DEVELOPMENT OF A NANO-RISK ASSESSMENT TOOL BASED ON A HOLISTIC APPROACH

P. Karayannis[1,2], E.P. Koumoulos[1, 2], C. A. Charitidis[1, *]

[1]Research Unit of Advanced, Composite, Nano Materials & Nanotechnology, School of Chemical Engineering, Department of Materials Science and Engineering, National Technical University of Athens NTUA, 9 Heroon Polytechniou St., Zographos, Athens, Greece GR-157 73
[2]Innovation in Research & Engineering Solutions (IRES), Boulevard Edmond Machtens 79/22 - 1080 Brussels, Belgium
(*charitidis@chemeng.ntua.gr)

ABSTRACT

The identification of various assorted occupational and consumer hazards in nanotechnology necessitates the development of efficient risk management systems, in order to adequately safeguard vulnerable parties, while not hindering research progress. Driven by the need for advanced risk assessment methods, we initiated development of a digital tool intended to support such operations. Our tool is being designed as an assistive platform for small- and medium-scale facilities/laboratories producing and using nanomaterials. Studying the progress made in analogous systems in recent years [1] [2], it was determined that our approach should be steered towards more specialized risk assessment techniques. Specifically, the risk assessment process is organized in three connected but discretely studied parts (Hazard, Probability and Exposure Assessments). This platform combines existing scientific advances in nano-risk assessment with established methods in the field of workplace safety and health and scientifically approved computer programs, presenting improved levels of adjustability and flexibility. We maintain that judicious use of a system of this character can be a helpful tool in risk prioritization and decision- making processes.

INTRODUCTION

While the field of nanotechnology exhibits widespread growth in R&D, manufacturing and commercial aspects, the potential uncertainties and information gaps involved in this unique discipline present significant barriers to nanomaterial risk assessment. As Nanotechnology is a relatively recently developed scientific area, there is insufficient epidemiological data on the possible adverse effects of nanomaterial exposure on humans, and no official thresholds for determining safe levels of exposure have been released yet. Published in vitro and in vivo studies generally demonstrate evidence of toxicity, however there exists uncertainty on the interpretation of results. This is due to the facts that high doses are used, the routes of exposure in some experiments are uncommon for human exposure, and the data obtained for a single nanoparticle cannot be confidently extrapolated to a class of nanoparticles, given the high variance of nanoparticles in terms of physico-chemical characteristics.

Control banding is a practical tool that can be employed to address many of the uncertainties presented in the risk assessment of nanomaterials, combining risk assessment and management. The term control refers to the proposed control approaches of the occupational risk. Such control measures could be, among others, adequate ventilation and a change in working practices. The term band in control banding is considered as a category of relevance to risk. Based on data input, a substance or a process can be categorized into a certain risk related band.

Several research groups have developed nanomaterial Control Banding Tools that share a similar approach based on risk prioritization. However, to our best of knowledge and evidenced in relevant literature reviews evaluating currently used nano-risk assessment tools, an approach that covers all applicable domains is missing at the moment, challenging the potential for result consistency on a broad scale [1] [2] [3] [4] [5]. The development of a thorough, more refined and adjustable tool will provide stakeholders with an efficient system of assessing risk and constitutes a decisive step towards the setup of an appropriate risk management plan for nanomaterial processes.

Our tool will be referred to in this presentation as the “Nano-Risk Assessment Framework” (“n-RAF”). N-RAF’s function is based on the application of a risk banding/prioritization scheme on nanomaterial processes, with the basis being provided by distinct hazard, probability and exposure assessments. The program’s design directions were decided upon in line with current state of the art, based on contemporary literature. In this presentation, the outline of the architecture of our system will be explained, and a case study of the risk assessment of MWCNT processes will be briefly presented.

AIMS AND METHODOLOGY

Risk is defined as “A situation involving exposure to danger”, but the concept is delineated in many ways according to the application, being given different definitions, depending on the context. Risk is defined as the “effect of uncertainty on objectives”, according to ISO 31000:2018, Risk management – Guidelines [6]. A more analytical definition of Risk can be formulated by distinctly analysing the concept’s constituents.

Risk = Hazard x Probability x Exposure x Vulnerability

One of the focal points of our work is the examination of each constituent of nanomaterial Risk distinctly, in order to produce a more accurate and flexible assessment. Other key aspects that determined the design directions of the present methodology are the following:

- The incorporation and adaptation of conventional risk assessment techniques established in process industry to our work approach.
- Parallel assessment of all materials, processes and exposure schemes expected to be encountered in a workplace, to enable uncomplicated comparative analysis and prioritization.
- The necessity to have output on exposure characteristics (dose, duration, exposure of each involved individual) for multiple exposure scenarios in every process.

In the following paragraphs, the function of the three constituents (Hazard, Probability and Exposure assessment) of our risk assessment methodology will be demonstrated.

HAZARD ASSESSMENT

The main concept of hazard assessment is based on the accumulation of all available information, leading to the detection of specific hazardous properties. The information gathered includes fundamental physicochemical properties, published (Eco)toxicological studies and occupational exposure limits. For nanomaterials, the Occupational Exposure Limits of parent substances, although not adequate to assess hazard, could provide the groundwork for a more analytical approach. As mentioned, the n-RAF employs a hazard banding approach, in order to cover hazard assessment. The tool analyzes and evaluates the input information and assigns the studied nanomaterial to a hazard band.

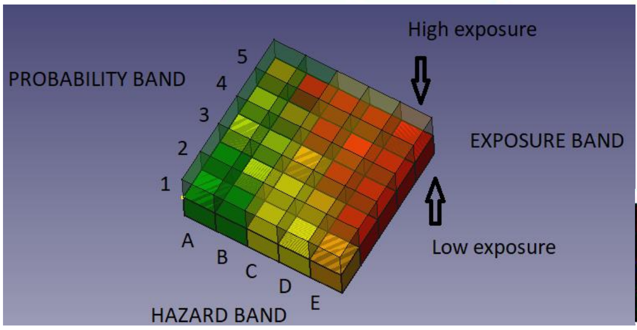
The biological and toxicokinetic properties of nanomaterials are reportedly dependent upon their characteristic physicochemical properties, for example particle size and shape, contaminants, solubility, hydrophobicity, surface charge and surface functionalization. The program requires input on these hazard parameters, in order to formulate a hazard profile for the studied nanomaterial, and assign it to an appropriate hazard band (A - Very Low, B - Low, C - Medium, D - High, E - Extreme). The hazard banding is realized through the combined use of a scoring system and a linear decision tree. The hazard parameters are assigned points according to their evaluated contribution in inducing toxic properties, while of 75% of the maximum score is applied in case of ‘unknown’ information. In addition to that, certain severity factors are considered more crucial than others, resulting in the immediate assignment of a certain hazard band, potentially overriding the score results. It is noted that the tool covers nanomaterials in powder form only, in its present development status.

PROBABILITY AND EXPOSURE

Exposure and Probability assessment results are merged into a single priority band in most currently available nano - Risk assessment Control banding tools (examples include Stoffenmanager Nano [7], ANSES CB Tool [8], Nanotool [9]), forming a two dimensional risk priority matrix. However, the nature of nanomaterial processes is such, that exposure can occur in several different ways during a process, each presenting different probability of occurrence and leading to various patterns of potential exposure intensity and duration. Based on this fact and the commitment to analyse each aspect of risk separately, the n-RAF presents a new and more targeted approach, uncoupling the two concepts. This more explicit examination is realized through the input of highly specific data from the customer, which is afterwards utilized to set up scenarios that describe exposure scenarios during occupational processes and accident situations most likely to occur. This approach provides enhanced preciseness and an estimation of the dose received by each exposed party in every case study. Based on such scenarios, quantitative exposure assessment simulations are conducted, using state of the art computer software. The simulation results are integrated into the tool in such a manner that the parameters of the studied scenario are easily distinguished and traced.

The results provided from the Hazard, Probability and Exposure assessment can be combined and formulated into a general overview of the Risk presented for each Nanomaterial, Process and distinct scenario. The resulting risk assessment is visualized through a three-dimensional diagram where risk levels for studied scenarios can be pinpointed, identified and studied in contrast **(Figure 1)**. This approach offers new and previously unexplored degrees of flexibility on control planning and risk mitigation. Through this methodology, the risk analyst can describe multiple exposure scenarios for each process, as is realistically expected to be the case. This degree of adaptability is absent in a conventional 2D approach, as every process is either uniquely linked to one specific exposure event or the details of the exposure schemes expected are not included in the assessment.

LIKELIHOOD	CONSEQUENCE				
	Insignificant	Minor	Moderate	Major	Catastrophic
Almost Certain	S	S	H	H	H
Likely	M	S	S	H	H
Possible	L	M	S	H	H
Unlikely	L	L	M	S	H
Rare	L	L	M	S	S



H	High Risk
S	Significant Risk
M	Medium Risk
L	Low Risk

Figure 1. *Conventional two-dimensional Risk banding (top) vs. three-dimensional Risk banding (bottom left). The axes represent the hazard band scale (X axis), the Probability band scale (Y axis) and the Exposure band scale (Z axis). The colour indicates the scoring and ranking of the nanomaterials and processes (bottom right), going from green (low risk), via yellow and orange (medium, significant risk), to red (high risk).*

PROBABILITY ASSESSMENT

The probability of occurrence is an estimate of how often a hazard event occurs. In this step, the likelihood that the hazard consequences will be realized, is determined according to user input. This is accomplished by analysing key aspects of the work process that concern accident vulnerability. Some of these are duration, frequency, level of training and number of employees working simultaneously in the workplace. The tool assigns five bands for probability (Extremely Unlikely, Unlikely, Less Likely, Likely, Probable), derived from the sum of the scores allocated for each parameter. Training, specific process modifications, situational awareness, morale and attitude change can be factors that contribute to the minimization of exposure probability.

EXPOSURE ASSESSMENT

Inhalation exposure is described as the result of a series of processes that determine the transfer of an aerosol from the source, through emission, via the transmission compartment to the receptor. A thorough exposure assessment requires the definition of industry-specific and application-specific exposure scenarios considering operational conditions and risk management measures, in order to provide an estimate or a measurement of the magnitude, frequency and duration of exposure to a hazardous agent. It is of vital importance that the sources, pathways, routes, uncertainties and assumptions are considered in the assessment.

Workplace air measurements for manufactured nanoparticles present significant difficulties in terms of high cost and complexity, requiring specialized knowledge and skills [10]. Exposure models and simulations are used in our methodology as an alternative, cost-effective way to provide a first-tier exposure assessment. The Nano-risk Assessment Framework utilizes the data extracted from simulations based on exposure scenarios that have been formulated in collaboration with workers/researchers. The information provided by the employees includes geometry of the workspace, worker positioning, the site of the source of the exposure and ventilation and humidity data. In this way, the risk assessment is based on estimations of real-life exposure occurrences concerning the working conditions of the specific site. Thus, more precise exposure assessment results can be gathered, as the analytical process has been upgraded from the use of the general exposure occurrence framework (e.g. provided by an MSDS) to the setup of personalized exposure scenarios. The simulations are conducted with the finite element analysis, solver and multiphysics simulation software COMSOL Multiphysics [11].

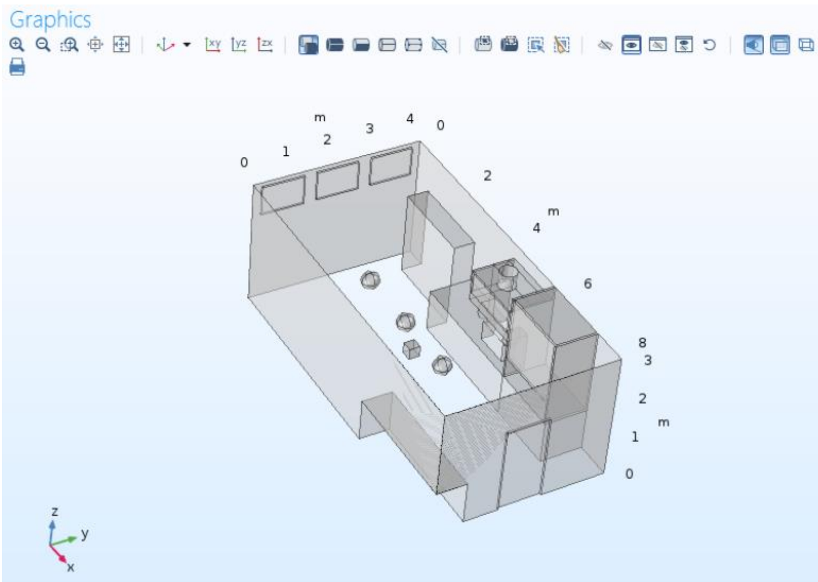


Figure 2. *Workplace geometry construction and set up of worker positions and exposure source in COMSOL Multiphysics (Case study concerning small scale MWCNT production and handling within a laboratory).*

Several exposure factors are considered and subsequently input into the tool; these include worker exposure intensity and duration, workplace exposure and time needed to remove the hazardous agent from the area. Occupational exposure limit values (of the parent substance) are also considered, representing the reference values regarding containment of the risk factor. These thresholds can be replaced, in the absence of adequate data, by derived exposure limits. These factors are analysed, and an exposure scoring system assigns an exposure score to each scenario. The score range is divided to five equal parts, resulting in five exposure bands (Very Low, Low, Medium, High, Very High).

RISK ASSESSMENT – RISK PRIORITY OVERVIEW

The final risk score is calculated by the multiplication of the Hazard, Probability and Exposure scores. The results from the scoring and banding schemes are combined into a 3D risk matrix, which is based on the calculation of the all-embracing risk score **(Figure 3)**. In this way, nanomaterials, processes and specific work configurations, represented by exposure scenarios, can be classified by order of increasing priority. This analysis can play a pivotal role in the design of risk-reducing scenarios, as it can provide preliminary information about the contribution of specific control measures, process changes and containment strategies on a risk mitigation plan.

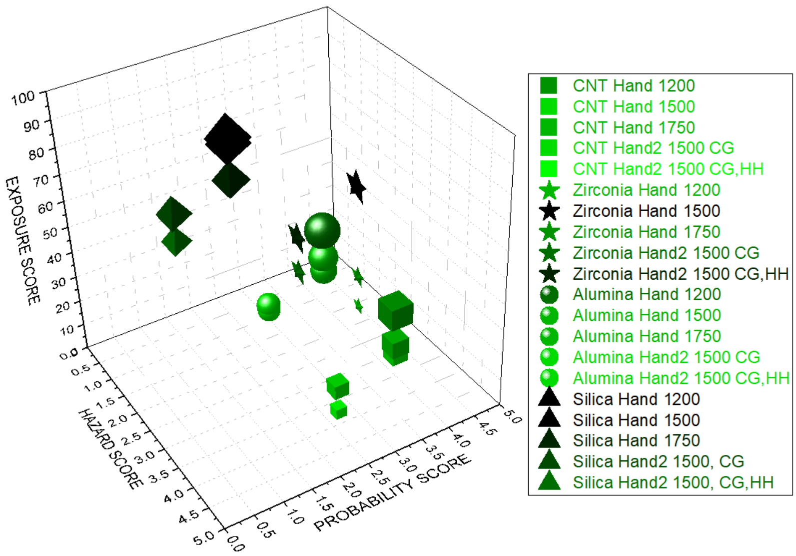


Figure 3. *Risk overview – Priority banding in several nanomaterials, processes and exposure scenarios.*

TOOL DEVELOPMENT

The tool is being developed in Microsoft Access®. This software has been selected because it renders the tool easily modifiable, it can be used with relative ease from non-experienced personnel and also offers potential for future expansion and integration with toxicological databases and QSAR models that can serve as a supplementing factor to the risk analysis.

CONCLUSIONS

The present work is an introduction to the logical basis for the design of a digital platform providing an integrated approach to nanomaterial risk assessment. Expanding upon the progress made in currently available nano-risk assessment tools, our methodology introduces novel approaches in the following areas:

- Set up of personalized scenarios concerning exposure incidents.
- Three-dimensional risk assessment, presenting the evaluation of exposure characteristics as a distinct assessment parameter and offering greater degrees of preciseness compared to 2D approaches.

- Easily expandable database and evaluation mechanisms through flexible design.
- Parallel assessment of the materials, processes and exposure events expected in a nanomaterial workplace, to render the risk visualization and prioritization procedures more straightforward.

Motivated by the continuously rising demand for precise risk assessment in the midst of heavy uncertainties, we suggest the above discussed application of appropriately accurate and distinct hazard, probability and exposure assessments for multiple materials and processes. The obtained data can provide a foundation for the formulation of an all embracing risk mitigation strategy.

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