

# A COMPARISON OF PERFORMANCE OF FOUR VIBRATING MESH NEBULISERS



Tia Dally

Vectura Ltd, Chippenham, UK.

## INTRODUCTION

- Vibrating mesh nebulisers (VMN) are a subset of nebulisers that aerosolise liquids by passing them through small pores in a mesh to create a fine mist of droplets<sup>[1]</sup>. However, there is great diversity within this group and each nebuliser faces a range of challenges regarding performance depending on the properties of the nebulised liquid.
- Four VMNs were selected for comparison:
  - Omron MicroAIR™ NE-U22; a mass produced, general purpose, passive VMN<sup>[2]</sup>
  - Philips InnoSpire Go; a general purpose active VMN<sup>[3]</sup>
  - PARI eFlow® Rapid; an active VMN used for drug-device combination products<sup>[4]</sup>
  - Vectura FOX®; an active VMN used for drug-device combination products<sup>[5]</sup>
- Three formulations were selected with the aim of challenging the operating space for each of the nebulisers:
  - Normal (0.9% w/v) saline was used for baselining performance, as it is a commonly used vehicle for active pharmaceutical ingredient (API)
  - VR325 formulation, which has similar viscosity to saline, low dissociation constant and moderate/low surface tension
  - VR134 formulation which has high viscosity, high dissociation constant and moderate/low surface tension.

**Figure 1: Nebuliser devices: Omron MicroAIR™ NE-U22<sup>[2]</sup>, Philips InnoSpire Go<sup>[3]</sup>, PARI eFlow® Rapid<sup>[4]</sup>, Vectura FOX®<sup>[5]</sup>**



## METHODS

### Particle Size Distribution

- Particle size distribution (PSD) was measured using the Sympatec INHALER Module at 20 L min<sup>-1</sup> flow rate.
- Each mesh was measured in triplicate with each solution using a 1.5 mL fill volume.
- PSD was calculated using Lorenz-Mie scattering and the WINDOX 5 software.

### Emitted Dose

- Each nebuliser was filled with 1.5 mL of formulation and weights recorded accordingly.
- Nebulisation until empty was timed.
- Percentage emitted dose (%ED) was calculated using:
 
$$\frac{\text{Nebuliser filled mass (g)} - \text{Nebuliser empty mass (g)}}{1.5\text{mL}} \times 100$$
- Gravimetric output rate (g min<sup>-1</sup>) was calculated using:

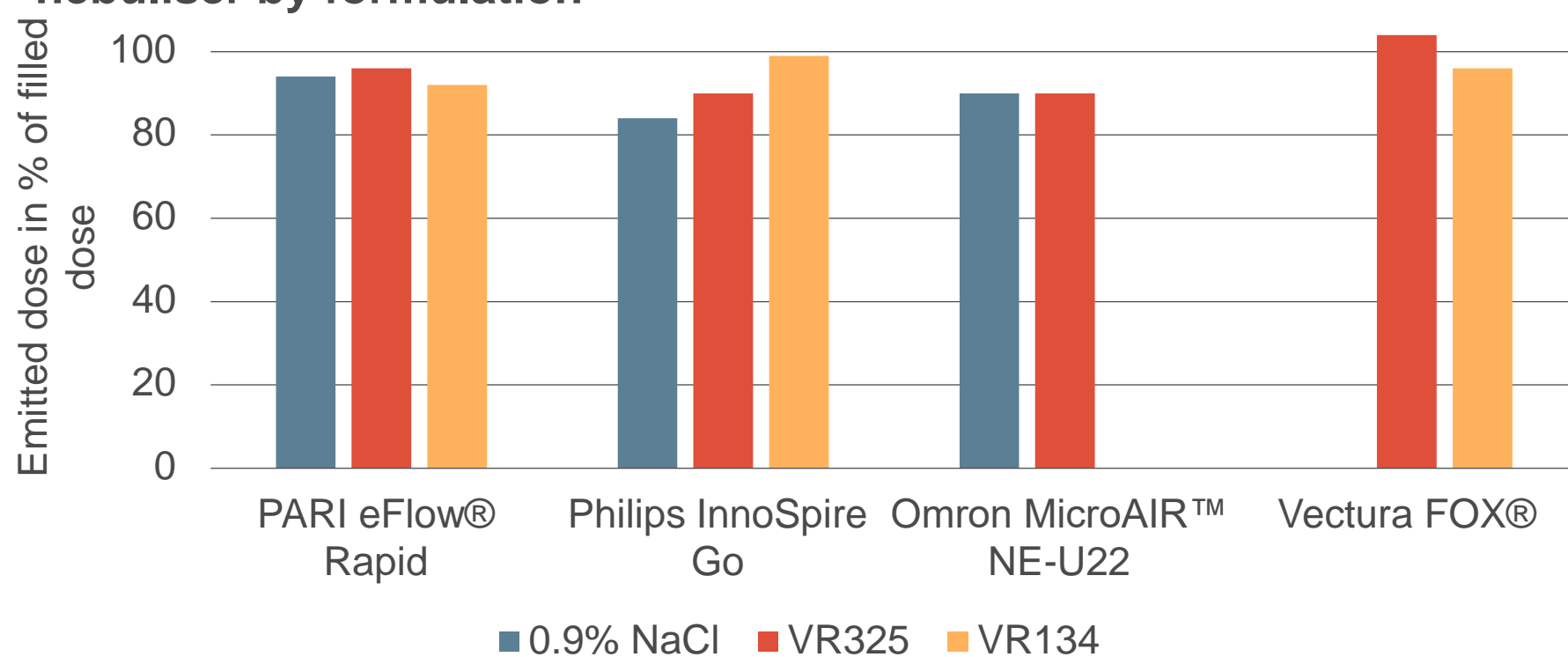
$$\frac{\text{Delivered dose (g)}}{\text{Nebulisation time (s)}} \times 60$$

## RESULTS

### Emitted Dose

- Average %ED with VR325 formulation was lower and more variable in Omron MicroAIR NE-U22 compared to the Vectura FOX® with 87% ± 5% compared to 104% ± 3%.
- Average %ED for both VR134 (92% ± 7%) and VR325 (96% ± 3%) formulation with the PARI eFlow® Rapid device were lower and more variable than with Vectura FOX®
- The %ED for Philips InnoSpire Go devices with VR134 formulation was higher than in Vectura FOX® but with increased variation, with 99% ± 11% delivered dose compared to 96% ± 3%.

**Figure 3: Emitted dose as a percentage of filled dose of each nebuliser by formulation**

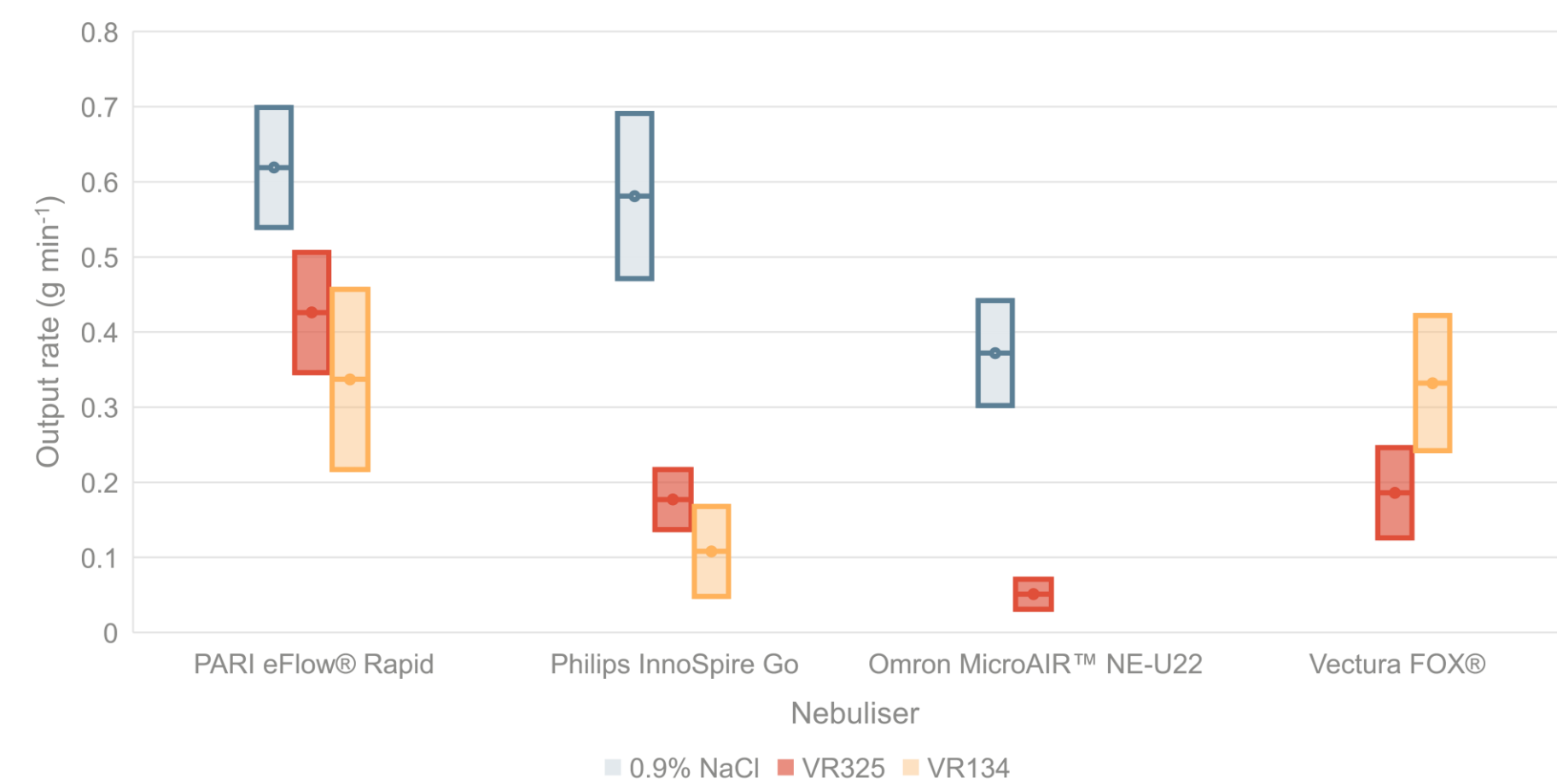


## RESULTS

### Output rate

- The Omron MicroAIR™ NE-U22 nebuliser could nebulise 0.9% w/v NaCl readily but struggled to nebulise VR325 formulation and could not nebulise VR134 formulation. The average output rate of VR325 formulation with the Omron MicroAIR™ NE-U22 nebuliser was much lower than in the Vectura FOX®.
- The average output rate with VR134 formulation of PARI eFlow® Rapid (0.337 g min<sup>-1</sup>) was very comparable to Vectura FOX® (0.332 g min<sup>-1</sup>). The PARI eFlow® Rapid had a higher output rate than Vectura FOX® with the VR325 formulation with an average of 0.426 g min<sup>-1</sup> compared to 0.186 g min<sup>-1</sup>.
- The Philips InnoSpire Go nebulised VR134 with lower output rates than the Vectura FOX®, 0.108 g min<sup>-1</sup> compared to 0.332 g min<sup>-1</sup>. Output rates with VR325 formulation were comparable between the Philips InnoSpire Go device and the Vectura FOX® device, 0.177 g min<sup>-1</sup> and 0.186 g min<sup>-1</sup> respectively.

**Figure 3: Mean output rate and standard deviation of each nebuliser by formulation**



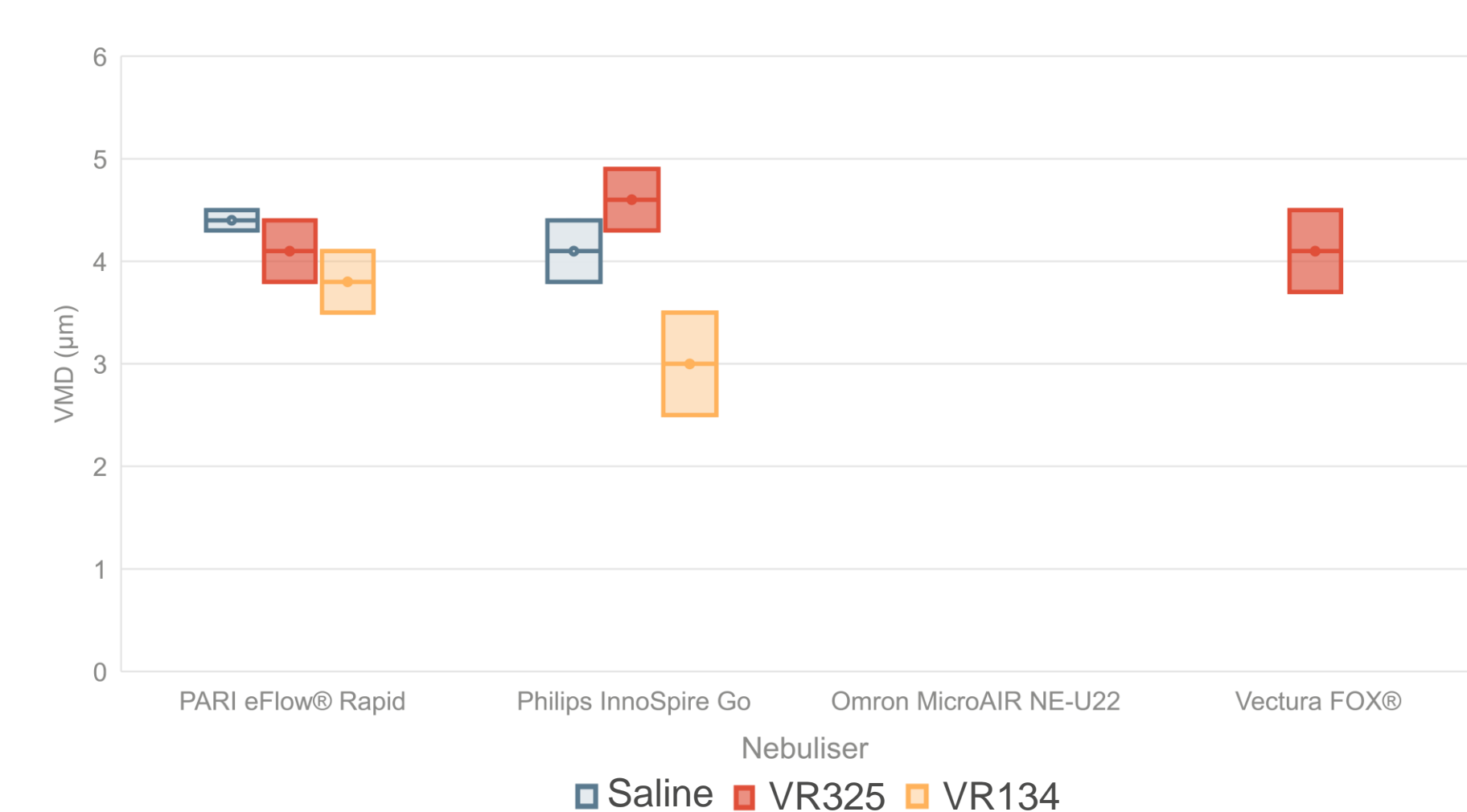
## KEY SUMMARY

The performance of vibrating mesh nebulisers is highly influenced by the properties of the nebulite. Vectura FOX® and PARI eFlow® Rapid perform more favourably than Philips InnoSpire Go and Omron MicroAIR™ NE-U22.

### Particle size distribution

- The Omron MicroAIR™ NE-U22 was unable to be tested due to limitations in equipment.
- In both the PARI eFlow® Rapid and Philips InnoSpire Go devices, the VR134 formulation showed the most variation in volume mean diameter (VMD) with standard deviations of 0.3 µm and 0.5 µm, respectively. This may contribute to the increased variation seen with output rate with this formulation.

**Figure 4: Mean VMD and standard deviation of each nebuliser by formulation**



- The mean particle size with VR325 was larger with Philips InnoSpire Go than with Vectura FOX®, with 4.6 µm compared to 4.1 µm.
- These higher particle diameters could be attributed to the low conductivity of the VR325 formulation. It also could be due to Philips InnoSpire Go device characteristics such as pore diameter or mesh frequency.

## CONCLUSIONS

- The Vectura FOX® device is more suitable for delivering the formulations evaluated here than the Omron MicroAIR™ NE-U22 and Philips InnoSpire Go.
- The physical properties of the solutions have been demonstrated to be highly influential in the success of nebulisation. In particular, in the Omron MicroAIR™ NE-U22 and Philips InnoSpire Go devices were not able to nebulise high viscosity and low conductivity formulations efficiently.
- The PARI eFlow® Rapid device has generally higher output rates than the Vectura FOX® device but comparable performance with the VR134 formulation.

## FURTHER WORK

- Philips I-neb was a notable omission which could not be acquired for comparison. If I-neb could be acquired, it is highly recommended that similar comparisons also be made with Vectura FOX®.
- Suitable test set up for PSD testing with the Omron MicroAIR™ NE-U22 should be investigated to measure data for comparison
- Delivered dose and PSD testing with 0.9% w/v NaCl with the Vectura FOX® should be conducted to produce data for comparison
- Evaluating the nebulisers with simulated patient use, i.e. tidal breath patterns, could be expected to yield more meaningful comparisons and the expectation would be that delivery rate would be reduced further for all continuous nebulisation devices.

## REFERENCES

- Pritchard, J. N., Hatley, R. H. M., Denyer, J., von Hollen, D., 2018. Mesh nebulizers have become the first choice for new nebulized pharmaceutical drug developments. *Therapeutic Delivery*, 9(2).
- Omron Healthcare, *Portable MicroAir® Nebulizer* [Online]. Omron. Available from: <https://omronhealthcare.com/products/microair-nebulizer-neu22v/>. [Accessed 19 August 2020]
- Philips, *InnoSpire Go Portable Mesh Nebuliser* [Online]. Philips. Available from: [https://www.philips.co.uk/c-p/HH1342\\_00/innospire-go-portable-mesh-nebuliser](https://www.philips.co.uk/c-p/HH1342_00/innospire-go-portable-mesh-nebuliser). [Accessed 19 August 2020]
- Pari. 2020. *eFlow® rapid Nebuliser System* [Online]. Pari. Available from: <https://www.pari.com/int/products/inhalation-devices-for-the-lungs/eflowrapid-nebuliser-system/>. [Accessed 19 August 2020]
- Vectura, 2020. *Device Platforms* [Online]. Vectura. Available from: <https://www.vectura.com/services/device-platforms/>. [Accessed 19 August 2020]

## About Vectura

- The company has around 200 members of staff at the Chippenham site so everyone is familiar with each other making it a very social and friendly place to work
- Due to the small nature of the company, the leadership team is very visible and hold regular business-wide meetings to keep everyone up-to-date
- Vectura has many social events and opportunities to get involved with such as a weekly badminton club, summer BBQ, winter ball and regular quizzes and raffles.
- Placement students are treated as if they are an entry level scientist, with lots of opportunities to write protocols and reports as well as leading presentations and sometimes training. Along with this, placement interns receive regular performance reviews and feedback which typically come with bonuses mid-way through the placement and at the end.
- During the COVID-19 pandemic, Vectura have been able to remain open but have given staff the flexibility to choose when they come on site. They also supported all the placement students if they chose to return home during lockdown

