# Efficiency assessment of 15 nebuliser systems by the Respirable Drug Delivery Rate

Fischer R[1], Jukic F[2] & Ledermüller R[1]

[1]PARI GmbH, Moosstraße 3, Starnberg, Germany; [2]PARI Pharma GmbH, Lochhamer Schlag 21, Gräfelfing, Germany;
Kontakt: ralf.fischer@pari.com

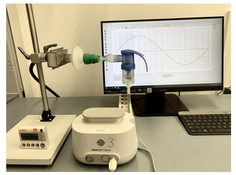


## Introduction and Explanation

Inhalation therapy with nebulisers is a relevant therapy option for respiratory diseases. The crucial factor for a clinically successful therapy is sufficient and targeted drug deposition, depending on the underlying lung disease, severity stage or patient population. Pulmonary deposition is significantly influenced by aerosol quality and the adherence of the patient. These depend on the drug formulation and the nebuliser system. E.g., infants require small droplets combined with a high Respirable Fraction (RF) and Aerosol Output Rate (AOR) in a short nebulisation time. Today, doctors can choose from a vast range of jet nebuliser systems with only limited information on objective comparison data. Thus, aerosol performance of commercial systems was tested on a standardised basis - the current European standard EN ISO 27427 - and used the Respirable Drug Delivery Rate (RDDR) for an objective evaluation.

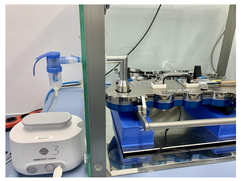
## Methods

Three different nebuliser systems of one brand were measured in duplicate (n = 6). The jet nebulisers were filled with 2 mL of 0.1% (w/v) Salbutamol. Drug amounts were determined by a validated HPLC-UV-System.



Aerosol Output (AO), Aerosol Output Rate (AOR) and nebulisation time (NT) were measured with a PARI COMPAS breath simulator using a tidal volume of 500 ml, 15 breath/min, I:E ratio of 50:50.

***Fig. 1:*** *Experimental setup Breath simulator measurements.*



Mass Median Aerodynamic Diameter (MMAD) and Respirable Fraction (RF= % particles < 5 µm) were measured with a cooled (17°C) Next Generation Impactor (NGI) at 50% relative humidity and 23°C ambient conditions at a flow rate of 15 L/min.

***Fig. 2:*** *Experimental setup NGI measurements.*

The RDDR was calculated as the product of AOR and RF. (Significance comparison of the mean values using ANOVA/Fisher Pairwise, significance level: $p < 0.05$).

## Results and Findings

- The parameters measured according to the EN ISO 27427 standard make the data comparable, but regarded individually they have little significance from a clinical point of view.

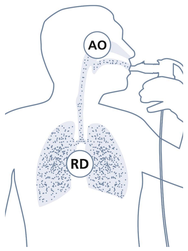



***Fig 3: Aerosol distribution***

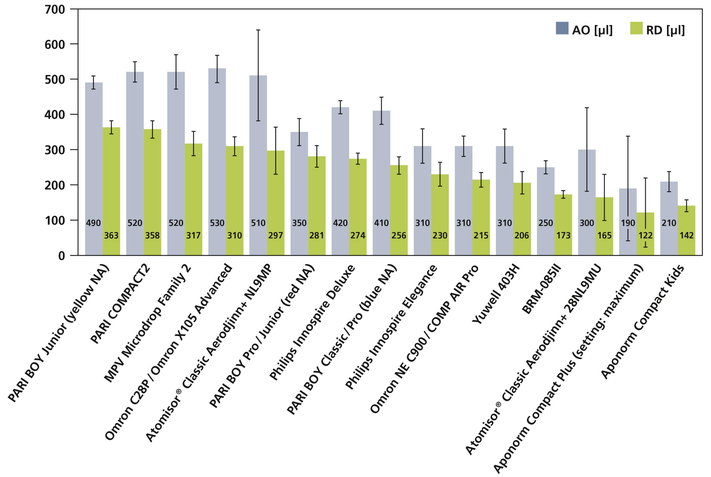



***Fig 4: Results of AO and RD*** *(MW ± SD, n= 6, NA = Nozzle Attachment).*

- Omron C28P (530 µl) followed by PARI COMPACT2 (520 µl) and MPV MicroDrop Family2 (520 µl) had the highest AO. These were almost 3 times larger compared to Aponorm Compact Plus (190 µl).
- A high AO does not necessarily mean a high amount of drug in the lungs. Only the combination of AO and RF (Respirable Dose; RD = AO x RF) shows how much therapeutically effective aerosol potentially reaches the lungs.
- Looking at the potential respirable amount, the PARI BOY Junior (363 µl, yellow NA) and the PARI COMPACT2 (358 µl) had the highest RD followed by the MPV MicroDrop Family 2 (317 µl).

**RDDR** = **≤ 5 µm** x **/**

**Respirable Drug Delivery Rate** — **Respirable Fraction (RF)** — **Aerosol Output Rate (AOR)**

- The RDDR also considers the duration of nebulisation. It is an **objective parameter** for the efficiency of a nebuliser system and describes how much **respirable drug per time** a system generates.

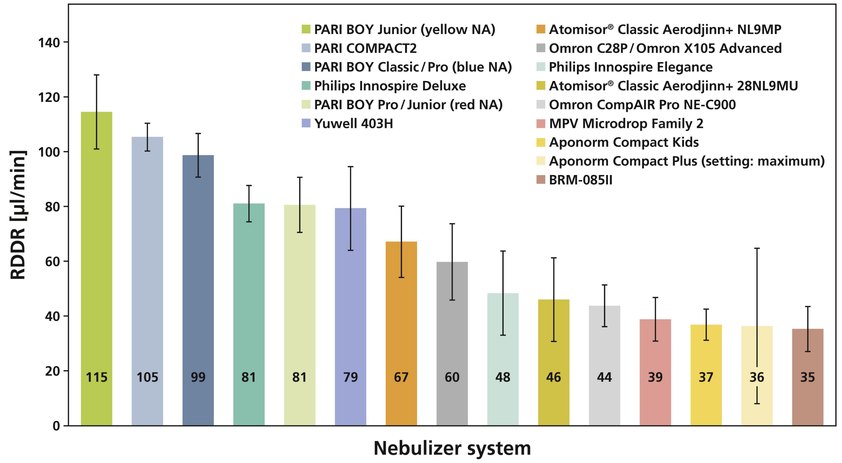



***Fig 5: Results of Respirable Drug Delivery Rate*** *((mean value ± 95% confidence interval, n = 6, NA = Nozzle Attachment).*

- The RDDR values varied by a maximum factor of 3. The PARI BOY Junior (yellow NA), the PARI COMPACT2 and the PARI BOY Pro (blue NA) had the highest RDDR values, which differed significantly from all other nebulisers tested.

## Conclusions

- **The efficiency of commercially available nebuliser systems differ significantly.**
- **Due to these performance variations the intended therapeutic success may be at risk, as underdosing or delayed symptom relief may occur. In the case of antibiotics, insufficient device quality can accelerate the development of resistance [1].**
- **The RDDR represents an objective parameter for the efficiency of a nebuliser system and can support the physician in selecting a suitable device.**
- **To ensure that patients receive clinically effective doses and thus achieve the best possible therapeutic effect, it is important that physicians choose a nebuliser system with a high RDDR.**

1. Moore JE et al., Respir Care. 2021;66(9):1446-57.