Alternative Metrics for the Physicochemical Characterization of UFP

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AIME: provide a tool box of relevant instruments for risk assessment, Characterisation, toxicity testing and exposure measurements of MNMs

OECD TG	Topic
105	Solubility in water
106	Adsorption/desorption (soil)
107/117/123	Partition coefficient
108	Complex formation in water
109	Density of solids
110	Granulometry
112	Dissipation constant
115	Surface tension of aqueous solutions

Impact on in vitro and in vivo toxicity tests: **Metrics and Dosage**

Solubility in water

105

Adopted:
27.07.95

OECD GUIDELINE FOR THE TESTING OF CHEMICALS

Adopted by the Council on 27th July 1995

Water Solubility

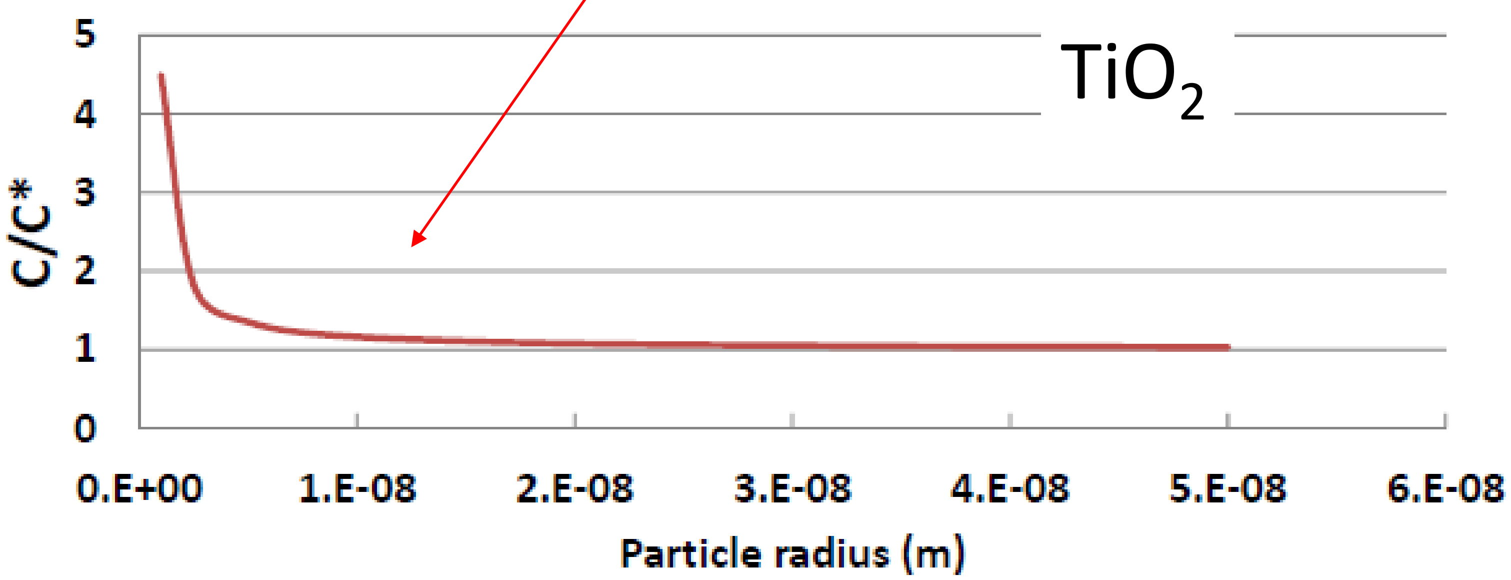
DEFINITIONS AND UNITS

4. The water solubility of a substance is the **saturation mass concentration** of the substance in water at a given temperature.

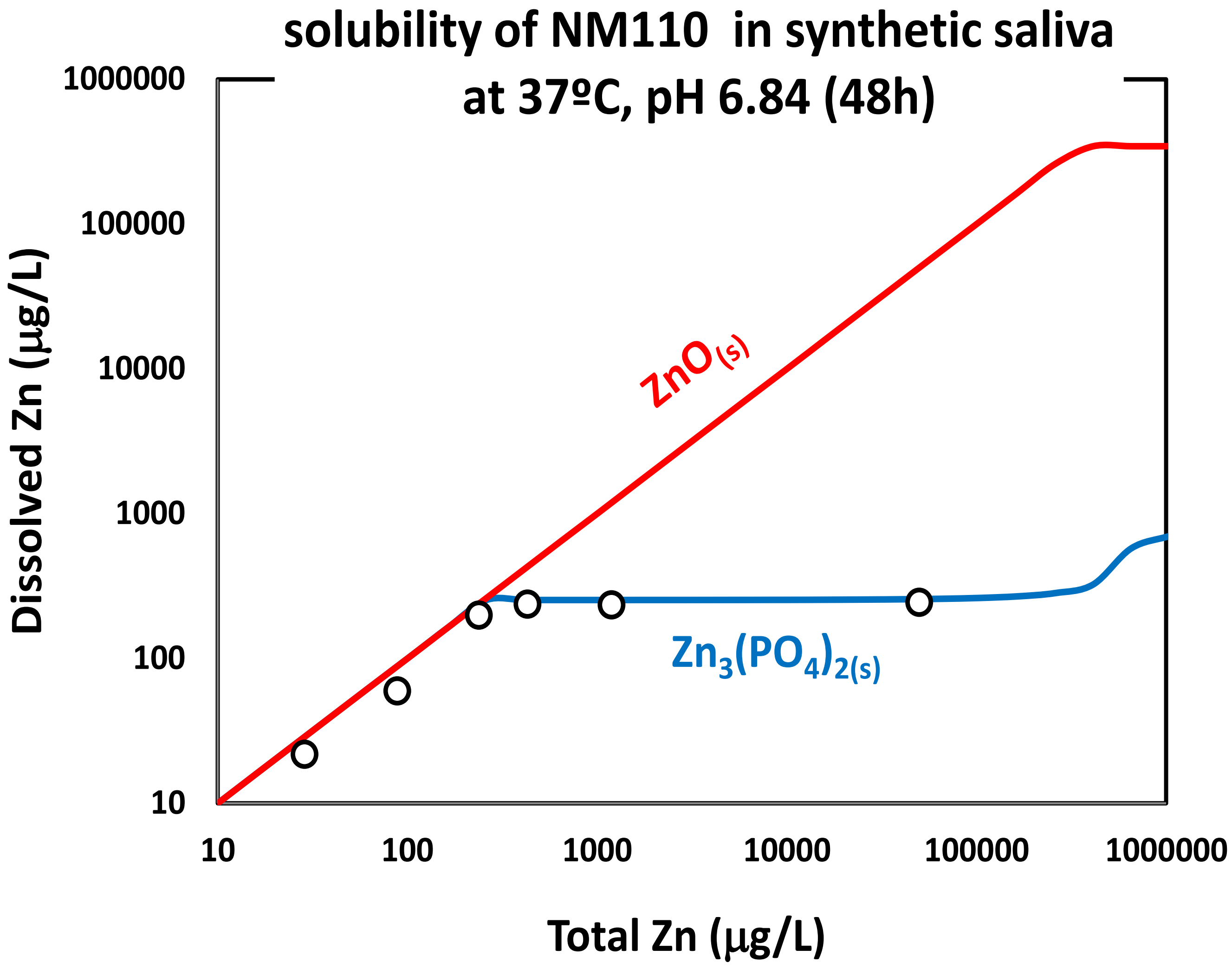
Solubility of Nanoparticles depends from size (Ostwald–Freundlich)

$$\ln\frac{\{C_{i(\mathrm{sat})}\}}{\{C^*_{i(\mathrm{sat})}\}} = \frac{V_i^*}{RT}\frac{2}{3}\gamma^{\mathrm{SL}}\frac{4\pi r^2}{\frac{4}{3}\pi r^3} = \frac{V_i^*}{RT}\frac{2\gamma^{\mathrm{SL}}}{r}$$

Commercial powder as used in sun screen (25 nm)



Measurement of solubility of Nanomaterial following the OECD TG 105 is in principle not possible


solubility of NM110 in synthetic saliva
at 37ºC, pH 6.84 (48h)
Dissolved Zn (µg/L)
1000000
100000
10000
1000
100
10
ZnO(s)
Zn3(PO4)2(s)
10
100
1000
10000
100000
1000000
Total Zn (µg/L)

Method for determination of the solubility kinetic

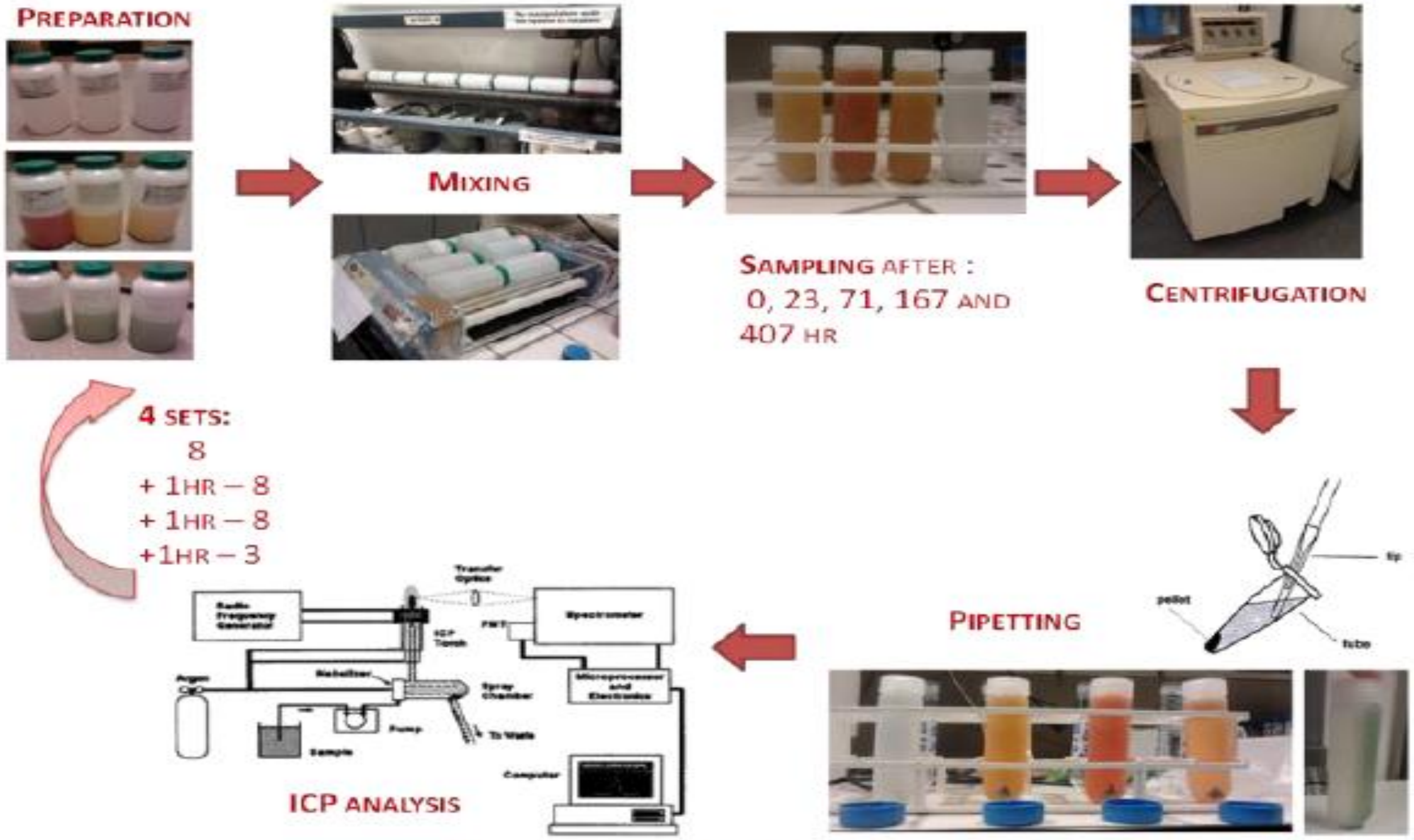


Figure 22: Protocol summary

Particle size

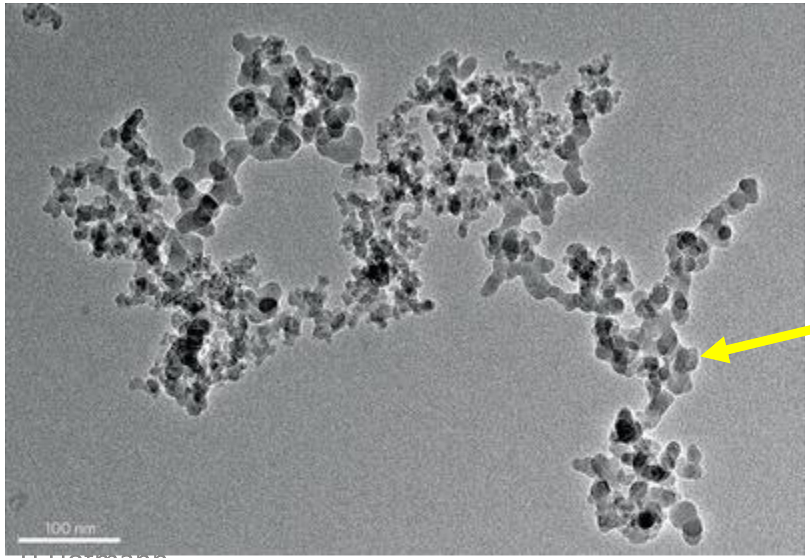
- No individual technique can satisfy a meaningful characterization.
- A combination of methods for primary particle size measurement and methods for hydrodynamic size measurement is necessary.
- **For primary particle size measurement, transmission electron microscopy techniques is the appropriate method.**
- In the case of granulometry of NM dispersions, there are 4 available techniques based on robust detection technologies: Centrifugal Liquid Sedimentation (CLS), **Dynamic Light Scattering (DLS),** Nanoparticle Tracking Analysis (NTA), Coulter counter
- Each technique requires proper calibration standards for the desired zones of interest.
- Use of a common dispersion protocol is mandatory

SOP's are established and in validation phase

A common European approach to the regulatory testing of nanomaterials

OECD TG109 Density of solids

- ***Poured density***, Schüttdichte, densité apparente,
- **Tapped density**, Stampfdichte, densité après tassement,
- **Density,** (Wahre) Dichte (Massendichte), densité,
- **New: Density of agglomerates, skeletal density, effective density**



Primary particle

Density

- The only method which gives reproducible results: He-Pycnometer

DRAFT

Version November 26th 2015

Protocol for true density measurement with He-Pycnometer

Method

This method measures the volume of gas (Helium) displaced by a known mass of powder, and gives the true density of the material. The sample must be completely dried.

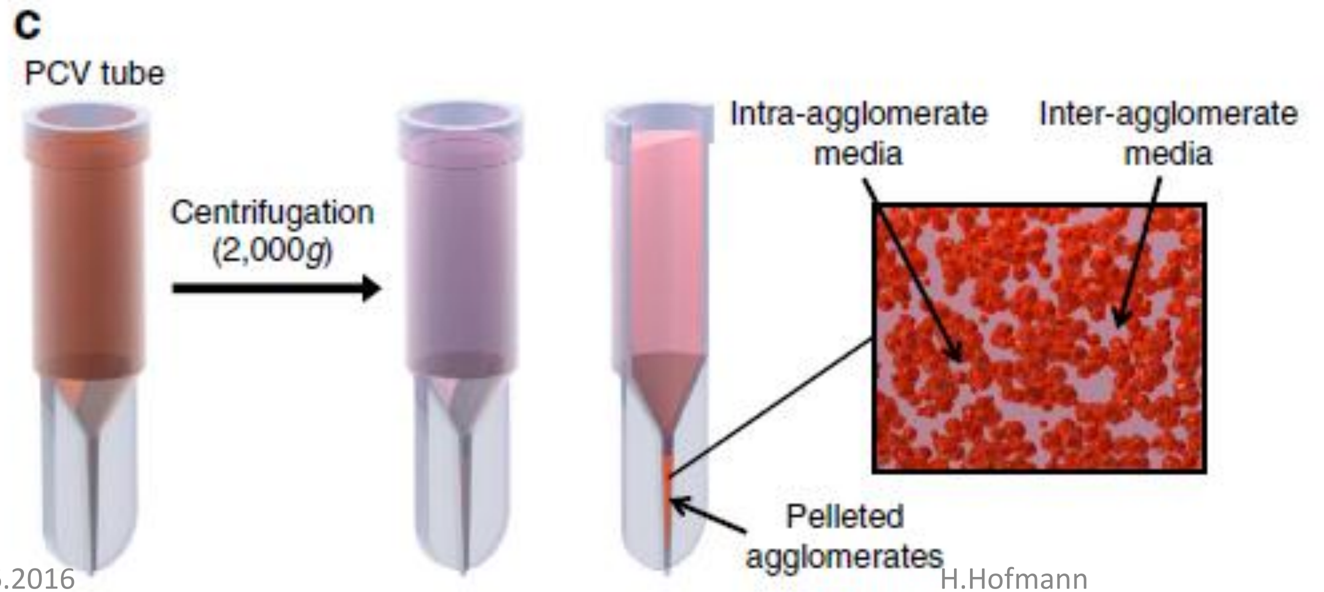
Densities of agglomerates

Received 15 Jul 2013 | Accepted 26 Feb 2014 | Published 28 Mar 2014

DOI: 10.1038/ncomms4514

Estimating the effective density of engineered nanomaterials for *in vitro* dosimetry

Glen DeLoid[1,*], Joel M. Cohen[1,*], Tom Darrah[2], Raymond Derk[3], Liying Rojanasakul[3], Georgios Pyrgiotakis[1], Wendel Wohlleben[4] & Philip Demokritou[1,*]



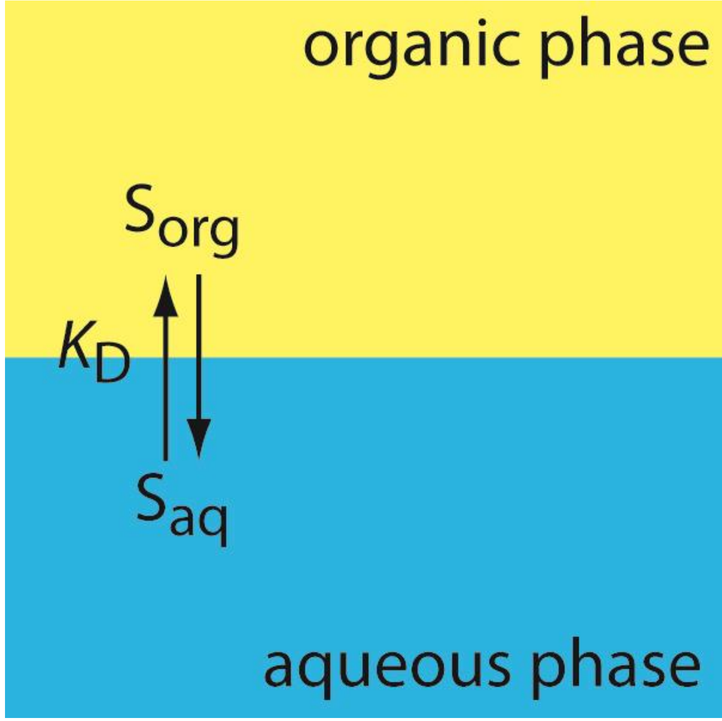
OECD TG 107/117/123 Partition coefficient (n-octanol/water)

Several reasons exists why for nanoparticles this Guideline is not applicable:

- nanoparticles forms colloidal dispersions, which are thermodynamically unstable.
- The results of a test following the OECD guidelines will depend strongly from the sample preparation and the energy added during the shaking process
- The colloidal stability influence the behaviour in the liquid

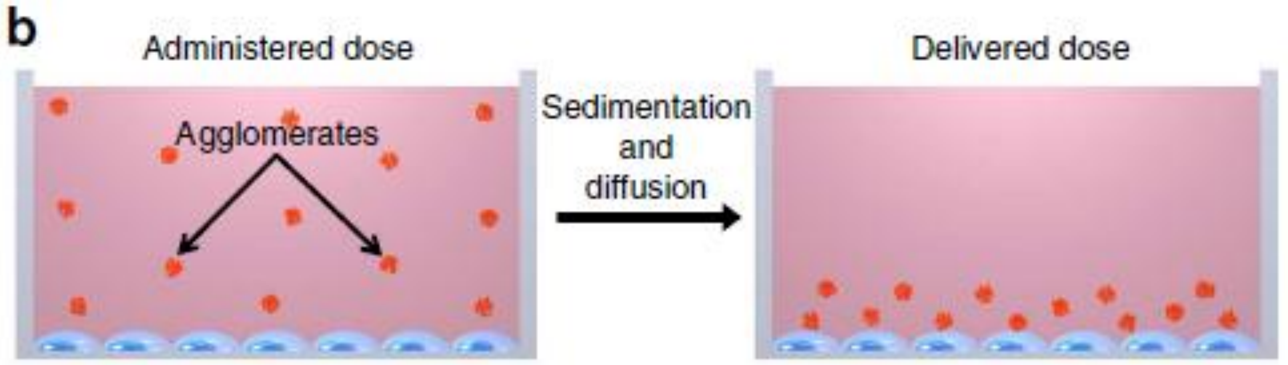
Conclusion:

The OECD Guideline is not applicable to nanoparticle suspension. The guideline has to be replaced by a determination of the colloidal stability of the nanoparticles in different liquids.



Antonia Praetorius, Nathalie Tufenkji,Kai-Uwe Goss, Martin Scheringer,Frank von der Kammer and Menachem Elimelech, Environ. Sci.: Nano, 2014, 1, 317 Groupe Prof. Hungerbühler ETHZ

Metrics and Dosage



Mass/area !!!

Administrated mass

Deposited mass

$$v_{sed} = \frac{2g(\rho_{NP} - \rho_{media})d^2}{9\mu}$$

All particles which are in a distance of t x v_{sed} could reach the cell membrane.

$$c / c_0 = erf(x / 2\sqrt{Dt})$$

$$M(t) = 2c_0\sqrt{\frac{Dt}{\pi}}$$

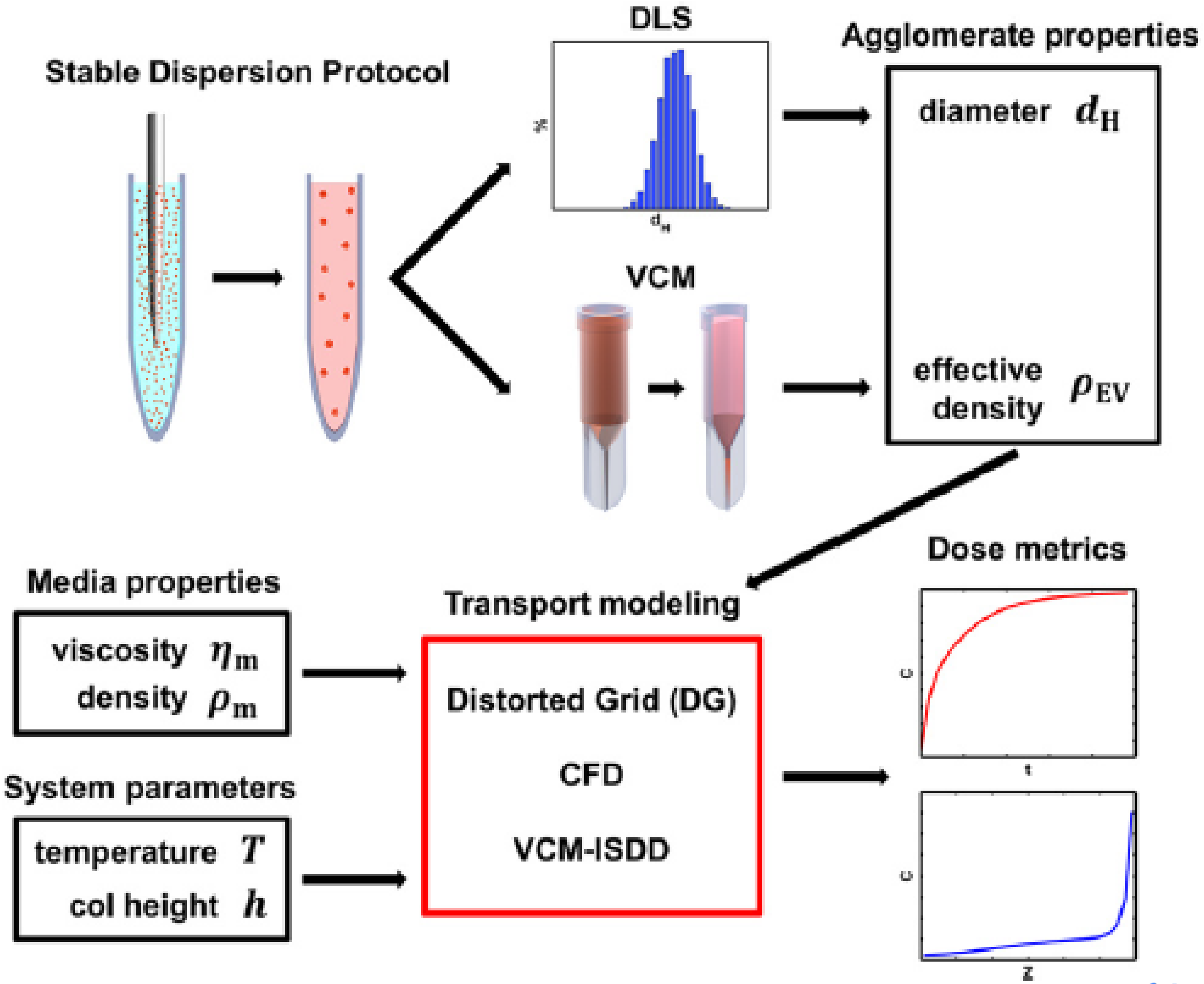
Sticking coefficient =1, newer model with SC <1

$$\frac{\partial n}{\partial t} = A\frac{\partial^2 n}{\partial x^2} - B\frac{\partial n}{\partial x}, \quad A = \frac{RT}{N6\pi\mu a};\ B = \frac{X}{6\pi\mu a} = \frac{\frac{4}{3}\pi a^3 g\delta}{6\pi\mu a} = \frac{2g\delta a^2}{9\mu},$$

Advanced computational modeling for in vitro nanomaterial dosimetry

Glen M. DeLoid*, Joel M. Cohen, Georgios Pyrgiotakis, Sandra V. Pirela, Anoop Pal, Jiying Liu, Jelena Srebric and Philip Demokritou

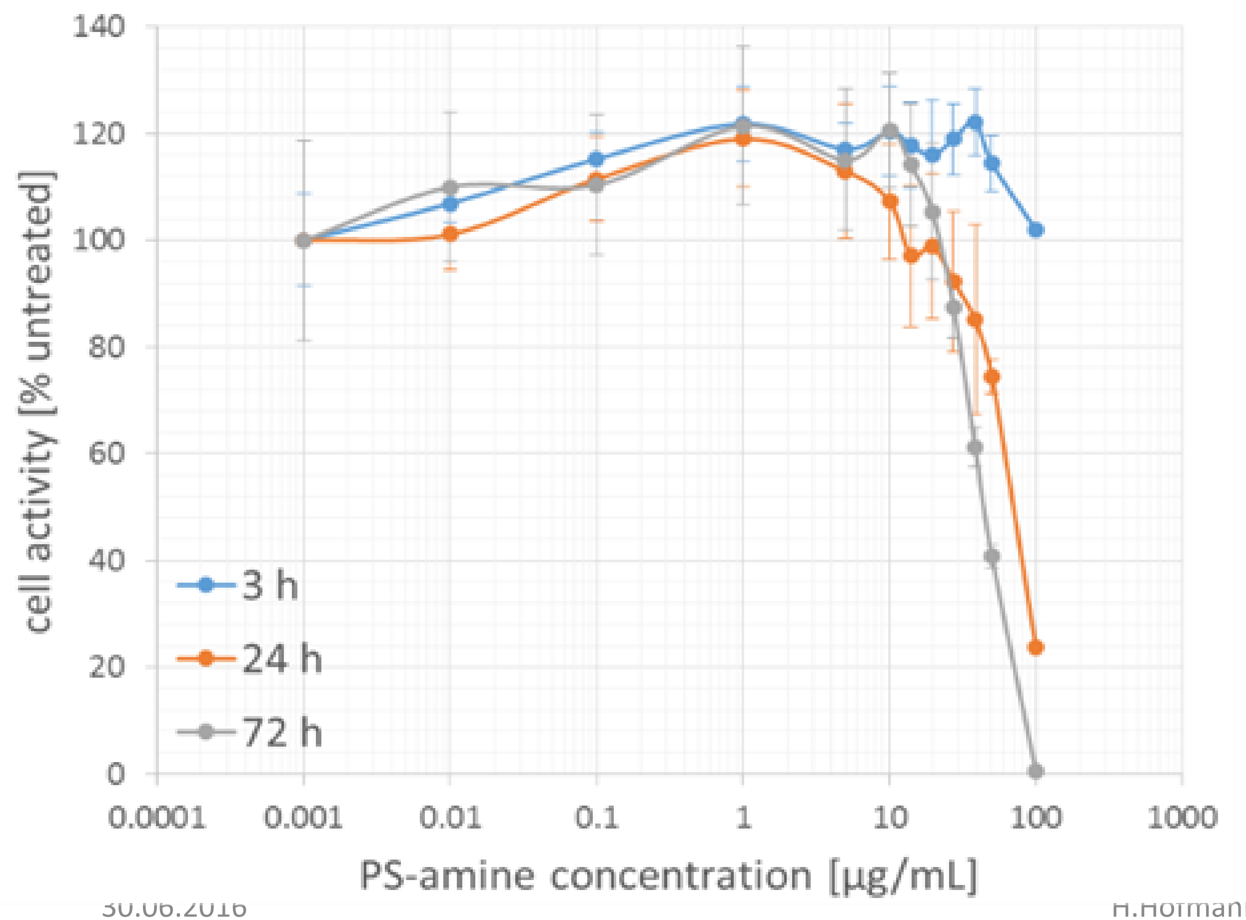
Particle and Fibre Toxicology (2015) 12:32



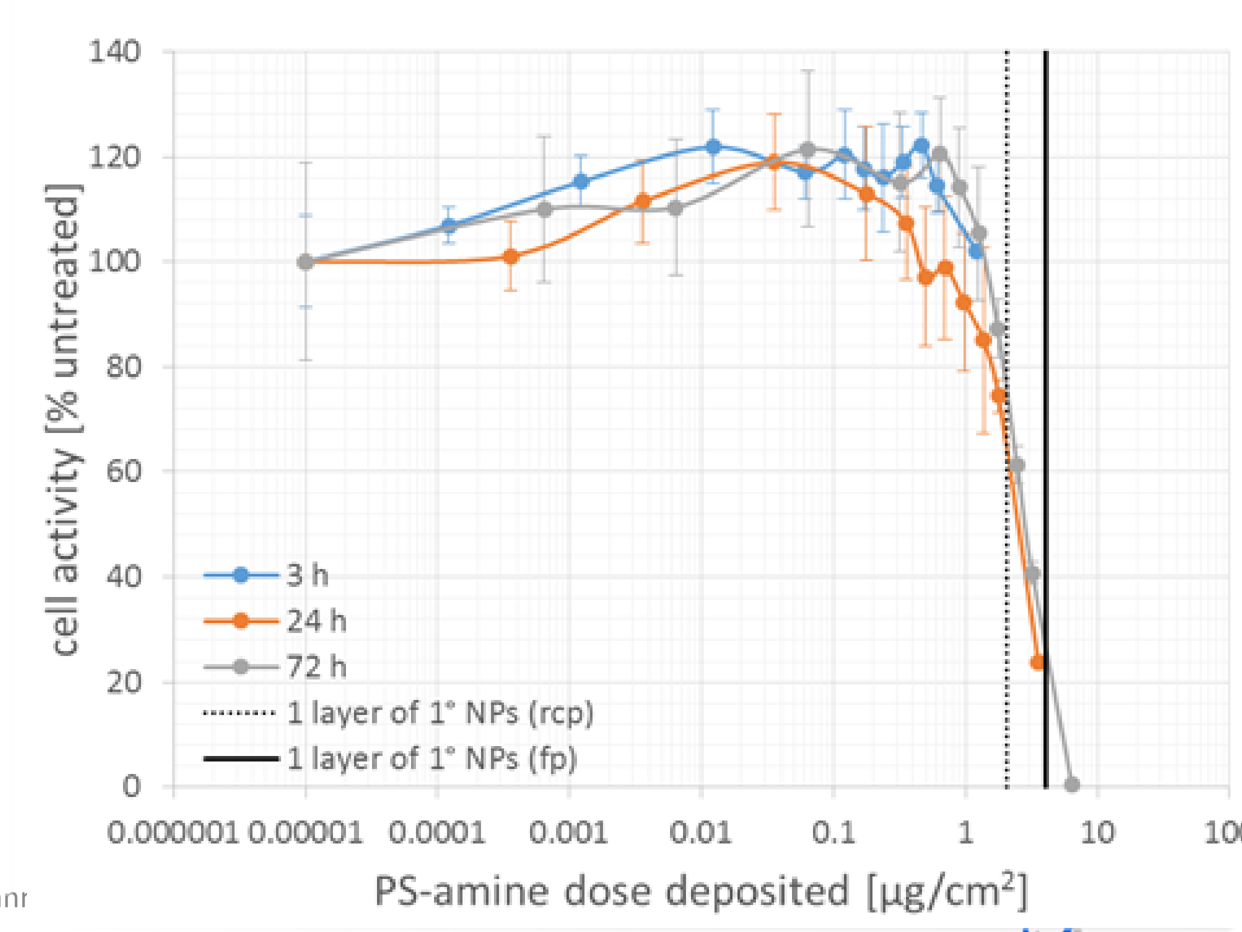
Viability A549 cells: MTS assay

Exposure to poly-styreneamine NP, 50 nm

standard metric: µg/mL

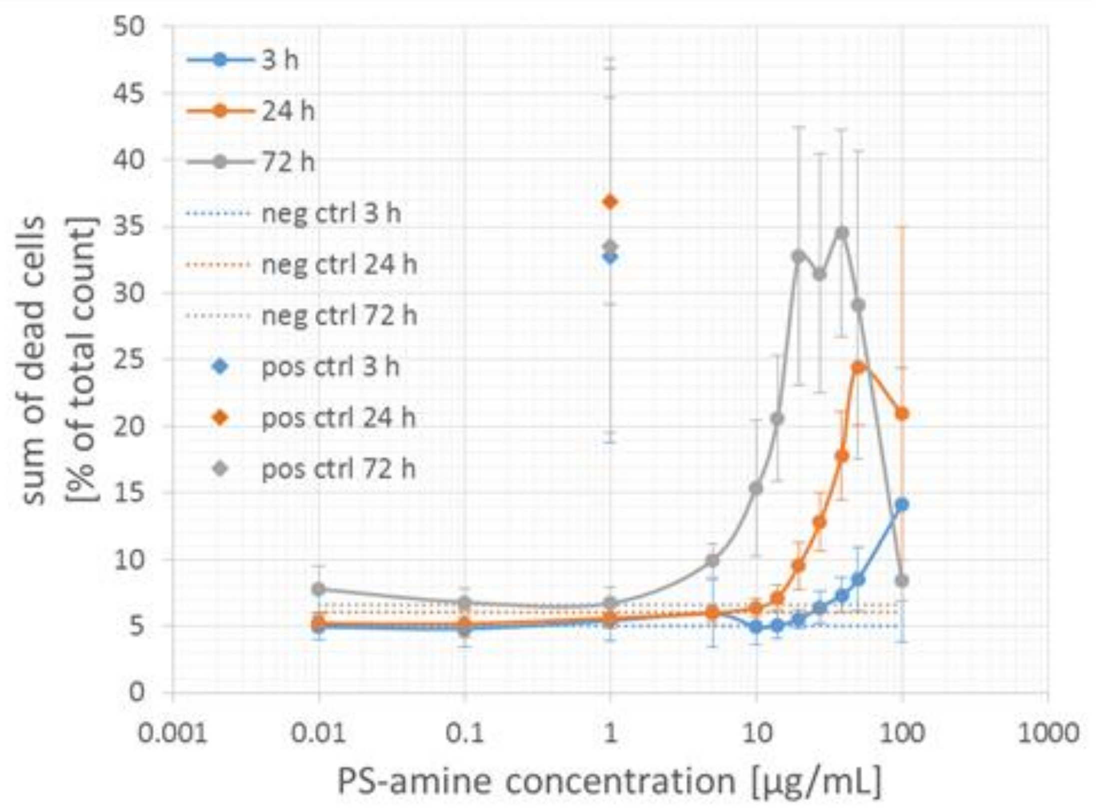


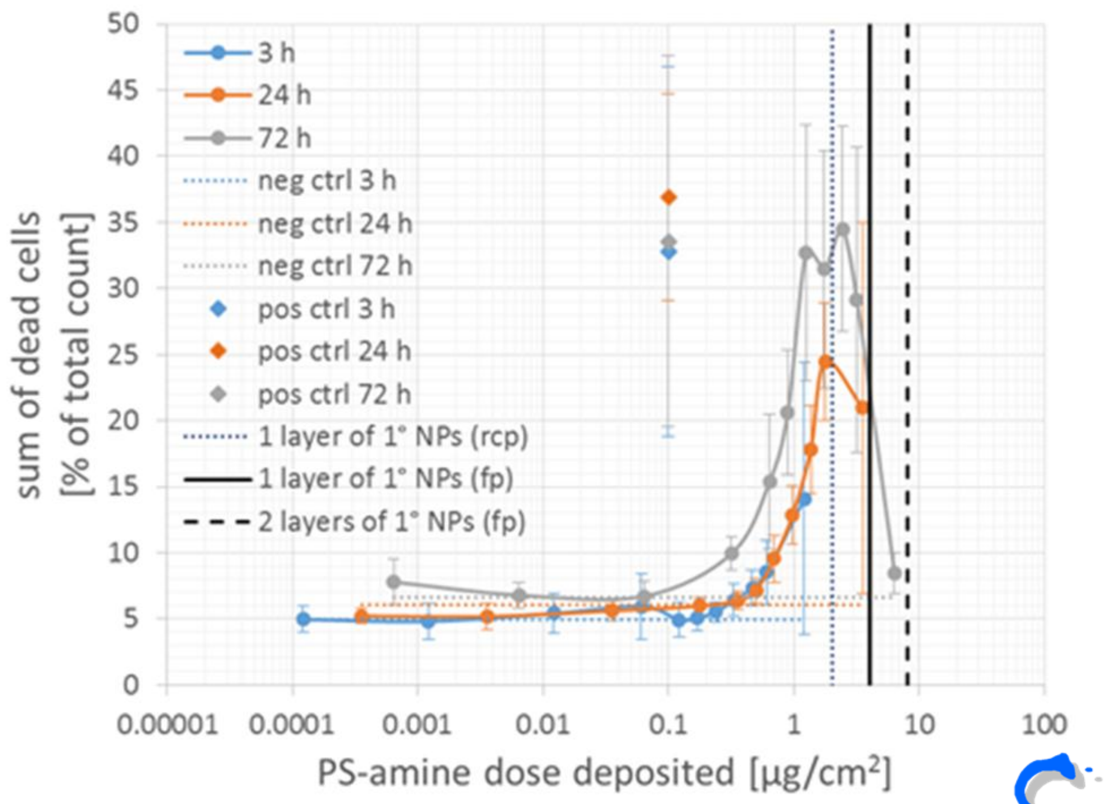
new metric: µg/cm² (ISDD)



Viability A549 cells: Annexin V/PI assay
Exposure to poly-styreneamine NP, 50nm

standard metric: µg/mL	new metric: µg/cm² (ISDD)





Conclusions

- Most of the OECD technical guidelines for physical and chemical characterization of NP needs modifications or are from a thermodynamic point of view not applicable

- Primary particles size, size distribution (shape) should be determined by TEM
- Agglomerate size and size distribution DLS or aequivqlent metods are useful (hydrodynamic diameter)
- Density of primary partilces and effective density has to be known
- For toxicity tests deposited mass/area is adequate metrics. If the particles are correctly characterized, mass could be transferred into number , surface and volume.

Thank you for your Attention

A common European approach to the regulatory testing of nanomaterials

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Carlos Rey-Castro, Josep Galcerán, Calin A. David (UdL)
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