Developing Methods for Automated Delivered Dose Uniformity (DDU) Testing for Nasal Sprays

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Introduction

The COVID-19 pandemic has further stimulated an already buoyant nasal drug delivery sector. Automation of compendial test methods promises to reduce analyst workload, improve reproducibility and increase data integrity.

Objective

To develop automated methods for DDU testing of nasal sprays.

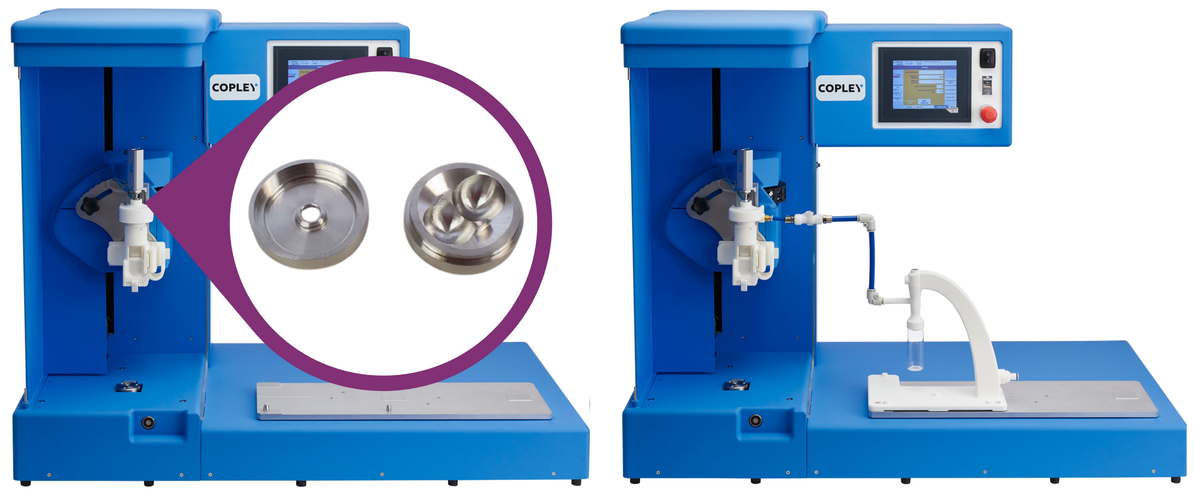
Method

The first set of experiments assessed the drug recovery from the Nasal Spray Dose Collector (NSDC) **Fig.1**, which allows dose collection from nasal sprays actuated in a vertical position. A nasal spray containing Beclometasone Dipropionate (BDP) and Fluticasone Propionate (FP) was well-shaken prior to testing and manually actuated by applying pressure on the upper surface of the dose collector.

Drug was recovered from the tip of the nozzle of the bottle and separately from the disassembled NSDC and analysed by HPLC to determine total drug recovery, for ten determinations.

Fig. 1 (left): Automated vertical nasal spray delivered dose collection with the NSDC. **Fig. 2 (right):** Automated test set -up for delivered mass measurement for nasal spray DDU testing, with waste dose collector for dose capture.

In a second set of experiments, delivered mass uniformity was assessed using an automated test set-up as shown in **Fig. 2**. Shot weight was recorded automatically via the inbuilt balance after each firing. Dose uniformity was assessed by averaging over 150 shots, post-priming. The number of deliveries relative to label claim was assessed simultaneously.



Results

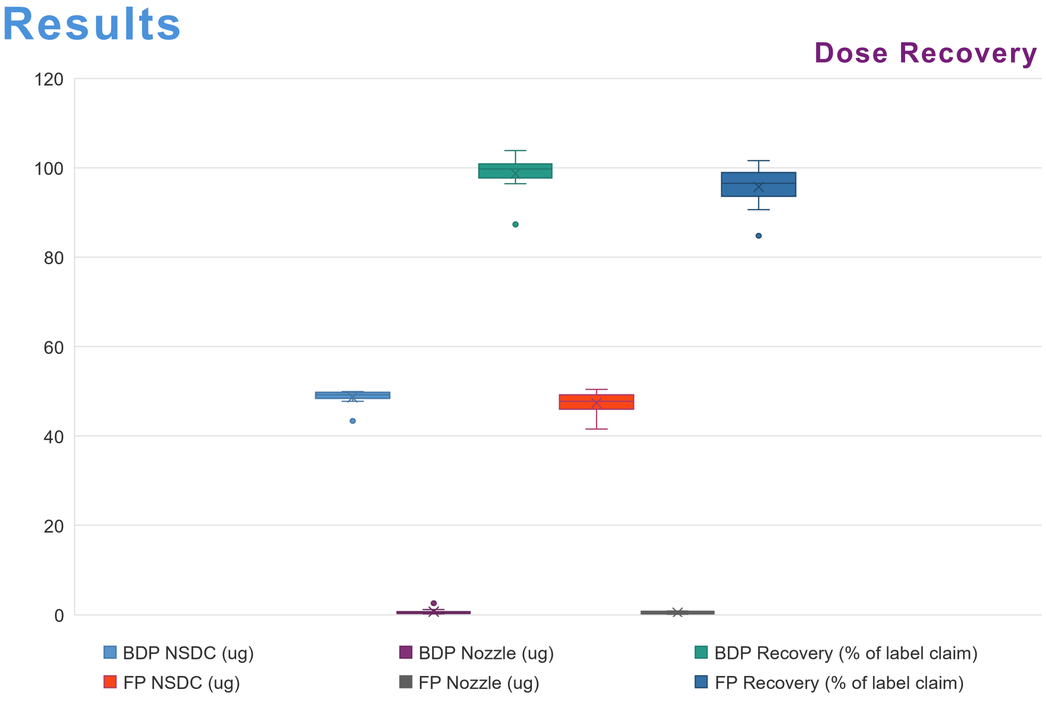
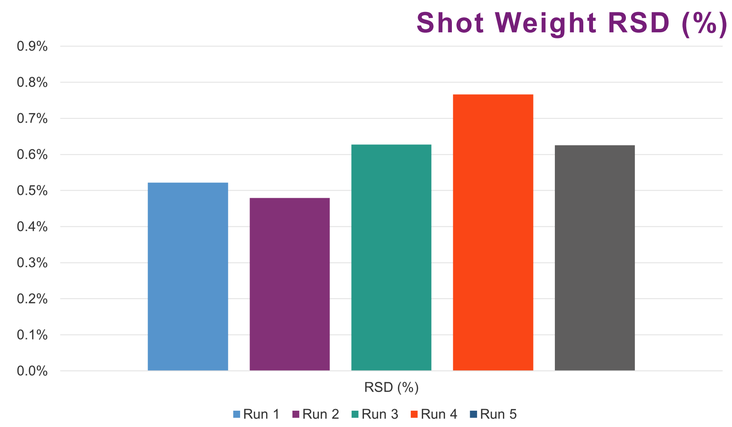


Fig. 3: Dose recovery data for BDP and FP from the NSDC and nasal spray bottle nozzle.



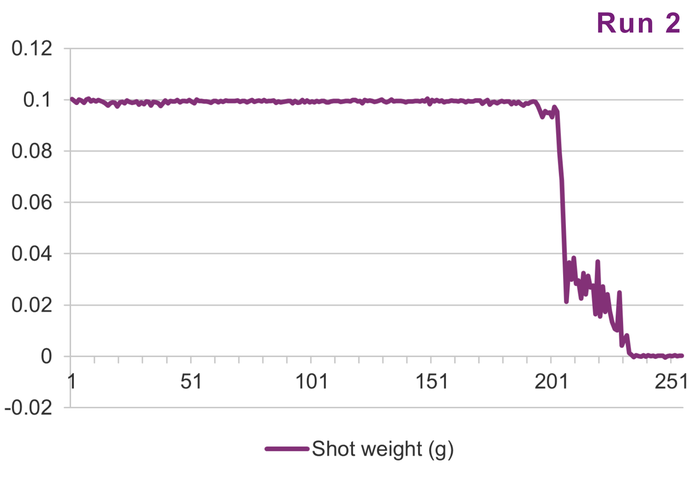


Fig. 4: Shot weight variability for five runs, determined in each case from data for 150 deliveries with the automated test set-up.

Fig. 5: Testing through to nasal spray bottle emptying shows a dramatic drop off in shot weight after shot 203 (exemplary data from **Run 2**).

Discussion

The internal geometry of the NSDC has a curved impaction surface designed to prevent splashing and dripping to achieve complete dose capture. The results presented here indicate the success of this design.

The second part of the study demonstrates the extremely high repeatability delivered by automated shot weight testing. By comparison, a study involving 250 manual actuations produced an average shot weight of 98.9 mg (RSD 1.6%) relative to a label claim of 100 mg. In our study, RSD measurements that are consistently less than 0.8% compares favourably to this data. Differences in applied actuation parameters are likely to be the main source of variability in the manual data.

Automation represents a considerable gain in terms of analyst time and health and safety (reduced risk of repetitive strain injury [RSI]).

Conclusion

Together the described novel dose collection device and automated shake, fire and flow control platform offer considerable potential for more productive DDU testing for nasal sprays, to a higher standard with respect to repeatability.

Further Reading

- Keller et al., Drug Delivery and Translational Research 2022;12: pp735-757
- Rees, European Pharmaceutical Review, published 3rd Feb 2021.
- News release ‘Altimmune begins trial of nasal vaccine for COVID-19’ Available at: https://pharmaphorum.com/news/altimmune-begins-trial-of-nasal-vaccine-for-covid-19/
- USP <601> ‘Aerosols, Nasal Sprays, Metered Dose Inhalers and Dry Powder Inhalers’
- Ph. Eur. 10.5 Nasal Preparations, Nasalia. 01/2021:0676.
- Guo & Doub, Journal of Pharmaceutical Sciences, 2006; 95, 9 pp2029 – 2040

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