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# Evaluation of Existing Control Measures in Reducing Health and Safety Risks of Engineered Nanomaterials

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**Abstract:**

While the risk management of engineered nanomaterials (ENMs) receives significant attention, there is still a limited understanding of how to select optimal risk management measures (RMMs) for controlling and mitigating the risks associated with exposure to ENMs. Clearly, there exists a need to expand current risk management practices to ensure safe production, handling and use of ENMs. Moreover, the performance of the existing RMMs should be re-evaluated for ENMs since control options that are proven to be effective for preventing or limiting risks associated with traditional particles might give unsatisfactory results in the case of nano-scale particles. This paper has brought together the evidence on the adequacy of traditional controls to minimize potential health and environmental risks resulting from exposure to ENMs. The aim here is to advance our understanding of the risk management approaches relevant for ENMs, and ultimately to support the selection of the most suitable RMMs when handling ENMs. To that end, evaluative evidence collected from the review of relevant literature and survey of nanotechnology institutions are combined and summarised to understand the level of protection offered by each control measure, as well as the relative costs of their implementation. The findings suggest that most relevant risk control options are based on isolating people from hazard through engineering measures (e.g. ventilation and chemical fume hoods) or personal protective equipment (PPE), rather than eliminating hazard at source (e.g. substitution). Although control measures related to the modification of ENMs have high efficiency in the occupational risk control hierarchy, they are not widely employed since there is currently a high degree of uncertainty regarding the impact of manipulating nano-characteristics on the performance of final product. Lastly, despite its low cost, PPE is the least effective category in the occupational risk control hierarchy and should not be used on its own when significant risk reduction is required. Clearly, further quantitative data is needed to fully assess the feasibility and cost-effectiveness of risk control options to prevent risks from exposure to ENMs. When there is little information on the efficiency of control measures specific to ENMs, the default efficiencies can be used for initial assessment purposes although it should not be

considered exhaustive.

## 1. Introduction

Nanotechnology is an emerging field of science and engineering that has already been applied to a variety of industrial fields. Given the ever increasing use of engineered nanomaterials (ENMs) in industry, it is essential to properly assess all possible risks that may occur as a result of exposure to ENMs[1]. Recent studies have shown that the distinctive characteristics of ENMs that have made them superior to bulk materials for some uses presumably, might also have a substantial impact on the level of risk they pose[2, 3]. However, the complex nature of ENMs presents a challenge for the existing general and product specific regulation[4]. In order to facilitate sustainable manufacturing of ENMs, it is desirable to develop transparent and comprehensible tools for risk assessment and management[5].

The risk assessment process involves identification and evaluation of occupational, consumer and environmental exposure to hazardous substances, while risk management primarily focuses on the selection and implementation of effective measures to control unacceptable risks. It is generally agreed that traditional risk management frameworks and tools do not cover all the issues associated with manufacturing, handling and using ENMs and hence need to evolve to become more sensitive to nano-specific issues[6]. Although a revised risk management methodology for nano-scale objects has not been approved yet, there are a number of technical reports and guidelines published by (inter)national organizations[7-11] and standard setting bodies[12-15] that provide guidance on risk management issues and control measures relating to ENMs. Additionally, numerous control-banding tools have been proposed[16-19], that associate predefined hazard and exposure levels with risk management measures and link hazard with physical characteristics in a qualitative or semi-quantitative way.

As in traditional risk management approach, once all potential hazards are identified, assessed and thoroughly evaluated, risk reduction strategies should be considered in a systematic approach (e.g. hazard control hierarchy). Essentially, there are two ways of mitigating or reducing the risk: *hazard control* through modification of ENM properties while maintaining their original features and functionality and *exposure control* reducing the release of ENM from industrial processes or consumer products or limiting the exposure of workers and consumers to ENM by means of administrative measures and behavioral guidelines. Although it is widely agreed that traditional methods used to control exposure to particles can be implemented to ENMs, there is a need to re-test their level of control against ENMs[20].

This paper is concerned with the current availability of information on the effectiveness and cost of risk control measures for reducing risks associated with ENMs. To that end, evaluative evidence collected through the review of the scientific literature and survey of nanotechnology companies are combined and summarised to understand the level of protection offered by each control measure, as well as the relative costs of their implementation. The main aim here is to support the appropriate selection of effective and economical risk control option when dealing with ENMs.

## 2. Methodology

Published literature from 2008 to 2015 was searched for studies on risk management of ENMs and risk control options applicable to ENMs using Web of Science database. The following keywords have been used to identify the relevant studies: nano*, risk management, risk reduction, risk prevention measures, risk control measures, risk management strategies. More than a hundred papers were found; however, only 41 papers were identified as being relevant and further analysed. The relevant papers from the literature review were divided into two categories: review or opinion papers on risk management of ENMs and research papers that quantitatively studied the efficiency of risk control measures for ENMs. Two main criteria was employed when assessing the feasibility of control measures: efficiency and cost. These two criteria are important because they signify the technical, economical and contextual feasibility of risk control options. While a considerable amount of quantitative literature data on the effectiveness of controls for specific types of ENMs have been collected, no information on the costs that can be attributed to each control option has been reported in literature.

The project search on CORDIS with the same keywords revealed five directly relevant EU-funded projects, namely Scaffold, NanoMicex, NanoSafePACK, GUIDEnano and SANOWORK, selected from more than 10 ongoing/completed projects in the field. The scientific findings from these projects were also inspected to find out whether they obtained information that may be relevant for supporting the appropriate selection of risk control measures when dealing with ENMs. In addition to the review of projects and scientific literature, a questionnaire was developed to survey organisations that are involved in the manufacture, distribution, supply, handling, use and disposal of ENMs and to understand the efficiency and cost of the control measures that are currently available. Potential participants and their contact information were identified from nano-safety projects, nano-related websites, European NanoSafety Cluster Compendium 2015 and personal communications with relevant individuals. The questionnaire was organized around several categories: engineering controls, organizational measures, personal protective equipment (PPE) and future research directions. The draft questionnaire was tested internally by 4 industrial companies and revised according to their feedback. The results obtained from 36 organizations are presented in this paper.

## 3. Risk Management Approaches and Tools for ENMs

Considering the rapid growth of nano-industry and consequently the increasing rate of exposure to ENMs, it is required to have effective risk management strategies in order to ensure and maintain a significant level of protection for consumers and the environment. Although the aim here was to address the safety of both workers and consumers, an extensive search of literature and other useful sources resulted in much more information available on risk management for nanotechnology workers compared to end-users. Therefore, this section is mostly focused on the available risk management approaches and tools that are dedicated to reduce the level of risk for workers.

In this section, the existing tools, scoring systems and strategic approaches for aiding in the selection of appropriate risk prevention measures and minimizing risks of exposure to ENMs are briefly described based on the literature information. The basic nano-tools for risk management and prioritization is given in Table 1, whereas the risk management strategies proposed by different researchers to establish a safe environment when working with ENMs are summarised in Table 2.

The safe and healthy workplace for employees exposed to ENMs is essential but challenging, which can be achieved by identifying and managing risks, such as recognition of hazards, assessing exposures, characterising actual risk, and implementing measures to control the identified risks. In this section, existing scoring systems and strategic approaches for minimizing risks of exposure to ENMs are described based on the literature information.

It has been mentioned in many of the published guidelines that RMMs should follow the standard hierarchy of control strategies in order to eliminate hazard or to reduce exposure[7, 8, 12, 21]. The traditional hierarchy of controls given in Figure 1 describes the order that should be followed when choosing between viable control options for controlling risks in a reliable and cost effective manner. According to the traditional hierarchy of control, the most effective hazard control is the elimination of all hazards within a process (e.g. by replacing the process or use of a non-hazardous substance). If the complete elimination of hazard and risk at source is not practical, risk should be minimized by substituting the process or compound with a less hazardous (i.e. safer) alternative. The third most effective risk management strategy is the use of engineering controls, which require physical change to the workplace. The remaining control measures, namely administrative controls that are designed to enforce operational procedures to minimize release to a working area and PPE aiming to protect an individual person from risks to health and safety, are least effective when used on their own because they rely on human behavior and supervision. Ideally, these measures should be used in conjunction with more effective control measures if control at source of risk is very impractical.

Risk management tools used to mitigate risk and manage exposure can be divided into three main categories: qualitative, semi-quantitative and quantitative. Qualitative or semi-quantitative tools are currently favorable for the control of potential risks associated with ENMs since there is still lack of knowledge or understanding in relation to the safety assessment of nano-scale materials[22]. A control banding approach is a potential solution to assess and manage workplace risks where there is limited information, particularly relating to safety procedures and workplace exposure limits. It combines risk assessment and management to simplify risk complexity in the scarcity of input data[23]. To date, a number of control banding tools such as CB Nanotool[16], ANSES Nano[17, 18], NanoSafer[19] and Swiss precautionary matrix[24] have been developed to protect the health of workers handling ENMs. Table 1 lists the basic nano-tools for risk management and prioritization. A low-cost/evidence based tool[25] was one of the earliest control banding tool developed for assessing and managing the potential risks resulting from workers' exposure to Carbon Nanofibers. Similarly, Hansen et al[26] developed a systematic tool, NanoRiskCat, to support companies and regulators in their first-tier assessment and communication on the hazard and exposure potentials of consumer products containing ENMs. The outcome is related to five colored dots representing the qualitative exposure potential for professional end-users, consumers and the environment, and the hazard potential for humans and the environment. Each dot is assigned one of four different colours (red, yellow, green, and grey) indicating high, medium, low or unknown level of exposure/hazard potential, respectively. With the obtained results, users can identify the top priority to apply proper risk measures for the reduction of the exposure and hazard risks. In US, Grieger et al[27] developed a risk ranking tool (i.e. Tool for ENM Application pair Risk Ranking) to screen human health risks of ENMs, using both qualitative and quantitative information. Most of these nano-tools seem to use reasonable approaches and provide promising results, while their main limitations are the extensive input data requirements and solely theoretical, rather than observational, considerations being made. More detailed information about the existing tools for risk management and prioritization of ENMs can be found elsewhere[28, 29].

A number of risk management strategies have been proposed to support the reliable risk management of ENMs are summarised in Table 2, including risk management approaches, methods and models. Kuempel et al[1] suggested an integrated procedure for risk management of ENMs including research and tools (toxicology & epidemiology, exposure and risk analysis), risk characterisation (weight of evidence, severity & likelihood, variability & uncertainty), risk management (occupational safety & health guidance, exposure limits, communication) and workplace actions (engineering controls & PPE, exposure monitoring, worker training, medical monitoring). Schulte et al[30] proposed that risk management process for ENMs should be a part of an enterprise-wide risk management system, including both risk control and a medical surveillance program assessing the frequency of adverse effects among groups of workers exposed to ENMs. Goudarzi et al[31] proposed a 10-step qualitative risk management model for detecting significant risks in a systematic approach and providing decisions and suitable actions to reduce the exposure and hazard to an acceptable level. Ling et al[32] developed a risk management strategy based on the precautionary risk management, which is a modified version of Luther's method[33]. The risk management strategies were constructed according to the different levels of precautionary risk management, which includes the measures relating to technology control, engineering control, PPE, and monitoring of the working environment for each level.

Fadel et al[34] highlighted that the use of multi-criteria decision analysis (MCDA) for risk management purposes and the integration of risk and life cycle analysis using MCDA can be helpful to support the next generation of sustainable nano-enabled product designs and effective management of ENM risks. They proposed that the integration of risk and life cycle analysis using MCDA can be helpful to support the next generation of sustainable nano-enabled product designs and effective management of ENM risks. Tervonen et al[35] proposed a multi-criteria-based decision support system for clustering nanomaterials into ordered risk classes. Linkov and Seager[36] discussed how to integrate risk assessment and life-cycle assessment using MCDA approach in order to prioritize research strategy in the context of emerging environmental threats. In another study, Malloy et al[37] successfully applied MCDA methods as part of regulatory alternatives assessment in which products, processes or technologies are compared on the basis of their hazard, technical feasibility and economic viability. More recently, Bates et al[38] applied analytical tools including value of information and portfolio decision analysis for risk research prioritization for nanomaterials. MCDA was also applied to combine data on hazard and exposure for risk prioritization of ENMs in order to inform suitable risk mitigation strategies. For example, Hristozov et al[39] applied an MCDA methodology for human hazard identification, which incorporated data quality evaluation and generated results of relevance for comparison and selection of relevant safety by design options. Similarly, Hristozov et al[40] applied MCDA for ranking of nano-specific exposure scenarios in occupational settings, which was useful to check how the implementation of different risk management measures (e.g. PPE) would change the final worker exposure levels. More recently, Hristozov et al[41] proposed a quantitative risk prioritisation tool, which combined advanced exposure modelling with dose-response analysis to calculate Margins of Exposure for a number of ENMs in order to rank their occupational risks and thus inform risk management decision making.

In the European project SCAFFOLD, the structure, content and operation modes of the Risk Management Toolkit[42] were developed to facilitate the implementation of “nano-management” in construction companies with the consideration of 5 types of nanomaterials ($TiO_2$, $SiO_2$, carbon nanofibres, cellulose nanofibers and nanoclays), 6 construction applications (Depollutant mortars, self-compacting concretes, coatings, self-cleaning coatings, fire resistant panels and insulation materials) and 26 exposure scenarios, including lab, pilot and industrial scales. The proposed risk management model included the following main tools: Risk management to open checklist for diagnostic, implementation or audit; Risk assessment to evaluate the identified risks; Planning to schedule the implementation of control measures specified in the evaluation tool; Key performance indicators to define, customise, calculate and visualise the indicators; Documents and templates to provide a list of templates with procedures, instructions, registers and manuals. Groso et al[43] developed a practical, user-friendly hazard-classification system for the safety and health management of nanomaterials. The process starts using a schematic decision tree that allows classifying the nano laboratory into three hazard classes similar to a control banding approach (from Nano 3 - highest hazard to Nano 1 - lowest hazard). For each hazard level they provide a list of required risk mitigation measures (technical, organizational and personal) such as protective measures, technical measures, organizational measures, personal measures and cleaning management. Yokel and MacPhail[44] reviewed the exposures, hazards and risk prevention measures of ENMs, in particular the occupational exposure assessment and the approaches to minimise exposure and health hazards including engineering controls such as fume hoods and personal protective equipment, and the efficiencies of the control measures. The recommendations to minimise exposure and hazards were largely based on common sense, knowledge by analogy to ultrafine material toxicity, and general safety and health regulations, due to the lack of available information and/or un-verified research findings. Chen et al[45] reviewed the eco-toxicological effects of ENM and the existing regulations that can be related to ENMs. They concluded that the variety of ENMs and their properties make the identification and characterization of ENMs a challenging task, and hence, an improvement in sensitivity and selectivity of analytical methods to detect and quantify ENMs in the environment is essential. They proposed a risk assessment framework as a practical alternative for the environmental assessment and effective management of ENMs. Based on the occupational hazard band (OHB) method, a new approach to assess the risks inherent in the implementation of powders was developed[46], which considers exposure based on seven parameters which take into account the characteristics of the materials used, their emission potential, the conditions of use, as well as classic parameters of exposure characterization like duration and frequency. The result of the reflection is then positioned on a hazard versus exposure matrix from which 4 levels of priority of action are defined, as in the classical OHB method used to manage pure chemical risk.

In summary, most researchers appear to agree on the conclusion that although we do not need an entirely new risk management paradigm to manage ENM risks, there is a need to expand existing practices to better address nano-related issues and ensure safe production, handling and use of ENMs. Although the existing risk management approaches applies well for ENM, their ability to transform from one form to another which leads on to changes in exposure and hazard (and hence risk) makes the process much more complex. At present, the main limitation in the field of ENM risk management is the insufficiency of the hazard/exposure research data that will be used to adopt existing risk management approaches and translated into modified practices. This problem is originated by not only the lack of data available, but also lack of systematic approaches for collecting and managing the information needed. One strategy to overcome this limitation in a timely manner is to collate available data from various sources (e.g. literature, ongoing/completed projects and nanotechnology companies) through an inventory and convert it into meaningful information that can be applied to risk decision-making process.

Additionally, there are a number of ongoing studies and projects dedicated to improving the knowledge and understanding of risk management of ENMs. A short description of relevant EU-funded projects, together with their relevance to RMMs, is given in Table 3. It should also be noted that most of these projects are recent or ongoing and results are, in most cases, not yet published. Although the review of relevant projects allowed identification of the main sources of information relevant to RMMs, only a small amount of data is currently available from these projects. As the projects reach their conclusion much more data will be available.

## 4. Workplace Controls for ENMs

This section is focused on occupational risk and managing the risks of ENMs in the workplace since studies on consumer risks estimates for ENMs and consumer protection are lacking in literature.

### 4.1.Risk Control Measures Relevant For ENMs

Most of the technical exposure control methods (e.g. glove boxes, dust suppression systems, fume cupboard, safety cabinet, good hygiene practices and personal protective equipment) can be applied to ENMs since these measures rely on the bulk properties of nanoscale materials, not on their nano-specific properties. However, their performance in controlling ENM exposure should be evaluated since control measures that are proven to be effective for controlling exposure to traditional particles might give unsatisfactory results in the case of nano-scale particles [47]. Table 4 gives a list of traditional risk management measures that are considered to be relevant for ENMs.

Between 2006 and 2011, NIOSH conducted site visits to 46 U.S. companies that produce and/or use ENMs and collected information on the most frequently used engineering controls, housekeeping methods and PPE types[48]. Their assessment showed that the most frequently employed engineering controls for reducing occupational exposures to ENMs were local exhaust ventilation (59%) and chemical fume hoods (54%) followed by ventilated enclosures (50%), enclosed production (48%) and glove boxes (22%). Additionally, 37% and 30% of the visited companies were observed to be employing wet wiping and HEPA vacuum as housekeeping methods, respectively. Moreover, the most frequently used PPE type was observed to be gloves (89%) followed by lab coats/Tyvek suits (83%) and respirators (76%)[48]. Similarly, it was noted in NIOSH's guidance document[8] that the most common control measures used for ENMs are fume hoods, local exhaust ventilation systems, filtered vacuum cleaners, walk-in ventilated enclosures and isolation techniques such as negative pressure rooms or boxes.

In 2007, Conti et al carried out an international survey among 83 nanotechnology companies and research laboratories to find out (nano-specific) health and safety programs and risk control measures implemented by these organizations to ensure safe working practices and environmental protection[49]. The results demonstrated that the most common type of engineering control measure was fume hoods (66%) followed by some kind of exhaust filtration (49%). 82% of the interviewed companies said they had nano-specific PPE recommendations for their employees. In 2010, Schmid et al conducted a survey between 1626 Swiss Companies investigating the quantity of nanoparticles and current protection measures that are in place[50]. Closed process was identified to be the most common protection method in liquid applications while PPE was observed to be the most prominent safety measure followed by local exhaust ventilation in case of powder applications. Similarly, in 2010, NEPHH project conducted a survey on occupational health and safety procedures that are in place in nano-manufacturing sector with the aim of collecting information on engineering controls, PPE and waste management[51]. They reported that the majority of their respondents (66%) use fume hoods, followed by laminar flow clean blench (34%), glove boxes (29,8%), biological safe cabinet (27,7%), cleanrooms (23,4%), glove bag (21.3%), closed piping system (21.3%), pressure differentials (19.1%), separate HVAC (Heating Ventilation and Air-Conditioning) (8.5%) and chemical box (2.1%) to reduce worker exposure to ENMs[51]. Moreover, 95% of survey respondents indicated that they employ PPE and/or clothing recommendations for their employees while only 78% kept the use of PPE compulsory when handling ENMs. In terms of waste management, only 31% were observed to use nano-specific spill control methods and the most common equipment cleaning technique was identified as “wet wipe”. Moreover, the majority of the respondents were observed to treat nano-waste as any other chemical waste[51]. The review of literature on efficiency of different control measures for ENMs showed that the most widely used RMM according to these surveys (e.g. local exhaust ventilation and chemical fume hoods) have indeed high efficiencies in reducing ENM emissions and particle concentrations [52-54].

In our questionnaire, we asked respondents to score four risk management categories (engineering controls-elimination and substitution, engineering controls-technical measures, organisational measures and personal protective equipment) in terms of their relevance to their firms’ activities in risk reduction process on a scale of 1 to 4, with 4 being most relevant and 1 being least relevant for reducing potential risks that are associated with ENMs. The answers given to this question by 36 nanotechnology companies are summarised in Fig 2. In this context, relevance can be considered as a subjective parameter. Overall, the respondents selected the PPE (e.g. body, hand respiratory and face protection) and technical measures (e.g. design of manufacturing processes that reduce workers’ contact with raw nanomaterials, such as containment, isolation and ventilation) to be the most relevant control strategies for ENMs followed by organizational measures (e.g. monitoring, health surveillance and good hygiene practices). It is also worth mentioning that the difference in the relevance score of risk management categories is very small. Despite their high efficiency, survey respondents ranked substitution and elimination (e.g.

physical manipulation of raw materials into forms that reduce hazard or exposure such as change of physical state and coating) as the least relevant control methods.

### 4.2.Efficiency of Risk Control Measures

Although it is widely agreed that traditional methods used to control exposure to particles can be implemented to ENMs, there is a need to re-test their level of control against ENMs[20]. Currently, there is a lack of knowledge on the efficiencies and practicality of particular risk management measures for control of worker exposure to ENMs. A number of studies (quantitatively) examining the efficiency of different control measures for ENMs are summarised in Table 5, while the data collected from reviewed projects are given in Table 6-7. Many researchers have employed different approaches (e.g. percent reductions based on mass or particle number concentrations, process to background ratios etc.) to quantify the efficiency of control measures being tested. Most of these studies have concluded with a set of recommendations for controlling worker exposure to ENMs. Overall it has been recommended that, after *substitution of hazardous material and process changes*, *isolation of emission sources* is the top priority to control and prevent worker exposure to ENMs while, *ventilation system* used for removing or diluting air containment is the next priority to consider[55]. It has been also demonstrated by many researchers that *combination of isolation with ventilation* remarkably increases the performance of exposure control systems[55-58].

Among 36 survey respondents, only 5 of them provided quantitative data on the effectiveness of control measures. Moreover, provided answers are incomplete and mostly conflicting, suggesting that more research is needed with respect to the efficiencies of risk control measures for clarification. Overall, all type of ventilation methods except dilution ventilation and controls such as embedding in matrix were observed to have high efficiency (>80%) while surface modification approaches and automation were observed to have very low efficiency (<50%) for ENMs. The main difficulty here is defining which nano-form the efficiency applies to. When there is no information on the efficiency of control measures specific to ENMs, the default efficiencies can probably be used for initial assessment purposes although it should not be considered exhaustive. Specialized databases including scenario-specific efficiency values of risk management measures, such as exposure control efficiency library (ECEL[59]), can be a good starting point for this purpose. Therefore, future directions could include how ECEL-like libraries can be used to better address nano-specific needs.

### 4.3.Cost of Risk Control Measures

The achievement of environmental protection at low cost is an integral feature of several risk management principles (e.g. European Commission's Precautionary Principle[60], UK Health and Safety Executive‘s As Low as Reasonably Practicable (ALARP) principle[61]) and regulations (e.g. REACH Authorisation's Analysis of Alternatives[62] and Socioeconomic Analysis[63]). Although cost is not a direct factor in REACH, measuring economic viability of alternatives to the company is a factor within Authorisation. Therefore, this section would of particular use to downstream users trying to compare and implement alternative control measures.

Given the significant uncertainties around ENM risk and ambiguous risk perception of stakeholders, evaluation of costs is even more critical to support a rational risk management approach. Helland et al[64] report that small firms identified cost as the biggest barrier to occupational risk management. Fleury et al[65] pinpoint difficulties in implementing risk management for nanocomposites based on acceptable risk thresholds, and propose risk management and cost evaluation based on the ALARP principle[65].

Key methodologies used to assess the balance between environmental protection and the personal or societal costs to achieve it include Cost Benefit Analysis (comparison of net benefits and net costs of an action for manufacturer or society) and Cost Efficiency Analysis (assessing which action maximizes the level of risk reduction per unit cost)[66]. To illustrate how efficiency and cost criteria can be integrated, emerging findings (Fig. 3) from the questionnaire on respondents ranking on cost (on a scale from 1 to 4 with 1 meaning low cost and 4 meaning high cost) are compared with the occupational risk control hierarchy for efficiency (Fig. 1). As can be seen from

Fig. 3, automated control and process control are observed to be costly risks management solutions. However, despite their relatively high investment and implementation costs, they significantly reduces the likelihood of different forms of risks before they occur and ultimately, serves to save costs. Survey respondents rank PPE for hand, face/eyes, feet and body as the least expensive RMMs. In most cases, the respondents did not specify whether their responses were related to one piece of PPE for single or repeated use. Although PPE is a low-cost intervention, it is the least effective category in the occupational risk control hierarchy and would not be useful in situations where significant risk reduction is required. It should also be noted that the effectiveness of PPE in real-life conditions might be higher if they are used adequately.

Organizational and work practice control measures are rated by the respondents among the more expensive RMMs, but are penultimate in the occupational control hierarchy. On the other hand, most of the engineering controls (except operator containment) are little higher than PPEs in cost, but more preferred according to the occupational risk hierarchy, suggesting that engineering controls could have the optimum tradeoff between efficiency and cost for medium to high risk scenarios. Elimination (e.g. limiting concentration of hazardous material) and substitution (e.g. change of physical state, change in physicochemical properties) have high efficiency in the occupational risk control hierarchy but also ranked among the most expensive RMMs by respondents, suggesting that they will be used in high risk scenarios. By developing quantitative estimates of efficiency and cost for ENMs, RMMs can be clearly compared to find the alternative that makes the most optimum tradeoff between these factors toward the achievement of risk thresholds. Specifically, once the sufficient amount of quantitative data is available, it would be possible to find an optimum set of financially efficient RMMs using efficiency-cost ratio as an indicator.

The cost of risk management is also expected to have an inverse relationship with insurance premia for nanomanufacturing. Insurance sector attending the first SUN Stakeholders' Workshop in Utrecht in 2014[34] expressed a willingness to offer discretionary insurance premium discounts if industry demonstrated an understanding of risk, regulation and Standard Operating Procedures[67]. Therefore, along with supporting industry in implementing RMMs that will prevent adverse effects on human beings and the environment, finding an optimum set of financially efficient RMMs will also enable industry to reduce insurance costs for nanomanufacturing.

## 5. Conclusion and Direction for Future Research

This study is concerned with the current availability of information on the efficiency and cost of existing RMMs for managing the risks of ENMs. The ultimate aim here is to contribute towards the development of an inventory of RMMs that offers a systematic approach to select optimum control options (e.g. embedding in matrix, local exhaust ventilation, vacuum cleaner etc.) for safe nanoscale product and process design. To compare the technical and economic feasibility of existing risk prevention measures for ENMs, both qualitative and quantitative data have been collected through the review of relevant literature and the survey of nanotechnology institutions. The findings show that isolating people from hazard through engineering measures and reducing employee exposure to hazards through protective clothing are more commonly used to reduce ENM risks, compared to eliminating hazard at source. It has been also observed that despite the high efficiency and sustainability of risk prevention measures such as the elimination and substitution (e.g. modification of ENMs in a way that reduces the risks they pose) in the hierarchy of hazard control, their current use is not widespread due to the unknown effects of manipulating nano-characteristics on the desired functionality. Clearly, more quantitative research is needed with respect to the efficiency and cost of each RMM to fully understand and compare their suitability in preventing risks that may arise as a result of occupational or consumer exposure to ENMs.

The limited knowledge on nanoEHS issues points to important gaps in research on the environmental and health risks associated with nanotechnology. Clearly, much research remains to be done on the risk management of ENMs, including identification and categorization of ENMs (e.g. classification of nano-enabled materials based on key parameters or biological interactions) data collection (e.g. scientific data pertinent to hazard and exposure), standardization (e.g. definitions, control limits, measurement methods and metrics etc.), safety-by-design research (e.g. integrating safety into design), development of new measurements (e.g. developing a combination of different analytical methods for determining nanomaterial mass concentration, particle concentration, morphological information etc.), and risk prediction/management tools (e.g. tools for the predictive risk assessment and management including databases and ontologies). Lastly, nanotech companies participating in SUN's survey were asked to score the importance of these research directions on a scale of 1 (lowest) to 4 (highest) in order the understand their perspective on future research needs (Fig. 4). Data acquisition was ranked to be the most important research area followed by standardization, nanomaterial identification and classification, risk prediction and management tools and new measurement methods/tools. The apparently less importance attributed by companies to safety-by-design research may be caused by the high degree of uncertainty regarding the potential impact of manipulating nano-characteristics on the performance of final product. However, the ability to remove the source of risk through safety-by-design approaches (e.g. use of a nanoform encapsulated in micro/macro form that reduce human and environmental exposure while preserving nanoscale reactivity) is one of the most effective risk management strategy and deserves further investigation.

The existing challenges in risk management of ENMs are not only scientific but also related to insufficient communication and integration between different scientific disciplines, which might lead to unnecessary overlapping of studies. More focused research, integrated processes, and more dialogue is required. In part, this is currently being addressed by a growing number of European projects and international efforts. For example, SUN is a collaborative EU project aiming at making best use of available knowledge on environmental and health risks of ENMs to develop a user-friendly, versatile software-based DSS for practical use by industries and regulators. It aims to contribute to the sustainability of nanotechnology by addressing health and safety issues of ENMs throughout their complete life cycle in close collaboration with research organisations, industry and regulating bodies. These projects will undoubtedly lead to many insights into the risk management issues involved in nanoscale production and products.

## Declaration of interest

The authors declare no conflict of interest.

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**Table 1.** Risk prioritization and management tools for ENMs

| Tool | Description |
|---|---|
| **CB Nanotool** [16] | A control banding tool for assessing risks associated with ENM operations and selecting effective engineering controls |
| **Stoffenmanager Nano** [68] | A generic online tool for ranking potential human health risks as well as risk management measures applicable to ENMs |
| **ANSES Nano** [17, 18] | A control banding tool for managing the potential risks of ENMs |
| **Swiss precautionary matrix** [24, 42] | A risk prioritization tool for safe handling of synthetic NMs |
| **NanoSafer** [19] | A semi-quntitative risk priorization tool for managing ENMs in the workplace |
| **NanoRiskCat** [26] | A conceptual decision support tool for risk categorization and ranking of ENMs |
| **A low-cost/evidence-based tool** [25] | A low-cost/evidence-based for assessing and managing the risks associated with exposure to Carbon Nanofiber |

**Table 2.** Risk management strategies for ENMs

| Ref. | Description |
|---|---|
| 1 | — It provided a detailed overview on making use of current hazard data and risk assessment techniques for the development of efficient risk management guidelines for ENMs.<br>— The authors proposed an integrated approach for risk management of ENMs including research and tools, risk characterisation, risk management and workplace actions. |
| 30 | — This paper provided an overview on the application of risk management approaches for ENMs.<br>— The authors concluded that risk management process for ENMs should be an internal part of an enterprise-wide risk management system, including both risk control and a medical surveillance program that assesses the frequency of potential side effects among groups of employees (potentially) exposed to ENMs. They also suggested that the medical surveillance can be used to estimate the effectiveness of risk management program. |
| 31 | — The researchers proposed A 10-step qualitative risk management model for nanotechnology projects: the basic knowledge of the work; a thorough risk assessment; identifying nanoparticles; identifying hazardous nanoparticles; obtaining latest information; evaluating exposure routes; identifying risks; performing actions; documenting the whole process; and reviewing the risk management. |
| 32, 33 | — The investigators constructed a risk management strategy to protect employees working with ENMs based on the precautionary risk management and reported the results of case studies with ENMs.<br>— Overall, they developed four risk management approaches: technology control (removing potential hazards from raw materials, manufacturing processes, mechanical equipment and factory facilities and other operating environments, changing operating pattern, confining production process systems), engineering control (adopting additional protective methods such as preventing and limiting sources of risk, using local ventilation and high efficiency particulate filters), personal protective equipment (breathing apparatuses, gloves or protective clothing), and working environment monitoring (exposure monitoring and special health examinations). |
| 34, 69 | — These papers outlined latest efforts and outcomes in regard to risk assessment and management of ENMs.<br>— The authors highlighted the importance of integrating risk and life cycle analyses to guide engineering design using multi criteria decision analysis. |
| 35-39 | — These papers discusses the use and integration of multi-criteria-based decision support systems for effective management of ENM risks. |
| 43 | — The researchers introduced a methodology for nano-safety and health management.<br>— The procedure they developed employs a schematic decision tree to classify risks into three hazard classes with each class being provided with a list of required risk mitigation measures (technical, organizational and personal). |
| 44 | — This extensive review drawn together finding from a broad range of research on risk assessment and management of ENMs and outlines some good workplace practices.<br>— The authors investigated the elements of occupational health protection and hierarchy of exposure control, including primary prevention (e.g. elimination, substitution, engineering controls, environmental monitoring, administrative controls and PPE), secondary prevention (e.g. medical examination of workers) and tertiary prevention |

| | |
|---|---|
| | (e.g. diagnosis, therapy and rehabilitation), for ENMs. |
| 45 | — This paper provided an overview of eco-toxicological effects and risk management of NMs.<br>— The authors noted that a ENM risk assessment framework should include three main steps: (1) Emission and exposure pathway, nanoparticle characteristics and exposure metric, (2) Effects and impacts on both ecosystem and human health, (3) Risk assessment (risk characterisation and risk levels). |
| 46 | — The authors proposed a new risk assessment approach based on the "control banding" approach comprising five occupational hazard bands (1-5).<br>— The methodology they proposed considers exposure based on seven parameters including the main properties of the ENMs, their emission potential, the condition of use and exposure characterization parameters such as duration and frequency. |

**Table 3.** EU-funded research projects for risk assessment and mitigation of ENMs

| Project | Duration | ENMs covered | Main aim | Relevance for RMM |
|---|---|---|---|---|
| *SUN* | 2013-2017 | Ag, $TiO_2$, WC-Co, CuO, $SiO_2$, MWCNTs and organic pigment | Development of a Decision Support System (DSS) to facilitate safe and sustainable manufacturing and risk management of NMs | Data on in-use efficiencies and protection factors for engineered ventilation control and PPE |
| *Scaffold* | 2012-2015 | $TiO_2$, $SiO_2$, Cellulose Nanofiber(NF), CNF, Nanoclays | Development of risk management models and tools for NMs in the construction industry | Data on the efficiencies of collective protections (e.g. LEV, glove-box) and PPEs |
| *NanoMicex* | 2012-2015 | ZnO, $Fe_2O_3$, $TiO_2$, $Al_2O_3$, $CoAl_2O_3$ | Development of methods and strategies to reduce the potential risks of workers' exposure to NMs in the pigment/ink industry | Data on the efficiencies of common RMMs (PPE and engineering controls) against ENMs |
| *NanoSafePACK* | 2011-2014 | Nanoclays, Ag, $SiO_2$, ZnO, $CaCO_3$ | Development of a best practices guide for safe handling and use of ENMs in packaging industry | Data on the efficiencies of PPE and Engineering Controls (LEV systems and filtration) against common nanofillers |
| *GUIDEnano* | 2013-2017 | Pristine synthesized NMs | Assessment and mitigation of nano-enabled product risks on human and environmental health | Data on the efficiencies of. safer-by-design approaches and exposure control measures (e.g. fumehoods, closed systems and ventilation) tested on ENMs |
| *SANOWORK* | 2012-2015 | $ZrO_2$, Polyamide and$TiO_2$ NF, $TiO_2$ and Ag nanosols, CNTs, | Development and implementation of design option-based risk remediation strategies for NMs | Data on the efficiency of safety-by-design approach in decreasing nanoaereosolization and control hazard determinant properties (ROS production, surface ions dissolution) |

**Table 4.** The proposed classification system for technological alternatives and risk management measures of ENMs

| | |
|---|---|
| **Product/Substance Controls** | |
| Substitution of hazardous material | Purification |
| Limiting concentration of hazardous ingredient | Embedding in matrix |
| Change of physical form and solubility | Packaging |
| Change in physicochemical properties | Granulation, Controlled aggregation, |
| Surface modification | |
| **Process and Waste Controls** | |
| Change of env. conditions (e.g. humidity) | Reduction/cleaning of air emissions |
| Automation | Reduction/cleaning of general waste |
| Suppression systems- wetting at point of release | Disposal of general waste |
| Suppression systems- Knockdown suppression | Reduction/cleaning of nano-specific waste |
| Use of mechanical transportation | Disposal of nano-specific waste |
| Containment of operator (e.g. cabin with filtered air for operator) | |
| **Engineering (enclosure, isolation and ventilation) Controls** | |
| Physical containment (e.g. covers, sealing heads) | Glove bags and glove boxes |
| Chemical fume hoods | Enclosed (isolated) operations |
| Biosafety cabinets | Sealed operations |
| Local exhaust ventilation systems (e.g. with enclosing, capturing or receiving hoods) | |
| Mechanical room ventilation | Dilution (general exhaust) ventilation |
| Natural ventilation | Laminar flow booths & benches |
| **Good Work Practices and Administrative Controls** | |
| Cleaning and maintenance of process equipment | Management systems |
| Vacuum cleaner with an air filter (e.g. HEPA) | Operating practice |
| Spill containment measures | Supervision |
| Workplace housekeeping | Monitoring |
| Personal hygiene facilities | Health surveillance |
| Restricted or prohibited process areas | Worker training |
| **Personal Protective Equipment Controls** | |
| Body protection | Face / Eye protection |
| Hand protection | Feet protection |
| Respiratory protection | |

**Table 5.** Studies evaluating the efficiency of control measures for ENMs

| Measure | NM Type | Efficiency | Ref |
|---|---|---|---|
| Process change (harves wait time) | CNTs and/or graphene | 99.6 and 100% reduction in conc. (from 2.4 and 0.36 to 0.06 and 0.05 mg/m3 ) | 57 |
| Process change (isolation valves) | CNTs and/or graphene | 99.9% reduction in con. (from 2.27 to 0.017 mg/m3) | 57 |
| Process ventilation (exhaust fan) | CNTs and/or graphene | 82.6% reduction in WBZ (from 0.71 to 0.18 mg/m3) | 57 |
| (furnace) Exhaust ventilation system-with enclosure | CNTs | 93-96% filtration efficiency on average | 70 |
| Biological safety cabinet | CNTs | 36% reduction in con. In WBZ (from 4291 to 2749 particles/cm3) and 40% reduction outside the hood | 56 |
| Canopy hood (cutting area) | CNTs | 15-20% increase in conc. In WBZ | 56 |
| Custom fume hoods and biological safety cabinet (BSC) | Epoxy/CNT nanocomposites | Process/Background conc. in BZ Ratios; None: 5.9, Custom hood: 24.4, BSC:0.66 | 71 |
| Fume hood (fan ON and OFF) | Titanium tetraisopropoxide NPs | Particle number con. reduced from 150 000 to ~6 300 (background level) particles/cm3 | 53 |
| Cabin air filter- high fan speed | Diesel engine exhaust | 55% and 48.9% reduction in exposure based on particle number and surface area con. | 72 |
| Cabin air filter- medium fan speed | Diesel engine exhaust | 65.6% and 60.6% reduction in exposure based on particle number and surface area con. | 72 |
| Personal protective clothing (cotton, polyester and Tyvek) | Nanoalumina | Mass of NP deposit (C:3364, P:2463, T:2121 μg/swatch)<br>Mass of NP release (C:1674, P:1312, T:877 μg/swatch) | 73 |
| Ventilated feeder enclosure | Nanoalumina | Particle number con. reduced from 6060 to 360 particles/cm3 | 55 |
| Ventilated full enclosure | Nanoalumina | Particle number con. reduced from 360 to -520 particles/cm3 | 55 |
| Ventilated feeder enclosure | Nanoclay | Particle number con. reduced from 97 380 to -20 particles/cm3 | 55 |
| Ventilated full enclosure | Nanoclay | Particle number con. reduced from -20 to340 particles/cm3 | |
| Unventilation full enclosure | Nanoclay | Particle number con. reduced from -20 to 0 particles/cm3 | 55 |
| Sealed and unsealed respiratory protection device | Nanoscale NaCl aerosol | When the RPD is sealed, the protection factor is 100 to 1 million greater than the protection factor in an unsealed fit. | 74 |
| Local exhaust ventilation with a custom-filtered flange | Nanometal oxides | 92% reduction in emission and 100% reduction in particle conc. | 54 |
| Local exhaust ventilation (portable fume extractor) | Nanometal oxides | 88-96% reduction in conc. | 52 |
| Thermo-denuder | CNT-containing polystyrene | 99.9% reduction in the number of released NP | 75 |

**Table 6.** The experimental penetration factor (e.g. the ratio between the number concentration of particles inside and outside the protective device) of PPE[76]

| ENMs | PPE | $PF_{Av}$ % | ENMs | PPE | $PF_{Av}$ % |
|---|---|---|---|---|---|
| ZnO | Aut. Mask | 7.40 | $Fe_2O_3$ | Latex Gloves | 0.040±06 |
| ZnO | Half Mask 1 | 8.50 | $Fe_2O_3$ | Nitrile Gloves | 0.03±0.07 |
| ZnO | Half Mask 2 | 12.00 | $Fe_2O_3$ | Lab coat | 2.0±0.5 |
| $Fe_2O_3$ | Aut. Mask | 5.52 | ZnO | Latex Gloves | 0.00±0.09 |
| $Fe_2O_3$ | Half Mask 1 | 6.58 | ZnO | Nitrile Gloves | 0.00±0.1 |
| $Fe_2O_3$ | Half Mask 2 | 8.55 | ZnO | Lab coat | 0.8±0.2 |
| $TiO_2$ | Aut. Mask | 6.24 | $Al_2O_3$ | Latex Gloves | 0.35±0.19 |
| $TiO_2$ | Half Mask 1 | 5.88 | $Al_2O_3$ | Nitrile Gloves | 1.2±0.8 |
| $TiO_2$ | Half Mask 2 | 6.51 | $Al_2O_3$ | Lab coat | 5.0±1.4 |
| $Al_2O_3$ | Aut. Mask | 6.50 | TiO2 | Latex Gloves | 0.04±0.03 |
| $Al_2O_3$ | Half Mask 1 | 9.99 | TiO2 | Nitrile Gloves | 0.0±0.4 |
| $Al_2O_3$ | Half Mask 2 | 6.26 | TiO2 | Lab coat | 8.5±1.9 |
| $CoAl_2O_3$ | Aut. Mask | 7.80 | $CoAl_2O_3$ | Latex Gloves | 0.0±0.4 |
| $CoAl_2O_3$ | Half Mask 1 | 7.16 | $CoAl_2O_3$ | Nitrile Gloves | 0.0±0.4 |
| $CoAl_2O_3$ | Half Mask 2 | 7.87 | $CoAl_2O_3$ | Lab coat | 12±4 |

**Table 7.** Scores for modifying respiratory and dermal exposure through protective measures [77]

(Generally, a score of 1 is considered to be the default value that leads to a certain concentration. Values >1 indicate situations with increased exposure and values <1 situations with reduced exposure.)
*based on the work of [78] ; **based on the work of [79]

| RMM | Score | RMM | Score |
|---|---|---|---|
| **General Ventilation*** | | **Localised Controls*** | |
| No general ventilation, room size<100m3 | 10 | No control measure | 1 |
| Mechanical and/or natural ventilation, room size<100m3 | 3 | Limiting emission (e.g. wetting a powder, spraying of water) | 0.3 |
| Spraying booth, room size<100m3 | 0.1 | Local exhaust ventilation (LEV) | 0.3 |
| No general ventilation, room size=100-1000m3 | 3 | Containment of the source without LEV | 0.3 |
| Mechanical and/or natural ventilation, room size100-1000m3 | 1 | Containment of the source with LEV (e.g. fume cupboard) | 0.03 |
| Spraying booth, room size100-1000m3 | 0.3 | Glove boxes/bags | 0.001 |
| No general ventilation, room size>1000m3 | 1 | **Gloves**** | |
| Mechanical and/or natural ventilation, room size>1000m3 | 1 | No gloves | 1 |
| Spraying booth, room size>1000m3 | 1 | Woven clothing | 0.3 |
| **Respiratory PPE*** | | Gloves-Non-woven permeable, not connected well to clothing or arms | 0.3 |
| No PPE | 1 | Gloves-Non-woven permeable connected well to clothing or arms | 0.1 |
| FFP2 filtering half masks | 0.4 | Gloves-Non-woven impermeable, not connected well to clothing or arms | 0.03 |
| FFP3 filtering half masks | 0.2 | Gloves-Non-woven impermeable connected well to clothing or arms | 0.09 |
| P2 replaceable filter Half Mask | 0.4 | **Clothing other than gloves**** | |
| P3 replaceable filter Half Mask | 0.2 | No clothing | 1 |
| A1P2 combined half mask | 0.2 | Woven clothing | 0.09 |
| A1P3 combined half mask | 0.1 | Non-woven permeable | 0.03 |
| Full-Face masks with P3 filters | 0.1 | Non-woven impermeable | 0.009 |
| A powered filtered device incorporating a TH1 hood | 0.2 | **Personal Enclosure*** | |
| A powered filtered device incorporating a TH2 hood | 0.1 | No cabin for workers | 1 |
| A powered filtered device incorporating a TH3 hood | 0.05 | Cabin without specific ventilation system | 0.1 |
| | | Separated room with independent clean air supply | 0.03 |

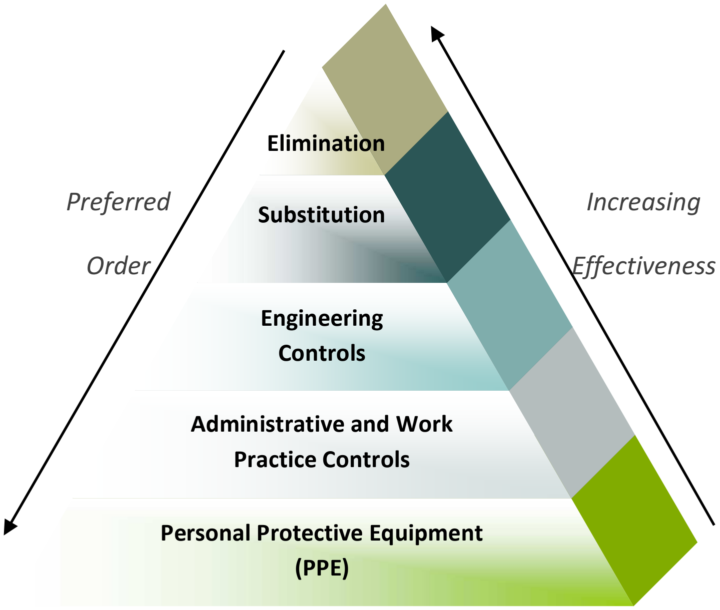

**Fig. 1** The traditional hierarchy of risk control

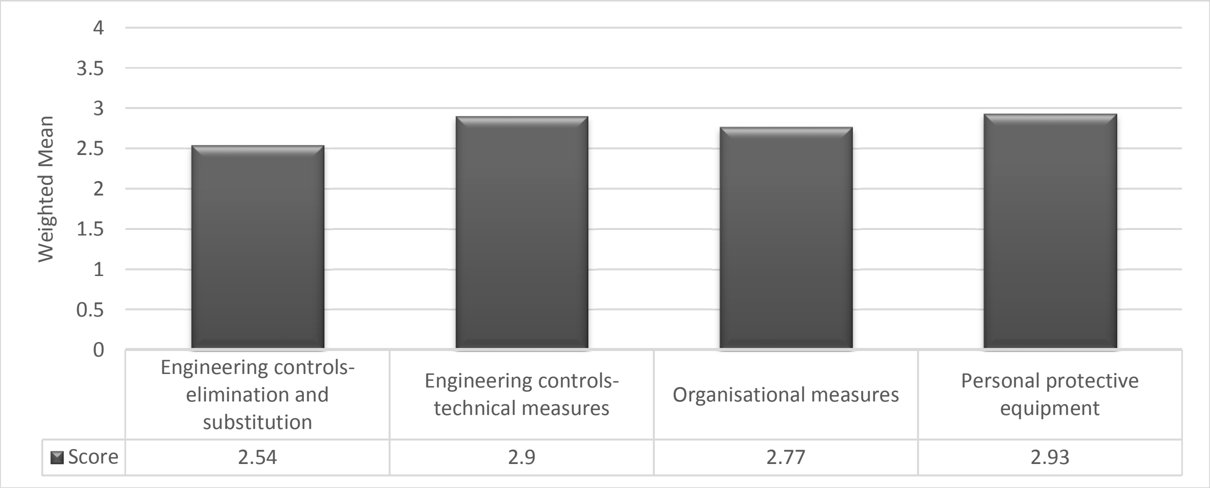

**Fig. 2** Relevance of risk management measures for survey-respondent companies measures on a scale of 1 (lowest) to 4 (highest)

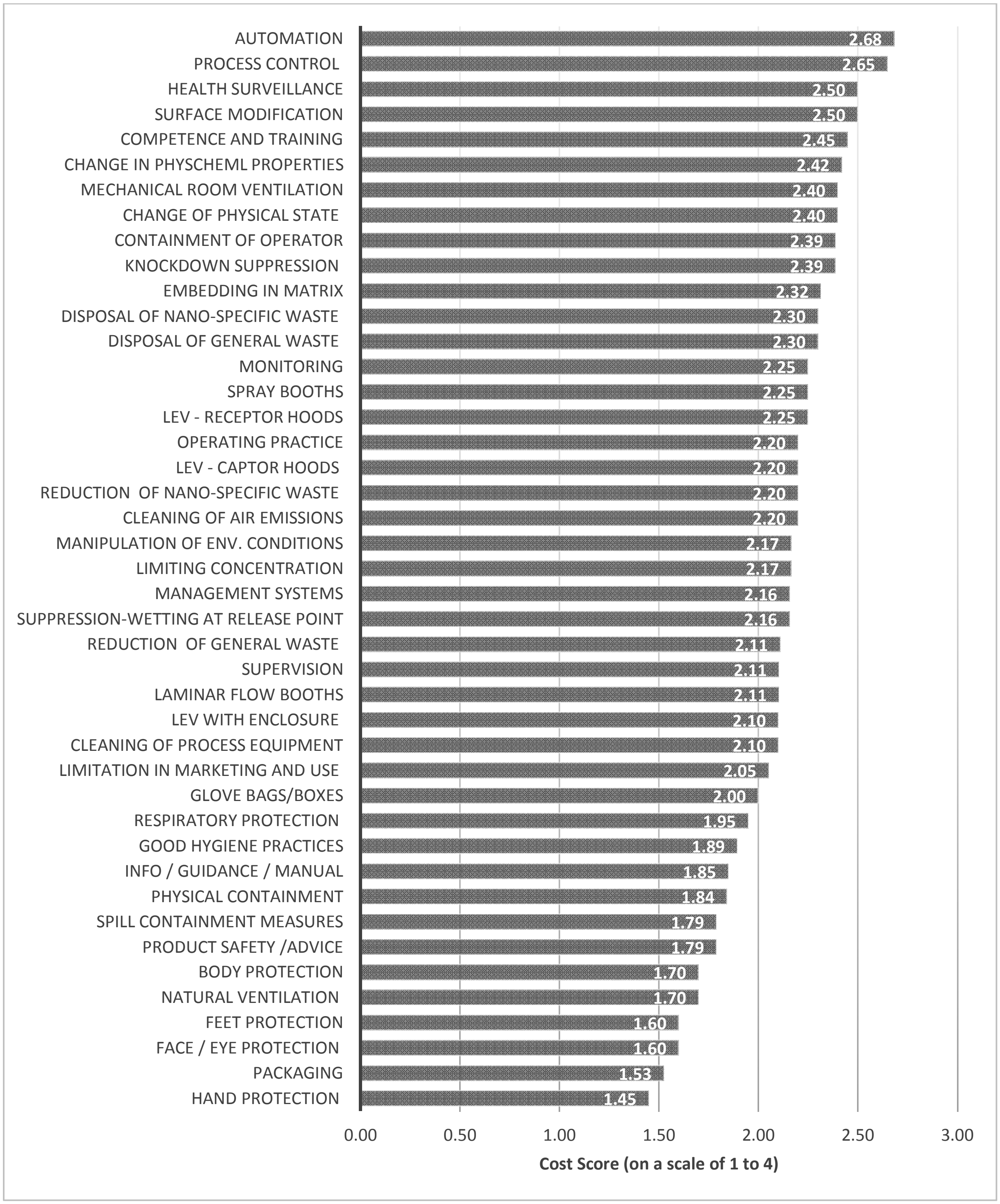

**Fig. 3** Relative cost of risk management measures on a scale of 1 (lowest) to 4 (highest)

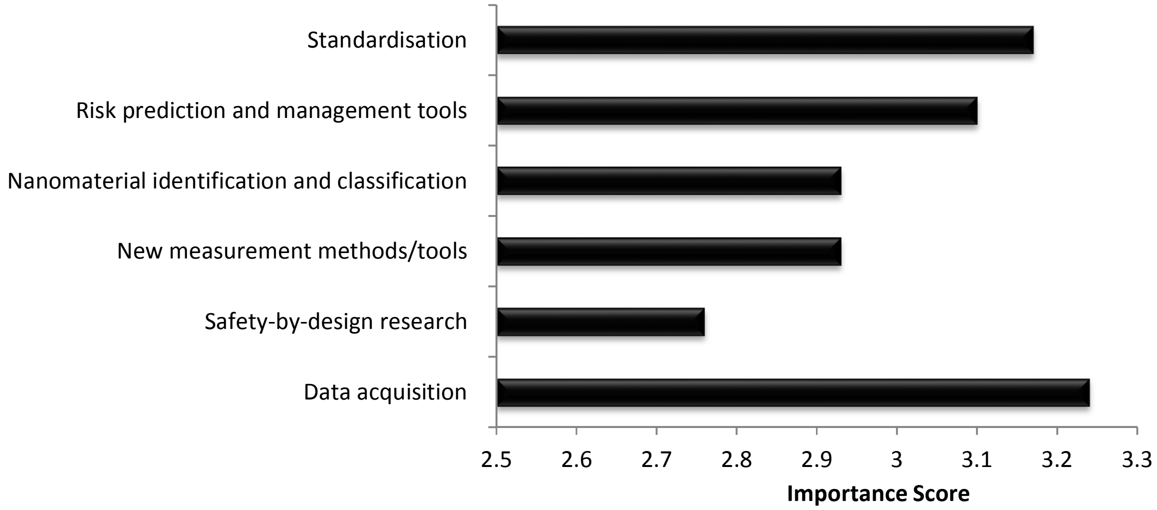

**Fig. 4** The importance of future research directions on a scale of 1 (lowest) to 4 (highest)