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

<table>
<thead>
<tr>
<th>Capsule-based DPIs</th>
<th>Reservoir-based DPIs</th>
<th>Reservoir-based pMDI</th>
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<tbody>
<tr>
<td>Foradil® (Novartis)</td>
<td>Formagal® (SMB)</td>
<td>Oxis® (Astra Zeneca)</td>
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<tr>
<td>Novolizer® (Meda)</td>
<td></td>
<td>Formoair® (Chiesi)</td>
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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

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<tr>
<th>Green: low deposition</th>
<th>Orange: moderate deposition</th>
<th>Red: high deposition</th>
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Mass Median Aerodynamic Diameter

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<tr>
<th>Green: optimal deposition</th>
<th>Orange: intermediate deposition</th>
<th>Red: unsatisfactory deposition</th>
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Reproducibility

Uniformity of delivered doses

Fine particle dose

Dose delivery throughout device life

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<th>Green: no significant difference between the DD throughout device (δ)</th>
<th>Red: some DDs are significant throughout device (δ) * indicated the DD differing significantly with the respective DDs</th>
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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 the induction port.


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