



Activities of the European Virtual Institute for Integrated Risk Management (EU-VRi) in the area of Nanotechnologies, Risk and Public Health

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EU-VRi: Raison d' être

The one-stop-shop for integrated risk management related product and services Two main lines of activities:

- EU
- Industry

1. EU

- EU Projects
- TP Industrial Safety ETPIS and German TPIS

2. Industry

- Joint services (the ""one-stop-shop" > all products and services available from "one hand")
- Products: software, tools, guidelines, information, ...



Members

Founding:

- INERIS, France
- Technologica, Belgium
- 3. BZF, Hungary
- 4. University of Stuttgart, ZIRN, Germany
- Steinbeis GmbH & Co KG, Germany

Associated:

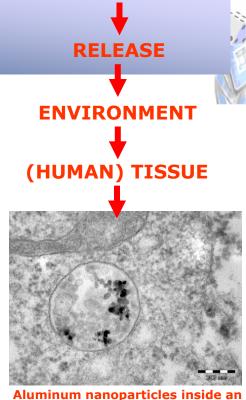
- 6. CONPRICI, Italy
- 7. BAM, Germany
- 8. CNR-IRC, Italy
- 10. CIOP, Warsaw, Poland
- 11. TUV, Germany
- 12. ...





The starting point ...

- What is the REAL safety concern and/or safety impact of nanotechnologies:
 - ("mere") presence in the environment?
 - ("mere") presence in tissues?
 - occupational and/or other health issues/problems/diseases?
- From the Public Health (PH) point of view the answer is simple: possible and actual effects on humans! ... Individuals and groups ...
- Much of the current research stops before reaching the level of Public Health



TECHNOLOGY

Aluminum nanoparticles inside an endosome of an A549 cell from an in vitro toxicity experiment (cf. ToxSci 2006)



Short-term and long-term adverse effects: disorders/diseases



Human exposure to nanoparticles



> yes, we are exposed ... and this IS a problem of INDUSTRIAL SAFETY!

Process	Total concentration in measurement range 14-673 nm, (particles.cm-3)	
Outdoor, office	up to 10 000	
Silicon melt	100 000	
Metal grinding	up to 130 000	
Soldering	up to 400 000	
Plasma cutting	up to 500 000	
Bakery	up to 640 000	
Airport field	up to 700 000	
Welding	100 000 up to 40 000 000	

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ref: SCENIHR 2006, Möhlmann, 2004

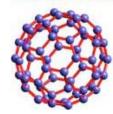


Human exposure to nanoparticles

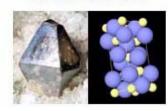
Examples!

- pulmonary and dermal toxicity of fullerenes
- distribution and dermal penetration and pharmacokinetics
- physicochemical characteristics and dermal penetration of metals oxides in sunscreens
- potential photocarcinogenicity of titanium dioxide

Fullerenes



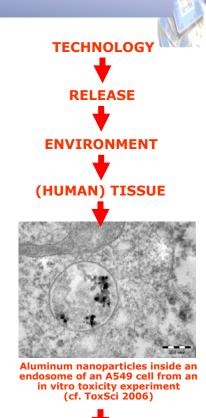
Metal oxides



The starting point ...

Can Nanomaterials be Toxic? ... YES!

- Wide range of materials can be made "nano"
- Nanometer range is where life processes happen e.g. inhaled ultrafine particles are toxic to lung and cardiovascular system
- Transported easily, go unexpected places
- Accumulate in cellular organelles
- Some components are toxic as chemicals, i.e. they can be toxic both as chemical and nano!
- Many (most?) of possible effects belong to the category of "low-doses-long-term-exposure" which is an unsolved problem in itself, also for "non-nano" materials!
- ... Huge knowledge gap: Currently we have "a nano part" of knowledge needed to assess the toxicity of nanomaterials! ... probably just about 10⁻⁹ of knowledge we have about the toxicity of chemicals! ... think about REACH!



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Short-term and long-term

adverse effects:

disorders/diseases

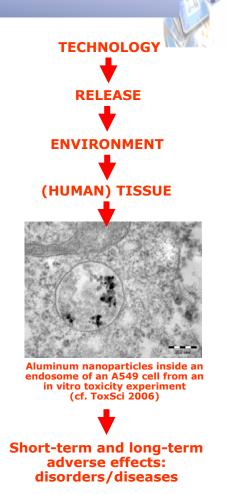
The starting point ...

What do we have ("good news")?

- public and scientific interest
- Overall methodology/approach (e.g. the IRGC)
- Running research (US, EU, ...)
- Some methods and tools

What we still miss (for sure!)

- clinical research
- targeted epidemiological research/surveys
- integration of research: analytical, in silico, in vitro, in vivo ...
- integration of nano-issues into the routine practice of public health ... regulatory framework missing!



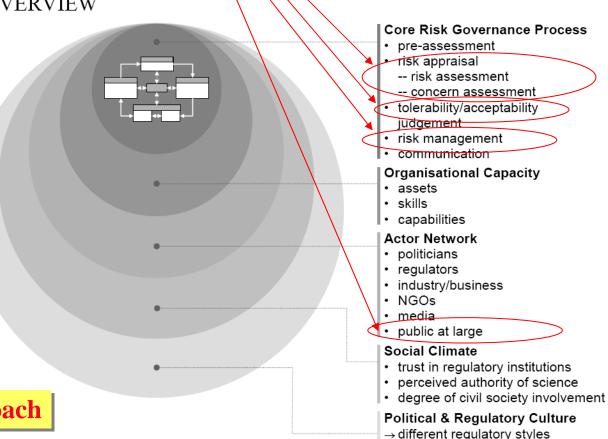


What is so specific about nanotechnologies with respect to public health?

Public Health (primary concerns)

IRGC RISK GOVERNANCE FRAMEWORK (I/III): OVERVIEW





methodology/approach

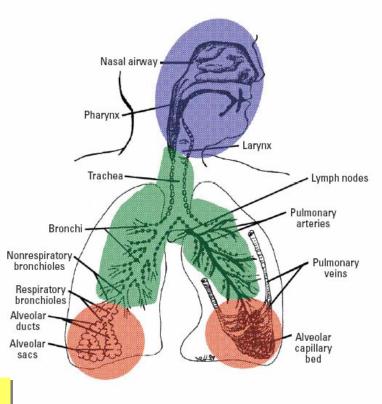


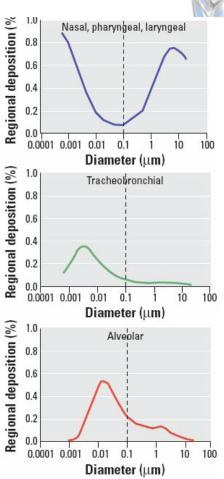
IRGC RISK GOVERNANCE FRAMEWORK (II/III): ORE PROCESS

ORE PROCESS Public Health (primary concerns) What is so lanagement Sphere: Assessment Sphere: specific ecision on & Implementation of Actions Generation of Knowledge about nano-Pre-Assessment technologies Problem Framing with respect Early Warning Screening Determination of Scientific Conventions to public health? Risk Management Risk Appraisal Implementation Risk Assessment Option Realisation Hazard Identification & Estimation Monitoring & Control · Exposure & Vulnerability Assessment Communication Feedback from Risk Mgmt. Practice Risk Estimation Decision Making Concern Assessment Option Identification & Generation Risk Perceptions · Option Assessment Social Concerns · Option Evaluation & Selection Socio-Economic Impacts Tolorability & Acceptability Judgement Risk Evaluation Risk Characterisation Judging the Tolera- Risk Profile bility & Acceptabiliy Judgement of the Need for Risk Seriousness of Risk Reduction Measures · Conclusions & Risk methodology/approach Reduction Options



Example
(US):
Pulmonary
Deposition as
a function of
particle size
(not so
straightforward - PH
research
needed!)





running research

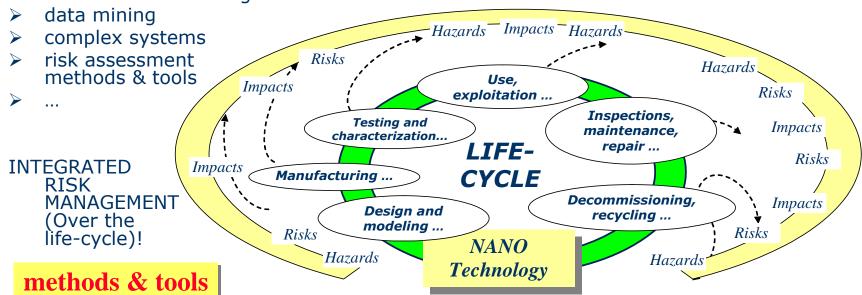
ref: Bucher, NTP 2006



Methods and tools – part of the solution:



- IT infrastructures (databases, communication possibilities ...)
- simulation
- bio-inspired modeling (e.g. artificial organs, artificial life)
- advanced methodologies

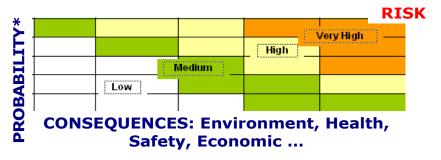




(integrated) Risk assessment and management should:

- combine quantitative and qualitative assessment
- deal with low-quality, scattered, inconsistent and few data
- match the model-based and behavior-based assessment be seamlessly combined with the preliminary screening analysis
- provide a preliminary assessment of risks and effects of low-doses long exposure effects in the (usually!) short times available in research projects





* - Calculated and/or perceived by the society

Conclusions: we still lack a lot!

Comparison / Differences			
	Chemicals / particles	Nanomaterials	
Can we reasonably predict?			
Structure/ properties	yes	no !	
Absorption	yes	no	
Distribution	often	no	
Metabolism	often	sometimes	
Excretion	often	no	
Toxicity	often	no !!	
Target organs	often	no !!	
Persistence/reversibility of effect	often	no !!!	
Do we know how to design, perform and interpret studies? !!!			
Material preparation	yes	no	
Study designs	yes	no	
Interpretation	yes	yes	

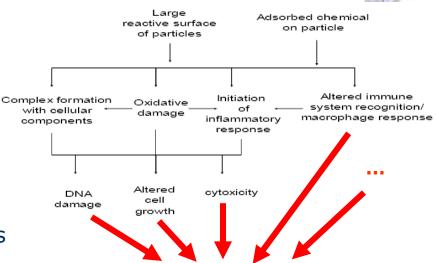
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CONCLUSIONS ...

- General conclusion:
 - Yes, there is a cause for concern/caution
 - No, there is no quick answer
 - Yes, we (as public health people) know what questions to ask
 - Yes, were we making progress
- Main issue: effects on humans can be far more complex than "just" DNA damage ... e.g. chronic diseases, reduced work ability ...

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Short-term and longterm adverse effects ON HUMANS (also "work force"!): disorders/diseases???

... in other words ...

- Health effect are:
 - not only "depositions" and "concentrations", but more
 - how the people feel ("thick" or "well"!)
 - if exposed to nanoparticles, nanomaterials, nanotechnologies ...
- ...and for industry and industrial safety it means the exposure of:
 - work force
 - users of their products
 - general population

