Simulation of the dose from a dry powder inhaler

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Vision

A DPI simulation tool to

Support device development:
- Speed up development process
- Reduce device testing
- High performance and robust device

Support formulation development:
- Right formulation for right device
- Narrow the design window
Dry powder simulations – the tools

CFD = Computational Fluid Dynamics

- Simulation of air flow profiles
- Complex flow geometries
- Turbulence
- Large eddy simulations
- Multiphase flow

DEM = Discrete Element Method

- Simulation of particle interactions, trajectories, collisions, deformation, breakage

Material characteristics can be taken into account:

- Size
- Density
- Surface energy
- Friction
- Cohesivity/Adhesivity

the MultiFlow code
Simulation of the dose from a DPI: The inhalers


How to simulate the dose from a DPI?

THE FINE PARTICLES CONSTITUTE A CHALLENGE !!

1. Too many particles  
   Current simulation limitation approx. 100 000 particles

2. The fine particles are very small  
   Limits the simulation time
   
   100 times smaller diameter → 100 times shorter time step

Our approach: Combine DEM simulations of the fine particles with CFD-DEM simulations of the inhaler + carrier
Simulation of the dose from a DPI

Adding fines to the carrier
Simulation of the dose from a DPI

Adding fines to the carrier
How to handle the micro-particles?

The fine particles are followed via **MICRO-MODELS**

1. Carrier – carrier collision
2. Carrier – wall collision
3. Fine release by drag forces
4. Fine particle re-attachment to carrier
5. Fine particle release from wall due to carrier-wall collisions
Simulation of the dose from a DPI

Micromodel for carrier – carrier collision

The Hamaker constant, $Ha$, is a measure of the interaction force between carrier and fine particles.
The integrated model: FOSID

Time: 0.018400 s
The integrated model: Output

The "fines source" monitors where the fines are released.

Full simulation of a "normal powder" in the screenhaler.
Validation: Emptying time

Screenhaler: Excellent agreement with experimental data

Particles exiting

Simulation

Experiment

Optical conc.

Fines fraction

Fines fraction < 5μm

Measurement time (ms)

Normalised number of particles

Flow Time (ms)
Validation of flow rate effects

Flow dependence

Predict the flow dependence of the device

Good match between simulation and experiment

Any inhalation profile can be simulated
Conclusions and Future aspects

A powerful DPI simulation tool has been developed
✓ Posesses the right physics
✓ Can be adapted to different APIs, carriers, drug loads
To be used for:

Device development and optimization
- Drug retention
- Fine generation zones
- Robustness

Application to formulation development

The interaction between formulation and device

Fundamental understanding
- Which mechanism are important for fines generation?
- Understanding / optimizing the effects of
  - Carrier particle size
  - drug load
  - Lactose fines
  - Drug cohesivity/adhesivity
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And YOU