(Scientific) Comments on the Public Consultation's Summary

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on emerging and newly identified health risks
on health and environmental risks

General Issues

- Moratorium on use unless full RA is available
  - For all ENM?
    - Large investments needed
    - Time needed would limit technological progress
- Precautionary approach
  - Based on technological development there are already products on the market using nanotechnology and/or containing ENM
  - Currently an educated guess/evaluation may be possible based on developing knowledge
- Do we need product registration/notification?
  - Some nanomaterials are already in use for a long time
  - Voluntary registration failed (matter of ongoing debate)

General Issues continued

- Assessment of control measures
  - For control measures you need demonstration of absence and/or presence
    - Detection of a specific type of ENM is a problem
    - Problem of discrimination ENM from natural NM
- Raising awareness in public
  - Communication of uncertainties and/or risk to public
  - Explanation why RA of ENM is lagging behind technological/product development

Comments on Regulatory Issue

- Regulations existing for 'normal' chemicals apply to ENM
  - REACH for chemicals, and the existing regulations specific for pharmaceuticals and medical devices
  - The problem is how to obtain data to comply with requirements
    - Specific guidance needed for ENM
- Main questions
  - When is a material/chemical a nanomaterial?
    - ISO definition: ....approximately between 1 – 100 nm.
    - SCENIHR definition: ....dimensions of the order of 100 nm or less
  - Do we need specific regulations?
    - Probably not but there is a need for a REGULATORY definition of ENM

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What do we know of the RA of engineered nanomaterials ? (SCENIHR 2009)

- Nanomaterials are not by definition harmful because of their size
  - Size reduction > increase in surface area > more reactive > more toxic?
    - NO, some are toxic others are not
- There are areas of specific concern
  - Protein fibrillation found in vitro
  - Carbon Nanotube (CNT) effects
  - Genotoxicity testing
  - Altered tissue distribution
  - Environmetal toxicity demonstrated
- No general paradigm for ENM hazard identification
  - Case by case approach proposed

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What do we know of the RA of engineered nanomaterials ? (SCENIHR 2009)

- The necessity of a high quality characterization of the ENM used in the hazard identification assays
  - Size and size distribution
  - Agglomeration/aggregation presence
  - Shape
  - Chemical composition
  - Surface area
  - Surface charge
  - Surface chemistry (coating)
  - Crystallinity
  - Solubility, hydrophobicity, lipophilicity
  - ……

Comments on ENM Risk Assessment 1

- Full RA of all ENM before use
  - Use of high number of animals for hazard identifictaion
    - Aim of REACH to limit animal testing
    - Consultation: some NGOs asked for ban on animal testing
- The knowledge on testing of ENM is growing but not yet similar to that of chemicals
  - OECD sponsorship program for evaluation of the applicability of the OECD guidelines for the testing of chemicals for ENM
  - Various governmental (incl. EU) research programmes
- RA is more than hazard identification (toxicity testing)
  - Exposure identification and characterization, hazard identification and characterization (dose response?), risk assessment

Comments on ENM Risk Assessment 2

- Case by case approach
  - How to do the testing?
    - More guidance may be needed
    - Adaptation of existing assays to nanospecific problems (dose evaluation, administration of ENM)
  - Do groups/clusters of ENM exist with similar properties?

- Lack of reference materials
  - What to use as reference?
    - The 'bulk' materials?
    - Specifically prepared nanomaterials (negative, positive controls)?

Comments on ENM Risk Assessment 3

- Focus for risk assessment
  - Work place
    - Highest chance for exposure when containment fails
    - Depending on type of ENM respiratory exposure
    - Chance for exposure to free non bound nanoparticles
- Full RA to guarantee safety
  - Use of in vivo assays versus in vitro assays
    - In vitro assays not yet sufficiently developed/evaluated for use in RA
  - Conflict between societal emphasis on safety versus reduction of in vivo testing
- Life cycle approach
  - Need for high quality information on use

Comments on ENM Risk Assessment 4

- Environmental issues
  - Life cycle analysis needs also to address environmental issues
  - Fate and behavior in the environment largely unknown
    - ENM does not necessarily ends in sediment/soils
    - NOM (natural organic matter) can stabilise ENM
  - Adaptation of assays may be needed
  - Some parameters (K_{ow}) may not be relevant for ENM
  - Effects on environmental species have been demonstrated

Issues of concern

- Dose metrics
  - Mass may not be the best, but is easy to use and to understand
  - Surface area has shown better correlation for some ENM
    - Toxicity in vitro equal between bulk and nanomaterial when dose expressed as surface area
    - ENM does not have an increase in toxicity due to its size
- Migration/toxicokinetics
  - Most ENM end in liver and spleen, organs dedicated to clear contaminants from blood
    - Specific organ distribution/targetting may be possible depending on surface characteristics of ENM
- Biological effects
  - Chronic inflammation

Issues of concern

- CNT, nanofibers
  - Harmful effect may be similar to asbestos
    - Dependent on characteristics of fiber (lenght, rigidity, biodegradability)
- DNA damage
  - Contradicting results
    - Needs further evalauation/research
    - In vitro versus in vivo difference?

Summary
Where are we today?

- Risk Assessment frame work is available (SCENIHR 2009)
  - We do not know yet how to fill the existing gaps
  - Exposure measurement/estimation remains a problem
- Not all ENM are toxic
  - Case by case approach
- Specific problems need to be solved
  - Nanofibers/tubes
  - Genotoxicity
- Lack of reference materials
- Lack of in vivo toxicity studies
  - OECD sponsorship program
- Environmental behavior needs attention
- Regulatory issue
  - what is considered a nanomaterial from a regulatory viewpoint

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