ACHIEVING CONSISTENT, USER INDEPENDENT, NASAL DOSE DELIVERY USING A SPRING DRIVEN DEVICE

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INTRODUCTION

- Unit dose nasal drug delivery devices are used to administer a variety of drugs to a broad range of patients, without the need for more invasive delivery methods or the assistance of a healthcare professional (HCP). Due to the large variation in user strength, dexterity and finger size, the device design should aim to minimise the performance impact of differing user interaction.
- The FDA guidance for performance specifications of nasal sprays includes tolerances for the target metered shot weight (MSW)[1]. Droplet size distribution (DSD) - alongside other spray parameters - also needs to be specified and controlled in nasal spray products, although no target values or tolerances are provided in the guidance[2].

EXPERIMENTAL METHODS

Two sets of sumatriptan-filled nasal spray samples, were each tested in non-clinical user and laboratory studies under representative use conditions:

- Reference device (RD) – a marketed user driven nasal spray, Imigran® (24 samples for user testing and 30 for lab testing)
- Recipharm proprietary device (PD) – a novel, spring driven nasal spray, currently under development (13 samples for user testing and 52 for lab testing)

The studies were conducted by Proveris Scientific Corporation (Massachusetts, USA), collecting data for a full suite of Essential Performance parameters. Lab-based testing was run on an NSx actuator. Drug effectiveness was not relevant for this study.

Figure 1. Recipharm's proprietary device (left) and the reference device (right).

RESULTS AND DISCUSSION

- Actual mean MSW values across all devices tested were always within upper (USL) and lower (LSL) specification limits (figure 2) , assuming a target of 100 mg. The spring driven devices consistently delivered a MSW within specification limits and with little variation, particularly when actuated by hand (see table 1).
- Similarly, droplet sizes remained within a narrow range for spring driven devices (table 1). User driven devices appeared to be affected by actuation speed of the thumb (figure 3), unlike spring driven devices. This supports the hypothesis that a spring driven delivery system can provide a more consistent device performance.

Table 1. Mean EPR values and their associated standard deviations (SD) and statistical significance (p), across a representative range of actuation velocities.

Device/ Actuation method	Mean MSW/mg & (SD)*		Mean droplet size @ 60 mm/µm & (SD)*					
	MSW	p**	DV10	p**	DV50	p**	DV90	p**
Imigran®/ user	101.1 (8.23)	0.031	N/A	N/A	N/A	N/A	N/A	N/A
Proprietary/ user	98.5 (1.17)		N/A		N/A		N/A	
Imigran®/ NSx	102.1 (1.85)	0.937	23.7 (6.34)	0.000	46.7 (13.34)	0.000	91.2 (31.34)	0.000
Proprietary/ NSx	98.8 (1.88)		20.6 (0.64)		39.7 (2.01)		75.9 (7.92)	

*Mean and SD taken across all velocities for each category.
**Based on test for equal variances; p<0.05 indicates significant difference in SD.

- Actuation force measurements revealed that a nasal spray user would need to apply a mean force of 2.77 kg (SD 0.191) to Recipharm's PD, in order to receive a full dose. This is well within the range for the approved RD, which had a mean maximum actuation force of 6.76 kg (SD 0.238).
- Despite the smaller sample size for Recipharm's PD, the small variation in data indicated potential for the device to have emergency use applications. This was based on calculation of tolerance intervals for MSW data with 99.999% reliability and a 95% confidence level.

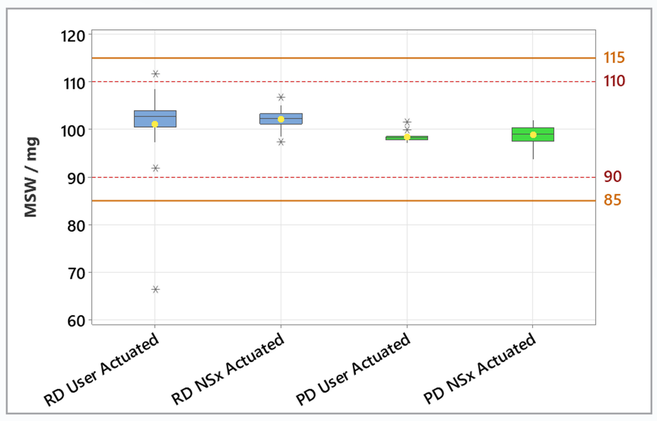

Figure 2. Metered shot weights (MSW) for RD (blue plots) and Recipharm's PD (green plots), with mean values indicated by yellow dots and reference to FDA recommended specification limits: ±10% (red dashed lines) and ±15% (orange solid lines) of target mean.

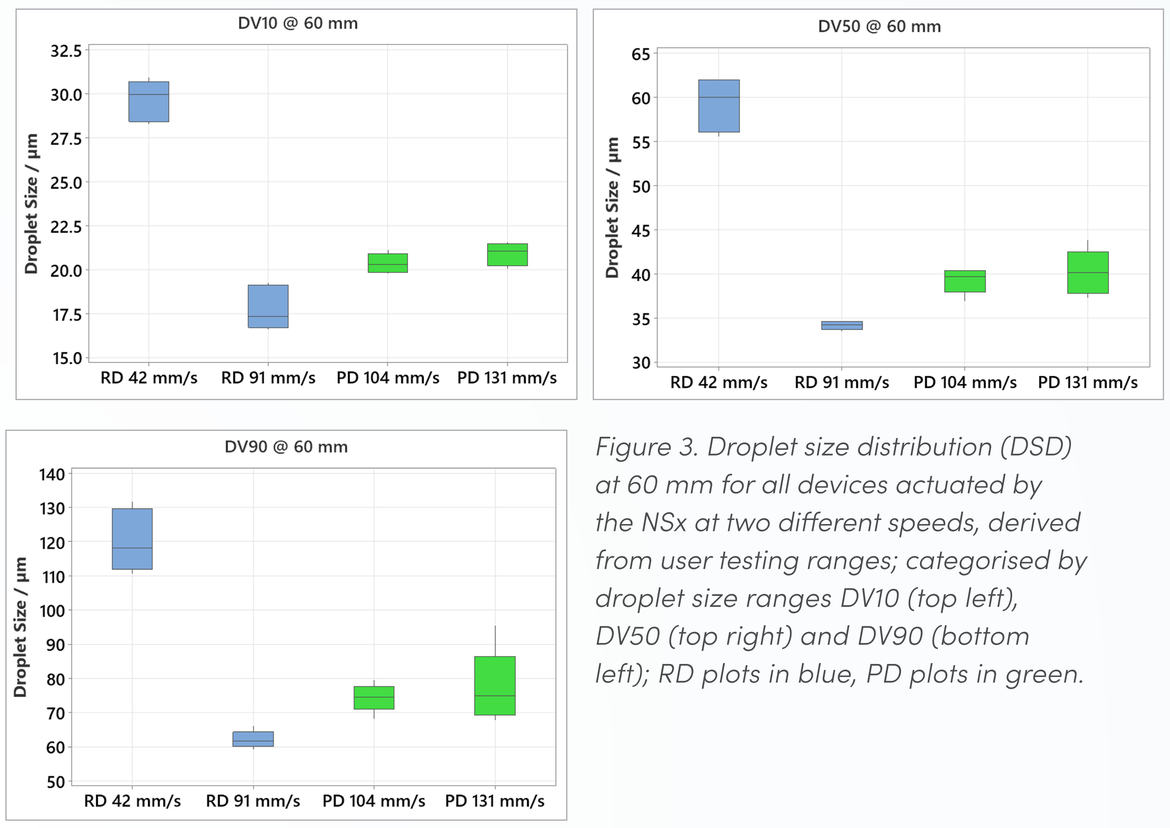

Figure 3. Droplet size distribution (DSD) at 60 mm for all devices actuated by the NSx at two different speeds, derived from user testing ranges; categorised by droplet size ranges DV10 (top left), DV50 (top right) and DV90 (bottom left); RD plots in blue, PD plots in green.

CONCLUSIONS

- EPR parameters (MSW and DSD) have shown an overall significant reduction in variation for novel, spring driven, unit dose nasal delivery devices filled with marketed sumatriptan formulation. This opens applications for geriatric users or those with limited dexterity or strength, as well as more consistent delivery of higher viscosity fluids in the hands of a user. An important consideration for applications where dose accuracy and dispersion are critical to therapeutic performance.

REFERENCES

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ACKNOWLEDGEMENTS

Testing conducted and data provided by Proveris Scientific Corporation, USA.

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