Digital Twin of Pharmaceutical Spray Drying Process for Production of Inhaled Therapeutics

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1. Motivation

Value Statement:

As of 2019, COPD affects approximately 12.5 million Americans and asthma affects about 27.5 million Americans [1]. The most effective way to treat COPD and asthma is through local drug delivery to the airways. Spray drying allows for precise control over particle size, density, surface energy rugosity, porosity, and microstructure while also allowing production of particles with the desired dose ratio of precursor components [2]. Spray drying is the most efficient way to engineer particles for inhaled therapeutics.

Application of Spray Drying for Inhalation Products:

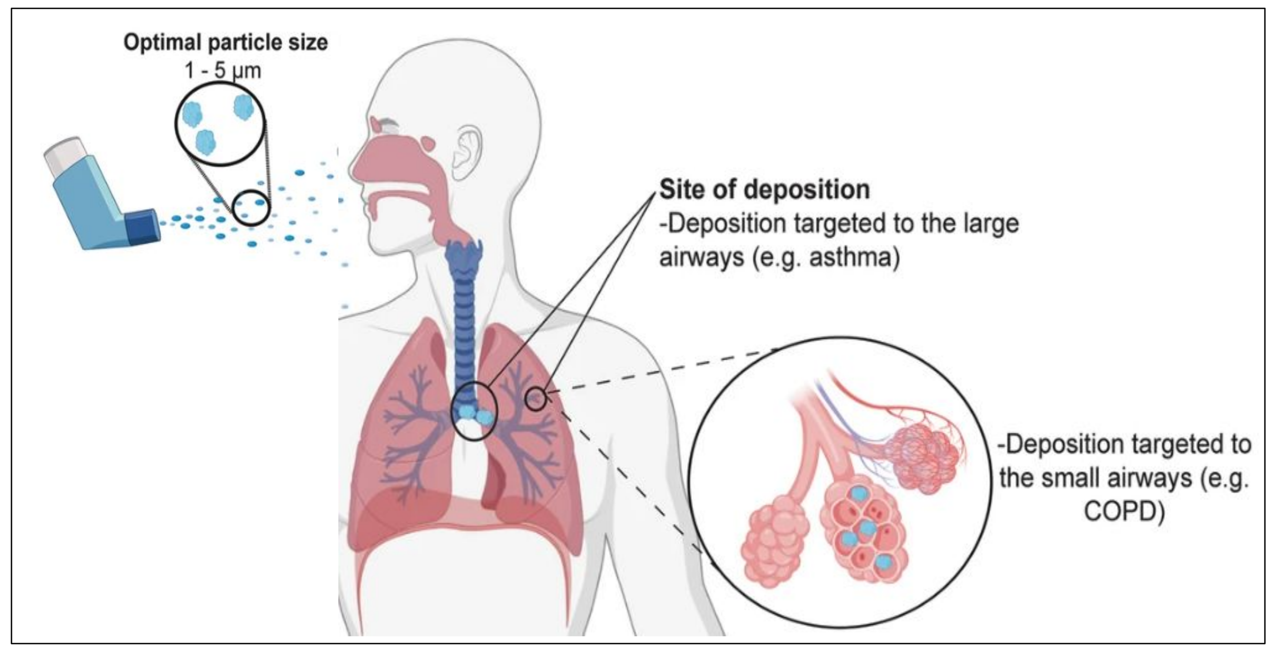


Figure 1: Depicts particle deposition in the lungs [3].

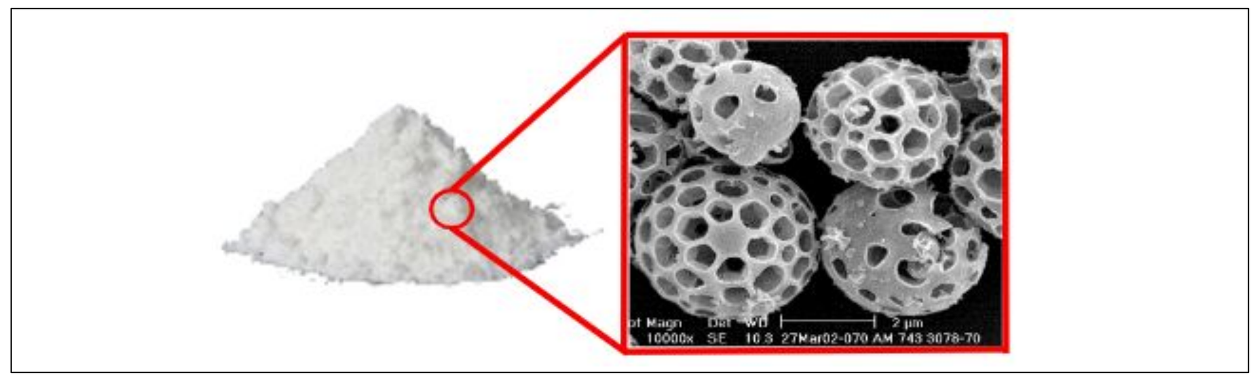
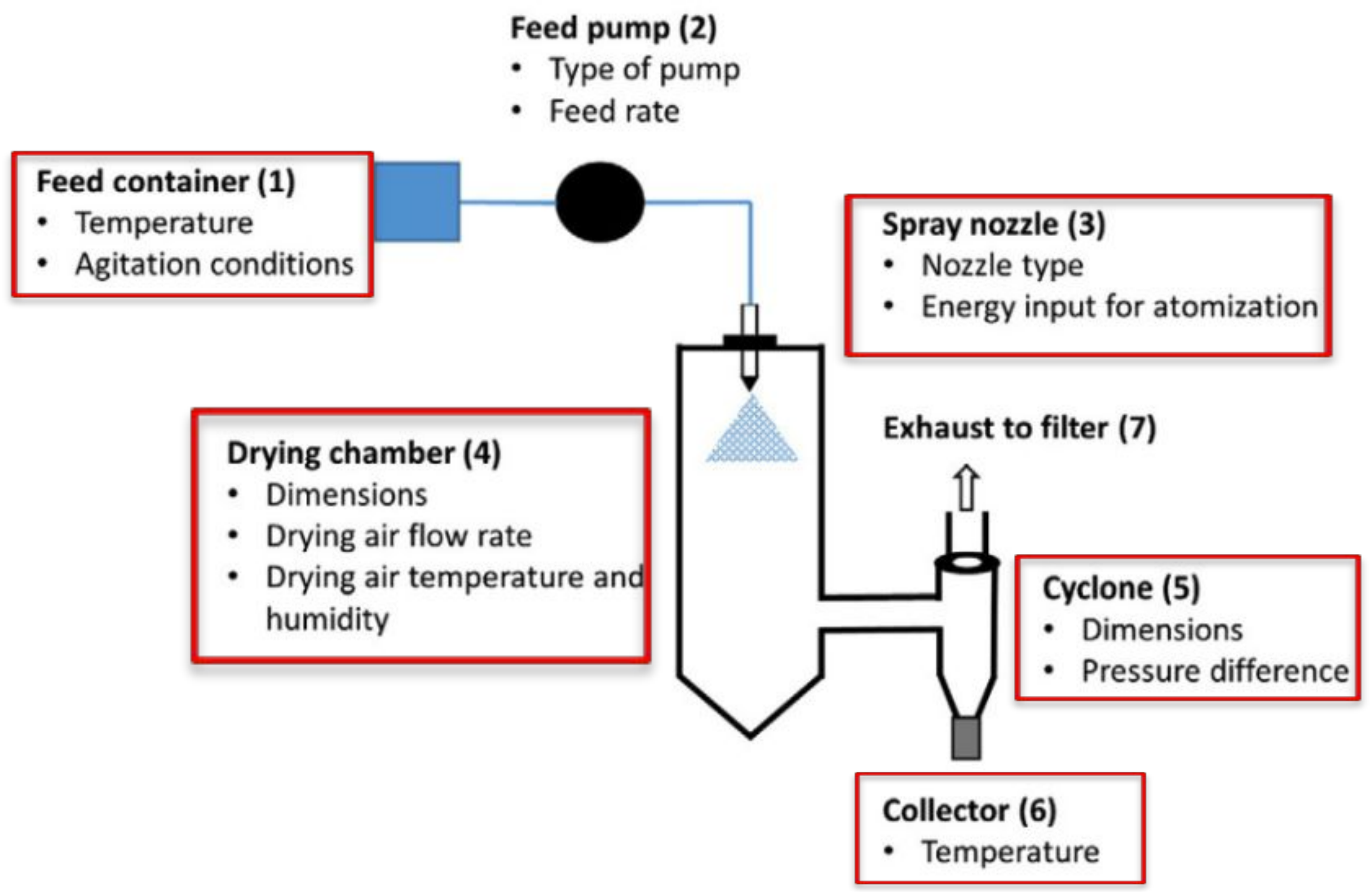


Figure 2: An example of an inhalation product with porous particle morphology [4].

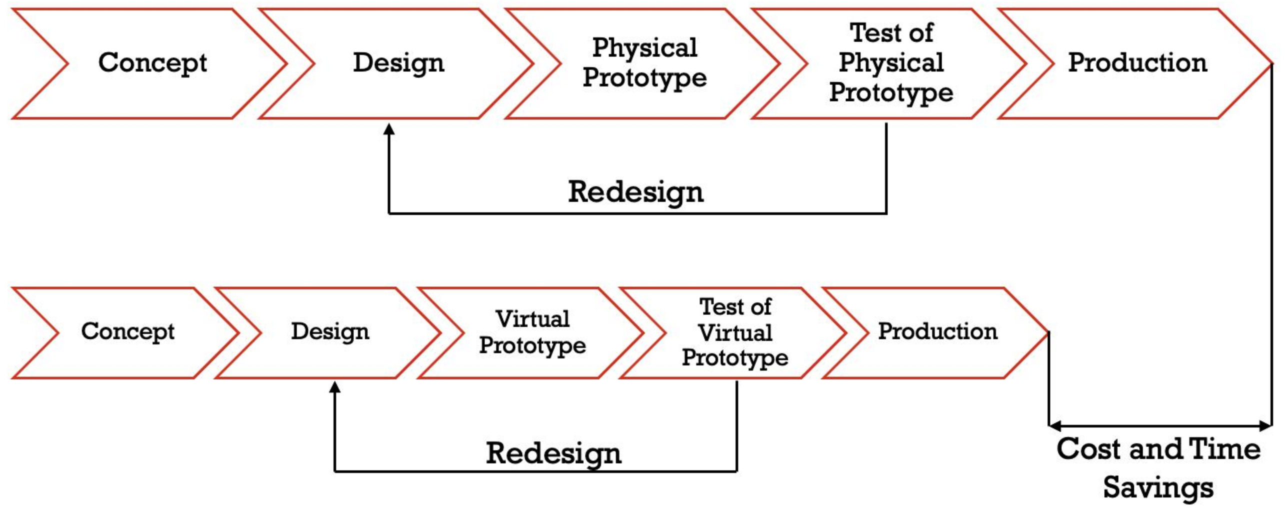
5 Main Process Components:

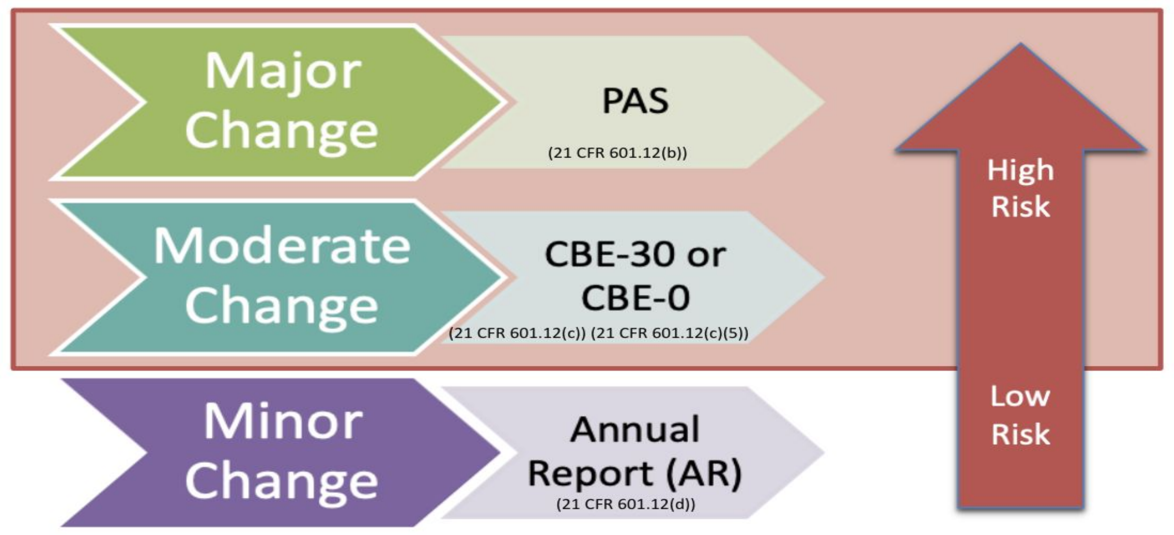


2. Process Modeling and Benefits

Our process model functions as a digital twin to the physical spray drying process and provides:

- An updated model in modern software
- Increased Efficiency of Troubleshooting
- Reduction in Development Costs
- Ability to Leverage Simulated Data in Regulatory Submissions

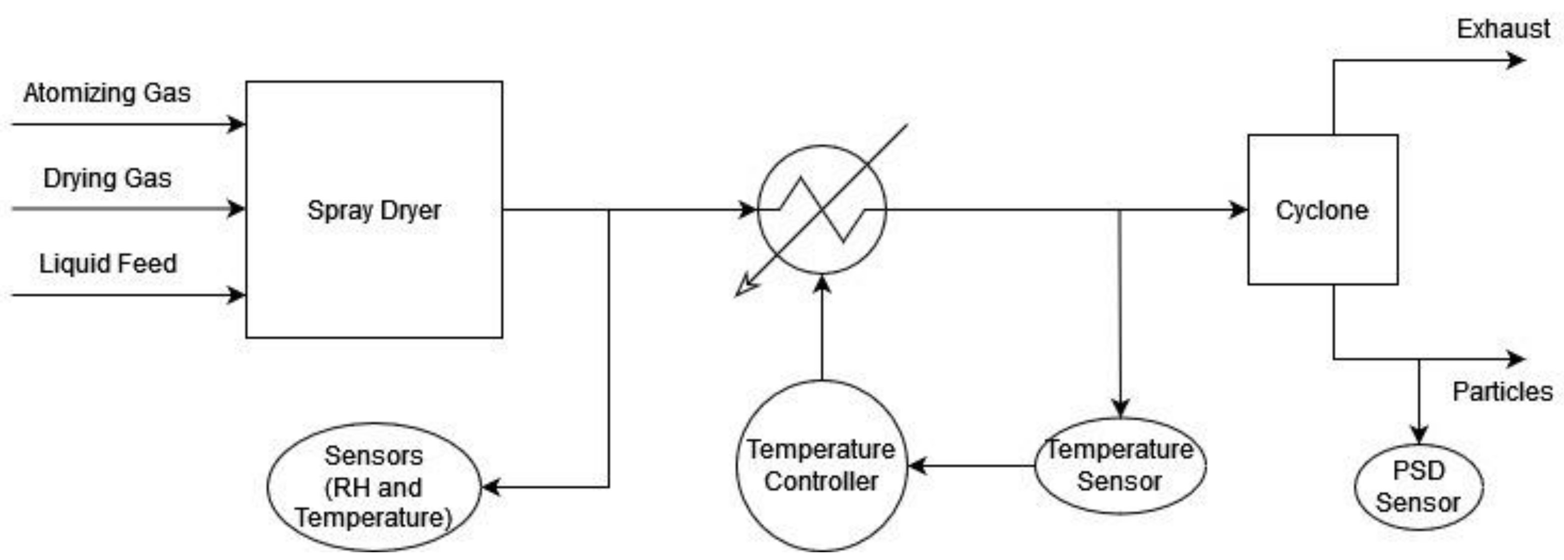




Goals of our Process Model:

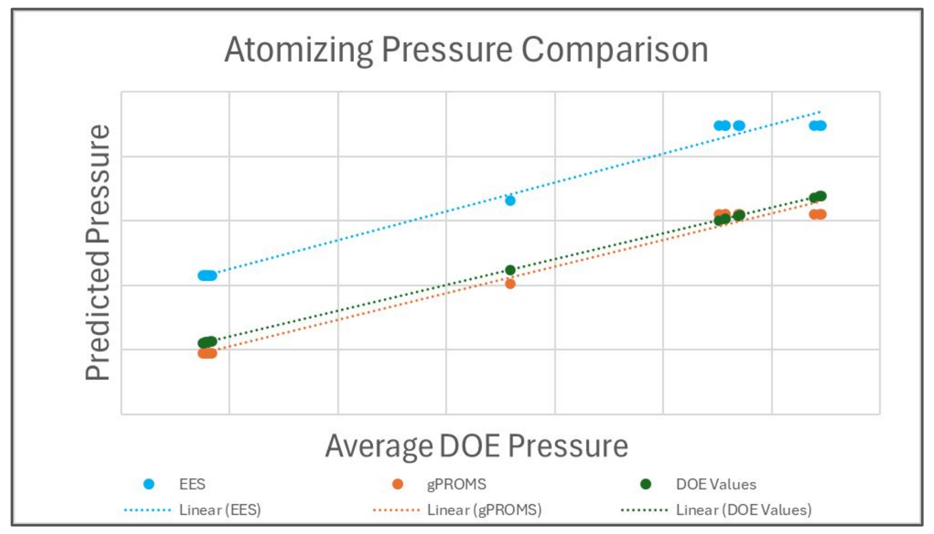
- To **predict steady state output values** given various input conditions.
- Model Inputs:
  - Liquid feedstock flow rate
  - Drying gas flow rate
  - Drying gas temperature
  - Atomizing gas flow rate
- Model Outputs:
  - Dryer temperature and relative humidity
  - Particle size distribution
  - Final particle moisture content

3. gPROMS Spray Drying Model

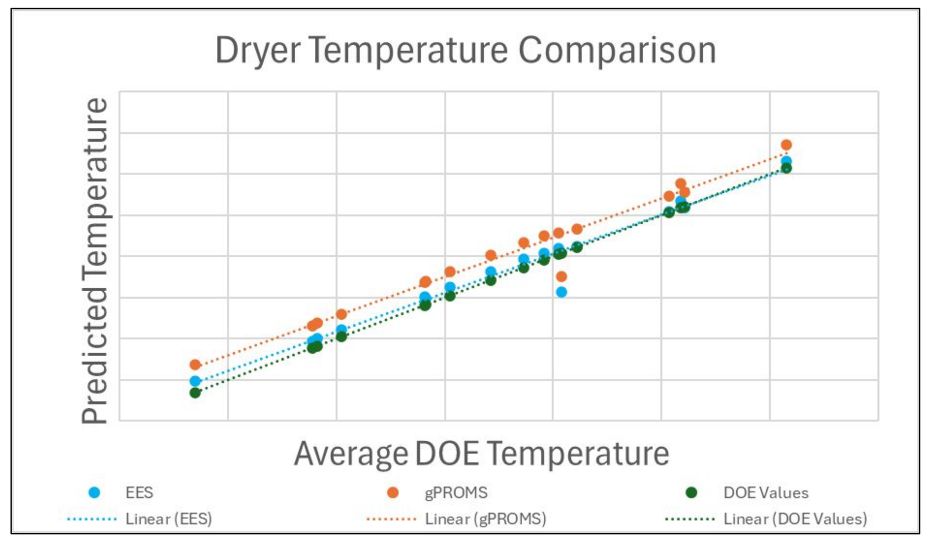


4. Model Validation

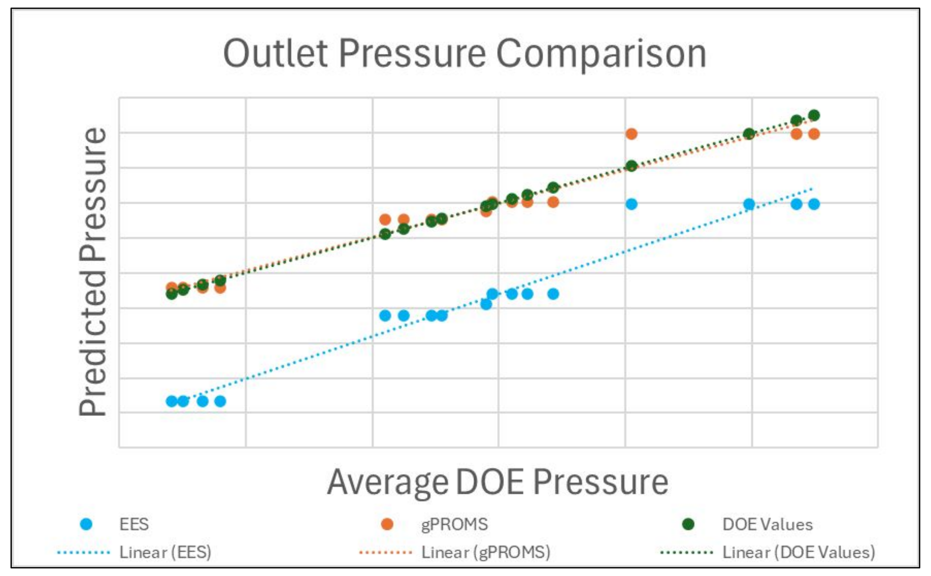
Validation was completed by comparing the team's process model to large-scale experimental data from water run DOE and to the previous version of the process model.



Average Percent Difference:
- Old Model: 9.56%
- Our Model: 1.28%



Average Percent Difference:
- Old Model: 0.51%
- Our Model: 1.38%



Average Percent Difference:
- Old Model: 7.46%
- Our Model: 0.66%

5. Next Steps/Future Directions

1. Incorporate ability to model a multi liquid feed to the spray dryer
2. Validate with formulation data

6. Acknowledgements

Thanks to Jeremy Saunders, Patrick Teung, David Lechuga, and Kassidy Wallace for their dedication and support on this project. And a special thanks to Astrid and Duy for their continued support with gPROMS modelling.

References

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[2] Lechuga-Ballesteros, D., Noga, B., Vehring, R., Cummings, R. H., & Dwivedi, S. K. (2011). Novel cosuspension metered-dose inhalers for the combination therapy of chronic obstructive pulmonary disease and asthma. *Future Medicinal Chemistry*, *3*(13), 1703–1718. https://doi.org/10.4155/fmc.11.133
[3] Matthews, A. A., Ee, P. L. R., & Ge, R. (2020, October 30). *Developing inhaled protein therapeutics for lung diseases - molecular biomedicine*. SpringerLink. https://link.springer.com/article/10.1186/s43556-020-00014-z/figures/1
[4] Lechuga, D. (n.d.). *Porous Particle SEM*.