Risk assessment of nanomaterials – further considerations

The risks of nanomaterials and how to assess them has been given a lot of attention over the past years. Efforts by scientists, regulators and industry have been devoted to understand if the current methods and tools used to assess the risks of chemicals in general can also be used for these materials. The reason behind the concerns is that some nanomaterials have shown different effects and properties compared to those with bigger particle sizes.

Nanomaterials are able to move into the body through the lungs, gastro-intestinal tract or skin into circulatory and lymphatic systems and from there to other tissues and organs. This ability to move depends mostly on their composition and size. Due to their decreased size, nanomaterials have a greater surface area which enhances their chemical reactivity. This can result in increased production of reactive oxygen species (ROS), including free radicals, which is one of the main causes of symptoms such as inflammation.

It has been confirmed that the main concepts of chemicals risk assessment also apply to nanomaterials; the risk is the result of hazardous properties of the substance combined with the exposure to it. At technical level though some testing and assessment methods need adaptations due to the specific properties on nanomaterials. Over the past decade knowledge is increasing about these materials, which has generated several important guidance documents at international level (e.g. OECD and EU).

A RISK IS ONLY RELEVANT IF THERE IS A LIKELIHOOD FOR EXPOSURE

Nanomaterials can enter our bodies either orally via food intake, when penetrating the skin or inhaled as part of the ambient air. Depending on how we interact with nanomaterials, the most likely route of exposure may differ. For workers, inhalation is recognised as the most relevant route and should be considered when conducting a risk assessment in the workplace.

For the general public, exposure patterns is less clear. Some nanomaterials are taken up by inhalation, for example, due to air pollution, but often the most likely route is predominantly oral. In this context, it is important to realise that some nanomaterials have been shown to be beneficial or even essential for human health such as certain metals and nutrients.
The risk of nanomaterials is based on two aspects: the identified toxicity (hazard characterisation) of a chemical substance or nanomaterial, and the likelihood of exposure based on the measured or expected concentrations in humans and the environment.

The risk assessment of nanomaterials should be based on robust data or estimations of exposure such as measured or expected concentrations (Fig. 1), and toxicological behaviour in humans, animals and the environment.

To assess possible exposure levels to workers, epidemiological studies may provide useful information. In fact, exposure limits in the workplace have already been established for a number of chemicals that need to be followed by regular workplace measurements. For nanomaterials, there is still a lack of measured exposure data and often risk assessment relies upon estimations resulting from modelling.

Fig. 1
THE LIFE CYCLE OF NANOMATERIALS IN A RISK ASSESSMENT PERSPECTIVE

Like all chemicals, nanomaterials are being produced, used and disposed of and this is called the life cycle. When assessing the risk of a certain chemical, taking all these steps into account is necessary but may also be complex.

Many nanomaterials are used in numerous products on the market, i.e. they have a widespread use, which makes the life cycle consideration even more challenging. Some nanomaterials are, for example, incorporated into a matrix of plastic which in turn may impact on the likelihood of exposure and therefore also the potential risk.

Other nanomaterials end up in the environment where, depending on their structure and properties, they will transform, dissolve, combine with others or on other constituents, and can sediment or be transported further away. These processes affect both the behaviour of the particle and how it interacts with organisms.

A risk assessment of a nanomaterial throughout its life cycle (Fig 2) should also be able to distinguish between risks to different populations such as workers and consumers. The risk assessment of nanomaterials for the general public needs to also cover an estimation of their indirect exposure through the environment e.g. from ground water or crop production following an uptake of substances through soil.

Fig 2.

INHALATION

In most workplaces, the most relevant route of exposure to nanomaterials is breathing them in. When inhaled, nanomaterials are sometimes able to reach deep into the lung, where uptake into blood is more likely.

Fig 3 shows that after landing on lung lining fluids (1) the particles must cross the pulmonary epithelium (2) to reach the underlying tissue or the systemic circulation, respectively, and must also overcome some effective clearance processes (3): mucociliary clearance in the airways and the clearance by macrophage in the deep lung.

If the particles are taken up, the particles can be transported to other organs in the body. This is called ‘translocation’. It is important to note that both the likelihood for uptake and translocation, are not only influenced by the size, but also by the particle’s chemical and physical properties or by the any surface treatments made.
Some nanomaterials also cause an effect at their point of entry. When inhaled, they may cause a local effect such as an irritation. The irritation is a sign that the defence system of the lungs is working, which results in the body’s natural clearing mechanism being activated causing the lining of the lung to produce phlegm that helps to move particles up and out of the lungs. However, inhalation studies in rats have shown that nanoparticles may induce more irreversible inflammation and result in more tumours than an equal mass of larger particles.

Science has pointed out a link between inhalation of nanoparticles through air pollution and respiratory illnesses such as asthma, chronic bronchitis, emphysema, or even lung cancer) and/or cardiovascular problems (angina pectoris, ischaemic heart disease etc.).

**Fig. 3**

![Diagram of lung structure and nanoparticles](image)


De Souza Carvalho et al. 2014

Even inhaling fine dust (fine inert particles of micrometric size—see Fig 4 on how different size particles can reach the lungs) may cause lung diseases e.g. pneumoconiosis (derived from Greek and simply meaning ‘dusty lungs’). This is an especially important issue to consider when assessing risks for workers such as miners and bakers.

Recently several reports have been published regarding potential risks to exposure to diesel nanoparticles. Although not fully understood scientifically, there is enough evidence to indicate that inhaling diesel exhaust fumes may cause acute and chronic health effects.
DERMAL

Absorption of particles in the nano-range through the skin is possible although it occurs to a very low degree. When it does occur, the level of penetration of nanomaterials may be greater than for larger particles. While size is important with regard to the penetration/absorption of particles, other parameters such as the composition, solubility and surface chemistry play a role in dermal toxicity.

ENVIRONMENTAL EFFECTS

Nanomaterials have the capacity to affect organisms in the environment and its physical compartments (ground, surface and ground water, atmosphere, sediment). Most of the studies underpinning this have been performed in the aquatic environment, mainly in fresh water. Currently, there is still fairly limited data available to characterise and identify nanomaterials in particular, in soil or sediments. At present, it is difficult to establish if the current use of nanomaterials poses a risk to the environment.

CHALLENGES IN ASSESSING THE TRUE ENVIRONMENTAL IMPACT OF NANOMATERIALS

The assessment of the environmental impact of nanomaterials is challenging due to the many ways nanoscale particles can interact with the surrounding compartments. Because of this, both the direct effects and the indirect effects have to be considered.

Indirect effects are mostly related to the transformation and interactions of nanoparticles with the environment and further on with organisms in their transformed state. Indirect effects of nanoparticles are
difficult to be distinguished from direct effects. Indirect toxicity to organisms implies modifications of the particles not existing in its original form.

Nanomaterials can be dissolved in the water, attached to other substances or degraded into another type of particle creating difficulties in quantifying or measuring the relevant concentrations of nanoparticles to which organisms are exposed in the environment. These transformed nanomaterials may have more or less severe effects than the original nanomaterials.

As such, indirect effects are not quantified easily in ecotoxicological experiments. Overall, careful assessment of the particular fate is needed before the overall impact of direct and indirect effects can be quantified. Currently, microcosms and natural ecosystem experiments (see below) allow the combined direct and indirect effects of nanoparticles to be studied. However, these are highly complex studies (e.g., in terms of exposure measurements and effects assessment) which can take long time and create additional challenges at the level of data interpretation.

**IS LABORATORY EXPERIMENTATION REALISTIC?**

The properties of nanoparticles can vary according to experimental conditions and the effects observed on organisms under laboratory conditions can vary from those observed under real environmental conditions. Nevertheless, laboratory tests and the organisms chosen provide a good picture of the potential effects of the nanoparticles tested even if conditions are simplified. This holds not only for nanomaterials, but also for other chemicals substances.

For a large majority, the ecotoxicity studies have been performed with model species (algae, bacteria, small crustaceans, worms and fish) exposed to a nanomaterial in a single medium (water, ground or sediments) for rather short periods (from 2 days up to 8 weeks). It is, thus, possible to assess the toxicity and the toxic mechanisms of the effects of nanomaterials concerning individual species.

In some cases, more complex experiments were carried out simulating effects on whole microcosms. These studies are done over a long period (up to 1 year) and performed on a variety of species, including plants, algae, fish and others zooplankton, which allow comparable conditions to small ecosystems (river or pond, cultivated or natural fields) to be created.

While increasing the realism of the test and of the observations made, the complexity of the analysis and interpretations of the results creates additional challenges. Overall, these tests can be used to evaluate the impact of nanomaterials under more realistic environmental conditions, but are very expensive, difficult to repeat and still leave challenges to extrapolate results to apply to real life freshwater, ground water and sediment conditions.

**FATE: HOW NANOPARTICLES INTERACT WITH THE ENVIRONMENT?**

Nanoparticles may change significantly once released into the environment by being transformed or even disappearing fully during their life cycle. This evolution is related to the properties and structure of particular nanomaterials. For instance, in various compartments (e.g., sludge from wastewater treatment plants, soil or surface water) nanoparticles can interact with other pollutants and constituents of the environment (e.g., oxides, silicates, phosphates, organic matter) and as a result become transformed or no longer exists as particulate material.

Furthermore, nanoparticles may dissolve, combine with other constituents, and can be deposited in the sediment or be dispersed.
An overview of the main interactions and transformations pathways for nanomaterials are summarised below.

Because of their size, nanoparticles may have different physico-chemical properties compared to non-nanomaterials, which may alter their environmental behaviour.

For the moment, it is challenging to assess fate and behaviour of nanomaterials in the environment and in particular on how these aspects potentially effects the toxicity. The methods to measure and evaluate the fate of the nanoparticles in the environment is still under development in several research projects at EU level.
RELEVANT LINKS:


Figure 3 copyright information


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