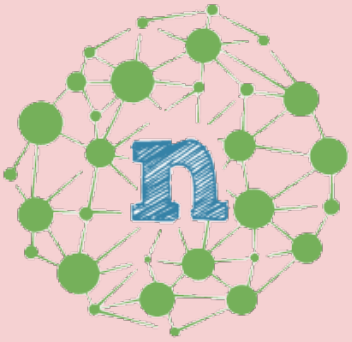
Revision of REACH Annexes for Nanomaterials – Position Paper

- **The inclusion of a nano-definition in REACH Annex VI gives legal certainty on when nano-specific rules in the REACH Annexes apply. However, further including the definition in the main body text would make it binding for all stakeholders to whom REACH applies.**
- **Under REACH, nanoforms of a substance have to be assessed and documented separately in order to assess and control their possible risks adequately.**
- **Registrants should not only be obliged to describe the test material and sample preparation but also to justify why the selected test material and test method is the most appropriate form for the test and whether the results are significant across multiple forms.**



- **Physicochemical and (eco-)toxicological information should be included in the registration dossier when "nanoforms are used in consumer preparations or incorporated into consumer articles."**
- **Tests for the environmental fate and environmental hazards should consider the surface functionalization of nano-objects.**
- **Registrants shall fully characterize all nanoforms before grouping them for (eco-) toxicological assessment.**
- **The supplier should give information on nanomaterials in the following categories of the Safety Data Sheet (SDS): composition, handling, exposure controls, physical and chemical properties, and toxicological information.**

1. Aim of this paper

REACH is the primary EU regulation on chemicals to address the health, safety, and environmental risks of substances, mixtures, and articles containing specific substances produced or put on the market in the European Union. Producers and importers, as well as down-stream users (e.g. formulators or producers of articles), have to submit registration dossiers to the European Chemical Agency (ECHA) in which they identify, characterize, and evaluate their substances, mixtures, and products. The registrant duties are found in the main legal text of REACH and fleshed out in several Annexes to REACH. So far no nano-specific provisions have been included in the REACH Annexes, and according to latest findings, the registration dossiers available so far do not contain information on nanoforms.[1] This may be partly due to the fact that nanomaterials with the same chemical identity as non-nanoforms are not considered to be discrete substances.For these nanomaterials, REACH does not stipulate a separate obligation to register, rather the nanoform[2] of a substance has to be registered together with the associated non-nanoforms of the material. In May 2014, the European Commission presented a project of annexes amendment to the Competent Authorities Sub-group on Nanomaterials (CASG Nano) to ensure efficacy of nanomaterial registration. This position paper discusses these proposed amendments.

2. Amendments to Annexes in discussion

This chapter focuses on nano-relevant amendments within the REACH Annexes with regard to general issues (in Annexes I and III), substance identification (Annex VI), and the duties of registrants. Annexes VII to XI REACH require substances to be tested for their environmental fate and behavior as well as their (eco-)toxicological hazards.

2.1 General issues (REACH Annex I, II, and III)

Although nanoforms of a substance are not considered to be discrete substances in REACH, they have to be assessed and documented separately in order to control possible risks adequately. This applies especially to the registration dossier, the chemical safety report (CSR), the safety data sheet, and in communication with downstream users.

2.1.1 Chemical Safety Report (CSR), Grouping and Exposure assessment

According to the proposed amendment of the Commission (in REACH sections 0.1 and 0.3 of Annex I) manufacturers and importers of a nanoform of a substance have to state whether and which different nanoforms of a substance are included in their chemical safety report. If manufacturers and importers use information on a nanoform of a substance to demonstrate the safe use of other forms of the substance they have to document this in their CSR. Consequently, the registrant must justify that the safety assessment adequately includes all nanoforms covered by the registration.

The Commission plans to amend the provisions for grouping different forms of a substance or for using read-across in exposure scenarios and risk management measures in order to cover nanoforms, too (cf. sections 0.4 and 0.5 of REACH Annex I REACH). To that end, whenever data from one nanoform is used to demonstrate safe use of other forms of the same substance, the registrant must provide scientific justification and record it.

Regarding the substance-specific exposure assessment of nanoforms "incorporated in an article in which it is permanently embedded in a matrix or otherwise rigorously contained by technical means," the Commission proposes that the emission estimation for nanoforms, "where relevant," takes the conditions in REACH Annex XI section 3.2 point c) into account (cf. Annex I section 5.2.2 of REACH).

Our Position:

The proposed amendments are welcomed as they clarify that nanoforms of a substance must be assessed and documented separately. With respect to the exposure assessment of nanoforms, the addition of "where relevant" in REACH Annex I section 5.2.2 places an added step for nanoforms compared to non-nanoforms that requires legal interpretation leading to uncertainty and should be removed.

Moreover, the Commission proposed to add the following sentence to Annex I section 0.1: "The chemical safety report shall also describe whether and which different nanoforms of substances manufactured and imported are included, including a statement [on] when and how information on one form is used to demonstrate safety of other forms. The requirements specific to nanoforms of a substance in this Annex are without prejudice to requirements applicable to other forms of that substance."

Our Position:

It should be stated clearly in REACH Annex I that the uses of nanoforms have to be identified by the registrant in the chemical safety report. If there are indications that a nanoform for an identified use shows different expositions and/or risks than the non-nanoform or other nanoforms, a separate determination of harmful effects, exposure assessment, and description on risks indicated by that use must be made.

2.1.2 (Eco-)toxicological information for Phase-in Substances (REACH Annex III)

The registration dossier for substances produced between 1 and 10 tonnes shall include physicochemical and (eco-)toxicological information available to registrant (cf. REACH Art. 10 and 12 in connection with Annex III). For the nanoforms of substances that were already manufactured or placed on the market before REACH entered into force on 1 June 2008 (called "phase-in substance") the registrant is not required to deliver toxicological and (eco-)toxicological information. The registrant is only required to provide information on physicochemical properties (cf. REACH Art. 12 (1) lit b)). In contrast to that duty, registrants of substances that are put on the market after 1 June 2008 (called "non-phase-in substances") and registrants of phase-in substances which are likely to be carcinogenic, mutagenic or toxic for reproduction, or substances with dispersive or diffuse use, for example in consumer mixtures and consumer articles, must provide physicochemical and (eco-) toxicological information according to Annex VII (cf. REACH lit. a) and b) in Annex III). According to the latest amendment proposal, the Commission wants to include phase-in-substance that have one or more nanoforms in Annex III.

Our Position:

As a consequence of the proposed amendment, registrants would have to include physicochemical and (eco-)toxicological information in the registration dossier for phase-in substances that have one or more nanoforms. Additionally, it should be stated in paragraph b) (i) of REACH Annex III that physicochemical and (eco-)toxicological information has to be included in the registration dossier if "nanoforms are used in consumer preparations or incorporated into consumer articles" (corresponding to paragraph b) (ii) of REACH Annex III). With this amendment, an important loophole regarding the risk assessment for most of the existing nanomaterials (i.e. a nanoform of a substance itself or those used in a consumer product already on the market) would be closed.

2.1.3 Detailed description of the test material and sample preparation

In order to ensure the validity of data provided, it is critical that registrants describe the test material and sample preparation they have used.

The Commission wants to address that aspect in all tonnage bands by introducing the following amendment in the introductory text of the Annexes VII to X:

"Without prejudice to the information submitted for other forms, any relevant physicochemical, toxicological and ecotoxicological information shall include characterisation of the nanoform tested and test conditions. The same shall apply when information is provided by application of quantitative structure activity relationships (QSARs) or evidence obtained via other means than testing."

Our Position:

We welcome the amendment that makes it mandatory for registrants to describe the test material and sample preparation. However, the registrant should also justify why the selected material and test method is the most appropriate and whether the expected results could be used for multiple forms. The justification is necessary to control the quality of a read-across result, i.e. is the hazard assessment for a specific nanomaterial (e.g. titanium dioxide 20 nm) true for another nanomaterial (e.g. titanium dioxide 30 nm). Moreover, the justification should also apply to the use of historical data.

2.2 Substance identification & physical-chemical properties (REACH Annex VI)

There is consensus that the definition of substance in REACH Art. 3 No.1 covers nanoforms of a substance as well. Nevertheless, it is still unclear whether nanoforms and non-nanoform (bulk form) of a substance with an identical chemical composition are one and the same substance or if, and according to which, criteria they are discrete substances from a regulatory point of view. One solution would be to treat non-nano forms and nanoforms of a substance as discrete substances. The Commission does not follow this option, but rather treats nanoforms and non-nanoforms as different forms of the same substance and proposes to include a definition for "nanomaterial" as well as criteria to identify nanomaterials according to REACH Annex VI, Section 2. Regarding a definition of the term "nanomaterial," the Commission proposes to implement its recommendation of 18 October 2011 in Annex VI.[3]

Where the registration of a substance also covers a nanoform of the substance, the proposed amendment requires characterization of the nanoform according to the following criteria:

- Names or other identifiers of the nanoforms of the substance,
- Particle number size distribution with indication of the fraction of constituent particles in the size range 1 nm – 100 nm,
- Description of surface functionalization or treatment,
- Shape, aspect ratio, and other morphological characterization; information on assembly structure including shell like structures or hollow structures, if appropriate,
- Surface area (volume specific surface area and/or mass-specific surface area),
- Description of the analytical methods or the appropriate bibliographical references for the identification of the information elements in this sub-section. This information shall be sufficient to allow the methods to be reproduced.

Our Position:

The inclusion of a nano-definition in REACH Annex VI is welcomed. It gives legal certainty on when to apply nano-specific provisions. However, further including the nano-definition in the main body text would make it binding for all stakeholders for whom REACH applies. Regarding the proposal for the characterization of nanoforms, it only covers minimum characterization requirements. Important characterization information is missing, including information on the particle size distribution outside the 1 nm and 100 nm range; surface chemistry and surface charge; the formation of agglomerated/aggregated forms during use and (environmental) release; the stability of aggregates/agglomerates; and the possible "crystalline state" of the nanoform. Information required on surface treatment, coating, or functionalization is extremely limited, although this is considered to be one of the key parameters relevant for risk assessment of nanoforms.[4]

2.3 Human- and Eco-toxicology (REACH Annexes VII – XI)

Under REACH, registrants must comply with different registration and testing requirements depending on the production volumes per registrant and per year:

- Tonnage band 1 – 10 t/y: Annex VII requirements
- Tonnage band 10 – 100 t/y: Annex VIII requirements
- Tonnage band 100 – 1,000 t/y: Annex IX requirements
- Tonnage band over 1,000 t/y: Annex X requirements

It must be noted that the information required for higher tonnage bands registrations include those of the lower tonnage band, i.e. the information requirements increase with production volume.

Nanoforms of a substance can differ, both from chemically identical non-nanoforms of a substance and other nanoforms with regard to their (eco-)toxicity and environmental behavior. Previous studies have shown that for the (eco-)toxicity of nanomaterials, criteria other than size may be important, e.g. crystalline form (e.g. TiO2), possible contamination, 3-D structures (e.g. CNT), and surface-treatment.[5] In 2012, nano-specific requirements were introduced in the ECHA "Guidance on Information Requirements and Chemical Safety Assessment,"[6] for example regarding endpoint-specific test requirements. There are currently no nano-specific provisions included in Annexes to REACH. The Commission is discussing the following amendments to REACH Annexes:

Our Position:

It should be obligatory for the registrant of a nano form of a substance to conduct inhalation or dermal studies instead or in addition to oral tests if they are a more appropriate route. Additionally, it should be mandatory for the registrant to give scientific justification about which route(s) is considered to be most relevant for the nanoform(s). Unfortunately, testing of additional exposure routes will lead to more animal tests. We contend however, that not requiring these tests could amount to testing the material on human instead.

2.3.1 Address relevant endpoints for human health hazards

Acute toxicity

In terms of acute toxicity of nanoforms, "inhalation" is considered the most relevant exposure route for human health in general. Currently, only an oral toxicity test is required for substances produced above 1 tonne (Annex VII, Section 8.5.1). However, the oral toxicity test is not required when the substance is classified as corrosive to the skin or a study on acute toxicity by inhalation is available.

The Commission is discussing requiring inhalation or dermal studies according to Annex VIII Sections 8.5.1 and 8.5.3 for substances produced in volumes above 1 tonne instead of oral tests if they are the more appropriate exposure route.

Our Position:

It should be made clear that what needs to be tested is the discrete "nano-object" not its aggregates or agglomerates. Additionally, it should be obligatory to consider the surface treatment of the nanoform in the test.

2.3.2 Address relevant endpoints or environmental fate and environmental hazards

Stability

To predict the fate of nanoforms in the environment, certain physic-chemical properties (such as hydrolysis) are relevant factors (cf. REACH Annex VIII Section 9.2.2.1). However, for nanoforms, other abiotic degradation mechanisms such as ion dissolution may be more relevant. The Commission is discussing this aspect in Annex VIII Section 9.2.2.1 and plans to require a more appropriate study for nanoforms if another abiotic degradation mechanism (such as photolysis or interaction with other chemicals) is more relevant than hydrolysis.

Bioaccumulation

Potential for bioaccumulation must be tested for substances within the 100 to 1000 tonnes tonnage band (cf. REACH Annex IX Section 9.3.2). In this regard, the fat solubility of a substance is important. It is measured by the octanol-water partition coefficient (called "logKow"). If the logKow is found to be > 3 this is seen as a trigger for the substances bioaccumulation potential. However, according to Annex IX Section 9.3.2, the bioaccumulation test can be waived if the substance is not fat soluble (has a logKow ≤ 3). As the logKow may not be an appropriate indicator to determine the bioaccumulation potential of nanoforms, the Commission proposes that waiving the test cannot be justified by the logKow of the nanoform alone.

Transport and distribution

Similarly, the European Commission is discussing limiting the waiving of tests for nanoforms regarding the parameters "adsorption/desorption" (cf. REACH Annex VIII Section 9.3.1, Annex IX Section 9.3.3). The Commission is planning to amend Section 9.3.1 to specify that the "Kow" alone cannot serve as a justification for waiving tests based on the low potential for adsorption.

Long-term toxicity

Registrants of substances produced between 100 and 1000 tonnes have to conduct long-term toxicity tests (cf. REACH Annex IX Section 8.6.2). So far, long-term testing can be waived if short-term toxicity tests do not show evidence of toxicity (cf. REACH Annex IX Section 8.6.2 second column). The Commission proposes to suppress the possibility of waiving long term toxicity testing based on a lack of short-term toxicity evidence.

To assess the long term sub-chronic toxicity of a substance, Annex IX Section 8.6.2 contains criteria to help the registrant decide whether the dermal or inhalation route is most appropriate. The Commission is now proposing to include "cardiovascular toxicity" and "respiratory sensitisation" as additional criteria when a nanoform is covered by the registration.

Hazards for soil and sediment

In order to assess the hazard of a substance for soil organisms, the equilibrium partitioning method may be applied if toxicity data for soil organisms is not available (cf. "effects on terrestrial organism" in Annex IX section 9.4 second column). According to the Commission's proposed amendment, the equilibrium partitioning method may be applicable to nanoforms too, but its use must be scientifically justified.

2.3.3 Scientific justification for grouping/read-across/QSAR (REACH Annex XI)

According to REACH Art. 13, registrants may generate information on intrinsic properties of substances by means other than tests, provided it meets the general rules in Annex XI to adapt the standard testing requirements set out in Annexes VII to X. In particular, vertebrate animal tests should be avoided when testing human toxicity. Instead, alternative methods should be used, such as in vitro testing, use of qualitative or quantitative structure-activity relationship models (QSARs), or use of data from substances that are structurally related (grouping or read-across). Registrants may omit testing in accordance with Annex VIII, sections 8.6 and 8.7, Annex IX and Annex X if justified by available information on exposure and risk management measures, as specified in Annex XI, section 3.

The Commission basically proposes to address nanoforms separately when they are registered together with a substance. Additionally, the rules for grouping substances and read-across in Annex XI section 1.5 shall apply to nanoforms too.

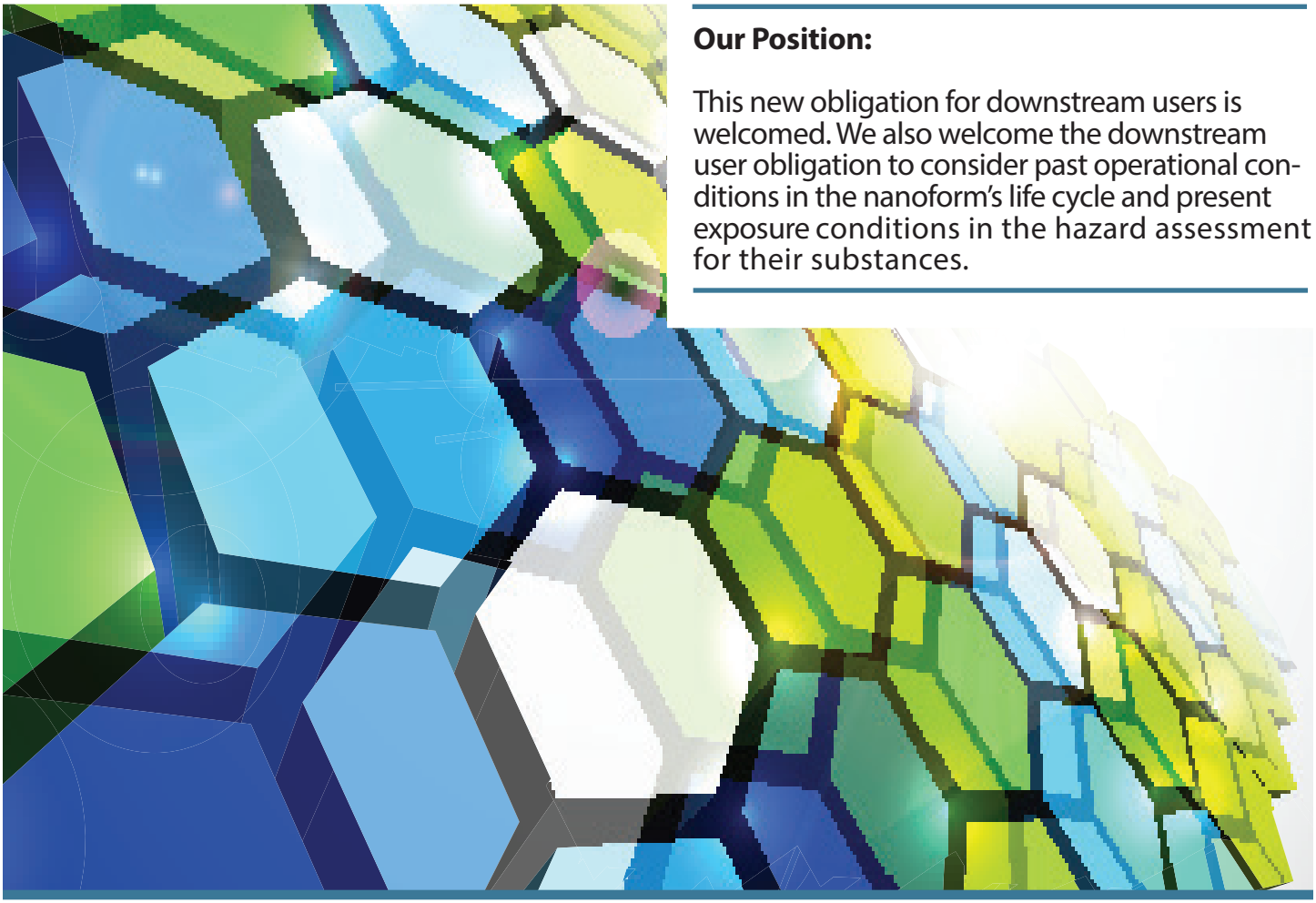
Our Position:

An analogy concept for grouping of nanoform on a case-by-case basis is welcomed. The controversy on this provision relates to whether registrants must provide full characterization of all forms before deciding on grouping those nanoforms for (eco-)toxicological assessment. Allowing the grouping for (eco-)toxicological assessment of non-characterized nanoforms would defeat the purpose of most of the proposed amendments. Grouping for the purpose of hazard assessment is based on the hypothesis that information on the safety of one nanoform can be used to demonstrate the safety of another nanoform. Nanomaterials can have a multitude of physical-chemical characteristics (e.g. size, coating, shape, surface characteristics, solubility), which influence their (eco-)toxicity (cf. Fact sheet "Toxicity of Engineered Nanomaterials"). These characteristics are identified through a material characterization process. It is therefore scientific nonsense to group several uncharacterized materials for the purpose of hazard assessment. Instead, it is essential to require the characterization of nanoforms before they can be grouped for hazard assessment purposes.

2.4 Downstream users (REACH Annex XII)

Downstream users[7] (e.g. formulators or producers of articles) are also responsible for the safe use of chemicals by implementing safe use at their own site and communicating relevant information both to their suppliers and their customers. They are required to prepare a Chemical Safety Report (CSR) in accordance with Annex XII for any use which the supplier (registrant) has excluded in his exposure scenario or any use the supplier advises against (cf. REACH Art. 37 (4)). Annex XII contains the general provision for downstream users to assess substances and prepare a CSR.

The Commission proposes to introduce an obligation for downstream users to "keep available information on the physical state, concentration, concentration range or quantities of nanoforms in mixtures and articles that they use" in the chapeau of Annex XII. According to the Commission this duty applies to all information the downstream user has received from the supplier´s safety data sheet (cf. REACH Art. 31 and 32).



Our Position:

This new obligation for downstream users is welcomed. We also welcome the downstream user obligation to consider past operational conditions in the nanoform's life cycle and present exposure conditions in the hazard assessment for their substances.

Footnotes:

1. RPA et al (2014): Study to Assess the Impact of Possible Legislation to Increase Transparency on Nanomaterials on the Market, Evaluation Report for DG Enterprise and Industry, November 2014, p. 110.
2. In this paper, the term "nanoform of a substance" relates to nanomaterials with a chemical identity that is equivalent to the substance within REACH.
3. The definition reads as follows: "a nanomaterial is a natural or 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. By derogation, fullerenes, graphene flakes and single wall carbon nanotubes with one or more external dimensions below 1 nm shall be considered as nanomaterials. For this purpose, 'particle' means a minute piece of matter with defined physical boundaries; 'agglomerate' means a collection of weakly bound particles or aggregates where the resulting external surface area is similar to the sum of the surface areas of the individual components and 'aggregate' means a particle comprising of strongly bound or fused particles. A nanomaterial may be a form of a substance or a distinct substance. A nanomaterial may have different nanoforms".
4. Stone, V.; Hankin, S.; Aitken, R.; Aschberger, K.; Baun, A.; Christensen, F.; Fernandes, T.; Hansen, S.F.; Hartmann, N.B.; Hutchison, G.; Johnston, H.; Micheletti, C.; Peters, S.; Ross, B.; Sokull-Kluettgen, B.; Stark, D.; Tran, L. (2009): "ENRHES – Engineered nanoparticles: review of health and environmental safety".
5. Stone, V.; Hankin, S.; Aitken, R.; Aschberger, K.; Baun, A.; Christensen, F.; Fernandes, T.; Hansen, S.F.; Hartmann, N.B.; Hutchison, G.; Johnston, H.; Micheletti, C.; Peters, S.; Ross, B.; Sokull-Kluettgen, B.; Stark, D.; Tran, L. (2009): "ENRHES – Engineered nanoparticles: review of health and environmental safety", EC contract number 218433.
6. See the website of ECHA: http://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment (as from 21.11.2014).
7. Downstream users are companies or individuals who use a chemical substance, either on its own or in a mixture, in the course of their industrial or professional activities.