Marketed Formoterol Inhalation Aerosols:

A Comparative Evaluation to Determine the Place of Capsule-based Dry Powder Inhalers (DPIs)

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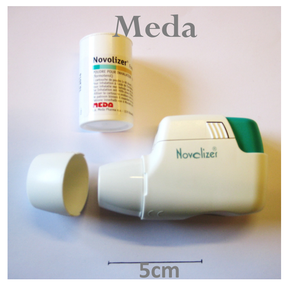
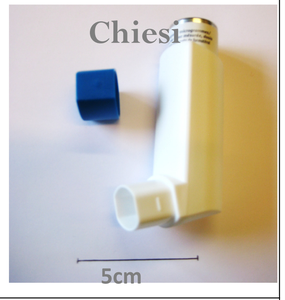
Introduction

The success of inhalation therapy depends on the patient, the device and the formulation. Indeed, the ideal inhalation medicine has to present reproducible and robust drug delivery throughout the device life but also features that improve the device handling and preference by the patients [1,2].

Therefore, the aim of this study is to compare marketed inhaled medicines based on formoterol, a long-acting β2 agonist frequently used to treat asthma and chronic obstructive pulmonary disease.

AIM OF STUDY

Capsule-based DPIs		Reservoir-based DPIs		Reservoir-based pMDI
Foradil®	Formagal®	Oxis®	Novolizer®	Formoair®
Novartis	SMB	Astra Zeneca	Meda	Chiesi
				
Gelatin capsules 5cm	Hypromellose capsules 5cm	5cm	5cm	5cm

Inhaled medicine based on 12 µg formoterol fumarate dihydrate/nominal dose

Dose delivery and Aerodynamic Performance

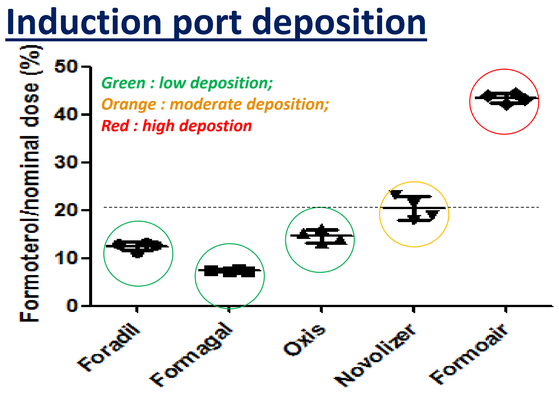
- ➔ *In vitro* deposition using a Next Generation Impactor (NGI) to determine Fine Particle Dose (FPD ≤ 5 µm), MMAD and induction port deposition
- ➔ Reproducibility of Delivery Doses (DD) and FPD

Device Handling

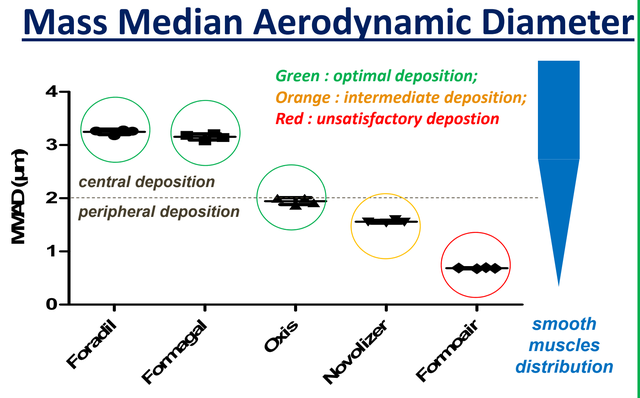
- ➔ Ease of use (dexterity and number of steps)
- ➔ Feedback to the user of dose delivery
- ➔ Device resistance

Drug Delivery and Aerodynamic Performance

Induction port deposition

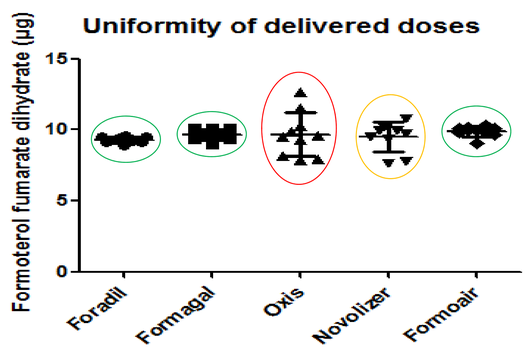


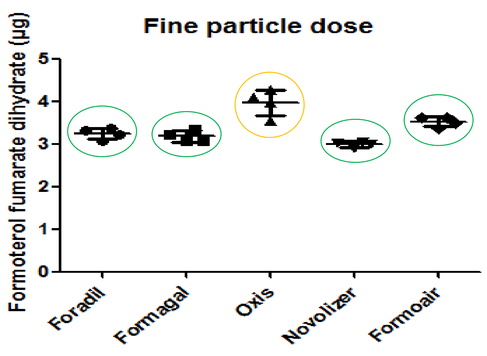
Mass Median Aerodynamic Diameter



Reproducibility

Green: low variability (CV<10%); Orange: moderate variability (10> CV <15%); Red : high variability (CV>15%)

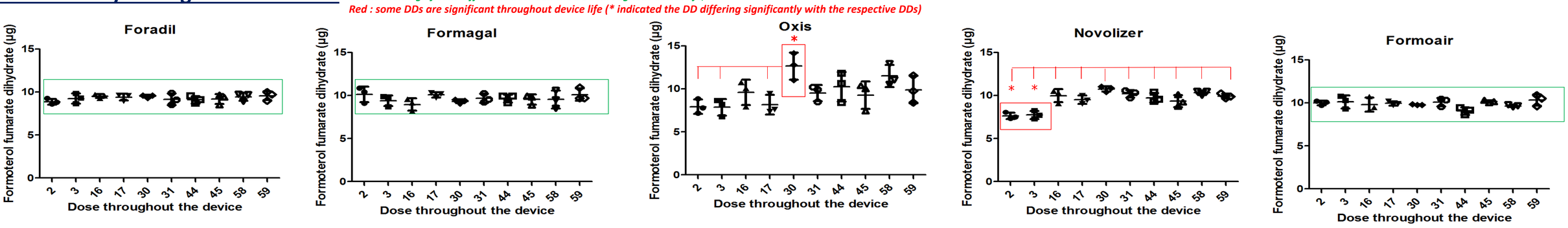




Robustness ➔ one-way ANOVA (* if p < 0.05) with post hoc test (Bonferonni)

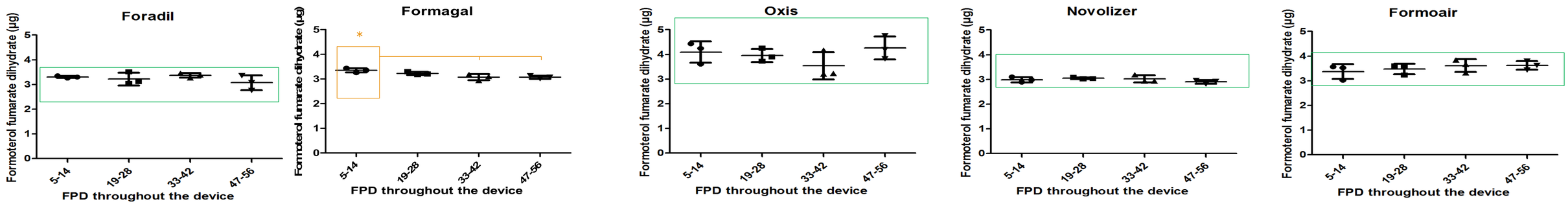
Dose delivery throughout device life

Green : non-significant difference between the DDs throughout device life;
Red : some DDs are significant throughout device life (indicated the DD differing significantly with the respective DDs)*



Fine Particle Dose throughout device life

Green : non-significant difference between the FPDs throughout device life;
Orange : some FPDs are significant throughout device life (indicated the FPD differing significantly with the respective FPDs) due to a very low FPD variability (CV< 5%)*



Device Handling

	Foradil	Formagal	Oxis	Novolizer	Formoair
Priming steps	0	0	1	4	1
Dose loading steps	6	6	3	3	1
Inhalation steps	5	5	5	5	5
Cleaning steps	4	4	2	2(+8*)	2(+4*)
Dexterity	High	High	Low	Medium	High
Feedback	Visual, Auditory, Taste		(Taste)	Visual, (Auditory), Taste	Cold and high velocity plume
Airflow (Resistance)	100 L/min (Low)	100 L/min (Low)	57 L/min (High)	75 L/min (Medium)	/

* For complete cleaning

Conclusions:

Capsule-based DPIs:
No priming step
Excellent feedback
Low device resistance
Higher dose loading and cleaning steps inducing high dexterity

Reservoir-based DPIs:
Lower dose loading and cleaning steps inducing lower dexterity
Priming step
Lower feedback
Higher device resistance

Reservoir-based pMDI:
Low dose loading steps
High Feedback
No device resistance
Priming step
Hand-mouth coordination inducing high dexterity

Conclusions:

- ➔ **Reservoir-based pMDI:** good reproducibility of DD and FPD which are consistent throughout the device life but present as main disadvantage the highest deposition in the induction port and peripheral lung.
- ➔ **Reservoir-based DPIs:** poor reproducibility of DD which are not consistent throughout the device life for both, poor reproducibility of FPD only for Oxis which is consistent throughout the device life and moderate deposition in the induction port for Novolizer.
- ➔ **Capsule-based DPIs:** good reproducibility of DD and FPD which are consistent throughout the device life except for FPD of Formagal certainly due to electrostatic charges and the lowest FPD variability (CV : 4%). They present the lowest deposition in induction port.

References: [1] Virchow JC *et al.,* Expert Opin Drug Deliv 2014, 11(12):1849-57; [2] Chrystyn H, Int J Clin Pract 2007, 61(6):1022-36

Respiratory Drug Delivery Europe, Palais des Congrès d'Antibes, Nice, France, May 5-8, 2015