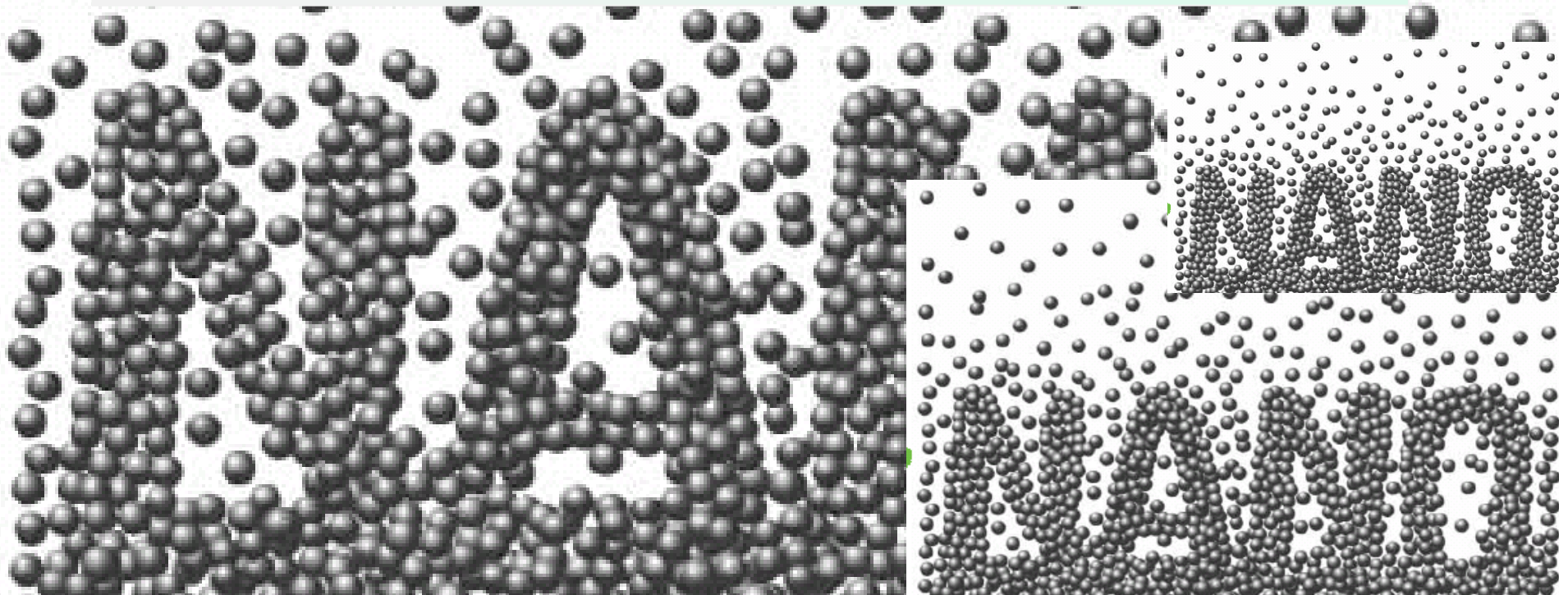
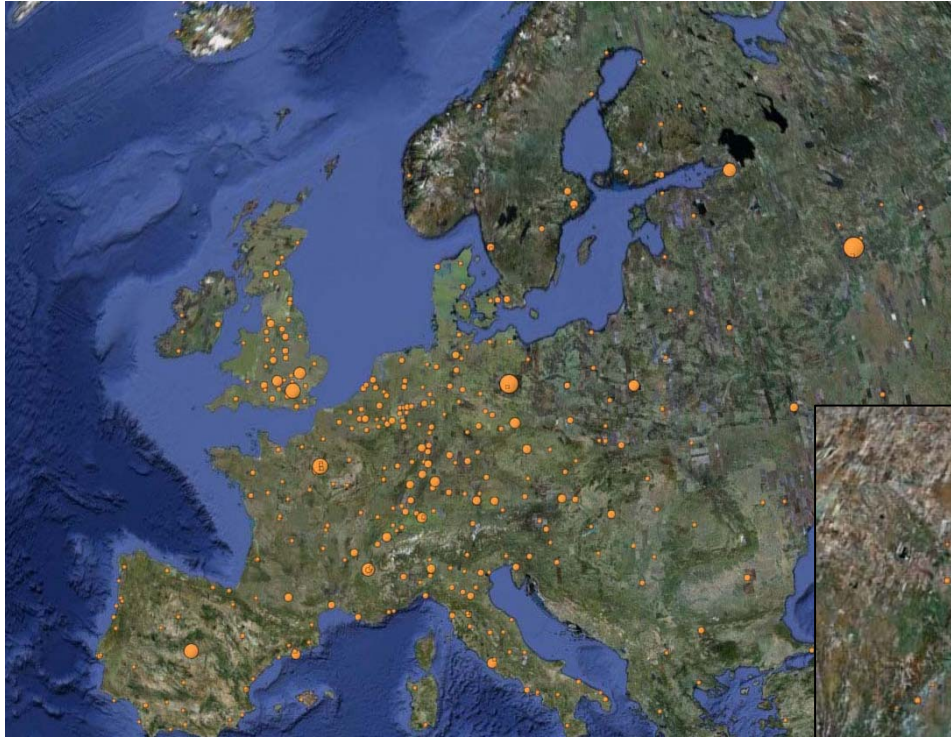


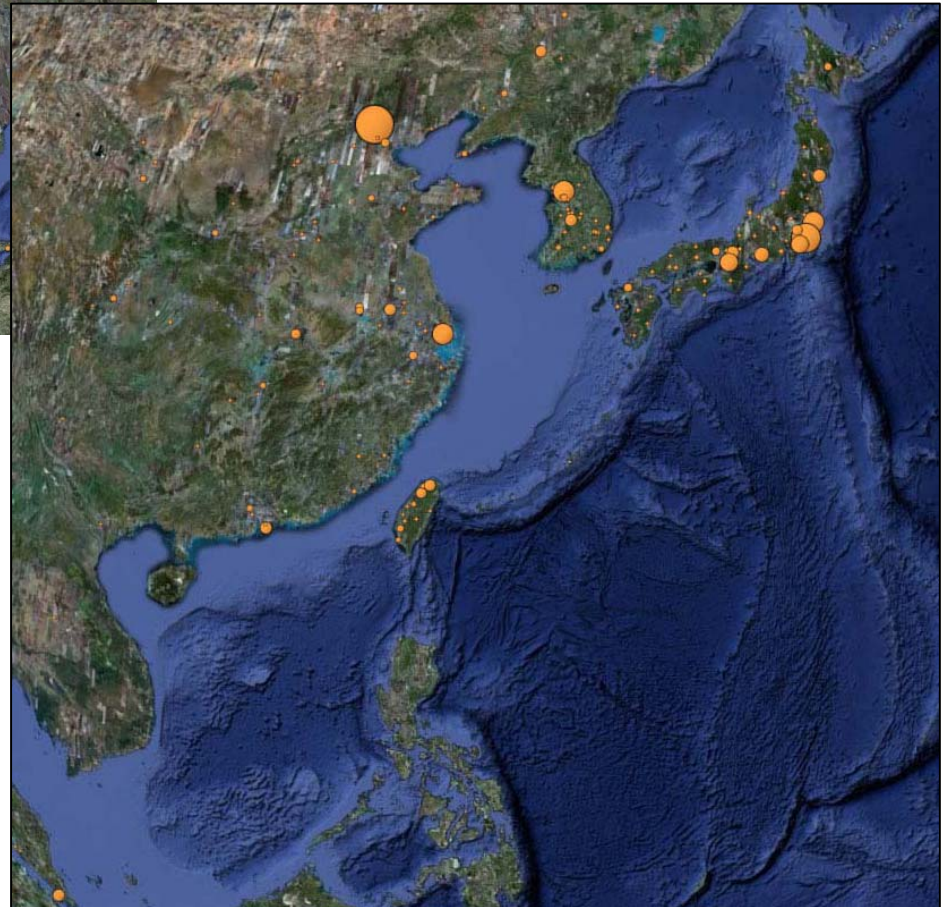
Best practices in handling nanomaterials in the workplace- - a survey in the Netherlands

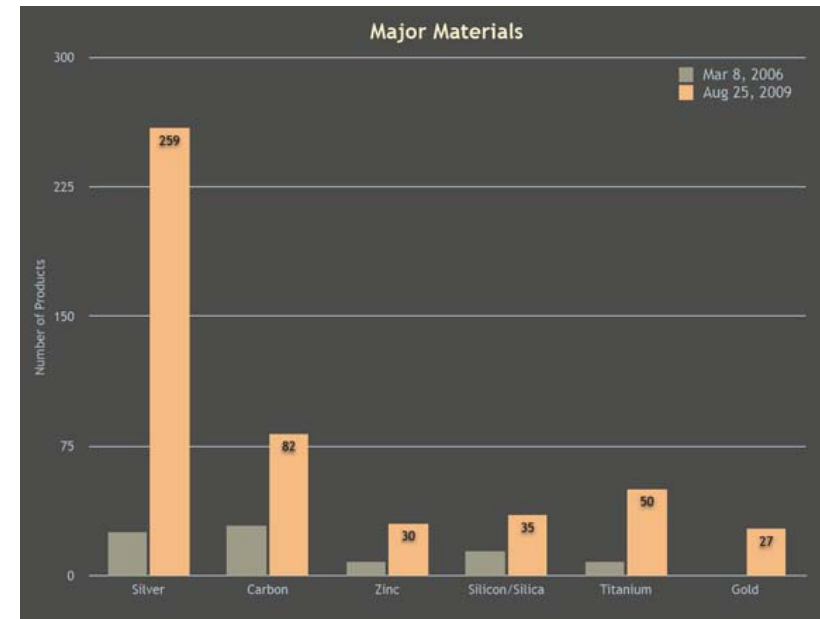
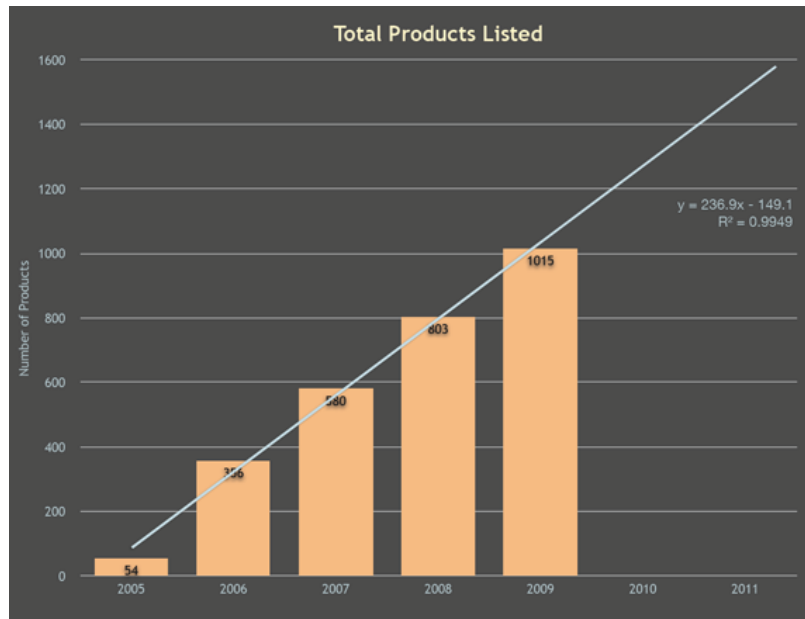
Paul Borm





Publication activities in East Asia and Europe. All cities with at least 100 Nano publications between 1998 and 2007 are highlighted

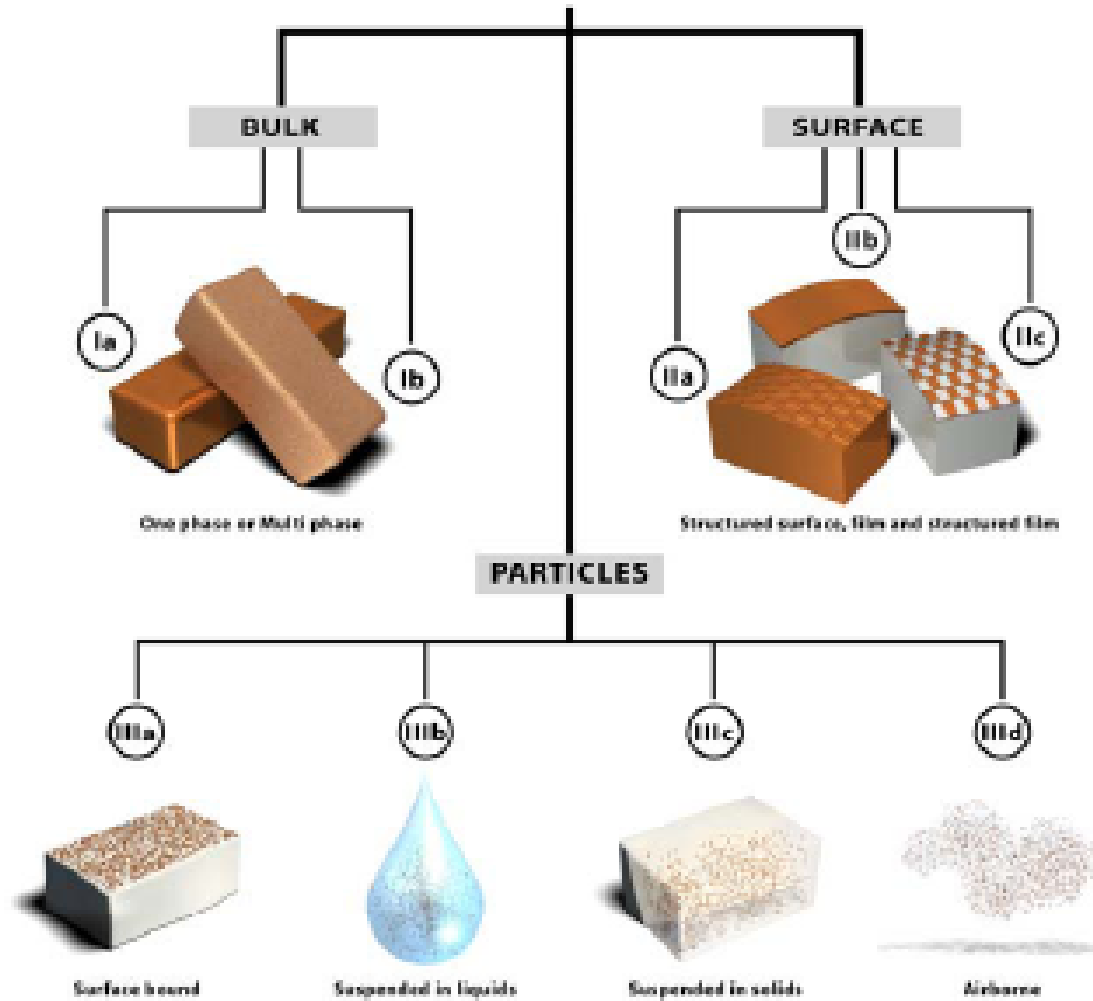




Total products (left panel) with nanocomponents on the US-market,
And –right- the major **nanocomponents** determinings its functionality

Data from Woodrow-wilson database (jan 2010).

NANOMATERIALS



$$\text{Risk} = \text{hazard} \times \text{exposure}$$

**Hazard: the “ability” of a chemical to
cause harm**

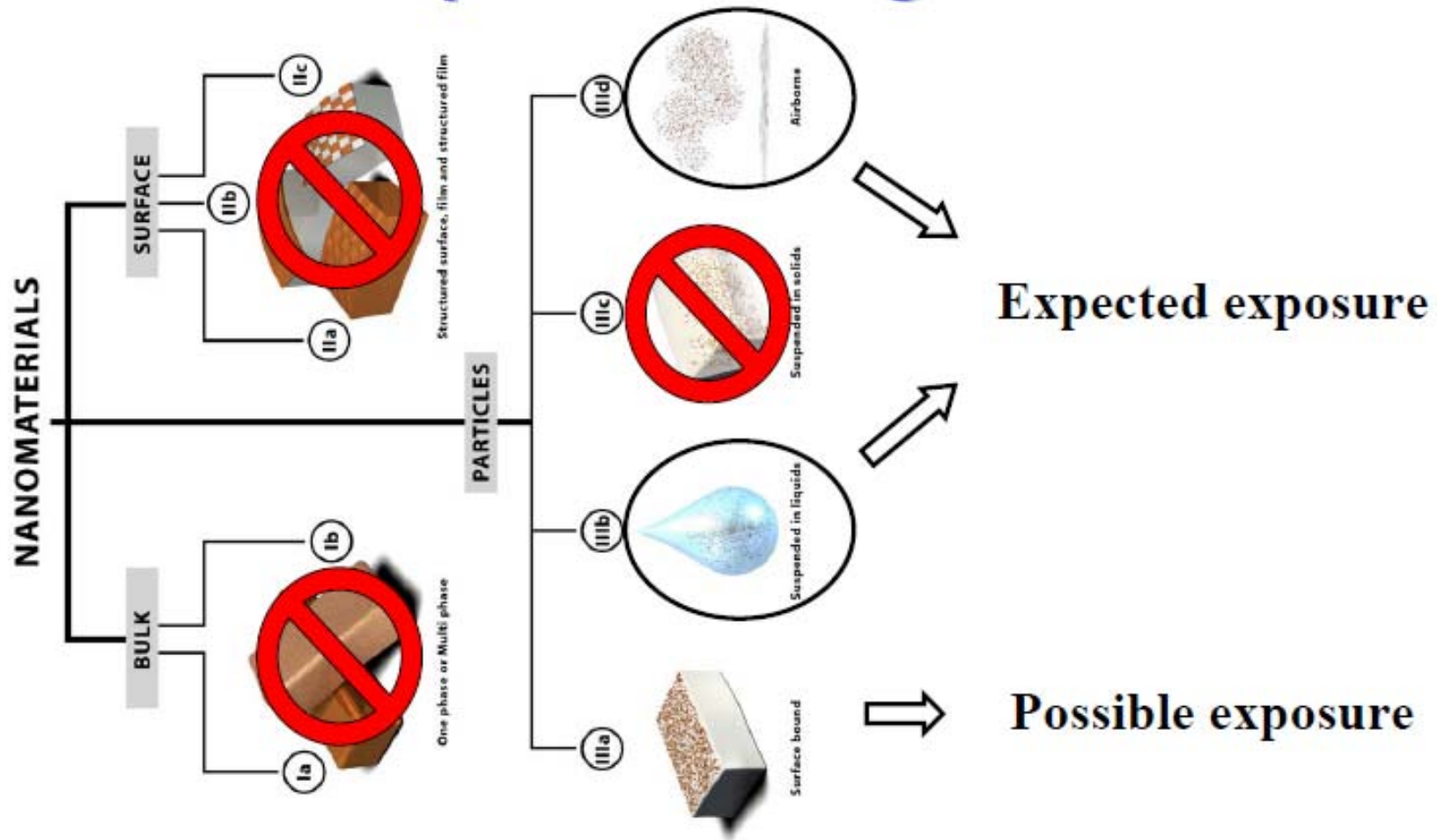
Risk: the “probability” it will do so

Early handling of carbon nanotubes (NASA)



Raw single walled nanotube material

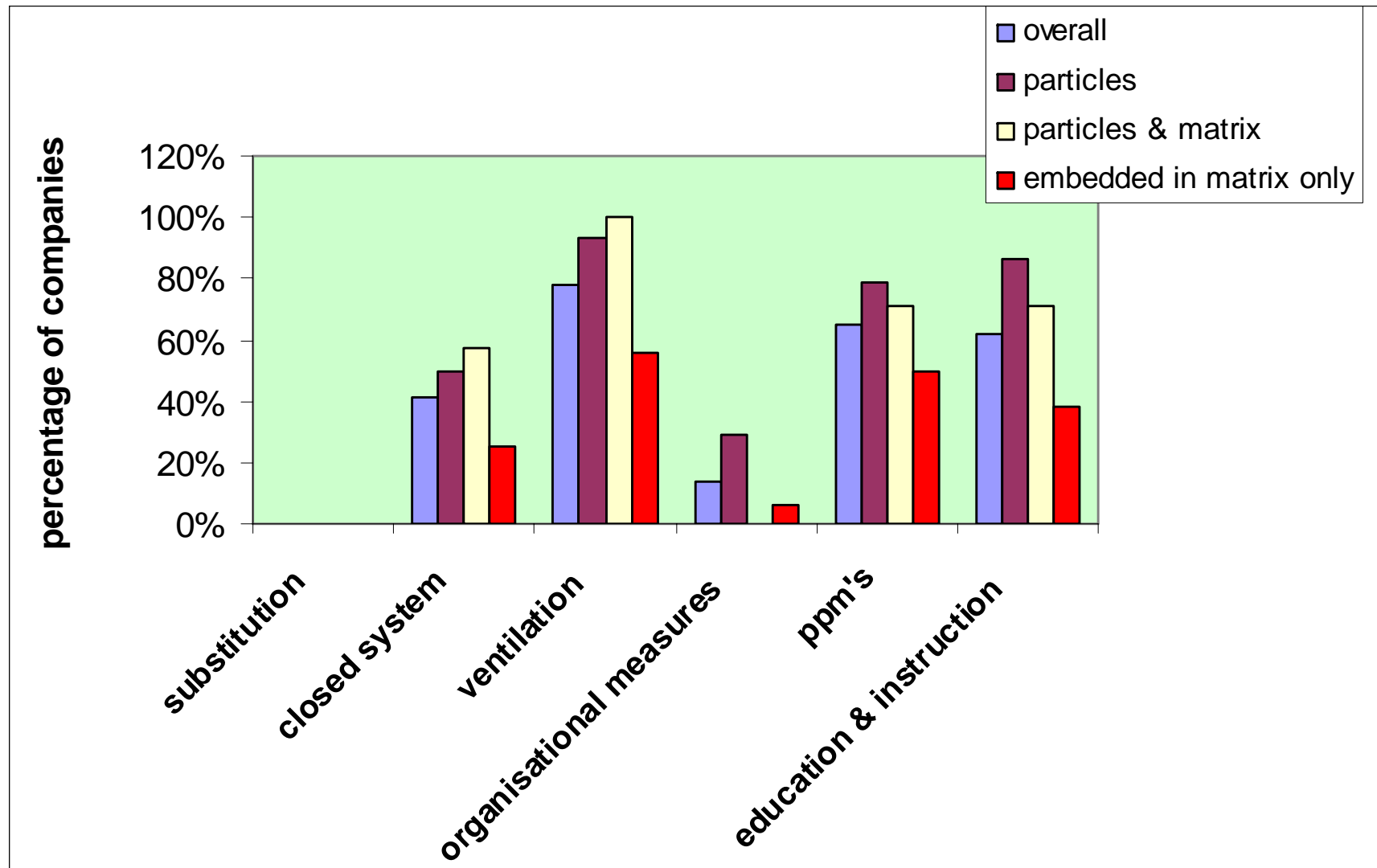
Exposure Categories



Company policies for nanomaterials

- Defined by 9 out of 32 companies (24%)
- 3 most important elements:
 - Pre-emptive choice on specific nanoparticles
 - Handling all nanomaterials as toxic substances (safety principle)
 - Choices on the physical form of nanoparticles

Occupational hygiene strategies by approach



Validation of risk assessment

- 29 companies (78%): not supported by any exposure measurements
- 8 companies (22%): some kind of exposure measurements:
 - 2 gravimetric only (nanoparticles?)
 - 1 chemical analyses of specific component
 - 5 meas. with condensation particle counter (CPC) and/or air sampling analyzed with SEM/TEM

Poor information exchange within the chain

- Information exchange on nanoparticles (from suppliers and to customers)
 - 19 (51%) no information exchange at all
 - 18 (49%) at least some information exchange
 - Only 7 (19%) active support by suppliers
 - Only 12 (32%) active communication to customers

Application	nr	Most prevalent Nanomaterial	Amount (kg/yr)
Assembly.recycling	2	Carbon black CNT	2000 0.1-1
Electronic equipment	3	TiO ₂ , SiO ₂	Unknown 100-1000
Research	6	Metals Clays CNT-C60	0.10- 1.0 1 0.1-10
Health & Food	4	FeO, SiO ₂ fullerenes	10 - 100 10 - 100
Surface & coatings	13	TiO ₂ , SiO ₂ , CB Al-oxides	100 – 10,000 100,000 100 - 200
Energy	1	Not specified	

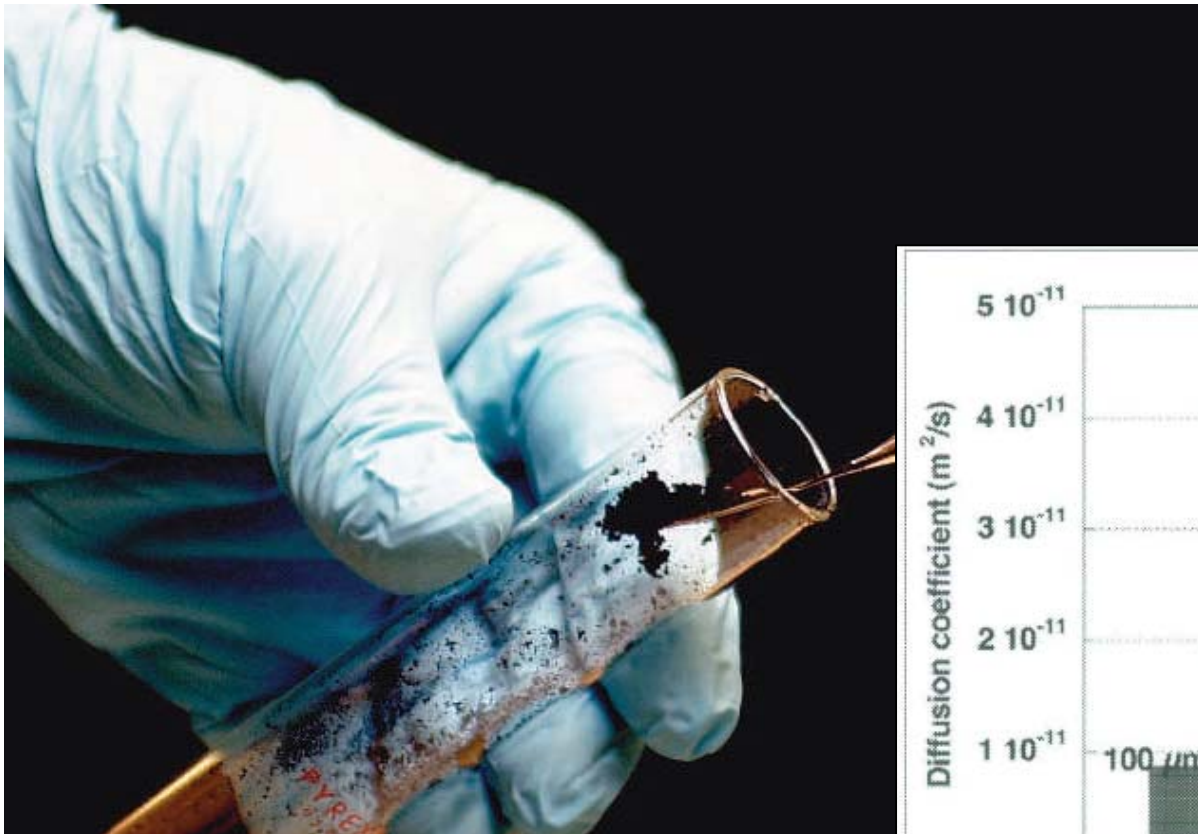
Country	Target/ response	NanoMaterials	C/Ac	NanoHSE	Reference
World	337/64	Carbon based Metal oxides	64/0	37	<i>Gerritzen et al, 2006</i>
Denmark	165/11	Metal oxides Silica, polymers Carbon black	6/5	1	<i>Tonning & Poulsen, 2007</i>
Switzerland	197/43	Silica, TiO2 Metal oxides, Ag Carbon black	43/0	N.D	<i>Schmid & Riediker, 2008</i>
Zwitzerland & Germany	?/40	No info	40/0	13	<i>Helland et al, 2008</i>
UK	? /9	No info	7/2	N.D.	<i>VRS, 2007</i>
Netherlands	98/8	No info	5/3	N.D	<i>Mikkers et al, 2007</i>
Netherlands	122/37	Carbon black metal oxides silica	30/7	9	<i>Borm et al (2008)</i>

Handling nanomaterials in European industry

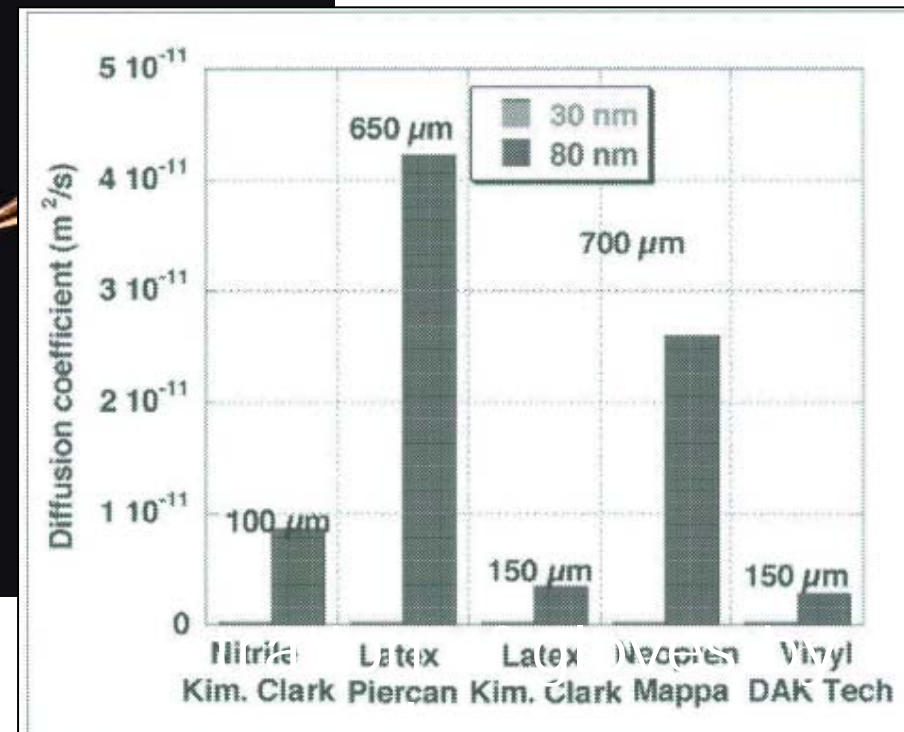
- Mostly first generation nanoparticles (CB, SiO₂).
- Ventilation most applied control measure.
- Little monitoring to check effectiveness of measures.
- Communication about hazards almost absent in the chain between producer and users; MSDS sheets are incomplete.
- Waste disposal according to classical pathways.
- Anticipated increase in production and use within 2-3 years.
- Guidelines available since late 2007, early 2008.

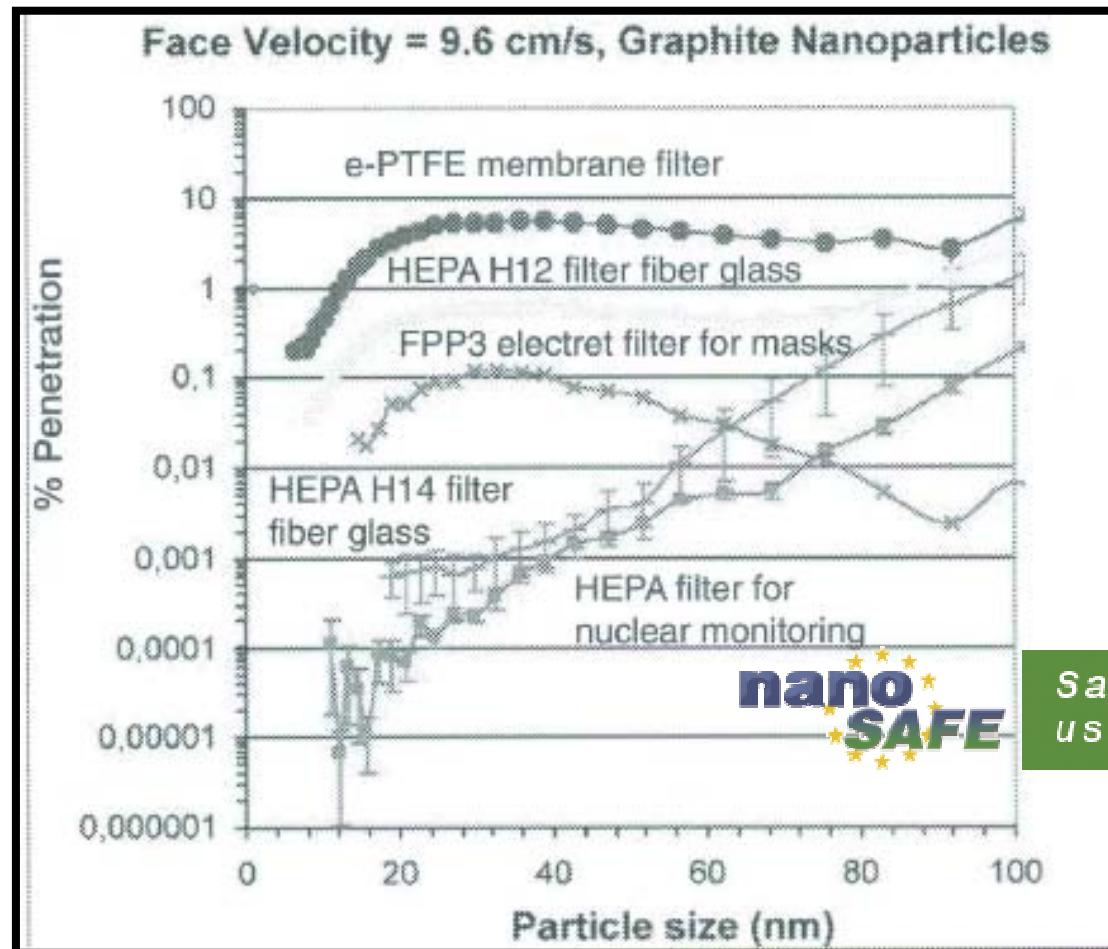
Borm et al, 2008; Schmid & Riediker, 2008; Gerritzen et al, 2006; Tønning & Poulsen, 2008

Know-how on safe handling of nanomaterials
Is emerging from current European research
Programmes (NanoSafe2, NANOSH, NOSH).



*Safe production and
use of nanomaterials*





*Safe production and
use of nanomaterials*

Tests performed with graphite nanoparticles confirm that conventional HEPA filters are very effective in capturing nanoparticles from ambient air.

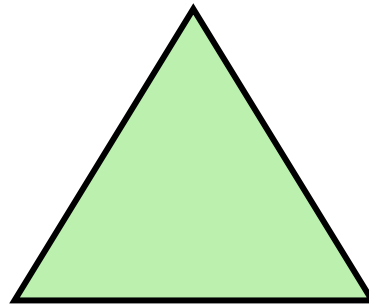
$$\text{Risk} = \text{hazard} \times \text{exposure}$$

**Hazard: the “ability” of a chemical to cause harm
and is usually tested by in vitro or in vivo
Toxicity assays**



Hazards of carbon nanoparticles: A Bermuda triangle

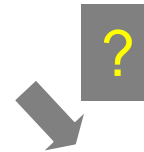
Combustion NP,
Diesel exhaust particles, UFP



Bulk industrial NP
carbon black



Engineered NP
MWCNT, C60



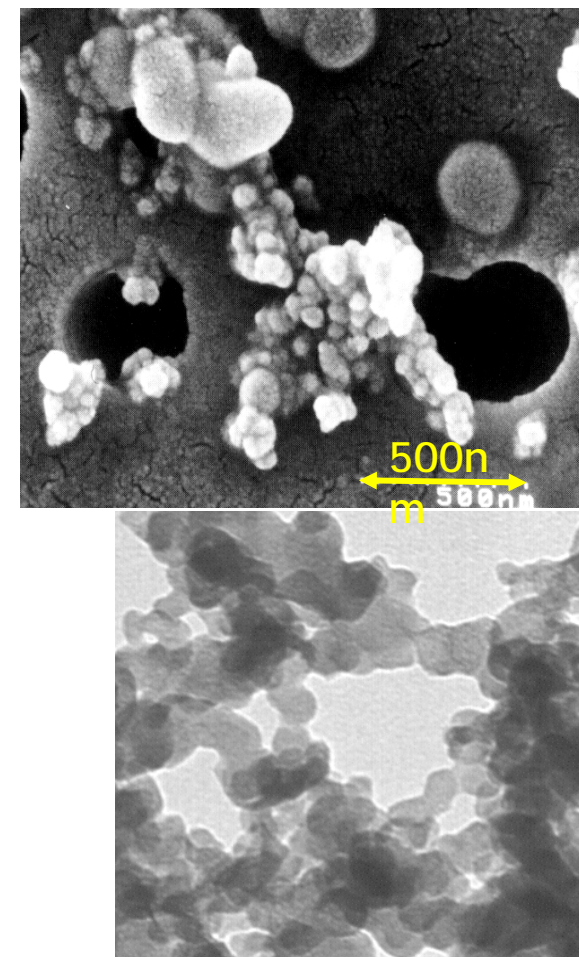
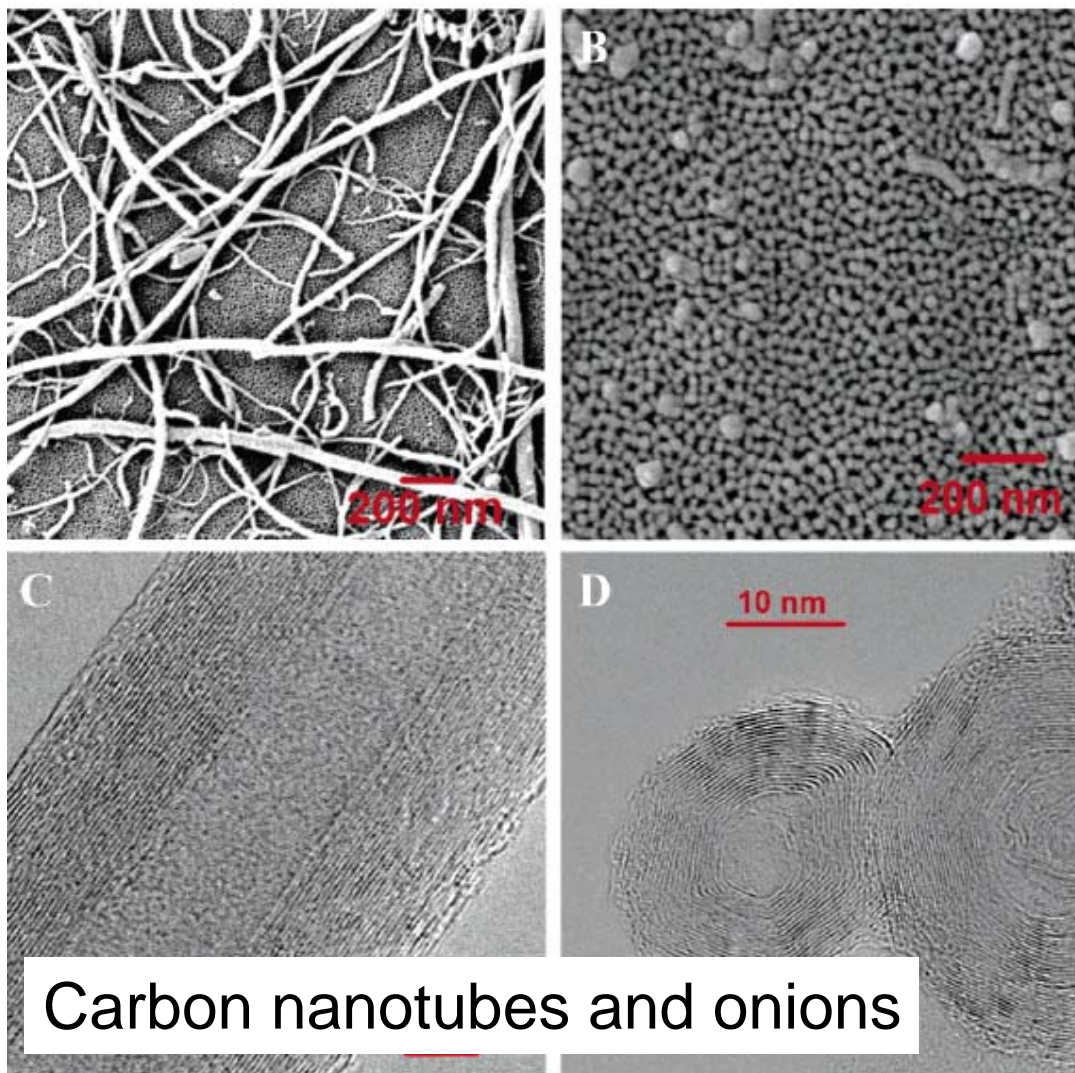
General paradigms in nanoparticles: true or not true?

- Size matters for many dynamic and kinetic issues.
- Inflammation is the key hallmark in effects.
- Surface area is the best metric for inflammation. For other effects no such consensus is present.
- At fine size, aggregates of nanoparticles have a larger effect than one fine particle of the same material.
- Aggregates of nanoparticles cannot be dissociated in epithelial lining fluid. Does that impede single NP uptake?
- Size is the main driver for current studies.

Priority questions and tasks

- What effects are caused by NP beyond those of fine particles? If so what are the mechanisms of these effects?
- What is the distribution of kinetics of NP in the body and its compartments? Is this relevant for the biological effects (ADME).
- Communicate that Nanomaterials are much more than just nanoparticles.
- Are we interested in stronger but similar effects (eg MWCNT, blood coagulation), or in effects not seen before (brain and cognition)?

Case: carbonaceous nanoparticles

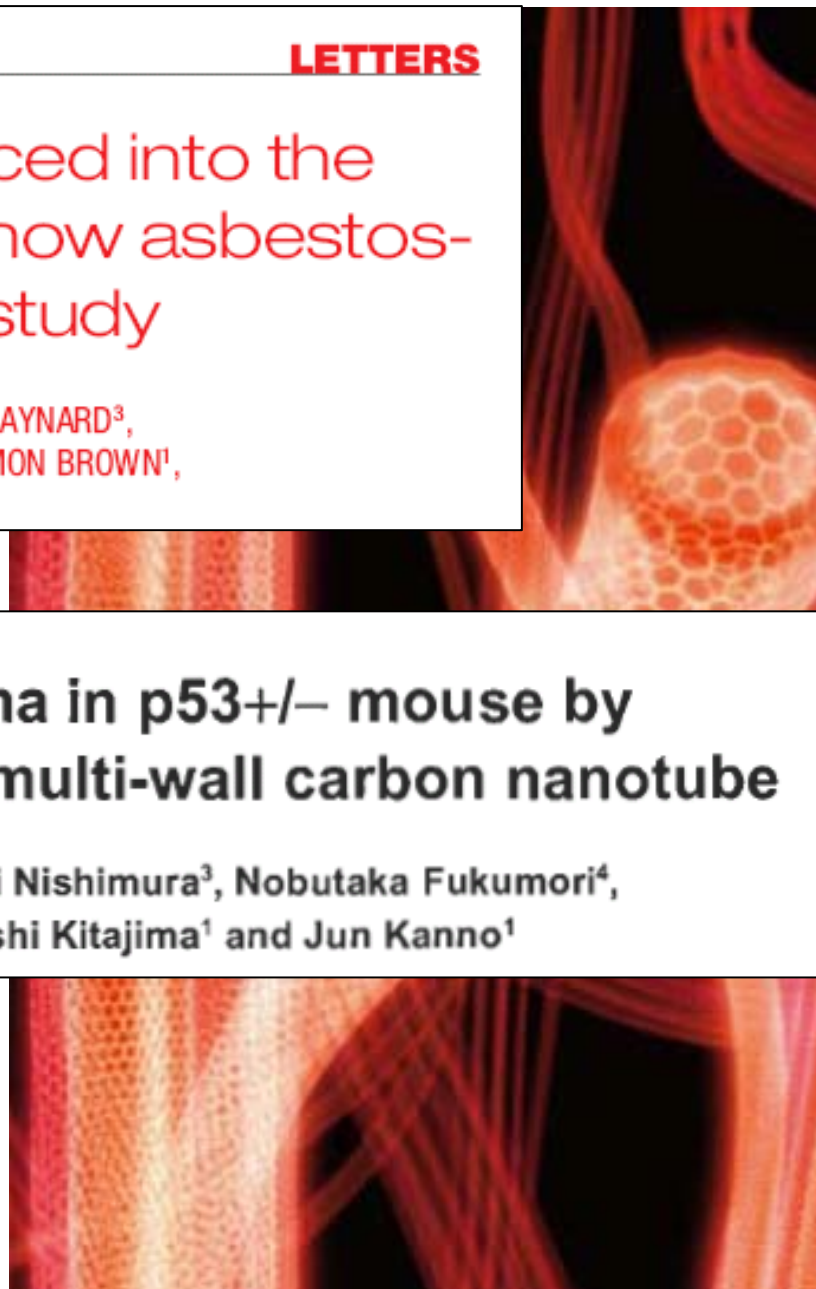


Carbon nanotubes introduced into the abdominal cavity of mice show asbestos-like pathogenicity in a pilot study

CRAIG A. POLAND¹, RODGER DUFFIN¹, IAN KINLOCH², ANDREW MAYNARD³,
WILLIAM A. H. WALLACE¹, ANTHONY SEATON⁴, VICKI STONE⁵, SIMON BROWN¹,
WILLIAM MACNEE¹ AND KEN DONALDSON^{1*}

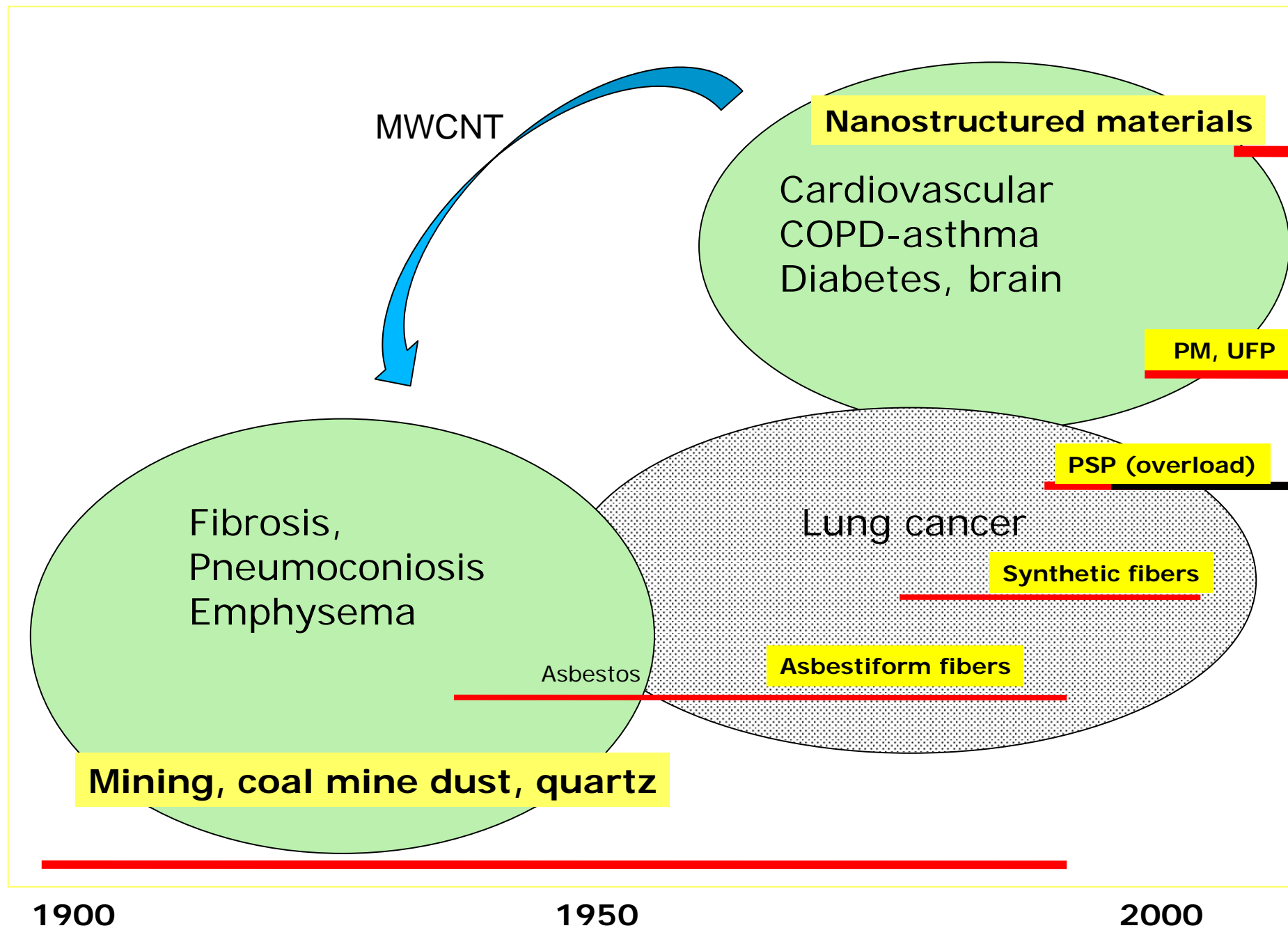
Induction of mesothelioma in p53+/- mouse by intraperitoneal application of multi-wall carbon nanotube

Atsuya Takagi¹, Akihiko Hirose², Tetsuji Nishimura³, Nobutaka Fukumori⁴,
Akio Ogata⁴, Norio Ohashi⁴, Satoshi Kitajima¹ and Jun Kanno¹



General conclusions:

- Ip model intended for hazard finding, but sensitive to artifacts and false positives.
- Poland et al is a short-time, mechanistic study not aiming to predict long term outcome.
- Takagachi study uses highly dosed in sensitive mouse model. Little data available for benchmarking.
- Both studies have used dose in a high-dose range that have been positive for most long fibres in rats. Unfortunately, little benchmark data are available in mice.
- The administration route and the test are only accepted in Europe, but recognized as overly sensitive.
- Pleural injection and inhalation of same materials at relevant dose are the logical next steps.



Future tasks and challenges

- Inventory of relevant nanoparticles and applications.
- Priority should be at preventing exposure
- Connect particle properties and effects
- Discriminate between role of particle size and chemistry.
- Are we interested in stronger but similar effects (eg MWCNT, blood coagulation), or in effects not seen before (brain, protein corona)?
- Communication and inclusion of new professional groups in debate (e.g. material scientists)



**Current legislation is driven by hazard and not by risk.
Nanomaterials deserve a more sophisticated approach**