Exposure Assessment of Nanomaterial-Containing Aerosols from Spray and Powder Products

Cosmetic Ingredient Review Panel
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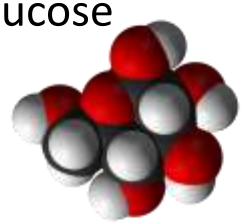
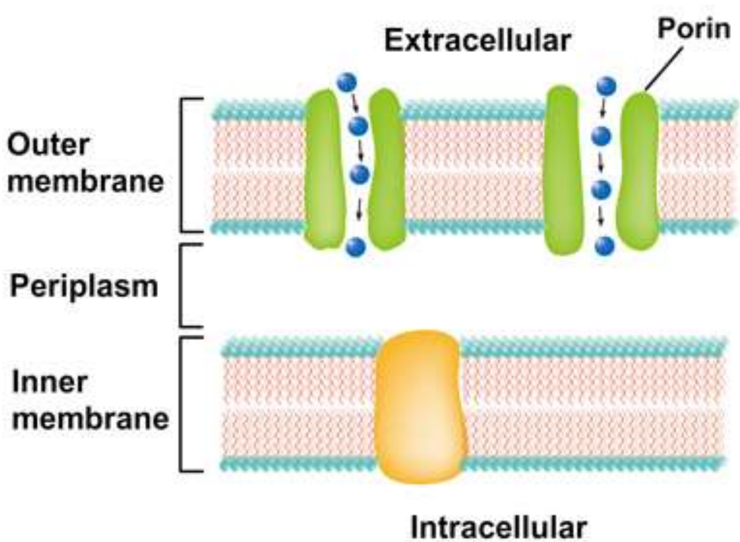
1 – 100 nm in Perspective

Glucose



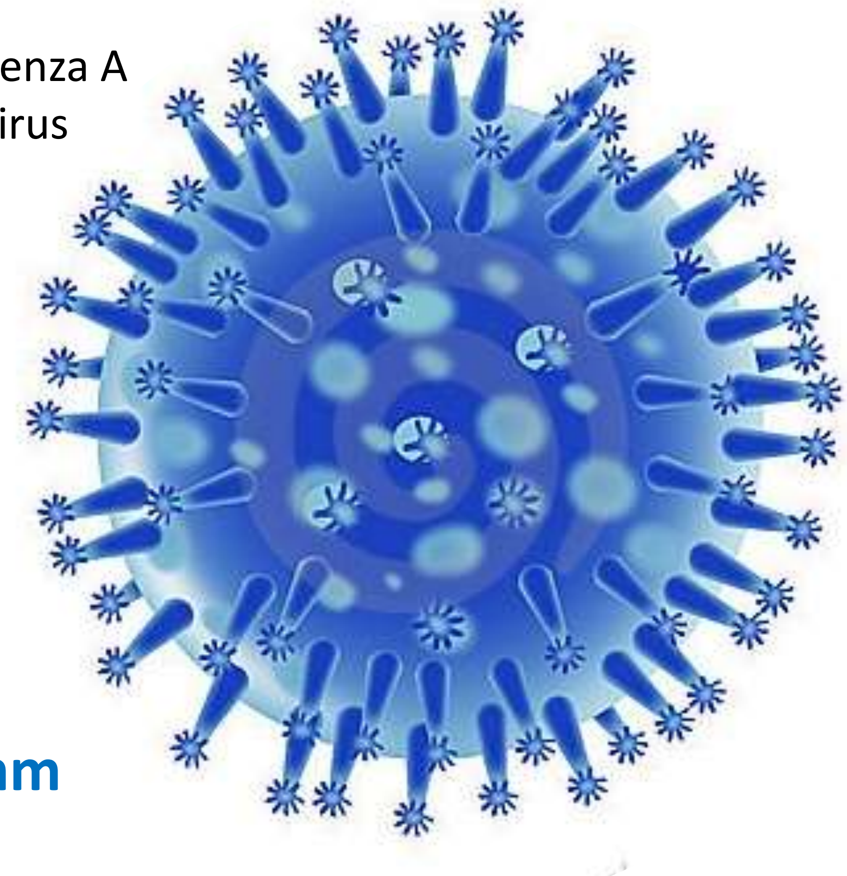
~1 nm

Double membrane of Gram-negative bacteria



~10 nm

Influenza A Virus



~100 nm

http://images.wikia.com/gcse/images/d/d5/Glucose.png
http://www.pdbj.org/eprots/images/2ODJ/2ODJ1.jpg
http://www.dreamstime.com/influenza-flu-virus-structure-thumb9252986.jpg

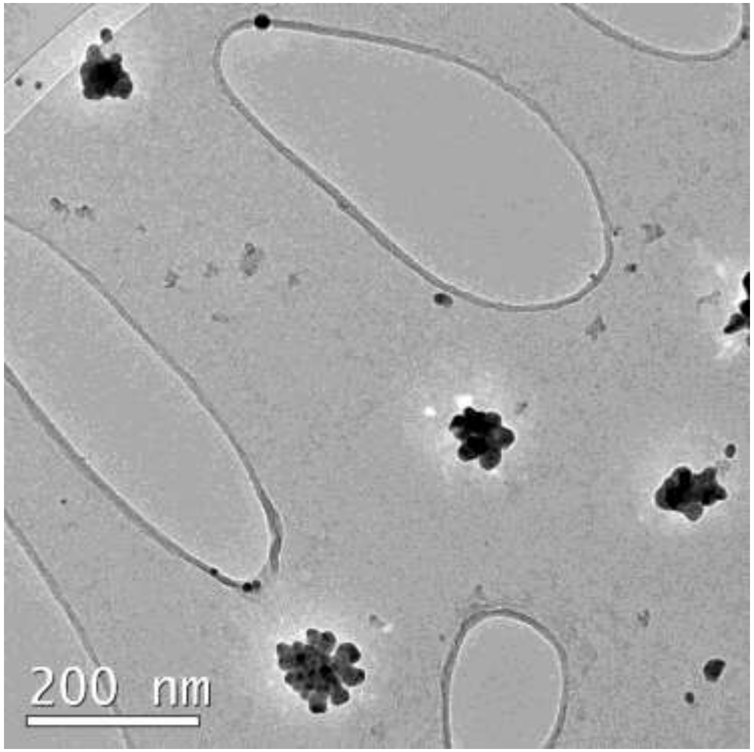
Nano-sized Particles and Materials

The US National Nanotechnology Initiative (NNI) defines nanotechnology as “the understanding and control of matter at dimensions between **approximately** 1 and 100 nanometers, where unique phenomena enable novel applications” (National Science and Technology Council, 2007).

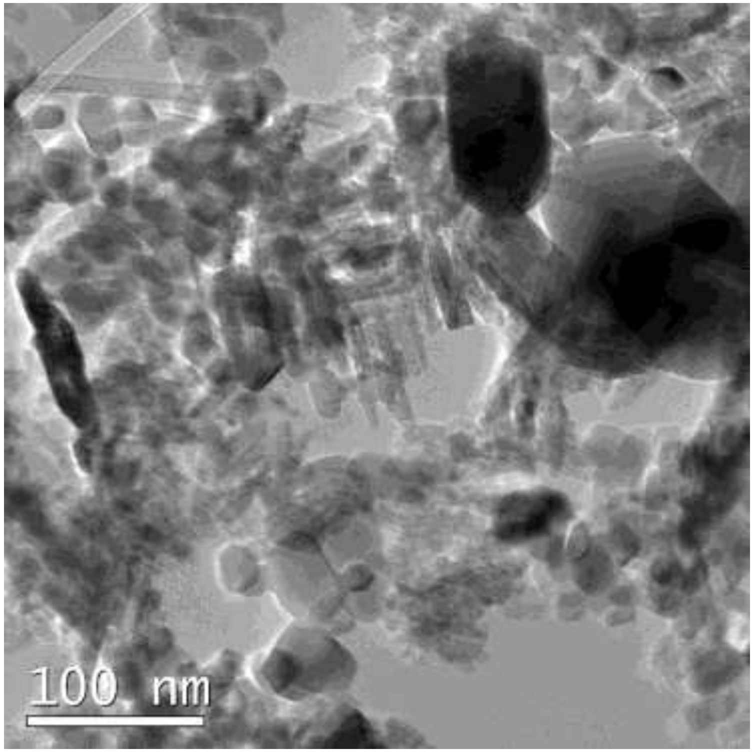
Under the EU’s “Recommendation on the definition of a nanomaterial (2011/696/EU)”
“A natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm - 100 nm.” *Includes some < 50 % and < 1 nm.

Nano-objects ≠ Nanomaterials

- Nano-objects can exist both as free nanoparticles and their agglomerates / aggregates or be attached to / incorporated into larger particles

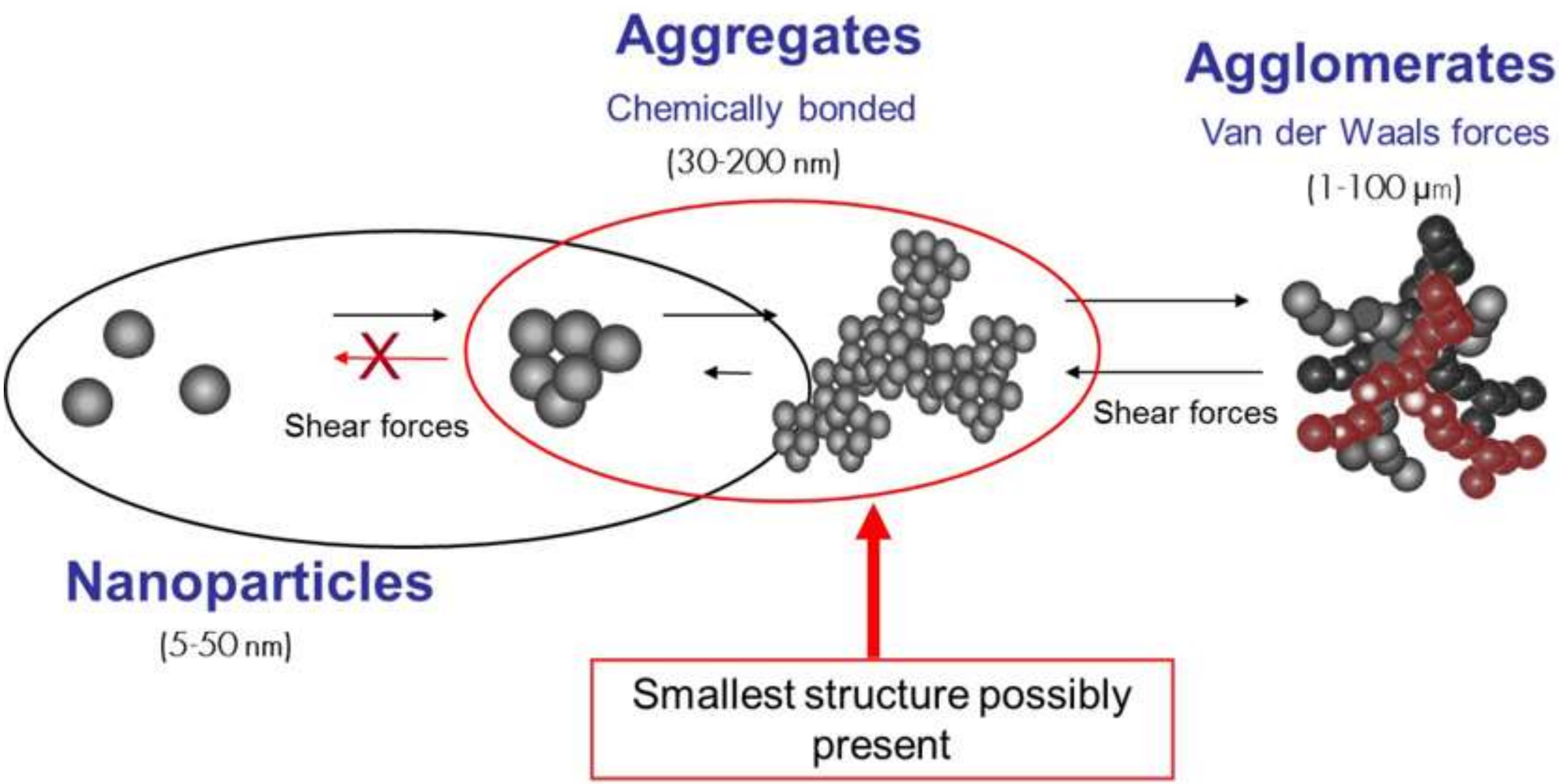


Sample 1



Sample 2

NOAA: Nano-objects, agglomerates and aggregates



http://www.teknoscienze.com/Articles/HPC-Today-Nanotechnology-and-Sun-Care-A-Risk-Review.aspx

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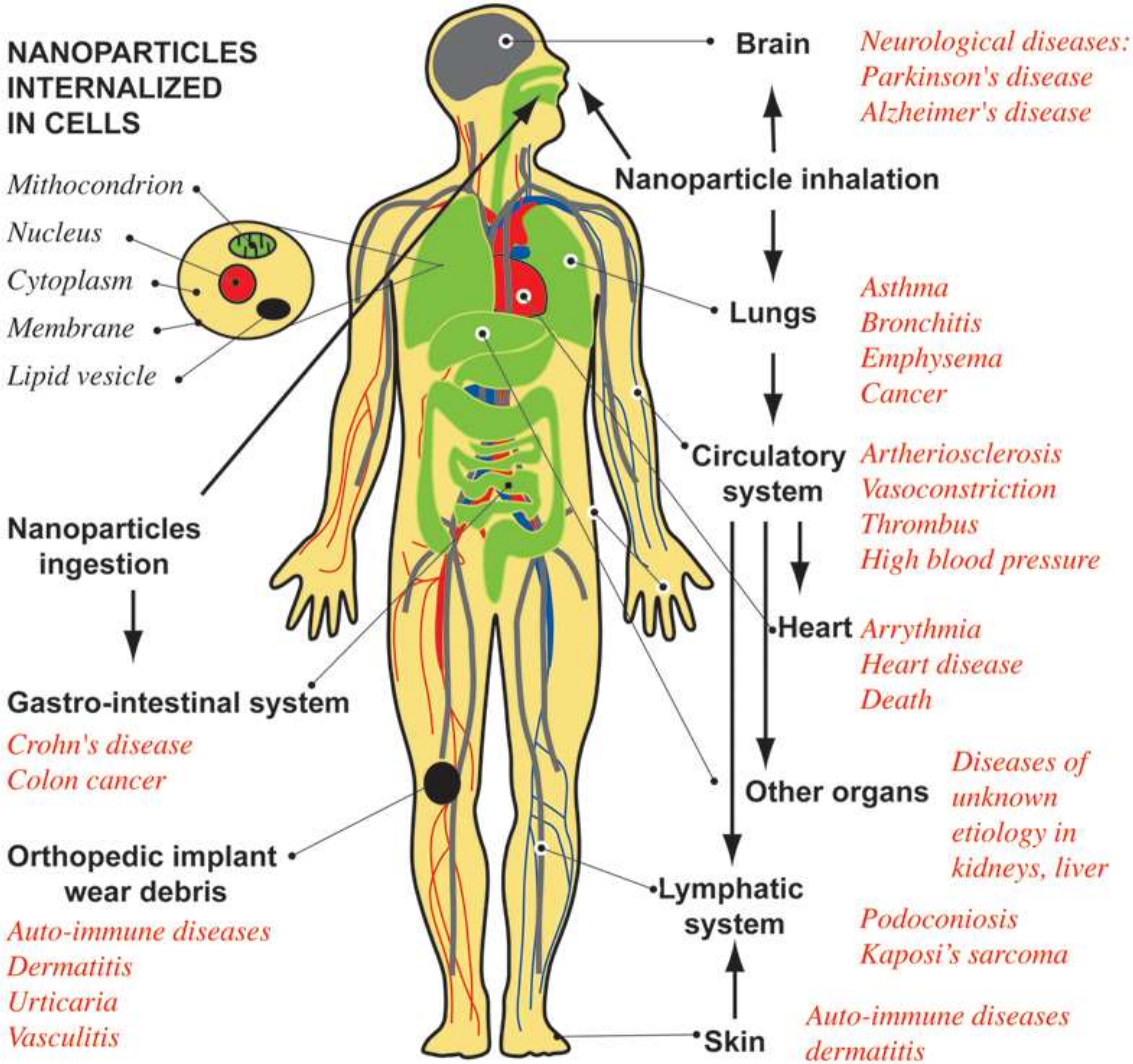
Human Exposure to Nanomaterials

C. Buzea, I. Pacheco, & K. Robbie, Nanomaterials and nanoparticles: Sources and toxicity, Biointerphases 2 (2007) MR17-MR71

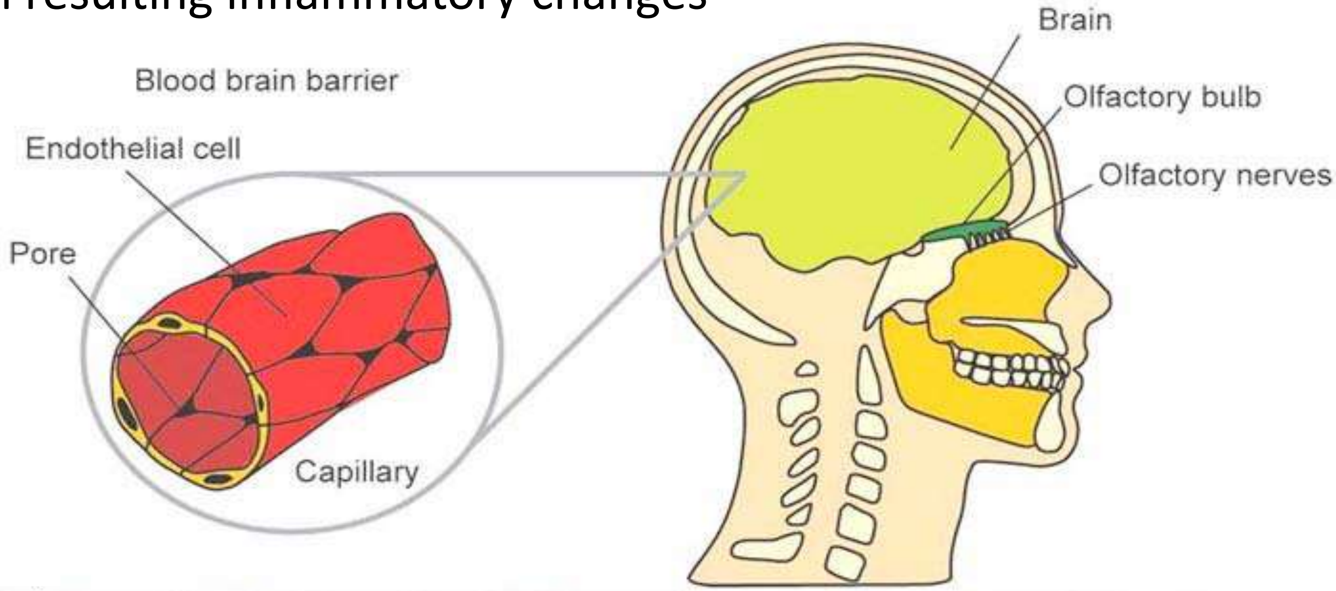


- Human exposure to nanomaterials is associated with **potential health risks**;
- Different routes of this exposure are possible: **ingestion, dermal, inhalation**

Health Concerns of Nanomaterial Exposure

The size distribution and structural state of matter at the nanoscale affects its toxicity and associated biological and health effects relative to mass dose of chemically the same substance:

- **Example 1:** graphite-derived carbon nanoparticles (median diameter 36 nm) were found to translocate from the respiratory system to the olfactory bulb of the rat central nervous system. The same effect was found for the manganese oxide nanoparticles (median diameter 30 nm) with resulting inflammatory changes*



*Elder A, Gelein R, Silva V, Feikert T, Opanashuk L, Carter J, et al. 2006. Translocation of Inhaled Ultrafine Manganese Oxide Particles to the Central Nervous System. Environmental Health Perspectives 114(8): 1172-1178; Buzea, C., Pacheco, I.I., Robbie, K. 2007. Nanomaterials and nanoparticles: Sources and toxicity. *Biointerphases*, 2(4): MR17-MR172;

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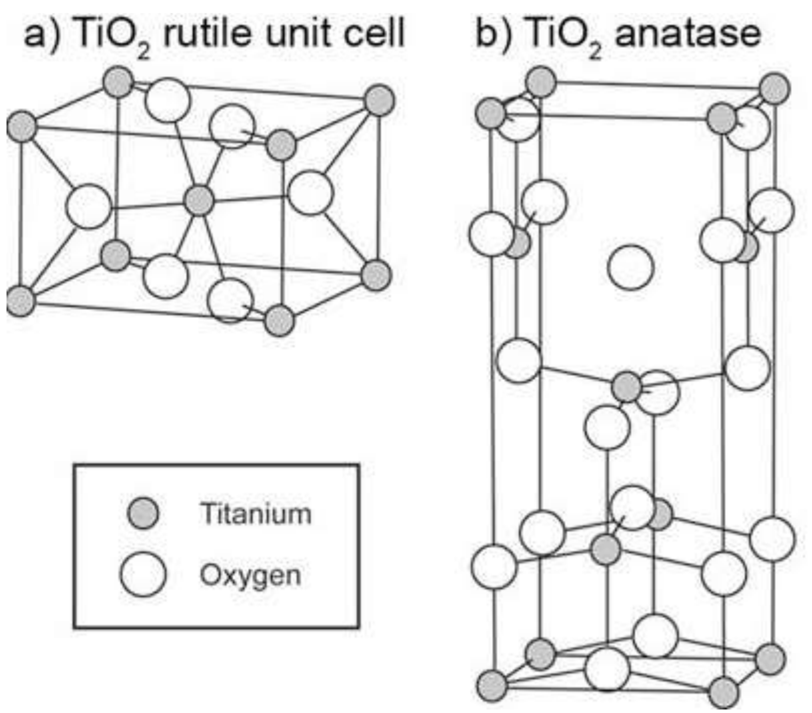
Health Concerns of Nanomaterial Exposure

Toxicity of nanomaterials can differ even for small variations of particle size and crystal structure:

- **Example 2:** following intranasal instillation, a more intense inflammation response resulted in mice exposed to 21-nm anatase/rutile nano-TiO_2 compared to 5-nm anatase nano-TiO_2.*

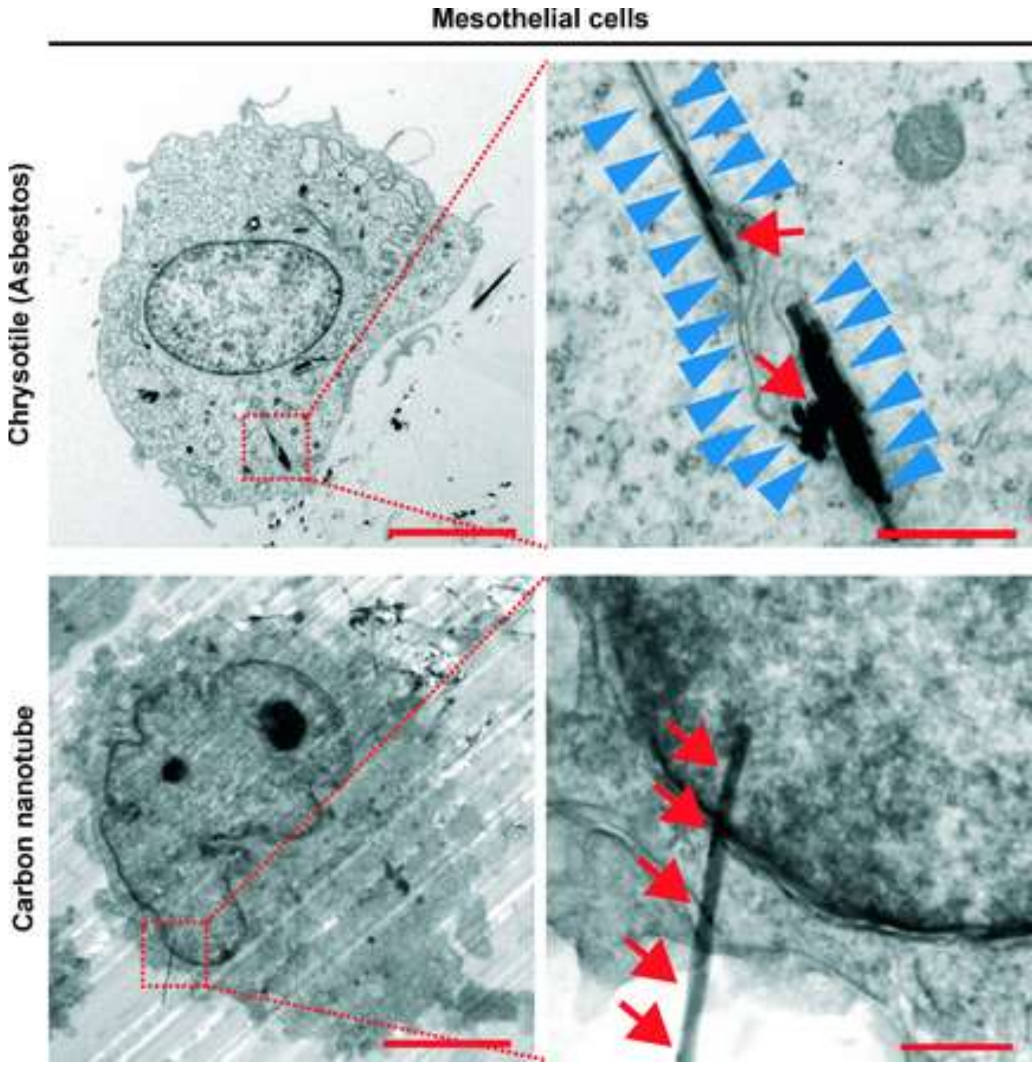


*Grassian VH, Adamcakova-Dodd A, Pettibone JM, O'Shaughnessy PT, Thorne PS. 2007. Inflammatory response of mice to manufactured titanium dioxide nanoparticles: Comparison of size effects through different exposure routes. Nanotoxicology 1(3): 211-226;
Buzea, C., Pacheco, I.I., Robbie, K. 2007. Nanomaterials and nanoparticles: Sources and toxicity. *Biointerphases*, 2(4): MR17-MR172.

Health Concerns of Nanomaterial Exposure

Differences and similarities between carbon nanotubes and asbestos fibers during mesothelial carcinogenesis:

The mechanism of fiber entry into the cells



Cancer Science
[Volume 103, Issue 8,](http://onlinelibrary.wiley.com/doi/10.1111/j.1349-7006.2012.02326.x/full#cas2326-fig-0001) pages 1378-1390, 14 JUN 2012 DOI: 10.1111/j.1349-7006.2012.02326.x
http://onlinelibrary.wiley.com/doi/10.1111/j.1349-7006.2012.02326.x/full#cas2326-fig-0001

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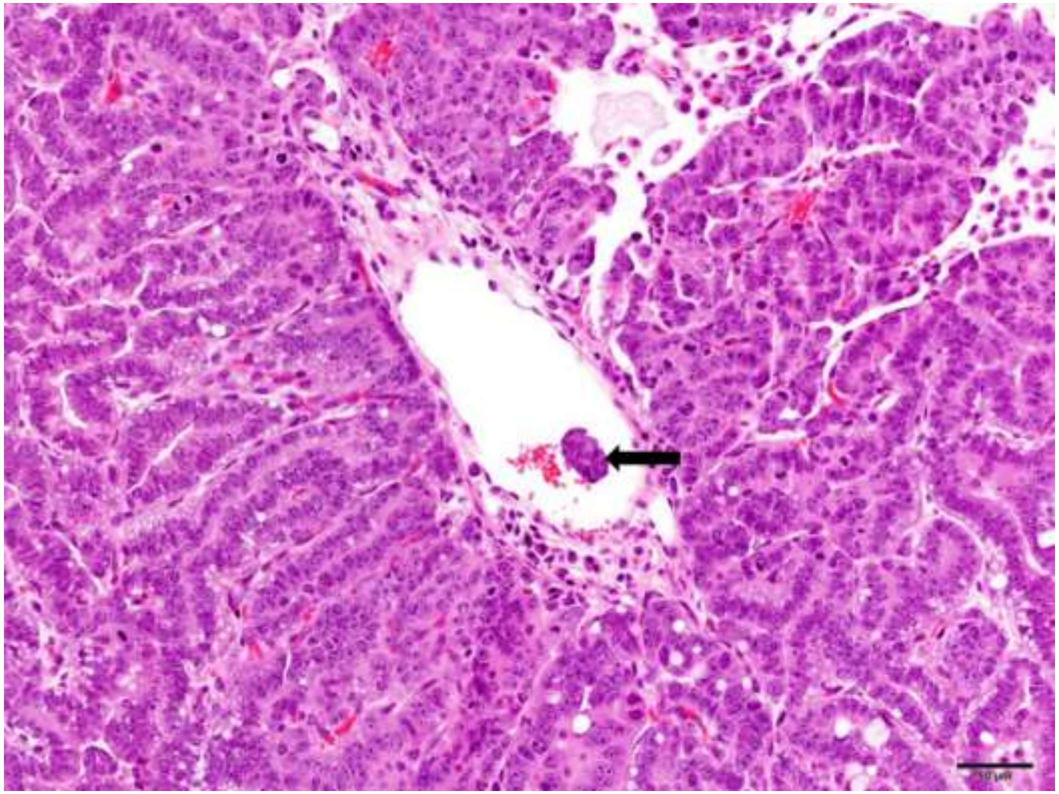
Health Concerns of Nanomaterial Exposure

Mice receiving both a known cancer initiator, methylcholanthrene, plus inhalation exposure to multiwalled carbon nanotubes (MWCNT)[1] were significantly more likely :

1. to develop tumors – **90% incidence and larger tumors**;
2. have **more tumors** than mice receiving the initiator chemical alone: all mice developed tumors (~3.3 tumors/mouse lung) vs. only 50% of mice developed tumors with ~1.4 tumors/lung).



Alveolar Bronchiolar Carcinoma of the Lung with Metastases in a Blood Vessel (arrow).

[1] Inhalation exposure at 5 mg/m^3 for 15 days, 5 hrs. per day

http://blogs.cdc.gov/niosh-science-blog/2013/03/mwcnt/

Health Concerns and Regulation

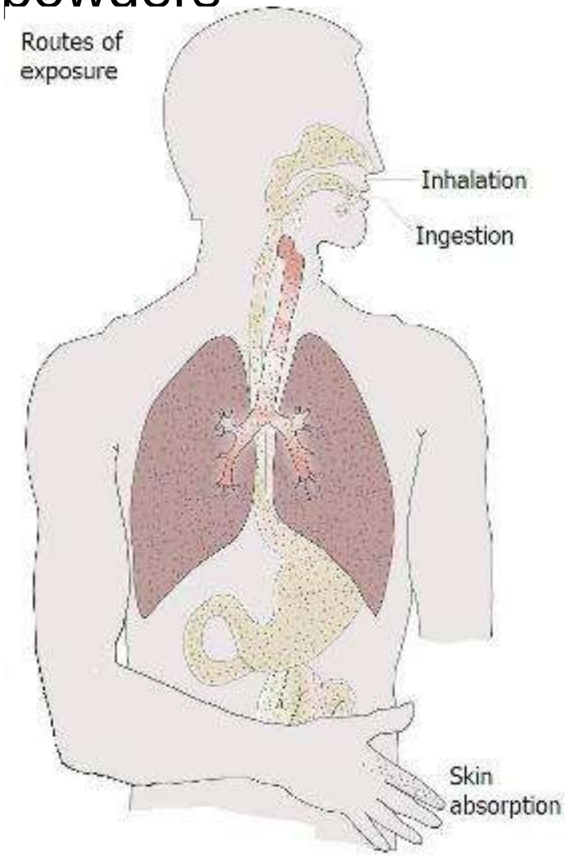
- Nanoparticles can be found ubiquitously in industrial and consumer products, claimed to contain nanomaterials and products not marketed as nanotechnology-based (regular products). **Nanomaterial exposure is possible - both occupational and end-user?**

- It is a challenge for modern analytical techniques to determine if nanoparticles, found in the products, are engineered or derived from natural ingredients. Manufacturers do not usually disclose such information about ingredients in their products. **Some regulations mandate disclosure of this information? Future regulations will likely require it too.**

- Inconsistency between advertising and marketing and the *de facto* “nano-status” of products that exist in the absence of regulations mandating accurate reporting of this information.

Nanotech Products → Exposure

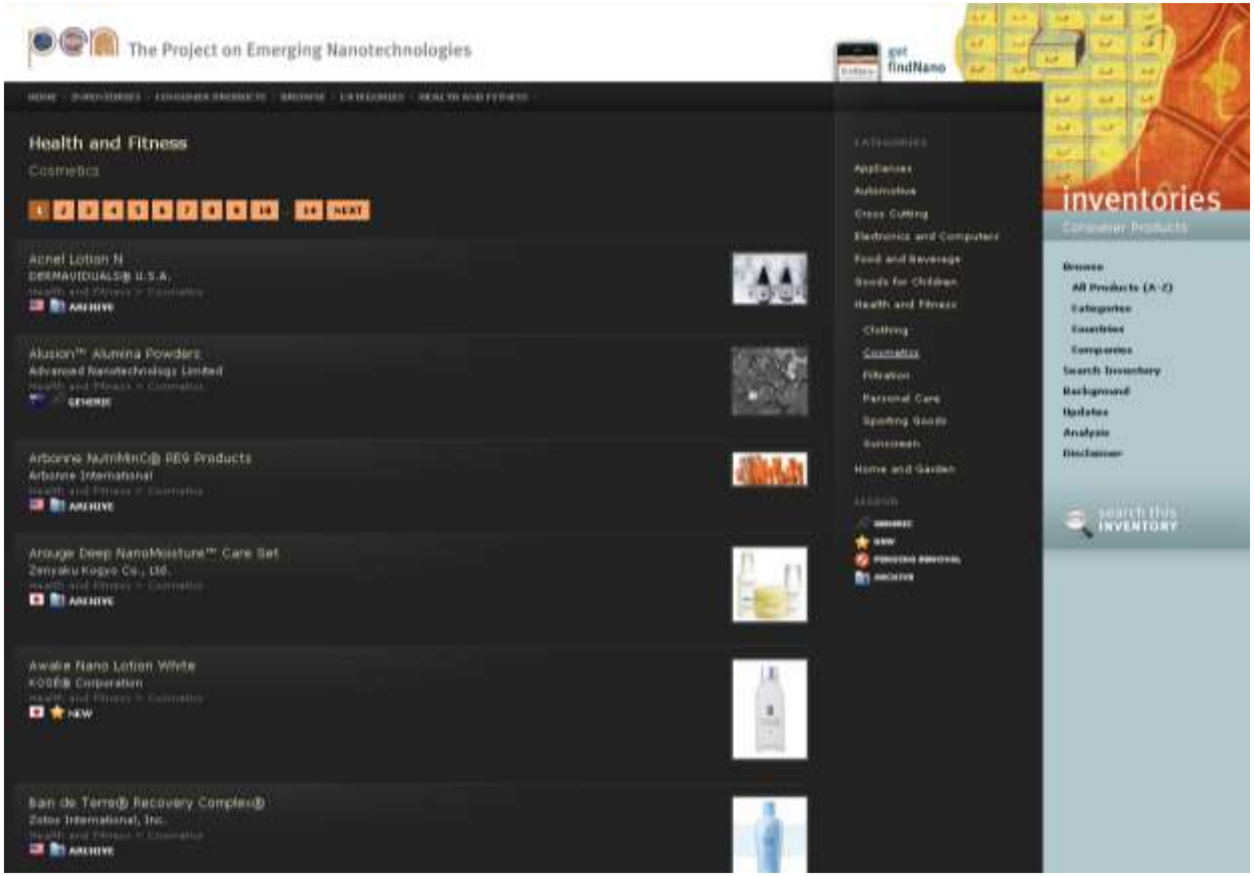
- Dermal and inhalation exposure may be especially high from nanotechnology-based consumer sprays and cosmetic powders



http://www.stewardshipcommunity.com/uploads/pics/hhroutes280.426.jpg

Our Research: Nanoproduct Selection

- The nanotechnology-based products were selected from the Woodrow Wilson Nanotechnology Consumer Products Inventory* that currently contains **>1300 such products**



*Woodrow Wilson International Center for Scholars, 2010 http://www.nanotechproject.org/inventories/consumer/

Non-Nanotech Products

- We added **Regular** products in our studies to study if and how their particulate composition and potential for inhalation exposure differ from the nanotechnology-based products

http://chemistscorner.com/wp-content/uploads/2009/12/new-cosmetic-products.jpg

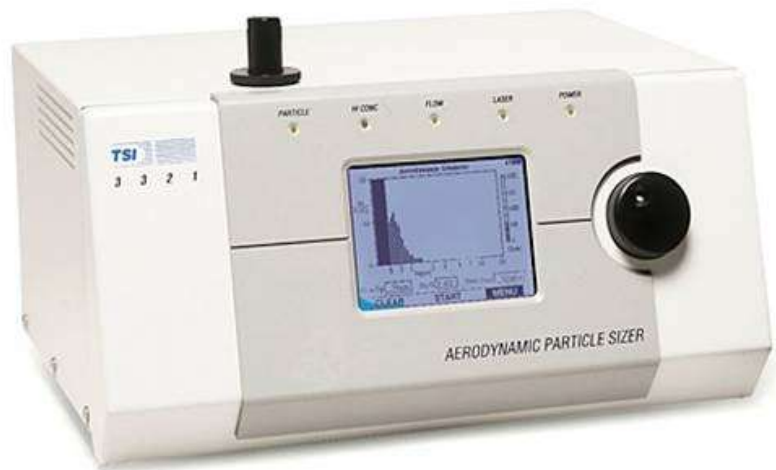
http://www.studiodirectcosmetics.com/cosmetics/pressed-powder-2.jpg

Problems Our Work Aimed to Address

- **Presence and content of nanomaterials** in consumer products on the market were largely unknown;
- **Potential of human exposure** to nanomaterial-containing aerosol particulate matter, released during use of nanotechnology-based products was unknown;
- **Doses of nanomaterials** that may result from the above-mentioned exposure were unknown.

Aerosol Measurement Techniques

- High importance of nanomaterials in all size fractions (both 1 – 100 nm **and above in the agglomerated form**) → we need to use **more than one measurement technique**, e.g. SMPS and APS



- **SMPS**: Scanning Mobility Particle Sizer
- **APS**: Aerodynamic Particle Sizer

http://www.tsi.com/ProductView.aspx?id=21939
http://www.tsi.com/ProductView.aspx?id=23007

Methods: All Aims

- Transmission Electron Microscopy (JEOL 2010F) to analyze particle **size, shape, and agglomeration** in the consumer sprays and cosmetic powders

Image from: http://www.virginia.edu/ms/images/JEOL2010.jpg

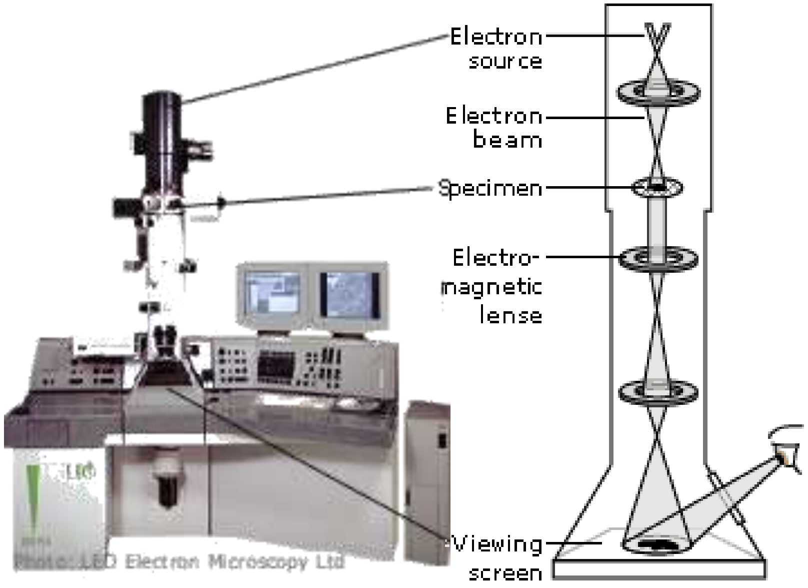
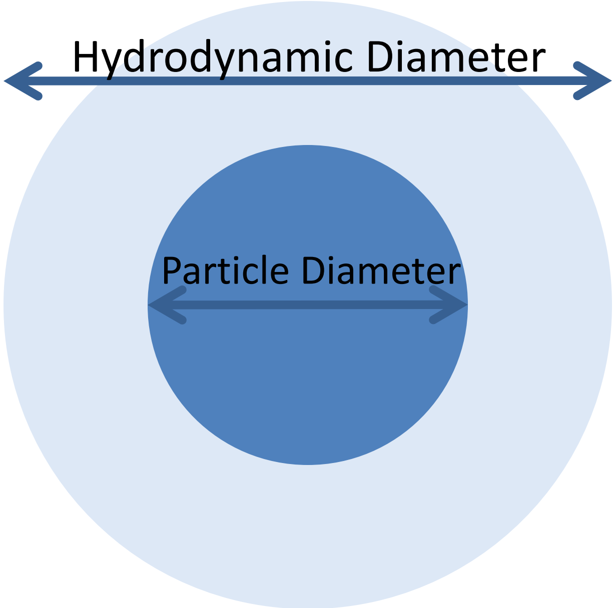


Image from: http://nobelprize.org/educational_games/physics/microscopes/tem/index.html

Methods: Consumer Sprays

- Photon Correlation Spectroscopy (Brookhaven ZetaPALS 90Plus Particle Size Analyzer) to obtain particle size distributions in spray products

http://www.wrrc.hawaii.edu/lab/ZetaPALS-250px.jpg



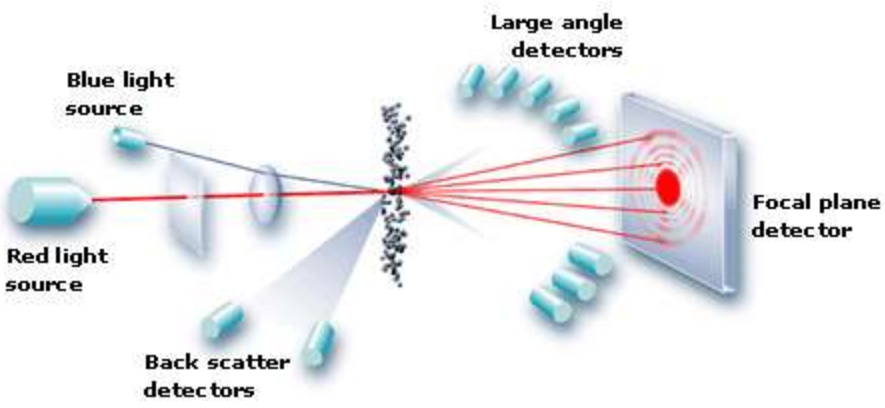
- Hydrodynamic diameter (HD) corresponds to the equivalent sphere with the same diffusion coefficient as that of the real particle

→ *Additional Explanation of HD*

Methods: Cosmetic Powders

- Laser Diffraction Spectroscopy (Malvern Mastersizer 2000) was used to obtain particle size distributions in cosmetic powders

http://www.leeds.ac.uk/particletechnology/Images/mastersizer.jpg



http://www.malvern.de/LabGer/technology/laser_diffraction/particle_sizing.htm

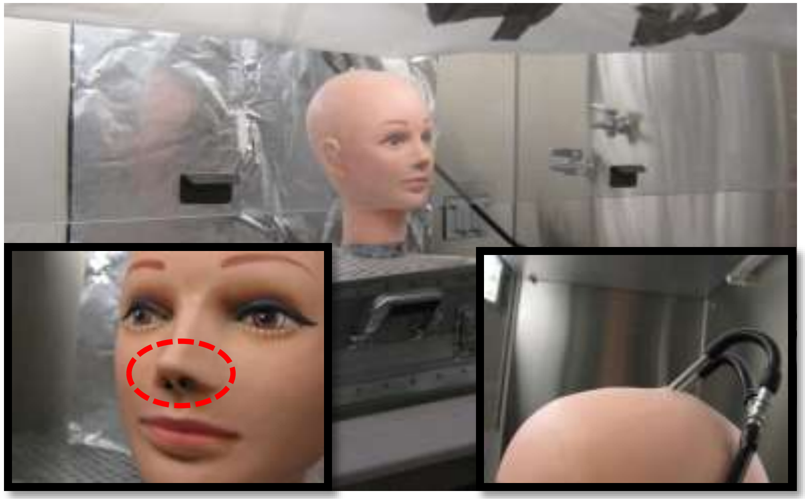
- Particles passing through a laser beam scatter light at an angle that is directly related to their size.

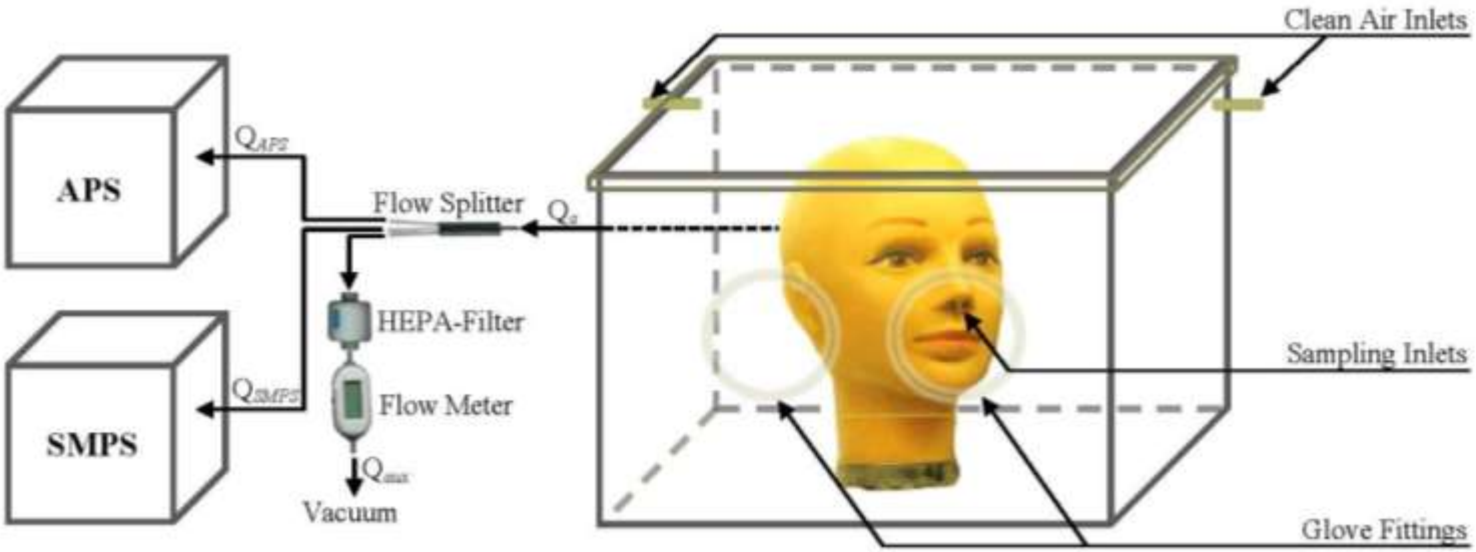
→ *Additional Explanation of the Principle of Operation*

Methods: Cosmetic Powders

- **Realistic exposure scenario**:

- application of the cosmetic powders with the supplied applicators and sampling in the way that mimics real life application and inhalation.





→ *Justification of the Sampling Flow Rate*

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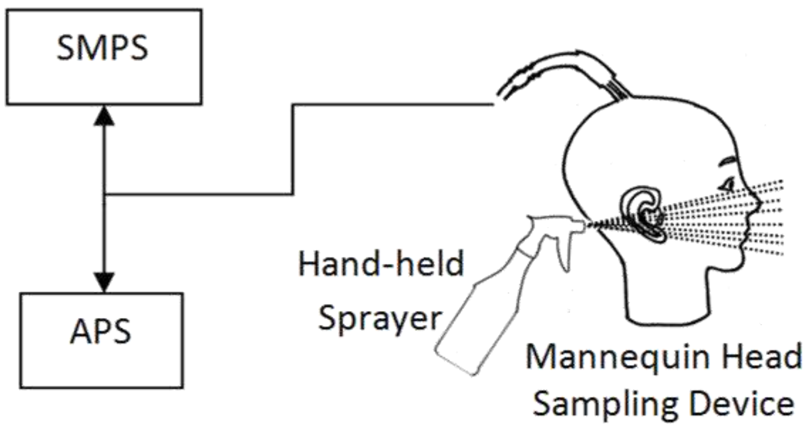
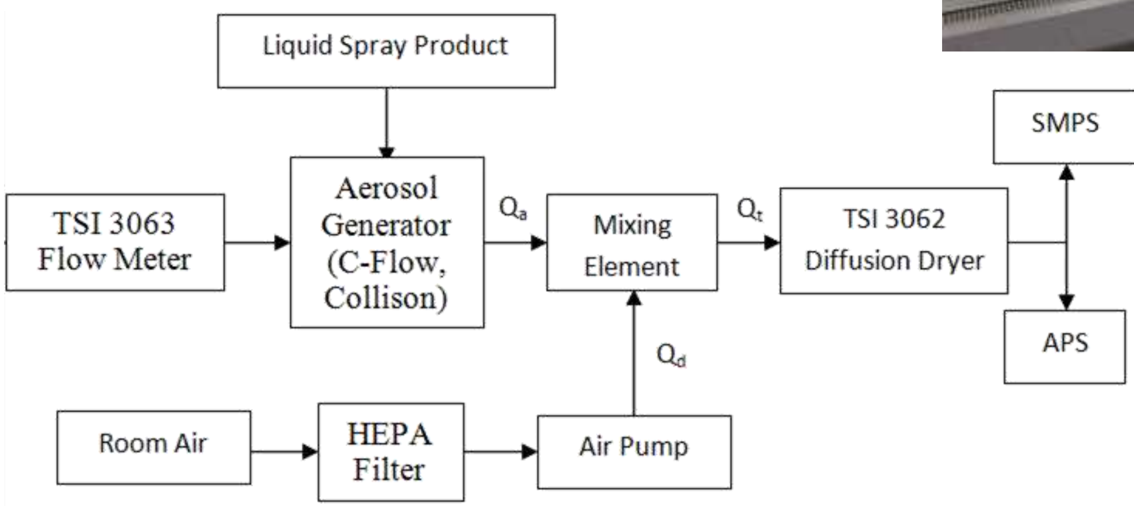
Methods: Consumer Sprays

Realistic Spray Use



Standard Nebulizers



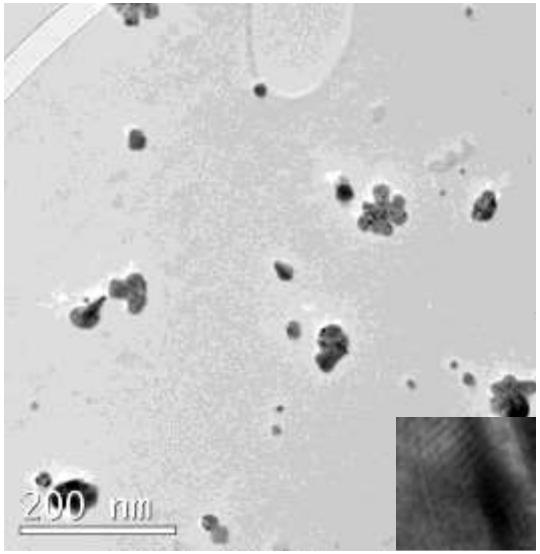
Tested Consumer Sprays

Nanoproduct	Regular Product
Silver Nanospray*	Regular Silver Spray
Facial Nanospray*	Regular Facial Spray
Hair Nanospray*	Regular Hair Spray
Disinfectant Nanospray*	Regular Disinfectant Spray
Skin Hydrating Nanomist*	Regular Skin Hydrating Mist
Wheel Nanocleaner*	*No Alternative Tested*

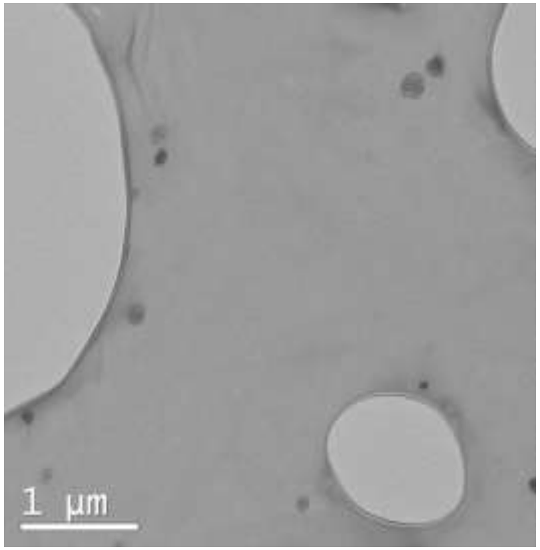
*Nanoproduct as per the Woodrow Wilson Nanotechnology Consumer Products Inventory

Results: TEM of Nano Consumer Sprays

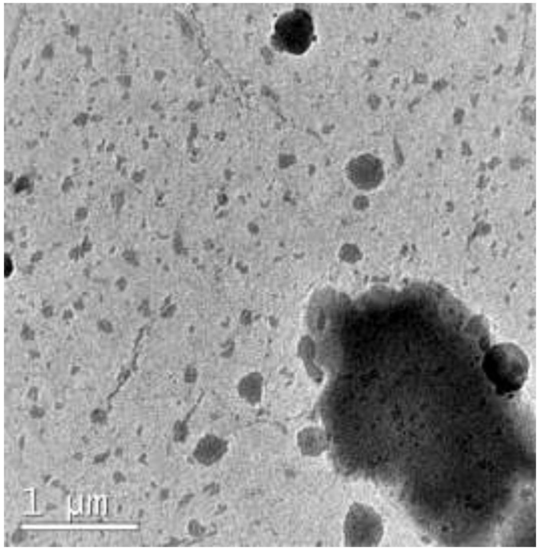
Nanotechnology-based Sprays



Silver **Nano**spray



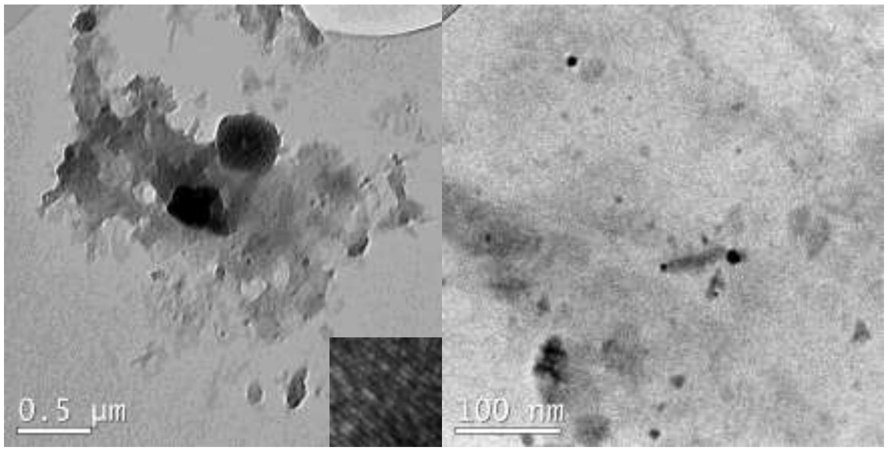
Disinfectant **Nano**spray



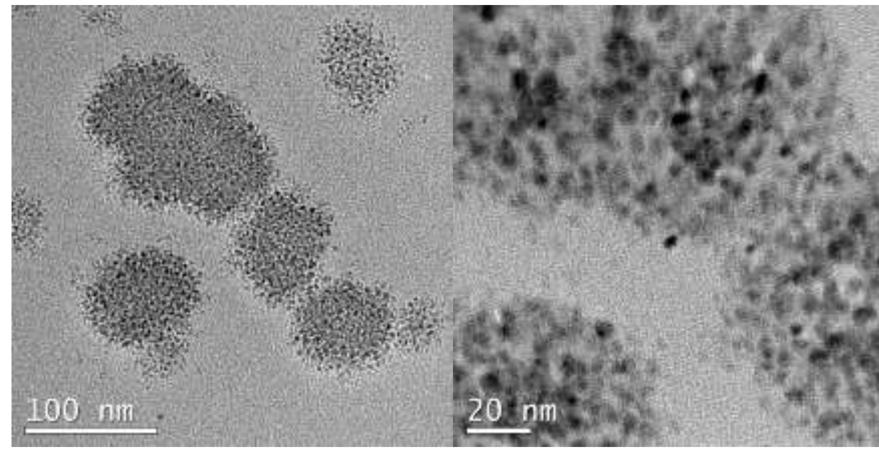
Wheel **Nano**cleaner

Results: TEM of Regular Consumer Sprays

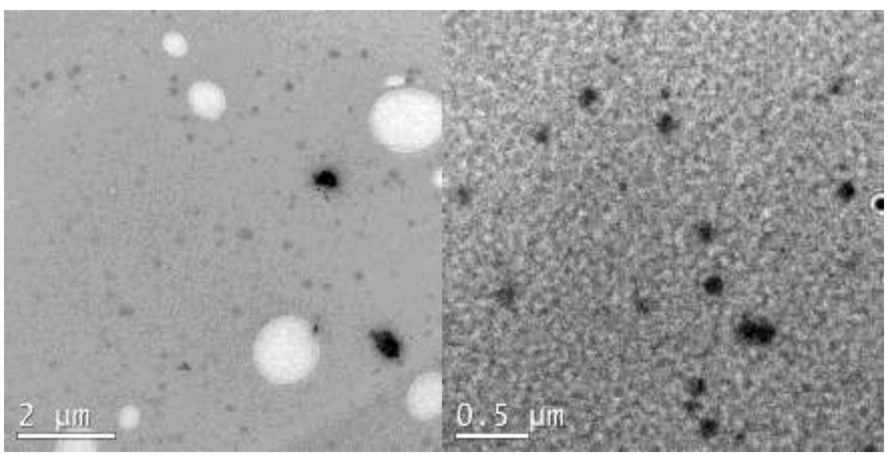
Regular Sprays



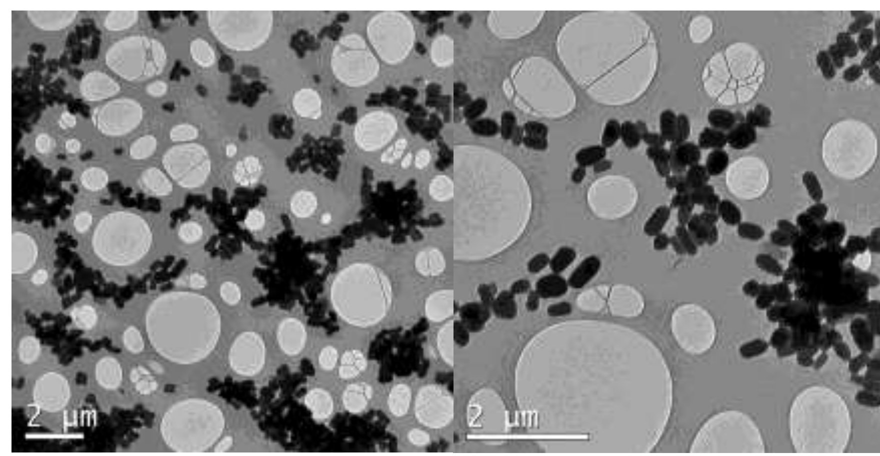
Regular Silver Spray



Regular Disinfectant Spray



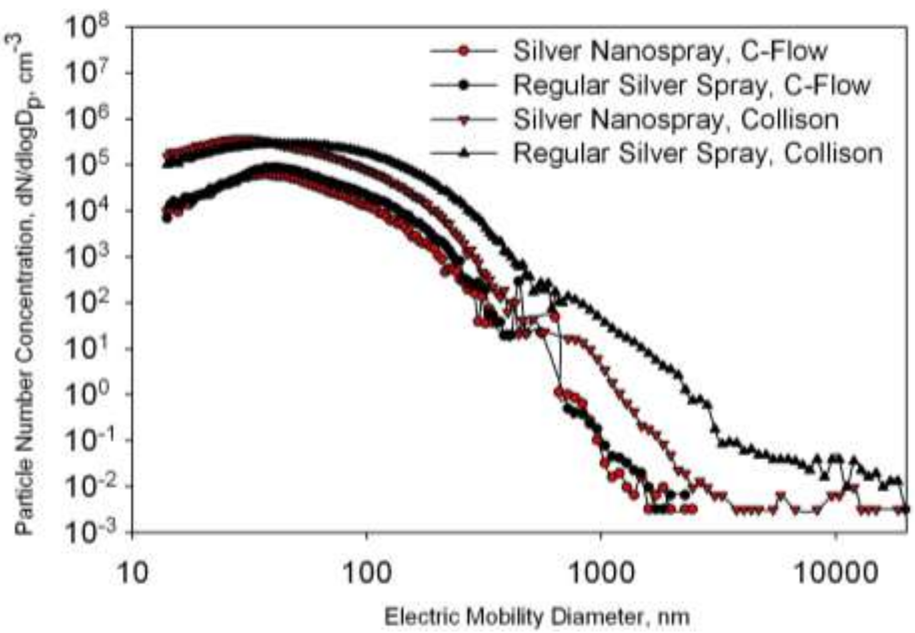
Regular Hair Spray



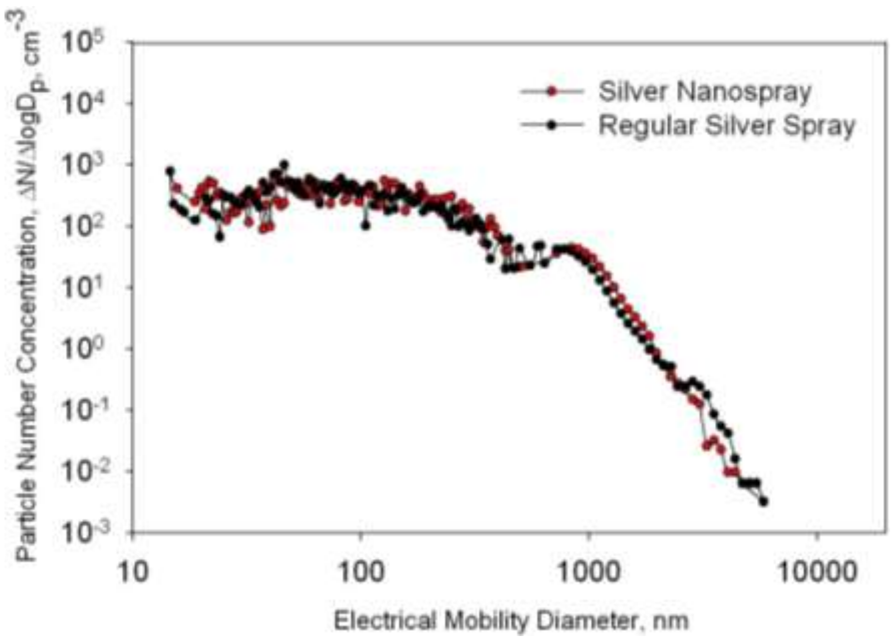
Regular Facial Spray

Results: Consumer Sprays

- The size distributions of aerosol particles and droplets likely to be inhaled during product application are different depending on the spraying technique



Using nebulizers



Handheld sprayer; Mannequin sampler

Selected Results: Nano Consumer Sprays

Product / Method	TEM	C-Flow Nebulizer Mode Diameter	Collison Nebulizer Mode Diameter
Silver Nanospray	**3 - 65 nm**, single particles and agglomerates, spheroidal, solid, beam insensitive	**37 nm**	**30 nm**
Facial Nanospray	No particles detected	**98 nm**	**61 nm**
Hair Nanospray	No particles detected	311 nm	No data (foaming)
Disinfectant Nanospray	**71** - 214 nm, single particles, spheroidal, solid, beam insensitive	**85 nm**	No data (foaming)
Skin Hydrating Nanomist	No particles detected	157 nm	113 nm

Results: Regular Consumer Sprays

Product / Method	TEM	C-Flow Nebulizer Mode Diameter	Collison Nebulizer Mode Diameter
Regular Silver Spray	**<3** - 435 nm, agglomerates and single particles, various shapes, solid, beam insensitive	**41 nm**	41 nm
Regular Facial Spray	**82** - >6000 nm, single particles and agglomerates, spheroidal and elliptical, beam sensitive	102 nm	No peak (concentration below water background)
Regular Hair Spray	**16.5** – 683 nm, single particles and agglomerates (two types), spheroidal, solid, beam insensitive	429 nm	334 nm
Regular Skin Hydrating Mist	146 - >2500 nm, single particles and agglomerates, spheroidal and elliptical, beam sensitive	102 nm	No peak (concentration below water background)

Tested Cosmetic Powders

Product	Purpose**
Nanopowder M*	Moisturizer
Nanopowder D*	Blusher
Nanopowder K*	Sunscreen
Powder F	Blot Powder
Powder G	Blot Powder
Powder E	Cosmetic Powder

*Nanoproduct as per the Woodrow Wilson Nanotechnology Consumer Products Inventory
**As per manufacturer

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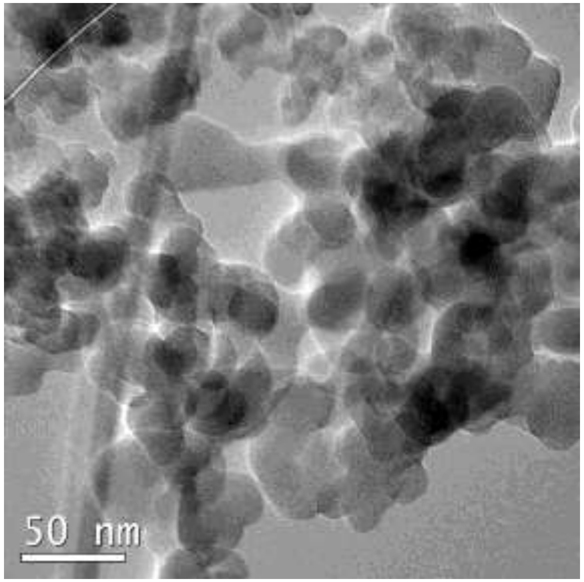
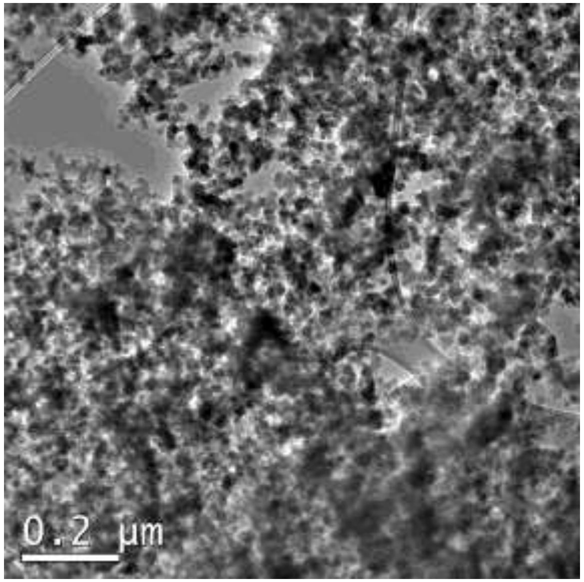
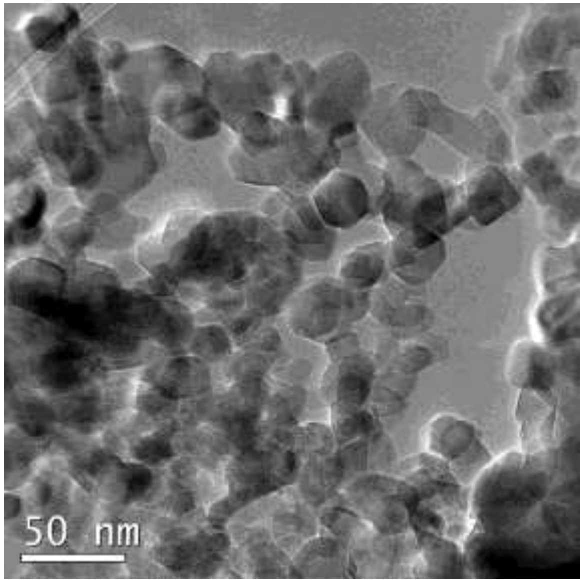
Cosmetic Powders, Confirmed as Nano by TEM

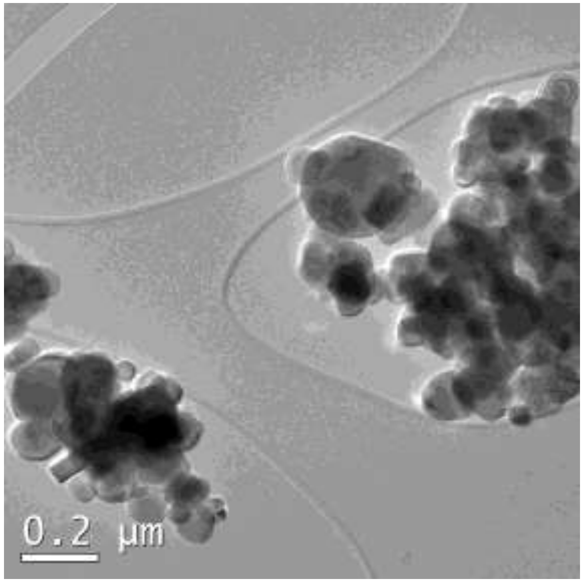
Nanopowder M
(Moisturizing Powder)





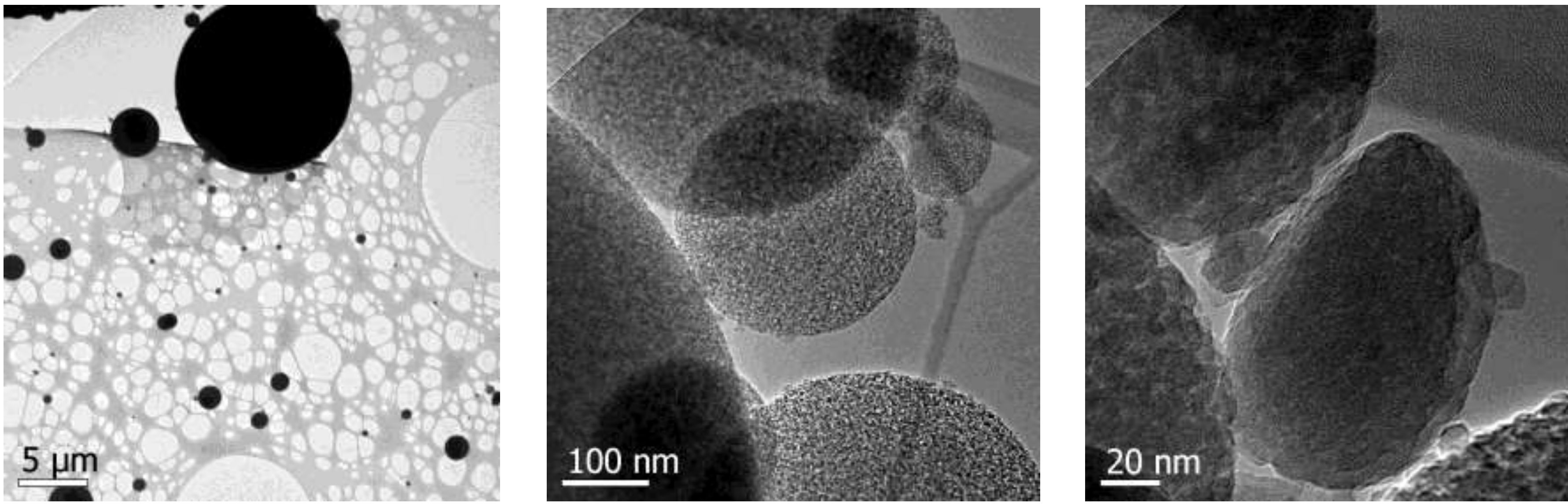
Nanopowder K
(Sunscreen)





Cosmetic Powders, Confirmed as Nano by TEM

Regular Powder E (Cosmetic Powder)



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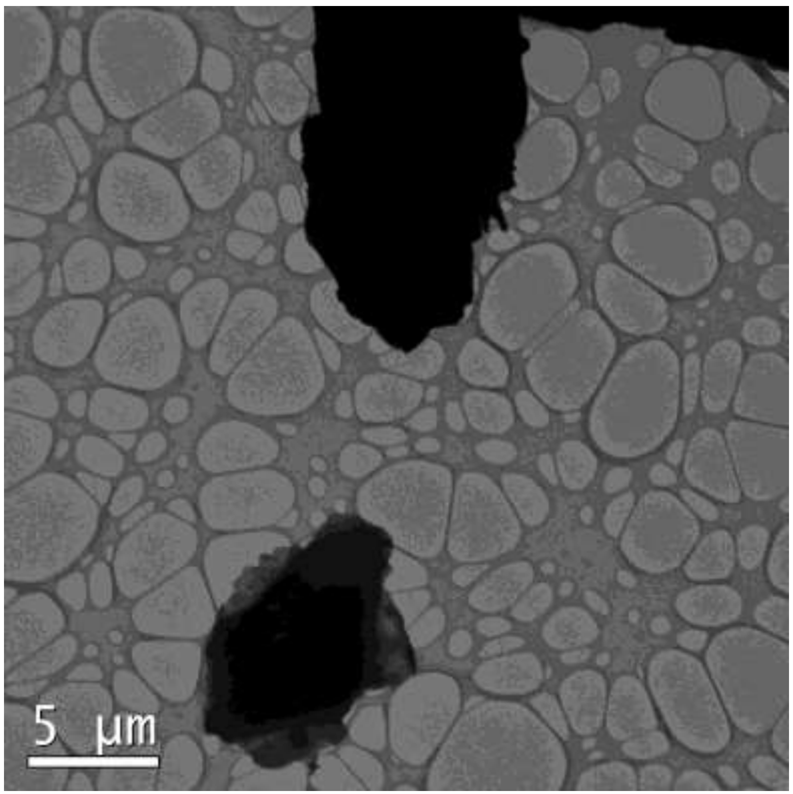
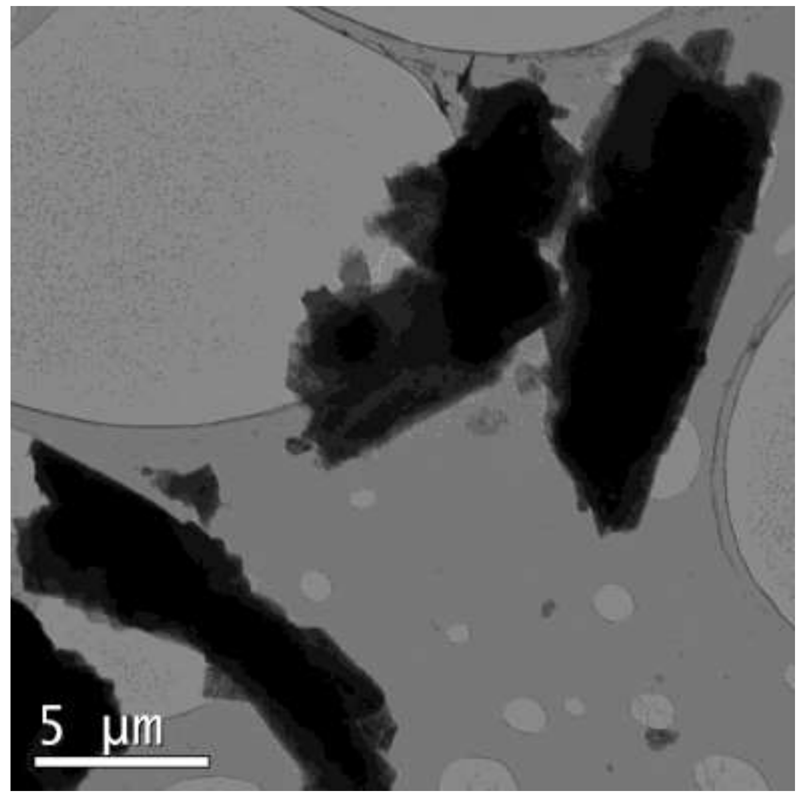
Cosmetic Powders, NOT Shown as Nano by TEM

- Similarities between certain nano and regular cosmetic powders;
- The “Nano” status of a product does not necessarily mean it contains detectable nanoparticles.



Nanopowder D (Blusher)



Regular Powder G (Blot Powder)

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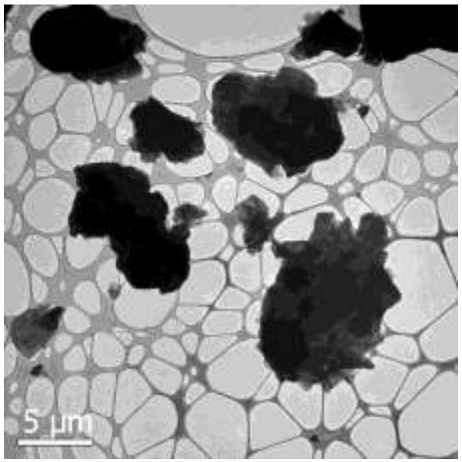
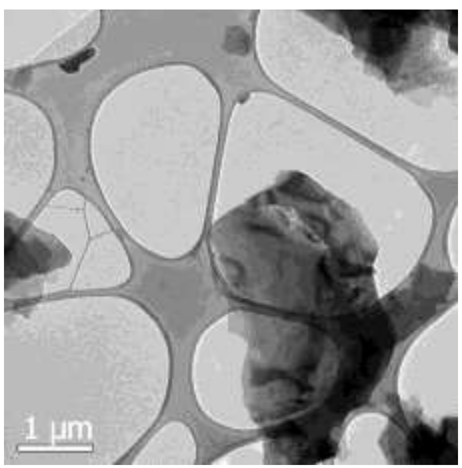
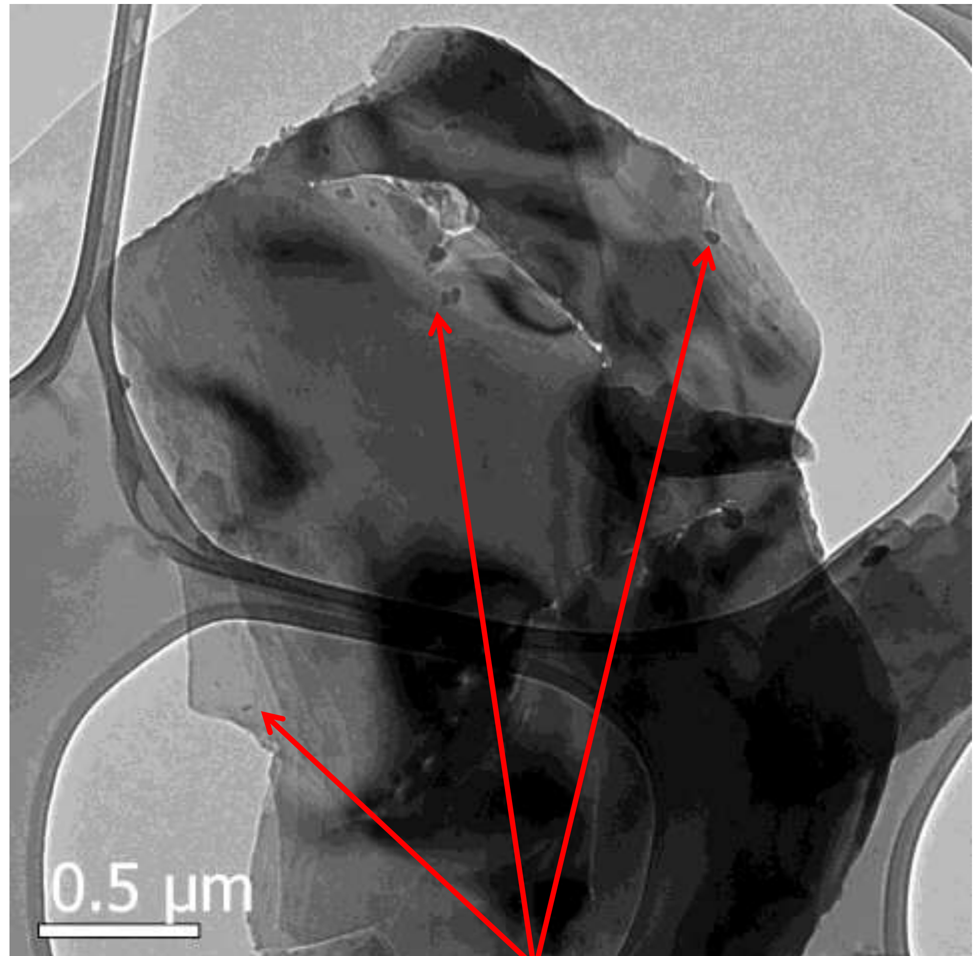
Cosmetic Powders, a Special Case – by TEM

Regular Powder F (Blot Powder)







Nanoscale inclusions, unclear if on the surface or inside larger particles

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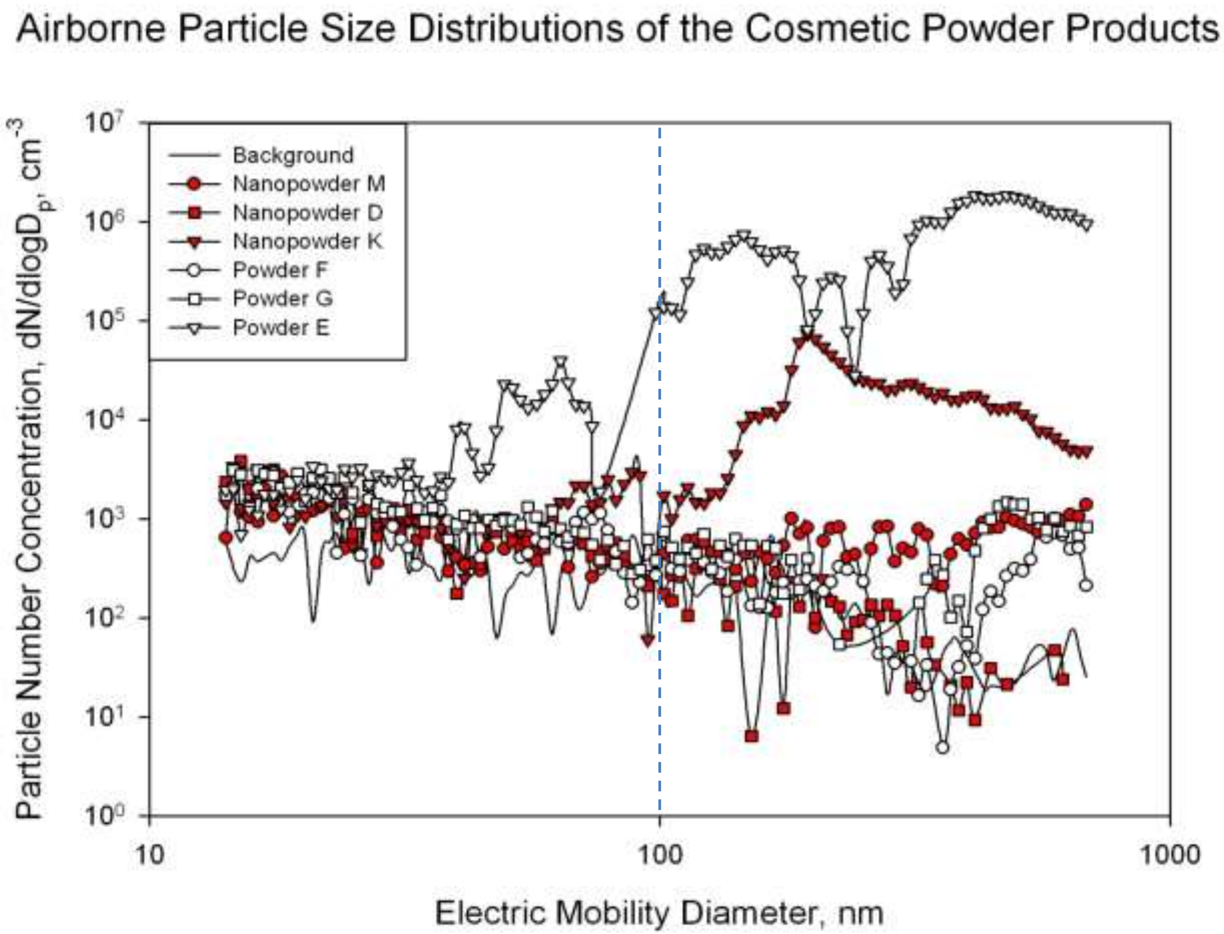
Results: Cosmetic Powders (TEM)

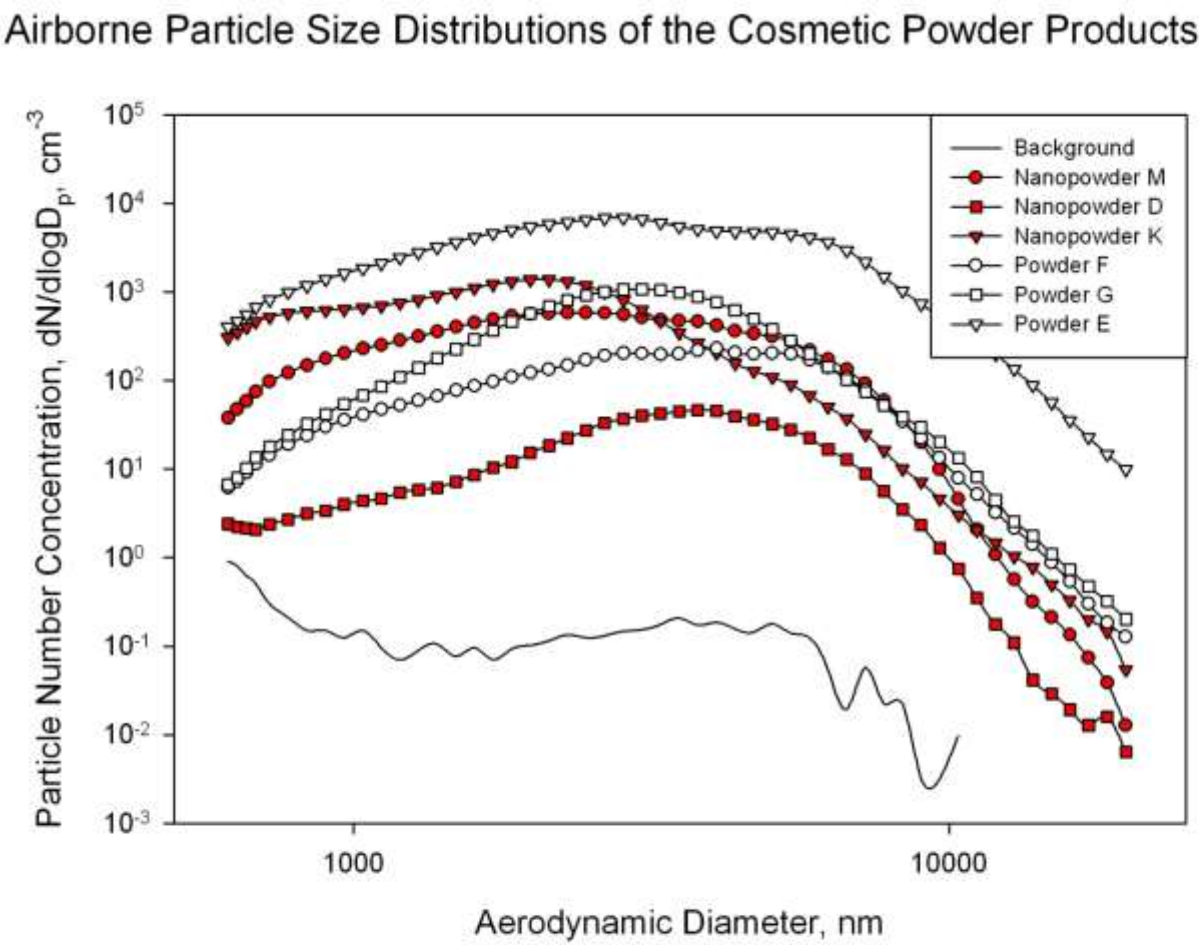
Product	TEM Range of Particle Diameters, Agglomeration, Shape, Structure, Electron Beam Sensitivity	Presence of particles <100 nm
Nanopowder M	**6 – 45 nm**	No separate, **all particles are <100 nm and agglomerated**
Nanopowder D	> 5 µm, single particles , irregular, solid, beam insensitive	No separate, no agglomerated
Nanopowder K	**7 nm** - > 3 µm, only agglomerates, angular spheroidal, solid, beam insensitive	No separate, **many agglomerated**
Powder F	**12 nm** – > 8.8 µm, single particles and agglomerates, angular composite, beam insensitive	No separate, **many in composites within large particles**
Powder G	**62.5 nm** – > 10 µm, single particles and agglomerates, irregular, solid, beam insensitive	**Very few** separate, unclear if larger particles are or are not agglomerates of nanoparticles
Powder E	**23.3 nm** – > 12.8 µm, single particles and agglomerates, spheroidal, solid, beam insensitive	No separate, **many agglomerated and attached** to the surface of large particles

Results: Cosmetic Powders



- In the nanosize range of the **SMPS** (14.1 nm – 98.2 nm), the aerosol particle size distribution for 4 cosmetic powders was very similar. **<u>Nano</u>powder K and especially <u>Regular</u> Powder E differed.**

Results: Cosmetic Powders



- In the **APS** measurement range (0.6 – 19.8 µm), the simulated inhaled particle concentrations resulting from the application of different powders **differed substantially from each other**.

Results: Cosmetic Powders (SMPS, APS)

Product	Purpose**	SMPS, Mannequin Head Sampler: Mode(s) Diameter	APS, Mannequin Head Sampler: Mode Diameter
Nanopowder M	Moisturizer	Not prominent **< 100 nm**	2.5 µm
Nanopowder D	Blusher	Not prominent < 100 nm	3.8 µm
Nanopowder K	Sunscreen	**88.2**, 194.6 nm	2.1 µm
Powder F	Blot Powder	Not prominent **< 100 nm**	4.0 µm
Powder G	Blot Powder	Not prominent **< 100 nm**	3.0 µm
Powder E	Cosmetic Powder	**63.8**, 145.9, 414.2 nm	2.8 µm

Nanomaterial Dose Assessment

- Performed for the cosmetic powders
  - Calculated for a **typical consumer** – a female 18 – 60 years old
  - Covered the total **14 nm – 20 µm** aerosol particle size range
  - Calculated how much particulate matter (PM) would be inhaled and how much would deposit in different regions of the human respiratory system: "**inhaled dose**" and "**deposited dose**" per 1-minute cosmetic powder application

http://www.pro-it-service.com/en/registration_and_user_profiles_with_movable_type.html
http://www.scarletcleaning.com/pages/commercial.html
http://phelan.en.china.cn/
http://www.superstock.com/stock-photos-images/1532R-38004

Methods: Nanomaterial Dose Assessment

Inhaled Dose

$$I_{inh} = f_{nano} \cdot C_{inh} \cdot IH_{air} \cdot T_{contact} / Bw \qquad (1),$$

where:
I_{inh} – inhaled dose of particulate matter per application **(ng/kg bw/application)**;
C_{inh} – mass concentration of particulate matter in inhaled air (ng/L);
IH_{air} – inhalation flow rate for a given gender/activity scenario (L/min);
$T_{contact}$ – duration of contact per application (min);
Bw – body weight (kg);
f_{nano} – mass fraction of nanomaterial(s) in the inhaled aerosol.

$C_{inh} = IF \cdot C_{air}$
where:
C_{air} – *mass concentration of aerosol particulate matter in the personal breathing cloud;*
IF – inhalability fraction.

It is assumed that the concentration of nanomaterial(s) in the initial product is proportional to the concentration of nanomaterial in the inhaled aerosol.

Equation (1) developed based on Hansen, S.F. et al. (2008) Categorization framework to aid exposure assessment of nanomaterials in consumer products. *Ecotoxicology*, 17: 438-447

Methods: Nanomaterial Dose Assessment

Deposited Dose = DF_{region of respiratory system} · Inhaled Dose

$$DF_{HA} = \left(\frac{1}{1+\exp(6.84+1.183\ln d_p)} + \frac{1}{1+\exp(0.924-1.885\ln d_p)} \right) \quad (4),$$

$$DF_{TB} = \frac{\left(\frac{0.00352}{d_p}\right)\left[\exp\left(-0.234(\ln d_p+3.40)^2\right)+63.9\exp\left(-0.819(\ln d_p-1.61)^2\right)\right]}{1-0.5\left(1-\frac{1}{1+0.00076 d_p^{2.8}}\right)} \quad (5),$$

$$DF_{AL} = \frac{\left(\frac{0.0155}{d_p}\right)\left[\exp\left(-0.416(\ln d_p+2.84)^2\right)+19.11\exp\left(-0.482(\ln d_p-1.362)^2\right)\right]}{1-0.5\left(1-\frac{1}{1+0.00076 d_p^{2.8}}\right)} \quad (6),$$

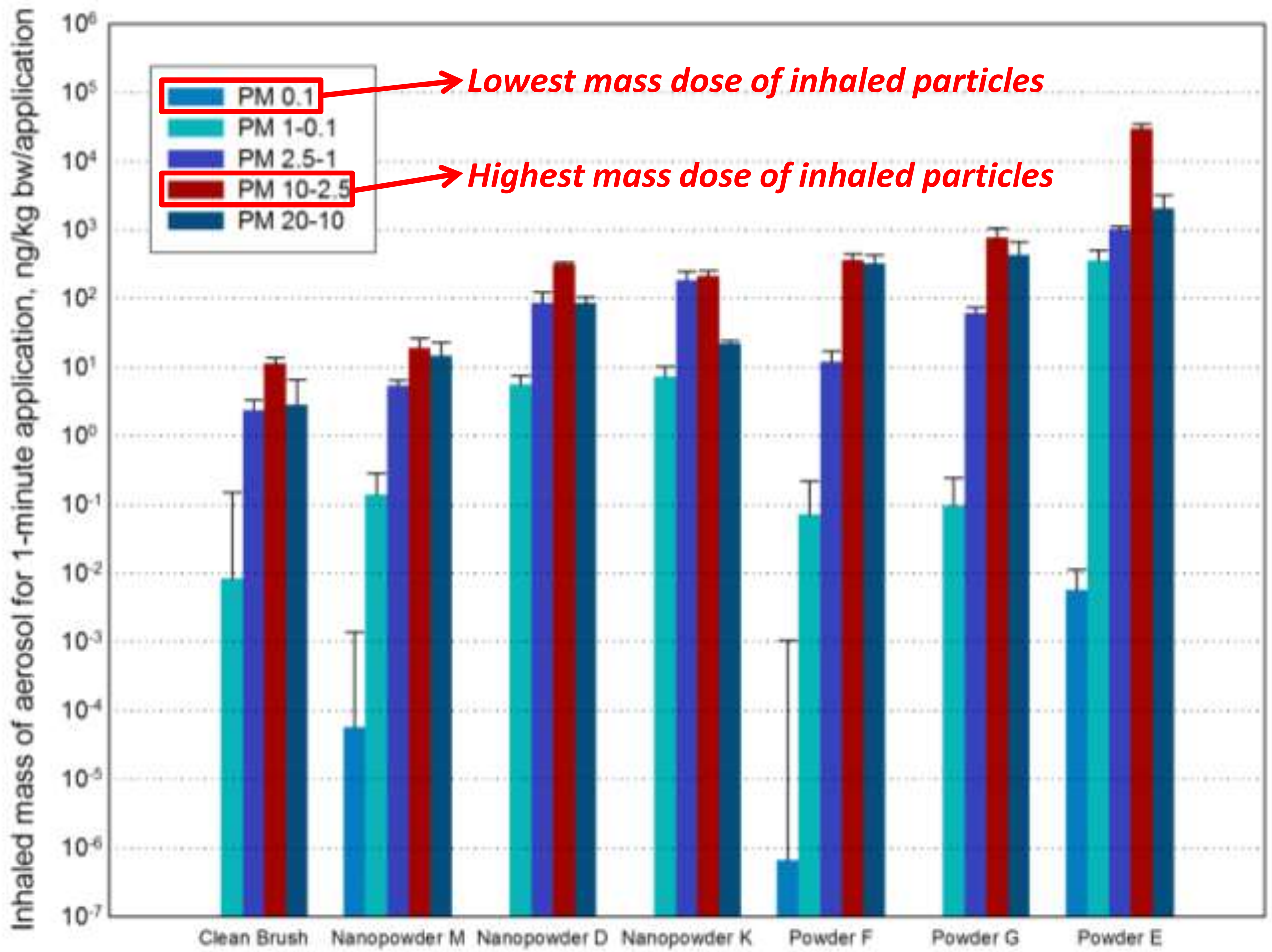
$$DF = \left(0.0587 + \frac{0.911}{1+\exp(4.77+1.485\ln d_p)} + \frac{0.943}{1+\exp(0.508-2.58\ln d_p)} \right) \quad (7)$$

where:
d_p – particle size (µm);
DF_{HA} – deposition fraction for the head airways;
DF_{TB} – deposition fraction for the tracheobronchial region;
DF_{AL} – deposition fraction for the alveolar region;
DF – the total deposition fraction of the inhaled particulate matter.

Equations (2, 4, 5, 6, 7) from Hinds, W.C. (1999) Aerosol technology: properties, behavior, and measurement of airborne particles. New York, NY: John Wiley & Sons, Inc., 483pp

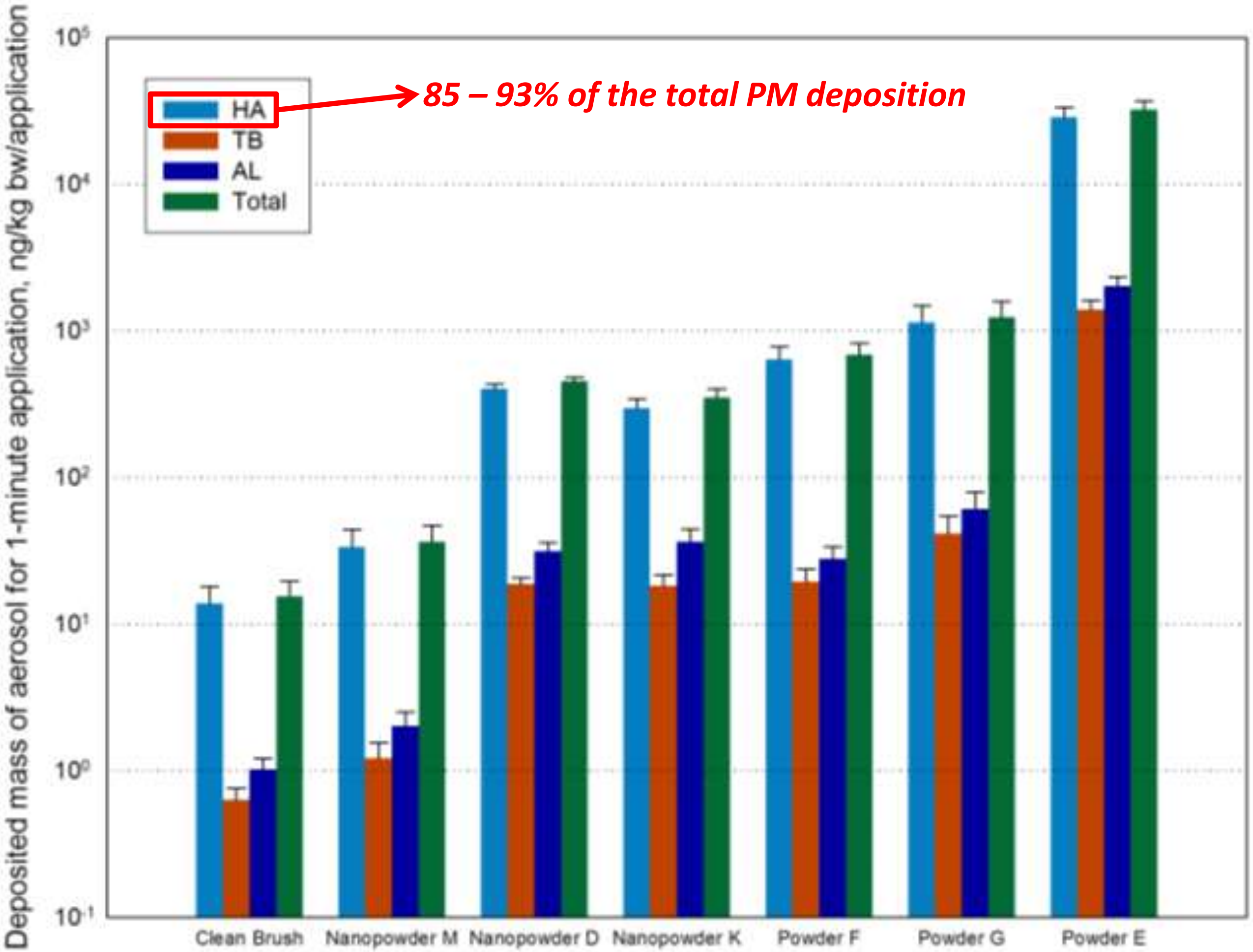
Results: Nanomaterial Dose Assessment

Inhaled Dose from 1-minute application of cosmetic powders



Results: Nanomaterial Dose Assessment

Deposited Dose from 1-minute application of cosmetic powders



→ *Deposited Dose as Percentage of Total PM Deposition*

Conclusions I

- Exposure to ultrafine including engineered nanoparticles can cause or contribute to adverse health effects;
- Nanoparticles can be found ubiquitously in consumer products, claimed to contain nanomaterials as well as "regular" (not marketed as nanotechnology-based) products;
- Use of nanotechnology-based consumer products can lead to inhalation exposure to single and agglomerated nanoparticles;
- Existing sampling and analytical techniques do allow collection and characterization of ultrafine particles including engineered nanomaterial particles;

Conclusions II

- By mass, inhaled dose of the aerosol fractions above 100 nm is much higher (3-8 orders of magnitude) than of individual nanoparticles or their agglomerates **smaller than 100 nm (nanoagglomerates)**;

- By mass, between **85 and 93%** of the total deposition of inhaled particulate matter occurred **in the HA region** of the human respiratory system in the case of the cosmetic powders we investigated;

- **The head airways and, to a lesser extent, the tracheobronchial region** are important in addition to the alveolar region as the **deposition sites** of nanomaterial-containing particulate matter.

Conclusions III

- The particle size distributions in the products and the derived aerosol are different;

- For the consumer spray products, different spraying (aerosolization) techniques produce different aerosol particle size distributions;

- It is currently hard or impossible to determine if nanoparticles, found in the products are engineered or derived from natural ingredients, especially when manufacturers do not disclose this information;

- Both natural and engineered nanomaterials are currently subject of the "**U.S. EPA Nanotechnology Reporting and Record-keeping Requirements Rule**" under TSCA section 8(a) and will likely be subject of future regulations.

Conclusions IV

- The European Union already regulates nanotechnology-based cosmetic products. It is unclear if and how the US will follow in the EU's footsteps, but it may so happen that the issue of inhalation exposure from cosmetic products in general could become subject of regulations in the US.

- Both natural and engineered nanomaterials are currently subject of the "**U.S. EPA Nanotechnology Reporting and Record-keeping Requirements Rule**" under TSCA section 8(a) and will likely be subject of future regulations.

Questions?

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