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Science-based grouping of nanoparticles for industrial application of safe-by-design

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Introduction

The number, variety and complexity of engineered nanoparticles (or nanomaterials) incorporated in products will increase rapidly over the next years. A variety of different surface modifications (capping agents) are used to modulate the surface properties. Importantly, in some cases modifications of the nanoparticle surfaces by capping agents have been shown to eliminate nanoparticle toxicity. The aim of safe-by-design is the optimization of nanoparticles towards no toxicity or at least markedly reduced toxicity by selecting specific structural features such as surface properties while maintaining the technological use. However, currently, there is a lack of knowledge on the behaviour of capped nanoparticles in real products and there is little systematic data on biological effects or toxicity in relation to surface modifications. Due to this, systematic integration into computational approaches is lacking.

Objective

To bridge the Mode of Action based computational modelling to the demands of grouping and safe-by-design of nanoparticles, and make it applicable for industry.

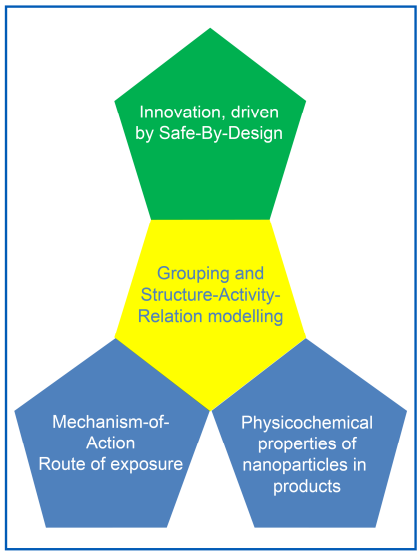

Figure 1. Structure of the project.

Deliverables

1) **Science based criteria for grouping nanoparticles** taking into account their behaviour and mode of action (*in vitro* and *in vivo*).
2) **New experimental data** for a panel of surface modified nanoparticles SiO_2 and TiO_2 on the functionality in relevant products and in relevant biological matrices.
3) **Proof-of-Principle grouping computational models.** Quantitative Structure Activity Relations Models incorporating route of exposure and behaviour of nanoparticles in products and biological matrices.
4) **Address barriers for the industrial application** of Safe-by-Design as standard practice and support value chain studies of NANoREG.

Approach

Criteria for and availability of *in silico* models for safe-by-design approaches can only be developed based on large datasets. In the absence of this we:

1) Perform similarity analysis and grouping of available data or simple nano read-across predictions.

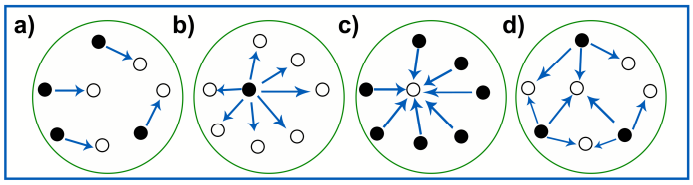

Figure 2. Different types of grouping and read-across methods to be evaluated in the project: a)one-to-one b)one-to-many c)many-to-one d)many-to-many, that can be used depending on amount of data available.

2) Assemble toxicity data retrospectively from existing data while the application data and data on the behavior in relevant biological media will be generated in this project

New data produced in project		Existing data, available for consortium			
Nanoparticles	SiO_2[a,b,c], TiO_2[a,b,c]	Nanoparticles	Phys-chem	In vivo data	In vitro data
Application data	Product 1,2,3	SiO_2[a,b], TiO_2 ZrO_2[a,b,c], ZrO_2[a,b,c], Ag[a,b,c,d], ZnO, $BaSO_4$, AlOOH	In suspension Coating, DLS, NTA,TEM	Inhalatory	Available
Phys chem	In vitro digestion Protein coating	SiO_2	In suspension and digestive juices	Oral	Available

Combined to produce science-based grouping computational model for Safe-by-design

Table 1: Content of nanoGEM toxicological database and link with data generation in the current project. The combination of the data will be used as input for the computational modelling

3) Proof-of-Principle grouping computational models. Extension of current state of the art computational modelling of nanoparticles incorporating route of exposure and behaviour of nanoparticles in products and biological matrices.

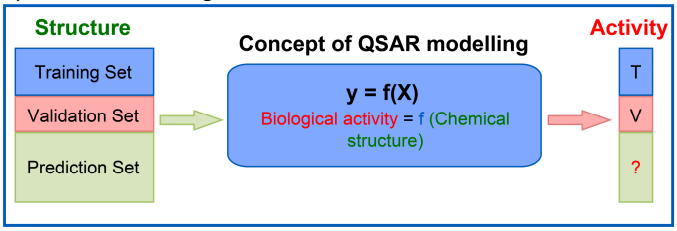

Figure 4. Concept of computational modelling using different data sets.

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