Feasibility and challenges of human health risk assessment for nanomaterials

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Background

The unique properties of many types of nanomaterials has led to their increasing manufacture and use in many promising applications. In order to assess the current status of hazard, exposure and risk information pertaining to different nanomaterials, in 2008 the EU funded a 12-month FP7 project called Engineered Nanoparticles: Review of Health and Environmental Safety (ENRHES). ENRHES – coordinated by Edinburgh Napier University with the Institute of Occupational Medicine acting as Scientific Coordinator - involved a comprehensive and critical scientific review of the health and environmental safety of different classes of nanomaterials, as published in the open literature. The review (available for download here) considered sources, pathways of exposure, impacts on health and the environmental in order to generate information and data suitable to attempt a risk assessment. Drawing on the results of the ENRHES report and complemented with some more recent findings, experts from the ENRHES team, with the activity led by project partners Frans Christensen and Karin Aschberger from the European Commission Joint Research Centre's Institute for Health and Consumer Protection, have now published a series of articles assessing the feasibility and challenges of conducting a human health risk assessment for four types of nanomaterials: carbon nanotubes (CNT), titanium dioxide nanoparticles (nano-TiO2), silver nanoparticles (nano-Ag) and carbon fullerenes (C60). These publications were highlighted in a recent news article from JRC and are discussed in more detail below.

Scope and approach

Very few publications up to now have dealt with risk assessment methodologies for nanomaterials. In an opinion report published in 2007, the EU Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) stated that the current methodologies are generally likely to be able to identify the hazards associated with the use of nanomaterials, but that modifications are required for the guidance on the assessment of risks. This was further detailed the SCENIHR opinion published in 2009, pointing, between others, to main limitations in high quality exposure and dosimetry data. Nevertheless, in the assessments for CNT, nano-TiO2-, nano-Ag and C60 published by members of the ENRHES team, a traditional risk assessment approach was applied to determine the extent to which conclusions could be drawn in relation to the potential risks associated with the current use of these nanomaterials and where relevant to recommend further data generation. In terms of endpoints covered, the assessment was designed using an approach inspired by the traditional method to assess risk under the previous EU chemicals legislation and the new EU chemicals legislation REACH. However, due to the limited data available the methods used did not follow frameworks or templates rigorously. Also, the assessment was not as comprehensive in terms of detail as would normally be conducted for some regulatory risk assessments. It is expected that more data are available than can be accessed via the open literature, therefore it is stressed by the authors that the results of these studies should not be applied directly for any regulatory decision making. In addition, it is important to highlight that the data used in these appraisals relates to different types of CNTs, nano-TiO_2, nano-Ag and C_{60} (with varying size, surface chemistry, solubility, aggregation/agglomeration etc.) and care should be therefore taken when drawing general conclusions across the parameters.

Key findings and recommendations

In the case of all four nanomaterials assessed using the approach outlined above, it was determined that gaps in the available data set, in relation to both exposure and hazard, do not allow any definite conclusions suitable for regulatory decision making to be made at the present time. Key findings of the appraisals and recommendations for future work in order to enable a full risk assessment are outlined on a material by material basis below.

Carbon nanotubes

CNTs possess many unique electronic and mechanical properties and are thus interesting for numerous novel industrial and biomedical applications. As the level of production and use of these materials increases, so does the potential risk to human health.

Results of the appraisal of the feasibility and challenges of human health risk assessment for CNTs by Ashberger et al. - published in Critical Reviews in Toxicology - indicate that:

- the main risks for humans arise from chronic occupational inhalation, especially during activities involving high CNT release and uncontrolled exposure;
- it is not yet possible to draw definitive conclusions with regards the potential risk for long, straight multi-walled carbon nanotubes to pose a similar risk as asbestos by inducing mesothelioma;
- the genotoxic potential of CNTs is currently inconclusive and could be either primary or secondary;
- possible systemic effects of CNTs would be either dependent on absorption and distribution of CNTs to sensitive organs or could be induced through the release of inflammatory mediators.

In order to enable a full human health risk assessment, Ashberger et al. recommend that future work should focus on the generation of reliable occupational, environmental and consumer exposure data. Data on toxicokinetics and studies investigating effects of chronic exposure under conditions relevant for human exposure should also be prioritised.

Titanium dioxide nanoparticles

Nano-TiO_2 is already widely used in a variety of consumer products, including paints, sunscreens, solar cells and catalysts. Key results of the appraisal of the feasibility of conducting a human health risk assessment of nano-TiO_2- – published in Nanotoxicology by Christensen et al. - suggest that repeated inhalation in the workplace and possibly consumer inhalation may cause risks, as may short-term inhalation following spray applications.

Christensen et al. suggest that the main future work to support a full risk assessment should focus on generating occupational and consumer inhalation exposure data, as well as toxicity data on absorption following inhalation, repeated dermal contact, and contact with damaged skin. Further information on possible neurotoxicity and genotoxicity/carcinogenicity is also required, as well as the establishment of a No Observed Adverse Effect Level (NOAEL) for acute inhalation of nano-TiO_2.

Silver nanoparticles

Nano-Ag is reported to be used in many consumer products owing largely to its anti-bacterial properties, including pharmaceuticals, clothing (for coating and for preventing odour), leisure equipment, toothpaste, plastics, sprays and paints.

Results of the appraisal of the feasibility and challenges for human health risk assessment based on open literature for nano-Ag – published in Nanotoxicology by Christensen et al. - show that repeated inhalation in the workplace and possibly consumer inhalation may cause risks. Also (uncontrolled) nano-silver drug intake and burn treatment of large parts of the body with wound dressings may cause risks.

Christensen et al. recommend that, in order to support a full risk assessment, future work should focus on generating occupational and consumer exposure data, as well as toxicity data on absorption (to assess questions such as whether particles or only ions are absorbed), information on genotoxicity, as well as further information on the toxicity following inhalation exposure to sizes and agglomeration states as uncounted in the workplace.

Carbon fullerenes

Current applications of C_{60} are focussed on targeted drug delivery systems, lubricants, energy applications (such as fuel cells, solar cells, and batteries), catalysis, and polymer modifications. Applications in the consumer market include surfaces for anti-wear applications, cosmetics and sporting goods. The anticipated market growth of fullerenes, in combination with the potential for direct human exposure via several applications (e.g. creams used on the skin or drug delivery) has led to widespread concerns about their potential to cause adverse effects to human health.

Results of the appraisal of the feasibility and challenges for human health risk assessment based on open literature for C_{60} – published by Aschberger et al. in Regulatory Toxicology and Pharmacology – indicates that:

- risks for humans exposed to fullerenes in the workplace cannot be excluded and exposure should be controlled;
- the main concern for consumers is exposure via direct dermal application of fullerenes present in cosmetics;
- available studies do not indicate a short term risk from the tested fullerene types, however no extrapolation to all fullerene types and to chronic exposure can be made.

Ashberger et al. recommend that the main future work to support a full risk assessment of C_{60} should focus on generating occupational and consumer exposure data, as well as suitable data on toxicokinetics and potential toxic effects following repeated inhalation and dermal exposure allowing to determine a NOAEL. It seems also relevant to clarify whether certain fullerene types may potentially induce genotoxic and/or carcinogenic effects via physiologically relevant routes.

Concluding remarks

As noted by the JRC, these publications represent a first attempt at conducting a human health risk assessment for a representative set of nanomaterials, with results clearly indicating that further work is required to generate data of sufficient quantity and quality to support a full risk assessment suitable for regulatory needs.

Overall, the results of the studies show that the main risk for human health may arise from chronic occupational inhalation exposure, especially during activities of high particle release and uncontrolled exposure. With regard to consumers, spray applications of nanomaterials may be of concern. The main risk for the environment (especially for algae and daphnia) is expected from metal and metal oxide nanomaterials, due to exposure to both particles and ions.

Publicly available hazard and exposure data for the investigated nanomaterials are however limited and there are high uncertainties in any conclusion on a possible risk. Furthermore, since the EU legislative framework on chemicals - REACH - and the associated guidance documents do not take into consideration any specific behaviour of substances in the nanoform, further work is required in the generation of data and the development of methodologies.

For further details on all of the appraisals discussed, as well as a number of other publications stemming from the ENRHES project, please see the full text articles referenced below.

Source

In preparing this article, materials from the following sources were used: European Commission Joint Research Centre ICHP, Critical Reviews in Toxicology, Nanotoxicology, Regulatory Toxicology & Pharmacology, Toxicological Sciences, Particle and Fibre Toxicology.

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