TOXICITY AND ECOTOXICITY OF NANOMATERIALS

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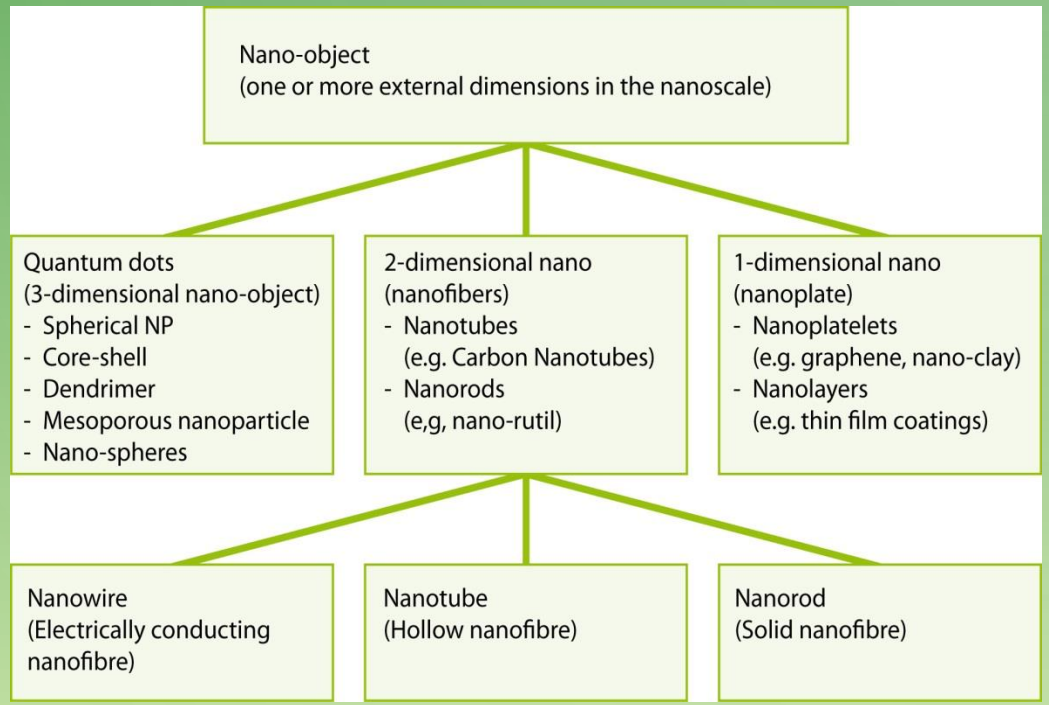
ENGINEERED NANOMATERIALS

Anthropogenic materials at nano-scale that are "**designed for a specific purpose** or function" (ISO/TS 80004

Categories of ENM according to ISO TS 27687



RISK ASSESSMENT FOR REGULATORY TOXICOLOGY

Risk = impact of uncertainty on objectives (ISO 31000)

Uncertainty:

- Empirical uncertainty (margin of error in measurement results)
- Lack of experiences
- Lack of scientific knowledge
- Ignorance (the white spots)

The objective of regulatory toxicology: to protect safeguard subjects from harm

RISK ASSESSMENT FOR REGULATORY TOXICOLOGY

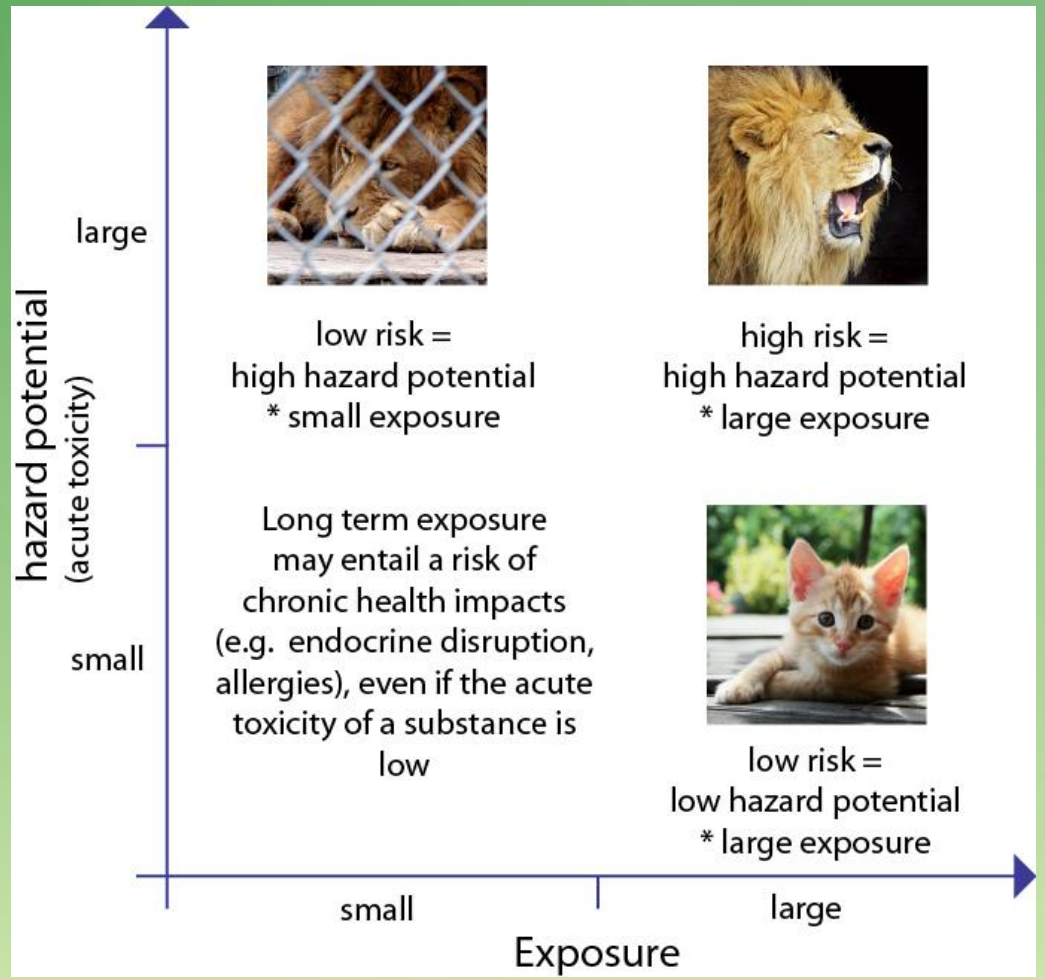
$$\text{Risk} = f_{(\text{exposure})} * f_{(\text{hazard potential})}$$

Exposure:
How much of a substance comes into contact with a target organism over a certain time period.

Toxicity:
The intrinsic ability of a substance to disrupt biological processes in living organisms (hazard potential).

RISK ASSESSMENT FOR REGULATORY TOXICOLOGY

Risk = $f_{(exposure)} * f_{(hazard\ potential)}$



For the regulatory purpose (thresholds, bans) scientific evidence about the dose–response relationship must be established

RISK ASSESSMENT FOR REGULATORY TOXICOLOGY

$$Risk = f_{(exposure)} * f_{(hazard\ potential)}$$

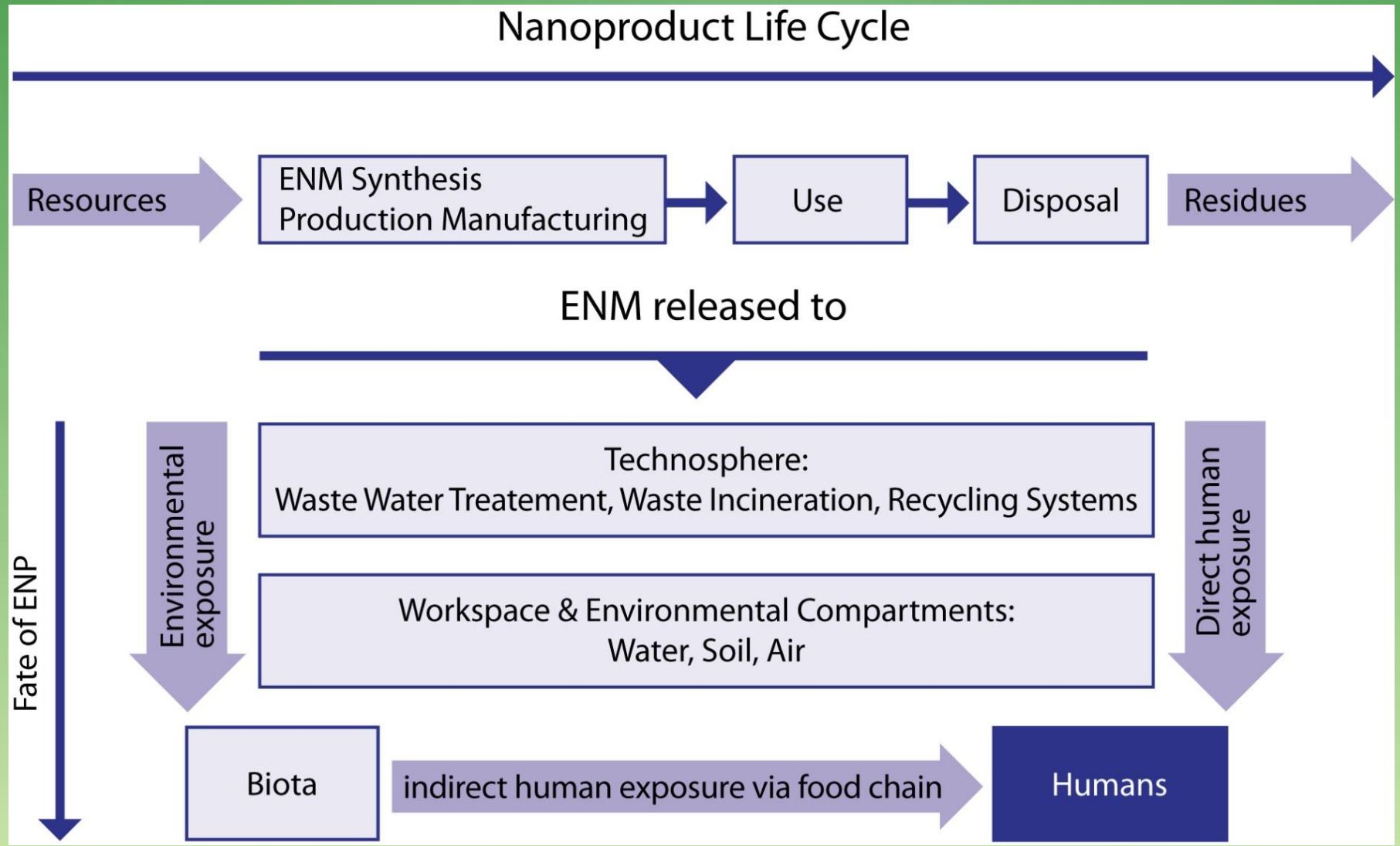
Exposure:

- by measurements (lab experiments, sample taking & analysis)
- by means of environmental fate scenarios
- by probabilistic modelling

Toxic hazard potential:

- experimental animal testing (in vivo)
- non-animal testing methods (in vitro)
- Experience-based methods
    - read-across method (analogy to a known reference substance)
    - grouping of substances by physico-chemical properties
    - quantitative structure activity relationships (QSARs).

EXPOSURE ASSESSMENT



EXPOSURE ASSESSMENT

Release of ENM can occur at each stage of the life cycle:

- during production and manufacturing processes,
- leakages during transportation, handling and waste disposal,
- accidents,
- detachment from products during their use phase (intended or unintended),
- recycling and final disposal of nano-products.

Transformations of ENM:

- physical-chemical properties (solubility, agglomeration/aggregation, absorbtion, etc)
- Interactions with technical systems (e.g. cross-contamination)
- Interactions with environmental compartments (dillution, sedimentation …)
- Interactions with biota (bio-persistency, bio-accumulation …)

HAZARD CHARACTERISTION

Toxicity depends from the kind of substance and its dosage
Toxicology is about measuring the dose-response relationship

Nanomaterials may show a different toxicity than bulk materials (classical chemicals) because:

- smaller particle size -> increased surface size
- different toxicokinetic mechanisms (bio-uptake, distribution, and elimination within an organism)
- different immune-system response
- there seems to be no size-relared threshold for nanotoxic effects

POSSIBLE MODES OF NANO-TOXICITY

- ***Oxidative stress:*** ENM can induce inflammatory reactions due to the formation of Reactive Oxygen Species within organisms.
- ***Inflammation:*** ENM can lead to a chronic overload of immune system cells that are responsible for removing foreign substances from the body.
- ***Genotoxic potential:*** possibility of DNA damage due to cellular uptake of ENM, which may result in cancer.
- ***Endocrine disruptors:*** various types of ENM can disturb the reproductive systems of male as well as female organisms
- ***Changes of body tissue*** (e.g. lung) caused by mechanical interaction with incorporated ENM. Accumulation of large amounts of foreign particles can clog normal tissue functions and lead to chronic diseases.
- ***Protein and lipid damage, enzyme disruption.***

STANDARDISATION ACTIVITIES

- ***CEN TC 352***
  - *WG 1 "Measurement, characterization and performance evaluation"*
  - *WG 3 "Health, safety and environmental aspects"*
- ***ISO TC 299***
  - *JWG 1 "Terminology and nomenclature"*
  - *JWG 2 "Measurement and characterization"*
  - *WG 3 "Health, Safety and Environmental Aspects of Nanotechnologies"*
- ***OECD Working Party on Manufactured Nanomaterials (WPNM)***
  - *Sponsorship Programme for the Testing of Manufactured Nanomaterials*
    safety testing of 13 specific Manufactured Nanomaterials and Endpoints
    Results: toxicological test results to be made publicly available by March 2015
    Series of guidelines for phys-chem characterization and toxicological testing