

# ***NANOFOOD: How to Assess Risks of a Nutritional Miracle?***



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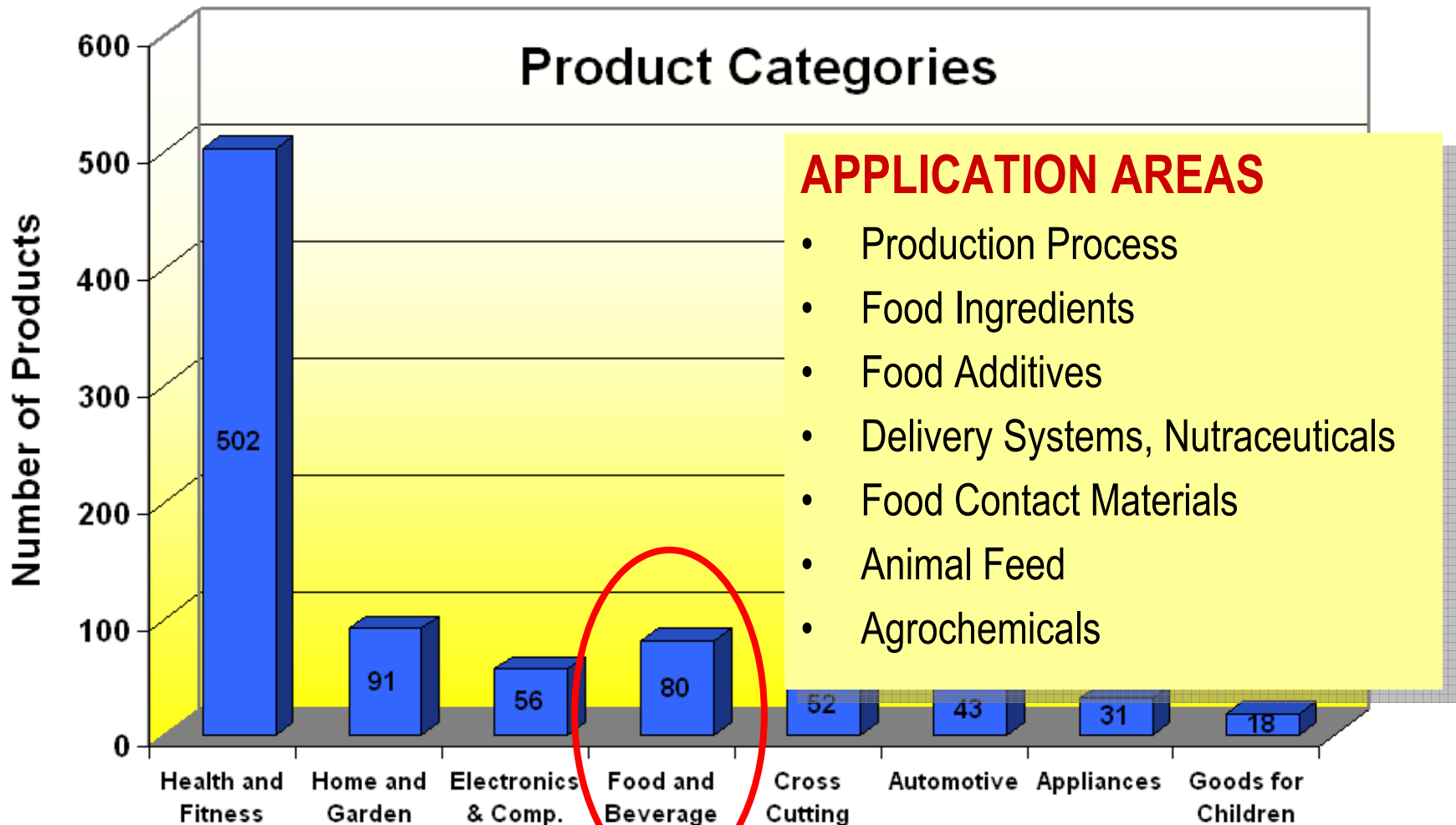
***3 European Food Safety Authority, Parma, Italy***

**<http://www.jrc.ec.europa.eu>**




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

# NT Consumer Products on the Market



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

## Knowledge gaps to overcome



European Food Safety Authority *Draft Scientific Opinion for Public Consultation*

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1 **DRAFT SCIENTIFIC OPINION**

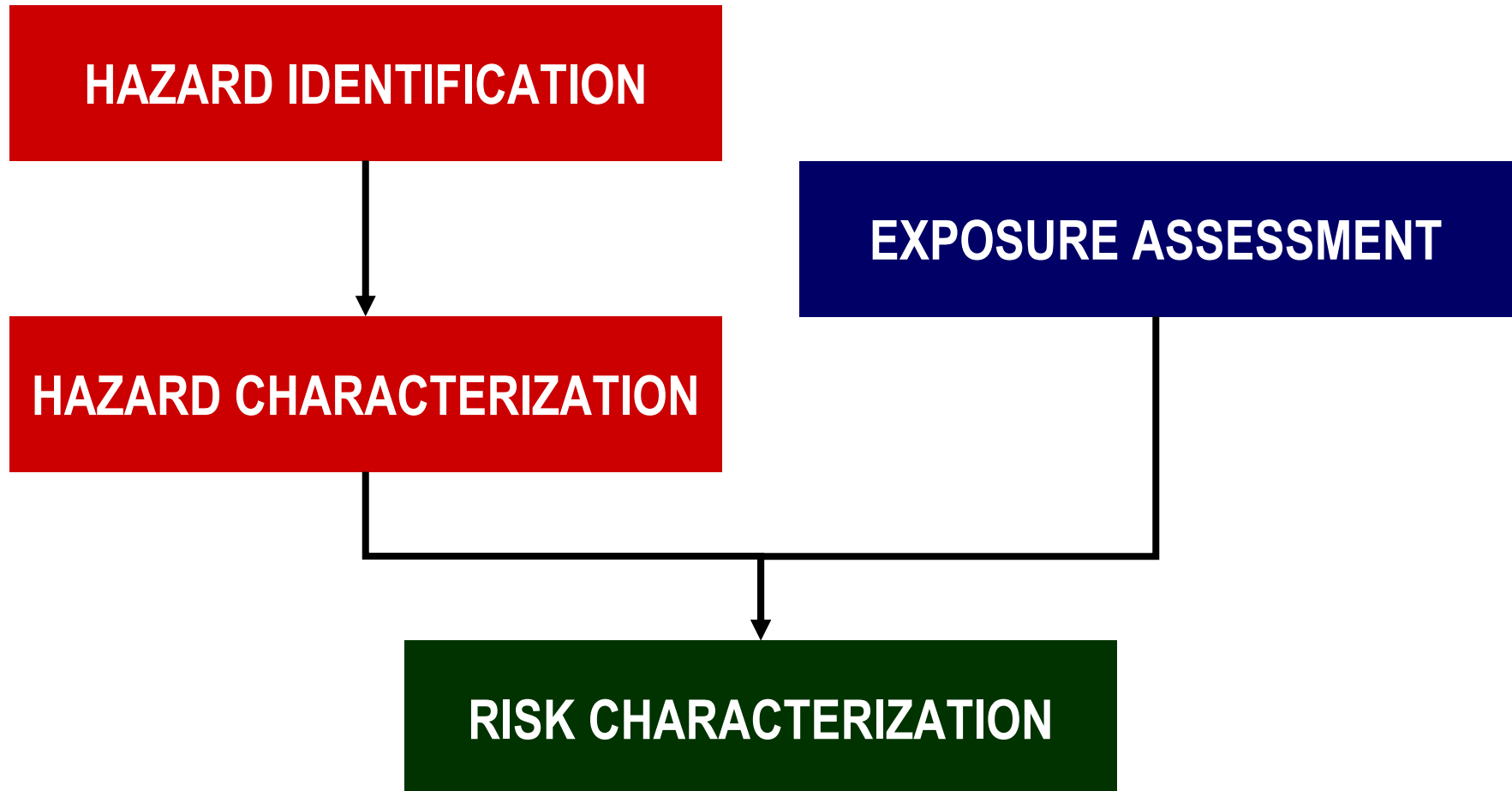
2 **Draft Opinion of the Scientific Committee on the Risks Arising from**

3 **Nanoscience and Nanotechnologies on Food and Feed Safety**

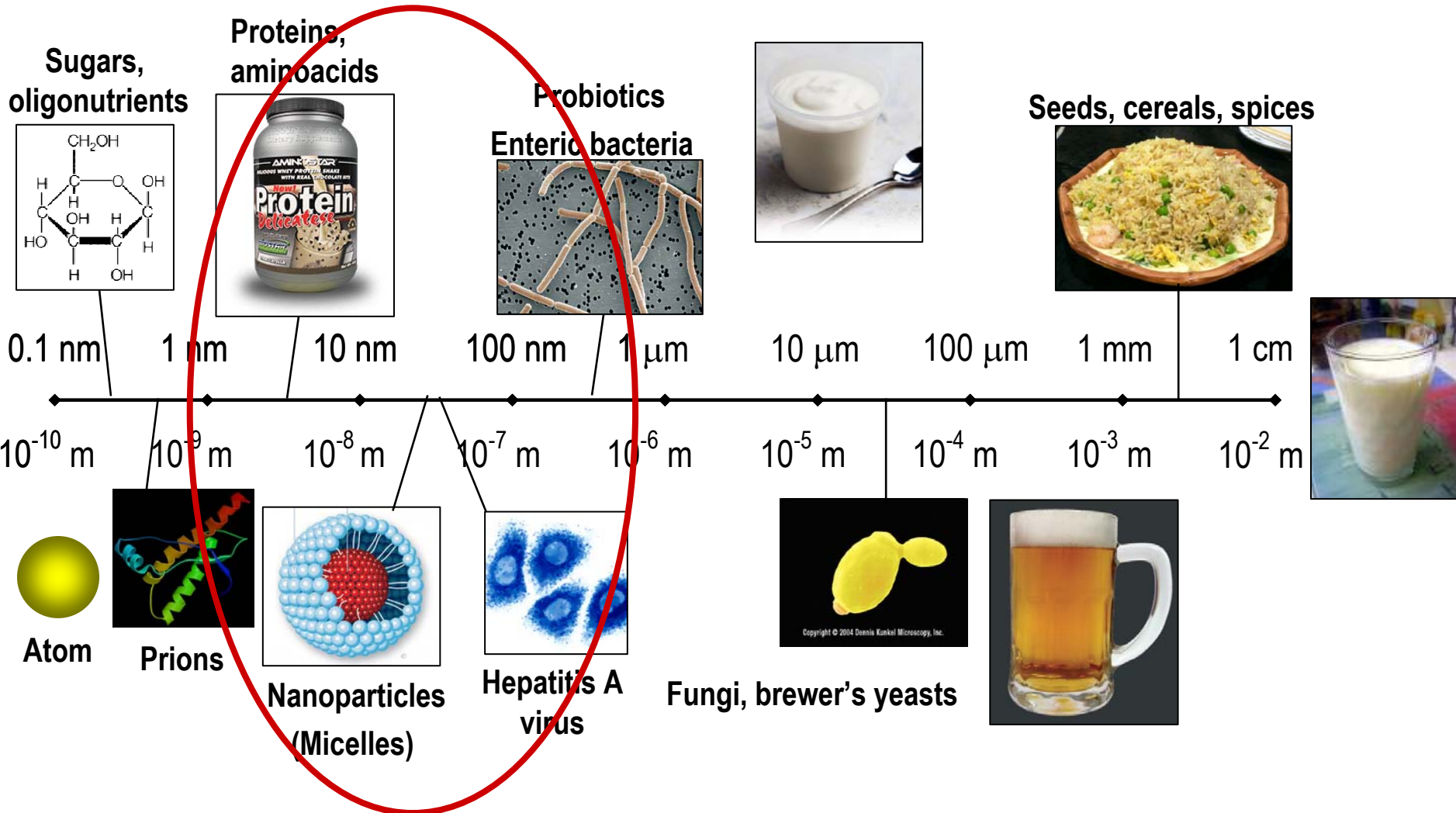
4 **(Question No EFSA-Q-2007-124)**

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

# RISK ASSESSMENT PARADIGM



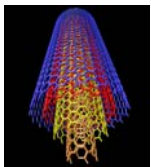
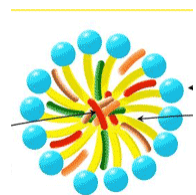
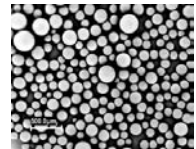
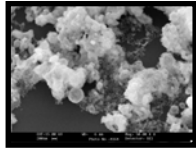
# NANOSCALE - FOOD



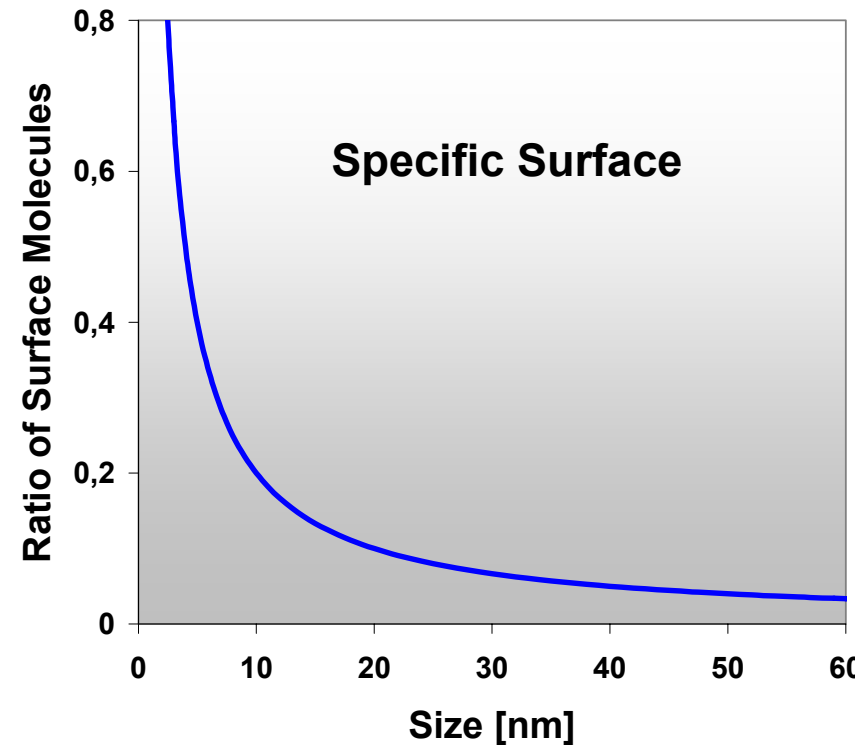
# **RISK ASSESSMENT**

## **(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

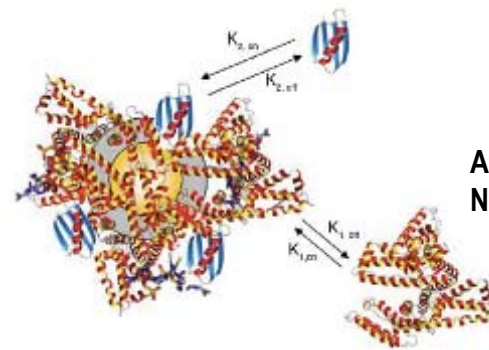
- NM are thermodynamically unstable or metastable
- Aggregation or agglomeration
- Interaction with surrounding matrix
- Ageing
- Adsorption of ions – surface charge
- Nuclei for heterogeneous crystallisation
- Catalytic effects

## 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) 1-2B

# Interaction of NM with biological matrices

## Consequences of phys.-chem. properties

- NM are thermodynamically unstable or metastable

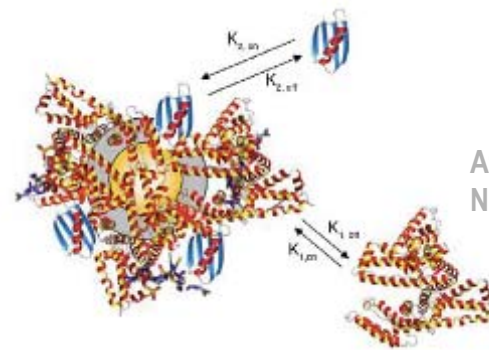
## Effect on Food Matrices:

- Changes in food consistency
- Influence on sensory properties

## Difficulties to characterize, detect and measure NMs in biological matrices

- Interaction with surrounding matrix
- Ageing
- Adsorption of ions – surface charge
- Nuclei for heterogeneous crystallisation
- Catalytic effects

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

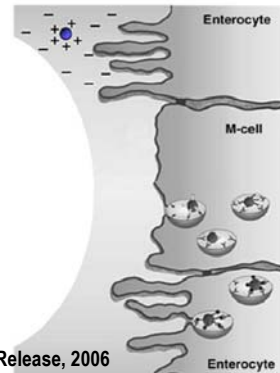
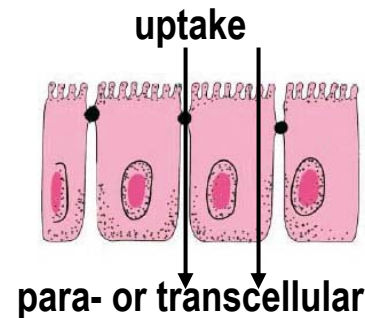
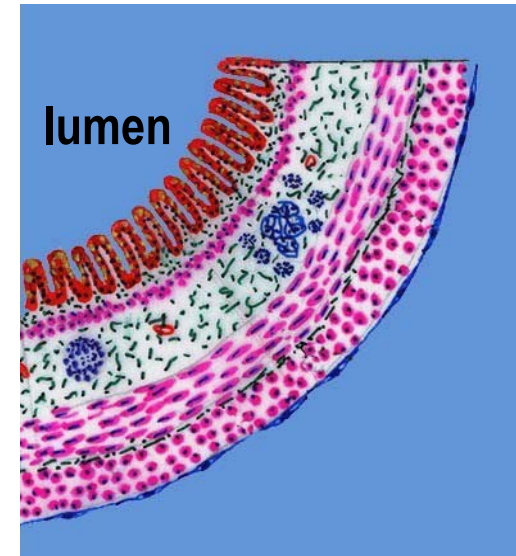


After Lynch and Dawson,  
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# Fate of Nanomaterials in the GI-tract

- 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

intestine



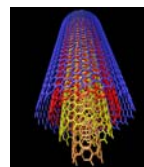
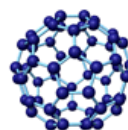
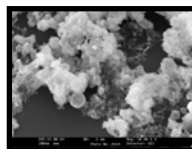
**Extremely limited data on biokinetics and fate of nanomaterials after oral exposure**



# 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
- Protein binding
- Cellular uptake
- Accumulation and retention
- Cell/tissue response

**Kinetics**

**Toxicity**

# **RISK ASSESSMENT**

## **(2) HAZARD CHARACTERIZATION**

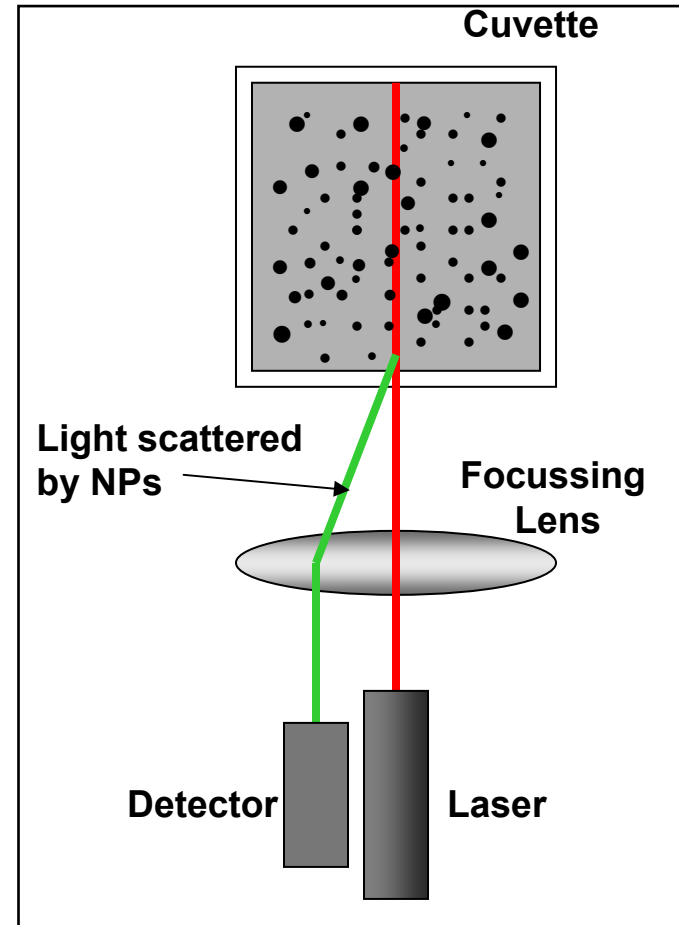
# Characterization and Detection Techniques

Single particle techniques  
vs ensemble techniques

A number of tools –  
no best techniques



**Electron Microscopy**



**Dynamic Light Scattering**

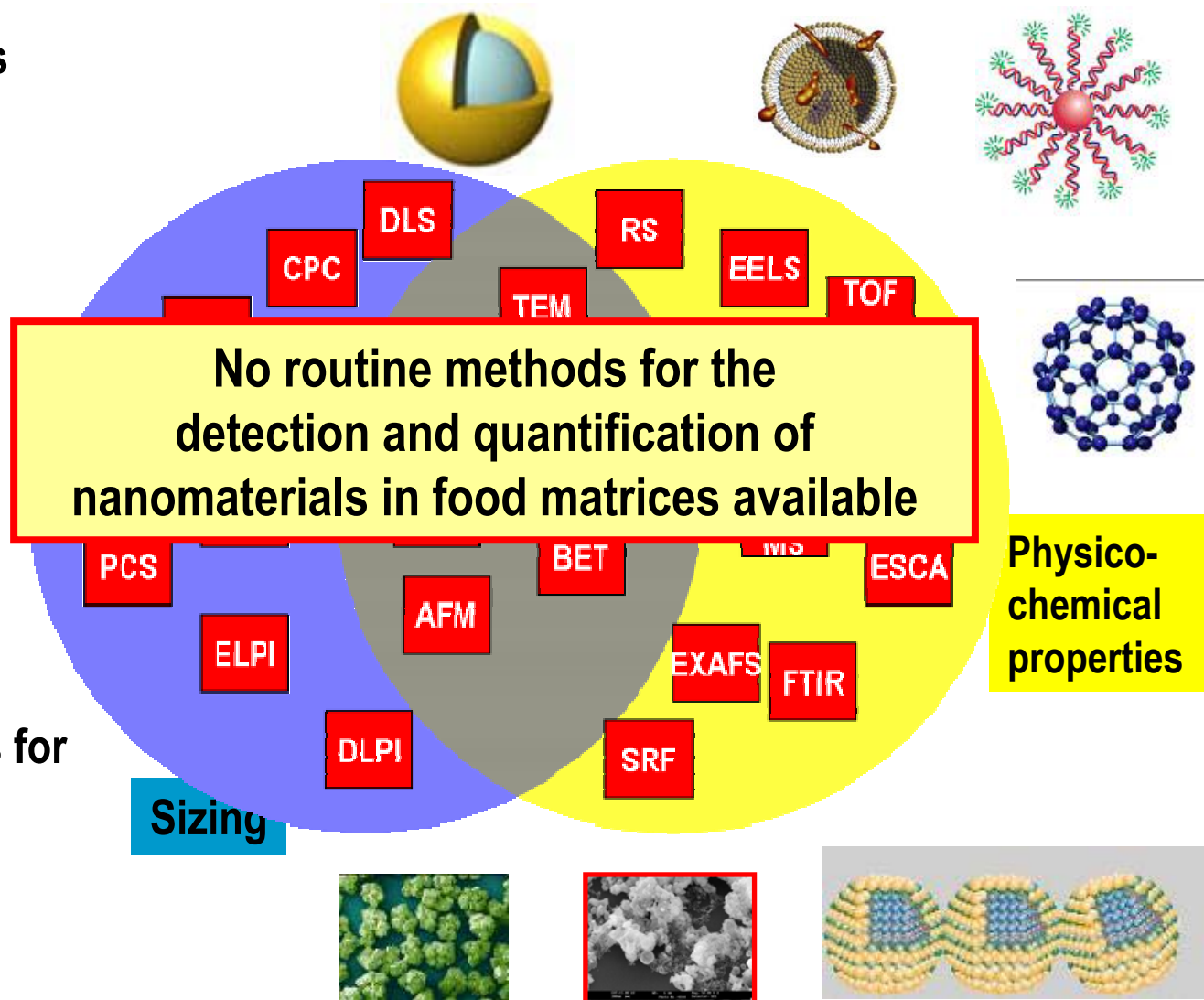
# Characterization and Detection Techniques

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?



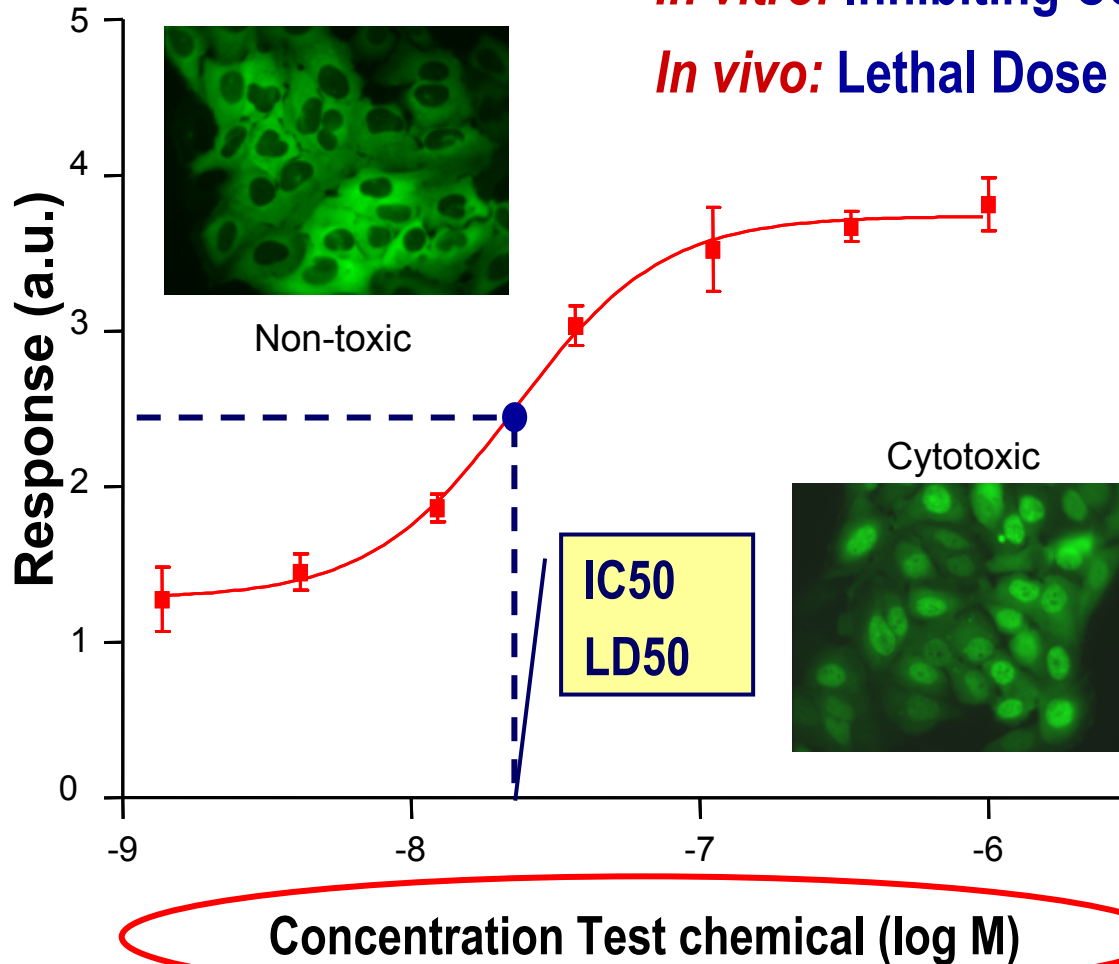
# BIOKINETICS: some 'knowns'

- 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 -  $IC_{50}$

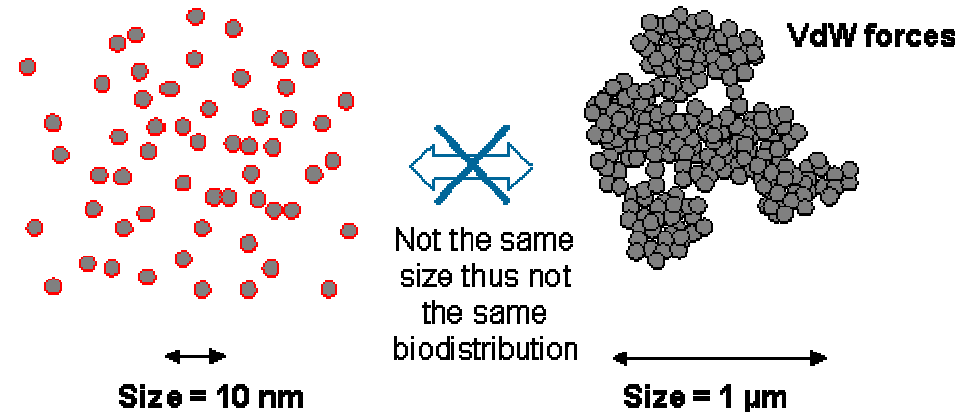
*In vivo*: Lethal Dose -  $LD_{50}$



# TOXICITY: Food Related Studies

## Dose metrics

- Mass?
- Surface area?
- Number concentration?

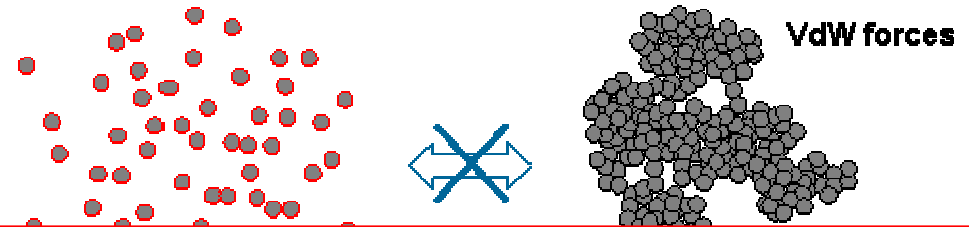


- **Few** studies on oral administration
- Adequate **characterization** of nanomaterials **lacking**
- Only a **narrow range of effects** have been studied
- Reported oral toxicity studies **restricted to acute toxicity**
- **properties - toxicity** relationship not yet established
- Current **toxicity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

# TOXICITY: Food Related Studies

## Dose metrics

- Mass?



**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*
- *properties - toxicity* relationship not yet established
- Current *toxicity testing adequate* to detect all aspects of potential toxicity?

# **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

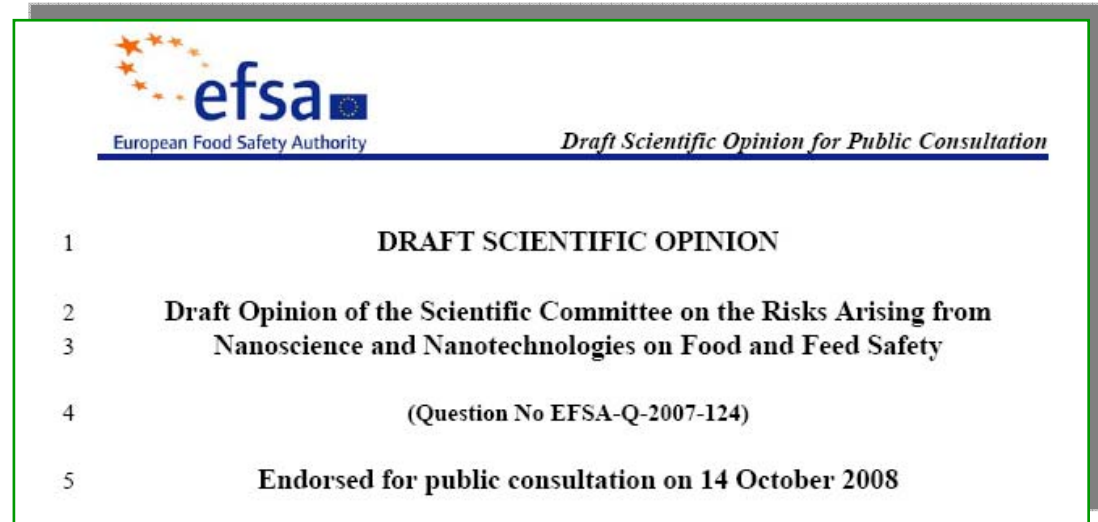
## AVAILABLE

- 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?

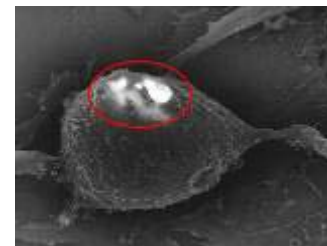
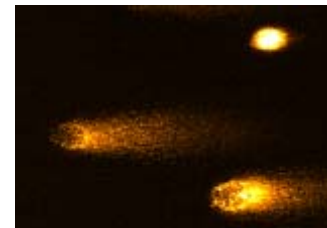
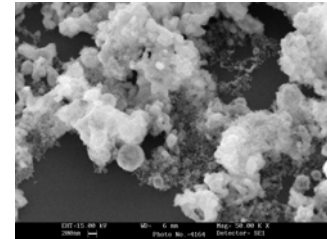
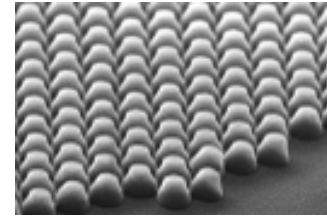
# Risk Characterization of Nanomaterials in Food



“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



## Joint Research Centre (JRC)

*Robust science for policy making*

# Thank you for your attention

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Contact: [jrc-info@ec.europa.eu](mailto:jrc-info@ec.europa.eu)