

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



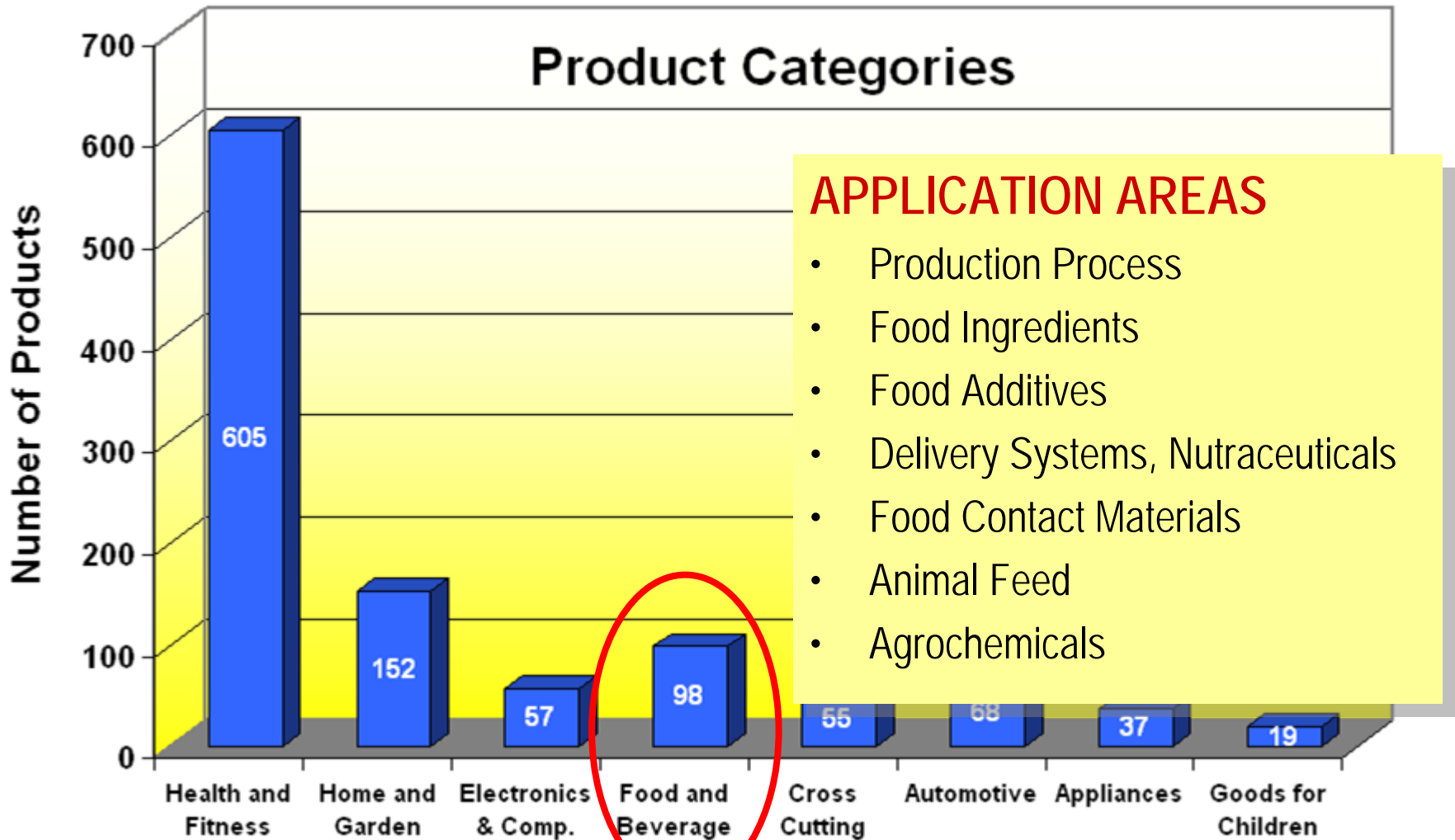
Hermann Stamm

*Institute for Health and Consumer Protection Joint Research Centre, Ispra*

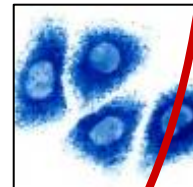
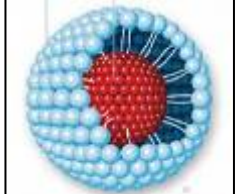
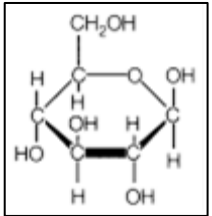
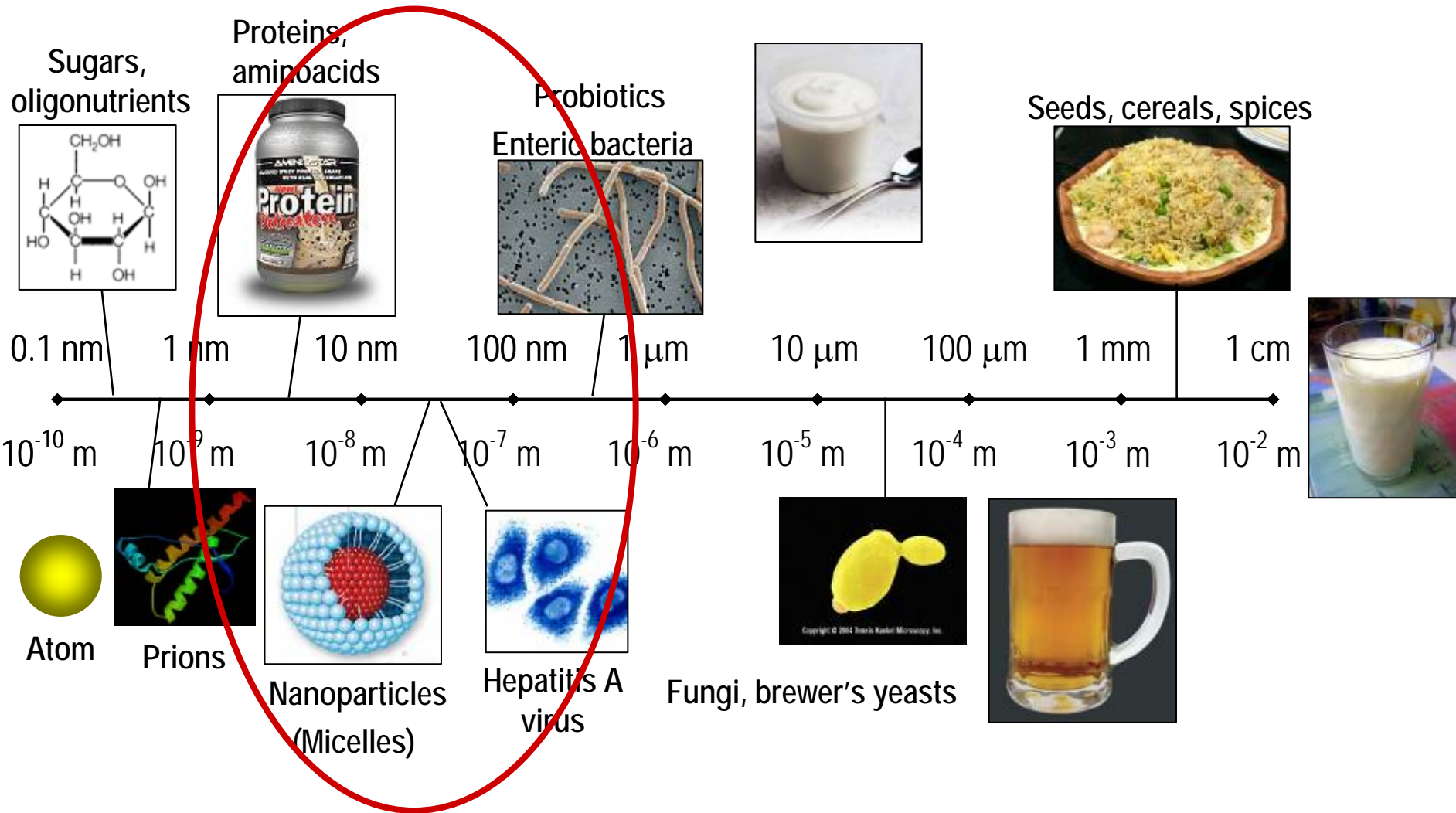
<http://www.jrc.ec.europa.eu>

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

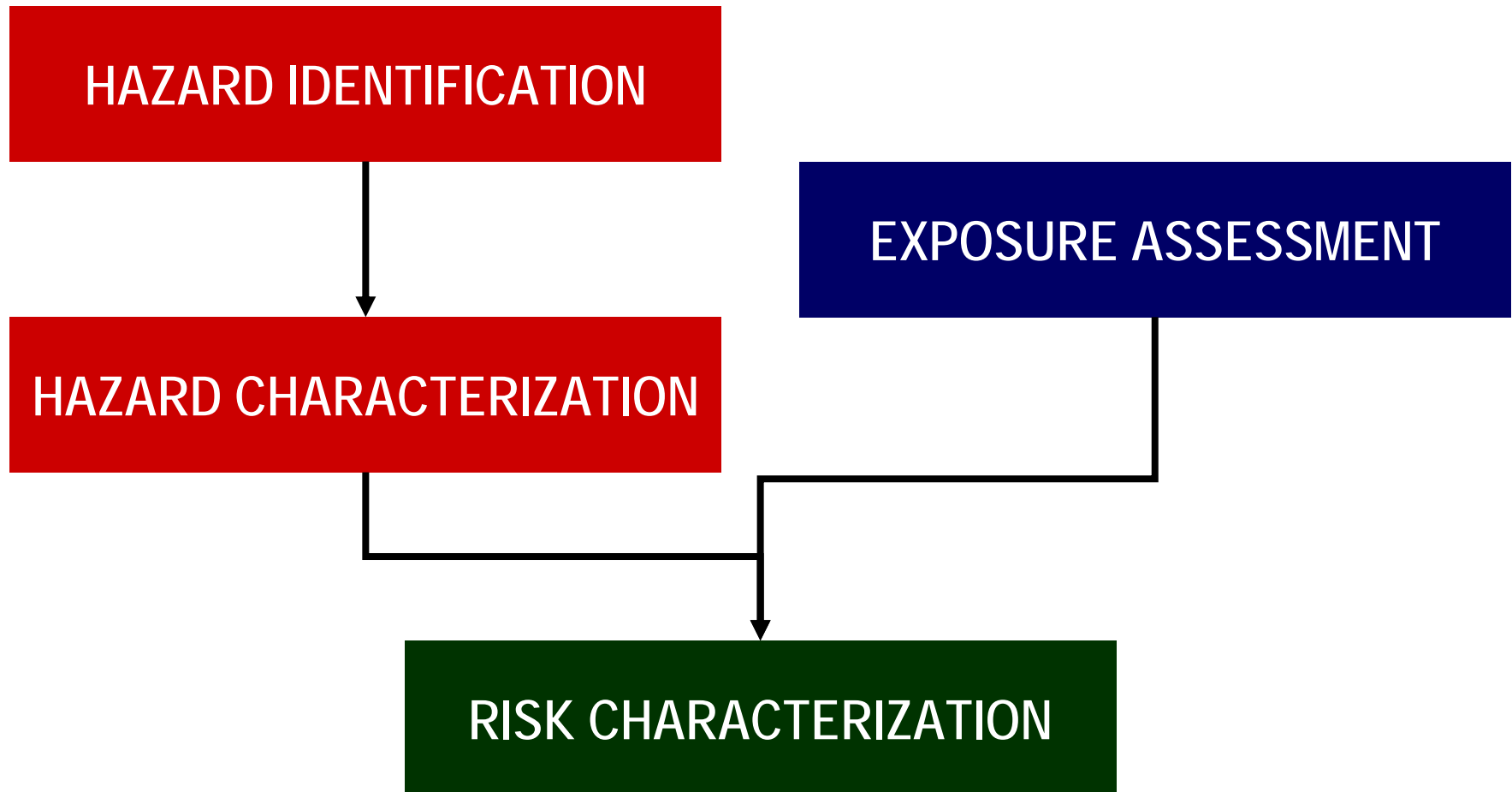
# NT Consumer Products on the Market

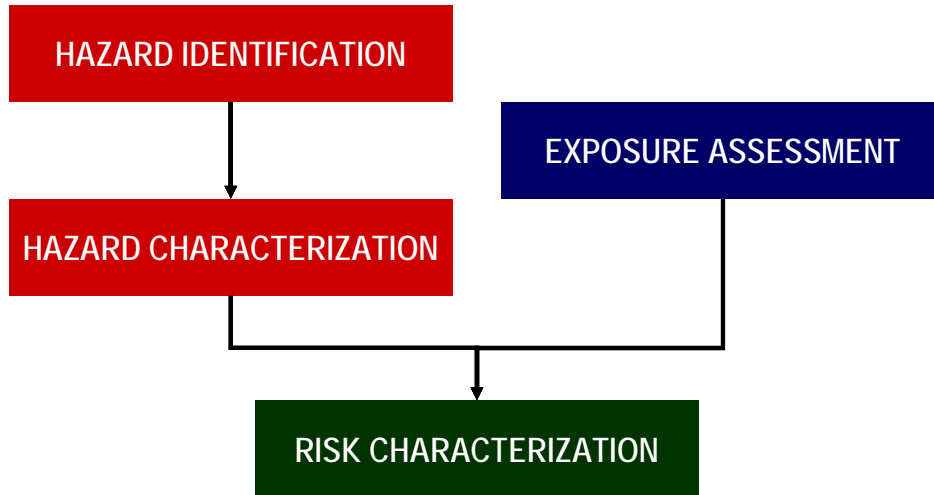


# NANOSCALE - FOOD



# RISK ASSESSMENT PARADIGM

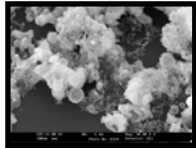




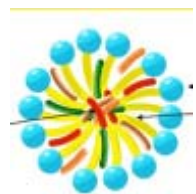
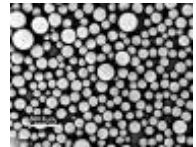
# RISK ASSESSMENT

## (1) HAZARD IDENTIFICATION

# Nanoparticles in Food – what makes them different?

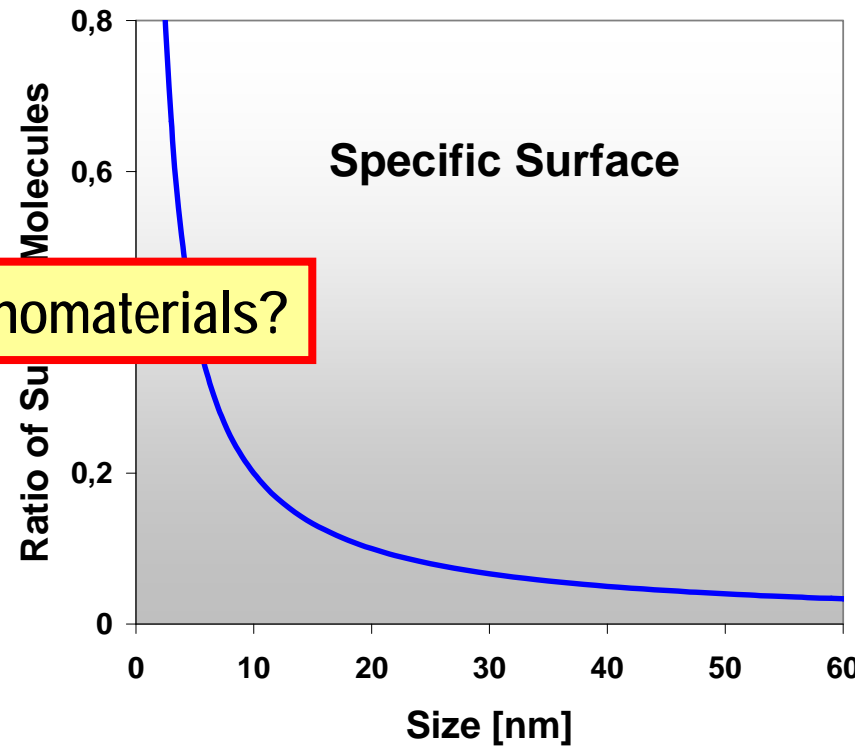
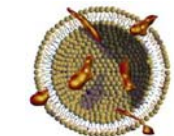
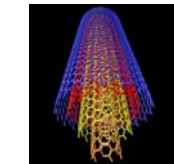


- Large specific surface
- Chemical reactivity very different compared to bulk material
- Quantum effects lead to special properties (e.g. optical ...)



- Matrix dependent properties
- Many forms: fullerenes, nanotubes, nanocarriers, nanoemulsions, nanoencapsulates, ...

**Definition of Engineered Nanomaterials?**



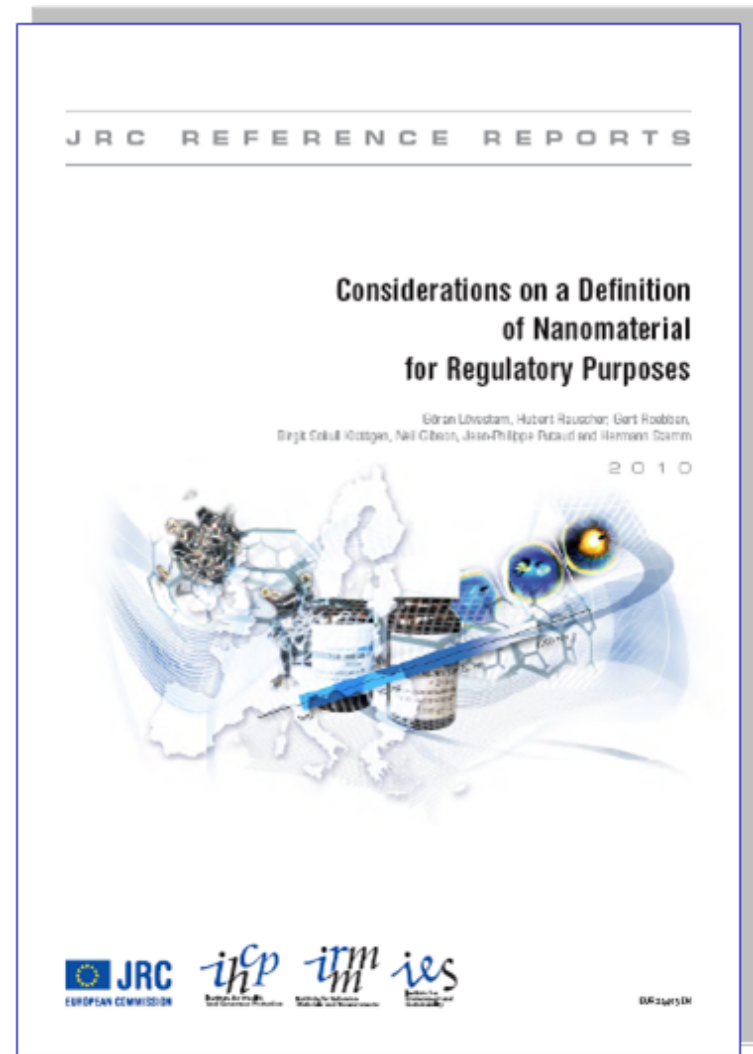
# Definition of Nanomaterial for Regulatory Purposes

## *Requirements*

- A single definition broadly applicable in EU legislation and policies
- Legally clear and unambiguous, i.e. enforceable

## *Questions concerning the key elements of a definition*

- What is the **nanoscale** and which size range should it encompass?
- Should other **properties** which are the consequence of the material being at the nanoscale be included?



# Interaction of NM with biological matrices

## Consequences of phys.-chem. properties

- NM are thermodynamically unstable or metastable

## Effect on Food Matrices:

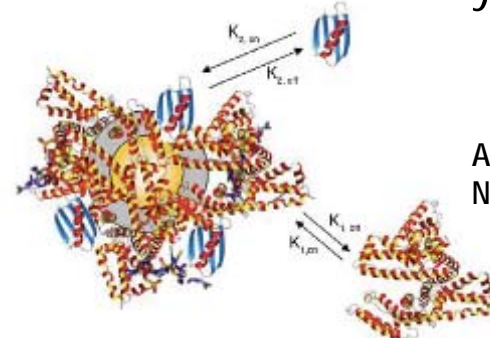
- Changes in food consistency
- Influence on sensory properties

## Effects of NM in living systems:

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

- Interaction with surrounding matrix
- Ageing
- Adsorption of ions – surface charge
- Catalytic effects

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



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

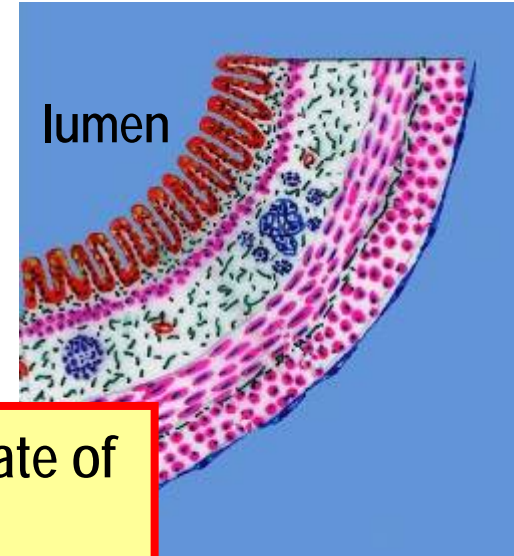
# Fate of Nanomaterials in the GI-tract

- Transformation in the
- Translocation through *wall*
- Translocation to *target* (liver, kidney)
- Biotransformation and little information

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



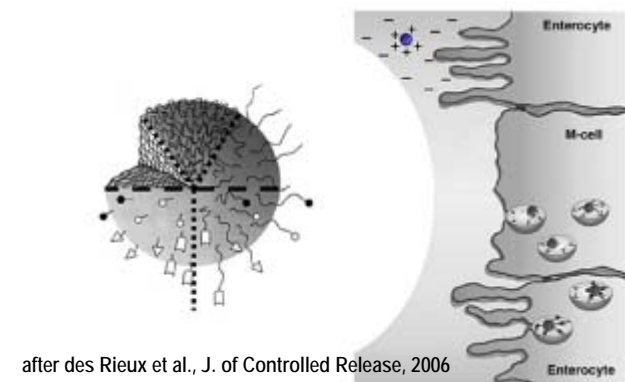
intestine



lumen



para-



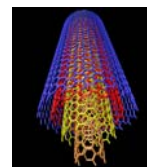
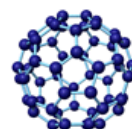
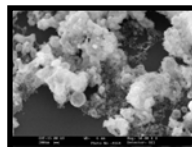
after des Rieux et al., J. of Controlled Release, 2006



# 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**

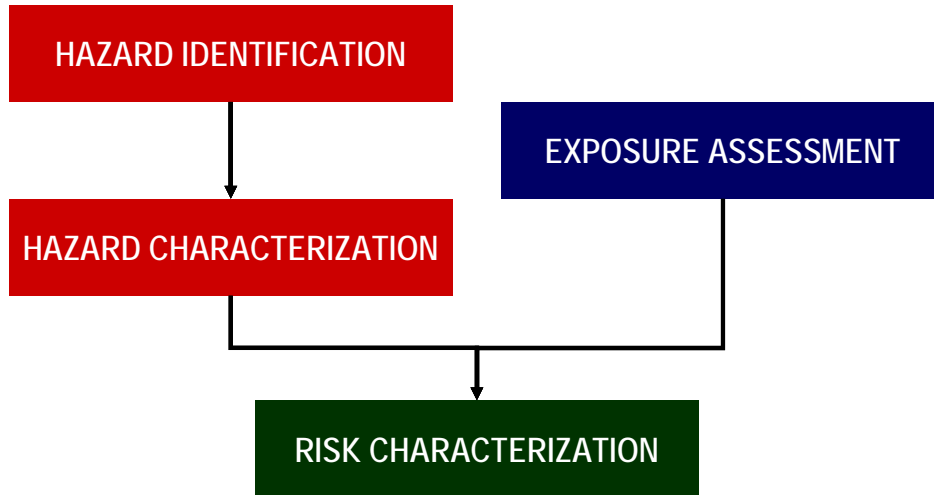


## EFFECT

- Translocation from GI-tract to target organs
- Protein binding
- Cellular uptake
- Accumulation and retention
- Cell/tissue response

**Kinetics**

**Toxicity**



# RISK ASSESSMENT

## (2) HAZARD CHARACTERIZATION

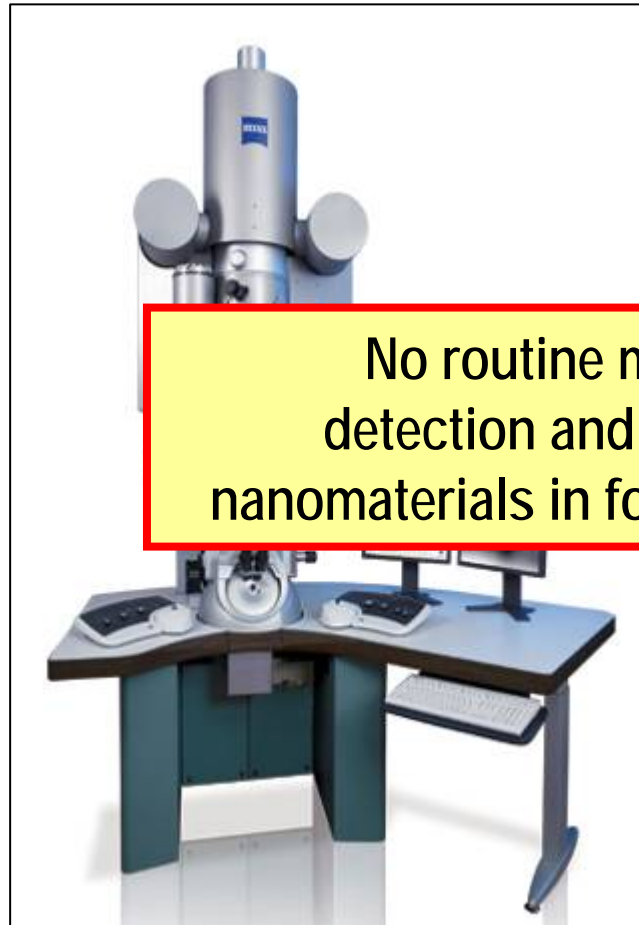
# Characterization and Detection Techniques

Single particle techniques  
vs ensemble techniques

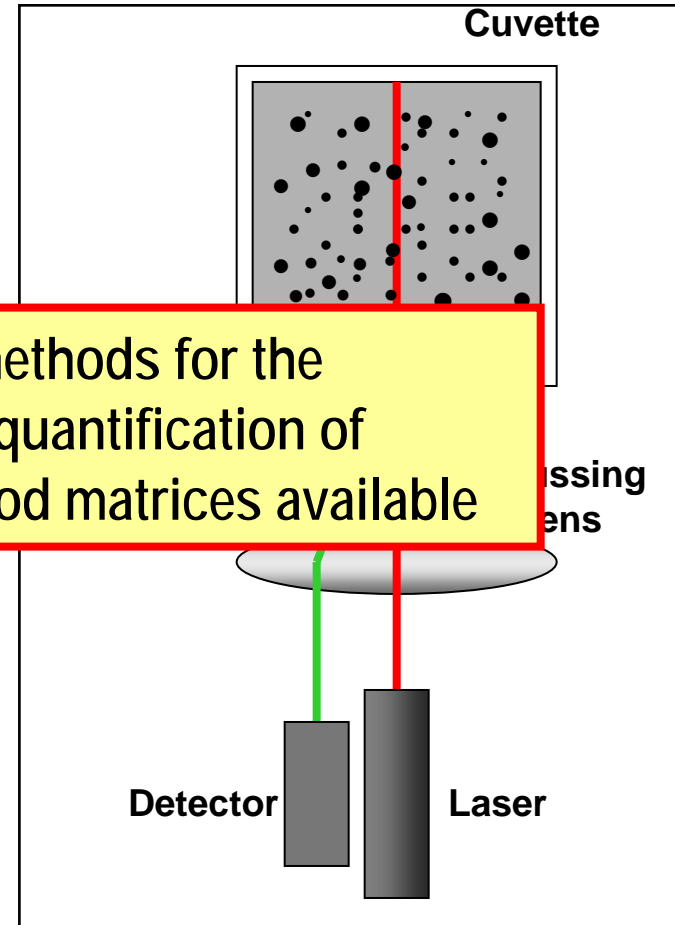
A number of tools –  
no best techniques

## ISSUES

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



Electron Microscopy



Dynamic Light Scattering

No routine methods for the  
detection and quantification of  
nanomaterials in food matrices available

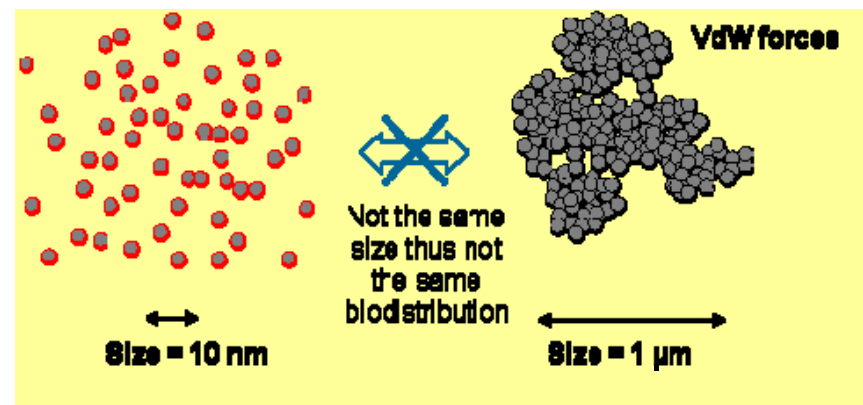
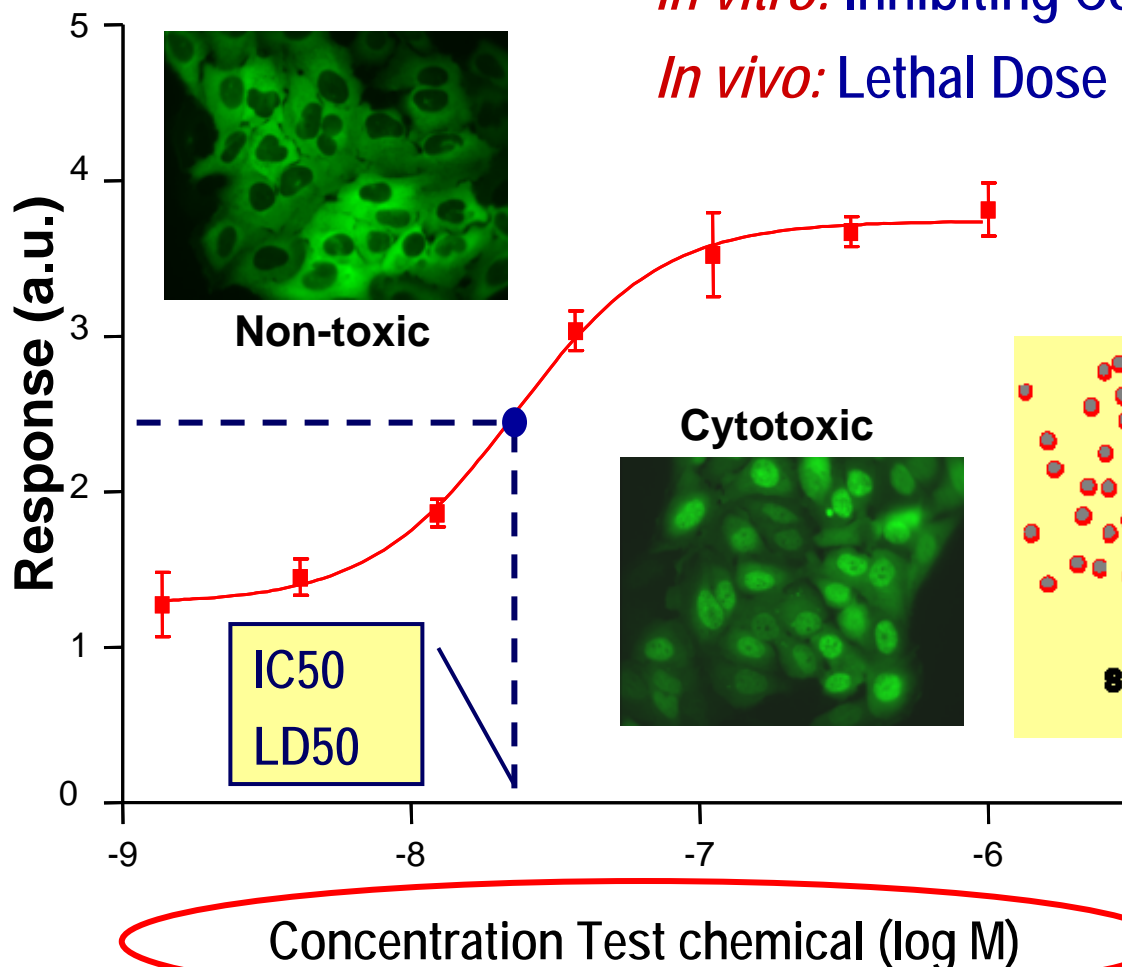
## BIOKINETICS: some 'knowns'

- 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 -  $LD_{50}$

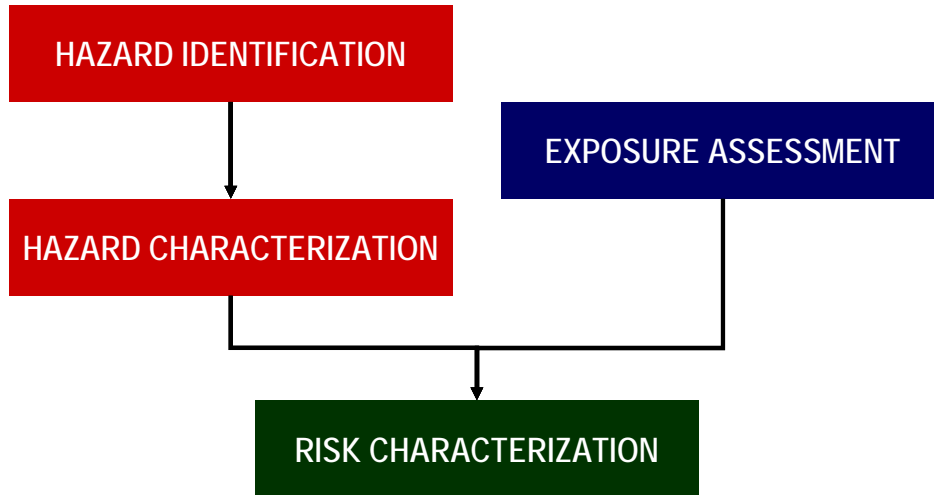


# TOXICITY: Food Related Studies

- *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?

Very limited information for risk characterization regarding oral exposure to NM

- Phys.-chem. Characterization
- Toxicokinetics
- Toxicity



# RISK ASSESSMENT

## (3) EXPOSURE ASSESSMENT

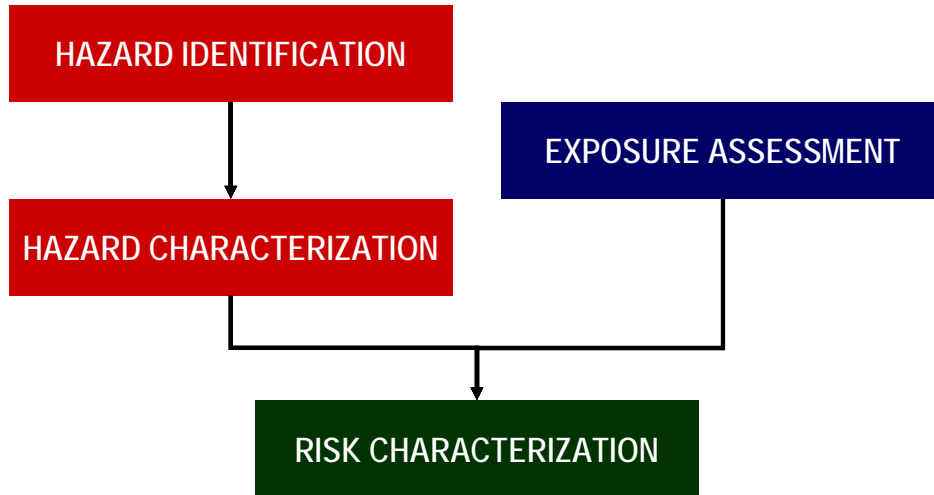
# Exposure to NMs from Food and Feed

## 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

## NEEDS and ISSUES

- More 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

## SCIENTIFIC OPINION

### The Potential Risks Arising from Nanoscience and Nanotechnologies on Food and Feed Safety<sup>1</sup>

Scientific Opinion of the Scientific Committee

(Question No EFSA-Q-2007-124a)

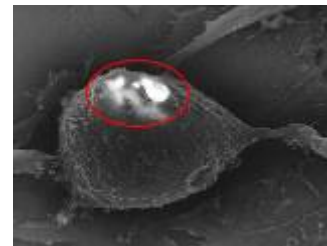
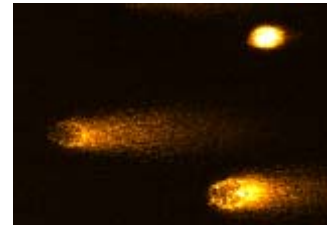
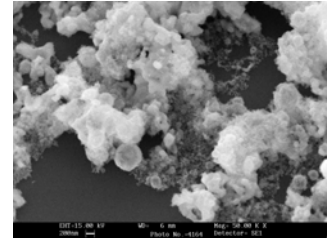
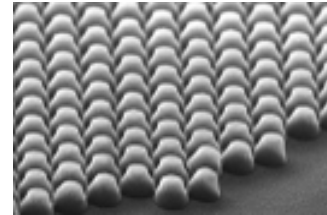
Adopted on 10 February 2009

“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
- Methods for safety assessment of nanomaterials
- 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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