

Comparison of different anatomical throats vs The USP throat

***Addressing the need
for in-vitro, in-vivo
understanding***

Samantha Holmes

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Introduction – inhalation drug development challenges



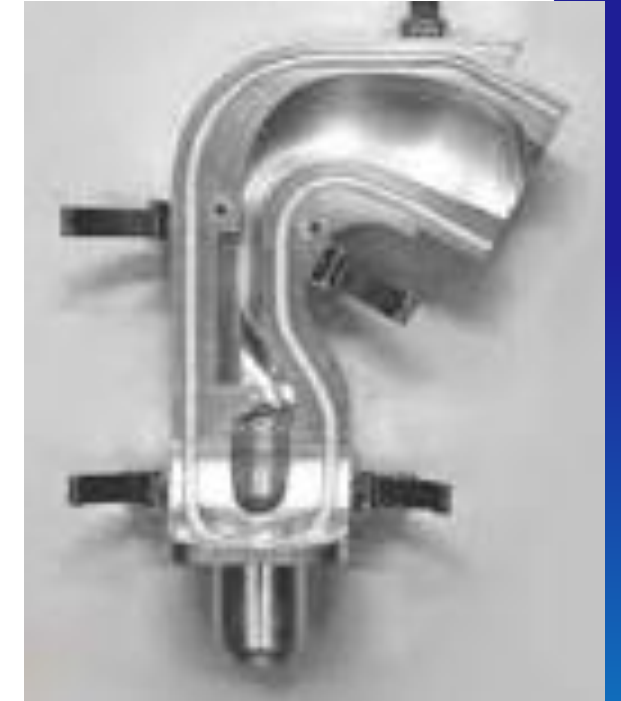
- ▶ Particle sizing is a critical parameter
- ▶ Often utilised to aid in-vitro, in-vivo understanding



- ▶ Regulatory and industry standard USP induction port (or throat) designed for quality control purposes
- ▶ Robust design

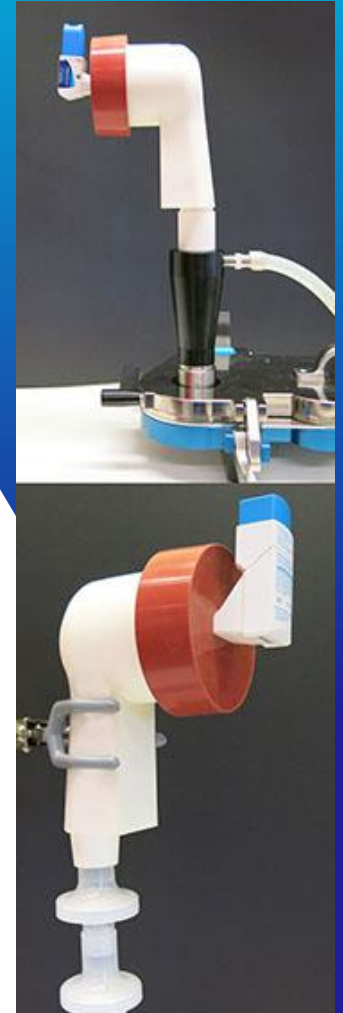
Evolution of the throat model

- ▶ Copley Scientific Alberta Idealised Throat launched in 2010
- ▶ Collaboration with University of Alberta, Canada
- ▶ Potential alternative to USP induction port
- ▶ More closely represents aerodynamic conditions in human throat
- ▶ Robust design



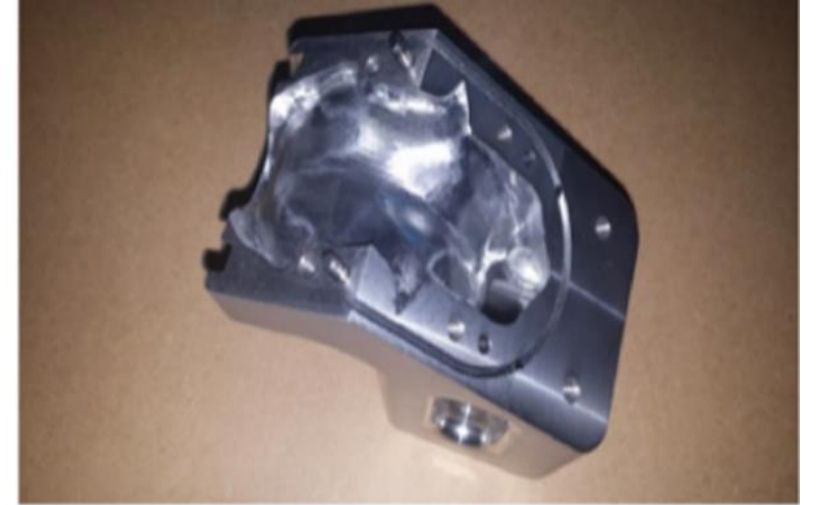
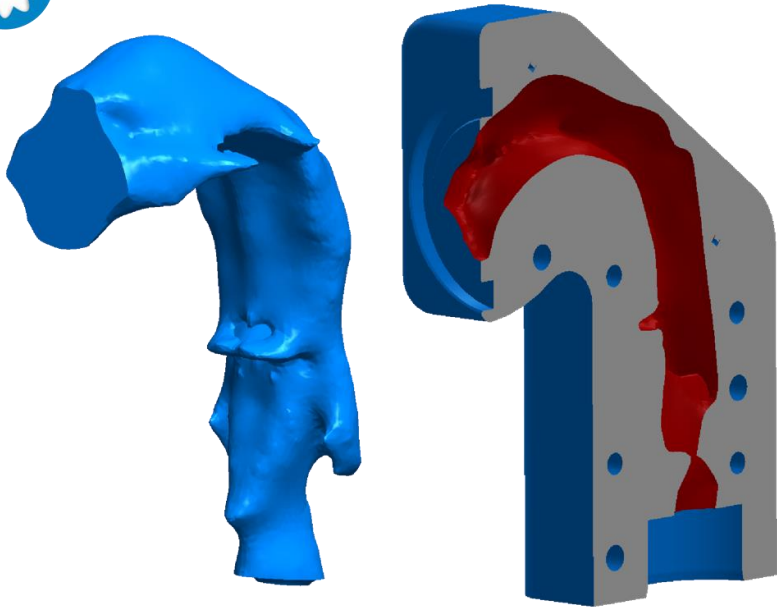
Emmace anatomical throat model

- ▶ Developed by a consortium consisting of AstraZeneca, GlaxoSmithKline and Sanofi Aventis
- ▶ The geometry of the models originates from MRI studies
- ▶ Available in three sizes small, medium and large
- ▶ These throat models are manufactured by Emmace Consulting



Nanopharm anatomical throat model

- ▶ Developed by Nanopharm Ltd
- ▶ Proprietary tool
- ▶ Based on MRI scan data from the OPC consortium



Study overview

Products

- ▶ Tiotropium pMDI Solution Formulation
- ▶ Respimat SoftMist™ Inhaler (RLD)

Variables

- ▶ Throat Model
- ▶ pMDI actuator exit orifice diameter

Test locations

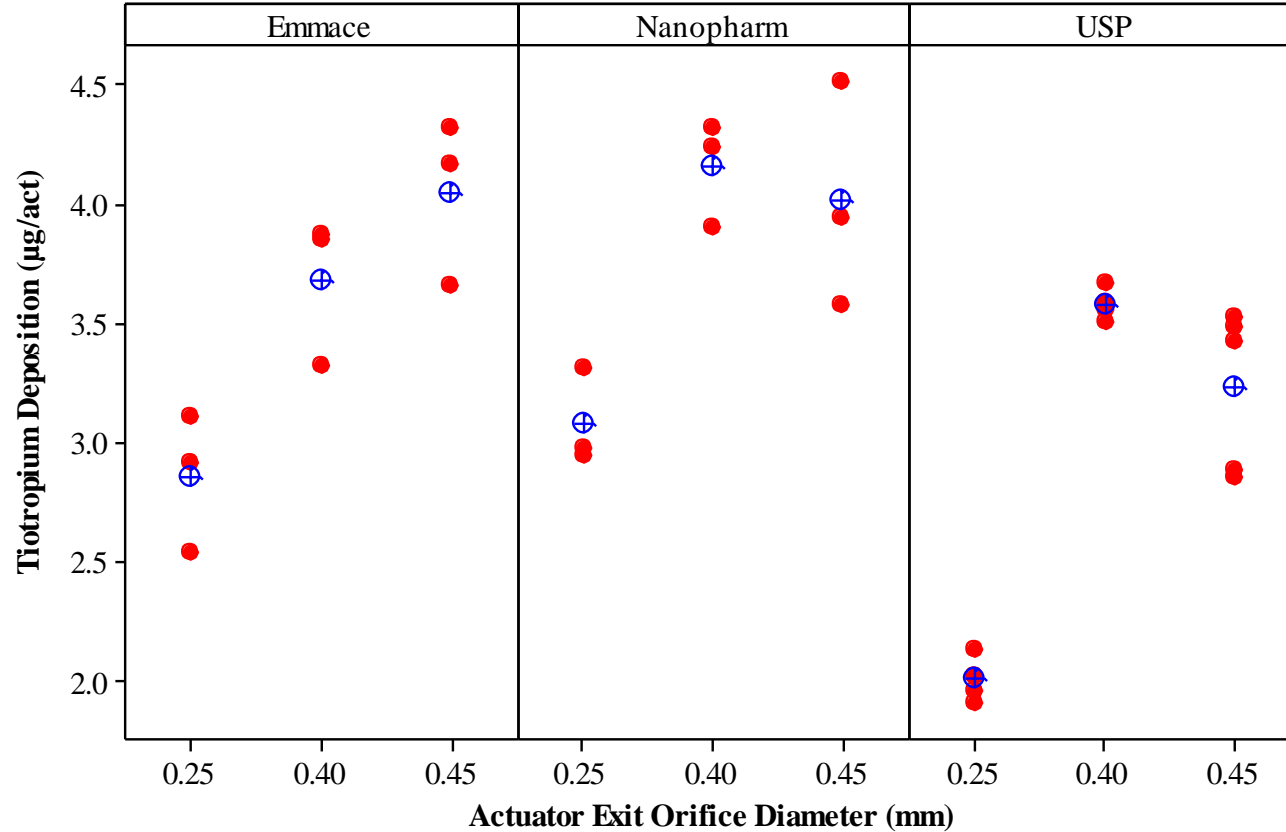
- ▶ Nanopharm – Newport, Wales
 - USP and Nanopharm Anatomical Throat
- ▶ 3M – Loughborough, UK
 - USP and Emmace Anatomical Throat

Test methodology

- ▶ NGI Impactor
- ▶ 30 L/min flow rate

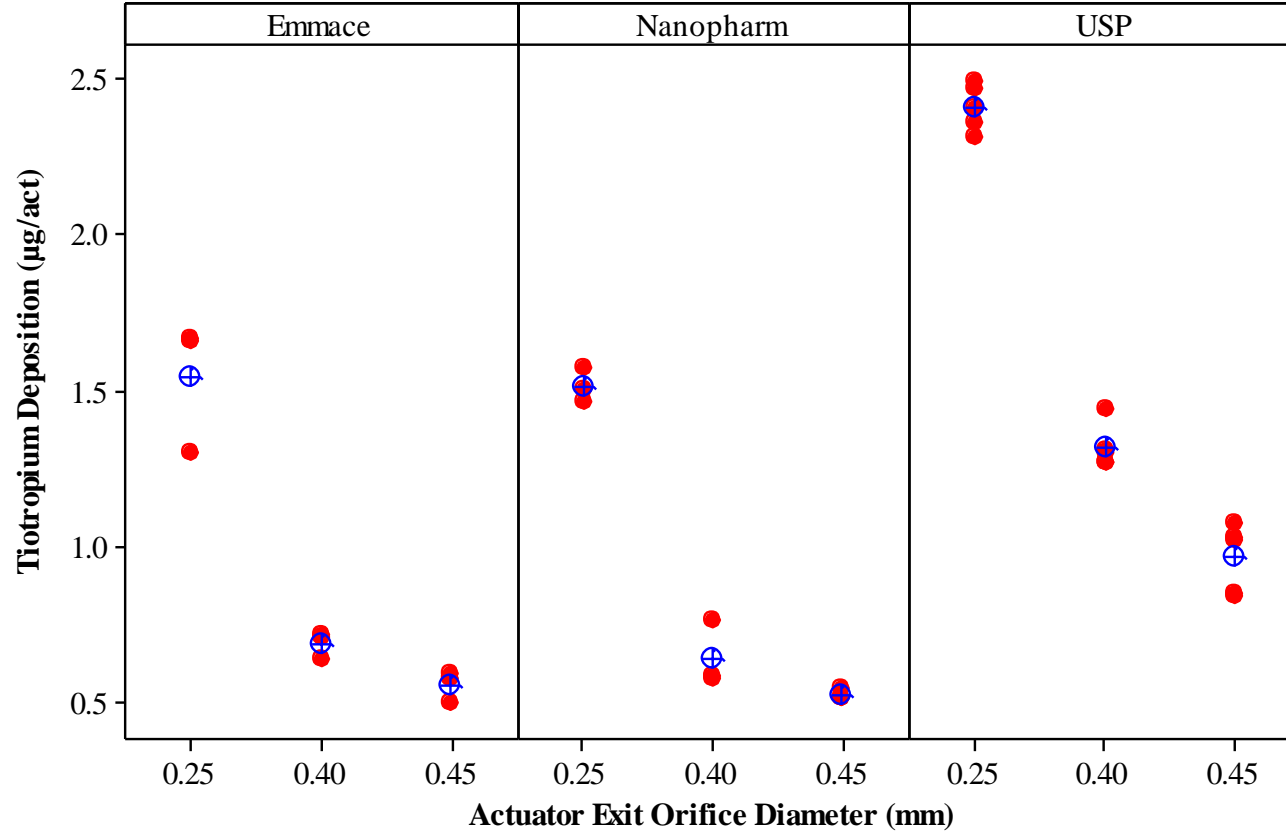


Comparison of throat deposition



Comparable throat deposition observed for anatomical throats
Anatomical throat deposition is higher than USP throat deposition

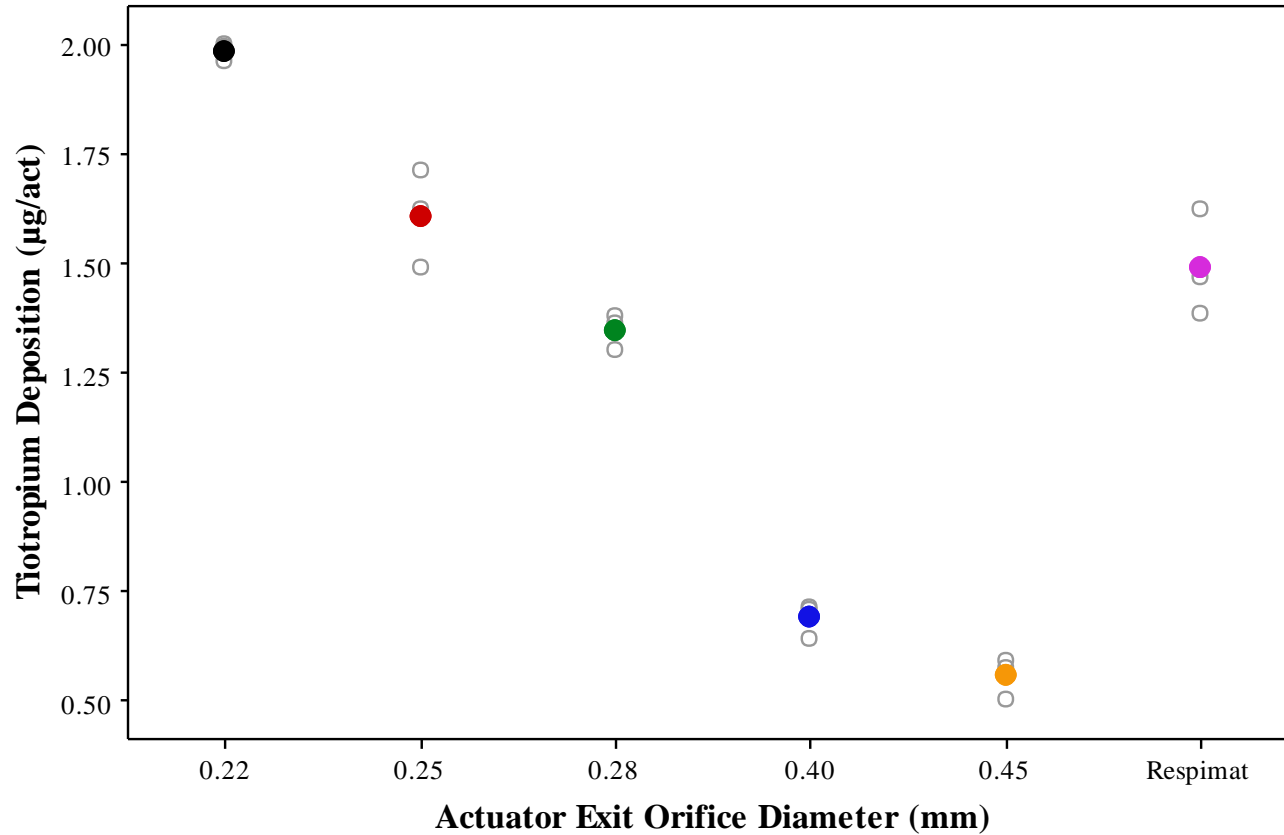
Fine particle mass (< 5 μ m)



Comparable FPM observed for anatomical throats
Anatomical throat FPM is lower than USP

Anatomical throat as a screening tool

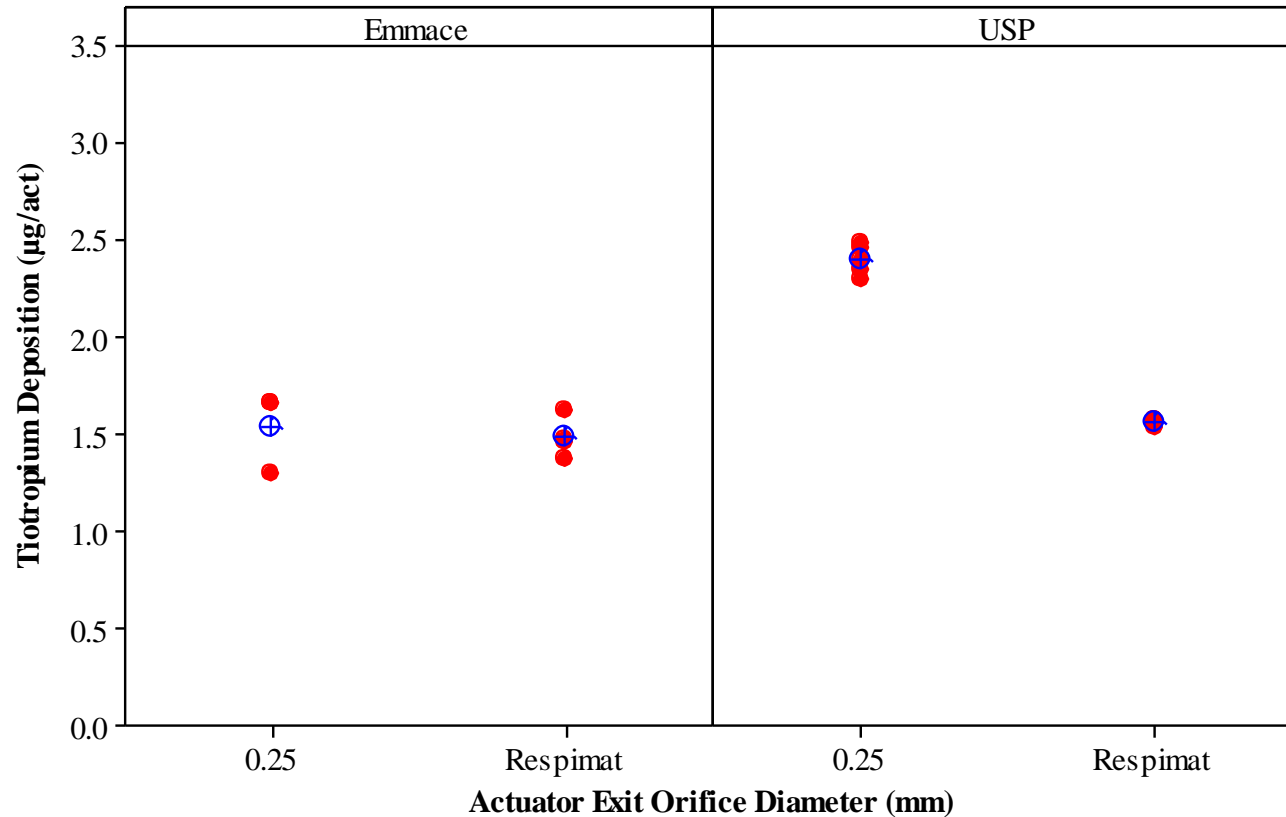
Fine particle mass (< 5µm)



pMDI configuration can be optimised to match a non-pMDI RLD in-vitro

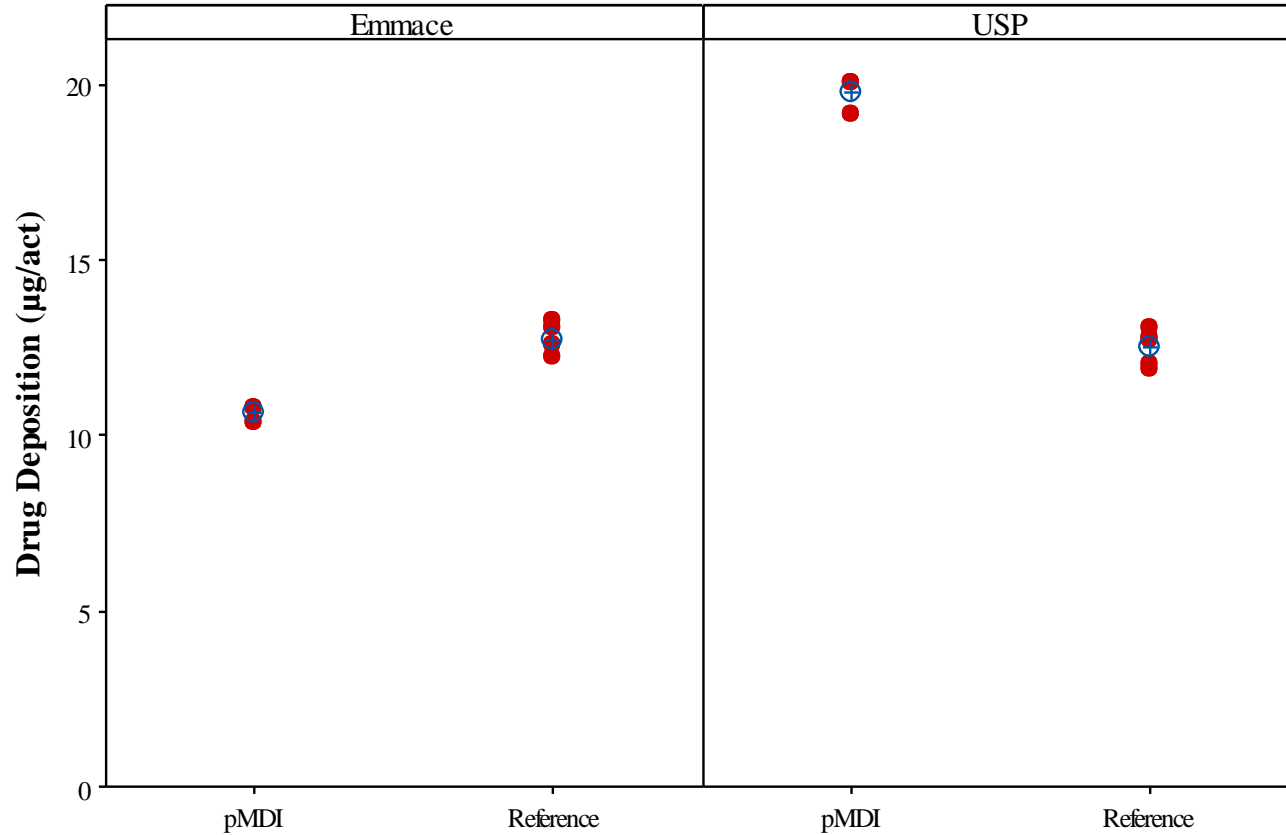
However...

Fine particle mass (< 5 μ m)



USP throat would predict a higher lung dose compared to anatomical throat

Suspension Product FPM using Emmace



Comparable effect on FPM observed for suspension formulations with anatomical throat

Conclusions

- ▶ Comparable throat deposition observed for Emmace and Nanopharm anatomical throat models
- ▶ Anatomical throat deposition is higher than USP throat deposition

- ▶ Comparable FPM observed for Emmace and Nanopharm anatomical throat models
- ▶ Anatomical throat FPM is lower than USP

- ▶ pMDI configuration can be optimised to match RLD in-vitro
- ▶ USP throat would predict a higher lung dose compared to anatomical throat

Future work



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Acknowledgements

- ▶ Nanopharm Ltd
- ▶ Copley Scientific
- ▶ Emmace Consulting