pMDI PLUME GEOMETRY AND SPRAY PATTERN, AN APPROACH TO METHOD VALIDATION

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INTRODUCTION

Characterisation of the plume geometry and spray pattern from the spray of a pMDI is a requirement for any product intended for the US market. Such measurements typically require the use of a high speed image capture system followed by a means of measuring the critical dimensions. The use of high speed video, modern computer processors and custom software packages have both simplified the testing process and made it more reliable and precise.

Whilst these advances have gone a long way towards making the analysis less complex, the validation of such a method is not as simple as for many ‘typical’ analytical procedures.

In the validation of an assay for example, the key to the process is to prepare solutions of known concentrations which are then analysed by the method being validated and the results compared back to the theoretical concentration. With a plume geometry or spray pattern method, this approach cannot be used due to the chaotic nature of the plume and the lack of a ‘standard plume’ of known dimensions. Thus an alternative approach is required.

INSTRUMENTATION

AstraZeneca R&D Charnwood are using a modified Image Therm SprayView™ system, figure 1, which has been developed to meet the needs of testing HFA pMDI products. This is a high speed video capture instrument using dual laser light sources and a custom software package allowing both spray pattern and twin-plane plume geometry measurements to be performed.

SYSTEM VALIDATION

The system has been validated according to normal in-house procedures used for analytical instrumentation.

METHOD VALIDATION

The lack of a ‘standard plume’ or a means of independently verifying a plume makes method validation in the traditional sense very difficult. The settings used to actuate the inhaler and capture the images are relatively easy to validate. However, due to the chaotic nature of the aerosol plume, it is not easy to accurately verify the dimensional measurements of the plume. To overcome these difficulties it was decided to take a different approach for the validation of the plume geometry and spray pattern test methods on the SprayView system.

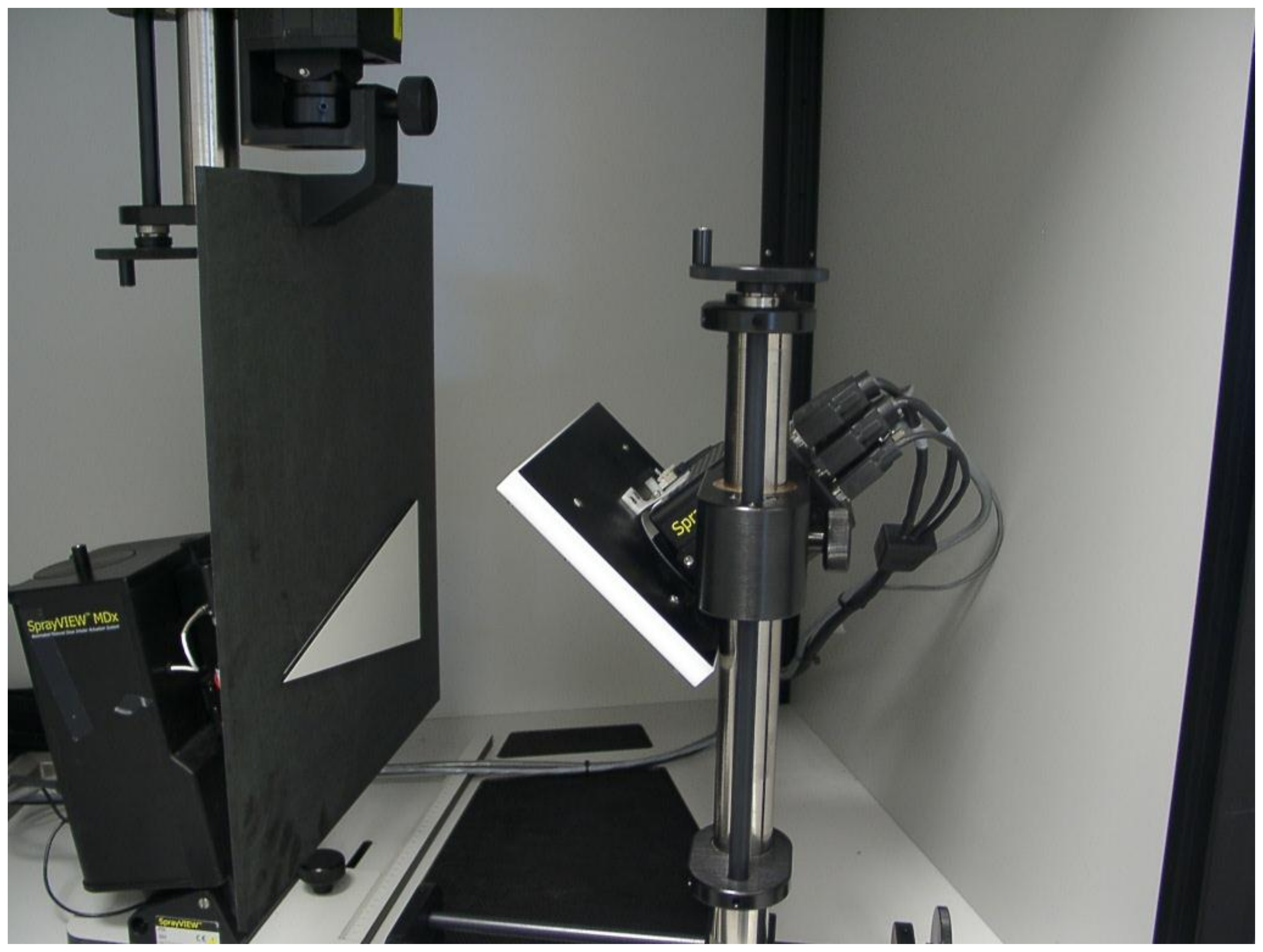

Figure 1: SprayView system set up to measure a plume validation target

The system was calibrated in the normal way but, rather than firing test inhalers and measuring the plume dimensions, the system was used to measure solid targets. The targets consisted of triangles, circles and ovals (figures 2 and 3) of known dimensions (accurately measured prior to the testing) e.g. plume lengths & angles and max/min diameters to represent typical plume and spray pattern measurements from the product(s). The initial measurements of the target dimensions, performed using calibrated callipers, were therefore traceable back to a controlled reference standard. Other parameters, such as the ‘cone angle’ of each target, were calculated using trigonometry.

Typical replica plumes and spray pattern targets tested and their dimensions are detailed in tables 1 and 2.

Table 1: Replica plume targets and acceptance criteria

Replica Plume Number	Cone Angle (°)	Plume Length (mm)	Plume Width (mm)
1	20.0 ± 2.5	349.7 ± 5.0	123.5 ± 5.0
2	25.0 ± 2.5	269.8 ± 5.0	119.7 ± 5.0
3	30.0 ± 2.5	189.8 ± 5.0	101.8 ± 5.0

Table 2: Replica spray pattern targets and acceptance criteria

Replica Spray Pattern	Circle	Ellipse	
	Diameter (mm)	Major (mm)	Minor (mm)
1	45.0 ± 1.0 mm	25.0 ± 1.0 mm	20.0 ± 1.0 mm
2*	30.0 ± 1.0 mm	30.0 ± 1.0 mm	15.1 ± 1.0 mm
3**	15.0 ± 1.0 mm	30.0 ± 1.0 mm	15.1 ± 1.0 mm

* Horizontal orientation ellipse, ** Vertical orientation ellipse

Spray pattern testing was performed at 30, 50 and 70 mm.

The measurements obtained from the validation targets (figure 2) using SprayView were then compared back to the measured dimensions.

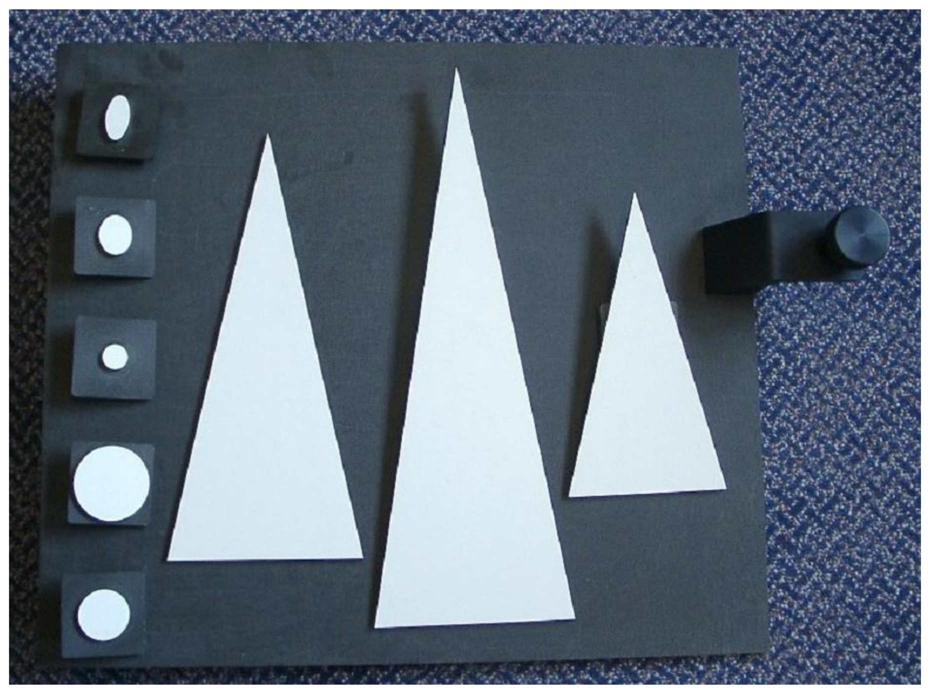

Figure 2: Plume and spray pattern targets

The test method would be considered to be validated if the system measurements of the targets agreed with the target measurements within the assigned acceptance criteria. Typical test images are shown, plume geometry (figure 3) and spray patterns (figure 4).

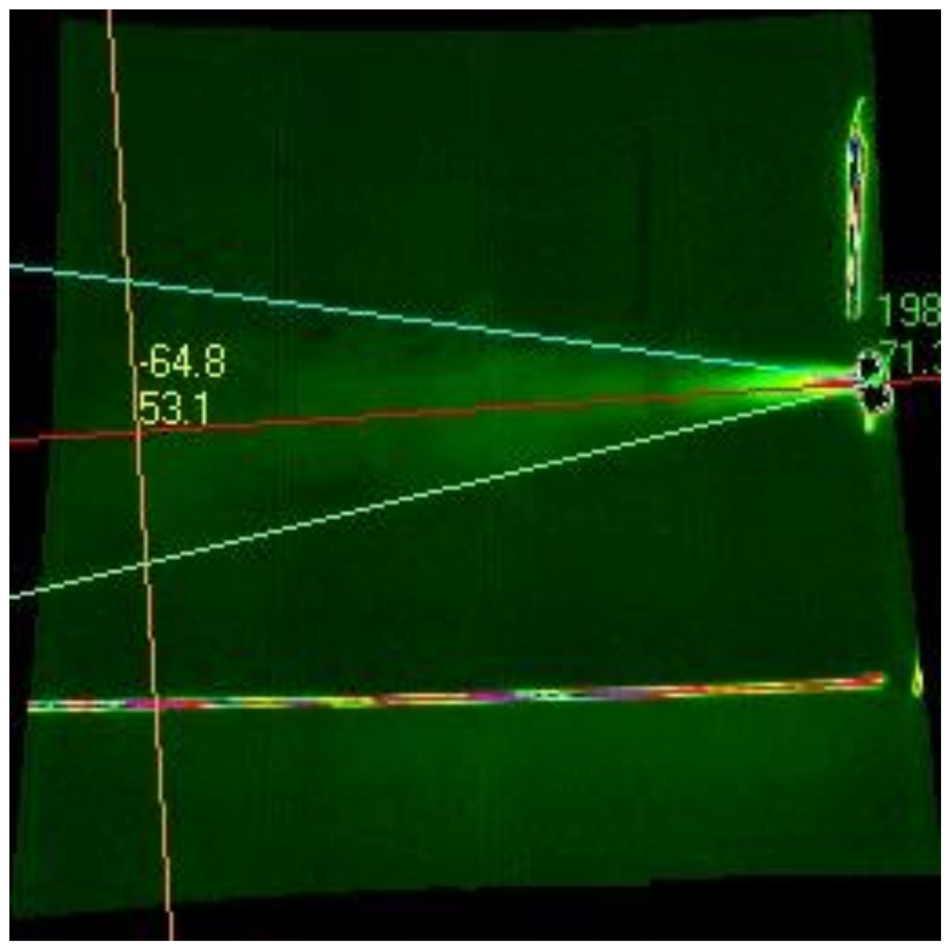

Figure 3: Typical plume geometry test image

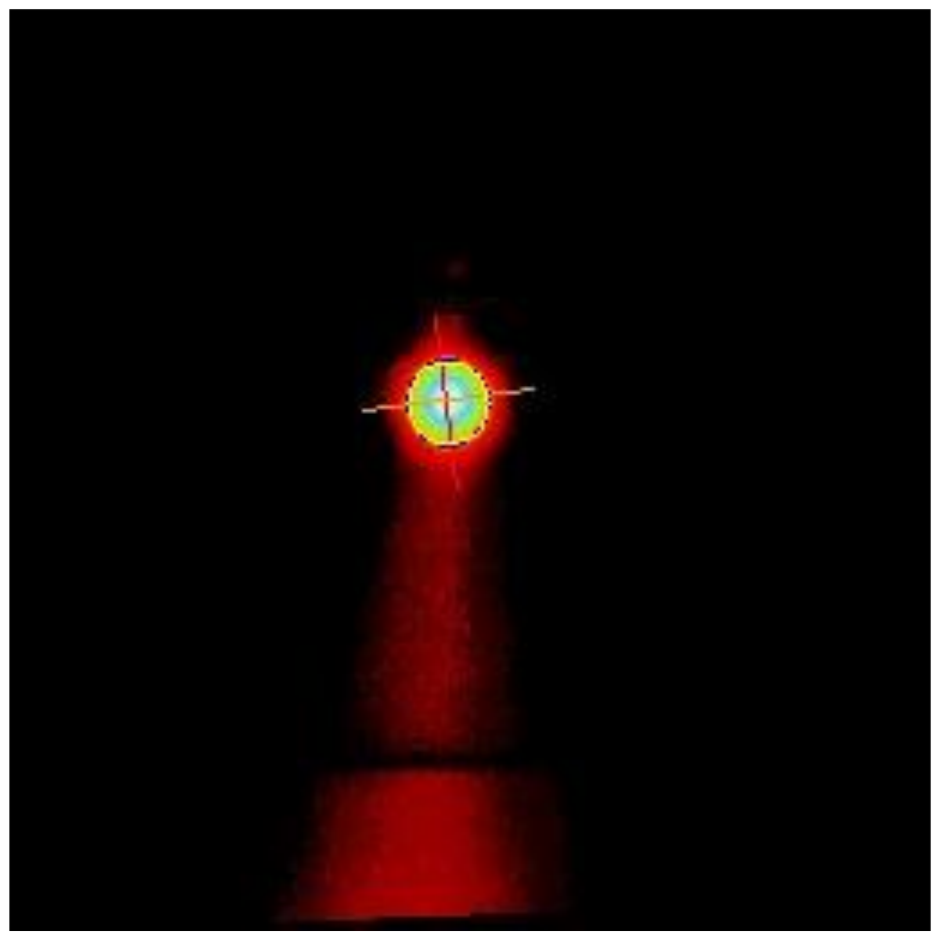

Figure 4: Typical plume geometry test image

RESULTS

Table 3: Plume geometry target measurements in primary mode (0°)

Plume Measurements	Plume Number		
	1 (n = 3)	**2 (n = 10)**	**3 (n = 3)**
Mean length (mm)	349.6	268.2	189.2
Max length (mm)	349.6	268.2	189.2
Min length (mm)	349.6	268.2	189.2
Mean width (mm)	122.1	119.7	103.0
Max width (mm)	122.1	119.8	103.0
Min width (mm)	122.1	119.7	103.0
Mean angle (°)	19.8	24.8	30.3
Max angle (°)	20.1	24.9	30.7
Min angle (°)	19.6	24.8	30.1

Table 4: Plume geometry target measurements in secondary mode (90°)

Plume Measurements	Plume Number		
	1 (n = 3)	**2 (n = 10)**	**3 (n = 3)**
Mean length (mm)	348.7	272.4	191.9
Max length (mm)	349.8	272.4	191.9
Min length (mm)	346.7	272.4	191.9
Mean width (mm)	124.8	122.0	104.2
Max width (mm)	126.9	123.8	105.2
Min width (mm)	123.8	120.7	102.1
Mean angle (°)	19.6	24.9	29.5
Max angle (°)	20.2	25.3	29.7
Min angle (°)	19.0	24.4	29.4

Table 5: Spray pattern target measurements

Measurements	Circle Diameter (mm)		
	15 (n = 3)	**30 (n = 10)**	**45 (n = 3)**
@ 30 mm			
Major length (mm)	14.9 (14.9 – 14.9)	30.2 (30.2 – 30.2)	45.6(45.6 – 45.6)
Minor length (mm)	14.8 (14.8 – 14.8)	30.0 (29.9 – 30.0)	44.8 (44.8 – 44.8)
@ 50 mm			
Major length (mm)	14.9 (14.9 – 14.9)	30.3 (30.3- 30.3)	45.5 (45.5 – 45.6)
Minor length (mm)	14.7 (14.7 – 14.7)	30.0 (30.0 – 30.0)	45.2 (45.2 – 45.2)
@ 70 mm			
Major length (mm)	15.0 (15.0 – 15.0)	30.3 (30.3 – 30.3)	45.2 (45.2 – 45.2)
Minor length (mm)	14.9 (14.9 – 14.9)	30.0 (30.0 – 30.0)	45.1 (45.1 – 45.1)
	Ellipse Number		
	1 (n = 3)	**2 (n = 3)**	**3 (n = 3)**
@ 30 mm			
Major length (mm)	25.1 (25.1 – 25.1)	30.2 (30.2 – 30.2)	30.1 (30.1 – 30.1)
Minor length (mm)	19.8 (19.8 – 19.8)	14.6 (14.6 – 14.6)	14.6 (14.6 – 14.6)
@ 50 mm			
Major length (mm)	25.2 (25.2 – 25.2)	30.2 (30.2 – 30.2)	30.0 (30.0 – 30.0)
Minor length (mm)	20.0 (20.0 – 20.0)	14.7 (14.7 – 14.7)	14.6 (14.6 – 14.6)
@ 70 mm			
Major length (mm)	25.2 (25.2 – 25.2)	30.3 (30.3 – 30.3)	30.1 (30.1 – 30.1)
Minor length (mm)	19.9 (19.9 – 19.9)	14.7 (14.7 – 14.7)	14.7 (14.7 – 14.7)

CONCLUSIONS

The determination of plume geometry and spray pattern characterisation is now a relatively simple task with the use of modern high speed capture techniques. However, the variable and chaotic nature of the aerosol plume, and the lack of an independent reference characterisation technique, means that such techniques are inherently difficult to validate in the traditional manner used for other analytical techniques. The process outlined here provides a means of validating plume geometry and spray pattern methods on the SprayView instrument back to a recognised reference standard.