NANOFOOD: How to Assess Risks of a Nutritional Miracle?

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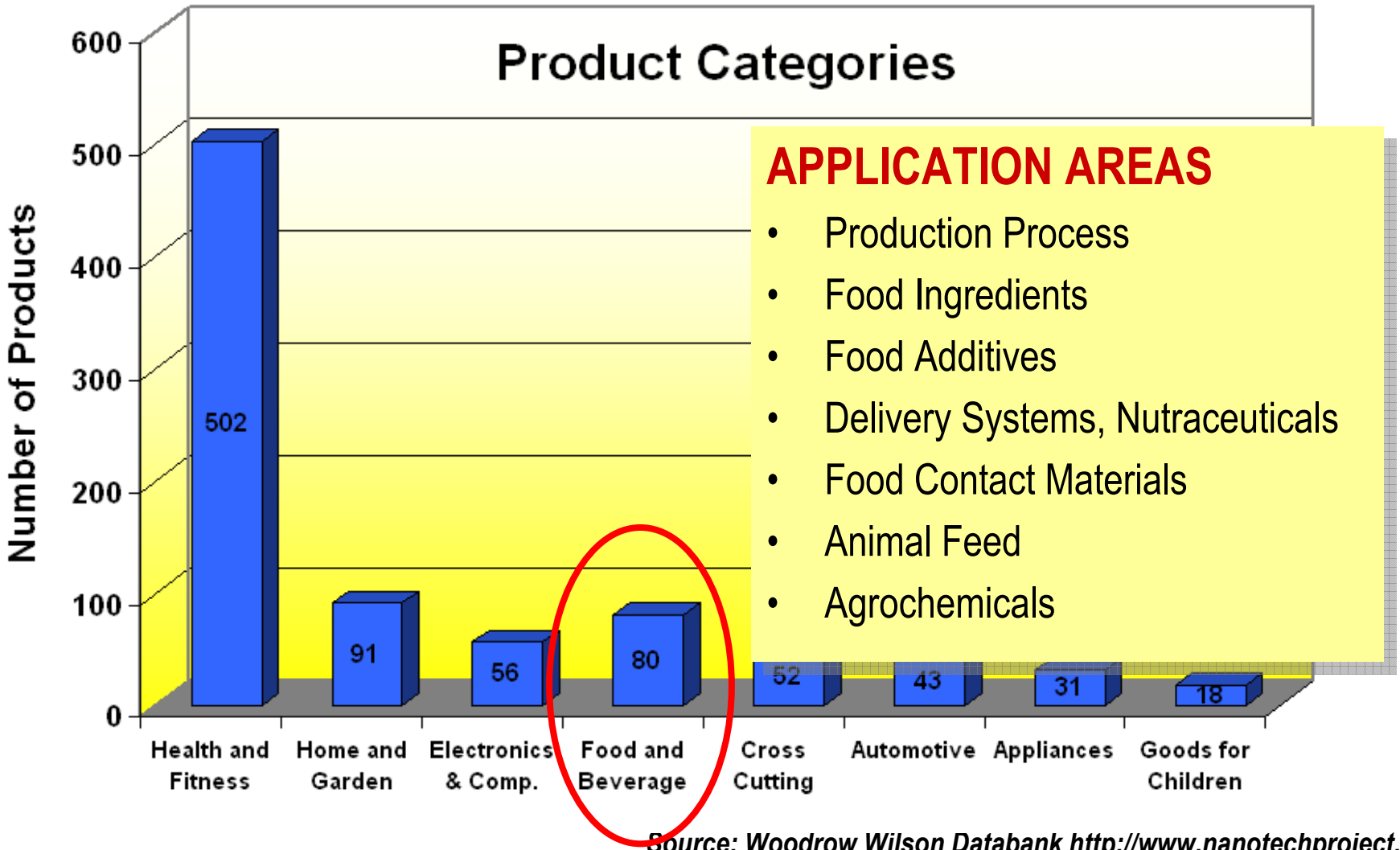
ihcp Institute for Health and Consumer Protection

*The views expressed in this presentation are personal and may not necessarily reflect those of the European Commission

NT Consumer Products on the Market



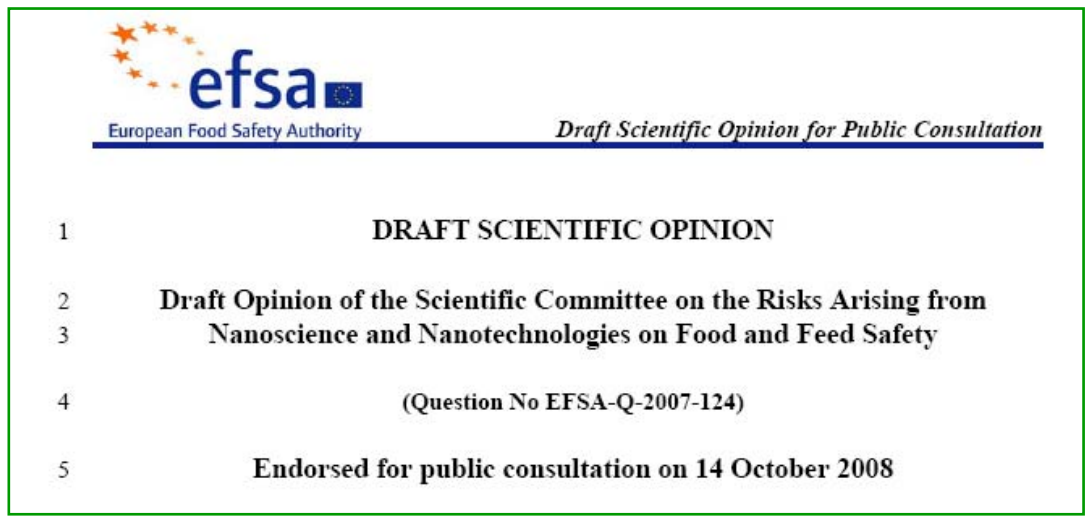
APPLICATION AREAS

- Production Process
- Food Ingredients
- Food Additives
- Delivery Systems, Nutraceuticals
- Food Contact Materials
- Animal Feed
- Agrochemicals

Source: Woodrow Wilson Databank http://www.nanotechproject.org/

How to assess risks?
What is needed for risk assessment?

Knowledge gaps to overcome



efsa
European Food Safety Authority
Draft Scientific Opinion for Public Consultation

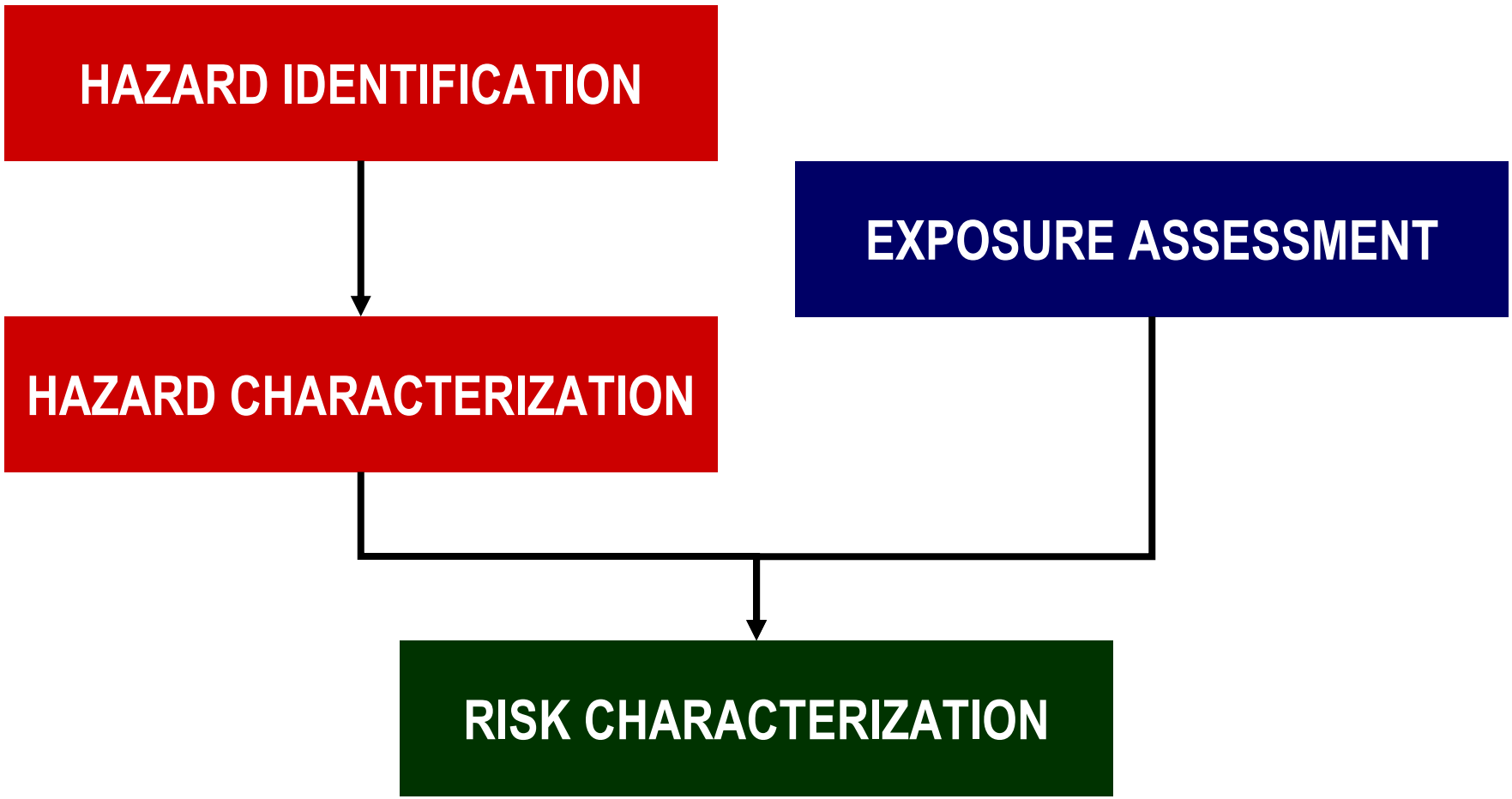
1 **DRAFT SCIENTIFIC OPINION**

2 **Draft Opinion of the Scientific Committee on the Risks Arising from**
3 **Nanoscience and Nanotechnologies on Food and Feed Safety**

4 **(Question No EFSA-Q-2007-124)**

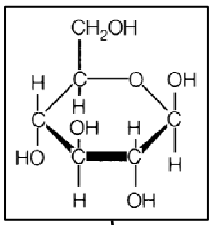
5 **Endorsed for public consultation on 14 October 2008**

RISK ASSESSMENT PARADIGM

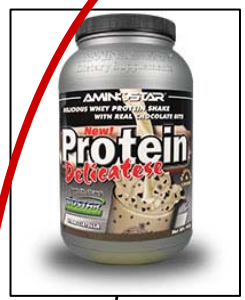


NANOSCALE - FOOD

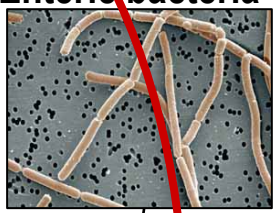
Sugars, oligonutrients



Proteins, aminoacids



Probiotics
Enteric bacteria

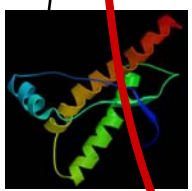


Seeds, cereals, spices

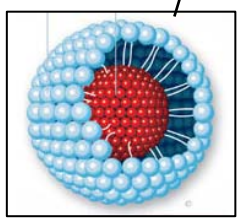
0.1 nm | 1 nm | 10 nm | 100 nm | 1 μm | 10 μm | 100 μm | 1 mm | 1 cm

10^{-10} m | 10^{-9} m | 10^{-8} m | 10^{-7} m | 10^{-6} m | 10^{-5} m | 10^{-4} m | 10^{-3} m | 10^{-2} m

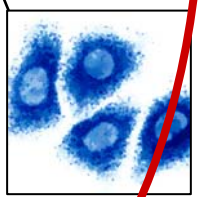
Atom



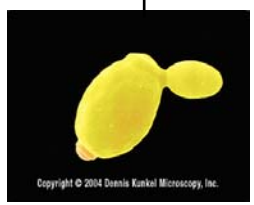
Prions



Nanoparticles (Micelles)



Hepatitis A virus

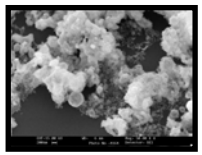


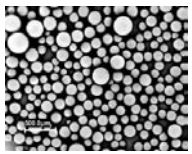
Fungi, brewer's yeasts

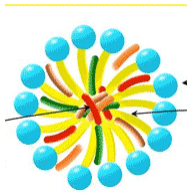
RISK ASSESSMENT

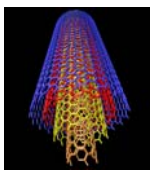
(1) HAZARD IDENTIFICATION

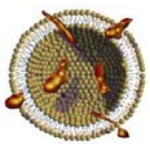
Nanoparticles in Food – what makes them different?



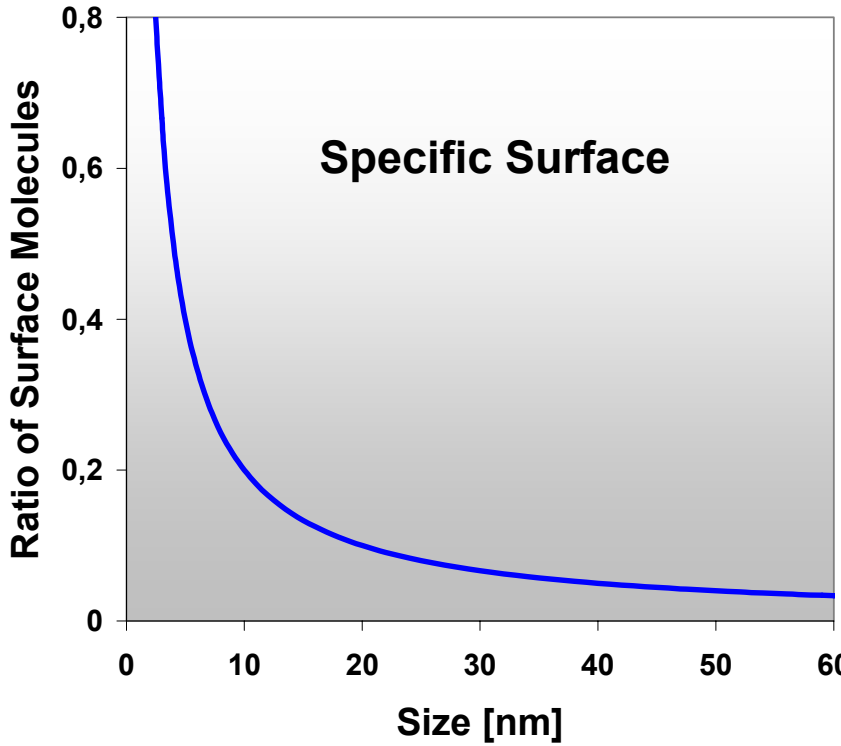








- Large specific surface
- Chemical reactivity very different compared to bulk material
- Quantum effects lead to special properties (electronic, mechanical, optical …)
- Matrix dependent properties
- Many forms: fullerenes, nanotubes, nanocarriers, nanoemulsions, nanoencapsulates, …



Definition of Engineered Nanomaterials?

Interaction of NM with biological matrices

Consequences of phys.-chem. properties

- NM are thermodynamically unstable or metastable
- Aggregation or agglomeration
- Interaction with surrounding matrix
- Ageing
- Adsorption of ions – surface charge
- Nuclei for heterogeneous crystallisation
- Catalytic effects

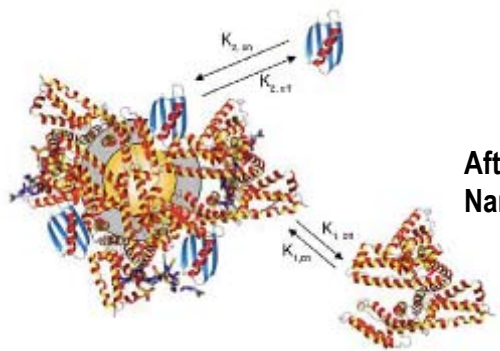
Simon and Joner, J. Food & Nutrition Research 47 (2008)

Effect on Food Matrices:

- Changes in food consistency
- Influence on sensory properties

Effects of NM in living systems:

- Interaction with functional groups of biopolymers
- Formation of reactive oxygen species
- Nuclei for induced crystallisation



After Lynch and Dawson, Nanotoday 2008, (3) 1-2ß

Interaction of NM with biological matrices

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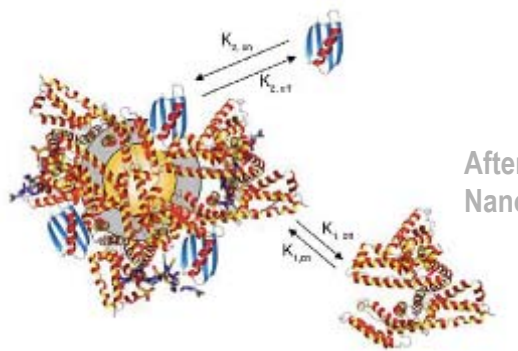
Simon and Joner, J. Food & Nutrition Research 47 (2008)

Effect on Food Matrices:

- Changes in food consistency
- Influence on sensory properties

Difficulties to characterize, detect and measure NMs in biological matrices

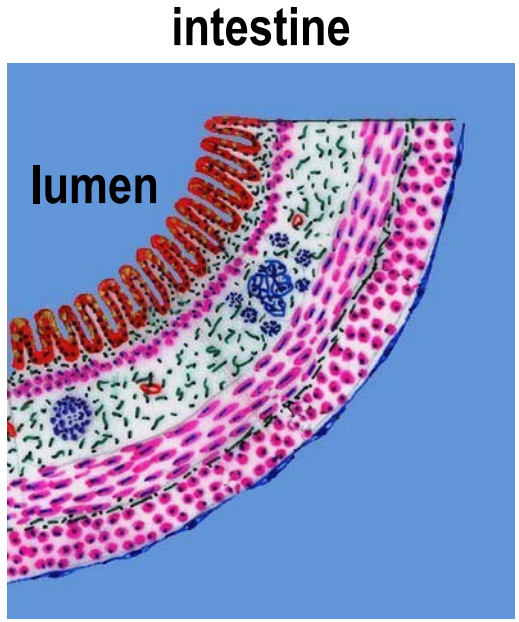
- Interaction with functional groups of biopolymers
- Formation of reactive oxygen species
- Nuclei for induced crystallisation

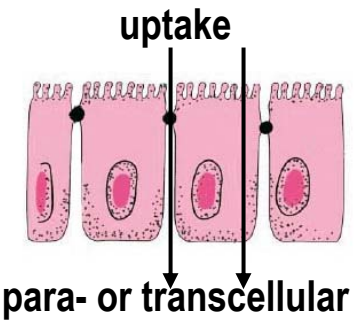


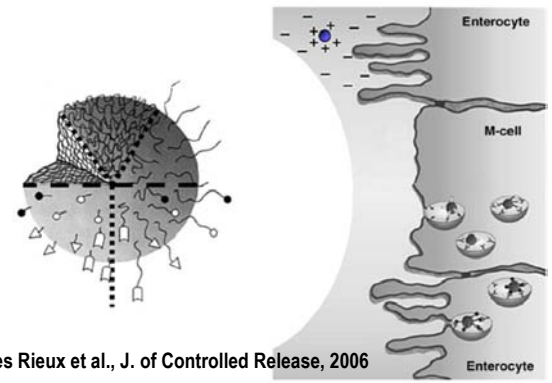
After Lynch and Dawson, Nanotoday 2008, (3) 1-2ß

Fate of Nanomaterials in the GI-tract

- Transformation in the ***lumen***
- Translocation through the ***intestinal wall***
  - Transcytosis and passive diffusion
  - phys.-chem properties dependent
  - Entering capillaries of lymphatic system
- Translocation to ***target organs*** (liver, kidneys, lungs, spleen, …)
- Biotransformation and excretion: little information







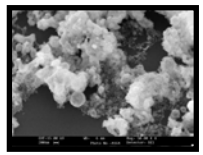
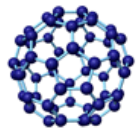
after des Rieux et al., J. of Controlled Release, 2006

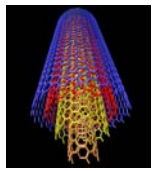
Extremely limited data on biokinetics and fate of nanomaterials after oral exposure

Understanding the biological response

- **Size and Shape**
  - Size distribution
  - Shape
- **State of Dispersion**
  - Agglomeration/Aggregation
- **Physical and Chemical Properties**
  - Chemical composition
  - Crystalline phase and crystallite size
  - Solubility
  - Impurities
- **Surface Area and Porosity**
- **Surface Properties**
  - Surface composition
  - Catalytic properties
  - Surface charge
  - Reactivity
  - Adsorption/desorption of molecules
  - Lipophilicity/hydrophilicity

Nanoparticle Characteristics




EFFECT

- Translocation from GI-tract to target organs

Kinetics

- Protein binding
- Cellular uptake
- Accumulation and retention

Toxicity

- Cell/tissue response

RISK ASSESSMENT

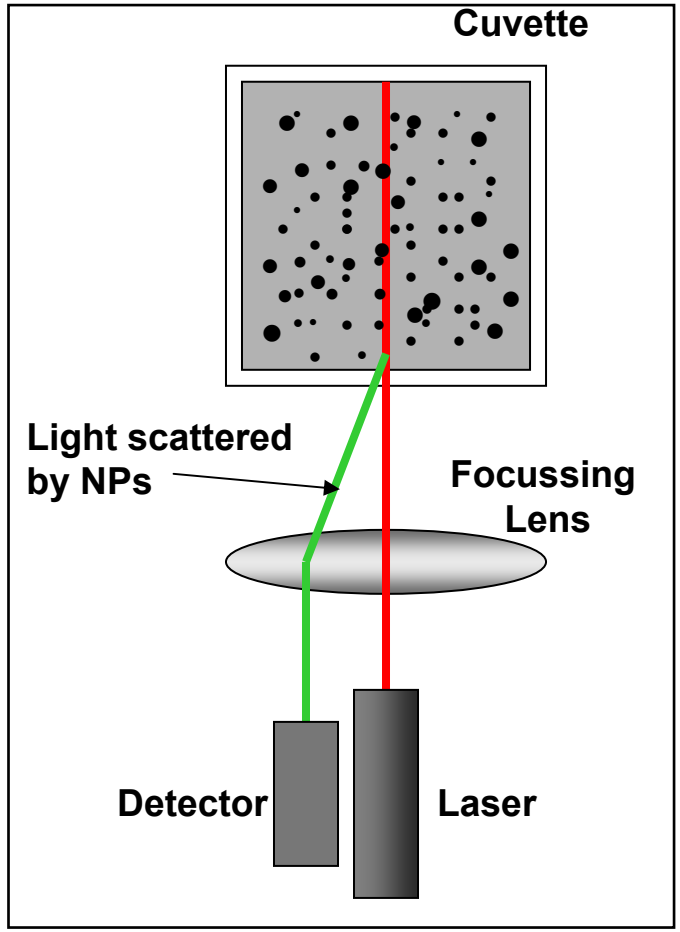
(2) HAZARD CHARACTERIZATION

Characterization and Detection Techniques

Single particle techniques vs ensemble techniques

A number of tools – no best techniques

Electron Microscopy

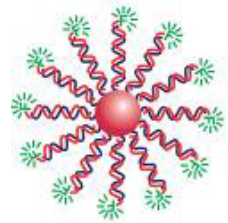


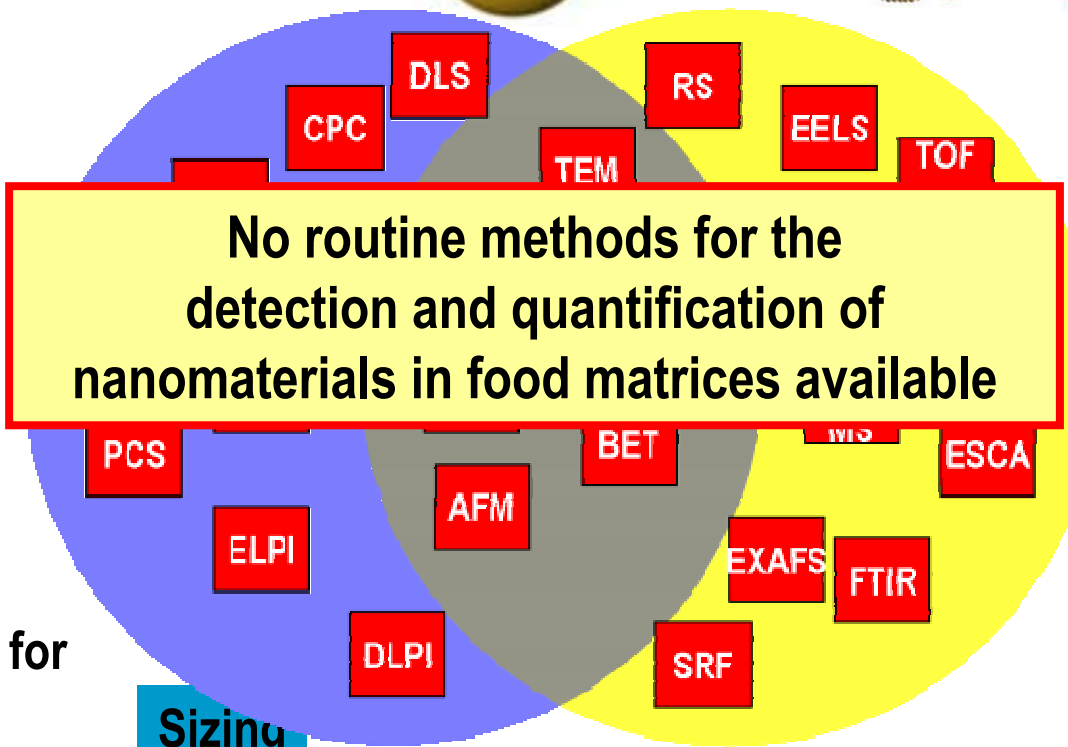
Dynamic Light Scattering

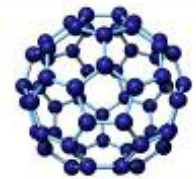
Characterization and Detection Techniques

Single particle techniques vs ensemble techniques

A number of tools – no best techniques

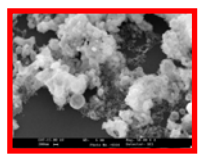


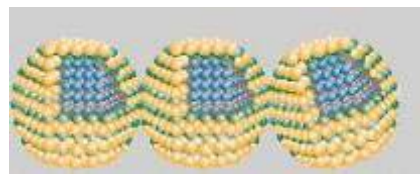




ISSUES

- Testing environment
- Sample preparation
- Laboratory vs routine measurements
- On-line measurements for safety analyses?
- Minimum set of characteristics?





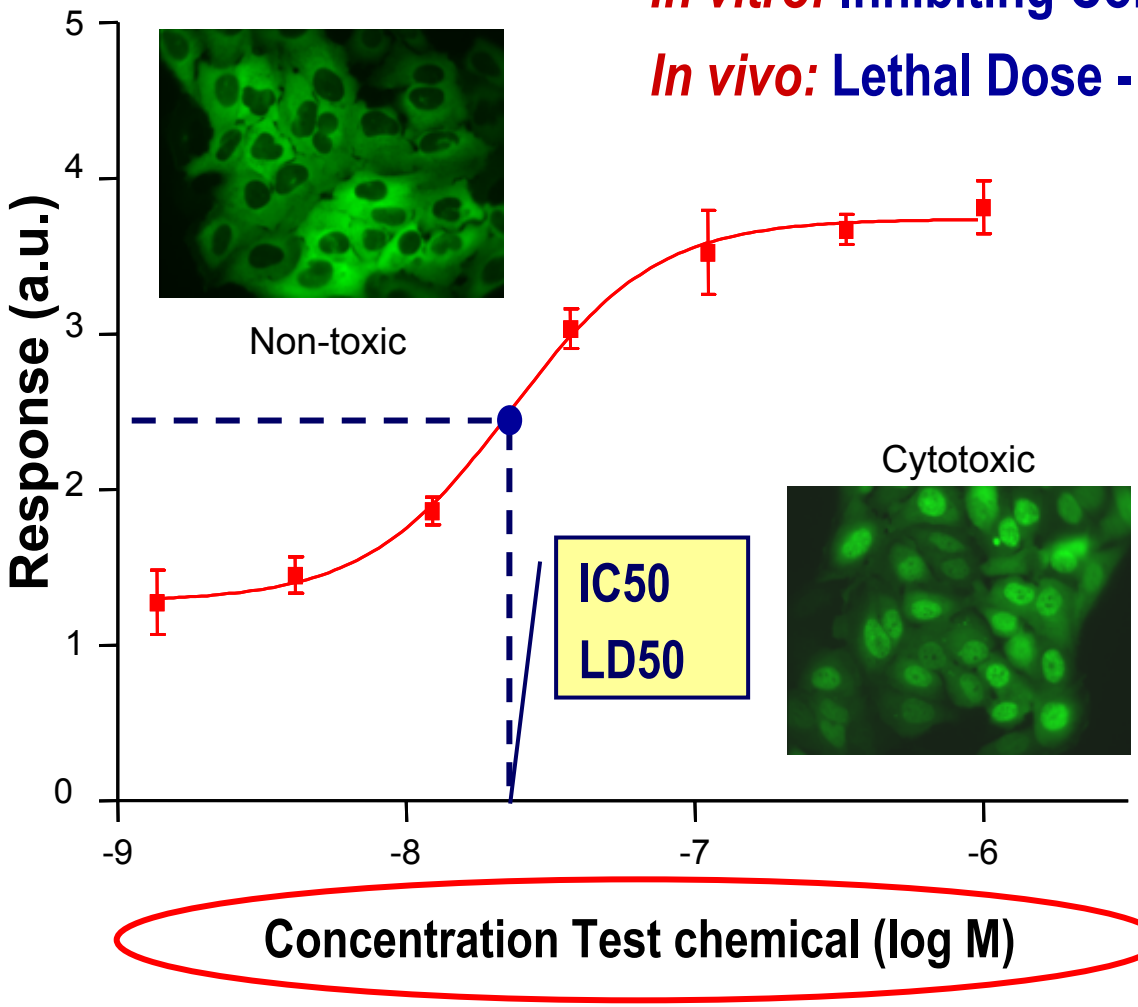
BIOKINETICS: some 'knowns'

- Toxicokinetic studies are ***limited to few types*** of insoluble nanomaterials (metals/metal oxides, gradually degrading polymers)
- Indications ***that small sized*** nanomaterials have a ***more widespread*** distribution than larger ones
- ***All organs may be targets***
- There may be ***large differences*** in the biokinetic behaviour for different types of nanomaterials (coatings, surface treatment, …)
- Nanomaterials were ***not characterized as administered***

TOXICITY: Dose – Effect Relationship

In vitro: Inhibiting Concentration - IC_{50}

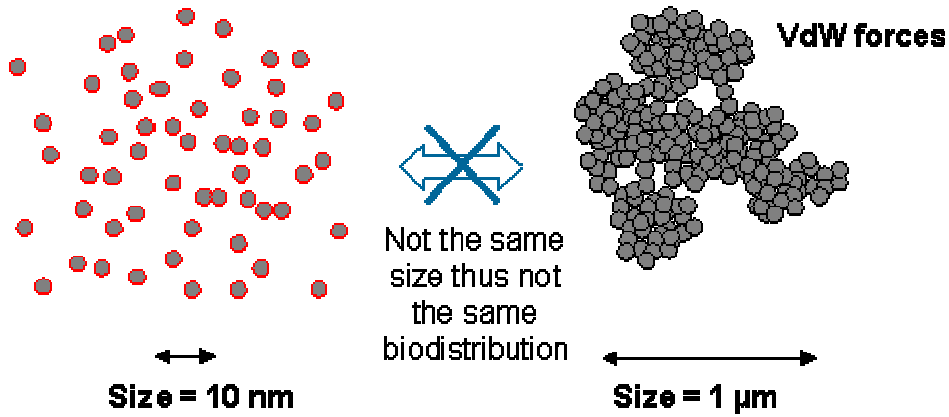
In vivo: Lethal Dose - LD_{50}



TOXICITY: Food Related Studies

Dose metrics

- Mass?
- Surface area?
- Number concentration?



- ***Few*** studies on oral administration
- Adequate ***characterization*** of nanomaterials ***lacking***
- Only a ***narrow range of effects*** have been studied
- Reported oral toxicity studies ***restricted to acute toxicity***
- ***properties - toxicity*** relationship not yet established
- Current ***toxicity testing adequate*** to detect all aspects of potential toxicity?

TOXICITY: Food Related Studies

Dose metrics

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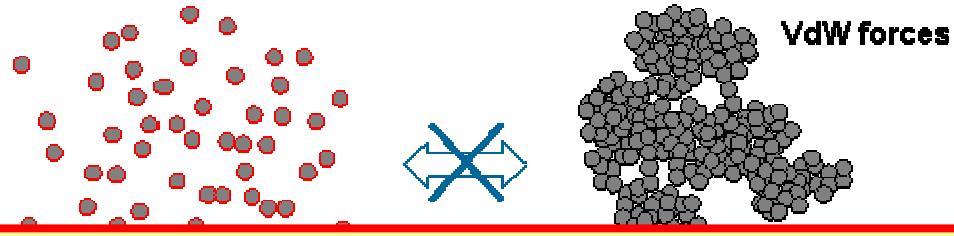

Very limited information for risk characterization regarding oral exposure to NM

- **Phys.-chem. Characterization**
- **Toxicokinetics**
- **Toxicity**

- Adequate ***characterization*** of nanomaterials ***lacking***
- Only a ***narrow range of effects*** have been studied
- Reported oral toxicity studies ***restricted to acute toxicity***
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RISK ASSESSMENT

(3) EXPOSURE ASSESSMENT

Exposure to NMs from Food and Feed

POTENTIAL EXPOSURES

- Migration from ***food contact materials***
- NM released in food ***processing***
- Nano-sized or nano-encapsulated ***ingredients***
- Residues from nano-formulated or nano particulate ***agro-chemicals***
- Contamination due to NMs released to ***environment***

EXPOSURE ESTIMATIONS

- Similar framework as for non-nanoscale materials
- No possibility to routinely ***determine NMs in situ*** in the food matrix
- Data on ***bioavailability*** of NMs after ingestion needed
- Data on ***release from FCM*** into food

RISK ASSESSMENT

(4) RISK CHARACTERIZATION

Risk Characterization of Nanomaterials in Food

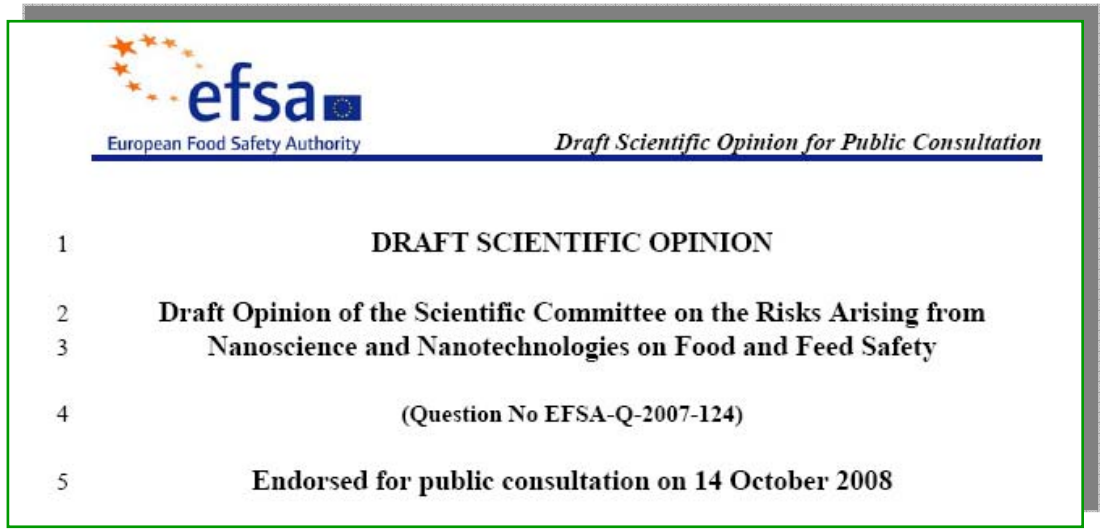
AVAILABLE

- Risk assessment paradigm is considered sufficient for application of nanotechnology in food
- Current toxicity testing approaches suitable to start case by case

KNOWLEDGE GAPS

- Lack of data for a comprehensive understanding of hazards
- Conventional toxicological test methods appropriate?
- No routine analytical methods for detection and analysis of nanomaterials in food matrices
- Current guidance documents appropriate for NM in food?
- Changes in regulation: on which level?

Risk Characterization of Nanomaterials in Food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Draft Scientific Opinion for Public Consultation

1 **DRAFT SCIENTIFIC OPINION**

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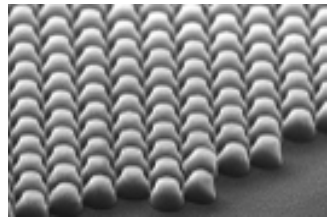
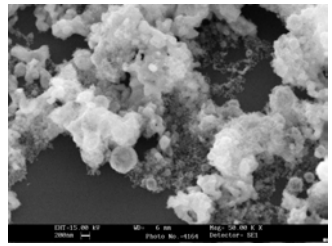
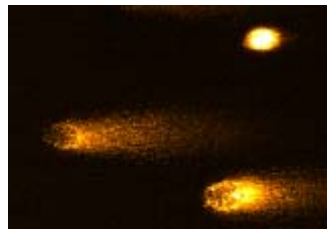
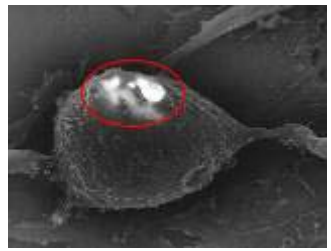
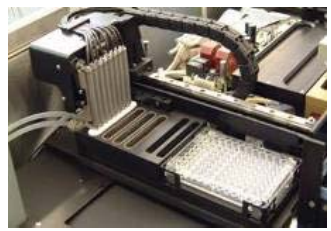
4 **(Question No EFSA-Q-2007-124)**

5 **Endorsed for public consultation on 14 October 2008**

"Appropriate data for risk assessment of an ENM in the food and feed area should include ***comprehensive identification and characterization*** of the ENM, information on whether it is likely to be ingested in nanoform, and, if ingested, whether it remains in ***nanoform at absorption***. If it may be ingested in nanoform, then ***repeated-dose toxicity studies are needed*** together with appropriate *in vitro* studies (e.g. for genotoxicity). ***Toxicokinetic information will be essential*** in designing and performing such toxicity studies."

JRC Nanobiotechnology Research

- Surface Science – Bio/non-bio interfaces
- Nanotoxicology
- Molecular and cell imaging for advanced *in vitro* testing
- Assay Automation
- Risk characterization and information management tools

SEVENTH FRAMEWORK PROGRAMME

ECHA

efsa Autorità europea per la sicurezza alimentare

OECD

ISO VAMAS cen

Joint Research Centre (JRC)

Robust science for policy making

Thank you for your attention

Web: www.jrc.ec.europa.eu
Contact: jrc-info@ec.europa.eu