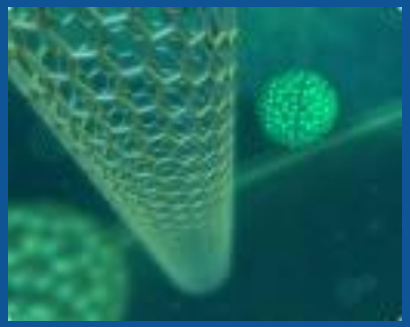
Nanogenotox Final Conference
22 February 2013
Paris, France



Perspectives on the risk assessment of nanomaterials

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Nano and Health and Consumers DG (DG SANCO)

Areas of interest for DG SANCO vis-à-vis nano include:

- ***Consumer products***
  - **No specific nano provisions in the General Product Safety Directive.**
- ***Cosmetics*** >>
- ***Medical devices*** *with nanomaterials*
  - **in Class III (the highest risk).**
  - **The Commission proposal (September 2012) for a Regulation on medical devices contains specific rules for them.**
- ***Pharmaceuticals***
  - **Authorisation of medicines applies similarly to nano containing medicines, 20 authorised to date. Further assessments are carried out as required.**
- ***Food*** >>
- ***Feed*** >>

Nano - cosmetics

The first legal instrument in the EU to contain specific rules on nanomaterials is the revised Regulation on Cosmetic Products (1223/2009).

- ***Entry into force on 11 January 2013***
- ***Applies also to products which are already on the market***

- Requires pre-market notification of information on nanomaterials

- ***Makes labelling obligatory in the list of ingredients***
- ***In risk assessment of cosmetics, nanomaterials have special attention. The Scientific Committee on Consumer Safety (SCCS) carries out these assessments.***
- ***The Commission will publish a catalogue of nanomaterials used in cosmetics, and annual status reports to the EP and Council***

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Nano – Medical

- ***Medical Devices with nanomaterials*** *are in Class III (the highest risk class). The Commission proposal, launched in September, for a Regulation on medical devices contains specific rules for them.*

- ***Pharmaceuticals****: Authorisation of medicines applies similarly to nano containing medicines, 20 authorised to date. Further assessments are carried out as required.*

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Food additives

- **Regulation 1333/2008 on food additives**

  For all **new food additives** EFSA evaluation takes into account nanotechnology.

  Previously authorised food additives are considered as new additives if there is a significant change in production methods or in the starting materials used, or if there is a change in particle size, for example through nanotechnology, and therefore they need to be evaluated and authorised.

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Food additives

- **Re-evaluation programme**

Particle size considered as part of the re-evaluation. E.g. Concerning calcium carbonate (E 170) EFSA concluded that *"the available data are sufficient to conclude that the current levels of adventitious nanoscale material within macroscale calcium carbonate would not be an additional toxicological concern"*.

Re-evaluation of silicon dioxide (E 551) to be completed by 2016 at the latest.

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Nanomaterials Risk Assessment

- **Advice of the Commission Scientific Committees**

  Opinions of the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) in 2006, 2007 and 2009

  Opinion of SCENIHR on nanodefinition in 2010

  Opinion of the Scientific Committee on Consumer Safety (SCCS) on nano-ZnO in 2012

  Guidance of the SCCS on the safety assessment of nanomaterials in cosmetics in 2012

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SCCS guidance on nanomaterials: physical chemical properties

Parameter	Description	Methods*
Surface characteristics	*Detailed information on nanomaterial surface must be provided. This should include information on surface charge (zeta potential), morphology/topography, interfacial tension, reactive sites, as well as any chemical/ biochemical modifications or coatings that could change the surface reactivity, or add a new functionality.*	*LDE, SPM, XPS, MS, RS, FTIR, NMR, AUC (for surface composition), GE, SPM, LDE, PALS (for zeta potential), Nano SIMS, SERS*
Solubility	*Information on solubility of the nanomaterial in relevant solvents and partitioning between aqueous and organic phase (e.g. log Kow for organic nanomaterials, and surface modified inorganic nanomaterials) must be provided.* ***Dissolution rates in relevant solvent for soluble and partially-soluble nanomaterials*** *should also be provided. Information on hygroscopicity of powders should also be provided.*	*Solubility/ dissolution rate in water and other solvents*
Surface area	*Information on BET specific surface area of the nanomaterial, and volume specific surface area (VSSA) must be provided (see Kreyling et al., 2010 for calculation of VSSA). At the moment the VSSA is only applicable to nanomaterials in powder formulation.*	*BET*
Catalytic activity	*Information on the chemical reactivity of the nanomaterial core material or surface coating must be provided. Information on photocatalytic activity, and radical formation potential of relevant materials must also be provided.*	*Kinetic measurements of chemical, biochemical and/or catalysed reactions*

SCCS guidance for nanomaterials : Physical chemical properties

Parameter	Description	Methods*
Concentration	*Information on concentration in terms of particle mass and particle number per volume must be provided for dispersions and per mass for dry powders.*	*A wide range of analytical methods, including UVVis, HPLC, GC/LC-MS, AAS, ICP-MS, etc.*
Dustiness	*Information on dustiness of dry powder products must be provided.*	*EN 15051:2006, DIN 33897-2.*
Density and pour density	*Information on density/porosity of granular materials and pour density must be provided.*	DIN ISO 697, EN/ISO 60
Redox potential	*Information on oxidation state and redox potential (for inorganic materials) must be provided, including the conditions under which redox potential was measured should be documented.*	*Potentiometric methods, X-ray absorption spectroscopy*
pH	pH of aqueous suspension must be provided.	pH in aqueous media
Viscosity	Information on viscosity of liquid dispersions must be provided.	OECD TG 114
Stability	Data on stability/ dissociation constant of the nanomaterial in relevant formulation/ media must be provided.	MS, HPLC, DLS, FTIR, NMR
Other aspects	UV absorption (extinction coefficient), light reflection	UV-Vis

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SCCS on testing of nanomaterials : specific considerations

- **Solubility/dispersion**
  - Some *in vivo* methods only suitable for soluble nanomaterials
  - Testing of insoluble materials to account for nano-dispersion
  - Properties of nanomaterials may change due to interactions with surrounding media
  - Dose of tested material - Need to ascertain stability, uniformity and maintenance of applied doses
- **Surface interactions**
  - Binding of various substances including test components on surfaces may affect results (false positives/negatives)
- **Metrics**
  - Weight/volume concentration may be more appropriate than traditional mg/kg or mg/ml
- **Bioavailability- Toxicokinetics**
  - Translocation

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SCCS advice on nanomaterials : mutagenicity/genotoxicity considerations

- **SCCS shares and confirms caution/concerns of NANOGENOTOX findings**

- **Doubts on the applicability of certain tests for nanomaterials (e.g. Ames)**

- **Questioned the use of metabolic activation systems**
  Most insoluble nanomaterials may not be metabolised
  Proteins in the metabolic system may interfere with nanomaterial or its bioavailability

- **Nano-agglomerates may interfere with microscopic evaluation test (micronucleus, chromosome aberration)**

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SCCS advice on nanomaterials : mutagenicity/genotoxicity considerations 2

In assessing mutagenicity/genotoxicity care should be taken to ascertain

- that test cells were actually exposed to the nanomaterials
- Composition of nanomaterials (including surface modification/coating)
- Size, size distribution and charge of nanoparticles
- Nanoform was retained throughout the test
- Agglomeration/aggregation state during the test
- Expected dissolution/solubility and fate of nanoparticles in test medium
- Cellular, nuclear uptake in cell line used
- Indications of toxicity
- No artefacts (e.g. cytochalasin control)
- Appropriate choice of tested concentrations

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www.ec-scientific-committees.eu

http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_s_005.pdf

Thank you!

Health and Consumers