Nanomaterials and REACH – What Do I Have to Do Differently?

Part 1: Regulatory requirements for nanomaterials

Author Neil Hunt Date February 2019
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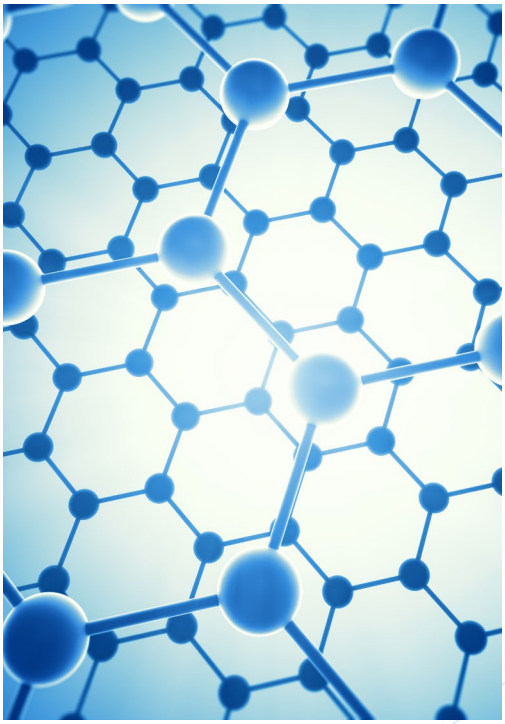
yordas Group

Business through Science

Due to their small size and high surface area, nanomaterials can demonstrate unique chemical and physical properties not seen in the meso-forms of the same substance. Their use is increasingly expanding from niche to widespread commercial applications. For instance, if you are wearing socks with "silver" technology for extra freshness, you are using a nanomaterial. There is concern that properties that give nanomaterials their unique commercial applications may also present new or increased toxicological impacts. Nanomaterials have been found in organs and cells inaccessible to the same substance in either bulk or solution form. These concerns have led to calls for greater regulatory control of these substances.

Many research projects over the last decade have indicated that, whilst there appears not to be a "nanospecific" novel toxicological hazard applicable to all nanomaterials, many different physicochemical factors can influence the toxicity of a nanomaterial. While it is good news that it cannot be assumed that all nanomaterials are toxic, these results mean that different nanoforms of a nanomaterial can demonstrate different toxicological profiles making the risk assessment of such materials complex. The update to REACH in December 2018, the key regulation for chemicals in the EU, has followed on from these research results in requiring that any manufacturer or importer of powders or nanomaterials should fully understand their product. This necessitates particle characterisation and risk assessment specific to the nanoforms placed on the market.

Nanomaterials – What are they?



Nanomaterials are forms of a substance that display extremely small internal or external dimensions usually in the solid form. Nanomaterials can exist in other forms, such as colloids and aerosols of liquids, but regulatory concern focuses on solid nanomaterials so the rest of this document will concentrate on these. In 2011, the European Commission's Scientific Committee on Newly Identified Health Risks proposed to define a nanomaterial as a substance where at least 50 % of the total number of primary particles in the substance display one or more external dimensions in the range of 1-100 nm. This means that not only ultrafine particulates, such as titanium dioxide in sunscreen and cerium oxide in fuels, but acicular rod-like structures including carbon nanotubes in tennis rackets and plate-like structures found in graphene are defined as nanomaterials. Some substances with a shortest dimension of < 1 nm can also be described as nanomaterials on a case-by-case basis. There has been a long delay in finalising this definition, with no firm date set for official publication.

It must be noted that other regulations, both regional and international, provide slightly different definitions for nanomaterials. For example, the Cosmetic Products Regulation defines a nanomaterial as insoluble, the Food Contact Regulation defines nanomaterials as deliberately manufactured and the US TSCA regulation requires the substance to display unique properties related to its size or shape to be a nanomaterial.

Why are they receiving regulatory attention?

The REACH regulations introduced into the EU in 2007 aim to identify and control risks arising from the manufacture and use of chemicals in the EU. As part of this, manufacturers and importers of a substance in the EU at over one tonne per annum must register the substance by May 2018. The registration dossier should assess the hazard and risk arising from all forms of the substance placed onto the market. As it was worded, REACH advised that registrants of nanomaterials should do a separate assessment to the bulk form but the regulation did not clearly make this mandatory. After a series of Board of Appeal decisions, it was decided to update REACH to more explicitly state the registration obligations for nanomaterials. These updates to the Annexes of REACH came into force in December 2018, introducing new concepts into the regulation and clarifying when additional testing is required and the nature of this testing (see the other white papers in this series). These dossier updates must be completed by January 2020.

The update has formally introduced new terms into REACH. An understanding of these terms is essential to identify how registration dossiers for nanomaterials should be constructed.

Nanoforms: Research has shown that two different grades of a substance might both be described as a nanomaterial but display different physical and chemical characteristics, and hence different toxicological profiles. These different grades are described as different nanoforms. The description "nanoforms" entered the regulatory lexicon in the update to REACH in December 2018 to describe forms of a substance that both meet the definition of nanomaterial while differing in their physico-chemical characteristics. Nanoforms can differ by their size, shape, surface-modification and other relevant parameters. Recent guidance has clarified that if two grades of a nanomaterial are manufactured to intentionally have different physical or chemical parameters, they would be described as two nanoforms of the substance irrespective of the similarity of their hazard or risk profile. Inter-batch variability within one grade is permitted to fall within the description of a single nanoform.

Sets of similar nanoforms: The update to REACH has also introduced the concept of "sets of similar nanoforms", which is intended to simplify the process of addressing nanomaterials under REACH. A "set of similar nanoforms" is one where more than one nanoform displays identical physicochemical, toxicological and eco-toxicological hazards. Only one set of characterisation and endpoint data will be required per "set of similar nanoforms". It will be necessary to provide scientific justification for setting the limits of a "set of similar nanoforms" and guidance is eagerly awaited from ECHA to describe the degree of justification required.

New obligations arising from the update to REACH

The update to REACH has clarified existing or introduced new obligations for the registrants of substances placed on the market as a nanomaterial. There may also be a need for registrants of all substances in the powder form to investigate whether they need to update their dossier. Some of these obligations are explicitly stated in the regulation whereas others may be implicit.

- All substances placed on the market as a nanomaterial will need to include particle characterisation in their registration dossier.
- Registrants of powders will need to investigate whether their substance is a nanomaterial or not.
- Different grades of a nanomaterial will need separate particle characterisation.
- Sets of similar nanoforms will need to be defined and justified, both by an individual registrant and between different registrants.
- Potential for conversion between nanoforms during the life-cycle will need to be assessed.

- Full hazard assessment, the information required defined by the total tonnage of the substance placed on the market by the registrant, will be needed for each set of similar nanoforms.
- Some endpoints will require different testing protocols to bulk forms of the same substance.
- Exposure scenarios for nanomaterials will be more likely, meaning that downstream users will also need to have some knowledge of the nanoform in their products.
- Safety data sheets may require updating.
- Communication between registrants (used to be called SIEFs) will need to be considered and further payments under Letter of Access agreements could be needed.

More detail on the new testing requirements for nanomaterials, including particle characterisation, hazard assessment and risk assessment are detailed in a subsequent white paper in this series.

New obligations arising from the update to REACH

If every set of similar nanoforms has a complete suite of endpoint testing commissioned, the amount of animal testing and the cost to registrants will be so excessive that large sections of the nanotechnology industry in the EU may cease to be financially justifiable. Therefore, it will be vitally important to identify approaches to avoid this level of new studies. Thorough and exhaustive literature searches through the vast research body of work will be crucial to identify 'Weight of Evidence' solutions to some endpoints. The use of grouping and read-across strategies between nanoforms and from bulk forms to nanoforms will also be a vital tool in the risk assessment of nanomaterials, whether to set the limits of a set of similar nanoforms or to justify read-across arguments, although it is likely that properly designed studies will also be needed for a comprehensive conclusion. Of crucial importance will be the guidance documents published by ECHA that will show how well justified a grouping strategy needs to be to meet the regulatory obligations to the regulator's satisfaction. There are a number of research projects that are focusing on the development of grouping and read-across strategies for nanomaterials, including GRACIOUS (www.h2020gracious.eu) and NanoGravur.

Yordas Groups Services

Yordas reviews the guidance documents for the European Chemicals Agency (ECHA) as an industry representative on the Partner Expert Group. As members of a number of EU-funded projects, influencing how the regulations have been updated, our experience places us in an ideal position to identify a client's regulatory obligations and to design cost effective registration strategies.

To discuss your requirements with a member of our expert team, call us on +44(0)1524 510278 or email info@yordasgroup.com.