WORKING FOR A HEALTHIER FUTURE

Characterisation of High Aspect Nanomaterials to Support Hazard Assessment

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Outline

- Introduction
- *In vitro* testing
- Methodology
  - Separation of respirable fraction from bulk material
  - Multi-instrumental approach
  - Mapping of aerodynamic and physical size
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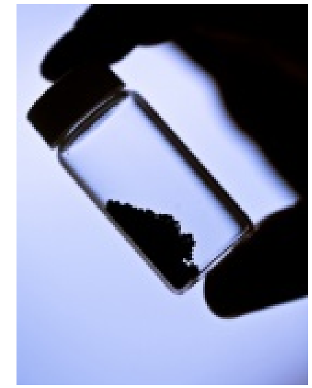
- Acknowledgments & Contacts

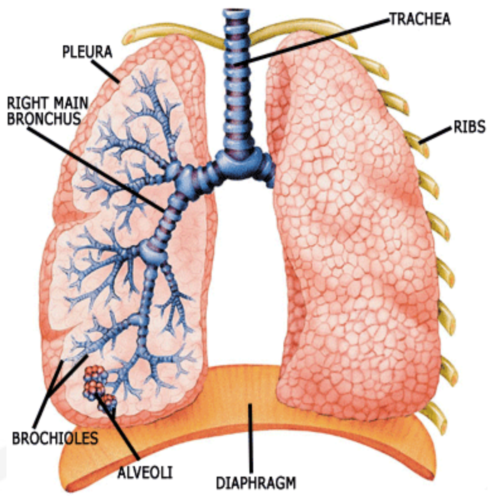
Introduction

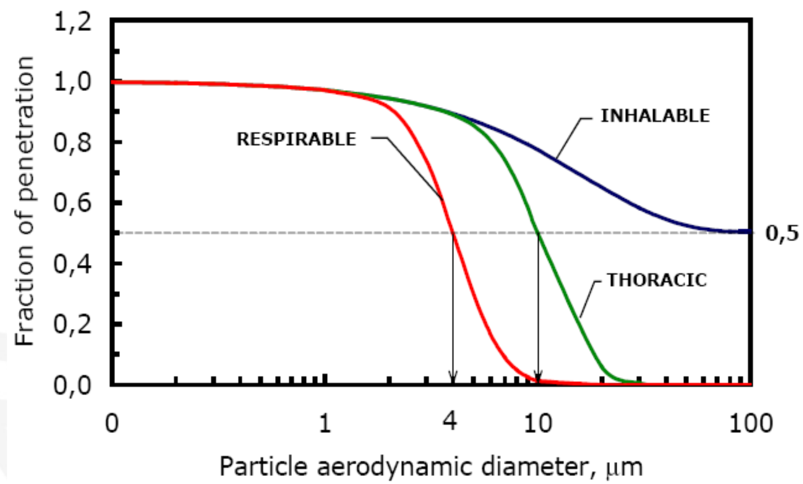
- Toxicology
  - Chemical
  - Particle driven toxicology
    - Surface charge
    - Surface functionalisation
    - Impurities
    - Morphology
      - Size
      - Shape



Understanding particle morphology is crucial for the investigation of inhalation toxicology

Introduction





Probability of aerosol penetration as a function of aerodynamic diameter, internationally agreed by CEN/ISO/ACGHI

Particles with an aerodynamic equivalent diameter < 10 µm will enter the alveoli region of the lung (High Aspect Ratio Nanomaterials)

Projected Area Diameter (µm)	Thickness (µm)	Aerodynamic Diameter (µm)
5	0.1	1.33
10	0.1	1.88
20	0.1	2.66
30	0.1	3.26
40	0.1	3.76
50	0.1	4.20
60	0.1	4.60
70	0.1	4.97
80	0.1	5.32
90	0.1	5.64
100	0.1	5.97

Schinwald et al. ACS Nano. 2011 Dec 23

Example HARNS

- Carbon nanotubes
- Graphene
- Nanoclays
- Platelet materials

In vitro testing

Current Approach

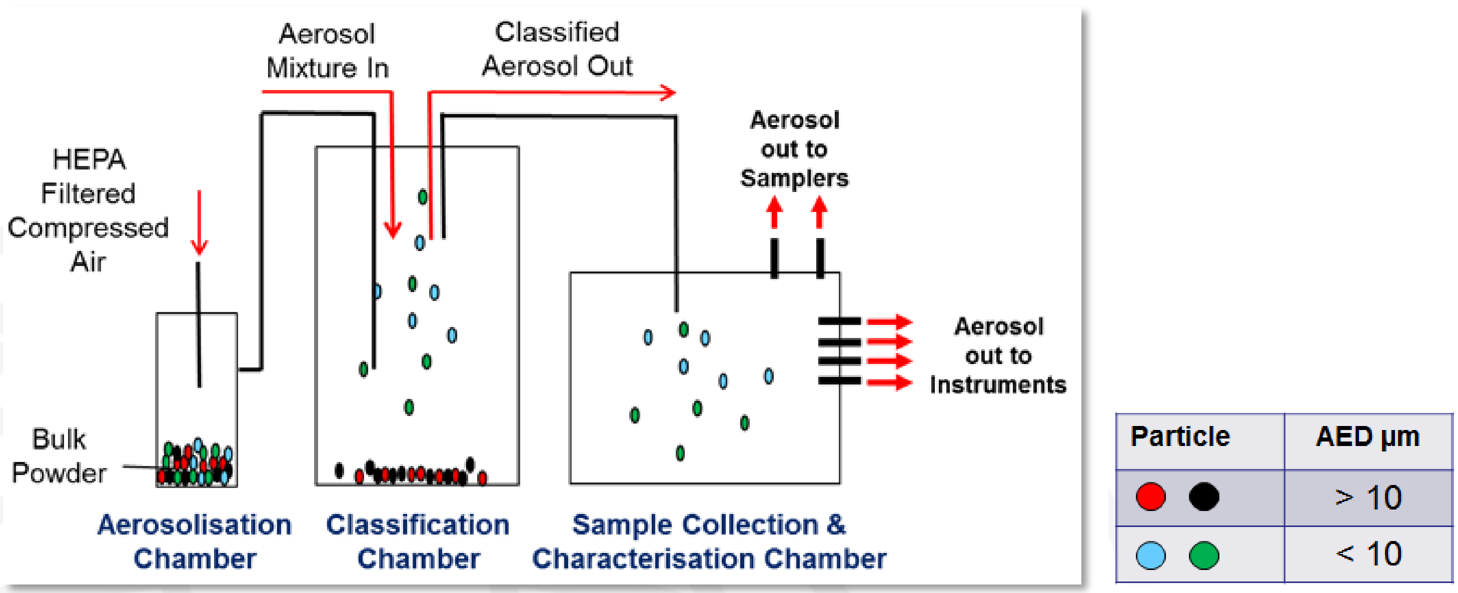
- Uses bulk material
- Size selection does not account for aerodynamic size
- Using bulk material gives a false indication of dose response
- Materials are reduced to <10µm physical size

IOM Approach

- Respirable fraction separated from bulk fraction for toxicological analysis
- Characterisation includes aerodynamic size information alongside physical and dynamic light scattering obtained particle size distributions
- Offers information to provide a more robust hazard assessment

Methodology

Separation of Respirable Fraction from Bulk Material

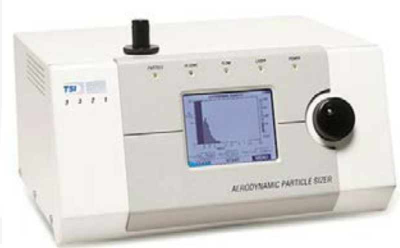


- Based on Stokes law – density, aerodynamic size and air flow
- Only particles with a certain aerodynamic size will leave the classification chamber
- Allows for the collection of respirable fraction onto samplers and subsequent toxicological analysis of the fraction rather than the bulk material

Methodology

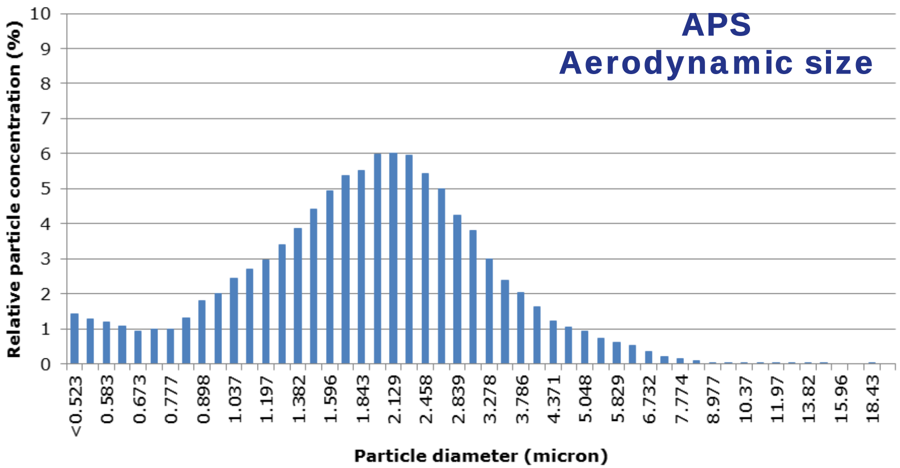
Multi-Instrumental Approach

Real Time Instrument	Size Range (nm)	Concentration Range (#/cm^3)	Measurement Principle	Metric			
				Number Conc.	Size Distribution	Mass	Surface Area
Fast Mobility Particle Sizer (FMPS)	5.6- 560	0- 1,000,000	Electrical mobility	✓	✓	✓	✓
Aerodynamic Particle Sizer (APS)	500- 20,000	0- 20,000	Light scattering	✓	✓	✓	✓
DustTrak	100-15,000	0- 60 mg/m^3	Photometric		✓	✓	

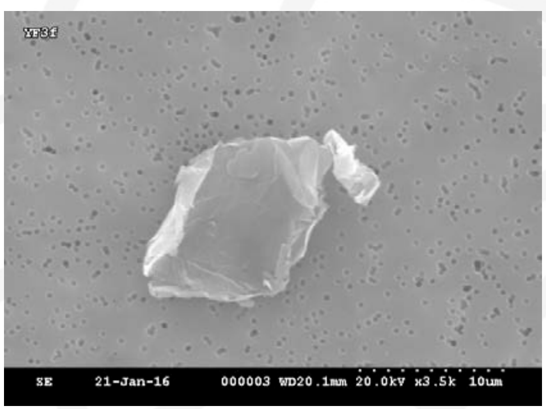


Methodology

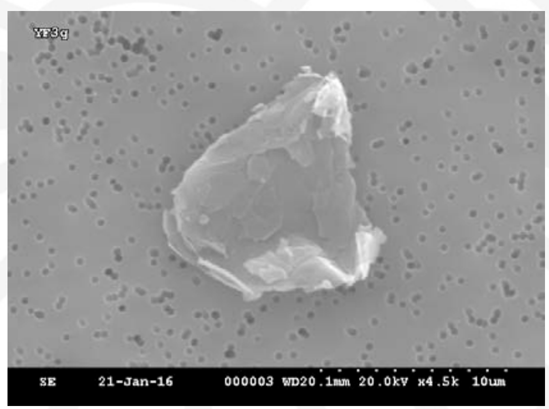
Mapping of Aerodynamic vs Physical Size



Nano ID Stage	Aerodynamic Diameter (μm)	Physical Size Found (largest dimension) – μm Graphite-based Particles
3	4.0- 8.1	50
4	2.0- 4.0	25
5	1.0- 2.0	5
6	0.5- 1.0	25
7	0.25- 0.5	5



11 μm GFN flake
Respirable head



15 μm GFN flake
Respirable head

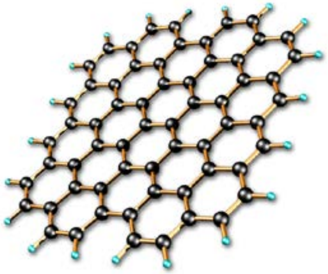
Summary

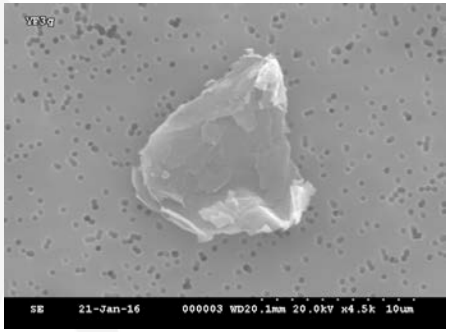
- Respirable fraction separation allows for a more relevant sample characterisation and preparation for use and interpretation in inhalation toxicity testing

- Detailed characterisation is integral to a robust material hazard assessment

- The need for this particular method extends beyond graphene and CNTs, to all high aspect ratio materials

- Essential in progressing the science to allow for realistic *in vitro* toxicological analysis





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