

# Computational Fluid Dynamics (CFD) Modeling for Optimization of Device Design and Understanding of Product Performance

## GRx+Biosims 2020: Complex Products Workshop

### Session 4: Device Considerations for Complex Drug-Device Combination Products

**Ross Walenga, Ph.D.**

Division of Quantitative Methods and Modeling, Office of Research and Standards

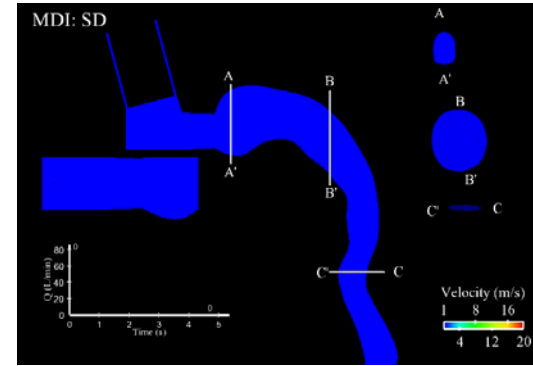
Office of Generic Drugs | CDER | U.S. FDA

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# Computational Fluid Dynamics (CFD) Modeling

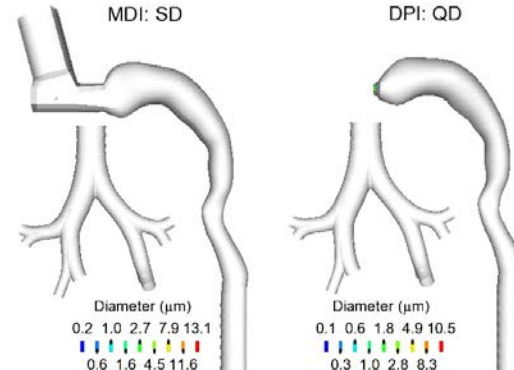


- Prediction of fluid and particle transport
- Allows for consideration of realistic geometries
- Validated with in vitro or in vivo data



Metered Dose Inhaler (MDI)

Simulations from Longest et al.<sup>1</sup>

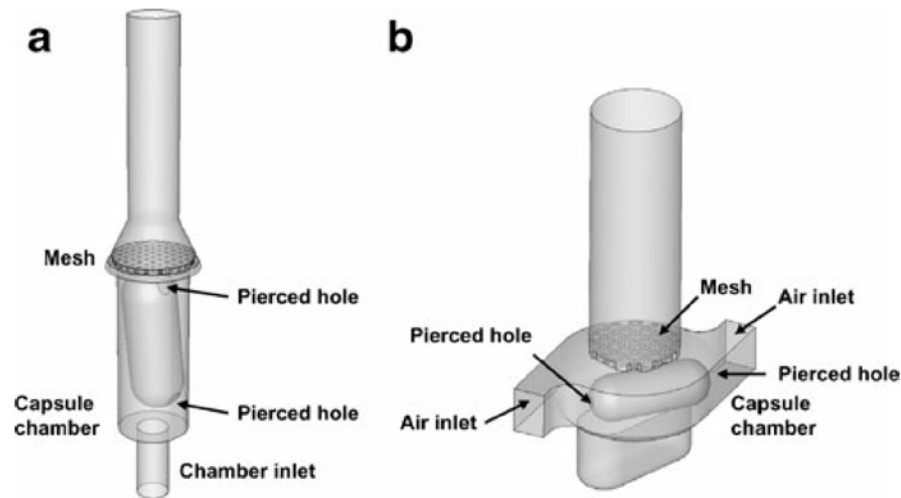


Dry Powder Inhaler (DPI)

# Device Modification to Match In Vitro Performance

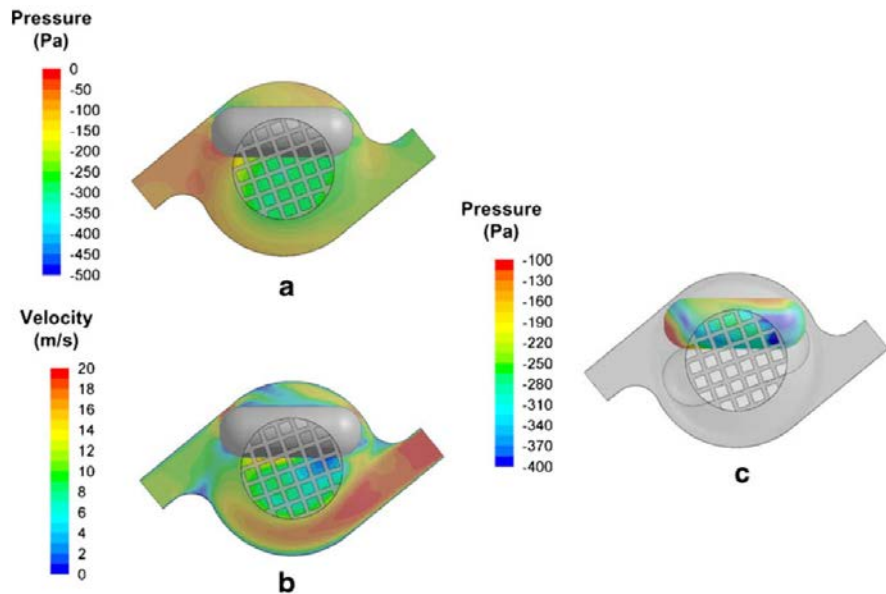


- Research funded by the Office of Generic Drugs (OGD)
  - University of Bath (PI: Jagdeep Shur)
- Two capsule-based dry powder inhalers (DPIs) with tiotropium bromide - Handihaler<sup>®</sup> and Cyclohaler<sup>®</sup>
- Model flow and particle transport using CFD
- Modify Cyclohaler<sup>®</sup> to achieve comparable predictions
- Compare in vitro particle size distribution

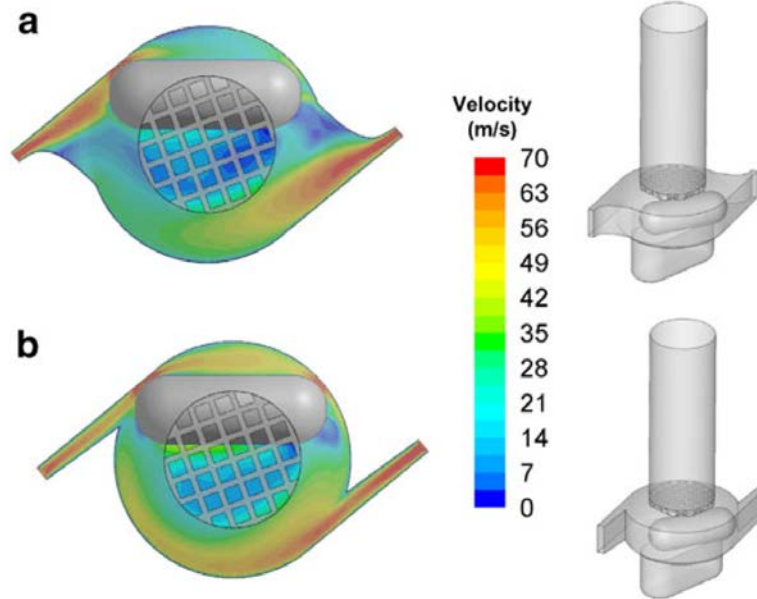


Computer aided design (CAD) representations of a) Handihaler<sup>®</sup> and b) Cyclohaler<sup>®</sup>. Fig.1 from Shur et al.<sup>2</sup>

# Velocity Comparison Following Device Modification

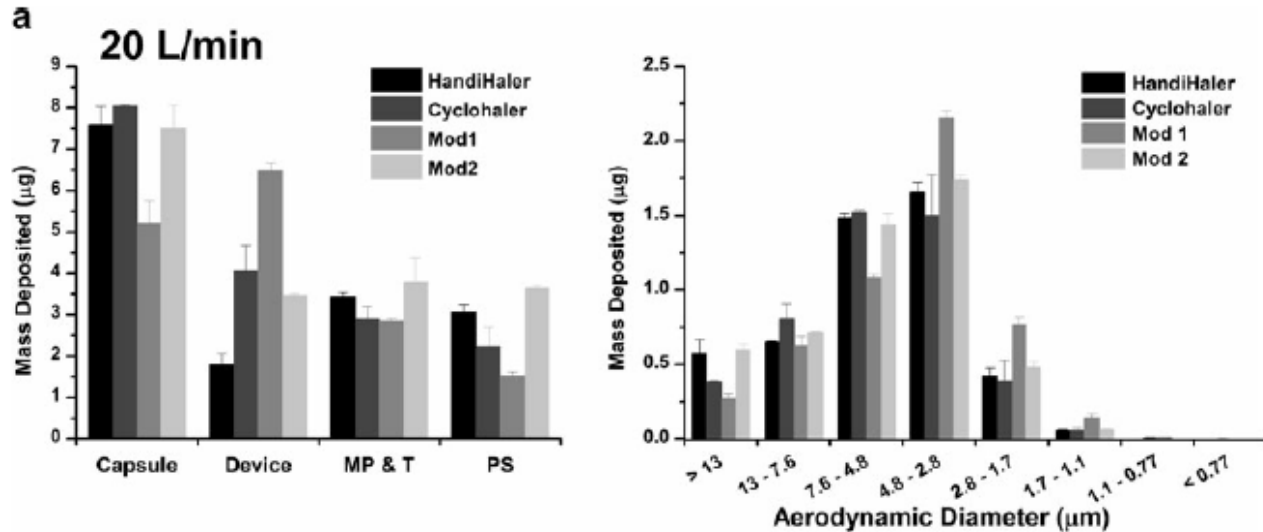


CFD Predictions in unmodified Cyclohaler<sup>®</sup> for a) device pressure, b) device velocity, and c) capsule pressure. (Fig 3. from Shur et al.<sup>2</sup>)



CFD predictions of Cyclohaler<sup>®</sup> device pressure in a) modification #1, and b) modification #2. (Fig. 4 from Shur et al.<sup>2</sup>)

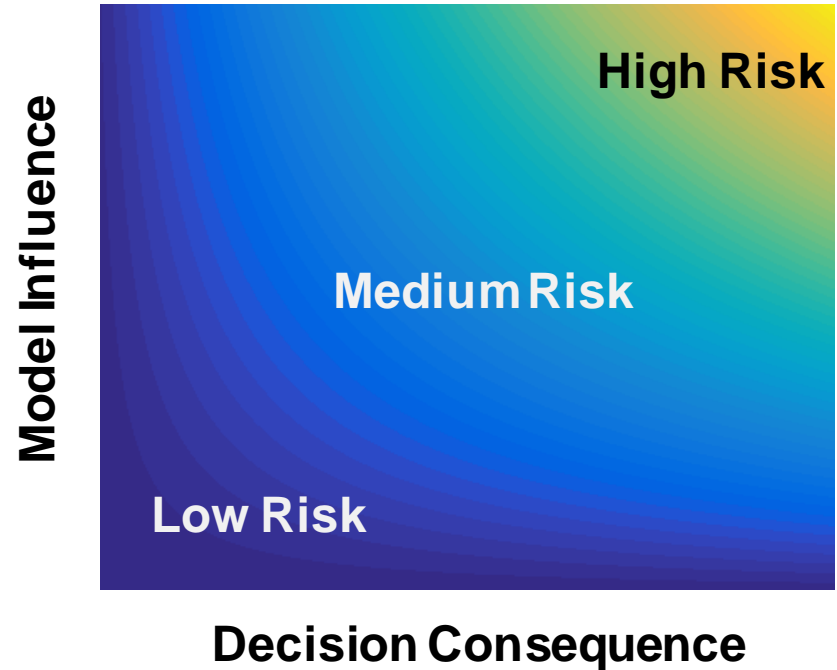
# In Vitro Particle Size Distribution Comparison



Stage measurements in Next Generation Impactor for Handihaler<sup>®</sup>, Cyclohaler<sup>®</sup>, and two modifications of Cyclohaler<sup>®</sup> for flow rate of 20 L/min. Abbreviations: mouthpiece (MP), throat (T), and preseparator (PS). (Fig. 6a from Shur et al.<sup>2</sup>)

# ASME V&V 40 Concepts

- American Society of Mechanical Engineers (ASME) Verification & Validation 40 standard<sup>3</sup>
- Context of Use: Describes what question the model addresses and to what extent
- Model Risk: Determined by decision consequence and model influence
- Credibility: Verification and Validation



(Figure from Walenga et al.<sup>4</sup>)

# Conclusions

- CFD is a modeling technique useful for understanding the effects of device differences on drug delivery from drug-device combination products.
- A case study with an orally inhaled drug product demonstrated that CFD-guided design may be used to alter device characteristics to more closely match in vitro properties.
- One suggested standard for assessing model credibility is ASME V&V 40.

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# References

1. Longest PW, Tian G, Walenga RL, Hindle M. Comparing MDI and DPI aerosol deposition using in vitro experiments and a new stochastic individual path (SIP) model of the conducting airways. *Pharmaceutical Research*. 2012;29(6):1670-88.
2. Shur J, Lee S, Adams W, Lionberger R, Tibbatts J, Price R. Effect of device design on the in vitro performance and comparability for capsule-based dry powder inhalers. *The AAPS journal*. 2012;14(4):667-76.
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4. Walenga RL, Babiskin AH, Zhao L. In silico methods for development of generic drug–device combination orally inhaled drug products. *CPT: Pharmacometrics & Systems Pharmacology*. 2019;8(6):359-70.