Ensuring the Consistency of Performance of Mesh Nebulizers

R. H M Hatley, L. E A Hardaker, A. P Metcalf, J. Parker, F. Quadrelli & J. N Pritchard

Respironics Respiratory Drug Delivery (UK) Ltd, a business of Philips Electronics UK Limited, Chichester, West Sussex, UK.

Summary

The consistency in aerosol performance of the mesh in a mesh nebulizer is important as variability can affect the respirable delivered dose and treatment time. In addition meshes should be replaced periodically as part of routine mesh nebulizer maintenance, here it is particularly important that the output rate and thus treatment time of the new mesh should be similar to the one it replaced as differences could be perceived by the patient as a less effective treatment if there is variability in treatment time. We tested the consistency of performance of 73 randomly selected InnoSpire Go meshes from 7 batches manufactured using new in-process controls intended to minimize variability in aerosol performance. The mesh was placed in an Aerogen fixture and attached through a connector to a Spraytec laser diffraction system (set to 6 L/min extraction with an additional 7 L/min sheath air). Data acquisition was started on the Spraytec and the generator was started. Two priming runs were performed by transferring 50 µL of 0.9% saline to the fixture then tests were performed in triplicate with 250 µL of 0.9% saline. This method was repeated for each of the 73 meshes. Volume median diameter (VMD) and output rate were comparable between the batches; mean VMD was 4.76 µm with a range of ±0.2 µm around the mean, and mean output rate was 0.55 mL/min with a range of 0.03 mL/min below and 0.01 mL/min above the mean. The maximum difference between the batches for VMD was 0.4 µm and for output rate was 0.04 mL/min. VMD and output rate were consistent between the batches of meshes tested; therefore, replacement of the mesh should not cause variation in treatment time or particle size.

Introduction

Correct nebulizer use is important to ensure that patients receive an effective dose, and factors such as consistent treatment time can indicate to a patient that they are correctly using their nebulizer. The mesh in a mesh nebulizer should be changed periodically as part of routine maintenance, and it is important that the performance of the nebulizer does not alter between mesh batches to avoid changes in treatment times and particle size when a mesh is replaced. New in-process controls have been developed for the InnoSpire Go mesh nebulizer (Respironics Respiratory Drug Delivery [UK] Ltd, Chichester, UK) in order to ensure that treatment time and VMD do not vary between mesh batches. [1] In this study, we aimed to assess the consistency of performance of 73 meshes from 7 batches that have been through the in-process control by assessment of particle size and output rate.

Methods

Prior to testing, the meshes, test fixture, and connector were washed in warm soapy water, rinsed, and air-dried. All equipment and solutions/reagents were stabilized to ambient laboratory conditions at least 2 hours before use (22-24 °C, 995-1016 mbar atmospheric pressure, and 46-56% relative humidity). The 73 meshes were randomly selected from 7 different manufactured batches (Table 1).

Table 1. The number of meshes randomly selected from each batch.

Batch	A	B	C	D	E	F	G
Number of meshes	3	12	20	15	8	8	7

A Spraytec laser diffraction system (Malvern Instruments Ltd, Malvern, UK) was set up to perform testing with the open flow cell method with a 6 L/min extraction and an additional 7 L/min sheath air with the flow cell in horizontal orientation, in line with the novel method reported in Slator et al., 2016. [2] A mesh was placed into a fixture (Aerogen Limited, Galway, Ireland), which was then attached to the Spraytec with a connector. Data acquisition was started on the Spraytec, and the controller attached to the generator was started. A priming run was performed by transferring 50 µL of 0.9% saline to the Aerogen fixture, and another prime was performed when the obscuration dropped to background levels. When the obscuration returned to background levels again, a test was performed by transferring 250 µL of 0.9% saline to the Aerogen fixture. The test runs were performed in triplicate; data acquisition was stopped and the controller turned off once the obscuration returned to background levels again after the final test. The test was repeated with each of the 73 meshes. The mean data of the 3 runs were recorded for each mesh. Output rate was calculated based on the nominal charge volume and the number of records produced by the Spraytec, according to Equation 1, as each record is equivalent to 1 second.

[Equation 1] Output rate (mL/min) = (0.25 x 60) / Number of records produced

Results

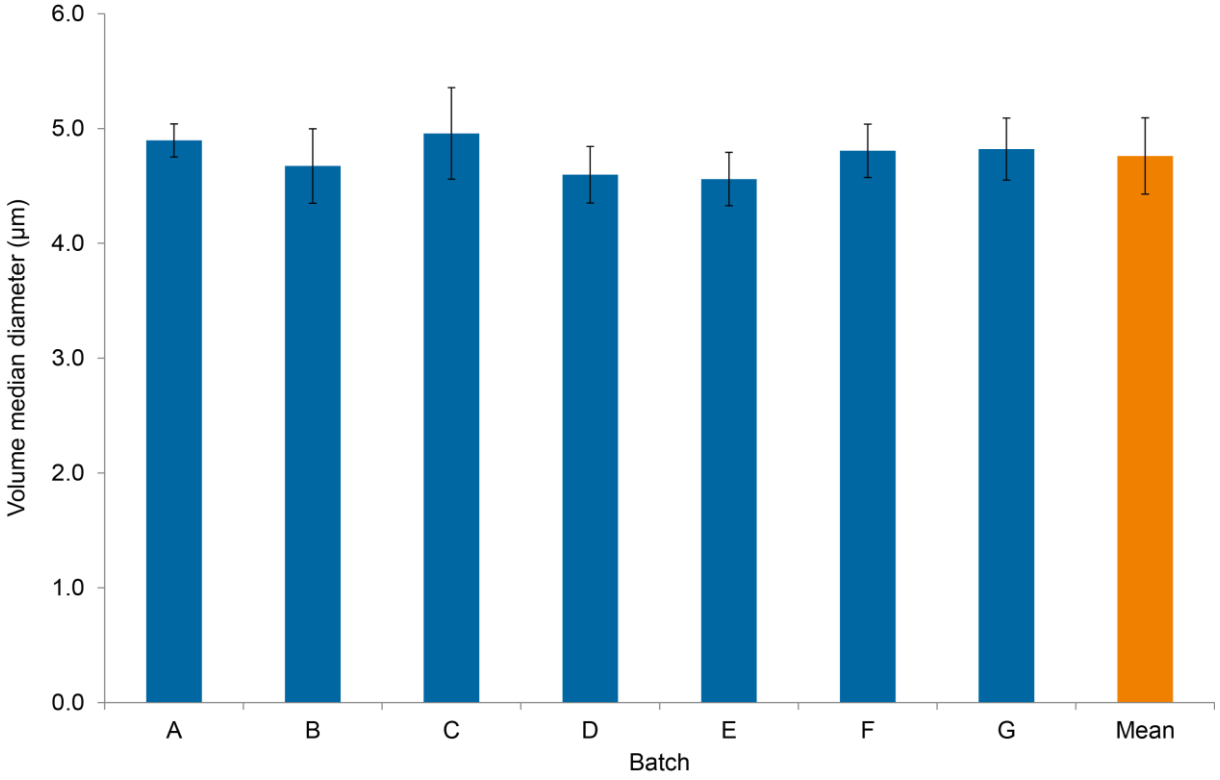

Figure 1 - Mean volume median diameter for each batch (■) and overall mean of all the batches (■). Error bars denote 1 standard deviation about the mean.

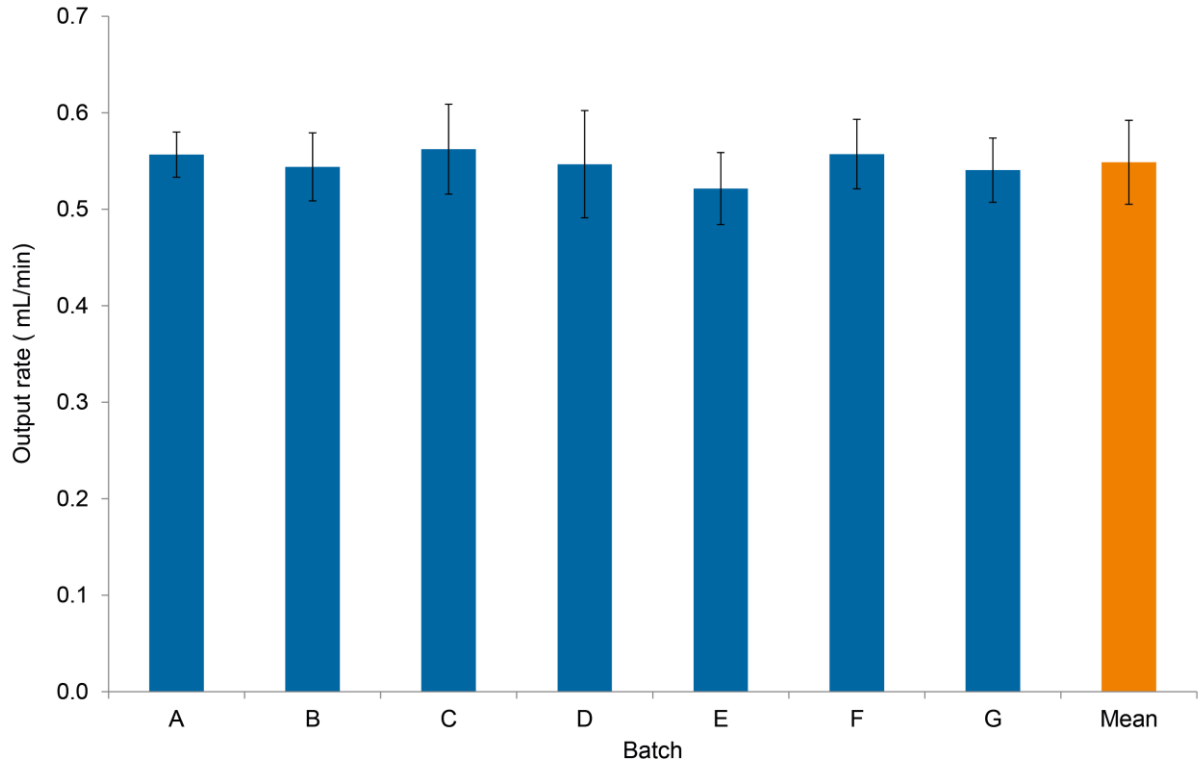

Figure 2 - Mean output rate for each batch (■) and overall mean of all the batches (■). Error bars denote 1 standard deviation about the mean.

Table 2. Mean particle size distribution span for each batch of meshes.

Batch	A	B	C	D	E	F	G
Span	1.53	1.59	1.56	1.56	1.53	1.54	1.56

The volume median diameter (VMD) was comparable between the batches of meshes, with a maximum difference of 0.4 µm between the batch means and a range of ±0.2 µm around the mean (Figure 1). The output rate was also comparable, with a maximum difference of 0.04 mL/min between the batch means and a range of 0.03 mL/min below and 0.01 mL/min above the mean (Figure 2). The relative standard deviations were 7% for the VMD results and 8% for the output rate results.

Discussion

The VMD and output rate were consistent between the batches of meshes, indicating that the replacement of these meshes as part of routine maintenance would not produce variations in particle size or treatment time. The VMD was below 5 µm for all of the batches of meshes, indicating that the meshes produced aerosol droplets of a size that would be likely to deposit in the smaller airways of a lung. [3,4] The output rate of 0.55 mL/min is relatively fast, and therefore short treatment times could be achieved. This may be a deciding factor for patients selecting an inhalation device, as short treatment times are desirable, and with conventional nebulizers, treatment times are usually longer. [5,6] The maximum difference in output rate between the batches was 7%, which would equate to a 6-second variation in a 3-minute treatment. Such a short variation in treatment time would be imperceptible to the user and could therefore provide them with confidence in the consistency of their treatments.

Conclusion

The performance of the meshes was consistent in terms of VMD and output rate. The output rate data indicated that short and consistent treatment times can be achieved between meshes, which is beneficial as users could therefore be confident in the consistency of the device's operation, even when the mesh is replaced as part of routine maintenance.

References

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