Improving dry powder inhaler performance: An integrated approach

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Advancement of dry powder inhalers (DPIs) is hindered by the limited understanding and control of de-agglomeration mechanisms and flow characteristics, which affect aerosol performance. These complex and intertwined phenomena are contingent to device design, inhalation flow, and formulation properties. To study these processes, an integrated approach is presented, combining three complementary methods: *in-vitro* deposition by cascade-impactor, computational fluid dynamics (CFD), and particle image velocimetry (PIV).

The impact of device design on its performance was assessed using 3D-printed DPI models with modified tangential inlets and the addition of a grid. Aerosol performance was investigated via a cascade-impactor (NGI-Copley), using a 1% w/w beclomethasone dipropionate-loaded lactose formulation, at 60 l/min. CFD was used to simulate the flow in the device and downstream region using a novel Scale-Resolving-Simulation approach to capture the turbulence structure and study particle behaviour (carrier and drug) via Lagrangian tracking. PIV measurements were performed using water-based experiments under geometrically and dynamically similar conditions to DPIs operating in air.

Inlets' modification did not affect fine particle dose assessed *in-vitro*. The grid inclusion decreased throat deposition due to a straightened outflow without lateral spreading, as observed from the PIV, which also showed a high-swirling and recirculating jet-flow emerging from DPIs without the grid. The CFD results showed close agreement with PIV data, validating the simulations, and providing detailed information on the flow and particle-dynamics.

Overall, this work demonstrates the correlation of fluid- and particle-dynamics with aerosol dispersion and particle deposition, within and from a DPI, that can be achieved.