CALL FOR THE DEVELOPMENT OF AN ADAPTATIVE TOOL FOR ASSESSING HUMAN HEALTH POSED BY ENGINEERED NANOPARTICLE RISK

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ABSTRACT

Assessing the risks associated with engineered nanoparticles (particles having at least one dimension in the 1–100 nm range) faces three major challenges: (1) lack of standard methodological approaches; (2) uncertainty surrounding the risk factors and their relative significance; and (3) lack of control strategies. Among the approaches that have been proposed are (1) adapting risk evaluation tools used in industrial hygiene; (2) use of evaluation concepts borrowed from the insurance industry; (3) determining the consensus among experts; (4) rating risk control measures; (5) construction of influence diagrams; and (6) use of techniques drawn from multi-criteria decision-making. Knowledge has advanced rapidly in the field of engineered nanoparticles, but comparison of studies is difficult and major gaps remain in the characterization of these materials and the risks they represent. Since they are already being introduced into commercial products and processes, the need is urgent for a flexible and dynamic tool for compiling and sharing detailed knowledge of the associated risks. Uncertainties need to be expressed and reduced. This tool must aid the decision-making of business managers, scientists, and other stakeholders. To the best of our knowledge, no approach suggested in the literature meets these criteria. Thus, the authors call to develop an adaptive, multidimensional decision support tool that indicates influence relationships among risk factors and fosters the gathering and sharing of knowledge, including uncertainties.

Keywords: Decision-making processes, decision supports, engineered nanoparticles, risk assessment, risk management.

1 INTRODUCTION

Nanotechnology makes it possible to manipulate, visualize, develop, and characterize materials and devices at the nanometer scale. The term ‘engineered nanoparticles’ or simply ‘nanoparticles’ is frequently used in this field to define particles of which at least one dimension is in the 1–100 nm range. Many types of engineered nanoparticles are known, including bulk nanostructured materials, surface nanostructured materials and materials carrying nanostructured particles on their surfaces (19% of market size), nanoparticles suspended in liquids (37% of market size), nanoparticles suspended in solids (13% of market size), and airborne or unbound nanoparticles (1% of market size) [1].

Such materials hold the promise of new chemical, physical, or biological properties not seen at larger scales. These new properties are expected to have applications in numerous industrial and medical fields. Nanotechnologies have led so far to the development of more than 1,000 commercial products listed in the Woodrow Wilson Center database in 2009 [2]. Lux Research reports that the value added by nanotechnologies to manufactured products is expected to reach US$3.1 trillion in 2015 [3].

The risk presented by these nanomaterials, which is of interest for this study, is created when they are released in the environment, into air or into a liquid either intentionally or accidentally. They are also referred in the literature as ultrafines. Much uncertainty currently

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surrounds the risks posed by these engineered nanoparticles [4–6]. The factors most likely to make them potential threats to human health have not been identified and the chemical and physical characteristics that could make them toxic as well as the mechanisms by which they might produce pathological conditions remain unclear [1, 7]. They can induce toxicological response(s) that differ principally from soluble or non-particulate toxicants. Knowledge in this area is being developed rapidly by interdisciplinary teams dispersed geographically, using methodological approaches and nanoparticles derived from various sources (cellulose, fullerenes, metals and metal oxides, and others), making it very difficult to do comparative studies. Moreover, no procedure currently exists for a standardized measurement by which to classify nanoparticles.

It is difficult to summarize what is known about nanoparticles and to draw general conclusions from the efforts made so far to characterize them [1, 7]. Engineered nanoparticles are produced and introduced into products and processes, while laboratories continue to create and handle still others for which uses have yet to be found. Market entry often precedes appropriate toxicology studies, raising growing concern and leading to recommendations for the development of risk management strategies in parallel with nanoparticle research and development [8].

The nanotechnology sector has remained outside the scope of regulatory legislation in many countries, until very recently [9]. A recent review has led to the conclusion that current European Community legislation covers in principle the potential health, safety, and environmental risks associated with nanomaterials [10], the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) framework being completed under directives from various agencies (e.g. British Standards Institution). Although numerous American agencies have regulatory, administrative, consultative, or normative responsibilities, for example, the Environmental Protection Agency (EPA), Food and Drug Administration (FDA), Occupational Safety and Health Administration (OSHA), National Institute for Occupational Safety and Health (NIOSH), American Conference of Governmental Industrial Hygienists (ACGIH), and the American Society for Testing and Materials (ASTM), the regulatory framework for engineered nanoparticles research and development in the USA is provided in the form of a single law enacted in 2003. Health Canada and Environment Canada apply a precautionary principle, while the Province of Quebec defines allowable levels of exposure to most particulate chemical substances regardless of particle size. However, nanomaterials may have toxicological and ecotoxicological properties that differ from those of the same chemical materials in the form of larger particles [11]. Since significant knowledge gaps continue to delay the characterization, evaluation, risk assessment, and management of manufactured nanoparticles, precautions should be taken to limit the level of exposure. The precautionary principle as applied by the Canadian Privy Council Office [12] needs the three following conditions: a decision is necessary; there is a risk of serious or irreversible damage; and there is no scientific proof of danger.

In view of the current situation, several researchers favor an adaptive or flexible risk management strategy [1, 13–15] that includes:

- Continuous evaluation of scientific information that is in-depth, balanced, reliable, and transparent with regard to the uncertainties surrounding risks [5, 7, 13–16];
- The drawing of a complete picture of the health effects of various products, processes, and laboratory tests [15, 17];
- A knowledge base that allows prediction of the health impact of new nanoparticles [17];

- Rapid identification of dangerous nanoproducts and those that may qualify for market entry on the short term [15];
- An effective and efficient way to meet the needs of targeted small, medium, and large businesses [15];
- The sharing of risk assessment methods and information on risks [18].

Adaptive management is a systematic approach defined by the US Department of the Interior as 'a decision process that promotes flexible decision making that can be adjusted in the face of uncertainties as outcomes from management actions and other events become better understood'. Careful monitoring of these outcomes both advances scientific understanding and helps adjust policies or operations as part of an iterative learning process. Adaptive management also recognizes the importance of natural variability in contributing to ecological resilience and productivity. It is not a trial and error process but rather emphasizes learning while doing [19].

Considering the diversity of engineered nanoparticles and their applications, other researchers advocate a case-by-case approach [7, 20]. This suggests that no generalized statement can be made concerning groups of substances. It will be a time-consuming process as a very important variety of nanomaterials exists [21]. Modes of use of engineered nanoparticles must be based on an approach that identifies and quantifies advantages, while taking potential risks into account [22].

2 METHODS

2.1 Research question

Applying risk management to engineered nanoparticles involves decisions based on exposure and the effects thereof in specific populations, as measured in terms of risk factors associated with significant consequences. Decisions arising from adaptive risk management in the case of engineered nanoparticles lead to one of three approaches: (1) use of scientific research and ad-hoc modeling of the human health effects of each potential risk factor for various particles and uses thereof; (2) development of a formal decision-making process describing a series of steps to follow in addressing the risks; and (3) development of decision supports applying to a segment of the decision-making process and supporting the decision maker at this stage in the process.

The present study examines the following questions: What decision-making processes and decision-making supports are suitable for assessing the risks posed by engineered nanoparticles? What are the foundations, limitations, and advantages of these processes and supports? Would it be useful to develop an adaptive, multidimensional decision support tool to assess human health risks posed by engineered nanoparticles?

2.2 Search strategy

To retrieve relevant studies from the peer-reviewed literature, six electronic databases, namely, Applied Science and Technology Abstracts, Chemical Hazards in Industry, Compendex, NIOSHTIC-2, PubMed/Medline, and Web of Science were searched for the years 2003 to 2010 using the keywords nanoparticle, uncertainty, risk management, risk assessment, decision-making process, and decision support. In addition to the database

search, references in relevant papers were reviewed to identify additional studies. The bulletins (2009–2010) of the nanotoxicology branch of the Quebec occupational health and safety research network were also consulted.

Studies proposing developments in decision-making processes and decision-making supports in addressing the problem of risk assessment of engineered nanoparticles were included. Decision supports are distinguished from decision-making processes by their partial application within such decision processes.

Results from research on decision supports were then sorted into the following categories based on the outcome: (1) representative decision supports (suggesting a synthetic image of lesional pathologies, referring to the judgments of experts, rating or classification scales); (2) descriptive decision supports (offering a schematic of causal links among lesional pathologies and how they function); and (3) normative decision supports (offering an estimate of risk based on historical data or statistical estimates for lesional pathologies).

3 RESULTS

3.1 Decision-making processes

The risk assessment and risk management paradigm of the National Academy of Sciences considers risk management to be a process consisting of four steps: (1) risk assessment; (2) risk treatment; (3) risk acceptance; and (4) risk communication [23]. Warheit *et al*. [24] proposed a five-step decision-making process covering mainly risk assessment: (1) describing, establishing, and anticipating activities that are sources of exposure (supplying raw material, manufacturing and producing, distributing, using/reusing/maintaining, discarding, and recycling); (2) identifying and characterizing the physical and chemical properties of nanoparticles, including variations in these properties; (3) establishing a risk profile; (4) identifying and characterizing exposures; and (5) analyzing the properties, risks, and exposures. Several other teams present similar reference frameworks [25–28]. Some point to the need to assess factors that aggravate exposure [29], while others insist on systematic analysis of manufacturing and production processes [30] by segmenting and prioritizing areas identified through classical industrial engineering techniques (material process diagrams or path diagrams). Robichaud *et al*. [31] favor a reference framework based on insurance concepts. This consists of identifying processes and matters involved (physicochemical properties, quantities, methods of synthesis, inputs, outputs, and detailed conditions of transformation), characterizing the materials and processes *in situ*, and disseminating the results using an insurance-style database.

Although scientifically valid risk identification and assessment of nanomaterials is an integral part of the decision-making processes, risk mitigation strategies need to be considered. These include precautionary measures to minimize worker exposure, such as enclosing hazardous processes, capturing airborne nanoparticles using local exhaust ventilation, and implementing emergency procedures. When engineering controls are not efficient or feasible, the use of personal protective equipment is required. Risk mitigation plans also include administrative (procedural) controls, good work practices, and educating and training of workers [32].

The scientific community generally recognizes that all decision-making processes or decision supports regarding the human health effects of engineered nanoparticles must be systemic and cover all stages of the nanoparticle lifecycle [13, 24–26, 33]. This lifecycle,

which includes production, transport or storage, distribution, use, recycling, or disposal, requires knowledge of the physicochemical transformations likely to occur when a nanoparticle passes from one environment to another or when products or sub-products are created by their decomposition or transformation. It is also important to know which producers and industries are using and handling nanoparticles and to update this information continually.

3.2 Decision supports

3.2.1 Using a representative approach

Citing similarity to the case of methyl tertiary butyl ether (MTBE), Davis [13] argues that experts in technical fields and social sciences could help reduce the uncertainty involved in attempting to anticipate the health effects of nanoparticles. Kandlikar *et al*. [5] likewise propose expert opinions and a Likert scale (psychometric scale specifying the level of agreement or disagreement of experts for a statement) to shed light on uncertainties surrounding preponderant risk factors, lesional mechanisms, and the classification of nanoparticles. Wardak *et al*. [34] queried eight experts on the effects of exposure to eight nanoproducts (solar creams, toothpastes, home fragrances, batteries, tennis rackets, screens of electronic devices, contrast agents used in magnetic resonance imaging (MRI) equipment). These experts were asked to evaluate the risks associated with various use-and-discard scenarios in terms of numerous indicators or markers (product newness, stability of recovery, properties dependent on the suspension medium, synergy with other products, means of disposal, particle dimensions, dispersion, aggregation, bioavailability, conditions of transport in the environment, photo-catalytic or catalytic activity, populations at risk, antibacterial properties, and level of uncertainty regarding these properties). This study concluded that experts lacked the knowledge to judge certain scenarios based on the indicators. Nevertheless, expert opinion combined with decision analytic frameworks is considered in many normative organizations to provide adequate assessment of the risks posed by nanomaterials [35].

Since developing occupational exposure limits for all new engineered nanoparticles is not feasible, some researchers and legislative bodies advocate a system of categorizing risks associated with nanoparticles in bands, commonly called control banding [21, 36–40]. Such classification systems are used for limiting exposure to chemical inhaler products [41, 42], in the pharmaceutical industry [39], by insurance companies [43], and to prioritize research in certain fields [17]. Based on the results of Sullivan [44], ISO [35], and Safe Work Australia [45] three bands 'to characterize exposure potential (as high, medium or low) for the degree of dustiness ("dispersability") for powders containing nanoparticles and for the quantity used in a specific occupational setting' are proposed. ISO is working on the development of such a qualitative risk assessment (TC229, WG 7). ANSES [21] has proposed a control banding tool assessing health risks based on physicochemical and toxicological properties of nanomaterials as well as their propensity to become airborne. This tool proposes five different bands of ventilation or confinement control.

Using a descriptive approach, Morgan [46] constructed influence diagrams (graphical representations of the decision situation) representing risk factors associated with the problem of nanoparticles based on the semidirected interviews conducted with 13 academic, governmental, and industrial experts. The conclusion of this unique study using this approach was that even under conditions of uncertainty, estimation and decision-making regarding the potential human and environmental risks is possible within the framework proposed, since it helps to structure the decision-making problem.

3.2.2 Using a normative approach

Bayesian methods are often recommended for situations in which there are few or no empirical data for some of the parameters of a risk analysis model and when it is necessary to employ subjective information from expert opinion as data to update a decision-maker's beliefs or to define a consensus [47]. To address risks when uncertainties regarding nanomaterials are significant, Hansen [1] proposes multi-criteria decision analysis, adaptive management, and Bayesian decision supports. This suggested use of Bayesian statistics means that decisions would be based on the scientific evidence available at a precise moment in time. Such decision models could be adapted as more data became available.

Several researchers [48–50] suggest using multi-criteria decision support techniques, such as multi-attribute utility analysis, the analytical hierarchy process (AHP), or ELECTRE, to classify nanoparticles. The AHP method, developed by Saaty in 1980 [51], decomposes one complex decision-making problem in a hierarchical structure. Using binary combinations to estimate every element of the same level of the hierarchy with regard to the elements of the upper level, the analyst can determine the best alternative as well as obtain a general appreciation of the desirability of every alternative. ELECTRE, developed in 1968 by Roy [52], is a multi-criteria decision technique based on the notions of concordance, discordance, and the comparison between several alternatives. The concordance and discordance thresholds are fixed according to the risk acceptability of the decision makers.

3.2.3 Using a mental model approach

Effective communication with the people potentially exposed to nanoparticles is a key element to consider. A message formulated by experts to warn non-experts against a set of potential threats may be ineffective if it contains technical jargon used only by experts. The message should add critical missing information, dispel misconceptions, and give realistic advice that can be followed in the workplace. In comparing a 76-member citizen panel to an expert panel in South Carolina, Priest *et al*. [53] found that citizens are concerned with economic, distributional, and privacy issues of nanotechnologies. Their perception of health and environmental risks increases, while experts are more concerned with how to evaluate potential toxicity. Citizens are in favor of regulation, while experts have difficulty reaching a consensus in this regard. To make safety information more relevant to the workplace of users, Cox *et al*. [54] proposed a generic methodology based on the mental models approach. Based on iterative comparison of experts and users understandings of chemical risks, these models provide useable information to workers, thereby enabling them to make appropriate decisions. Mental models are human conceptualizations of reality and possibilities, representing alternatives, structuring decisions and systems [55]. They can be valuable tools for understanding how workers perceive the risks, make decisions, and construct their behavior as a result of awareness of exposure to nanoparticles.

4 DISCUSSION

Some legislative organizations and research teams suggest assessing the risks posed by nanoparticles in the same manner as for chemical products [7, 26, 31, 32, 43, 56, 57], while others insist that they be treated differently [58]. Their dimensions are such that unsuspected means of exposure are imaginable, and once absorbed, their surface properties could have a significant impact on their kinetics and distribution, leading to new biological interactions and thus making it difficult to characterize and assess the potential risk. Evaluation of occupational exposure to airborne particles is based traditionally on the mass of pollutant in a unit volume

of air. However, some studies suggest that this standard industrial hygiene approach is inappropriate when dealing with nanoparticles [59–61] less soluble. However, it is clear that other parameters, such as morphology, crystalline structure, dimension, and dose expressed in number or surface per unit volume also influence particle toxicity. Considerable uncertainty currently surrounds the relative importance of these parameters for any given exposure scenario. Choosing an appropriate metric to measure occupational exposure therefore remains a major challenge. It might even be unrealistic to expect to find such a metric, since possible modification of the toxicity along the route of exposure must also be considered. Although it may be possible to measure the parameters most likely to be associated with biological response, no device or monitor currently exists to measure simple exposure.

All decision-making processes and decision supports proposed so far are based on the hypothesis that nanoparticles will become airborne and therefore behave according to the laws of aerosol physics and classic fluid mechanics. Nanoparticle behavior is thus thought to be similar to the behavior of a gas [16, 61]. At the nanometer scale, diffusional forces exceed gravitational and inertial forces. Deposition in the respiratory track or on a close body will be greatly affected by the high diffusion coefficients of these particles. However in the workplace environment, nanoparticles will be transported mainly by airflow convection, while still subject to diffusion. In the absence of other forces, such as temperature gradients and electromagnetic fields, nanoparticles will therefore closely follow air streamlines. One should not forget that once suspended in a liquid the behavior of these particles will be affected by new parameters. The health risk assessment should therefore take into account all the possible state that these nanoparticles could be aggressing on the workers or the environment.

4.1 Decision-making processes

Decision-making processes need to address the structure and consequences of the problem, if their aim is to describe all the steps to follow in addressing the risk. They must make it possible both to identify and rank risk factors. Further considerations include: (1) the persons for whom these decision-making processes are intended, in particular the resources at their disposal (time, information, funding) and the constraints they encounter in reaching decisions; (2) the assessment of uncertainties and the information needed to explore or quantify them need to be made more explicit and obtained in parallel with the assessment of consequences; (3) the relative severity of consequences needs to be identified clearly (discomfort, worrying damage, reversible pathology, and irreversible pathology); and (4) risk factors need to be assessed quantitatively and qualitatively. How to reconcile such results? How to limit the occurrence of biases (level errors, errors of omission, errors in the methods of assessing certain risks, etc.)?

Given the diversity of engineered nanoparticles now on the market and currently being developed, some argue that a case-by-case approach is no longer tenable, as currently used for other chemicals [58]. A rapid response to the possible pitfalls of this new technology is needed for regulatory purposes.

4.2 Decision supports

Representative and normative decision supports offer contextual scenarios to address the health consequences of nanoparticles in an aggregated manner, relying on historical data or statistical estimates. Explicative decision supports convey better understanding of interactions

among risk factors. The literature fails to provide a clear assessment of how uncertainties play a part in these consequences, though several techniques have been proposed to account for them.

A decision support is attractive because it allows repeated use of a model to make decisions, study choices, or offer diagnoses when consequences are significant and develop over time and when past experience is of little assistance. It does this while minimizing the occurrence of bias and makes it possible to integrate risks from several origins whether technological, operational, legal, regulatory, social, environmental, financial, consumer market-oriented or fiscal. The models are simplified and realistic, thus, making better decisions possible (in terms of resulting performance).

4.3 Representative outcomes

The human mind is limited in its capacity to deal with information: perception of information is selective, processing is sequential, the ability to calculate is limited, memory uses mainly heuristics and mechanisms of association, and biases in judgment are frequent [62]. Fortunately, individuals are capable of interpreting information. Viewed from the dynamic of human judgment, our problem calls for decision support techniques based on multiple decision makers who give careful consideration to the range of experts to be consulted [9]. The selection of experts needs to be made in compliance with an appropriate standard, such as AFNOR (*Association française de normalisation*) standard NF X50-110 [23] or equivalent. This standard requires selection of experts on the basis of their skills and their personal qualities. Other guidelines (e.g. in France) suggest choosing experts on the basis of their work experience in directly linked operational and managerial roles [63], their experience with assessment and the absence of conflicts of interests. The EPA [64] proposes selecting experts from multiple legitimate perspectives and on the basis of their technical expertise, experience, judgment and communication abilities, and their willingness to reveal any conflict of interest. All expert-dependent decision supports ought to be viewed as a photograph of their opinion at a clearly defined moment in time. Management of intellectual bias will be crucial, since as long as evaluation of risks posed by engineered nanoparticles remains delayed by insufficient technical knowledge, there will be no sensible alternative to consultation with experts in the field of engineered nanoparticle development. Any classification by bands is based on a relatively broad body of hypotheses: researchers assess characteristics of process activities qualitatively and controls are proposed accordingly. Partners (users) find them attractive because their use can be simple and straightforward [38]. However, caution should be exercised because these tools are developed by experts according to precise rules that are not always well understood and documented in practice: generalization of risks, errors and difficulties in the identification and relative importance of risks or inaccurate estimation of exposure may occur. Risk acceptance may also be a concern. According to Beauchamp [65], ‘acceptability of risk is more the fruit of an observation further to an exercise of information and consultation and negotiation than a concept a priori that we could measure scientifically’. Some consider control banding approaches to be good communication tools that can be an ‘integral part of a tiered strategy for risk assessment’ [38]. Paik *et al*. [40] studied the feasibility of using a control banding tool that they developed for five different research laboratory operations. They concluded that, ‘some level of expert judgment should be used to ensure that the recommended controls produced from the CB Nanotool are in fact the most appropriate for the activity in question’.

4.4 Descriptive outcomes

An influence diagram is a formal model of a complex and multidimensional problem. It serves as a user-friendly risk analysis and communication tool for clarifying the qualitative structure and dynamic of a phenomenon, which in this case includes identification of risk factors, logical links among risk factors, and uncertainties and mathematical relationships underlying relations of influence. However, this technique does not present decisional scenarios.

4.5 Normative outcomes

The Bayesian approach to decision-making is based on the use of prior knowledge to construct future scenarios and estimate the probability of their occurrence [1]. This method is used extensively to incorporate quantitative data as well as qualitative findings and subjective judgments, which it transforms into quantitative form [66]. However, the preferences of the decision maker cannot be discerned and the elicitation process and updating the decision model are complex [47]. A Bayesian method, nevertheless, could be used for engineered nanoparticles [67]. The current development of an advanced exposure assessment tool for REACH is a step in that direction [68]. This exposure assessment tool is built on a mechanistic model and an empirical component with exposure information from a database. A Bayesian process integrates the two sources of information to provide exposure estimates.

Multi-criteria methods are employed generally when several alternatives (nanoparticles) exist and arbitrage among criteria becomes necessary. Two challenges are encountered in the present case: (1) the definition of measurable and objective criteria and (2) the weighing of the various criteria in a transparent and acceptable manner for all social stakeholders [20]. While it is possible to represent the preferences of an individual using the so-called utility function, Condorcet demonstrated in the 18th century that it is difficult to construct such a relation for collective preference. Arrow developed a theorem of impossibility in the 20th century demonstrating that unless compromises are made among individual utility functions, it is impossible to establish a collective utility function. A coherent collective choice using multi-attribute utility theory requires identifying a unit of exchange that relies on a compensating mechanism to maximize total value collectively. The AHP method [51] makes it possible to classify alternatives (e.g. nanoparticles). However, this technique is vulnerable to the phenomenon of rank inversion. The ELECTRE method addresses alternatives in different classes by calculating indices of concordance and discordance. Each of the indices is confronted with a fixed threshold expressing the notion of acceptable risk. Alternatives are grouped in classes as a result, but cannot be ranked within a class. Linkov *et al*. [69] used stochastic multi-criteria acceptability analysis (SMAA-TRI), which is based on ELECTRE, to group nanomaterials into five risk classes, namely, extreme, high, medium, low, and very low. They used particle size as a quantitative criterion and six qualitative criteria measured as subjective probabilities estimated by experts. The indifference and preference thresholds for each criterion were defined logically because of knowledge gaps, which led to imprecise thresholds. Estimating the relative importance of each criterion based on their knowledge, the researchers were able to rank a fullerene, a multi-walled carbon nanotube, a quantum dot, a silver nanoparticle and an aluminum nanoparticle but could not quantify the risk that each represented.

5 CONCLUSION

An adaptive, multidimensional decision support tool should be developed to assess the risks that engineering nanoparticles and their processing represent to human health. This tool should indicate influence relationships among the risk factors and foster gathering and sharing of knowledge, including the degree of certainty. The tool we are developing will make it possible to share results of research among researchers in many fields. It might be viewed as a governance measure taken before introducing a more global regulatory framework. Such a tool will need to address all stages in the lifecycle of engineered nanoparticles and be transferable to partners (users). To have a real impact on individuals, knowledge must be shared and exchanged dynamically between the research community and the stakeholders. A standardized and practical approach must be taken to providing useful descriptions of the risks posed by engineered nanoparticles and to identifying the relationship between measured parameters of exposure and toxicity. Promoting adapted and acceptable risk reduction measures calls for a risk appreciation or assessment tool that gives due consideration to the perceptions, concerns, and values of the various social actors.

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