

REACH Annexes amendments to address nanoforms of substances: Cefic's perspective

Cefic welcomes the vote of the REACH Committee on REACH Annexes amendments for nanomaterials. The adaptation of the Annexes is a meaningful step to reduce existing legal uncertainties and provide more clarity for the registration of nanomaterials under REACH. The issue remains, however, complex and some of the amendments can even create further confusion.

After a detailed analysis of the Annexes amendments, Cefic has prepared a list of issues we believe need to be further addressed, in guidance or elsewhere (i.a. IUCLID).

- **Concept of nanoform (Annex VI introduction):** The inclusion of the term nanoform in Annex VI, defined as a form of a substance falling under the Recommendation on the definition of a nanomaterial (2011/686/EU), was already foreseen for some time. Cefic considers it necessary to clarify, in unambiguous terms, that a nanoform can comprise of several product grades of the same substance if they fit appropriately in the phys-chem parameters for nanoforms defined in section 2.4 of Annex VI.
- **Coverage of nanoforms (Recital 6):** The amendments of the REACH Annexes indicate that the chemical safety assessment needs to be adequately applied to the different nanoforms (and potential transformations) of the substances registered. This is yet a new concept for which supporting guidelines are currently being developed/updated; thereby flexibility should be given to properly address them.
- **Concept of "set of similar nanoforms" (Annex VI introduction):** Cefic agrees on the need for the inclusion of the concept of a "set of similar nanoforms" in the REACH Annexes. In our view, a "set of similar nanoforms" can be included in IUCLID by using the "assessment entity" function.
- **Tonnage:** Volume-dependent information requirements under REACH are related to the registered volume of the substance in all forms covered by the registration. Where several forms of a substance are covered in one REACH registration dossier, this may result in a huge number of new data requirements. Therefore, for reasons of workability, proportionality, animal welfare and cost-efficiency, formation of large groups ('sets of similar nanoforms') with similar characteristics should be supported and accepted. In addition, the formation of different 'sets of similar nanoforms' for different endpoints should be encouraged. This is especially important in terms of innovation, which could be the preparation of a new nanoform of an existing substance.
- **Dissolution rate (Annex VII 7.7):** The requirement to include the dissolution rate in the information requirements brings up some fundamental questions on test methods in general. The lack of validated methods implies that very different results might be obtained depending on environmental

media use, dispersion protocols and a long list of parameters. All (OECD) test methods for nanomaterials must, in the end, be validated to provide meaningful results

- **Partition coefficient octanol water (Kow) / dispersion stability (Annex VII 7.8): OECD Test Guideline 318** describes how to measure dispersion stability of nanomaterials in water. So far, there is no method defined for nanomaterials that cannot be wetted by water. Moreover, the dispersion method will alter the structure and hence sedimentation behaviour of certain aggregated/agglomerated materials.
- **Inhalation route (Annex VII 8.5.1):** Inhalation may be the more relevant route of exposure for nanomaterials compared to oral application. However, the acute inhalation toxicity study (OECD TG 403 and TG436) is not adequate for nanomaterials as materials of low intrinsic toxicity have to be tested at the limit dose of 5,000 mg/m³. Here, deaths are to be expected because this high nanoparticle concentration in the air will congest the trachea of the exposed animals, which will die due to a mechanical suffocation effect instead of the intrinsic toxicity of the substance. Therefore, we recommend requesting a short-term inhalation toxicity study (5d) instead of an acute inhalation toxicity study, regarding added value (get data on intrinsic tox) and animal welfare.
- **Toxicokinetics (Annex VIII 8.8):** The ECHA guidance for human health information requirements for nanomaterials indicates that:

“The standard information requirements defined by the REACH regulation can give useful information to help make a judgement about the possible toxicokinetics of nanomaterials (See Section R.7.12.2.1).

Information on the possible behaviour of the nanomaterials can be supplemented with in vitro and in silico predictions based on physicochemical and other data. This information may be used in grouping of nanomaterials to assist in the read-across of exposure and hazard characteristics, thereby reducing the total number of tests required.”

Cefic agrees with that statement, other required endpoints should be accepted as sources of toxicokinetic data. A full toxicokinetic analysis with no added value should be avoided.

- **Additional physico-chemical parameters (Annex VIII 7):** Cefic believes that a routine request from authorities for additional phys-chem parameters cannot be accepted; pragmatism should be the rule. A request for additional phys-chem information should be well justified. Cefic would like to encourage an open dialogue with the registrants before additional information is required.
- **Degradation (Annex VIII 9.2):** The text of the amended Annex VIII 9.2 indicates that

“For nanoforms that are not soluble, nor have high dissolution rate, such test(s) shall consider morphological transformation (e.g. irreversible changes in particle size, shape and surface properties, loss of coating), chemical transformation (e.g. oxidation, reduction) and other abiotic degradation (e.g. photolysis).”

Degradation can only be measured qualitatively, a quantitative analysis is not possible, the requirements for this endpoint need to be clarified in guidance.

Cefic thanks the Commission for their consideration and remains available for further clarifications and discussions to achieve a pragmatic implementation of the recently amended REACH regulation for nanomaterials.

For more information please contact:
Blanca Serrano, Product Stewardship Director, Cefic,
+32 2.676.72.40 or bsr@cefic.be.

About Cefic

Cefic, the European Chemical Industry Council, founded in 1972, is the voice of 29,000 large, medium and small chemical companies in Europe, which provide 1.2 million jobs and account for 14.7% of world chemicals production.