Nanomaterials: Occupational Health and Safety Issues

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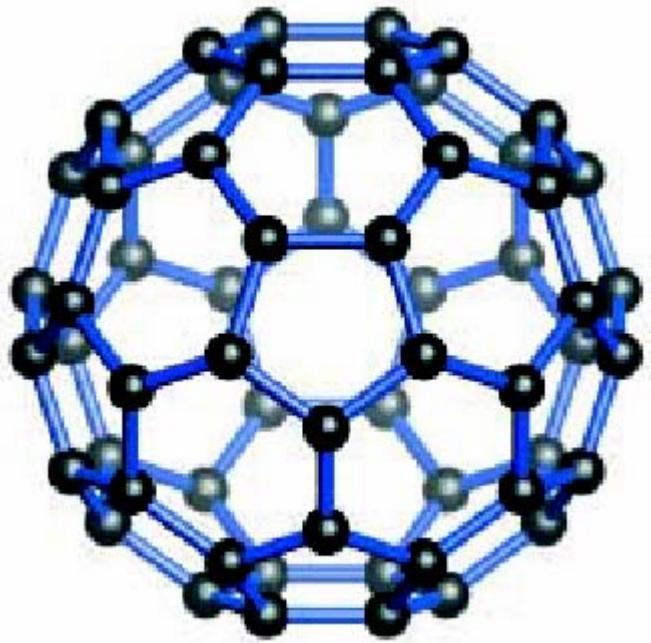
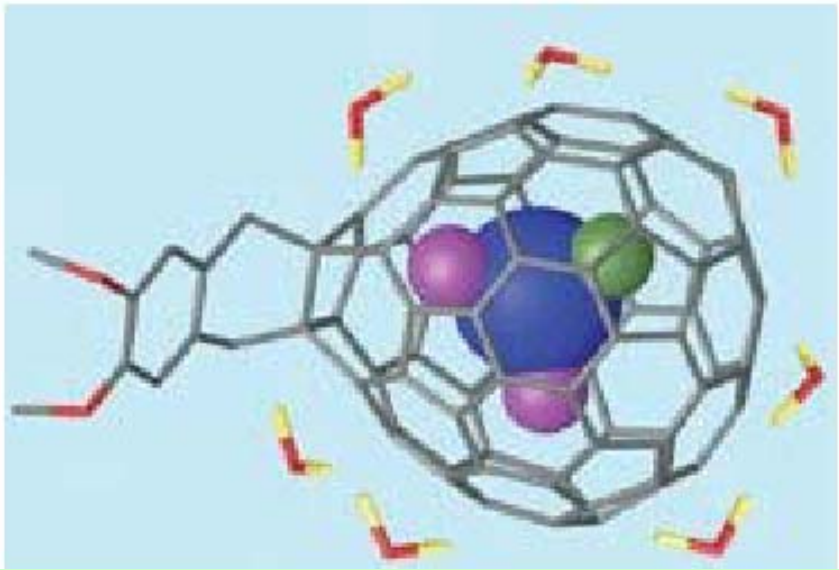
Fullerenes

- C_{28} to > C_{100}
- Hollow sphere
- C_{60} is the best known



- Insoluble
- No interaction
- Very compressible
- Resumes its shape

A modified fullerene



Made soluble by surface changes

Made chemically active by adducts

Incorporation of another product

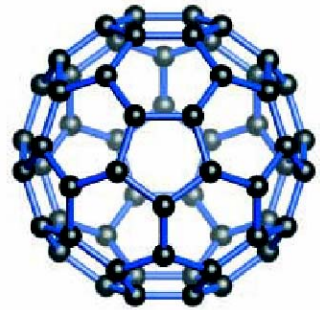
Interaction with the surrounding solvent

- **Very great variability in chemical, physical and biological behavior**

Do nanoparticles represent a health risk?

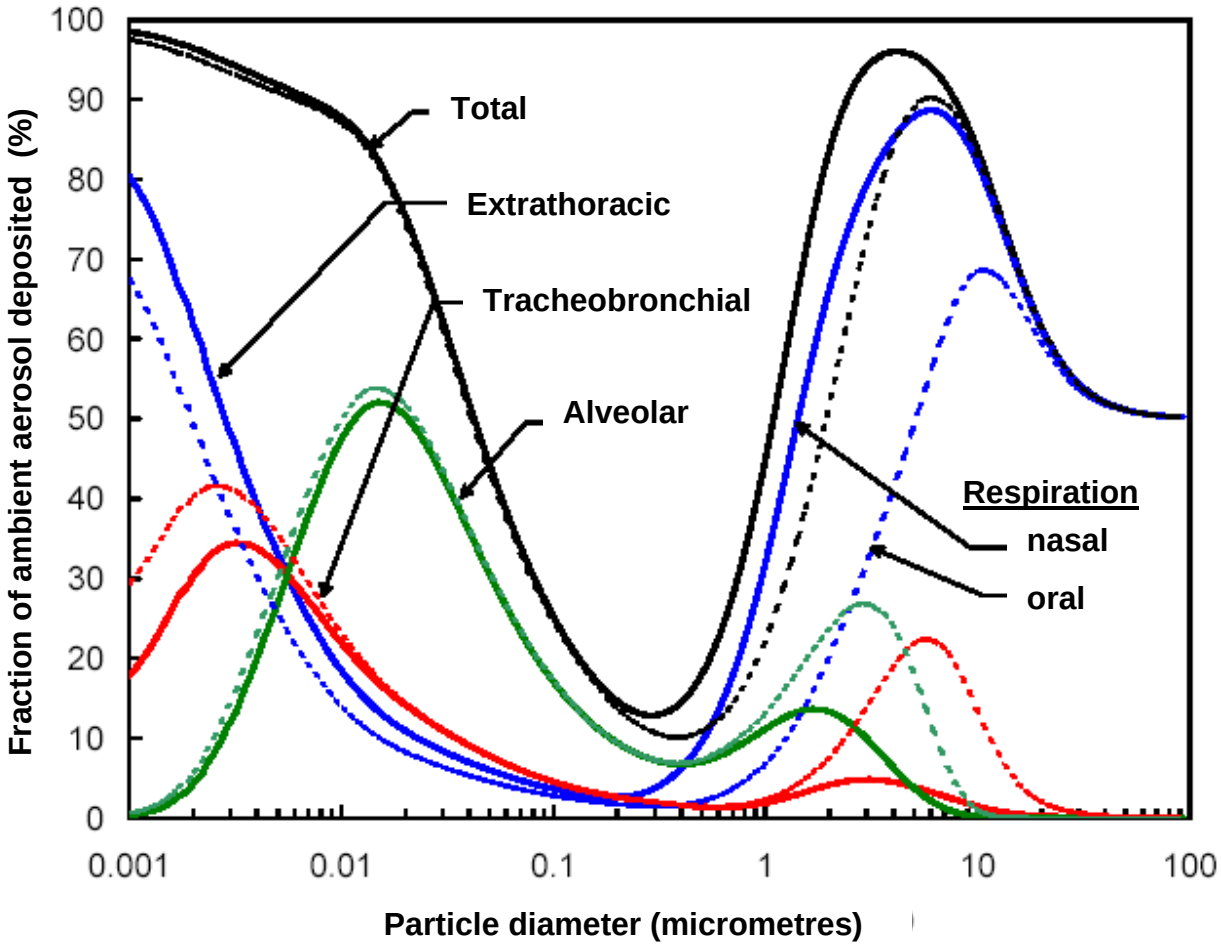
⇒ **Risk = toxicity x exposure**

Question of solubility



- **Two potential situations:**
  - **Nanoparticles are soluble into biological fluids**
    - **Toxicity related to the chemical composition only**
    - **Toxicity normally well documented**
    - ➢ **No difference between nano and microparticles deposited at the same biological site**
  - **Nanoparticles are insoluble into biological fluids**
    - ❖ ***Subject of our concern in health risk evaluation***

Pulmonary deposition of nanoparticles and ultrafine particles

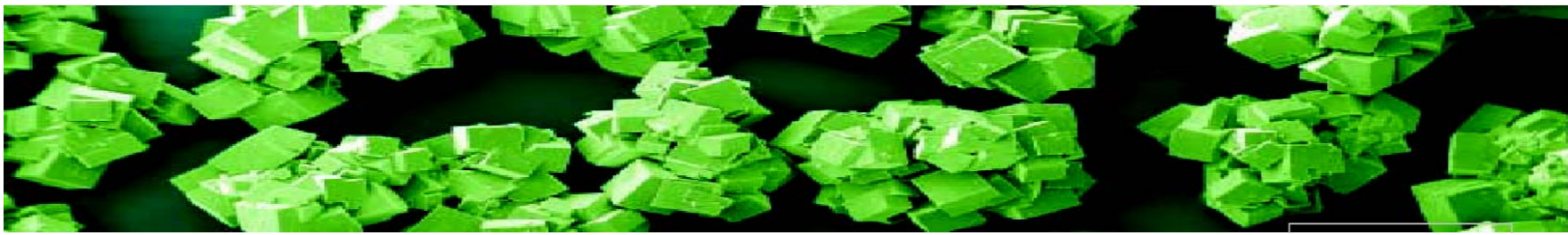


Elimination from the respiratory system

- **Extrathoracic level:**
  - **Normal mechanisms**
  - ***Olfactory nerve towards the brain***
- **Tracheobronchial level**
  - **Effective mucociliary elevator**
- **Alveolar level**
  - **Macrophages not very effective if < 1 micrometre**
  - **Macrophages: problems with fibres > 20 micrometres**
  - ***Interstitial and alveolar epithelium translocation → movement towards the blood and lymph nodes***

Insoluble inorganic nanoparticles

- **Digestive absorption (Au):**
  - **Absorption of nanoparticles by the intestine**
  - **Passage into the blood**
  - **Distribution: brain, lungs, heart, kidneys, intestine, stomach, liver and spleen**
  - **Absorption efficiency inversely proportional to the dimension of the particles**
  - **Significant accumulation (Au) at tumor sites**

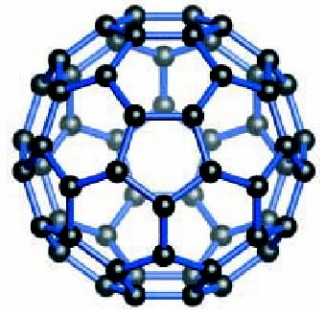


Inhalation (TiO_2)

- **Comparison of fine particles (250 nm) and agglomerated nanoparticles (20 nm) with the same final dimensions**
  - **Similar pulmonary deposition**
  - **20 nm are found in the lymph nodes**
  - **Slower pulmonary clearance → Greater pulmonary retention for nanoparticles**
  - **Greater translocation for nanoparticles**
  - **Greater pulmonary inflammation**

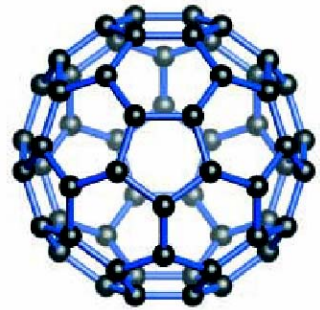
- ***Effects correlated with the specific surface area and not the mass***
- ***Effects related to surface composition and properties***

Fullerenes



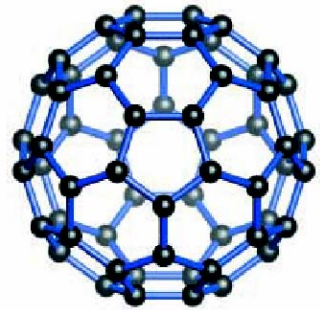
- C_{60} alone is documented
  - Intraperitoneal administration
    - Detection in the liver, blood, spleen
    - Decreases enzymatic liver activity (glutathion)
    - Kidney disorders
    - Crosses the placental barrier and is distributed throughout the yolk sac and the embryo
  - Oral administration
    - 98 % in feces, 2% in urine
  - Skin application
    - No effect on DNA and no cancer
- **No pulmonary study**

Chemically modified fullerenes



- **Intravenous administration**
  - **Distribution in tissues: detection in the liver (73-80%), lungs (5%), kidneys (3%), spleen, heart, brain**
  - **Lack of a renal clearance mechanism and nephropathy**
  - **Body, thymus and heart weigh loss**
  - **Spleen weigh increase**
  - **Intrauterine malformations and mortality**
- **Intraperitoneal administration**
  - **Kidney disorders C_{60} polyalkylsulfonates**
  - **Polyhydroxylated fullerenes have shown an antioxydant potential in the lungs**
  - **Hydroxylated and carboxylated functions dicrease the toxicity**
- **No pulmonary study**

Chemically modified fullerenes



- **Depending on the functional groups, toxicity varies**

From

very toxic

to

Benific

Singlewalled carbon nanotubes

- **Pulmonary toxicity**
  - Lung inflammation
  - No effect on macrophages for very short fibers
  - Bronchial pulmonary interstitial granulomas causing pneumonia and fibrosis
  - Potential pulmonary toxicity related to oxidative stress – increase in inflammation biomarkers
  - 10 to 25X> inflammation than silica – specific surface area
- **Cell**
  - Nanotube can cross the cellular membranes and be found in the nucleus - irritation
- **Skin and eyes (rats and humans)**
  - No allergy or irritation on skin or eyes

Multiwalled carbon nanotubes

- **Pulmonary toxicity: Intratracheal instillation**
  - **80% still in the lungs after 60 days**
  - **Phagocytosis efficiency is length dependent**
- **Cell**
  - **Nanotube can cross the cellular membranes and be found in the nucleus – irritation**
  - **Decrease in cell viability**

Insoluble organic nanoparticles

- **Interest in drug transport and targeting**
  - **Very selective therapy**
  - **Crosses the hematoencephalic barrier**
  - **Very promising tests**

- **Large variety in products but few toxicity studies on healthy organs**

Conclusion on toxicity

- **Exposure to engineered nanoparticles is likely to cause adverse health effects**

- **Surface area, surface activity (composition, Redox capacity…) and particle number should be better predictors of potential hazard than mass.**

Conclusion on toxicity (cont.)

- **Actual research results suggest that if the nanotubes are :**
  - **Longer than 20 micrometers and**
  - **In sufficient amount**

Then, we could expect the same kind of effects as biopersistent mineral fibers

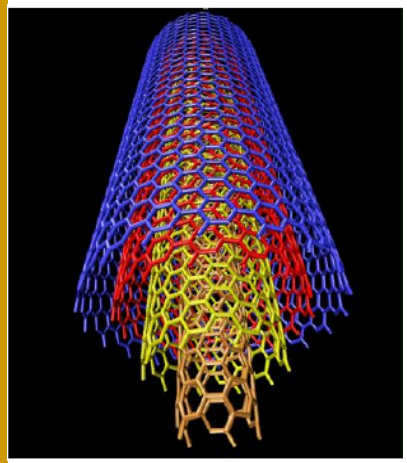
- **Fibrosis**
- **Cancer**
- **Pleura modifications**
- **Mesothelioma**

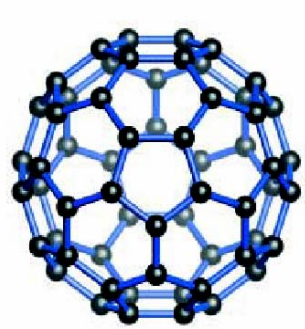
Workers' exposure potential

- During laboratory development
- During production:
  - Leaks from the reactor (high T, colloids, attrition)
  - Product recovery
  - Post-production processing
  - Packaging, storage, shipping
  - Equipment maintenance
  - Spills…
- Use and subsequent conversion:
  - Diversity of risks related to specific applications

Most production and conversion processes have a potential for worker exposure

Current knowledge on the exposure of Québec workers





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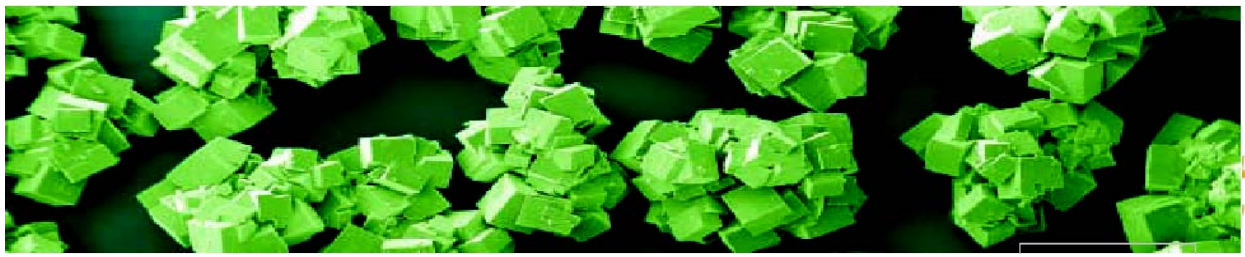

Other risks and aspects of prevention

- **Nanoparticles offer a large surface area**
  - nanoscale combustible material could present a higher risk than coarser material with a similar mass concentration given its increased particle surface area and potentially unique properties due to the nanoscale
  - **Explosion risks :**
    - Large and often reactive surfaces
  - **Fire risks :**
    - Nanometric metals and great chemical reactivity
  - **Storage:**
    - Environmental conditions: humidity, temperature, chemical compatibility

Occupational Exposure Control

Rule number 1:

- **Installations, processes, equipment, activities and workstations must receive particular attention**
  RIGHT FROM THE DESIGN STAGE

- **THREE main categories of means of control:**
  - **Engineering techniques**
  - **Administrative means**
  - **Personal protective equipment**

Recommended precautionary measures in the workplace

- Unless the toxicity of the product has been established, consider very toxic and minimize the exposure
- Apply existing exposure control techniques
- When possible, implement a risk management program
- Implement good work practices
- Consider implementation of an exposure assessment program
- Consider implementation of a health surveillance program

For more information

- **Two knowledge reviews are available on the IRSST web site (available in English)**

www.irsst.qc.ca

  - **R-469: Health effects**
  - **R-470: Risks and prevention measures**

Research team

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Questions ?