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Sunriser – An innovative platform tailored for efficient delivery of diverse formulations

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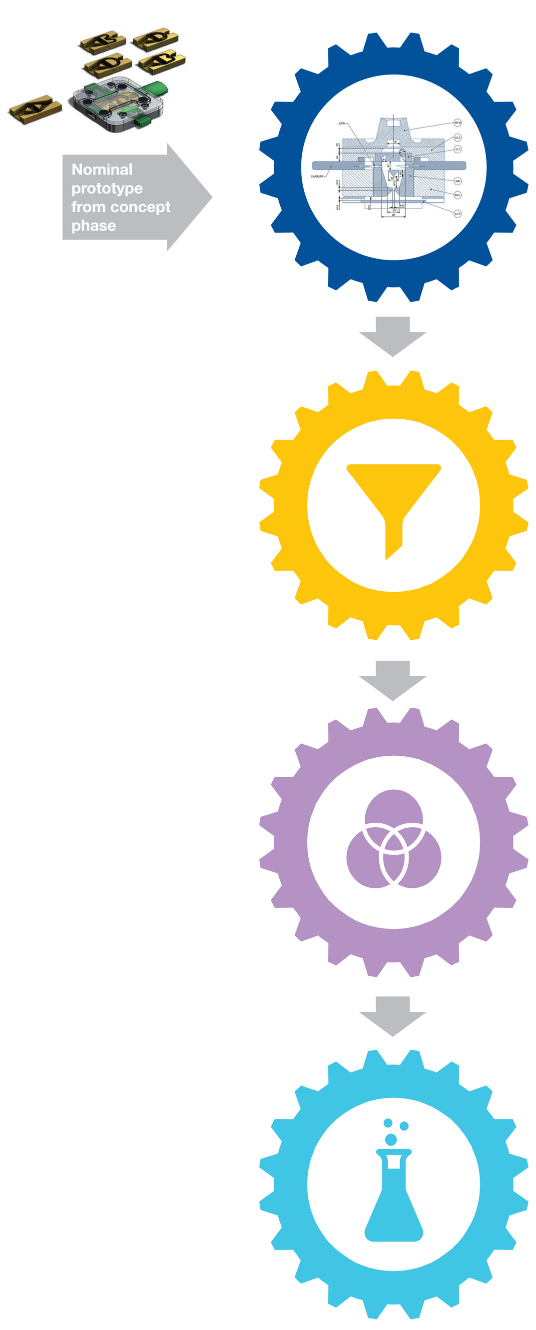
1. INTRODUCTION

The inhalation route is recognized as an effective method for delivering medications, targeting not only respiratory diseases but also systemic conditions. The recent trends in inhalation therapy for systemic applications, such as treatments for diabetes, Parkinson's, and Schizophrenia, highlight the versatility of this delivery method. These advancements have led to new formulation technologies being investigated for Dry Powder Inhalers (DPIs).[1] These new powders coming with new physico-chemical properties, are prompting also the development of new devices to achieve reliable and precise dosing to the patient. The device and formulation are intrinsically linked, as the drug delivery efficiency depends on both..[2]

A systematic stepwise approach of altering device parameters and link them directly to the aerodynamic performance for different formulations types was used to create a platform technology that is able to achieve high aerosolization properties and consistent performance even with cohesive powders and varying flow rates.

2. MATERIALS AND METHODS

A stepwise Methodology to gain a deep understanding of the Sunriser® Engine was combined with a modular 3D printed prototyping approach. From the first concept prototypes a design-space map was generated and subsequently tested. This identified the dimensions that significantly affect capsule motion and provided the statistical basis for the next phases. In STEP 1 aerodynamic performance was tested of the best performing configurations from STEP 0. STEP 2 expanded the design-space with new module combinations involving simultaneous dimensional changes. STEP 3 assessed additional part combinations and designs at two different flowrates (30 and 60 L min^{-1}) further refining the findings. A Next Generation Impactor (NGI) was used to characterize the aerosol properties of the formulation at flow rates of 45 L/min for Sunriser and 60 L/min for marketed capsule-based device and an actuation volume of 4 liter were tested. The fine particle fraction (FPF) was calculated.



Step 0:
Create Design Space Map for stepwise modeling of one dimension at a time of the nominal prototype. Test capsule motion (impact frequency, oscillation frequency, impact factor, movement factor) and evacuation time.

Step 1:
Screening & filtering based on factors improving capsule motion and evacuation time and aerodynamic performance.

STEP 2:
Combine modular parts to achieve an enhanced capsule motion and aerodynamic performance.

STEP 3:
Define new part designs to maximizing capsule motion and study reduction of capsule deposition. Test aerodynamic performance.

Increasing aerodynamic performance and reducing powder deposition in the device by systemic altering of dimensions and subsequent combination of best results

3. RESULTS

A design map of the Sunriser device was created to systematically vary critical dimensions. Modular prototypes composed of several interchangeable parts were 3D printed and used for the assessment of capsule motion and aerodynamic performance. Influential dimensions affecting especially capsule motion, powder retention in the device and aerodynamic performance within the Dry Powder Inhaler could be detected. From the 15 different studies we found that 9 dimensions are statistically significant in the range of study regarding impact frequency. All dimensions are located below the capsule position. Dimensions around the capsule chamber and the air inlet into the device are the most influential dimensions for reliable capsule motion. Changes of these dimensions are the foundation for the new combinations tested in the subsequent steps. By subsequent assembling of new prototypes and testing them with a carrier-based formulation and an engineered formulation in the following steps the capsule motion could be increased. Further the powder retention in the device could be decreased while achieving high fine particle fractions.

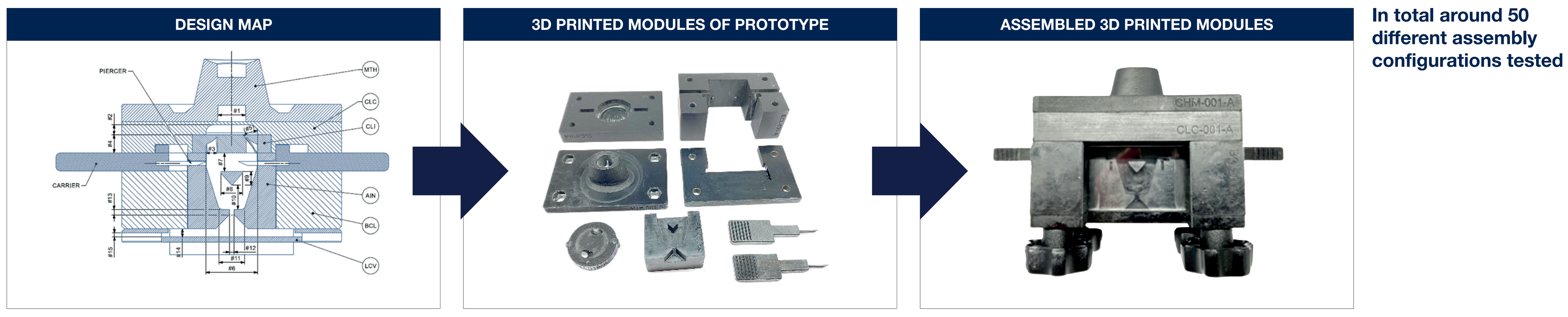


Figure 1. Design Map of Sunriser with crititcal dimensions and modular parts for the 3D printed prototypes.

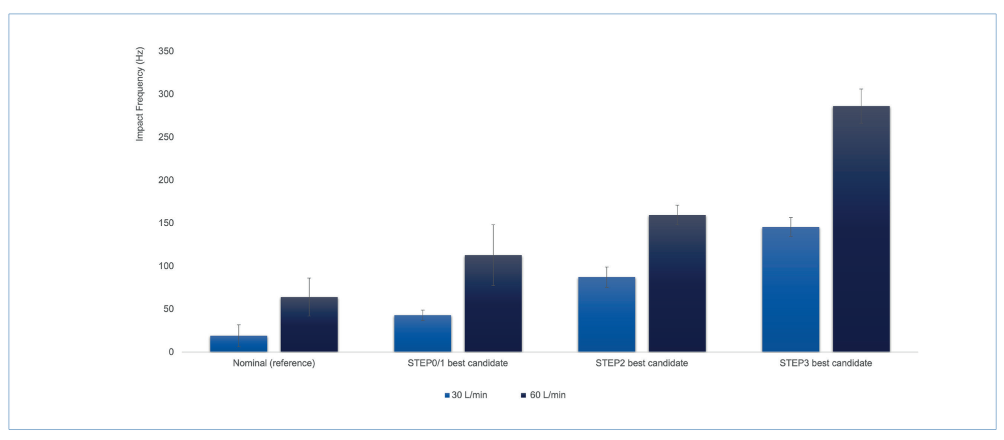
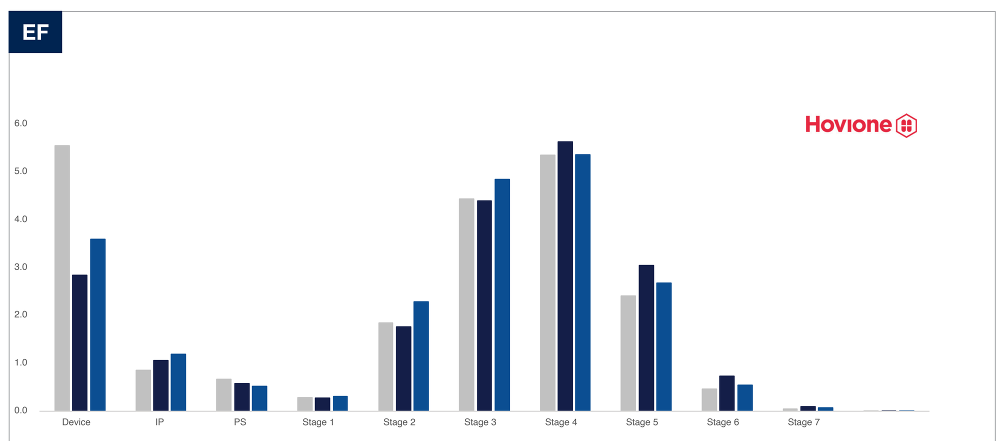


Figure 2. Significant improvement of capsule impact frequency from Step 0 to Step 3 for robust capsule movement

Several dimensions—particularly those governing local fluid dynamics around the capsule—proved critical for capsule motion. Conversely, dimensions seemingly unrelated to capsule displacement may still affect downstream aerosol particle-size distribution (APSD). Figure 2 summarizes impact frequencies for the top candidates at 30 and 60 L min^{-1}. Stepwise optimization greatly enhanced the DPI's ability to initiate capsule movement. Compared with the nominal design, the best STEP3 prototype increased capsule-motion efficiency by more than seven-fold at 30 L min^{-1} and showed similarly strong gains at 60 L min^{-1}. With the improvement of the innovative oscillating capsule movement the foundation for a enhanced and reliable performance of the overall Sunriser device was established.

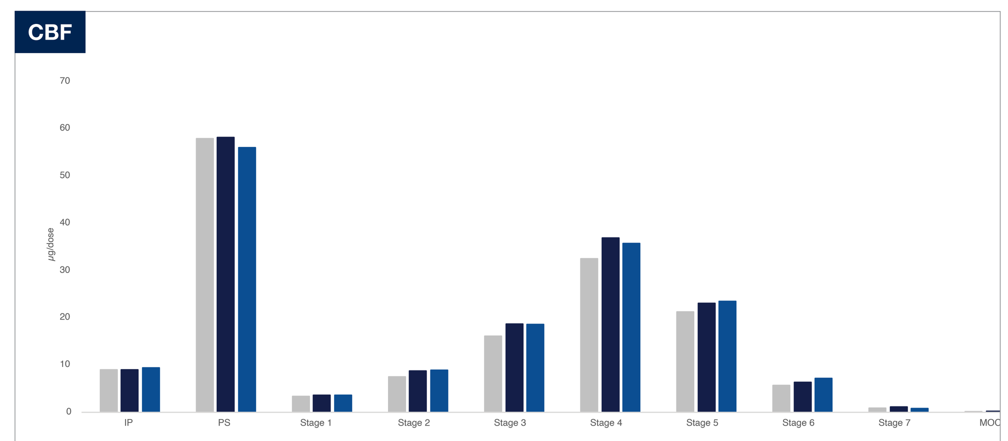
Those dimensional variations in combination with the introduction and testing of completely new parts of classifier and mesh design also resulted in an improved design for both engineered formulations (EF) and carrier-based formulations (CBF) compared to the nominal prototypes form the start. P3 Prototype was the best performing configuration with an increase in Emitted dose from the nominal prototype of 5% linked to the decrease of powder deposition in the device. Surprisingly the increase in performance was observed for engineered formulations as well as for carrier-based formulations, independent from the very different nature of those two formulation types.

EF



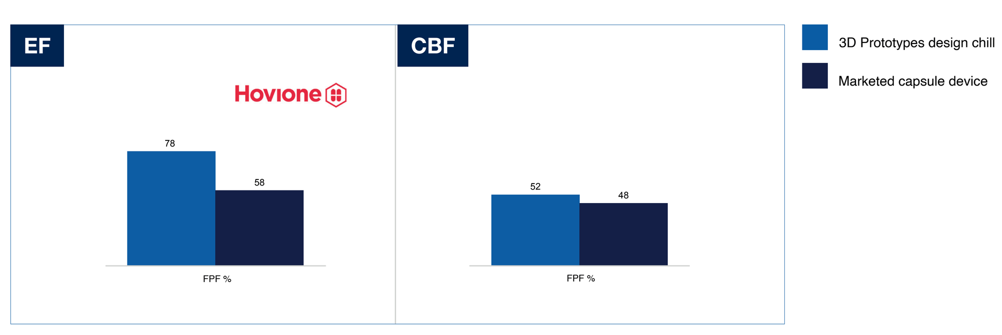
Engineered #3	ED (% LC), ±%RSD	Device deposition (%LC), ± %RSD	FPF (%ED), ± %RSD
NOM	72.9 ± 2.4	24.7 ± 13.5	76.3 ± 1.5
P3	78.6 ± 1.7	12.7 ± 9.1	77.5 ± 2.6
P4	79.6 ± 1.3	16.0 ± 6.2	74.3 ± 1.3

CBF



Carrier-based #3	ED (% LC), ± %RSD	FPF (%ED), ± %RSD
NOM	77.3 ± 3.3	76.3 ± 1.5
P3	83.1± 0.6	77.5 ± 2.6
P4	82.1 ± 4.7	74.3 ± 1.3

Figure 3. Step 3 configurations were tested with engineered formulation and a carrier-based formulation to find the best performing configuration to maximize FPF and minimize device powder retention.



The best configuration obtained during our development process was compared to marketed capsule-based devices again with testing the engineered formulation and the carrier-based formulation. For both formulation types a higher Fine particle Fraction was obtained delivering the formulation with the Sunriser prototype at 45 L/min compared to the marketed device at 60 L/min. This clearly indicates, that the powerful engine of the Sunriser device is able to de-agglomerate cohesive formulations and ensure a high fraction lung delivery.

4. CONCLUSION

Using an integrated approach and link fast prototyping of multiple device designs to the achievable performance for specific formulation types enables an accelerated development of a highly efficient DPI device. With this systematic approach a deep understanding of the key parameters for device design can be gained and thus with informed design iterations advancements in device performance could be achieved. By optimizing critical factors capsule motion, aerodynamic performance, evacuation time, and powder retention of the Dry Powder Inhaler (DPI) was substantially enhanced. Linking the systematic amendment of device configurations and performance outcomes specific to different formulations, enables a deep understanding of key design parameters. Consequently, informed design iterations can drive significant advancements in device performance, paving the way for innovative inhalation therapies that extend beyond conventional treatment paradigms. This highlights the device's potential as a platform device suitable for diverse inhalation therapies. Its ability to maintain high FPF across these diverse formulations suggests broad applicability, enabling the delivery of innovative inhalation therapies.

References

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