NANOPHARMACEUTICALS VS ENGINEERED NANOMATERIALS

WAR AND PEACE?

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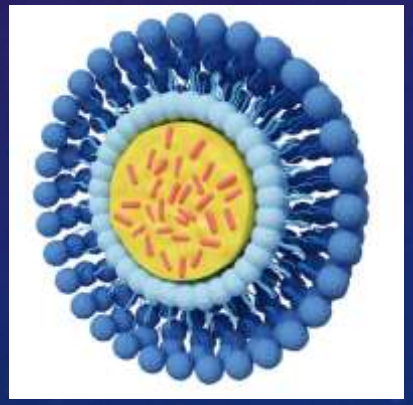
DEFINITIONS

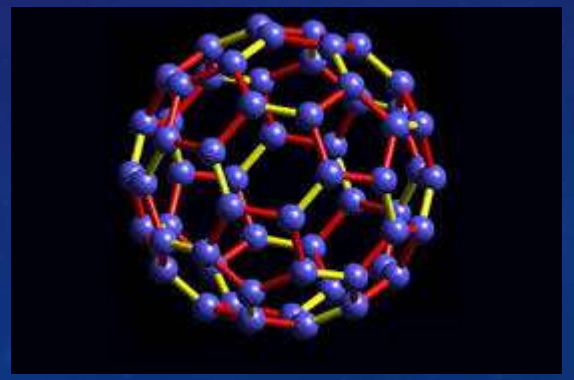
Nanopharmaceuticals

- Pharmaceuticals produced using nanotechnology, or manufactured in the form of nanoparticles
- Colloidal particles of 10 to 1,000 nanometers (1 micron) in size



Engineered nanomaterials

- A manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm - 100 nm … (EC, 2016)



CHARACTERISTICS

Nanopharmaceuticals

- Regulation: pharmacoeia, MDD/MDR
- Industry: pharma, medical devices
- Users: patients, medical profesisionals
- Agency: EMA
- Production: limited number of products on the market

Engineered nanomaterials

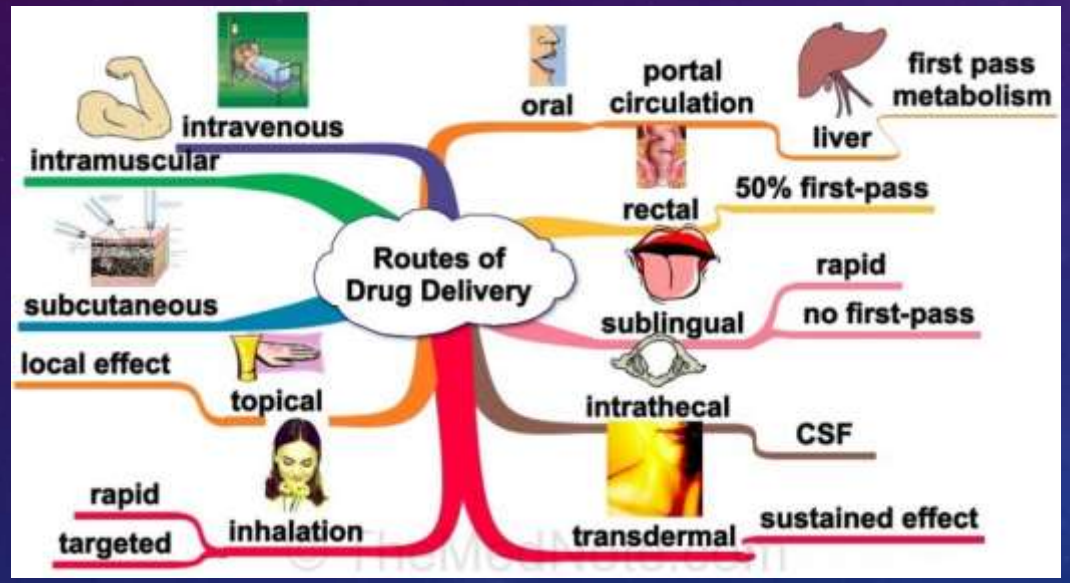
- Regulation: REACH
- Industry: chemical industry
- Users: workers, citizen
- Agency: ECHA
- Production: Many products on the market which sometimes are producd in high volumes (tons)

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

ECHA
EUROPEAN CHEMICALS AGENCY

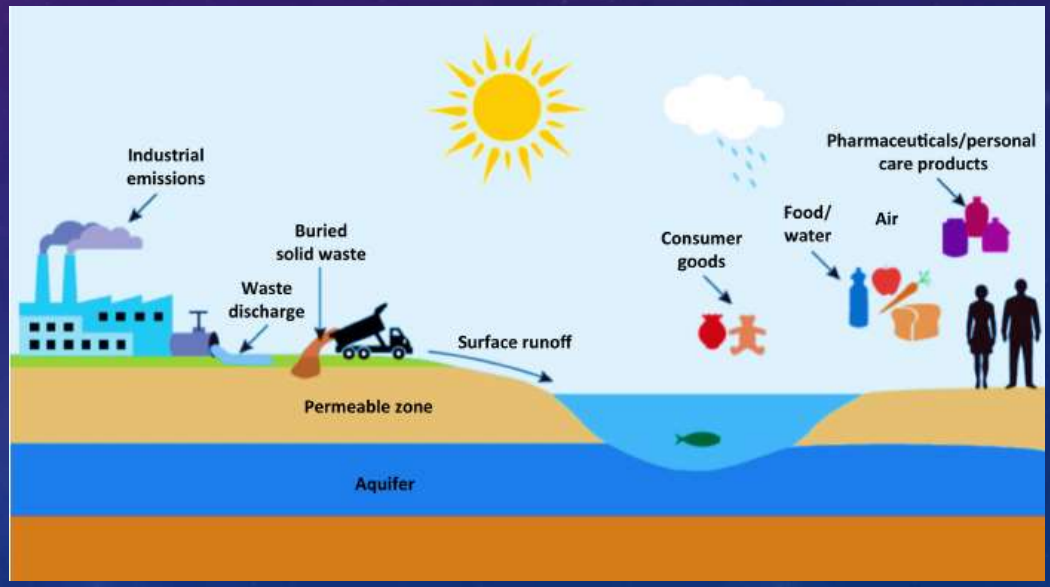
ADMINISTRATION VS EXPOSURE

Nanopharmaceuticals



Exposure (dose) well known

Engineered nanomaterials



Exposure unknown or difficult to assess

EC PROGRAMMES

Nanopharmaceuticals

- Nano2Life
- ETPN driven
- Heico FRIMA

Engineered nanomaterials

- NanoReg I, II
- Nanosafety cluster driven
- Georgios KATALAGARIANAKIS

TWO DEPARTMENTS EXAMPLE: CEATECH

LETI

- NanoBio infrastructure
- Development of organic nanocarriers
- Characterisation methods
- Non GMP Scale up manufacturing

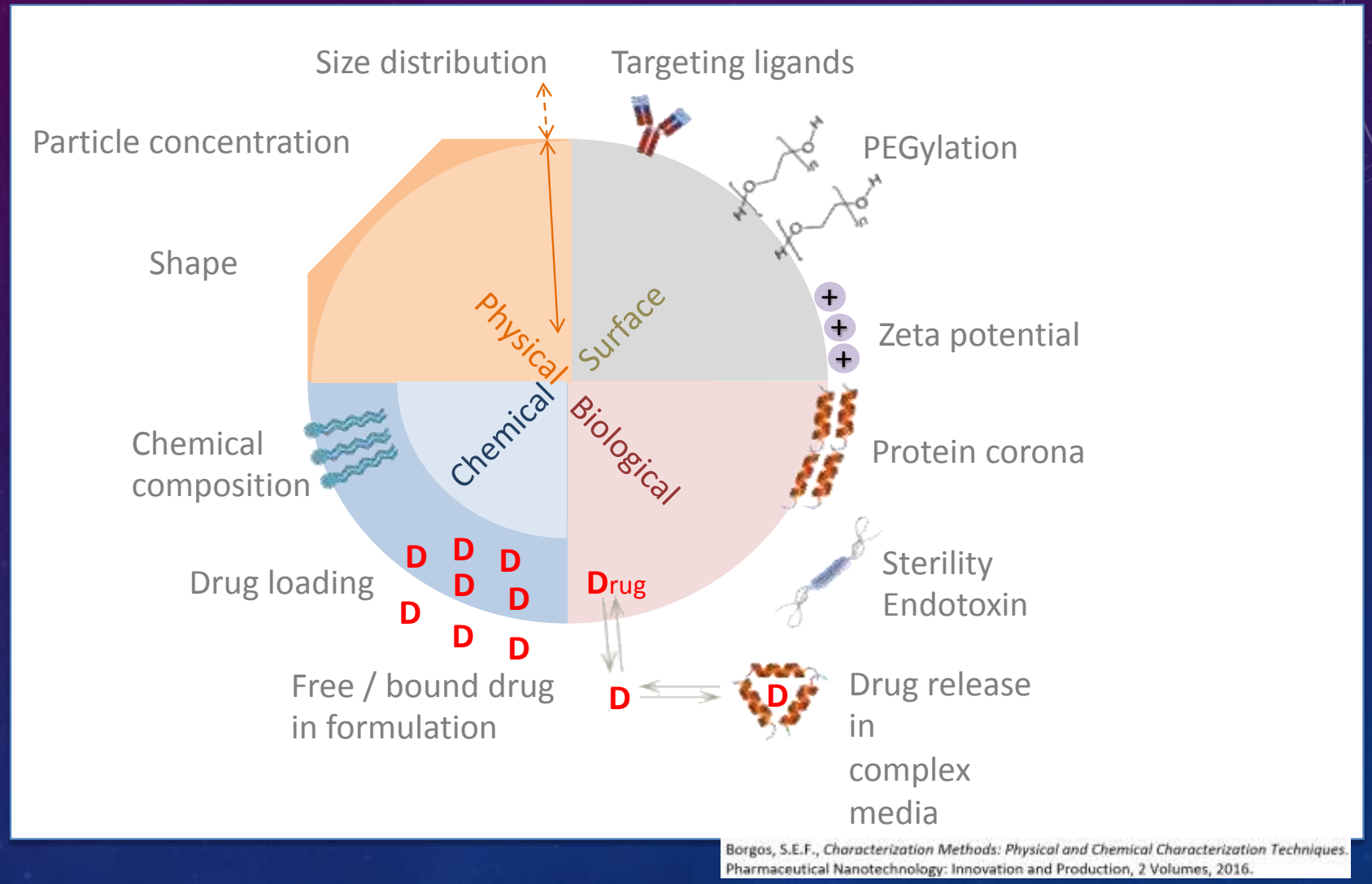
LITEN

- Platform on Nano-Safety
- Detection, characterisation methods
- Particle design, safe by design integration process
- Ecotoxicology, Lifecycle management

SIMILARITIES

- All nanomaterials have impacts on Human Health
- The potential risks of nanomaterials are mainly determined by
  - biocompatibility
  - biodegradability,
  - interaction with the complex biological environment
  - stability and accumulation in biological organisms and the environment
- Development of assessment methods for studying the safety and risks associated with a given material
- Mechanistic understanding of nano-bio interaction towards a «safe-by-design» approach
- Standardisation and development of testing guidelines for nanomaterials

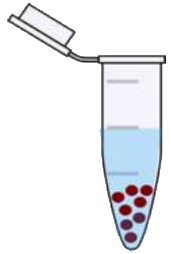
WHAT ARE THE PHYSICAL ASPECTS OF NANOMEDICINES?



Borgos, S.E.F., *Characterization Methods: Physical and Chemical Characterization Techniques.* Pharmaceutical Nanotechnology: Innovation and Production, 2 Volumes, 2016.

Source: F. Caputo and EUNCL Core Expert Team

OBJECTIVES OF THE CHARACTERIZATION AND SCREENING



Pristine Med-NPs, batch to batch consistency

- Particle size distribution (PSD)
- Shape
- Surface charge
- Free coating

Behavior in physiological conditions:

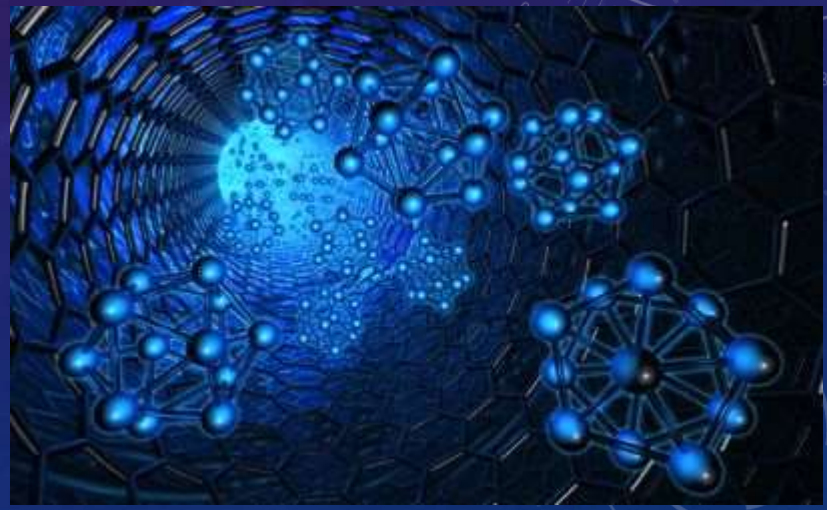
- NP immunotoxicity
- NP safety assessment
- NP biodistribution

Characterisation must be performed under biologically relevant conditions!

Source: EUNCL Core Expert Team (CET): TCD (A. Prina-Mello and O. Gobbo)

SAFETY ANALYSIS

- Basics are similar as we deal with particle behaviour versus soluble pharmaceutics/chemicals
- TiO2 nanoscreen, Silica in food: dermal and oral entry routes like nanopharmaceuticals
- More info is available on nanotox of ENM than nanomedicines
- Common understanding but different processes

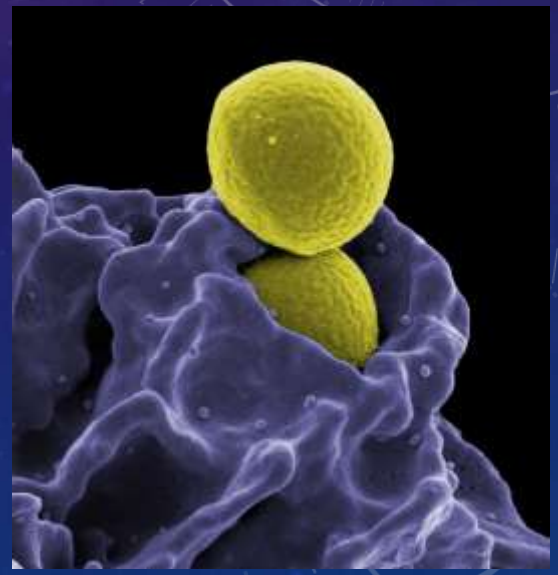


RISK ASSESSMENT

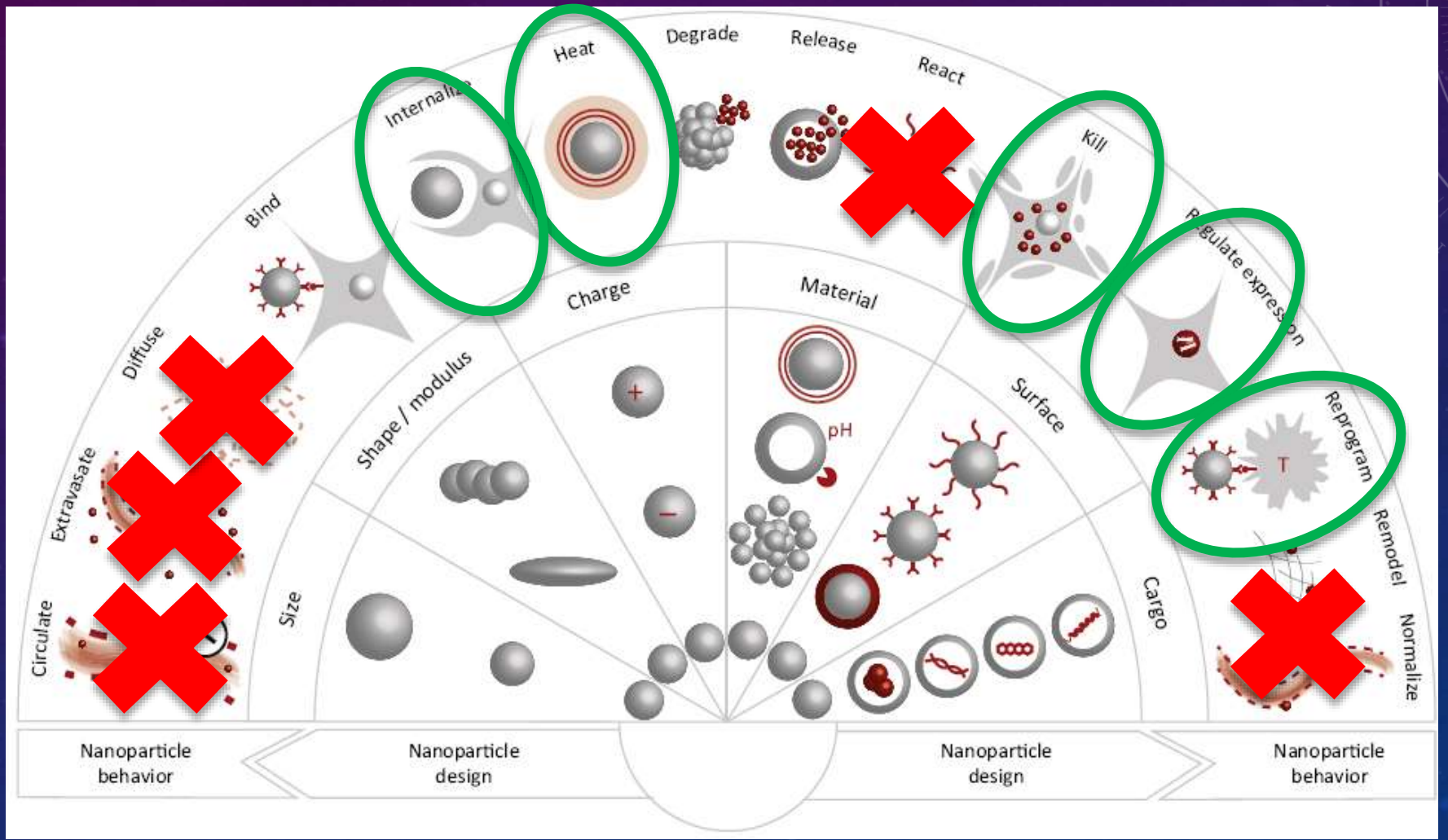
- Most particles end up in phagocytosing cells (MPS) and organs of the immune system
- This results in risk for immune effects
- Therefore nano immunotoxicity evaluation should be further developed

SAFETY AND IMMUNOTOX OF NANOMEDICINES

- Immunotoxicity is a critical issue from the early design and physico-chemical characterisation of nanomedicine
- Immunotoxicity has to be included and prioritised when developing nanomedicines
- Endotoxicity screening is the entry (first line) investigation assay for possible immunotoxicity reaction
- Strategy for screening is necessary for introducing check points during the nanomedicine development



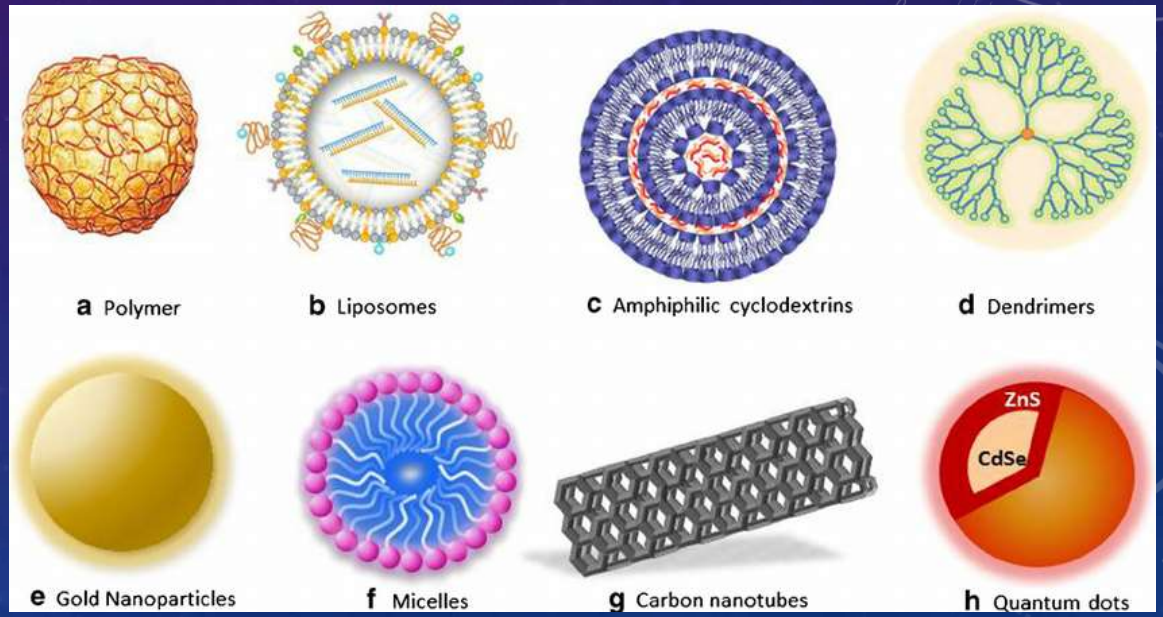
WHAT ARE THE SELECTED PROPERTY OF THE CARRIER? CASE STUDY FOR IONP FOR CANCER TREATMENT



Source: Hauert et al., Trends in Biotech, 2014;
Adapted by A. Prina-Mello (TCD)

ORGANIC VS INORGANIC, A RELEVANT CRITERIA?

- Physical nature (ex: Particle-like, small, tiny bowl like) and size count first
- Composition counts second
- What about fibers vs polymers?

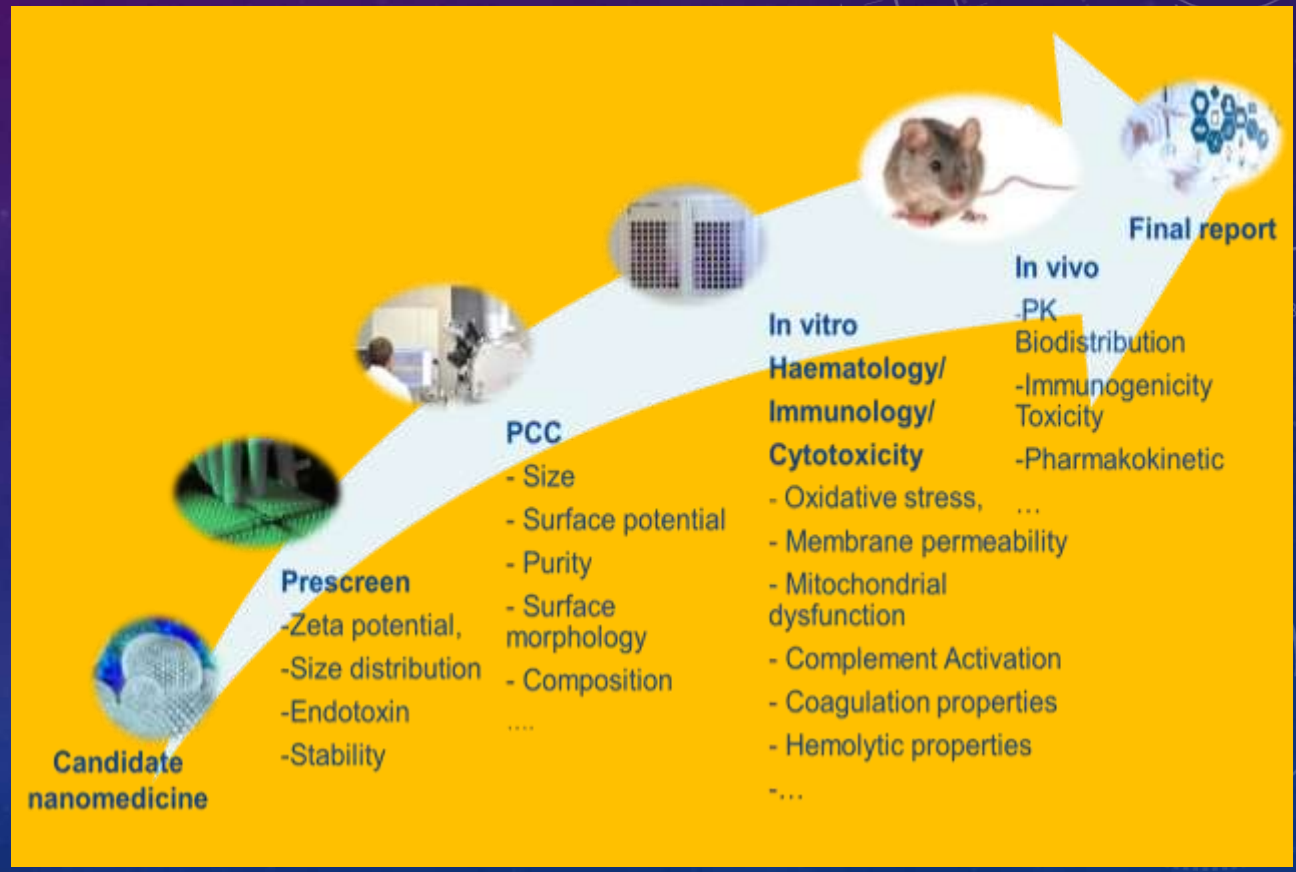


FUTURE PRIORITIES

- Safety by Design
- Quality by Design
- Borderline products
- Openess of data
- Format of data
- PBPK modelling

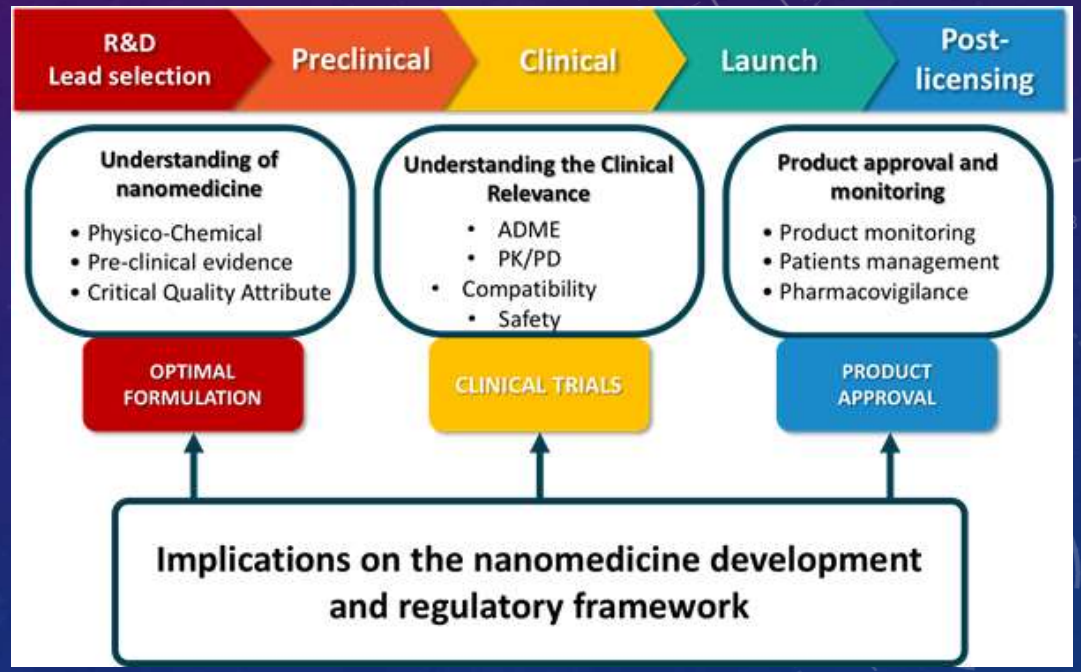
EUNCL
Nanomedicine Characterization Laboratory

- Service facility for nanomedicine developers
- Perform pre-clinical characterization of nanomedicines
- Identify and characterize critical parameter of nanomaterial in biological systems
- Develop improved analytical methods
- Interact with regulators to facilitate nanomedicine regulatory approval



REFINE

- Regulatory Science Framework for nano-bio-material based medical products and devices
- To support
  - Regulatory science to quickly analyse whether a new NBM raises new challenges to testing.
  - Producers, CRO/CDMOs to design safer products, and more efficient testing & manufacturing.
  - Researchers to meet urgent needs of regulators and define Adverse Outcome Pathways



Source: Siccardi et al., Computational Models for Nanomedicine, Book Chapter, Pharmaceutical Nanotech Innovation and Tech, Wiley- VCH

nanomedicine
EUROPEAN TECHNOLOGY PLATFORM

The Think Tank of Nanomedicine in Europe

Supporting public funding of the most promising R&D topics – "where Nanomedicine can bring something more" – through strategic inputs coming for all stakeholders, towards the E.C.

A driving force for industrialization

Detecting the best innovations in Nanomedicine and facilitate their access to the clinic through the Nanomedicine Translation Hub, a global set of premium services, free-of-charge for the beneficiaries.

POLICY OBJECTIVES:

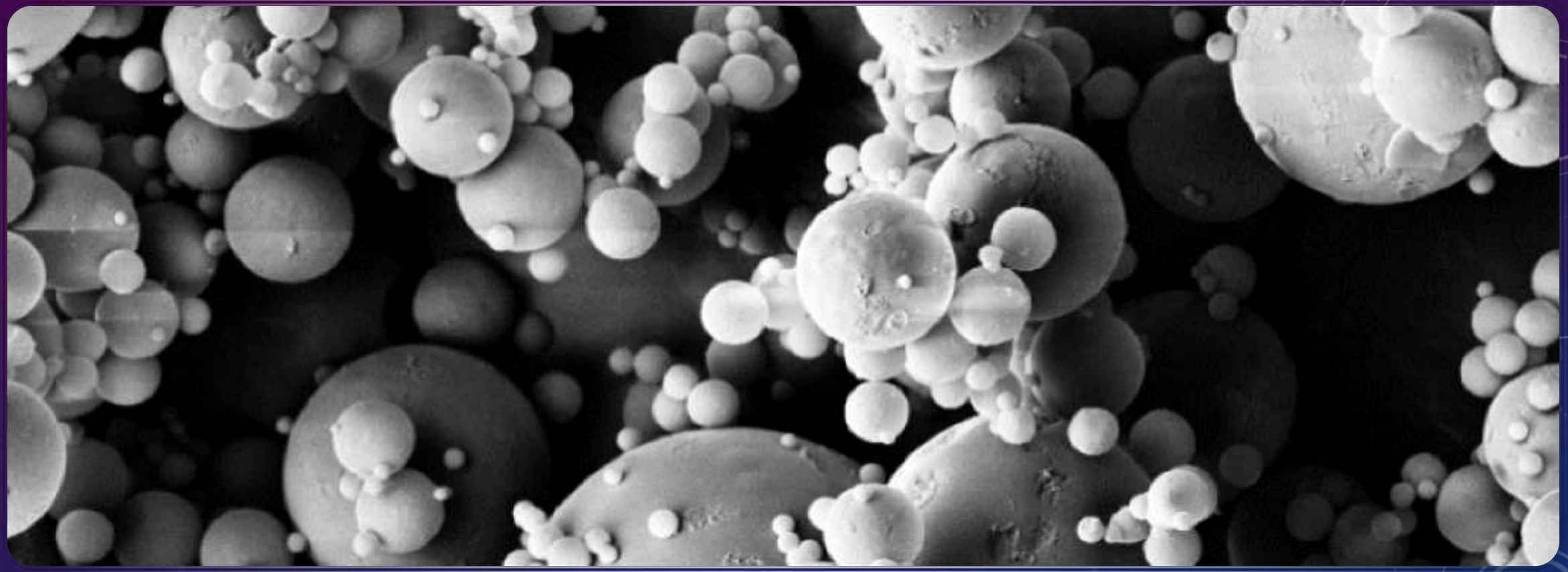
- Establish a clear strategic vision in the area resulting in a Strategic Research Agenda
- Decrease fragmentation in nano-medical research
- Mobilise additional public and private investment
- Identify priority areas
- Boost innovation in nanobiotechnologies for medical use

KEY TOPICS:

- Nanotechnology-based diagnostics
- Medical imaging
- Targeted drug delivery nanosystems and drug-free nanotherapeutics
- Regenerative medicine
- Vaccines

TAKE HOME MESSAGE

- Openess to share data
- Synergies in investment
- Design new products based on innovative material starting / adopting from QbD / SbD
- Improve efficacy and benefit on NEP applied to specific industrial needs



THANK YOU FOR YOUR ATTENTION