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# *Measuring the Agglomerate State of Dry Powder Aerosols for Pulmonary Drug Delivery*

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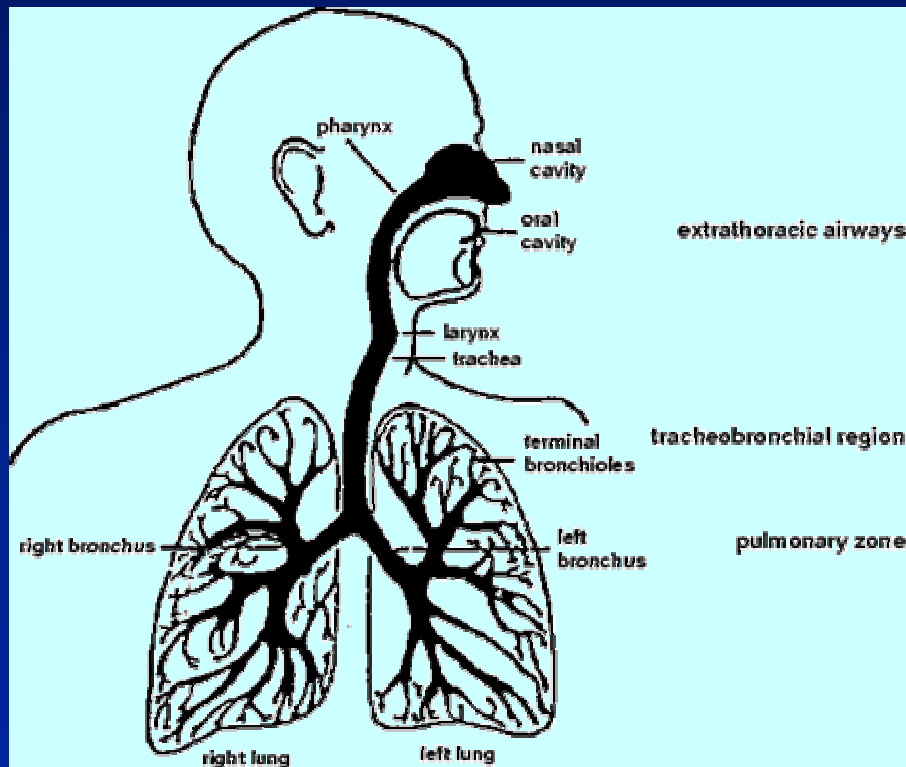
# Outline

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- **Introduction: Pulmonary delivery of pharmaceutical particles**
- **Aerosol particle agglomerates**
- **Agglomerate measurement apparatus**
- **Agglomerate state of model particle aerosols**
- **Measurements of pharmaceutically relevant particles**

# Goal: Pulmonary Delivery

- Non-invasive delivery of macromolecules to the deep lung via inhalation of aerosolized drug

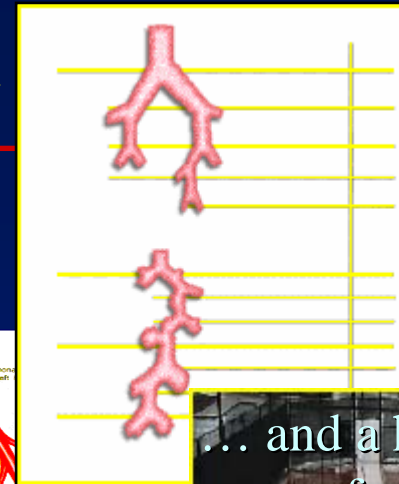


*...in addition to the classic application of treating locally.*

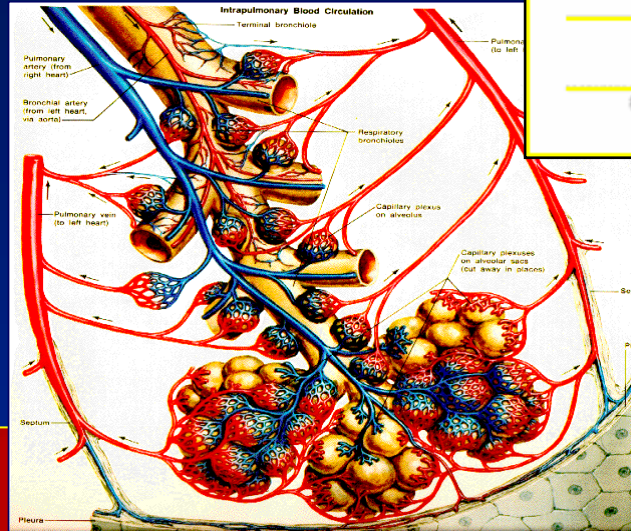
- Asthma
- COPD, CF
- Infections

# Delivery to the deep lung

... a tight contact with vasculature ...

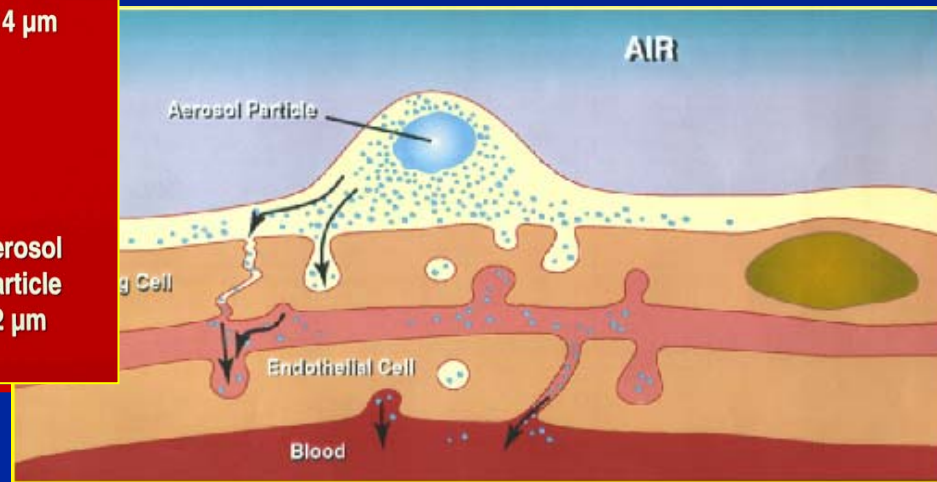
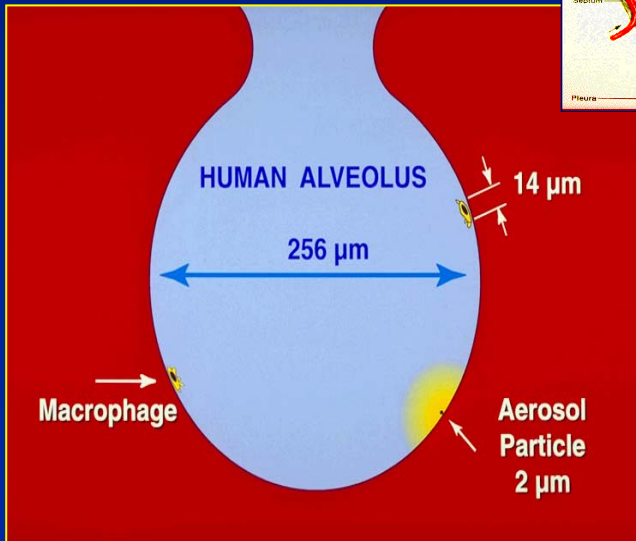


A branching structure leading to ...



... and a huge transport surface.

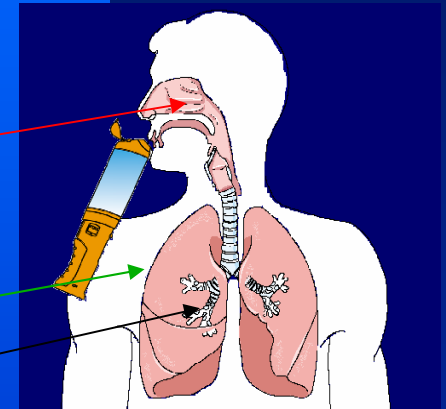
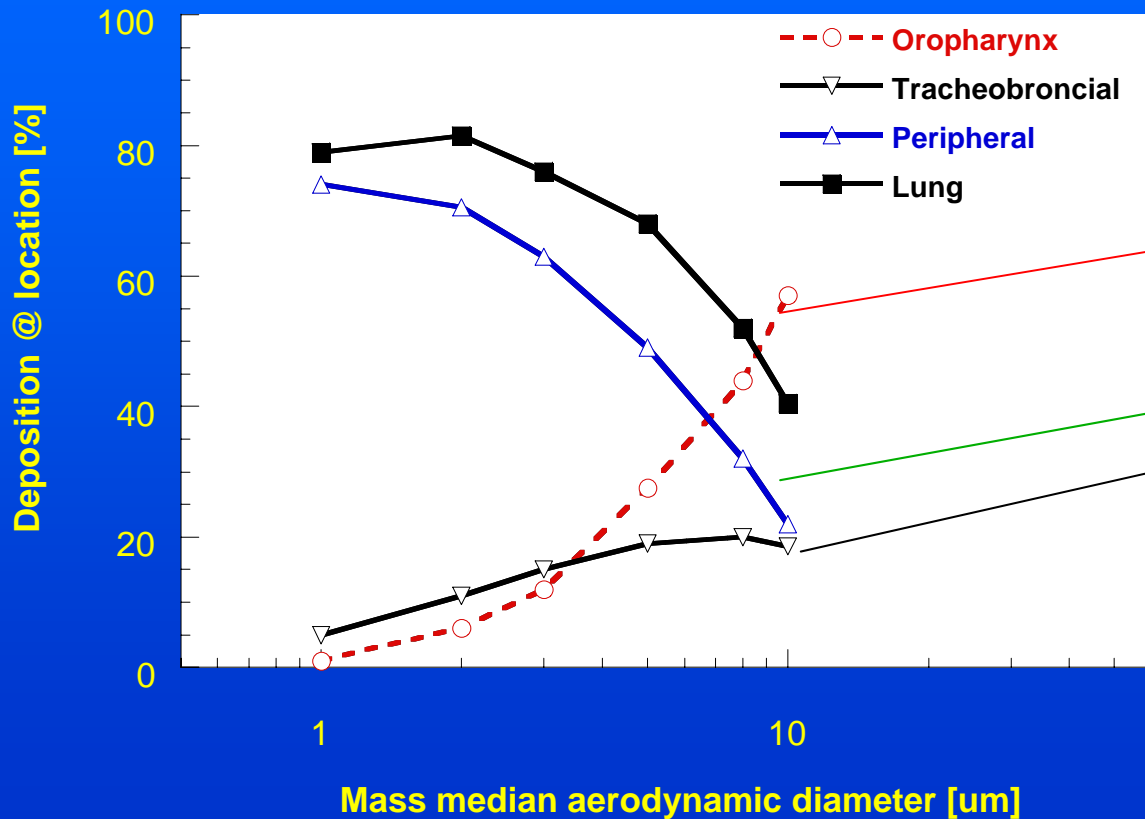
Deep lung deposition ...



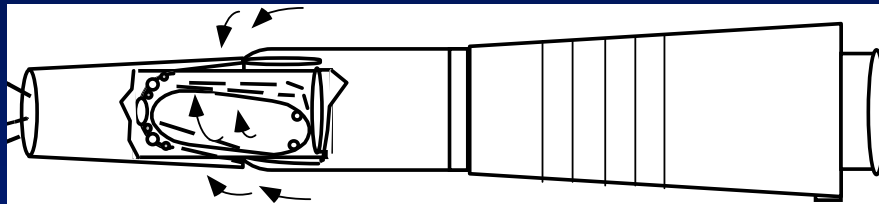
... leads to effective transport into the bloodstream

# Lung Deposition for Polydispersed Aerosols

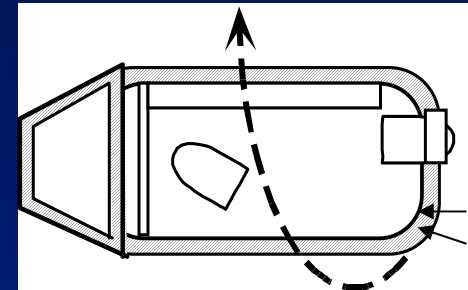
Inhaled volume 4 l  
Inhaled flow rate 30 l/min  
Breath hold 10secs  
GSD 2.2



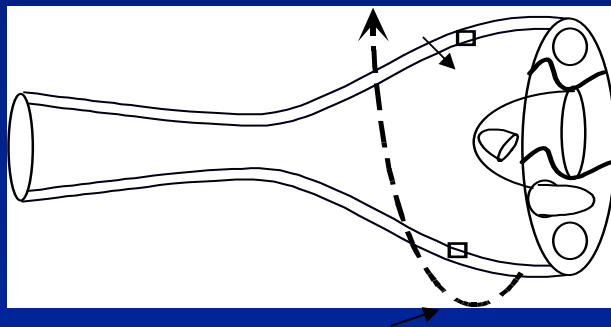
# Dry Powder Inhalers (DPIs)



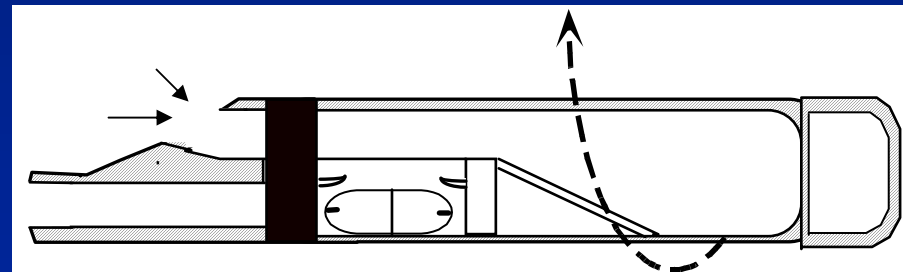
**T-326 (TURBOSPIN®)**  
(PHT, Inhale)



**ROTAHALER®**  
(Glaxo Smith Kline)

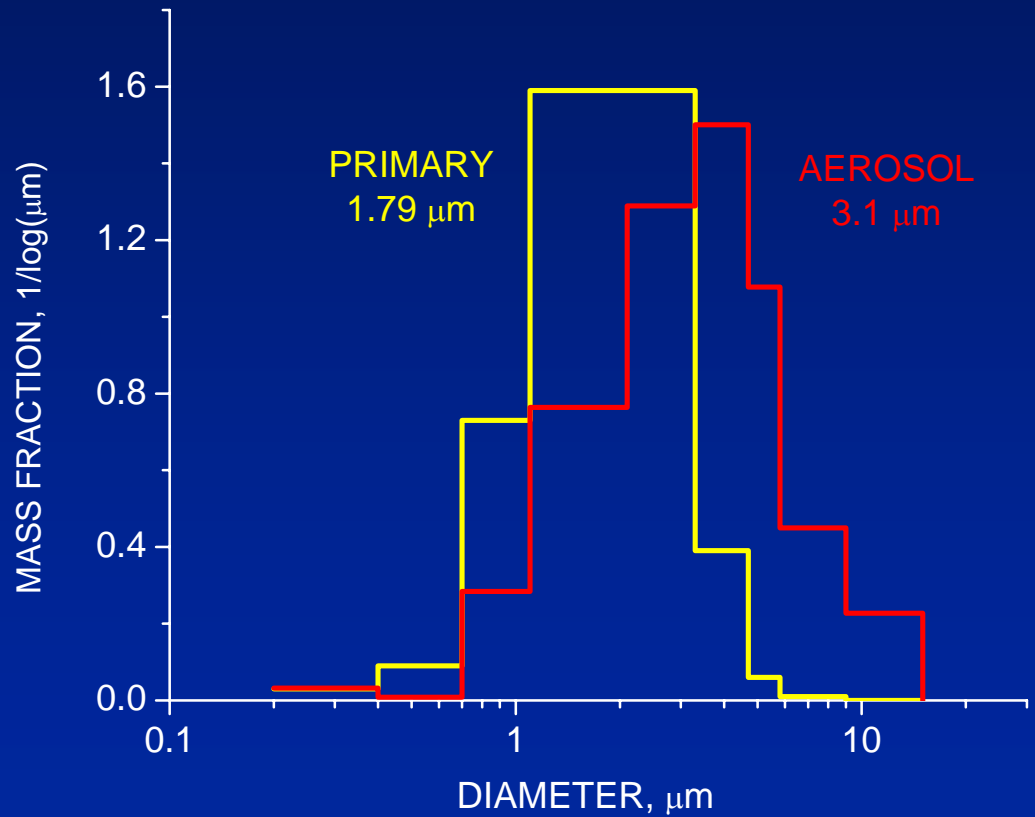
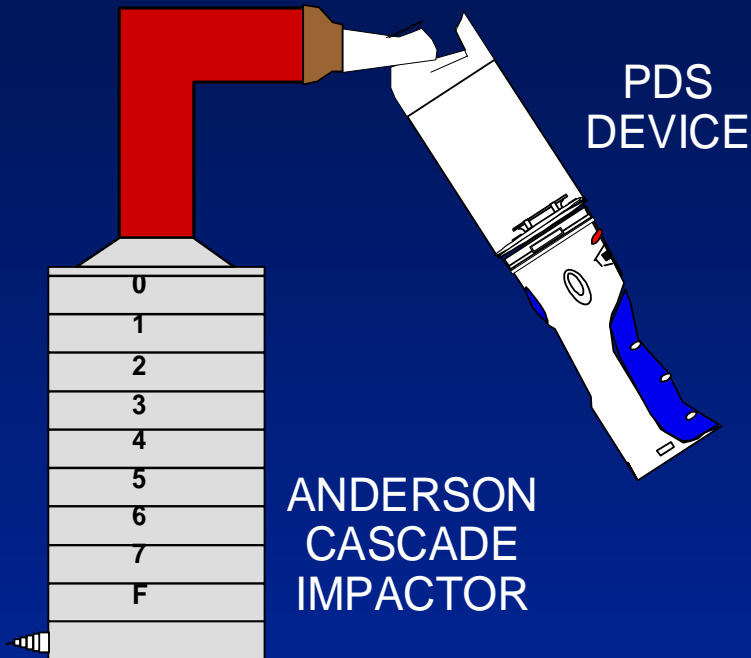


**ECLIPSE®**  
(Aventis Pharma)

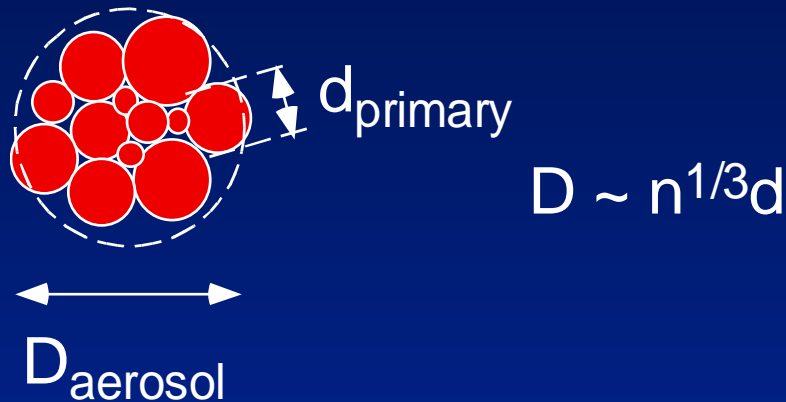


**FLOW CAPS®**  
(Hovione)

# Particle Size Distribution from a DPI



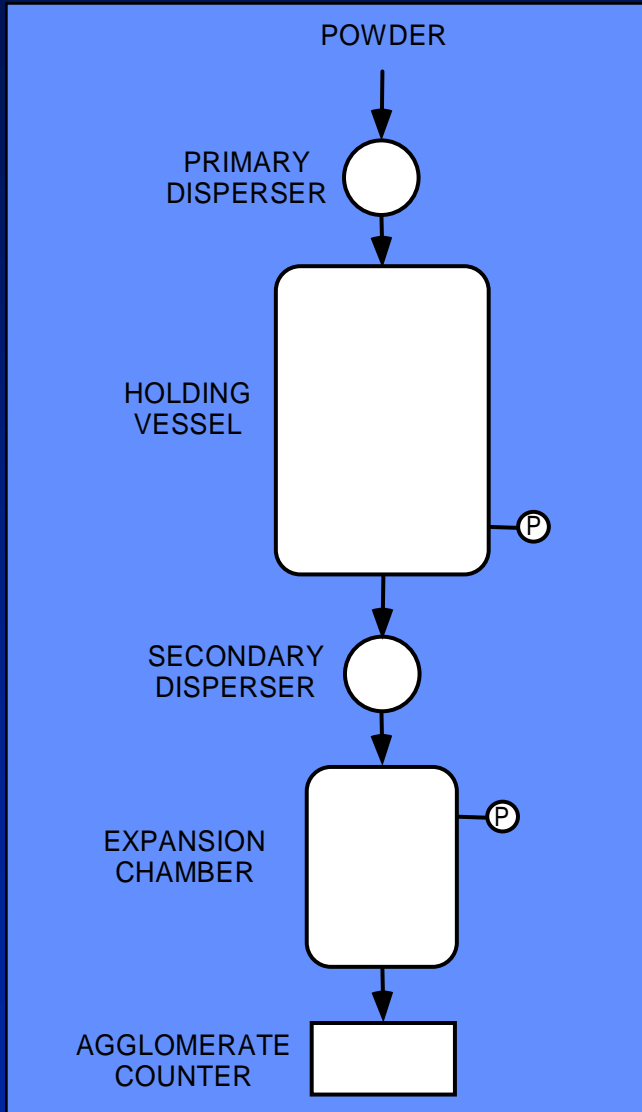
# Agglomerates in the dispersed aerosol



- Design particles that deagglomerate at the energies available in DPIs
- Measure agglomeration state of aerosols as a rapid formulation and process screening test

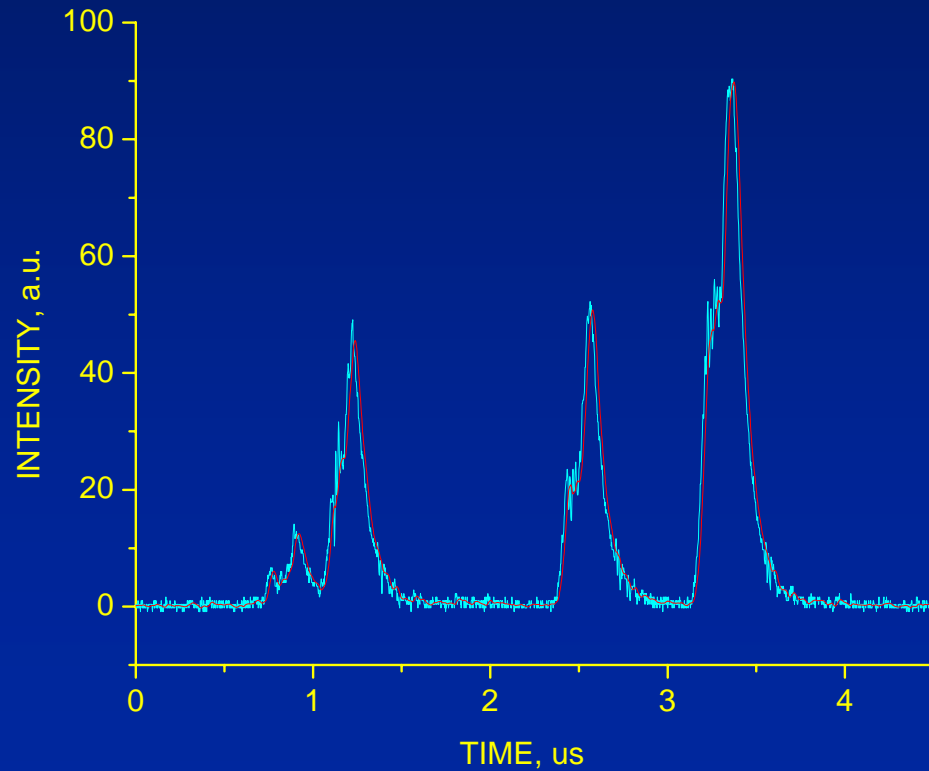
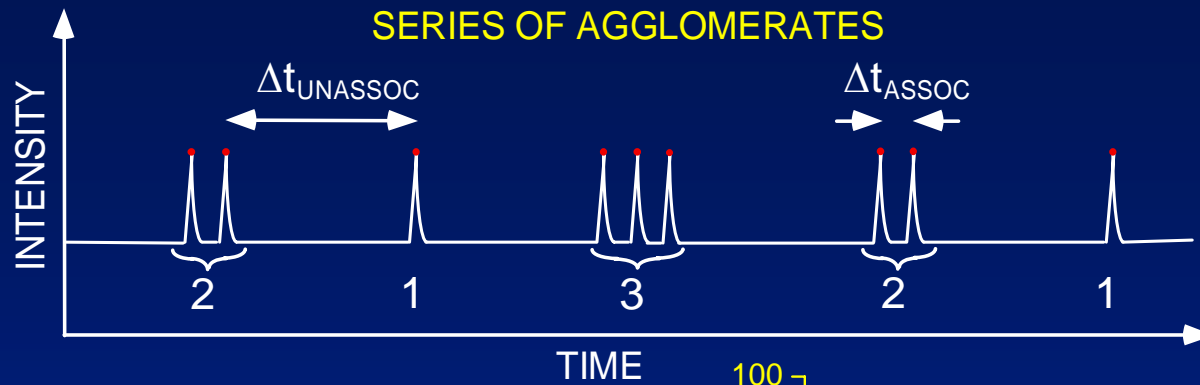


# Agglomerated Aerosol Test Apparatus

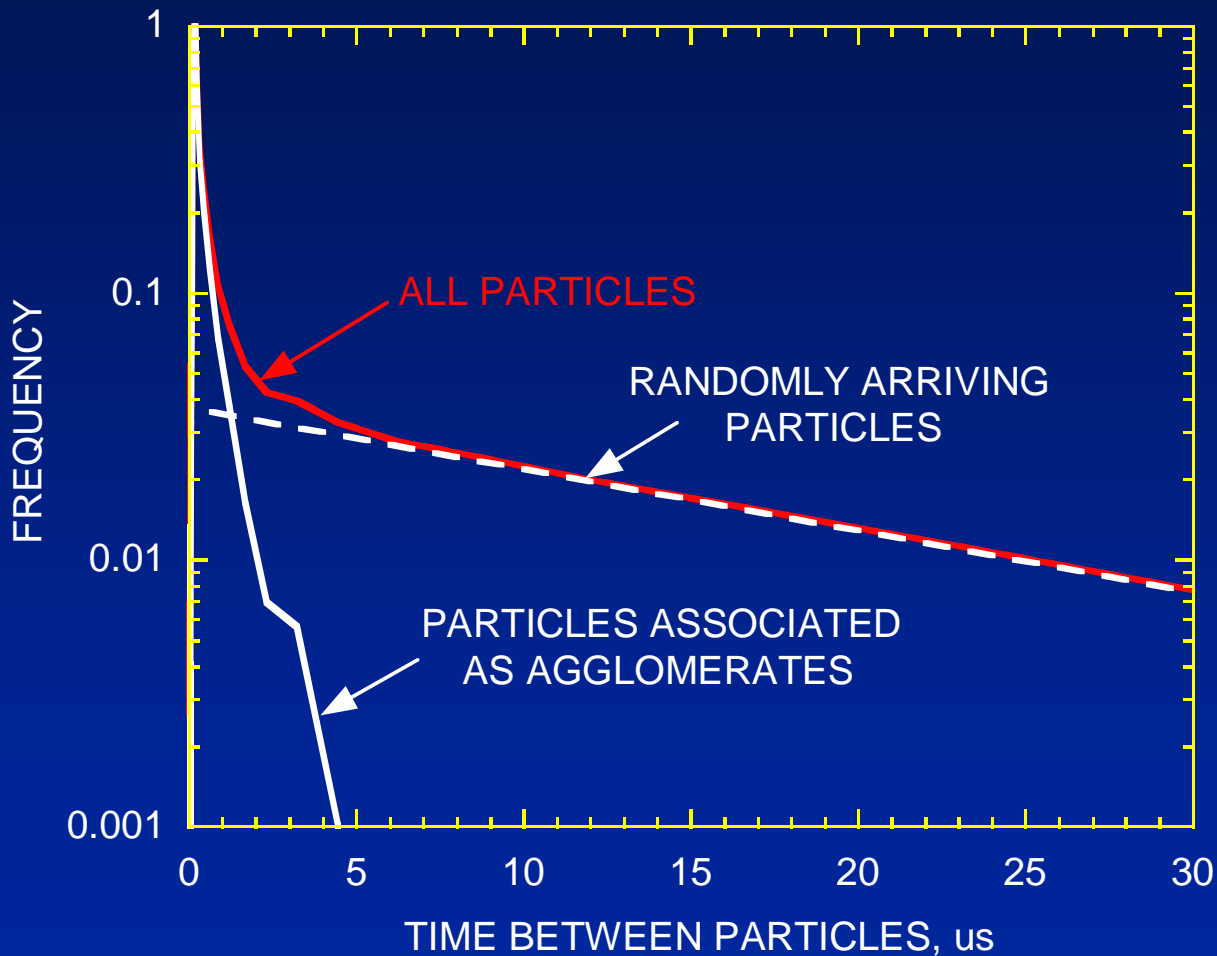


- Powder-based measurements
- DPI independent
- Primary dispersion:  
Consolidated powder into aerosol
- Secondary dispersion:  
Agglomerated aerosol into deagglomerated aerosol
- Agglomerate state
- Primary particle size

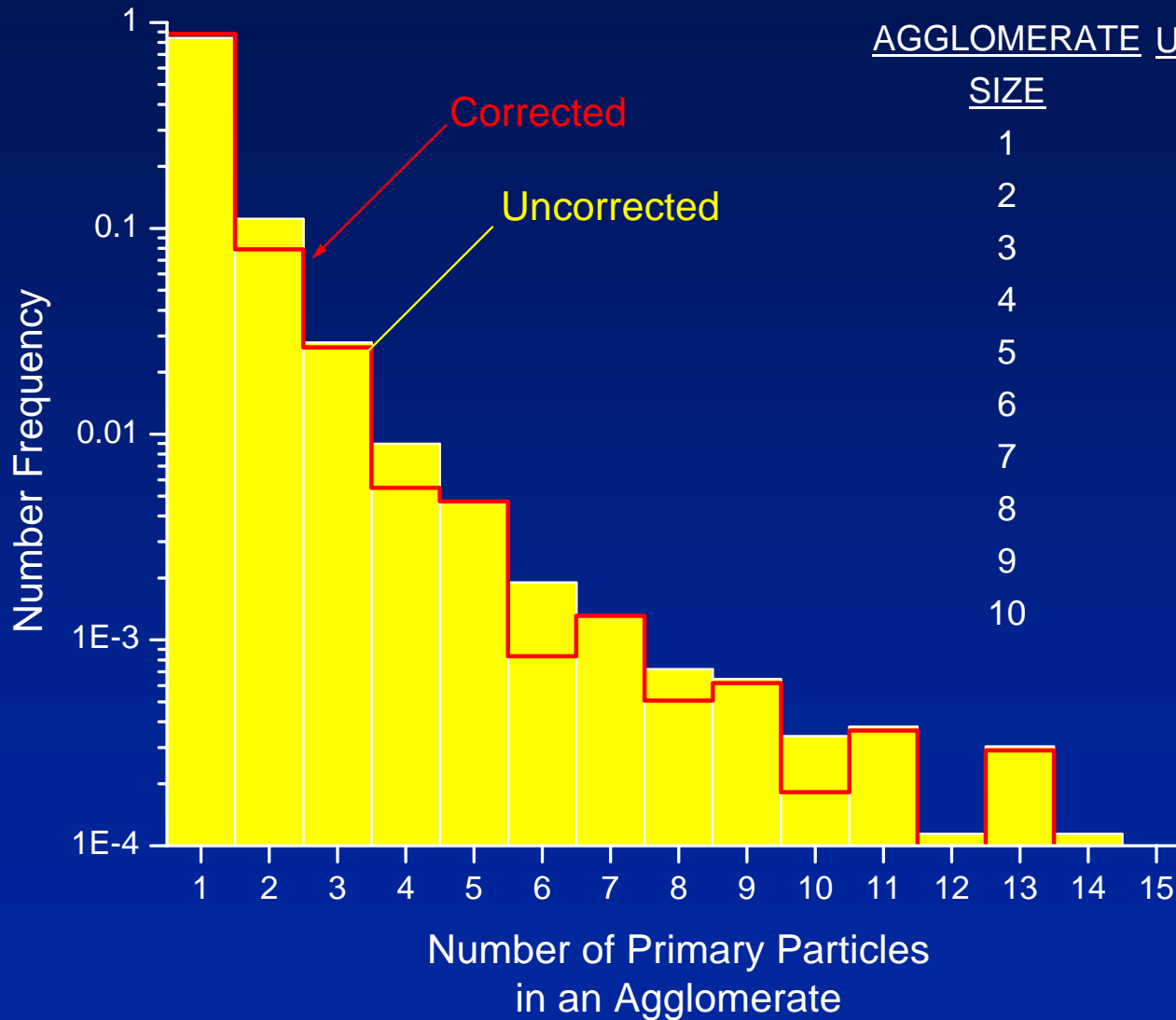
# Agglomerate Counter



# Statistical Evidence of Agglomerates

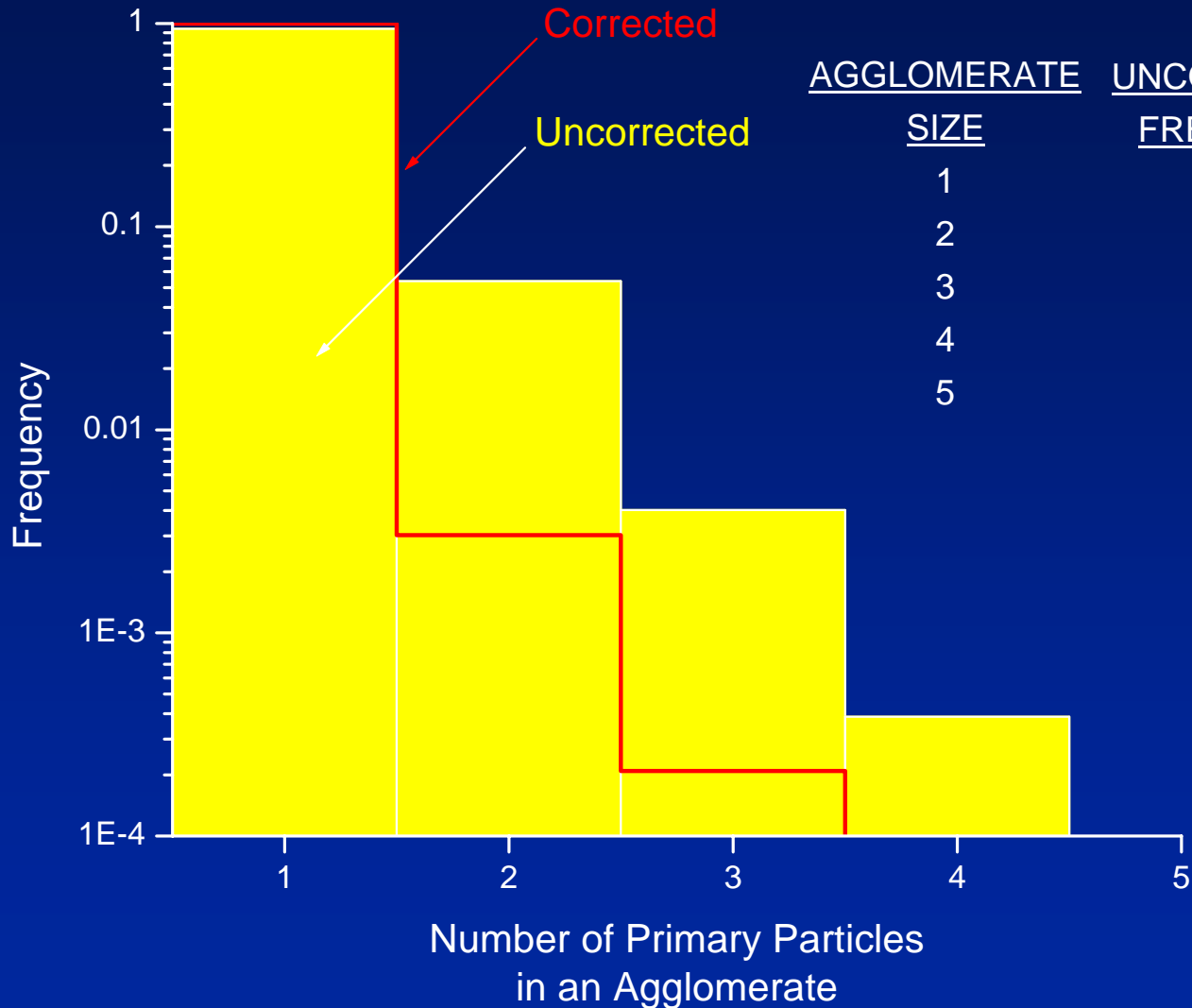


# Histogram of Agglomerates

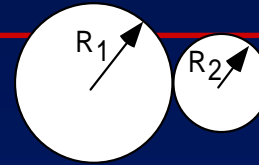
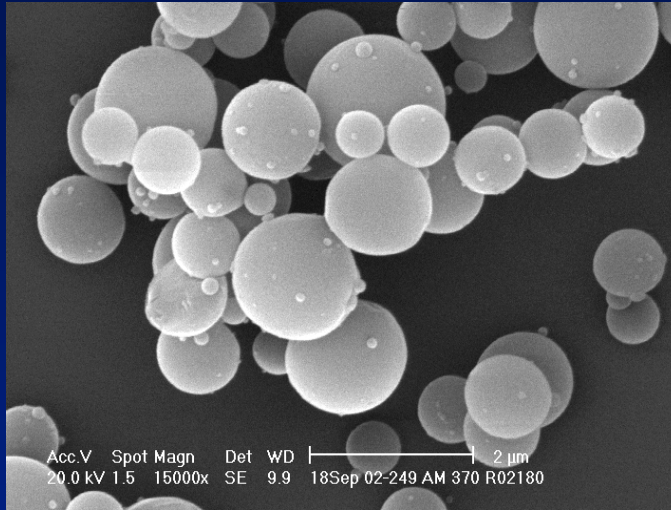


<u>AGGLOMERATE</u>	<u>UNCORRECTED</u>	<u>CORRECTED</u>
<u>SIZE</u>	<u>FREQUENCY</u>	<u>FREQUENCY</u>
1	84.09	88.02
2	11.12	7.09
3	2.78	2.64
4	0.90	0.55
5	0.46	0.47
6	0.19	0.08
7	0.13	0.13
8	0.07	0.05
9	0.06	0.06
10	0.03	0.02

# Histogram of Deagglomerated Powder

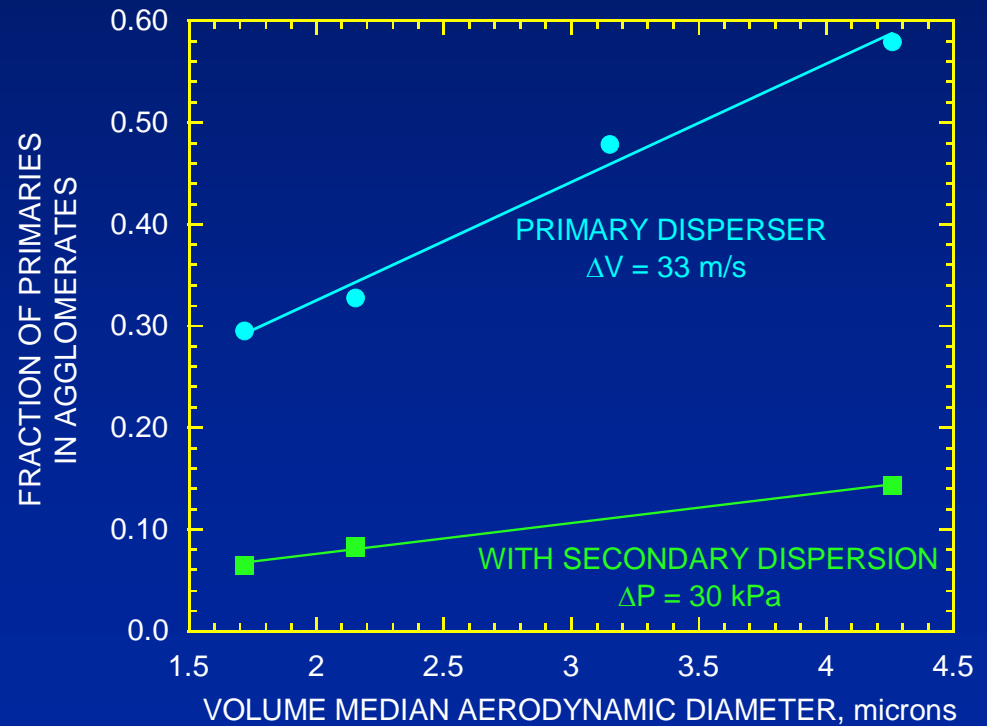
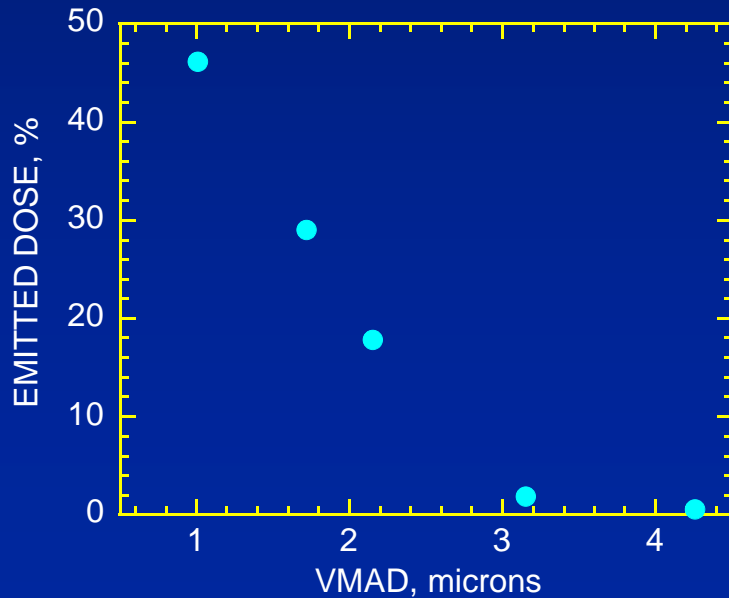


# Model Spherical Particles 100% amorphous raffinose

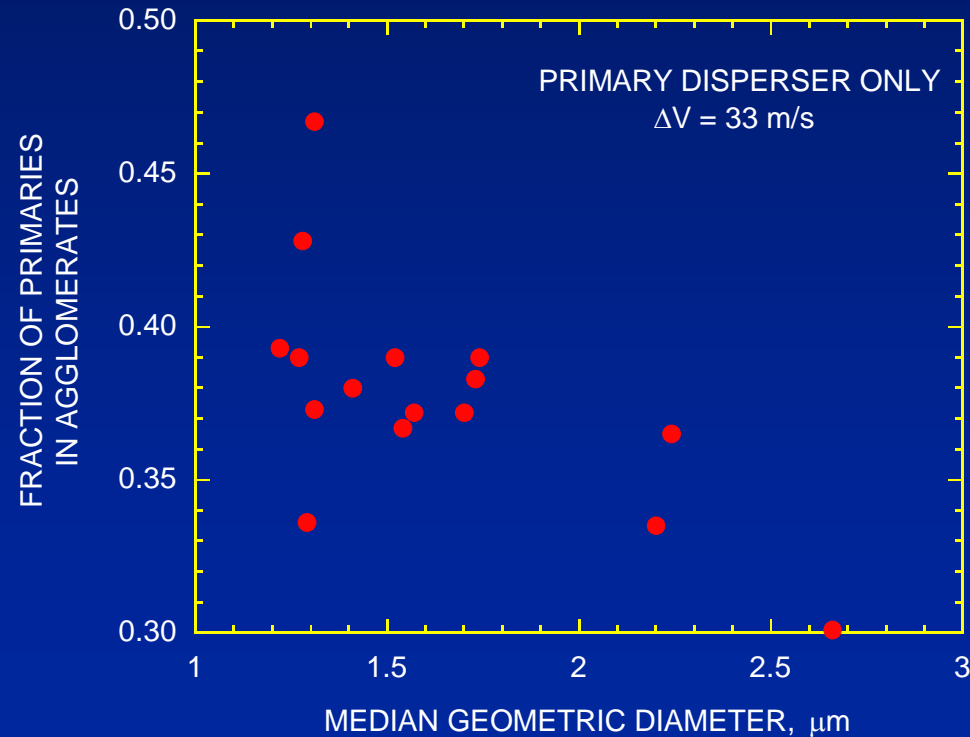
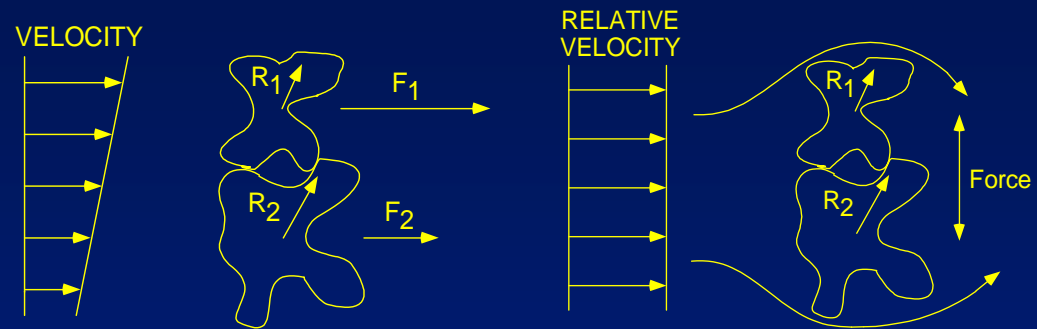
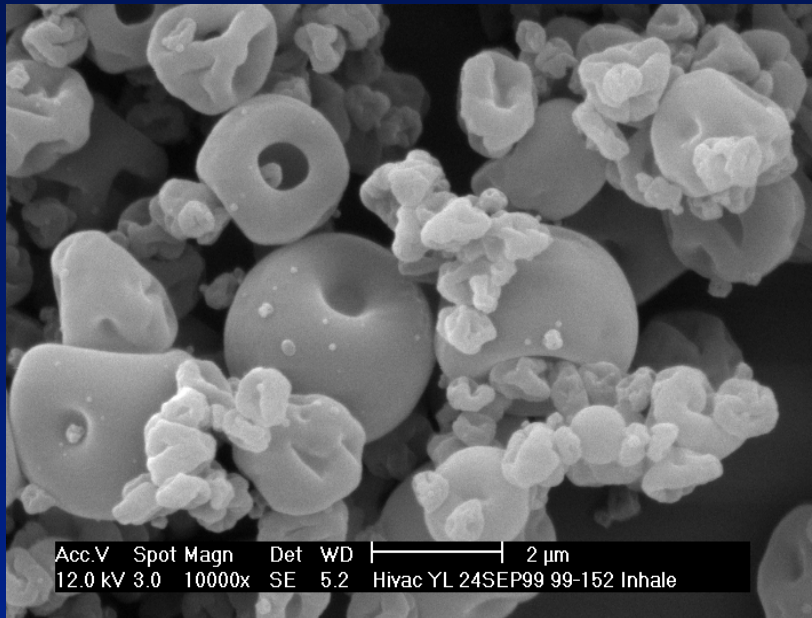


Van der Waals attractive forces:

$$F_{ad} = -\frac{A}{6z^2} \frac{R_1 R_2}{(R_1 + R_2)} = -\frac{AR}{12z^2}$$



# PulmoSol™ Protein Powders



100% protein

Aerodynamic forces  
 separating particles:

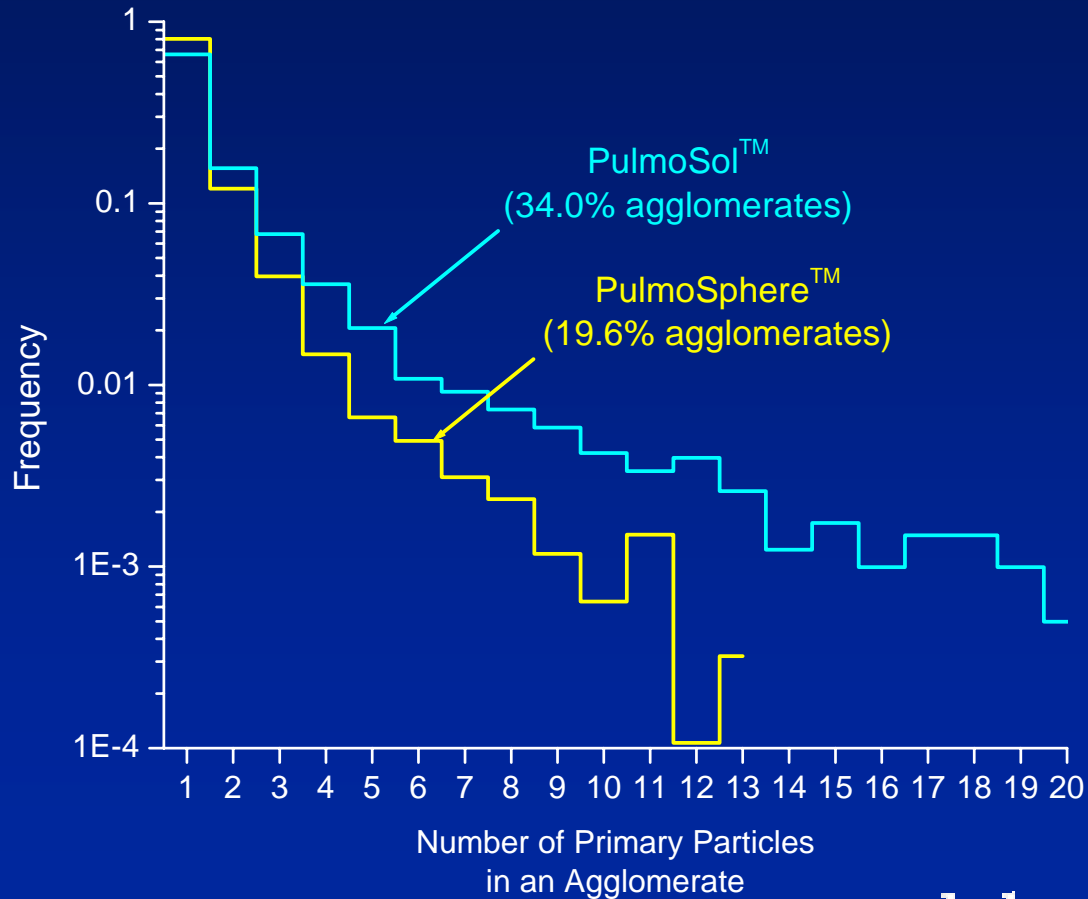
$$F_{sep} \propto R^2$$

$$F_{ad} \propto R_C$$

# PulmoSphere<sup>®</sup> Powders



Porous, low density  
Less surface contact





# *Summary*

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**Inhale has developed an advanced research and development tool to quantify and study deagglomeration of micron-sized powder particles.**

**Improved understanding of particle deagglomeration leads to optimized product performance, shorter development times and decreased scale-up risk.**