ECEG Working Group
Health & Safety and Responsible Care

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What role for the European social partners in the chemical industry

The scientific approach

Brussels, March 3, 2010

Science based HSE strategy

- Caring for **people** - Risk Assessment
  - Toxicological assessment review
  - Scenarios of exposure and exposure measurement
  - Risk assessment
  - Worker protection and training
  - Regulatory matters
- Caring for the **environment**
  - Eco-toxicity testing
  - Waste management

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TOXICOLOGICAL ASSESSMENT

Methodology

- **Acute toxicity**
  - Cytotoxicity
  - Oral
  - Dermal
  - Inhalation
- **Other assessments**
  - Mutagenicity, carcinogenicity
  - Specific organ toxicity
    - Single exposure (hematology and ingestion)
    - Repeated exposure (Inhalation)
  - Other tests

Acute Toxicity (1)

- **Cytotoxicity**
  - EU recommended *in vitro* testing carried out at JRC-IHCP
  - Cell viability assessment showed no to sign of toxicity of NC7000 on liver, lung, kidney, intestine, fibroblast and skin
  - The Colony Forming Efficiency test did not reveal any Cytotoxicity effects
- **Oral**
  - a modified OECD 420 test to assess oral acute toxicity showed no evidence of toxicity up to the highest dose that could be force fed.
  - Assessment after administration of the higher dose shows that the liver function and the kidney function are not affected by CNT administration.
  - No significant change in biochemical plasma values were observed.

Acute Toxicity (2)

- **Dermal**
  - In vitro tests used in cosmetic industry do not show dermal acute toxicity on human skin
  - There are no indications of irritation generated by CNT and no penetration into the skin could be seen, even under pressure.
  - Skin corrosion, irritation and sensitization tests did not reveal any effect of CNT
- **Inhalation**
  - A 5 days inhalation study according to OECD 403 (at doses of 2, 8 and 32 mg/m^3) indicates that CNT do not show acute toxicity through inhalation but can generate mild inflammation.

Other assessments (1)

- **In vitro mutagenicity and carcinogenicity tests (IHCP)**
  - The preliminary data revealed no mutation (genotoxicity) generated by any of the nanotubes tested
  - The tests show carcinogenic potential at high doses but it is unclear whether CNT are carcinogenic or they simply adsorb a lot of the nutriment of the cell culture media and thereby affect the cell function.
  - The carcinogenic potential is absent for OH functionalized tubes.
- **In vivo carcinogenicity study**
  - A two year study by Muller *et al.* (Toxicological Science 2009) shows an absence of carcinogenic response to multi-wall carbon nanotubes injected in the peritoneal cavity of rats
  - This result supports the conclusion that CNT are not carcinogenic as such but affect the relevance of the in vitro test.
  - According to Prof Donaldson, this result indicates that these CNT **are not asbestos like**

Other assessments (2)

- Hematological tests revealed that the CNT at concentration up to 500µg/mL did not affect the viability of red blood cells (Hemolysis), nor the coagulation cascade (Hemostasis). It shows that there are no risk associated with exposure following injuries
- In the acute inhalation tests, all organs of the animals were examined and beside the inflammation of the lung at high doses, none of the other organs were affected.
- 90 days sub-chronic inhalation test (OECD 413)
  - The study revealed moderate granulomatous inflammation,
  - The Lowest Observed Effect Concentration (LOEC) is 0.1 mg/m3.
  - With a Safety Factor of 40, the safe exposure level is < 2,5 µg/m³
  - Recent data obtained by a competitor suggest a recovery of the rats exposed to high doses. Based on such results, the Safety Factor could be reduced to 1.

Toxicological overview

	Test Item	Test method	Test conclusion
In vitro	Cytotox.	Modified OECD 476	No tox.
	Dermal tox.	Modified OECD 431	No tox.
In vivo	Chronic Inhalation	OECD 403 and 413	LOEC at 0,1 mg/m³
	Ingestion tox.	Modified OECD 401	No tox.
Ex vivo	Impact on hemolysis	Referenced method	No tox.
	Impact on hemostasis	Referenced method	No tox.
Ecotox	Green algae inhibition test	OECD 201	On-going
	Daphnia mobility & reproduction test	OECD 202 & 211	On-going
	Fish mortality, growth & larval test	OECD 203, 210 & 215	On-going

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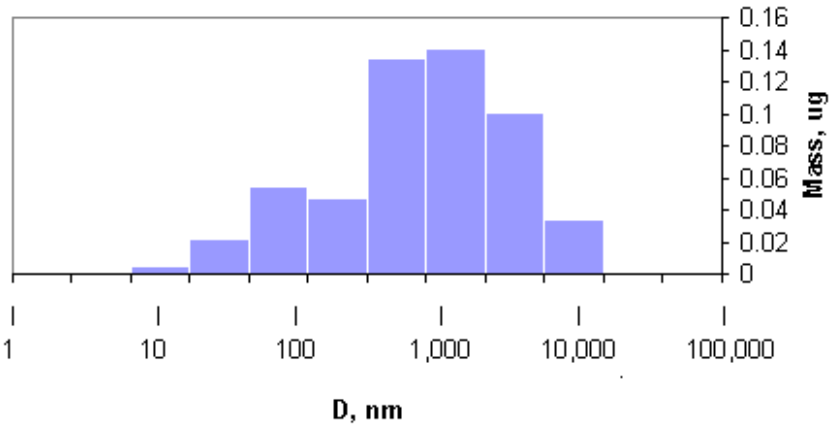
EXPOSURE ASSESSMENT

Measurement devices

- Collaboration with highly referenced partners: TNO for exposure assessment, IMEC for particle count, Belgian Federal Toxicological Office for exposure assessment
- Used devices to measure airborne particles:
  - ELPI (Electrical Low pressure Impactor)
  - CPC (condensation particle counter)
  - SMPS (Scanning Mobility Particle Sizer)
  - Diffusion charger
- Disadvantages:
  - Charging of particles
  - Difficulties to analyse data (measurements higher outdoor than indoor next to manipulation area !!!)
  - Not always specific for nanoparticles
  - No specificity for carbon nanotubes (general measure of airborne particles)

Complementary approach - Naneum

- Collection of particles from 2nm to 30µm on up to 15 size bins onto substrates to allow for chemical analysis and physical characterisation.
- **Particles >0.3µm** are collected by inertial deposition using a **cascade impactor** (normally from 0.3 to 30µm) and are selectively deposited onto microscope slides
- Particles from **2nm to 0.3µm** are collected by **diffusion deposition** onto Nylon nets.
- **Portable device** which works at atmospheric pressure and at ambient temperature.
- Conclusion: instrument that gives a **true distribution of particle sizes** in the size range 2nm to 30µm not distorted by condensation, evaporation or agglomeration.



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RISK ASSESSMENT

Risk associated to exposure

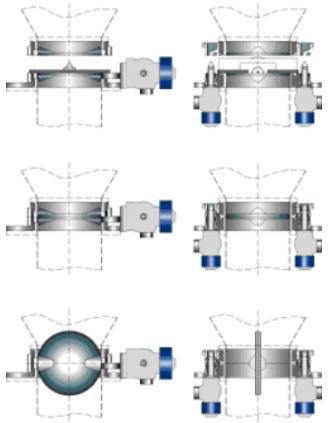
- Scenarios of exposure
  - Manipulation of large quantities of nanotubes as produced
  - Loading of a feeder
  - Exposure to abrasion particles
  - Permanent presence in a building where CNT are being used and produced

Scenario 1

- **Manipulation of large quantities of CNT**
  - Location: packaging unit at Nanocyl
  - Time of sampling: up to 72h
  - Particles collected in the air
    - 2.0 → 8.1 µm : 0.75 µg CNT/m^3
    - 0.25 → 2.0 µm : 0.5 µg CNT/m^3
    - 0.001 → 0.25 µm : 0.2 µg CNT/m^3
  - Total maximal potential exposure: 1.45 µg CNT/m^3
  - Safety factor to LOEC: 69
  - Additional measures recommended to prevent exposure:
    - FP3 respiratory capsules
    - Disposable glove, cover all and goggles

Scenario 2

- **Handling of large quantities of CNT**
  - Location: loading of the feeder of an extruder
  - Time of sampling: up to 144h
  - Particles collected in the air:
    - 2,0 → 8,1 µm : 1.00 µg CNT/m³
    - 0,25 → 2,0 µm : Below detection
    - 0,001 → 0,25 µm : Below detection
  - Total maximal potential exposure: 1.00 µg CNT/m³
  - Safety factor to LOEC: 100
  - Additional measures recommended to prevent exposure:
    - FP3 respiratory capsules, disposable glove, cover all and goggles
    - Use of special valves



Scenario 3

- **Potential exposure to particle coming from abrasion of CNT-based compounds and Master Batches**
  - Location: abrasion unit dealing with various polymers filled with up to 10% of CNT
  - Time of sampling: up to 20.000 abrasion cycles
  - Particles collected in the air:
    - 2,0 → 8,1 µm : Below detection
    - 0,25 → 2,0 µm : Below detection
    - 0,001 → 0,25 µm : Below detection
  - Total maximal potential exposure: below detection
  - Safety factor: no exposure to nano-particles
  - Additional measures recommended: FP3 respiratory capsules, disposable glove and goggles

Scenario 4

- **Long term exposure to low amount**
  - Location: office in production and R&D building
  - Time of sampling: up to 200h
  - Particles collected:
    - 2,0 → 8,1 µm : 0,25 µg CNT/m³
    - 0,25 → 2,0 µm : Below detection
    - 0,001 → 0,25 µm : Below detection
  - Total maximal exposure: 0,25 µg CNT/m³
  - Safety factor to LOEC: 400
  - Precautionary measures recommended: none

Worker training

- **Technical measures**
  - Production: close process
  - Transfer of powder: double valves
  - Ventilation: global and local
- **Personal Protection Equipment (PPE)**
  - Gloves
  - Respiratory masks: FP2 or FP3
- **Formation and information**
  - Regular information about possible hazard
  - Control if PPE are used

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REGULATORY ASPECTS

Global situation

- REACH
  - Pre-registration done
  - Identification of exposure scenarios
  - Registration foreseen in 2010 before the deadline
  - Participation to stakeholder dialogues on nanomaterials at EU level
- US-EPA
  - PMN and Consent ordre
- Japan
  - contribution to voluntary information exchange

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Caring for the environment

Caring for the environment

- **Eco-toxicity testing**
  - Acute and chronic tests on daphnia

    (first result: EC50 >100mg/l)
  - Test on algae
  - Test on fish
- **Waste management**
  - As a matter of precaution all waste are considered as hazardous

Conclusions

- **All routes of exposure to CNT seem safe except for the inhalation of high doses**
- **Risk assessment shows that simple precautionary measures can guaranty a very high safety factor**
- **Exposure assessment equipment provides a reliable tool to determine exposure and to define risk assessment**
- **The key is the collection of state-of-the-art information about toxicology and exposure in a proactive way.**