



# **An EC update on nanomaterials with emphasis on risk assessment methods**

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Risk Assessment

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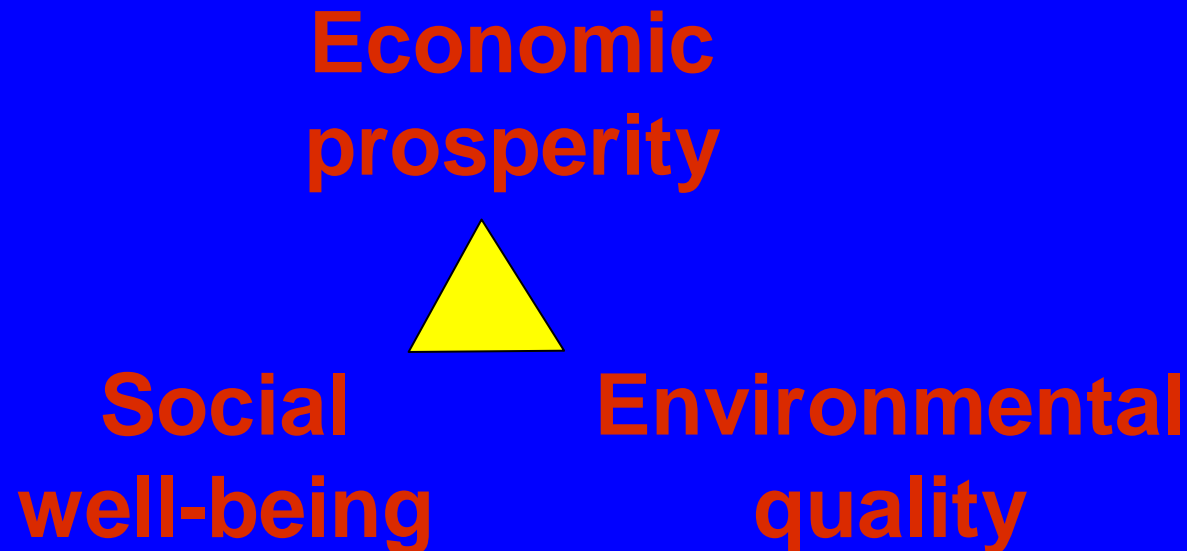


# Outline

1. Europe's "safe, integrated and responsible" approach to nanosciences & nanotechnologies
2. What the experts say on "the appropriateness of risk assessment methods for nanomaterials"
  - ◆ Risk characterization
  - ◆ Question 1: **Are current methods appropriate?**
  - ◆ Question 2: **How to adapt, complete them?**
  - ◆ Question 3: **Knowledge gaps?**
  - ◆ Regulatory implications
3. **Conclusion:** modifications are required



# 1. Europe's "safe, integrated and responsible" approach to nanosciences & nanotechnologies





# The European Nano Action Plan

- R&D
- Industry
- Society
- **Public Health, Safety, Environment and Consumer Protection**
  - Improve knowledge base
  - Examine regulatory aspects
- International Cooperation



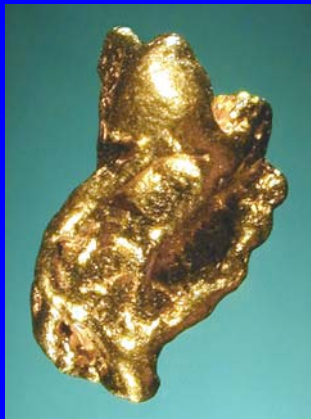
## 2. The scientific opinion

Are nano and bulk properties alike?  
→ No, generally, nano  $\neq$  bulk

Bulk gold:

■ yellow

■ inert



1 nm gold NP:

■ blue

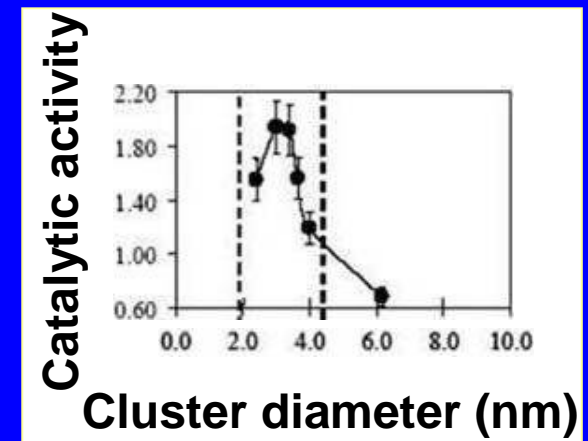
■ low reactivity



3 nm gold NP:

■ reddish

■ catalytic





Are toxicological inferences possible?

Generally, no.

Why?

At present, there are no systematic rules for toxicology (insufficient data).



## What does the hazard depend on?

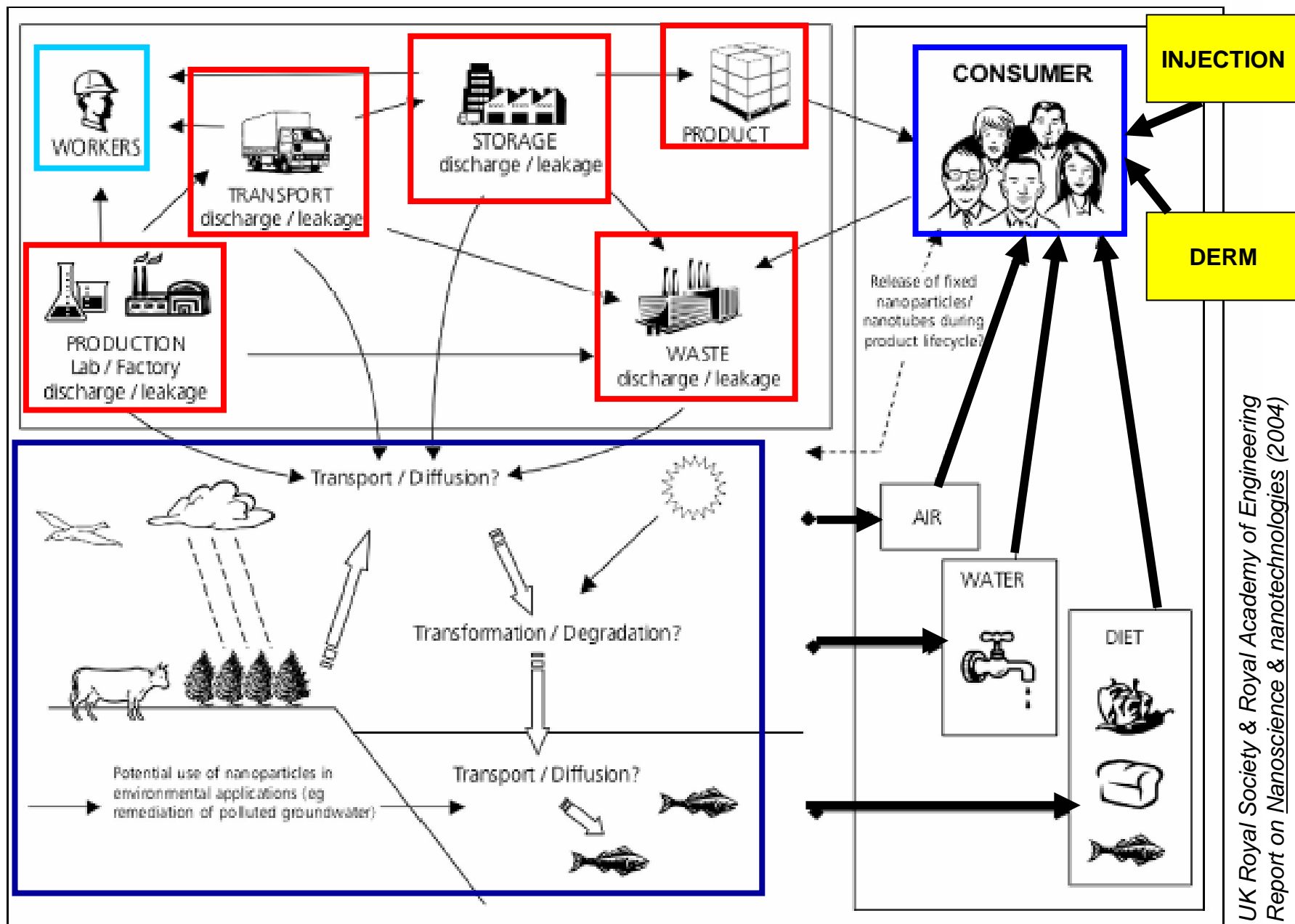
- Small size, shape and composition, including surface charge and adsorbed species
- Aggregation and dissolution or degradation
- Physiological response (lack of data)

### ➡ Implications of small size

- ▶ High surface to volume ratio → higher reactivity
- ▶ Quantum effects → new behaviors
- ▶ Significance of surface modification
- ▶ Greater toxic effects
- ▶ Interactions with biomolecules, e.g., DNA, RNA

<b>Diameter</b>	<b>Entity/Process</b>
7000-8000 nm	human red blood cell
800-3000 nm	bacterium
1000 nm	human cell nucleus
< 60 nm	NPs cross membranes
17-300 nm	virus
5.5 nm	hemoglobin
< 4 nm	NPs cross the blood-brain barrier
2 nm	DNA helix
0.3 nm	water molecule

# Exposure: sources, targets & routes





# Are current methods appropriate?

## 1. Hazards aspects (3)

- ➔ Toxicological & ecotoxicological methods don't address all hazards
- ➔ Attention needs to be given to the mode of delivery to reflect exposure scenarios
- ➔ Assays are not always comprehensive



Are current methods appropriate?

## 2. Exposure aspects (2)

- ➔ Mass characterization must be completed with surface and number of particles to express dose
- ➔ Existing methods used for environmental exposure assessment are not always appropriate



# Are methods appropriate?

## 3. Overall risk aspect

- ➔ Current risk assessment procedures require modification for nanoparticles.



# How to adapt and complete?

## ➔ Address issues

- Characterization of nanomaterials
- Routine measurements
- Characterization of hazards (including to assess exacerbation of pre-existing medical conditions and increased susceptibility to some diseases by nanomaterials)
- Systemic distribution of nanomaterials

## ➔ Use heuristic algorithms based, e.g., on likelihood of exposure, existing knowledge, homogeneity, solubility, size < 100 nm, coalescence, stability, etc.



## What are the knowledge gaps?

- ➔ Characterization of the mechanisms and kinetics of release
- ➔ Extent to which extrapolation is possible
- ➔ Toxicokinetic data after exposure
  - To identify target organs
  - To determine doses for hazard assessment
- ➔ Exposure levels to workers, the public and the environment and associated effects
- ➔ Fate, distribution and, persistence and bioaccumulation in the environment



## Regulatory implications (4)

- Dematerialization → reexamine thresholds
- New nanoproperties or uses → provide a unique CAS number-based identifier
- Small size and low mass
  - set new workplace exposure standards and reexamine worker protection devices
  - reexamine classification and labeling for human and environmental health
- Incompleteness of conventional tox and ecotox tests → require new tests (e.g., including systemic effects)





# Conclusion

- ➡ Risk assessment: Modifications required for nanoparticles (hazard x exposure)
- ➡ Toxicological profile: Nano ≠ bulk
- ➡ Toxicology: No systematic rules (lack of data)
- ➡ Implications
  - Testing guidelines
  - Health, occupational & environmental standards
  - Registration, classification and labeling of products
- ➡ Knowledge and data: Significant gaps