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Comparing Size Distribution of Particles Using Spraytec™ and Mastersizer™

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INTRODUCTION

The use of laser diffraction to measure the droplet size distribution within aerosol plumes (atomized particles in either propellant vapor or in air) expelled from either nasal or oral spray devices is widely accepted as the industry standard.[1] This technique is also used for measurement of the size distribution of primary drug particles in suspensions and drug formulations including liposomes, emulsions, and micelles.[2,3] The correlation between aerodynamic particle size determined by cascade impaction and the geometric particle size determined by laser diffraction in the plumes of pressurized metered-dose inhalers has also been reported in the literature.[4] Whereas the Malvern Spraytec™ is generally used to measure droplet size distribution of aerosols emitted from sprays, the Malvern Mastersizer™ is mainly used to measure particle size distribution of wet or dry products. The objective of this study was to determine if the Spraytec could serve in both roles.

METHODS AND MATERIALS

Equipment:
A Spraytec (Model STP5319) equipped with Spraytec wet-cell dispersion unit (Model STP2520) and a Mastersizer 2000 equipped with Hydro 2000SM dispersion unit (both from Malvern Instruments, Westborough, MA) were evaluated. Normal performance of both instruments was confirmed using standard latex particles obtained from Thermo Scientific (Fremont, CA).

Method:
Mastersizer: RI 1.59; Obscuration 10%; Mixing speed 2000-2500 rpm; Dispersant: water.
Spraytec: RI 1.59; Obscuration 8-13%; Mixing speed 2000-2500 rpm; Dispersant: water.

Materials:
Emulsion-1, a proprietary oil-in-water emulsion containing an active drug substance, and Suspensions A and B, each proprietary drug suspensions in aqueous media containing different actives and excipients (such as gelling and suspending agents) were used to compare instruments.

Robustness Testing on Spraytec:
The robustness of an analytical method is defined as its ability to remain unaffected by small variations in test parameters.[5] This work was performed using Emulsion-1 (nominal emulsion dispersed phase size = 0.4-5.0 µm).

Table 1: Robustness test parameters and acceptance criteria.

Test Parameter	Details	Acceptance Criteria*
Measurement Duration	Ensures that representative sampling has been achieved	RSD <20% for Dv50; RSD <30% for Dv10 and Dv90
Measurement Stability	Sample is stable over period of analysis – no agglomeration, de-agglomeration, or dissolution	RSD <20% for Dv50; RSD <30% for Dv10 and Dv90
Mixing Speed/Pump Rate	Material is suspended without formation of air bubbles (especially when surfactants are being used)	Determine plateau region where the recorded droplet size is independent of mixing speed
Obscuration Level	To obtain optimum concentration of the sample in the dispersion media	RSD <20% for Dv50; RSD <30% for Dv10 and Dv90
Reproducibility/Intermediate Precision	To assess sample-to-sample and analyst-to-analyst variability	For individual analyst and pooled data: RSD <20% for Dv50; RSD <30% for Dv10 and Dv90

*As described in USP <429>,[6] RSD should be <10% for values close to the center of the distribution and <15% for values approaching the distribution limits. For samples with a median size of <10 µm, the RSD limits are doubled.

Figure 1: Effect of measurement duration and measurement stability.

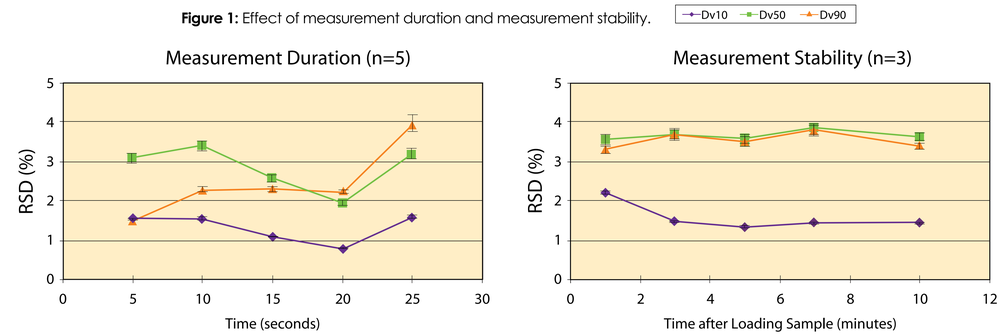


Figure 2: Effect of mixing speed and obscuration level with time.

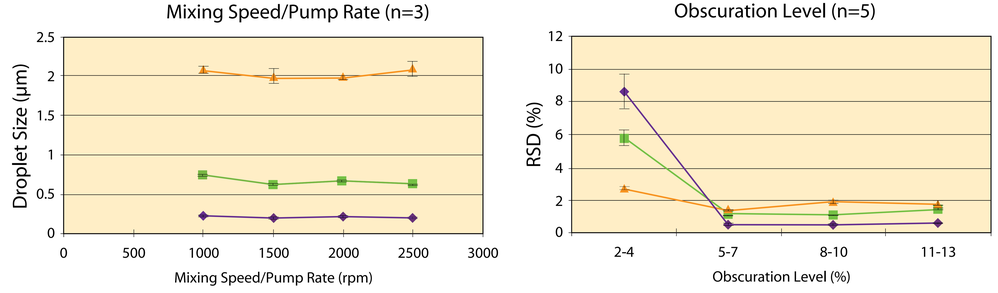
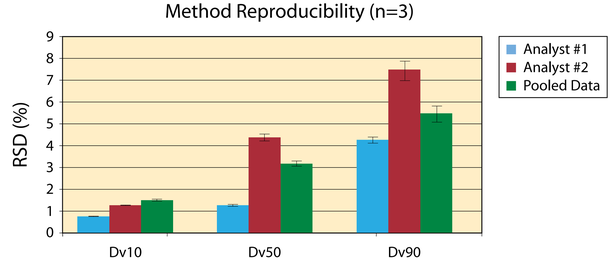


Figure 3: Data showing analyst-to-analyst reproducibility.



RESULTS AND DISCUSSION

Spraytec vs. Mastersizer Comparison

Table 2: Comparison of size distribution data obtained from Spraytec and Mastersizer for individual sample loadings (Run 1 and 2), average of the two runs, and standard deviation (SD).

Suspension A (µm)						
	Mastersizer			Spraytec		
	Dv10	Dv50	Dv90	Dv10	Dv50	Dv90
Run 1	5.879	20.565	45.696	9.421	23.157	46.647
Run 2	5.792	20.461	45.642	5.607	21.877	55.097
Average	5.836	20.513	45.669	7.514	22.517	50.872
SD	0.062	0.074	0.038	2.697	0.905	5.975

Suspension B (µm)						
	Mastersizer			Spraytec		
	Dv10	Dv50	Dv90	Dv10	Dv50	Dv90
Run 1	2.589	5.664	11.529	2.418	5.669	17.167
Run 2	2.482	6.094	13.904	2.418	5.732	17.703
Average	2.536	5.879	12.717	2.418	5.701	17.435
SD	0.076	0.304	1.679	0.000	0.045	0.379

As shown in Figure 1, Emulsion-1 size measurement using Spraytec was shown to be stable over the measurement period. Figure 2 indicates the speed of mixing has little influence on the size distribution, while an obscuration level of 5-13% showed similar size distribution – suggesting this to be an optimum range. The relative standard deviation (% RSD) is within the acceptable range, as defined in Table 1. Even though only two analysts were involved in the study, the method seems robust (Figure 3).

CONCLUSIONS

The robustness of the size distribution in emulsion formulations has been demonstrated using the Spraytec. In addition, when comparing the results obtained with those from the Mastersizer, the Dv50 values were in agreement to within the experimental error of ± 2 standard deviations plus the instrument accuracy (±2% for Dv50). This study demonstrates that the Spraytec (incorporating the wet-cell dispersion unit) can be used in place of a Mastersizer to accurately measure particle size of emulsions/suspensions in the range of 2-50 µm.

REFERENCES

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