



Easyhaler®

*Unique technical features as
demonstrated by recent data*

Introduction

The Easyhaler performs consistently, irrespective of a patient's inhalation flow^{1,2}

Patients receive a consistent fine particle dose with the Easyhaler¹

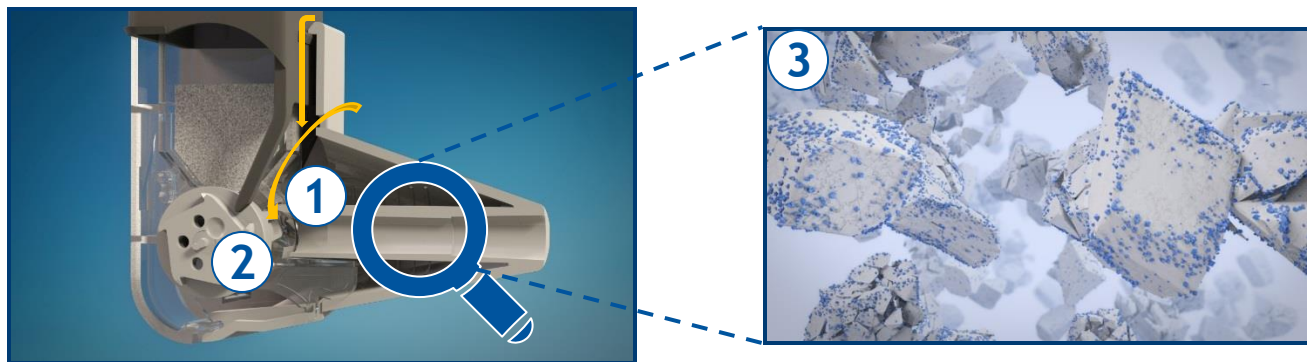
Patients prefer the Easyhaler to other dry powder inhalers^{3,4}

What are some of the unique technical features of the Easyhaler that may be behind these findings?



The Easyhaler is a high or medium-to-high resistance dry powder* inhaler generating highly turbulent air flow within the inhaler, even with low patient inhalation flows

- ① During an inhalation, air enters the Easyhaler around the actuator and encounters **high or medium-to-high resistance**,* due to the small size of the air vent

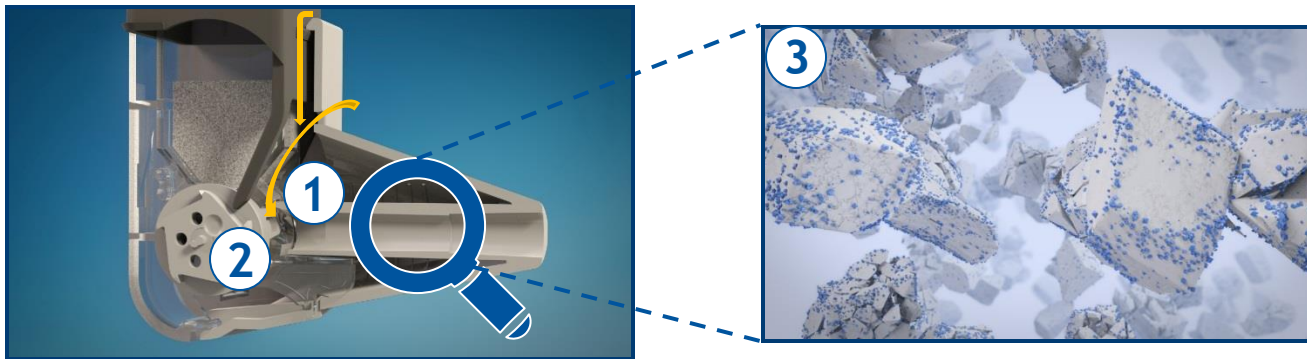


- ② **High or medium-to-high resistance** generates turbulent air flow to the dosing cup
- ③ Turbulent air flow ensures de-aggregation of drug particles and accurate dose delivery, even with **low patient inhalation flows**

*Easyhaler M (Monotherapy) is a high resistance inhaler and Easyhaler C (Combination) is a medium-to-high resistance inhaler
1. Chrystyn H. Clin Drug Invest 2006;26:175-83; 2. Malmberg LP, et al. J Aerosol Med Pulm Drug Deliv 2014;27:329-40

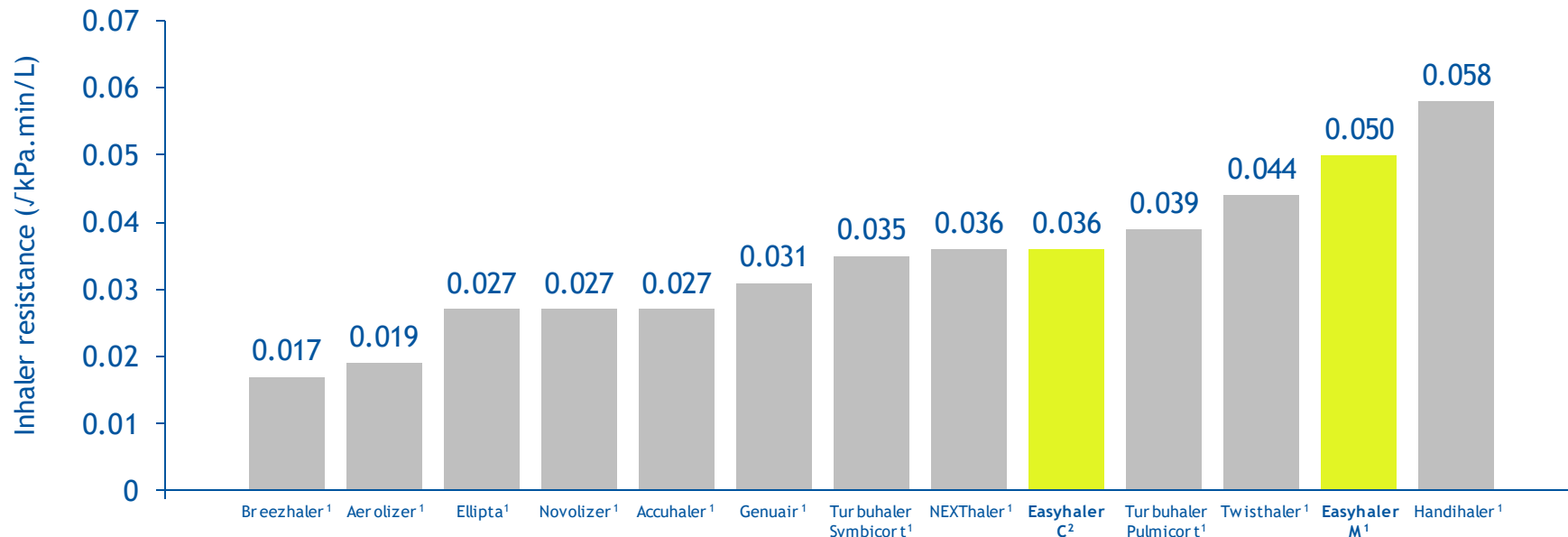
Why is turbulent air flow within an inhaler important?

- ✓ It generates high air flow speed and force to the dosing cup ①
- ✓ It guarantees the emission of all powder from the dosing cup ②
- ✓ It ensures de-aggregation of drug particles from carrier molecules, the formation of fine particles and an optimal speed for lung deposition ③



The Easyhaler is a high or medium-to-high resistance inhaler*

Inspiratory resistance of marketed dry powder inhalers^{1,2}

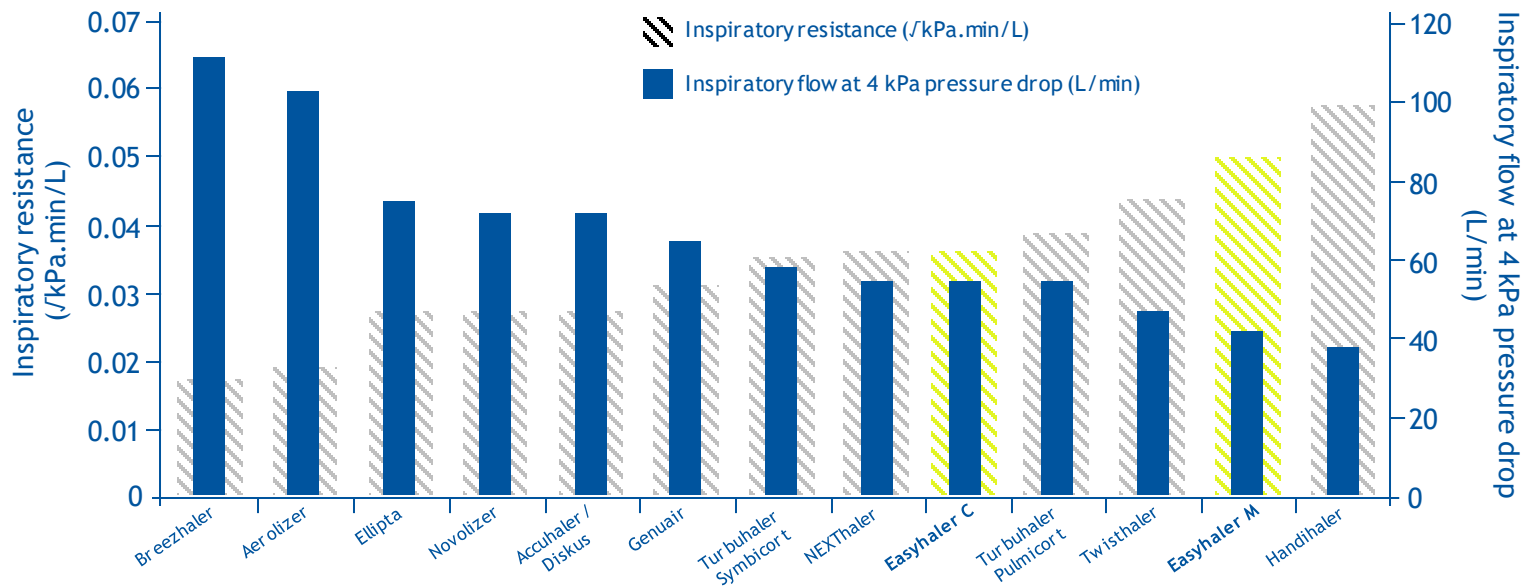


*Easyhaler M (Monotherapy) is a high resistance inhaler and Easyhaler C (Combination) is a medium-to-high resistance inhaler

1. Krüger P, et al. Eur Respir J 2014;44 Suppl 58:4635; 2. Malmberg LP, et al. J Aerosol Med Pulm Drug Deliv 2014;27:329-4

Higher resistance translates to a lower inspiratory flow through the inhaler

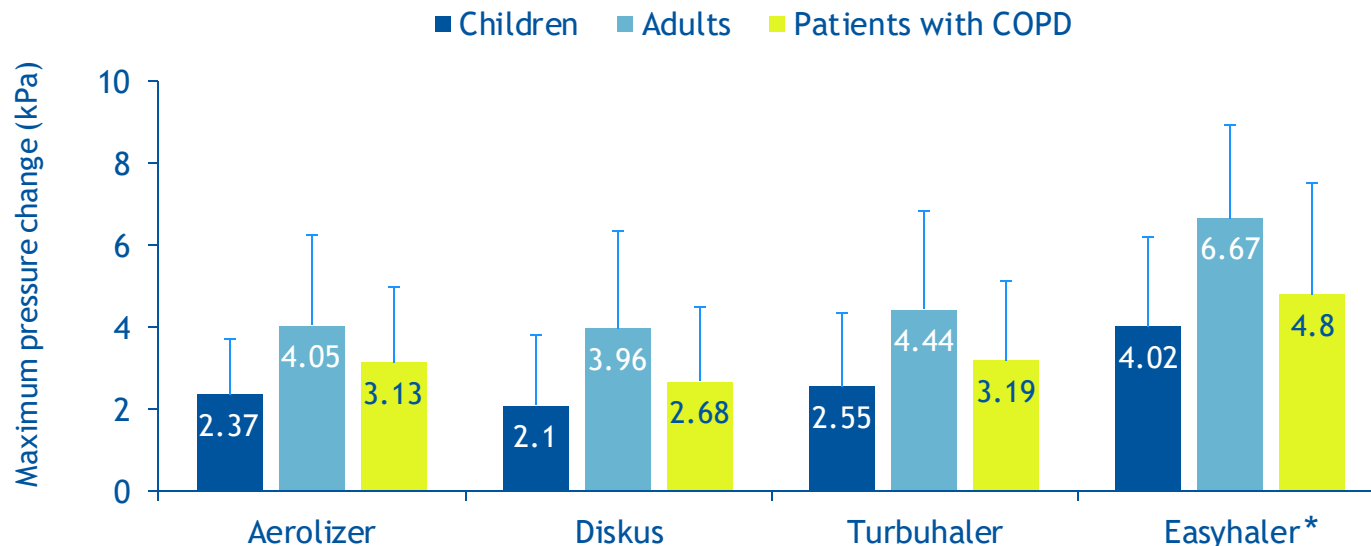
Inspiratory resistance of marketed dry powder inhalers and respective inspiratory flows studied at a pre-set equal pressure drop rate of 4 kPa^{1,2}



*Easyhaler M (Monotherapy) is a high resistance inhaler and Easyhaler C (Combination) is a medium-to-high resistance inhaler
1. Krüger P, et al. Eur Respir J 2014;44 Suppl 58:4635; 2. Malmberg LP, et al. J Aerosol Med Pulm Drug Deliv 2014;27:329-40

Easyhaler inhalers enable optimal turbulent air flow across all patient groups^{1,2}

Mean (SD) maximum pressure change, as a measure of turbulent air flow, generated through dry powder inhalers (N=98 [16 children, 53 adults, 29 patients with COPD])¹

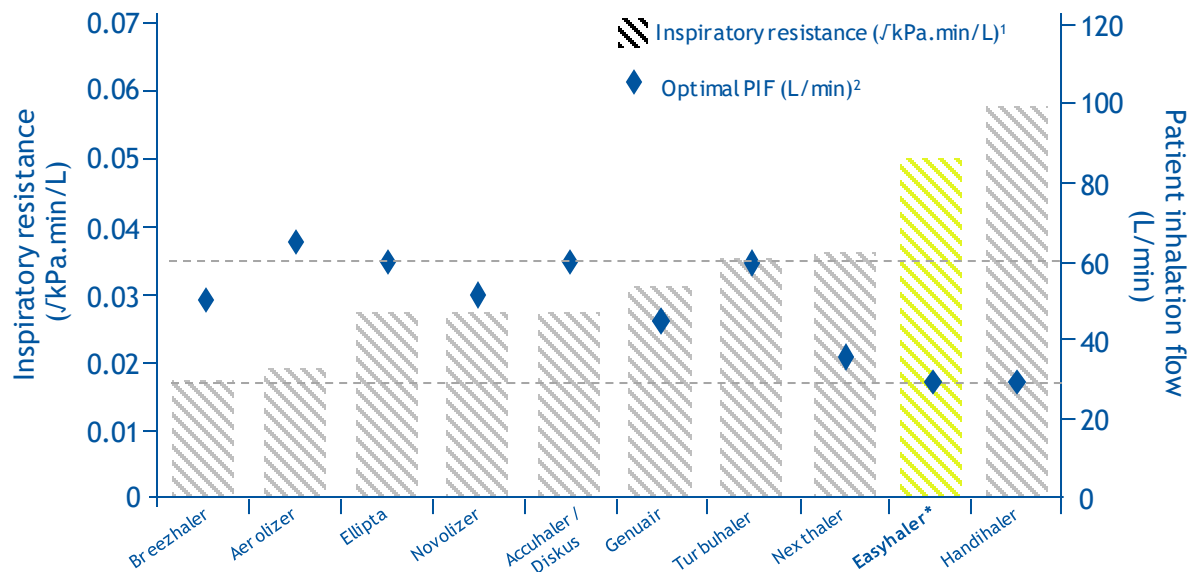


COPD: chronic obstructive pulmonary disease; SD: standard deviation; *data provided for the Easyhaler M (Monotherapy)

1. Azouz W, et al. J Aerosol Med Pulm Drug Deliv 2015;28:35-42; 2. Malmberg LP, et al. J Aerosol Med Pulm Drug Deliv 2014;27:329-40

With Easyhaler optimal drug delivery can be achieved even with low patient inhalation flow

Inhaler resistance,¹ and optimal PIF for adequate drug delivery² of marketed dry powder inhalers



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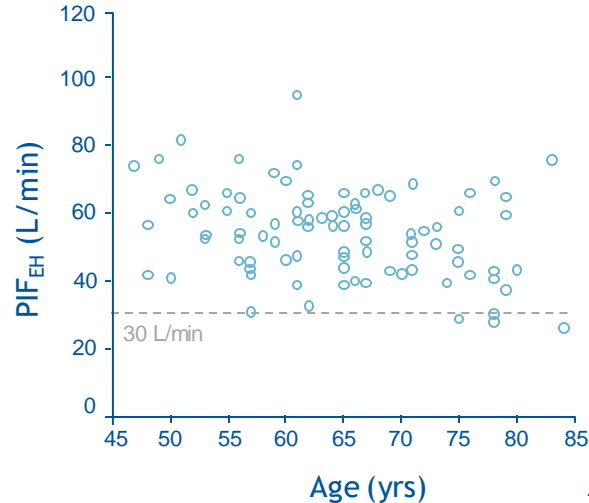
Optimal PIF level indicates that at this level, as well as any higher level, the patient receives the labelled dose.²

PIF of 30 L/min is reported as optimal for the Easyhaler.^{2,3}

Almost all asthma and COPD patients achieve a PIF of 30 L/min or higher^{1,2}

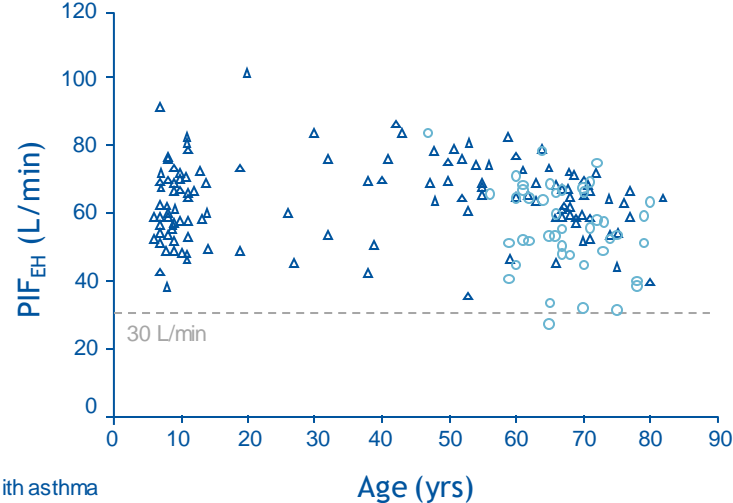
PIF rates (L/min) for Easyhaler Monotherapy¹ and Combination² therapy inhalers in patients with asthma or COPD^{1,2} (¹N=93 patients with COPD; ²N=181 patients [137 with asthma, 44 with COPD])

Easyhaler Monotherapy¹



△ Patient with asthma
○ Patient with COPD

Easyhaler Combination²

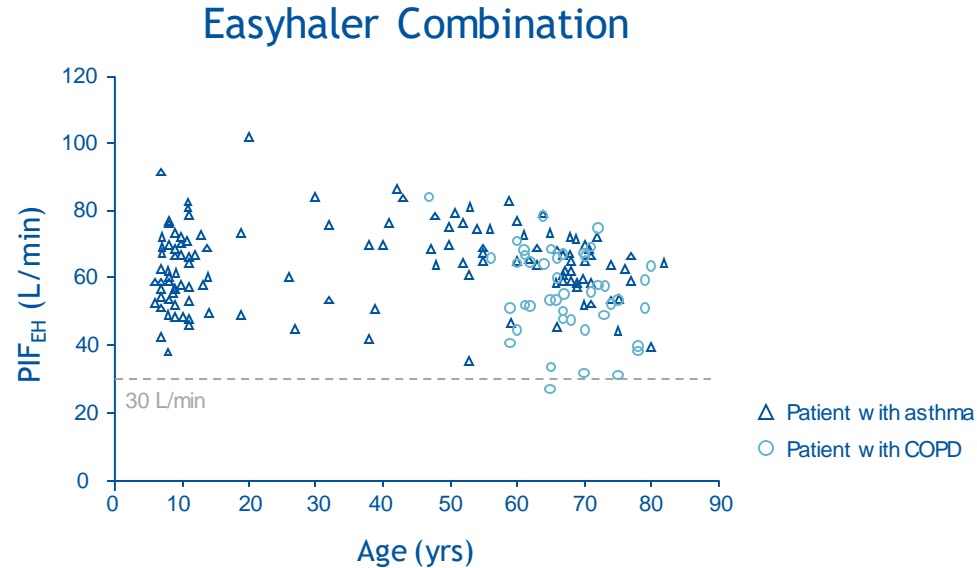


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The vast majority of asthma and COPD patients, of varying age and disease severity, achieve a PIF of 30 L/min or higher with both Easyhaler Monotherapy and Combination therapy inhalers.^{1,2}

Almost all patients achieve a PIF of 30 L/min or higher with an Easyhaler Combination therapy inhaler¹

Individual PIF rates (L/min) for the Easyhaler Combination therapy inhaler¹
(N=181 patients [137 with asthma, including 52 children, and 44 with COPD])



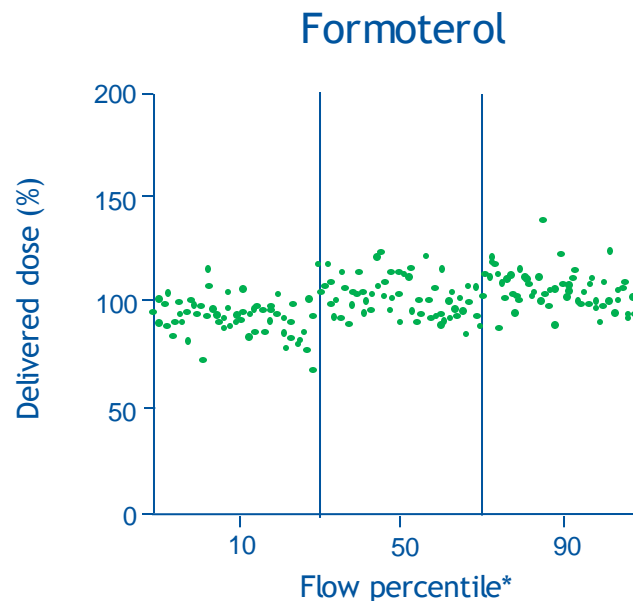
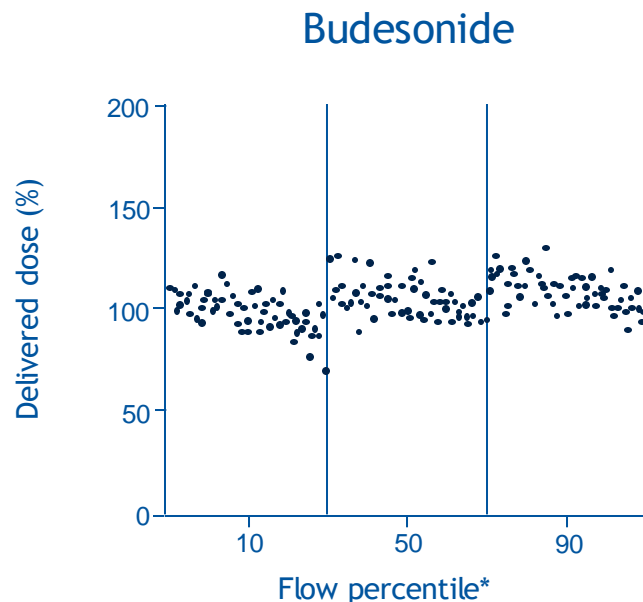
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All asthmatic patients and the vast majority patients with COPD, across a range of ages (6-82 years) and disease severities, are able to achieve a PIF rate of 30 L/min or higher with an Easyhaler Combination therapy inhaler.

In this study, Easyhaler PIF rates ranged from 35.4 to 101.4 L/min in asthmatic patients and from 27.0 to 83.7 L/min in patients with COPD.¹

The Easyhaler provides accurate and consistent dosing across patient inhalation flows

In vitro dose delivery from the Easyhaler Combination inhaler at three different peak inspiratory flows (each data point represents a single dose actuation)



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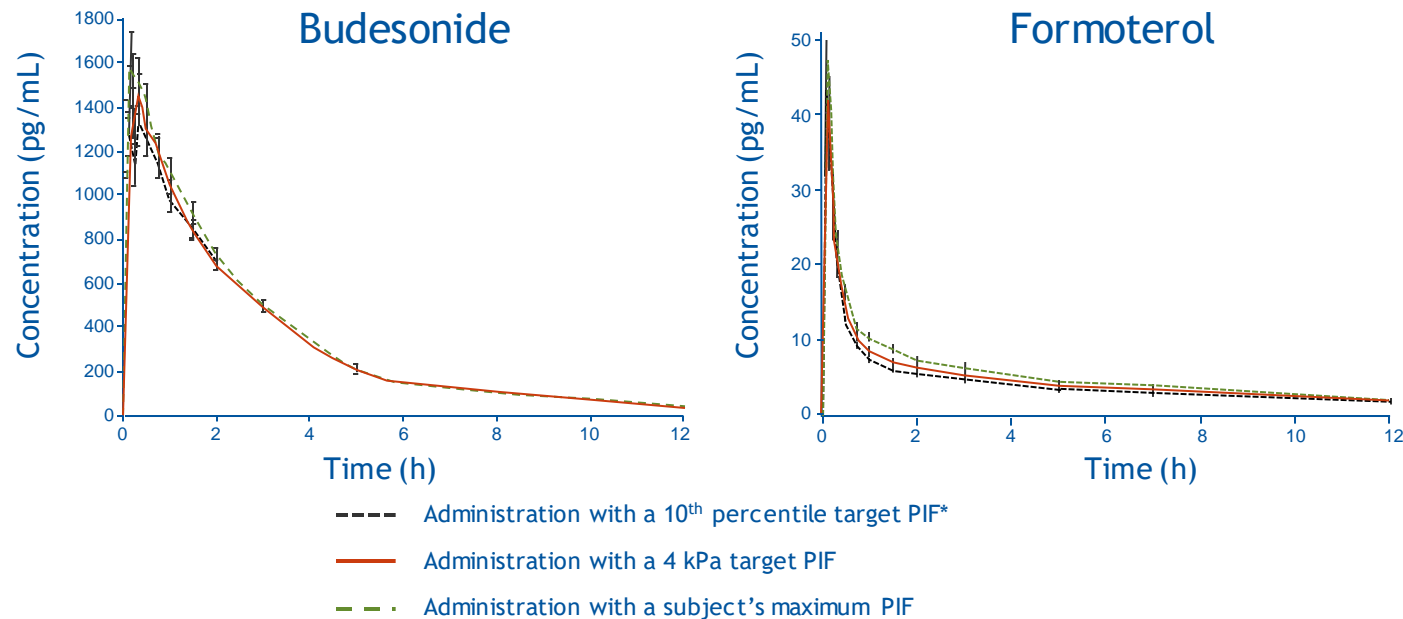
The Easyhaler produces consistent dose delivery irrespective of a patient's inhalation flow.

Even at low patient inhalation flows, turbulent air flow generated within the inhaler is enough to sufficiently break up drug particles from their carrier.

*10th/50th/90th percentile: peak inspiratory flows achieved by 90%, 50% and 10% of a patient population. These are indicative of high, medium and low inspiratory flows, respectively. Haikarainen J, et al. Pulm Ther 2017;3:125-38

The Easyhaler provides consistent lung deposition irrespective of patient inhalation flows

Mean drug concentrations (SE) in plasma after two inhalations from the Easyhaler Combination inhaler at three different PIFs (N=16 healthy volunteers)



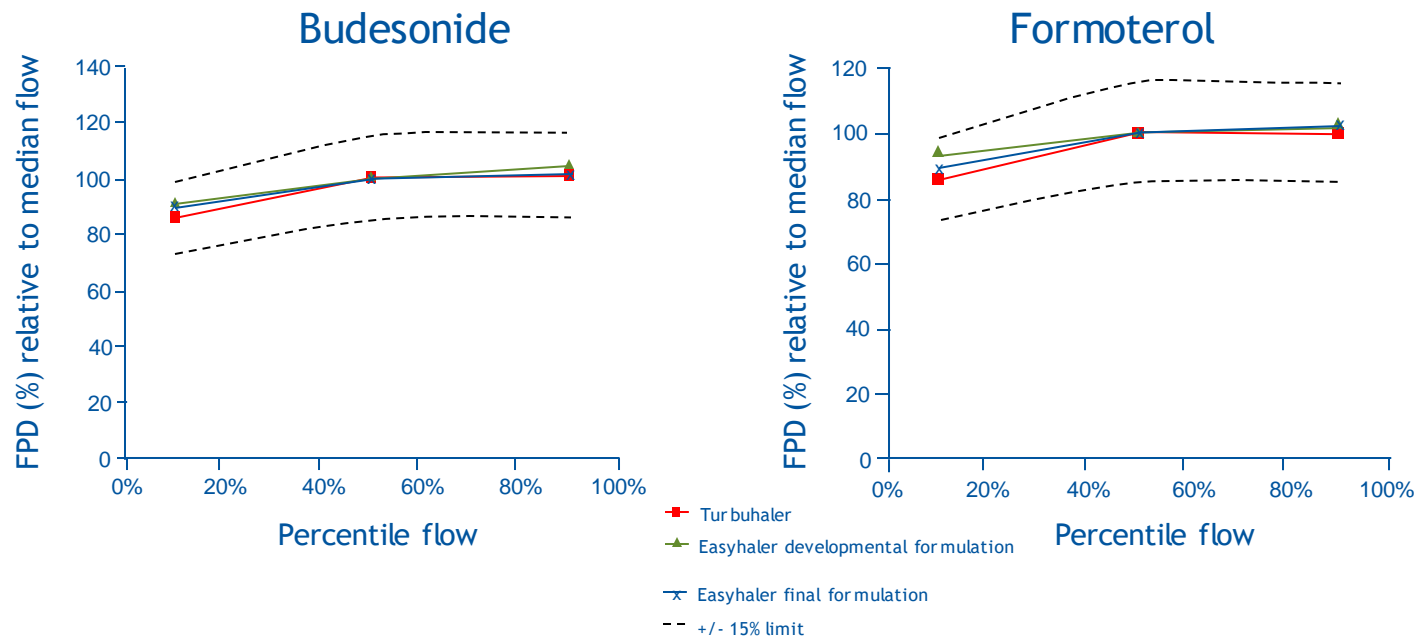
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The area under the curve is representative of lung deposition.

In this study, both drugs were administered with concomitant oral charcoal to prevent absorption via the gastrointestinal tract, and to assess absorption via the lungs only.

Fine particle doses with the Easyhaler are independent of patient inhalation flows

Delivered fine particle dose *in vitro* using the 10th, 50th and 90th percentile of the PIFs



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In this study, the delivered fine particle dose with Easyhaler was independent of patient inhalation flow, and comparable to that observed with Turbuhaler.

Summary

- Turbulent air flow generated inside a dry powder inhaler during a patient's inhalation is the main driver for efficient de-aggregation of the drug dose, and dose delivery¹
- The Easyhaler is a high or medium-to-high resistance inhaler generating highly turbulent air flow²
- With both Easyhaler inhalers (M and C), the vast majority of patients can achieve a PIF greater than 30 L/min,^{3,4} which is considered as optimal for the Easyhaler⁵
- Dose delivery with the Easyhaler is accurate and consistent across a wide range of patient inhalation flows, with efficient and consistent lung deposition and fine particle dose delivery irrespective of patient inhalation flows^{4,6}

Glossary

Fine particle

A particle with a diameter of $< 5\mu\text{m}$

Peak inspiratory flow

The fastest flow recorded during an inspiratory cycle

Resistance

Opposition to air flow

Turbulent air flow
(sometimes referred to
as *turbulent energy*)

The flow of air, in which molecules move in a random, non-ordered manner; the opposite of laminar flow, which is smooth, uninterrupted air flow
