A common European approach to the regulatory testing of nanomaterials

Report on identification and setting of categorization, read-across, and extra/intrapolation criteria Deliverable 5.1

Introduction

With the increasing number and variety of nanomaterials, the need to develop more efficient ways to evaluate potential adverse effects of a nanomaterial is becoming more important. Grouping and Read Across are considered as two methods that can contribute to this.

Grouping approaches allow the prediction of a substance's toxicity by comparing it to other similar substances. 'Read-across' is a technique to fill in data gaps where the test information for one chemical is used to predict the test information concerning the same endpoint for another chemical which is considered to be similar. Different from traditional chemicals, similarity of nanomaterials cannot be based on structural or chemical composition only. A wider spectrum of physicochemical properties determining identity and behaviour of nanomaterials including e.g. impurities, surface treatment, surface area, surface charge and shape have to be considered.

This deliverable presents a system for the grouping and read-across of nanomaterials from a risk assessment point of view based on expected biological, ecological and/or toxicological effects. The recommendations for grouping, read-across, extrapolation and interpolation will be used in the development of a flowchart (Task 5.7) and regulatory framework/toolbox (Task 1.4).

Description of Work

The regulatory context as well as existing and proposed approaches for Grouping and Read Across have been identified and analysed regarding their relevance and usefulness in the NANoREG context. Also the possibilities and limitations of using (Q)SARS (Quantitative Structure-Activity Relationships) for grouping and read across modelling have been evaluated. Currently available toxicological data have been used to describe the relation between (physical chemical) characteristics ("key properties") of nanomaterials and their interaction with cells and living organisms. Finally, aims and goals of grouping and read across in NANoREG context as well as different grouping approaches have been defined and elaborated. Practical applicability has been evaluated by analysing examples of grouping and read across.

Main results and conclusions

Existing or proposed approaches

There are many initiatives and proposals for grouping of nanomaterials, but only a few of these link physico-chemical properties to the environmental and/or human toxicity of the nanomaterials. For an effective grouping, a group needs to be well-defined to determine which nanomaterials belong or do not belong to a certain group. Groups are generally defined by benchmarks, i.e. a certain value for a specific physico-chemical property that sets a boundary of the group. For nanomaterials, such benchmarks need often be a combination of several different physico-chemical properties. Especially for nanomaterials, the need for setting multidimensional groups with several criteria is acknowledged by several institutions and working groups, but lack of data often hampers setting such benchmarks.

Data quality and predictive capacity of QSAR

The recent application of (Q)SAR to nanomaterials shows that researchers are starting to use such models in order to categorise nanomaterials in the same way as chemicals. This may be beneficial as it aims to improve the efficiency of hazard and risk assessment. However, it is clear that the valid imple-

mentation of nano-(Q)SAR is a long way off, as past experience with chemicals shows the considerable amount of time and effort needed to implement the use of such tools at an internationally acceptable level. Issues described in the deliverable cast serious doubts on the reliability of such models to support nano-regulation.

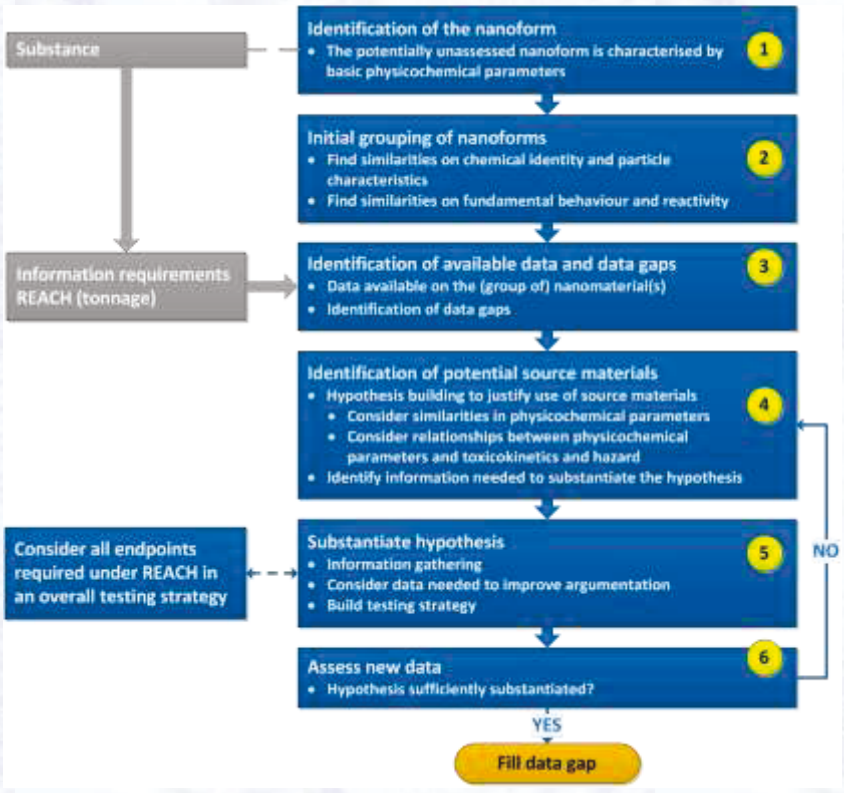
Properties for human and environmental behaviour

The behaviour and effects of a nanomaterial are influenced by a combination/interaction of several physico-chemical properties. These properties can tentatively be placed in four categories:

- **Substance identity**, including chemical composition, crystal structure, surface coating, functionalization and capping agents, impurities, all of which influence surface charge and reactivity.
- **Particle characteristics**, including size (distribution), surface area (which depends on particle size and porosity), surface roughness, shape and aspect ratio, all of which generally influence mobility and transport.
- **Transport behaviour**, which reflects characteristics of the nanoparticle that are (partly) influenced by the surrounding medium, such as solubility/dispersibility (rate of dissolution and equilibrium concentration, both size-related), surface charge, tendency to agglomerate and dustiness.
- **Activity and reactivity**, including redox potential.

Conclusions on Grouping, read-across, extra- and intrapolation within NANoREG

Two main goals of grouping are identified. The first is initial grouping for screening purposes and the second is grouping for the purpose of read-across to fill data gaps. In a working document of ECHA, RIVM and JRC on read-across between nanoforms (ECHA et al., 2015), a stepwise procedure was proposed for using data between (nano)forms. For grouping for screening purposes, the first two steps of this procedure may already suffice.



From the examples of grouping and read across, it becomes clear that initial grouping for screening purposes is already possible for some limited nanomaterials, route of exposures and endpoints. For nanoforms, examples of read-across used within regulatory risk assessment are only available for specific narrow groups of nanomaterials for a specific route of exposure and/or endpoint. Examples are the use of read across between high-aspect-ratio CNTs and asbestos (which is currently done in many control banding tools), the SCCS evaluation of TiO_2 in sunscreens and the NIOSH RELs for CNTs and TiO_2). Applying a stepwise approach to two hypothetical nanomaterials showed that detailed information on the physicochemical characteristics is already needed to support and justify read-across for specific exposure routes and/or endpoints.

For more details about NANoREG please visit the official website **www.nanoreg.eu**.

This project has received funding from the European Union Seventh Framework Programme (FP7/2007-2013) under grant agreement n° 310584