

# YOUR INHALATION GRADE LACTOSE



## Exploring the design space for dry powder inhalers, a case study with two types of capsule devices

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### Introduction

In the current Quality by Design paradigm, the development of a pharmaceutical product requires a thorough understanding of the design space to enable the built in of quality in the product.

### Methods

- Two capsule based devices (Handihaler® and Cyclohaler®)
- Lactose (Lactohale®, DFE Pharma) blended with 2 % budesonide
- A coarse grade of lactose complemented with different types of fine graded lactose.
- A development space was created with type of fine grade lactose (d50 of the fine grade varying from 5-15 µm) and amount of this fine grade (2.5-20 wt%) as factors and Fine Particle Fraction (FPF) and Hausner Ratio (HR) as the responses.
- Target was set on FPF (18-25%) and HR (Fair or passable).

### Results

The results were analyzed by a surface response design and gave a response plot for both HR and FPF as function of type and amount of fines. Overlap contour plots were constructed of both responses based on above stated borders and these are depicted in Figure 1.

### Discussion

For the constraints set, both types of DPI devices do show achievable design spaces. Handihaler has the largest white areas, with the largest at a fair flow constraint, whereas the Cyclohaler shows the largest white area in the passable flow range.

### Conclusions

In this study, Handihaler has in general a larger design space than Cyclohaler. At might be advisable to combine the choice for Handihaler with the choice of a piston capsule Filling system and Cyclohaler with tamping or disc-dosing filling system because this allows for the largest design area.

### References

1. Yu LX, Amidon G, Khan M a, Hoag SW, Polli J, Raju GK, Woodcock J: Understanding pharmaceutical quality by design. AAPS J 2014, 16:771–83.
2. Peters HJW, Hebbink GA: Selection of excipients for dry powder inhalers. ONdrugDelivery 2016, 2016.
3. Kinnunen H, Hebbink G, Peters H, Huck D, Makein L, Price R: Extrinsic lactose fines improve dry powder inhaler formulation performance of a cohesive batch of budesonide via agglomerate formation and consequential co-deposition. Int J Pharm 2014, 478:53–59.

## Contour Plot of Hausner Ratio FPD ED (%)

**Figure 1.** Red lines denote borders for flow (Hausner ratio), green lines denote desired FPF (21% ± 15%).

White areas show design space, grey areas are outside the design space.

### Fair flow

(HR=1.18-1.25)

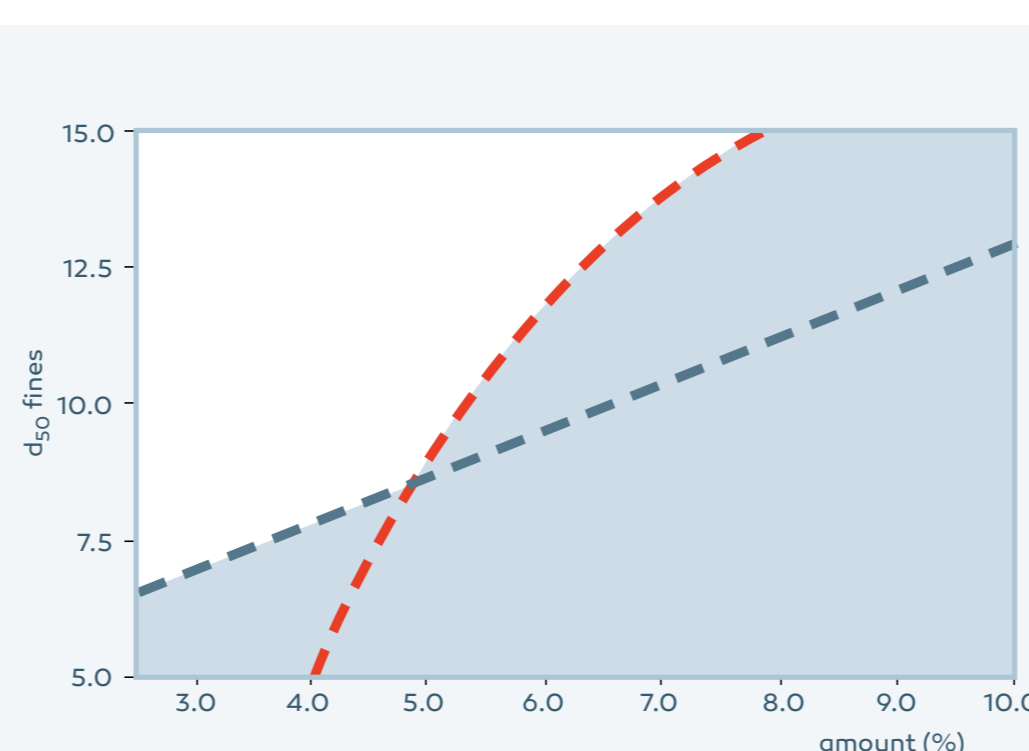
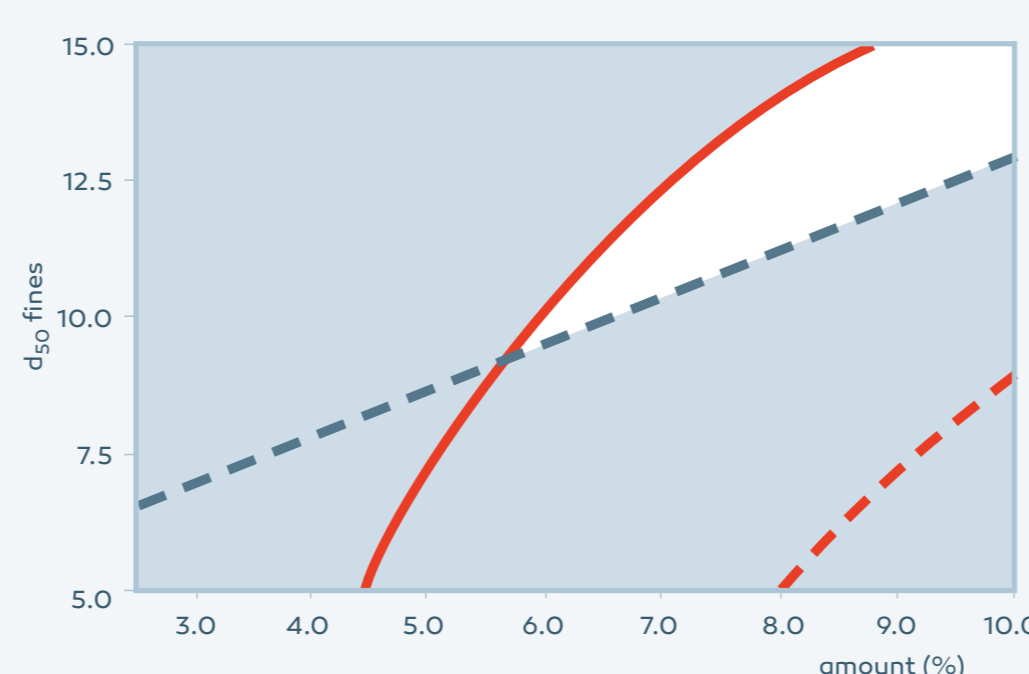
Line Style	Parameter	Value
Solid Red	Hausner Ratio	1.18
Dashed Red	Hausner Ratio	1.25
Solid Green	FPD ED (%)	18
Dashed Green	FPD ED (%)	25

### Passable flow

(HR=1.26-1.34)

Line Style	Parameter	Value
Solid Red	Hausner Ratio	1.26
Dashed Red	Hausner Ratio	1.34
Solid Green	FPD ED (%)	18
Dashed Green	FPD ED (%)	25

### HandiHaler



### Cyclohaler

