ROMANIAN ACADEMY
"Ilie Murgulescu" INSTITUTE OF PHYSICAL CHEMISTRY

NanoReg2

Development and implementation of Grouping and Safe-by-Design approaches within regulatory framework (NANOREG II)

Research and Innovation Action (RIA)

- an overview -

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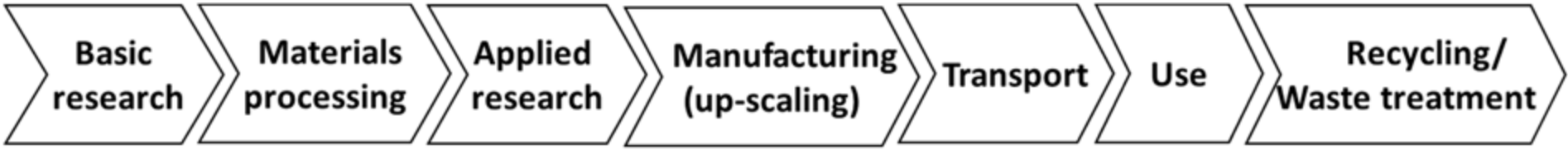
Main Objective:

to build a regulatory process by the implementation of **Safe by Design combined with Groupings principles:** enhancing Safety of MNMs along their value chain and therefore incorporating SbD both from an industrial and regulatory point of view.

Value chain of a product



In the process of innovation, when ideas are translated into marketable products, innovators need clear guidance about safety requirements from a regulatory point of view and take into account competitiveness and social constraints.

Specific Objectives:

•**To identify and define the regulatory requirements** in order to apply and implement **MNM grouping principles** in a regulatory framework.

•**To identify and select materials as candidates for value chain demonstrators** in collaboration with industry, then develop **life cycle maps** and **identify existing and potential exposure scenarios**

To evaluate **relative changes in environmental and human health risk** following implementation of the SbD process

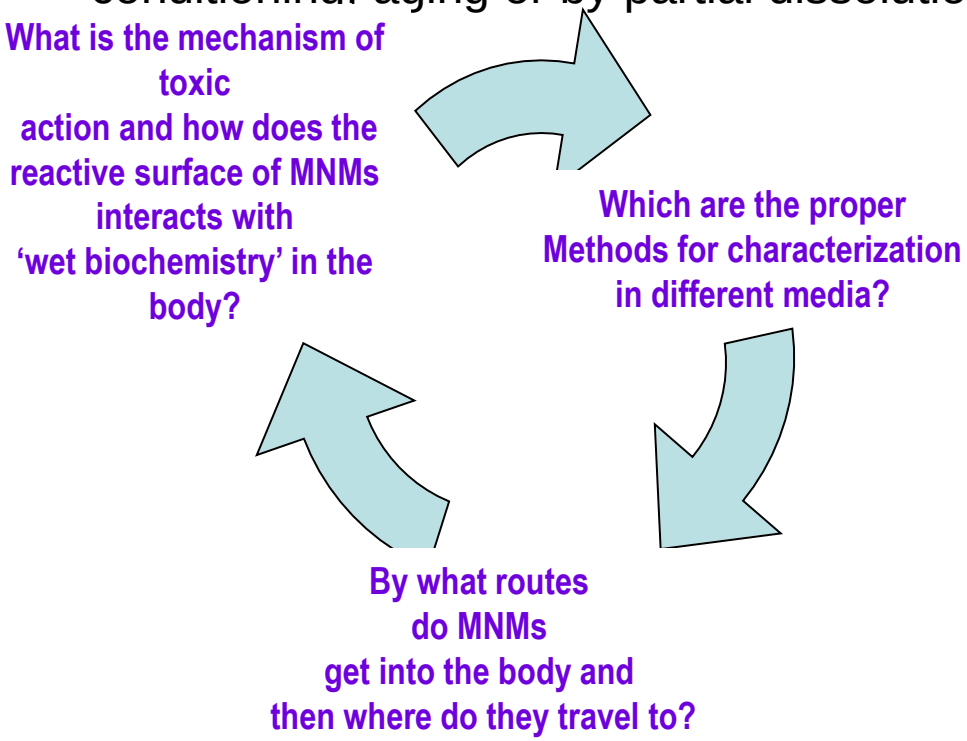
•Identify and overcome barriers to the application of **SbD concepts**, taking into consideration **grouping approaches** and **Risk Management** (RM) requirements

•Develop and adapt supportive technical and organizational tools for Safe by Design, based on **regulatory orientated grouping approaches**

•**Disseminate Safe by Design tools and SOPs, promoting regulatory orientated guidelines**

Challenging aspects related to the Grouping strategies

- MNMs are synthesized in a huge variety of different chemistries, sizes, shapes and charge surfaces.
- MNMs change during their life cycle for instance by agglomeration, surface conditioning, aging or by partial dissolution.



Since each physicochemical parameter can influence the behaviour and toxicity, risk assessment (RA) of MNM is a time and cost intensive process, performed on a case-by-case basis and requires large number of animal testing

Challenging aspects related to the Grouping strategies

- Grouping approaches can largely reduce the number of tests as they support a decision on which further tests are required and which ones may be waived. Thus, they would strongly facilitate Regulatory Risk Assessment (RA) and Management (RM).In addition grouping increases confidence in toxicological data for all substances in the group.

Task 1.2 *Monitoring future regulatory needs*:

- ❑Providing an overview on the regulation of chemicals under REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) and performing in-depth analysis of the currently available information.
- ❑Evaluate acquired information based on an integrative approach bridging NM characterization and toxicity evaluation
- ❑Identifying the possibilities how to implement SbD based on grouping approaches

Task 1.5 *Implementation of Technically Oriented instruments in a global ITS (Intelligent testing strategy)*:

- ❑ Prospective research on new key parameters for MNM grouping by using methods of Applied Chemical Thermodynamics
- ❑ Searching for adequate metrics for MNM grouping.
- ❑ Performing fundamental physico-chemical research into the interaction of NPs with bio-molecules: assessing the thermodynamics of binding interactions, protein corona formation and the effect of the NPs on the protein stability.

Challenging aspects –IPC contribution

- Thermodynamic investigations of protein stability in the presence of nanoparticles. Equipment: **NanoDSC calorimeter, TA Instruments**

  - Providing insight into the mechanism of protein adsorption and the evaluation of the impact of protein-nanoparticle interaction on practical applications

  - The influence of size, shape and surface reactivity of nanoparticles on the structure of the adsorbed protein molecules

  - Estimation of thermodynamic parameters of thermal denaturation of bound proteins

- Analysis of binding characteristics for protein-nanoparticle systems having different structures, shapes and functional properties. Equipment: **Isothermal titration calorimeter Microcal iTC200**

  - Evaluation of native protein - nanoparticle interaction parameters: ΔH, ΔG, ΔS, binding constant and stoichiometry

- Methodological overview of bacteria - NP interaction: Microcalorimetric measurements (by using **Setaram Microcalorimeters: µDSC3 and µDSC7**)

  - Microcalorimetric evaluation of MNM influence on bacterial growth: Thermal signal processing and kinetic modeling.

  - Standard microbiology lab.

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Thank you for your attention