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A Comparative Evaluation of the Aerosolization Performances of Marketed Fluticasone Multi-Unit and Single-Unit Dry Powder Inhalers (DPIs): The Effects of Product Use Life, Suboptimal Airflow and a Hot/Humid Environment

N. Wauthoz[1], I. Hennia[1], S. Ecenarro[2], K. Amighi[1]

[1]Université libre de Bruxelles, [2]Qualicaps Co, Ltd.

CONTACT EMAIL: **nawautho@ulb.ac.be**

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PURPOSE

An optimal inhalation medicine has to deliver an accurate delivered dose (DD) and fine particle dose (FPD) throughout the product use life, with low dependency on the patient's inspiratory airflows and with low impact of a hot/humid environment during use [Chrystyn Int J Clin Pract 2007].

In this study, a comparative evaluation was performed on marketed DPIs based on fluticasone propionate (250 µg) currently used for maintenance treatment of asthma and chronic obstructive pulmonary disease (COPD). The marketed products were the multi-unit Flixotide® Diskus (GlaxoSmithKline) containing doses in a blister strip, and the single-unit Flutaxa® Axahaler (SMB) containing each dose in a hypromellose capsule packaged in a container with a desiccant cap.

	Flixotide® GSK 	Flutaxa® SMB  Flutixon® (Poland)
Device (airflow)	Diskus or Accuhaler (84-87 L/min)	Axahaler (adjusted to 100 L/min)
Device type	Multi-unit DPI	Single-unit DPI
Powder packaging	Blister strip contained in the device	HPMC capsules in desiccant container
Excipients	Monohydrate lactose	Anhydrous and monohydrate lactose
Dosage	250 µg fluticasone propionate/nominal dose (60 doses)	

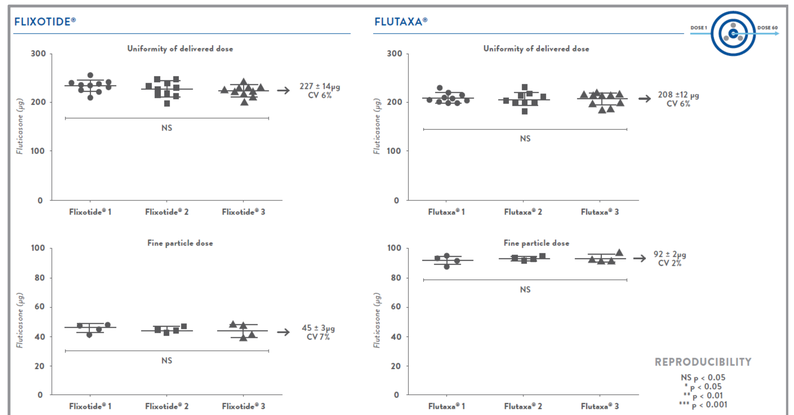
METHODS

The DD and the FPD were evaluated in terms of their **reproducibility** and **robustness** throughout the product use life (i.e. from the first to the last inhaled dose), different inspiratory airflows (30 L/min, 60 L/min, 87 or 100 L/min, the latters being the airflows recommended by the USP for Flixotide® and Flutaxa®, respectively) and by simulating the use of the medicines at high temperature and humidity conditions (i.e. 4 h at 40°C 75% relative humidity) on a DPI loaded with a dose.

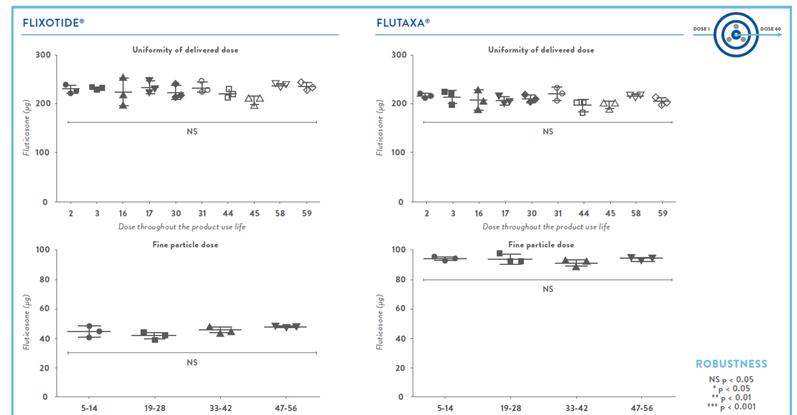
The DDs were determined on doses 2, 3, 16, 17, 30, 31, 44, 45, 58 and 59 of the product using the test recommended by the USP. The FPDs were determined after in vitro deposition in a USP apparatus 5 (i.e. the Next Generation Impactor, NGI) using the test recommended by the USP and using doses 5-14 (NGI 1), 19-28 (NGI 2), 33-42 (NGI 3) and 47-56 (NGI 4). The duration of each test lasted the time corresponding to an inhaled air volume of 4L through the device. The airflow was generated and controlled by a TPK2000 critical flow controller with two HCP5 high capacity pumps (Copley Scientific, Nottingham, UK).

RESULTS

DRUG DELIVERY AND AERODYNAMIC PERFORMANCE THROUGHOUT THE PRODUCT USE LIFE

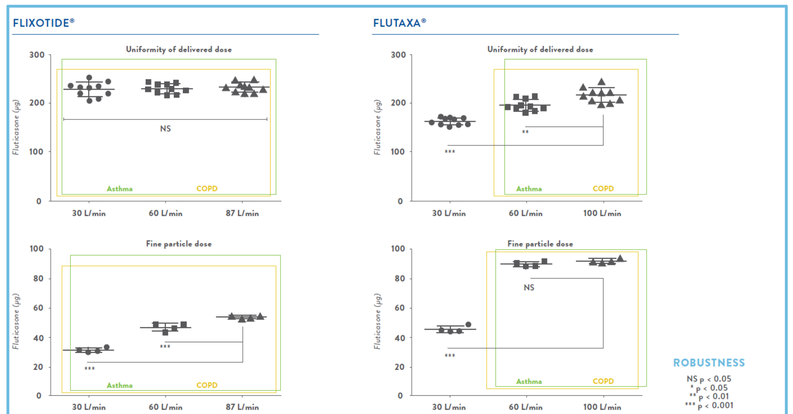


***Reproducible DDs and FPDs** with **low CV** but **a twofold FPD for Flutaxa** with the equivalent nominal dose*



***Robust DDs and FPDs** with non significant differences along the product life*

DRUG DELIVERY AND AERODYNAMIC PERFORMANCE AT DIFFERENT AIRFLOWS



*Flixotide® showed **robust DDs** but **significant difference for FPDs** at asthma and COPD patients' suboptimal flow*
*Flutaxa® showed **significant difference for DDs** but **robust FPDs** at asthma and COPD patients' suboptimal flow*

DRUG DELIVERY AND AERODYNAMIC PERFORMANCE IN DRASTIC CONDITIONS

*Flutaxa® showed **a slight but significant FPD decrease** from preloaded doses stored in drastic conditions*
*Flixotide® showed **almost no powder emission** from preloaded doses stored in drastic conditions*

CONCLUSION

Both the DPIs showed reproducible (equivalent CV) and robust (non-significant differences) DDs and FPDs along the product use life. Flutaxa® delivered double the FPD with less variability than Flixotide® despite a slightly lower DD. Moreover, FPDs from Flutaxa®, unlike Flixotide®, were robust at suboptimal airflows typical of those generated by asthmatic and COPD patients, and showed only a slight decrease, contrary to very low FPD due to almost no powder emission, when preloaded doses were exposed to a hot/humid environment.

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