BUILDING EXPOSURE SCENARIOS FOR SAFETY MANAGEMENT OF ENGINEERED NANOMATERIALS

Lucie SIKOROVÁ¹, Martie VAN TONGEREN², Pavel DANIHELKA¹, Araceli SÁNCHEZ JIMÉNEZ², Šárka BERNATÍKOVÁ¹

¹ Faculty of Safety Engineering, VŠB-Technical University of Ostrava, Lumírova 13/630, 700 30 Ostrava – Výškovice, Czech Republic, lucie.sikorova@vsb.cz
² Centre for Human Exposure Science (CHES), IOM Edinburgh, Research Avenue North, Riccarton, Edinburgh, Midlothian, EH14 4AP, United Kingdom, Martie.VanTongeren@iom-world.org

Abstract

Engineered nanomaterials (ENMs) have unique physical and chemical properties, which enable effective solutions in many aspects of our lives. They could help diagnose and cure diseases, reduce the environmental impacts or improve the function of consumer goods. However, the same properties which make them remarkable may make them potentially dangerous to humans and the environment. Despite the extensive research in the field of nanotoxicology, there is still not sufficient scientific evidence to make clear conclusions with respect to risk associated with the use of many ENMs. As a result, it is recommended to monitor occupational, consumer and environmental exposure and to control exposure as much as reasonably achievable. Exposure scenarios include a set of information on materials, operation conditions and applied risk management measures, and present a valuable tool for exposure assessment and subsequently for the risk management of ENMs. Building exposure scenarios belongs to one of the main research priorities in nanosafety worldwide, due to the need of harmonized, transferrable and effective data for decision making process. This contribution provides an overview of the state-of-the-art, obstacles and challenges in ENMs exposure scenarios development in the EU and implications for the Czech Republic.

Key words

Engineered nanomaterials, exposure scenario, exposure assessment, safety management

1. INTRODUCTION

Engineered nanomaterials (ENMs) and their applications could be beneficial in many areas of our lives – they may help diagnose and cure diseases (e.g. nanosensors for medical monitoring, targeted drug transport), reduce the environmental impacts (e.g. nanosorbents for water purification, soil remediation), enhance security (e.g. nanosensors for CBRNE detection, anti-counterfeiting applications), or just improve the functions of everyday consumer products (e.g. intelligent food packages, extremely thin ultra-high resolution displays) and make our lives more comfortable (e.g. self-cleaning surfaces, anti-odour textiles) [1]. Nanotechnology, which enables these solutions, has been identified as the key enabling technology (KET) for the EU providing the basis for further innovation and new products. However, nanotechnology can also bring new and emerging risks for human health and the environment. ENMs, which are intentionally manufactured for their unique physical and chemical properties different from bulk materials, show diverse behaviour regarding their safety as well. Health and environmental hazards have been demonstrated for a variety of ENMs [2]. Considering the huge possibilities that come with nanotechnologies and ENMs and the potential health and environmental risks, there is an urgent need to ensure their safety throughout the whole life-cycle. This is understood to be a prerequisite for the sustainable use of nanotechnologies and for the success of nanotechnologies in terms of market uptake and societal acceptance [3].

The framework for risk control from exposure to chemicals (i.e. chemical safety management) defined by the REACH regulation [4] is considered to be appropriate for ENMs as well. There are no provisions in REACH
referring specifically to nanomaterials. However, REACH deals with substances, in whatever size, shape or physical state. Substances at the nanoscale are therefore covered by REACH and its provisions apply [3]. Chemical safety management requires first of all a scientific, ideally quantitative, assessment of potential health effects at given exposure levels (risk assessment). Based upon the results of risk assessment, and taking into consideration other factors (i.e. social and economic impacts), a decision-making process aimed at eliminating or reducing to a minimum the risk to the chemicals (risk management), can be started. Risk assessment, consisting of hazard identification, dose-response assessment, exposure assessment and risk characterization, is a conceptual framework that provides the mechanism for a structured review of information relevant to estimating health or environmental outcomes. [5]

Many products containing ENMs are already on the market [6](see the Woodrow Wilson database [6]) or are very close to commercialization. The total annual quantity of nanomaterials on the global market is estimated at around 11.5 million tonnes [1]. People, especially at manufacturing sites, are exposed to ENMs. It is predicted that 6 million nanotechnology workers will be required worldwide by 2020 [7].

Currently, safety management of existing and newly developed ENMs is hindered by the lack of relevant scientific data. Despite the extensive research in the field of nanotoxicology, there are still many questions and uncertainties regarding potential risks and, due to the increasingly wide variety of nanomaterials that are being developed, completing proper risk assessment for every single ENM may not be possible or economically acceptable. In order to manage the risk from exposure to ENMs, it is essential that we understand and monitor occupational, consumer and environmental exposure to ENMs.

Development of exposure scenarios (ES) can be useful for sharing information on exposure in relation to contextual information. An ES, as defined by the REACH regulation, is a set of information on materials, operation conditions and risk management measures under which the risks associated with the identified use of a substance can be controlled. The ES is the basis for a quantitative exposure estimation and the communication tool in the supply chain [8]. Nowadays, building exposure scenarios for ENMs belong to one of the main research priorities within nanosafety worldwide, due to the need of harmonized, transferrable and effective data for decision making process [9]. The position of ES within the whole framework of safety management of chemicals, including ENMs, is shown in Figure 1.

![Fig. 1 Position of exposure scenarios within the chemical safety management framework (based on [10])]()
2. BUILDING EXPOSURE SCENARIOS FOR ENGINEERED NANOMATERIALS

Currently, ES for ENMs cannot be understood the same way as for conventional chemicals. Whereas for chemicals ES describe conditions under which the risks are controlled, for many ENMs it is not yet possible to ensure their safe use due to the lack of exposure limits for most of them. Nevertheless, they can be used to benchmark different process operations and control measures and to provide guidance to reduce exposure [11].

Exposure scenarios for ENMs have been or are currently being developed in several FP7 research projects (e.g. NANE, MARINA, GUIDEnano, SUN). Exposure scenarios are compiled in ES libraries which can be searched by ENM, life cycle stage, process or specific task. In such a library the user can search for a scenario similar to that under investigation and read-across the exposure information. The concept of read-across presents a very valuable tool for estimation of exposure to ENMs, since the measurements of ENMs are very expensive, complicated and requires well experienced operators.

The NANE and MARINA ES libraries focused on the inhalation route. Dermal ES and dermal transfer efficiencies are being investigated as part of the FP7 project SUN (Sustainable nanotechnologies project; http://www.sun-fp7.eu/) and will be part of an ES library for dermal exposure.

The first ES library for ENMs was developed within the NANE FP7 project (Development of Exposure Scenarios for Manufactured Nanomaterials; http://nanex-project.eu/). NANE was focused mainly on carbon nanotubes (CNTs), nano-sized titanium dioxide (nano-TiO₂) and nano-sized silver (nano-Ag). In total, 62 exposure scenarios (57 occupational and 5 consumer ES) were developed using publicly available data and data collected in several large-scale sampling campaigns (NANO SH project – FP6, NanoINNOV project – CEA). Only nine occupational ES were complete enough to be included in NANE Exposure scenario data library (http://nanex-project.eu/mainpages/exposure-scenarios-db.html). [12]

ES identified by NANE have been further elaborated within MARINA FP7-project (Managing risks of nanomaterials; http://www.marina-fp7.eu/project/). The MARINA ES library includes occupational ES for a range of ENMs (Carbon Nanotubes, CeO₂, CrO₃, TiO₂, ZrO₂, nano-Ag, nano-Cu, nano-Fe, Quantum Dots) and consumer and professional use of various nano enabled products (textiles, deodorant, paints, mortar, dental restoration material). The library will be available online (the project will be finished in 2015) and can be used as a first tier tool within a tiered exposure assessment methodology.

The FP7 project GUIDEnano (http://www.guidenano.eu/) will take the concept of ES library a step further. It will include an algorithm to quantify the similarity between the ES in a library and the scenario under investigation and will gather data collected within different FP7 projects.

The usefulness of the ES libraries depends on the quality of the contextual exposure information and measured data. It is a key issue that measured data are reported in a harmonized way and contextual information is properly recorded using ES templates. The information required by the current version of ES template developed within MARINA, is shown in Table 1. The completion of this information is crucial for efficient occupational ES, which can be further used for safety management of ENMs.

Examples of ES, based on information collected during the NANO DEVICE FP7-project, are presented in Read et al. (2014) [11].
### Table 1 Core information for occupational exposure scenario for engineered nanomaterials developed within MARINA FP7-project

<table>
<thead>
<tr>
<th>Description of the exposure scenario</th>
<th>Name of the exposure scenario (e.g. CNT production using Chemical Vapour Deposition)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description of tasks (e.g. sampling from reactor)</td>
<td>Life cycle stage (i.e. synthesis, manufacture of intermediate / end-product, waste treatment and recycling)</td>
</tr>
<tr>
<td>Operating procedure (i.e. raw material / final product handling, primary manufacture, cleaning, etc.)</td>
<td></td>
</tr>
</tbody>
</table>

**Description of premises**

<table>
<thead>
<tr>
<th>Production scale (mass/year)</th>
<th>Number of employees working with ENM / ENM-products</th>
</tr>
</thead>
</table>

**Substance characteristics**

<table>
<thead>
<tr>
<th>Type of substance (i.e. bulk ENM, ENM in suspension, composite solid material, etc.)</th>
<th>Name of the ENM used (e.g. silver nanoparticles, single-walled carbon nanotubes, titanium dioxide)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAS registration number</td>
<td>Physical state of the ENM / ENM-product at 20 °C and 101.3 kPa (e.g. powder, liquid, paste, film)</td>
</tr>
<tr>
<td>Primary particle size of the bulk ENM (nm)</td>
<td>Mean particle size of the ENM (nm)</td>
</tr>
<tr>
<td>Shape of the ENM (i.e. spherical, fibre, plate, etc.)</td>
<td>Surface area of the ENM (m² g⁻¹)</td>
</tr>
<tr>
<td>Density of the ENM (kg m⁻³)</td>
<td>Type of density (i.e. bulk, elemental, agglomerate)</td>
</tr>
<tr>
<td>Substance emission potential of the ENM / ENM-product (e.g. very high for fine and light powders, very low for firm granules)</td>
<td>Concentration of ENM in the mixture / product (%)</td>
</tr>
</tbody>
</table>

**Activity emission potential**

<table>
<thead>
<tr>
<th>Description of activity in terms of the energy applied to the process (e.g. very high for drilling, very low for manual handling)</th>
<th>Amount of ENM / ENM-product used during the ES (g, kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature at which process is carried out (°C)</td>
<td></td>
</tr>
</tbody>
</table>

**Technical conditions and measures at process level (source) to prevent release**

<table>
<thead>
<tr>
<th>Level of containment (semi-enclosed – e.g. fume cupboard, fully enclosed – e.g. glove box or reactor)</th>
<th>Effectiveness of containment (e.g. by quantification of residual losses or exposure)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of cabin for worker</td>
<td>Automation level (i.e. manual, semi-automatic, automatic)</td>
</tr>
</tbody>
</table>

**Technical conditions and measures to control dispersion from source towards the worker**

<table>
<thead>
<tr>
<th>Type of local ventilation at source (e.g. enclosing hood, capturing hood)</th>
<th>Efficiency of the local ventilation</th>
</tr>
</thead>
</table>

**Room conditions**

<table>
<thead>
<tr>
<th>Room volume (m³)</th>
<th>Room temperature (°C), pressure (Pa) and relative humidity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of general ventilation (i.e. natural, mechanical ventilation – incoming / outgoing air / both)</td>
<td>Air exchanges per hour (h⁻¹)</td>
</tr>
</tbody>
</table>

**Organisational measures to prevent / limit releases, dispersion and exposure**

<table>
<thead>
<tr>
<th>Frequency of the cleaning of the working area</th>
<th>Frequency of the maintenance of the engineering controls and ventilation system</th>
</tr>
</thead>
</table>

**Conditions and measures related to personal protection, hygiene and health evaluation**

<table>
<thead>
<tr>
<th>Type of personal protective equipment (PPE)</th>
<th>Level of effectiveness of the PPE</th>
</tr>
</thead>
</table>

**Exposure**

<table>
<thead>
<tr>
<th>Duration of the activity / process</th>
<th>Time the worker spends in direct contact with the ENM / ENM-product</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure pattern (i.e. continuous, intermittent, occasional)</td>
<td>Frequency of the activity (e.g. number of times the task / activity is done a week / month / year)</td>
</tr>
<tr>
<td>Distance from the source to the breathing zone of the worker (m)</td>
<td></td>
</tr>
</tbody>
</table>

**Measurements**

<table>
<thead>
<tr>
<th>Measurement type (e.g. personal during activity – inlet &lt; 30 cm from worker, area during activity – inlet 30 cm to 2 m from source)</th>
<th>Data description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of data + units (e.g. number concentration, particle size distribution, chemical characterization)</td>
<td>Instrument, model (e.g. Fast Mobility Particle Sizer Spectrometer 3091, TSI)</td>
</tr>
<tr>
<td>Size range</td>
<td>Date of survey</td>
</tr>
<tr>
<td>Measurement period</td>
<td>Descriptive statistics + value</td>
</tr>
</tbody>
</table>
Building ES for ENMs presents a big challenge. Publicly available data in literature regarding occupational exposure do not usually provide all key information, data on consumer exposure are scarce and environmental exposure could not been addressed yet due to analytical limitations [13]. Results from high quality surveys on real world industrial-scale occupational exposure situations are lacking. Many available release or exposure data are from experiments conducted under controlled laboratory conditions, which does not fully represent real on site situations. Furthermore, release and exposure measurement of ENMs present a difficult task due to temporal and spatial variability in both particle size distribution and number concentration through coagulation, scavenging by background particles and surface deposition [14]. Measurements require not just sophisticated instruments, but especially compliance with best practices protocols and experienced professional users.

At the EU level, there is an urgent need of more information on the use of ENMs, potential for release and exposure in occupational, consumer and environmental contexts in order to derive a comprehensive overview of possible human and environmental exposures [9]. Collecting exposure data in a comprehensive, structured and standardised way is essential for further decision-making process aiming to protect human health and the environment.

3. CURRENT SITUATION IN THE CZECH REPUBLIC

Similarly as in most EU countries, nanotechnology presents an important branch in the Czech business sector as well as in the field of research and development. The “nanotechnological map” of the Czech Republic has become much more dense during last several years. There has been a significant increase in the number of institutions involved in nanotechnologies (see Figure 2) [15].

![Graph showing increase in the number of organisations in the field of nanotechnology in the Czech Republic](image)

ASCR – Institutes of the Academy of Sciences of the Czech Republic; Uni – Universities; Contrib. org. – Contributory organisations; LM – Large enterprises (more than 250 employees); SME – Small and medium enterprises (up to 250 employees)

**Fig. 2** Increase in the number of organisations in the field of nanotechnology in the Czech Republic (numbers adopted from [15])

The Czech Society for New Materials and Technologies has been mapping the development in the nanotechnology field in the Czech Republic from its inception at the end of the 1980s until now. Thanks to their efforts, there is at least a rough picture about technological sectors, where ENMs could be used, and about workplaces with potential of exposure to ENMs.

Based on their publications ([16], [17]) the Czech National Institute of Public Health (NIPH) conducted a questionnaire survey to gain a better insight into occupational exposure to engineered nanomaterials in the Czech Republic during years 2008-2010. They asked enterprises and non-profit research organisations to provide basic information regarding the following topics: i) Introduction of the organisation (branch of economic activity, amount of employees etc.); ii) Characterization of produced/handled ENMs (chemical
composition, size of particles etc.); iii) Information about production (amount of ENMs produced, applications etc.); iv) Potential exposure to ENMs (enclosure of the system, form of ENM, exposure route, number of workers working with ENMs, safety measures in place); v) Observed health effects; vi) Perception of potential risks by management and employees; and vii) Provision of occupational health services.

In total, 53 enterprises and 37 non-profit research organisations answered at least some of the questions from the questionnaire. That presents 32 manufacture or processing workplaces and 99 R&D sites. Almost all known nanomaterials were reported – metals (Ag, Au, Fe, etc.) and metal oxides (TiO$_2$, Al$_2$O$_3$, SiO$_2$, ZnO, etc.), carbon nanomaterials (carbon nanotubes, fullerenes, nanodiamonds, carbon black) and others. Nanomaterials were presented in various different forms, such as free nanoparticles (NPs), densified NPs (e.g. in a form of granules), materials containing NPs embedded in a media (e.g. in polymer), as well as materials with nanocrystalline structure (e.g. hardened surfaces). ENMs were found to be used in many different applications – for surface modifications (structural and ceramic materials, paintings), fillers to rubber or other polymers, catalysts, filtration materials, composite materials, hard surfaces (PVD coatings) in engineering, sensors, semiconductors, optic components, biomedical applications etc. [18]

The survey provided valuable input information on potential occupational exposure situations in the Czech Republic. However, the level of detail in the data set is not enough to build ES described in the previous chapter. More comprehensive information on exposure is needed to be able to estimate potential risks at least at the quantitative level.

Some reports on measurements of nanomaterials in Czech occupational settings were found in publicly available literature (e.g. [19], [20], [21]). In contradiction to the frequently declared need of measurement of ENMs, most of them are focused on unintentionally produced nanoparticles. Only Pelclová et al. (2013) [19] deal with ENMs. This research group has been conducting a thorough investigation on urine and exhaled breath condensate markers of oxidative stress in workers exposed to aerosol containing TiO$_2$ nanoparticles. The Czech Occupational Safety Research Institute (VÚBP) conducted a measurement campaign on nanoparticles at different workplaces in the Czech Republic, such as administration, manufacture of fertilizers, metal products, wood products etc. [22]. Again, there were focused on unintentionally produced nanoparticles. Authors of this paper are not aware of any systematic measurements of ENMs at Czech workplaces, where ENMs or products containing ENMs are produced, processed or used.

Occupational exposure to ENMs is of high relevance in the Czech Republic, as shown by the NIPH survey. Occupational health and safety (OHS) of workers potentially exposed to ENMs has been set as one of the main research priorities at national level with particular focus on the following issues [23]: i) Monitoring of workplaces and particular tasks with ENMs; ii) Research on potential health impacts; iii) Development of methods for exposure measurements and assessment; and iv) Development of prevention tools (focus on personal protective equipment). However, systematic, long-term applied research in this field is still missing.

This is why the Czech Republic has joined the MODENA COST Initiative (Modelling Nanomaterial Toxicity; http://www.modena-cost.eu/Home.aspx) to share experiences and good practices with recognized European research teams. In the framework of this COST action, the national COST project NANOEXPO (Exposure to nanomaterials, assessment and management of risks associated with QSAR / QNTR; http://www.isvav.cz/projectDetail.do?rowId=LD14041) aims to address some of the above mentioned gaps. It is a multidisciplinary orientated project focused on management of health risks arising from exposure to ENMs. The project objectives are to develop:

- Database of occupational exposure scenarios in the Czech Republic, compatible with EU exposure scenarios libraries to be able to read-across from the libraries; and
- Guideline for an estimation of nanomaterial risks with the potential to use the QNTR modelling.

Real world exposure situations relevant for the Czech Republic will be investigated through structured face to face interviews, site visits and where possible supplemented with exposure measurements. The survey is supposed to start in winter 2015.
Involvement of the Czech Republic in the already running FP7 project NANoREG (A common European approach to the regulatory testing of Manufactured Nanomaterials; [http://www.nanoreg.eu/](http://www.nanoreg.eu/)) is a very important step forward. It will provide an access to standardized protocols for exposure assessment and the current state of knowledge in this field. VSB-Technical University is applying for a position of National coordinator of this project. The participation of the Czech Republic in the NANoREG is planned to start from January 2015.

It should be noted that consumer and environmental exposure has not been investigated in the Czech Republic at all. It is a big gap which should be solved as well.

4. CONCLUSION

The developments within nanotechnology open up an immense spectrum of opportunities and improvements in consumer and other products. However, in parallel with new functionalities new potential risks may appear with respect to health and safety. Due to gaps in current knowledge regarding hazard and risk assessment of ENMs resulting in high levels of uncertainty, there should be an increased emphasis on exposure assessment and control. Current precautionary measures aim to avoid or at least reduce the exposure to ENMs as much as possible.

Sharing of exposure data and development of comprehensive, well designed and realistic ES is essential for increasing our knowledge in exposure to nanomaterials in the workplace and among consumers. ES, providing conceptual information on particular ENM, operating conditions, applied risk management measures and release and/or exposure measurements, present a valuable tool for exposure estimation. Compiling ES into ES libraries enable to read-across particular exposure situation of interest and to benchmark different process operations and safety measures. The concept of read-across is of high importance, since the measurements of all exposure situations will not be achievable. In a wider context, ES could form a basis for exposure registries and further epidemiological research. Development of ES is an important step within the whole process of safety management of ENMs.

Despite the progress in ES building achieved at the EU level, there are still many obstacles and challenges in this field. Some of them arise from scientific reasons, e.g. the lack of knowledge on a relevant exposure metric, difficulties in conducting measurements associated with temporal and spatial variability in both particle size distribution and number concentration, non-existence of standardized protocols for exposure measurements or even the uncertainty in definition of nanomaterials. Others are linked rather to societal situation, especially to willingness of enterprises to share sensitive data regarding their production and processes involving ENMs, which are necessary for building real-world ES.

Nevertheless, ES libraries will enable necessary progress in nanosafety and the Czech Republic intends to be a valuable partner in this international activity. The Czech Republic has already joined the EU research in this field. However, more proactive approach should be adopted. There is an urgent need to open a dialog between stakeholders involved in occupational, consumer and environmental health and safety at the national level in order to share the knowledge and best practices so that the exposure data developed in the Czech Republic can be further used at the EU level.

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