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SPECIAL ISSUE ON ENVIRONMENTAL AND HUMAN EXPOSURE OF NANOMATERIALS

Evaluating the Control Banding Nanotool: a qualitative risk assessment method for controlling nanoparticle exposures

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Abstract Control banding (CB) strategies offer simplified processes for controlling worker exposures in the absence of firm toxicological and exposure information. The nanotechnology industry is an excellent candidate for applying such strategies with overwhelming uncertainties of work-related health risks posed by nanomaterials. A recent survey shows that a majority of nanomaterial producers are not performing a basic risk assessment of their product in use. The CB Nanotool, used internationally, was developed to conduct qualitative risk assessments to control nanoparticle exposures. Nanotoxicology experts have requested standardization of toxicological parameters to ensure better utility and consistency of research. Such standardization would fit well in the CB Nanotool's severity and probability risk matrix, therefore enhancing the protection of nanotechnology industry workers. This article further evaluates the CB Nanotool for structure, weighting of risk factors, and utility for exposure mitigation, and suggests improvements for the CB Nanotool and the research needed to bolster its effectiveness.

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Introduction

A fascinating case study for an industrial hygienist (IH) is presented in nanotechnologies due to the properties of some nanomaterials that include a high degree of reactivity, ability to deposit in various regions of the respiratory tract, ability to cross normally impenetrable barriers (e.g., blood-brain barrier, skin), and the lack of a clear toxicological basis for setting nanomaterial-specific occupational exposure limits. The applications for engineered nanoparticles seem endless, and substantial efforts are being put forth by both government and private industries into the research and development of nanotechnologies. However, it is becoming increasingly clear that the very properties that make nanoparticles technologically beneficial may also make them hazardous to humans and the environment, and news on nanoparticle health effects are often major news items at popular newspapers, such as the Dutch NRC (2008) and San Francisco Chronicle (Fernholm 2008). A recent Dutch NRC article refers to the similarity between carbon nanotubes and asbestos, both in their dimensions as well as their pathogenicity (Poland et al. 2008), and a recent San Francisco

Chronicle article refers to the potential adverse effects of silver nanoparticles on the environment.

While there is an increasing public demand for evaluating the risks associated with nanomaterials, any attempt to quantify the risks of nanoparticles is fraught with uncertainties. Just to name a few: (1) the contribution of a nanoparticle's physical structure to its overall toxicity is not fully understood; (2) lung deposition and alveolar clearance appears to be significantly different between nanoparticles and their larger counterparts; (3) there is no consensus on the relevant indices of exposure, as particle size and surface area are likely to be much more important than mass; and (4) there is a lack of clear information on exposure scenarios and populations at risk. Control banding (CB), which is described in greater detail below, has proven to be an effective strategy for controlling worker exposures in the absence of toxicological and exposure information, and has been mentioned as a potentially useful concept for managing nanomaterial exposures in the workplace (Warheit et al. 2007a; Thomas et al. 2006; Maynard 2007; Schulte et al. 2008). The CB strategy facilitates decisions on appropriate levels of control, based upon product and process information, without complete information on hazards and exposure scenarios. The CB Nanotool was recently developed and has been implemented in many countries utilizing a qualitative decision matrix for a risk assessment that leads to commensurate controls (Paik et al. 2008). Now that the CB Nanotool is beyond its pilot stage, it is appropriate to evaluate its construct, applications, and efficacy and to invite continued dialogue, use, and improvement of the tool within the IH community.

Control banding

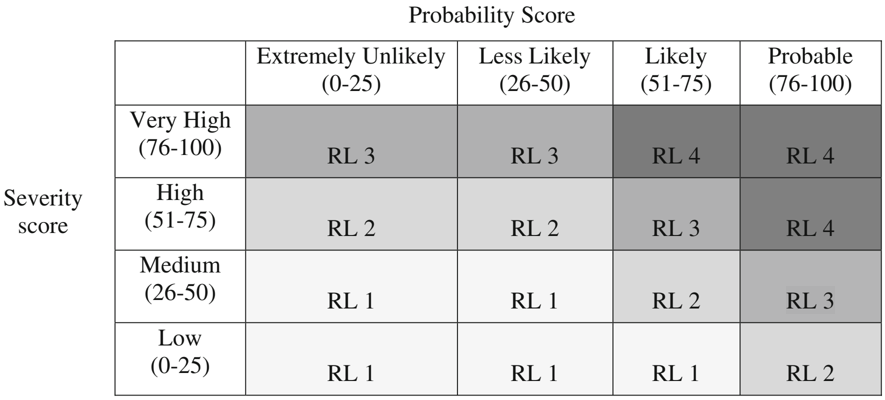
Control banding is not intuitively understood by name alone and can therefore be considered to be a notation for experts, which may come as a surprise to many people. The term originates from the field of IH and represents a qualitative instrument to assess risks for chemical substances to generate solutions and control measures (Russel et al. 1998). The instrument uses categories, or "bands," of health hazards, which are combined with exposure potentials, or exposure scenarios, to determine desired levels of control. The bands of health hazards for some control banding approaches are based upon the European Union risk phrases, while exposure potentials include the volume of the chemical used and the likelihood of the chemical becoming airborne, estimated by the dustiness or volatility of the source compound (Maidment 1998).

Originally, the concept of banding risks of chemical substances and their exposure controls started in the pharmaceutical industry around 20 years ago. Here, the limited availability of pharmacological and toxicological data of products handled by workers was the main motive to develop control strategies as part of a risk management approach. The foundation of the present movement for control banding is derived from a program of the British Health and Safety Executive (HSE) to assist small and medium enterprises in their risk management approach so that they could have a simplified method to comply with regulations requiring all users of chemicals to assess their risks and implement appropriate controls to protect their workers. In a series of papers in 1998, the instrument was published (Annals 1998). International CB workshops and activities further refined the instrument, and explored possibilities to apply the control banding approach to other domains, such as ergonomics, occupational safety, and recently to control nanoparticle exposure (Zalk 2001; Annals 2003; Swuste 2007; AIHA 2007; Zalk and Nelson 2008; Paik et al. 2008). Although CB has received criticism (see for instance Kromhout 2002; Swuste et al. 2003; Jones and Nicas 2006; ACGIH 2008), the focus on controls is a strong point of the instrument and makes it applicable for operations with many uncertainties in hazard, exposure, and consequence data (ACGIH 2008). Much of the criticism has focused on issues relating to the simplicity of the CB approach and the mistaken belief that CB has forsaken the experts and their traditional, quantitative methods. With nanoparticulate exposure and its many toxicological and quantitative measurement uncertainties, however, it can be argued at this time that the CB approach may in fact be superior to the traditional methods.

Risk assessment of nanomaterials with control banding

A recent survey indicates that 65% of companies working with engineered nanomaterials (NM) do not perform any kind of risk assessment relating to their product use (Helland et al. 2008). Therefore, the development of a standardized risk decision framework is necessary and has been called for in many of the latest investigative studies (Schulte et al. 2008; Warheit et al. 2008; Hallock et al. 2008). A conceptual CB model was presented by Maynard (2007) using "impact" and "exposure" indices. This conceptual model combines engineered NM composition parameters (shape, size, surface area and surface activity) with their exposure availability (dustiness and amount in use). These indices are linked to bands with four corresponding control approaches. The control approaches are a grouping of three levels of engineering containment, based on sound IH principles; (i) general ventilation, (ii) fume hoods or local exhaust ventilation, and (iii) containment. The fourth level is "seek specialist advice," referring to specialist IH expertise. In the recently published paper on the pilot "CB Nanotool," the feasibility of using CB principles is further developed and put into practice (Paik et al. 2008). Here, the control band for a particular operation is based on the overall level of risk determined for that operation. This risk level (RL) is the result of a combination of a severity score and a probability score for that operation (Fig. 1), analogous to the impact and exposure index described by Maynard.

The biggest challenge in developing the CB Nanotool was in the determination of the weightings for the different risk factors. In order to accomplish this, a group of experts at Lawrence Livermore National Laboratory (LLNL) was convened in more than 20 meetings over a 6-month period to address health, safety, and environmental control of NM to protect the health of both workers and the public while balancing the needs and requirements of researchers to continue their operations in a safe manner. These experts formed an "Institutional Project Team" (IPT) that was internally established at LLNL for the purpose of developing LLNL's first institutional NM safety program. Members of the NM IPT included: (1) LLNL's medical director, with over 30 years of experience, who oversaw the development of LLNL's medical surveillance program for Nanoparticle Workers and was to use the CB Nanotool's RL outcome as a basis for determining levels of medical surveillance; (2) The director of LLNL's Nanoscale Synthesis and Characterization Laboratory, with over 20 years of experience, who provided input into the physical characteristics that could affect the severity aspects of NM; (3) LLNL's Nanotechnology Safety Subject Matter Expert (SME), with over 10 years of experience, who played a key role in developing the tool and is a co-author of this article; (4) LLNL's medical programs division lead, with over 25 years experience, who developed a medical history questionnaire and medical monitoring scheme for higher risk workers; (5) A field environmental analyst, with over 20 years experience, who provided input on the proper waste characterization of NM; (6) An instructor from the safety training division, with over 15 years of experience, who developed an institutional web-based course on NM safety; (7) and an IH, with over 15 years experience, who provided a critique of the CB Nanotool and its practicality for use in the field. The NM IPT met on a weekly basis



Probability Score

		Extremely Unlikely (0-25)	Less Likely (26-50)	Likely (51-75)	Probable (76-100)
Severity score	Very High (76-100)	RL 3	RL 3	RL 4	RL 4
	High (51-75)	RL 2	RL 2	RL 3	RL 4
	Medium (26-50)	RL 1	RL 1	RL 2	RL 3
	Low (0-25)	RL 1	RL 1	RL 1	RL 2

Fig. 1 Risk level (RL) matrix as a function of severity and probability scores. Control bands are based on overall risk levels. Control bands by risk level: RL 1, General Ventilation; RL 2, Fume hoods or local exhaust ventilation; RL 3, Containment; RL 4, Seek specialist advice (Paik et al. 2008). Reprinted by permission of the British Occupational Hygiene Society, License #2114970359639

over these 6 months. These meetings were approximately one hour in duration and discussed not only the CB Nanotool itself, but also how it fit into the broader context of a comprehensive nanotechnology safety program.

Once the CB Nanotool was developed, integrated into the LLNL nanotechnology safety program as the required risk assessment approach for all work with NM, and implemented as part of the LLNL pilot program, further expert review and input was sought. One mechanism was through expert solicitation via email and phone correspondence prior to submission of the original "CB Nanotool' manuscript. Dr. Remko Houba, who is currently affiliated with the ArboUnie Expert Centre for Chemical Risk Management in The Netherlands, provided valuable input. Dr. Houba, who has over 15 years experience as an IH and investigated the population at risk in the Dutch NM research and manufacturing industries, offered his insight in the CB Nanotool including issues regarding the validity of the tool versus IH professional judgment and the importance of including mistiness (e.g., from spraying applications) as part of the dustiness index. He also concurred with the weighting for "unknown" factors and believed it adequately addressed the uncertainty that is prevalent in this relatively new field of NM safety. Another mechanism was through peer reviews of the original "CB Nanotool" manuscript that was submitted to the Annals of Occupational Hygiene Journal. One reviewer commented on whether or not dermal considerations were adequately addressed in the design of the CB Nanotool. Another reviewer commented on the role of total surface area of the nanoparticles and how this factor is addressed. Both of these issues are discussed in greater detail in the current study. While the actual identities of the peer reviewers are not known to the authors of this article, they are presumed to be experts in this field as they were chosen by the editor of the Annals of Occupational Hygiene Journal as peer reviewers of the manuscript. Yet another mechanism was through presentation of the CB Nanotool as part of two international conferences. One of them was on October 20, 2008, during the Organisation for Economic Co-operation and Development (OECD) Working Party on Manufactured NM Workshop on Exposure Assessment and Exposure Mitigation. Another was the International Commission on Occupational Health (ICOH) Congress in Cape Town, South Africa at the fifth International CB Workshop on 25 March 2009. At these workshops, the value of the CB Nanotool became quite apparent; however, there were many excellent questions asked that focused on the expert judgment behind the CB Nanotool, the weighting values to determine RLs, and whether additional risk assessments were available to further evaluate its outcomes as compared to expert IH judgment. This article is presented as a direct outcome of the OECD NM Workshop and the information presented is bolstered by professional consultation at the ICOH Congress. In addressing these cumulative questions, and in developing a further transparency of the CB Nanotool, this article was developed to offer an expert review of the most recent research in evaluating the initial judgment behind the CB Nanotool and revisits the tool's scoring parameters based on this cumulative information available to date.

Pilot CB Nanotool scoring parameters

As described in Paik et al. (2008), an important consideration in developing the CB Nanotool was that information on many of the factors related to severity would be unknown or uncertain. While it was recognized that traditionally, an unknown hazard would be treated as a high hazard, it was also that defaulting to the worst-case assumption is overly conservative for most hazards and would place an unnecessary burden on those managing the risk and limit the tool's usefulness. For that reason, it seemed appropriate to assign a given factor with "unknown information" 75% of the point value of "high." The implication, seen in Fig. 1, is that for a nanotechnology operation where nothing is known, RL 3 (containment) is required. In this scenario, if just one rating of any of the factors were to be "high," the tool would require an RL 4 assignment for the activity, the maximum control. The breadth and depth of the scoring factors is provided in greater detail within the original Paik et al. (2008) article and therefore will not be included to the same degree within this article. The information presented below reflects a summary of the severity factors, probability factors, and the maximum scores attributed to each of these factors.

Severity factors

Based on the literature available prior to publication of the pilot CB Nanotool, the list of factors below were considered to determine the overall severity of exposure to nanoscale materials. These factors influence the ability of particles to reach the respiratory tract, to deposit in various regions of the respiratory tract, to penetrate or to be absorbed through skin, and to elicit biological responses systemically. The division of severity factor points taken cumulatively is 70% for the NM and 30% for the parent material (PM). Research to date does not contraindicate the potential for engineered NM to be more toxic than its PM. The individual factors that make up the NM severity factors are as follows.

Surface chemistry of NM: Surface chemistry is known to be a key factor influencing the toxicity of inhaled particles. Points are given based on a judgment of whether the surface activity of the nanoparticle is high, medium, or low.

High: 10 Medium: 5 Low: 0 Unknown: 7.5

Particle shape of NM: The highest severity score is given to fibrous- or tubular-shaped particles. Particles with irregular shapes (anisotropic) have higher surface areas than isotropic or spherical particles.

Tubular, fibrous: 10 Anisotropic: 5 Compact/spherical: 0 Unknown: 7.5

Particle diameter of NM: The severity score was based on the particles' deposition in the respiratory tract, regardless of the region in the respiratory tract. Additional research on the toxicological significance of particle size is needed to improve the basis for these weighting factors.

1–10 nm: 10 11–40 nm: 5 <41–100 nm: 0 Unknown: 7.5

Solubility of NM: Poorly soluble, inhaled nanoparticles can cause oxidative stress, leading to inflammation, fibrosis, or cancer. Since soluble NM can also cause adverse effects through dissolution in the blood, severity points are assigned to soluble NM as well, but to a lesser degree.

Insoluble: 10 Soluble: 5 Unknown: 7.5

Carcinogenicity of NM: Points are assigned based on whether the NM is carcinogenic or not, regardless of whether the material is a human or animal carcinogen. Little information is available.

Yes: 7.5 No: 0 Unknown: 5.625

Reproductive toxicity of NM: Points are assigned based on whether the NM is a reproductive hazard or not. Little information is available on this factor.

Yes: 7.5 No: 0 Unknown: 5.625

Mutagenicity of NM: Points are assigned based on whether the NM is a mutagen or not. Little information is available on this factor.

Yes: 7.5 No: 0 Unknown: 5.625

Dermal toxicity of NM: Points are assigned based on whether the NM is a dermal hazard or not. Little information is available on this factor.

Yes: 7.5 No: 0 Unknown: 5.625

Toxicity of PM: Although research agrees that NM can be more toxic than PM, it is a good starting point for understanding the NM toxicity. Points are assigned according to the OEL of the bulk material.

0–1 μgm^{-3}: 10 2–10 μgm^{-3}: 5 <41–100 μgm^{-3}: 2.5 >100 μgm^{-3}: 0 Unknown: 7.5

Carcinogenicity of PM: Points are assigned based on whether the PM is carcinogenic or not.

Yes: 5 No: 0 Unknown: 3.75

Reproductive toxicity of PM: Points are assigned on whether the PM is a reproductive hazard or not.

Yes: 5 No: 0 Unknown: 3.75

Mutagenicity of PM: Points are assigned on whether the PM is a mutagen or not.

Yes: 5 No: 0 Unknown: 3.75

Dermal hazard potential of PM: Points are assigned on whether the PM is a dermal hazard or not.

Yes: 5 No: 0 Unknown: 3.75

The overall severity score is determined based on the sum of all the points from the severity factors. The maximum score is 100. Since nanoparticles usually behave much differently than their PM due to their small scale, greater consideration was given to the NM characteristics (70 possible points out of 100) than to the PM characteristics (30 possible points out of 100). An overall severity score of 0–25 was considered as low severity, 26–50 was considered as medium severity, 51–75 was considered as high severity, and 76–100 was considered as very high severity.

Probability factors

The probability scores are based on factors determining the extent to which employees may be potentially exposed to nanoscale materials.

Estimated amount of NM used during operation: For NM embedded on substrates or suspended in liquid, the amount is based on the NM compound itself and not the substrate or liquid portion.

>100 mg: 25 11–100 mg: 12.5 0–10 mg: 6.25 Unknown: 18.75

Dustiness/mistiness: Since employees are potentially exposed to nanoparticles in either dry or wet form, this factor encompasses both dustiness and/or mistiness of the NM. Knowledge of the operation (e.g., handling dry powders versus liquid suspensions of nanoparticles) would be a means to estimate dustiness/mistiness. Due to the size of NM, visibility may not be a reliable means to estimate overall dustiness/mistiness. A CB Nanotool design feature is that a rating of "none" for dustiness/mistiness level (and only for this factor) automatically causes the overall probability score to be "Extremely Unlikely," regardless of the other probability factors, since the other factors will not be relevant if no dust or mist is being generated. Examples of operations resulting in a "none" rating are handling of carbon nanotubes embedded on fixed substrates and working with non-agitated liquid suspensions.

High: 30 Medium: 15 Low: 7.5 Unknown: 22.5

Number of employees with similar exposure: Points are assigned by the number of employees assigned to this activity. More employees means a higher probability an employee being exposed.

>15: 15 11–15: 10 6–10: 5 Unknown: 11.25

Frequency of operation: Points are assigned based on the frequency of the operation, as more frequent operations are more likely to result in employee exposures.

Daily: 15 Weekly: 10 Monthly: 5 Less than monthly: 0 Unknown: 11.25

Duration of operation: Points are assigned based on the duration of the operation, as longer operations are more likely to result in employee exposures.

>4 h: 15 1–4 h: 10 30–60 min: 5 <30 min: 0 Unknown: 11.25

The overall probability score is based on the sum of all the points from the probability factors. The maximum score is 100. An overall probability score of 0–25 was considered extremely unlikely, 26–50 was considered less likely, 51–75 was considered likely, and 76–100 was considered probable. Based on the severity score and probability score for an operation, the overall level of risk and corresponding control band is determined by the matrix shown previously in Fig. 1.

Judgement behind the score weighting

There was a great deal of research and consideration of the collective information available during the development of the CB Nanotool. In concept, as described above, it was easiest to begin with the realization that traditional IH did not provide a comprehensive and accurate quantitative risk assessment of NM. The use of available quantitative instruments, such as condensation particle counters and nanoparticle surface area monitors, needs to be balanced with their potential biases (summarized in ISO 2007). Condensation particle counters can have both positive and negative biases depending on the particle size distribution of the particles they are measuring. The CPC Model 3007 (TSI Inc., Shoreview, MN), for example, measures particles in the 10 to >1,000 nm range and provides a number concentration. This instrument would significantly underestimate the actual number concentration of nanoparticles if the particle count median diameter was less than 10 nm or significantly overestimate the actual number concentration of nanoparticles if the particle count median diameter was greater than 100 nm. This would be problematic in most environments where naturally occurring nanoparticles would tend to co-exist with the engineered nanoparticles in question. Similarly, nanoparticle surface area monitors that rely on diffusion charging of the sampled particles can have significant biases when particles greater than 100 nm exist in the sampled air stream. Below 100 nm, active surface (inferred from the attachment rate of positive unipolar ions to particles) is a function of the square of the particle diameter and is considered a good indicator of external surface area. However, this relationship breaks down for larger particle size; therefore, the measurement would no longer correlate well the particles' external surface area. In addition, the expense of the available and more accurate exposure monitoring tools could be seen as cost-prohibitive, especially in the face of so much uncertainty. Once a decision was made to build a qualitative approach, it was also easy to decide on using the 4 × 4 risk model that is utilized in many of the CB strategies. The 4 × 4 risk matrix has been found over time to balance ease-of-use with an appropriate level of rigor to develop a binning of established and graded control approaches in a historically acceptable manner (Maidment 1998; ANSI 2000; Zalk and Nelson 2008). The research also presented a relatively consistent set of factors that should be used in the model, of which each is needed to be included in the scheme for scoring input; however, the weighting of each factor relative to the others was a bit more involved and required a relative risk approach in line with the available research (Robichaud et al. 2005).

Severity

Physicochemical characteristics NM (40 points)

Research showed a strong agreement that the physicochemical aspects of NM structure have a predominant effect on their potential toxicity (Maynard 2007; Warheit et al. 2007a; Thomas et al. 2006). Therefore, both the physical parameters (particle shape and diameter) and chemical parameters (surface chemistry and solubility) were weighted equally with 20 points attributed to each parameter, as research did not indicate that one parameter or the other led to a more elevated risk. This decision was also based on the fact that appropriate standardization of testing did not appear available in the literature, only that both of these considerations were necessary when evaluating the potential toxicity of a given NM (Powers et al. 2006).

Toxicological characteristics NM (30 points)

Having taken into account the more generic health hazard parameters of NM, it was also necessary to account for the toxicological concerns that might be related to research on specific NM effects. As the research on NM as a whole had not delved into these specific toxicological aspects to date, agreement by experts invariably noted that the more classic toxicological outcomes for an individual NM product should also be considered (Maynard 2007; Powers et al. 2006). Therefore, the toxicological adverse outcomes that would lower any prospective occupational exposure limit were included and these were: carcinogenicity, reproductive toxicity, mutagenicity, and dermal. From an IH perspective, it is difficult to consider weighting these adverse outcomes as anything other than equally as any one of these toxic effects will lead to an appropriate lowering of its OEL to avoid a health hazard.

Toxicological characteristics of PM (30 points)

As stated earlier, the properties that make NM unique in their utility also have the potential to create unique toxicological considerations. Without more specificity of this issue presented in research publications, it is necessary to start with the likelihood that much more of this toxicological information would be available for the bulk PM. Therefore, equal weight was given for the research-derived toxicological characteristics for both the NM and PM, with both at 30 points. This also gave an appropriate greater weighting to the physicochemical aspects of NM (40%), which are being heavily researched, than for the specific toxicological outcomes of both the NM (30%) and its PM (30%). A decision was made to use the same toxicological characteristics for PM and NM, dividing each of their points equally, although greater weighting was given to the NM (30%) then to the PM (20%) to reflect concerns expressed in the research. In order to make up the additional 10 points to equalize the PM toxicity with NM toxicity, the PM's OEL was included in the PM toxicological outcome determination, as this is more holistic in offering a relative weight to a more broad classification of epidemiology and toxicology issues. Thus, the PM OEL (10%) was given twice the value of any of the individual PM toxicological characteristics (5%).

Probability

Dustiness/mistiness (30 points)

In determining the factors that would lead to potential exposure to employees, the primary consideration would be based on the opportunity for the NM in question to become airborne. Experts are in agreement that the most important factor for determining the potential for exposure, and therefore the potential for bioavailability and translocation systemically, is in regards to inhalation (Warheit et al. 2007a; Maynard 2007; Thomas et al. 2006; Powers et al. 2006; Tsuji et al. 2006; Holsapple et al. 2005). The consideration was therefore a balance between its ability to become airborne, to disperse easily, and the amount of material used. It was determined to give dustiness/mistiness the greatest weight of the probability factors (30%). It was also given consideration that many of the CB Nanotool users performing an initial screening of NM activities could default here to "unknown" if no other parameters for airborne potential were readily available (Donaldson et al. 2006). Then, if the RL outcome was too restrictive with the weighting of an "unknown" score, a decision could to made to use quantitative measurements to assist in scoring this category. This focused use of quantitative monitoring tools is considered a more appropriate and cost-efficient application and is not confounded by the biases of using multiple monitoring devices simultaneously. In addition, although dustiness and mistiness are characterized together, mistiness in isolation would likely have a lower score then dustiness as the nanoparticles would be in the form of wet suspensions. This score for mistiness would therefore be more analogous to a lower score for dry, agglomerated particulates than when compared to non-agglomerated, highly dispersed particulate in a similar operation.

Estimated amount of chemical used (25 points)

The more material that is used, the better chance that it will become available as a potential source term for employee exposure. The weighting of the amount of chemical used in a given task was considered to be a slightly lower relative risk (25%) than the consideration for the airborne potential (30%). The authors also considered the combination of dustiness and amount used as being the primary exposure probability factors, in deference to Maynard's (2007) use of this as the only exposure factors, and therefore wanted this combination to be greater (55%) than the remaining factors that are task-specific (45%). This overall weighting is not entirely based on the relative risks presented in research for these factors due to the fact that this information is acknowledged as not being available in sufficient depth to make such a determination (Nasterlack et al. 2008; Tsuji et al. 2006; Holsapple et al. 2005). Therefore, IH expertise was utilized to make this relative risk delineation based on the decades of combined field practitioner experience for the factors culminating in exposure.

Opportunity for exposure (45 points)

For all of the discussion on the toxicological aspects of working with nanoparticles, the focus can now be given to the more classical nature of the traditional IH profession. Exposures and the potential for employee uptake are typically seen as a function of the length of the task at hand and the periodicity of where that task is performed. Taking on aspects of epidemiology and a statistical view of the potential for variance from the mean, the more the number of workers performing a given task, the higher the probability of exposure. Therefore, these three aspects relating to exposure opportunity were given an equal weighting with frequency of operation, duration of operation, and the number of employees performing each given 15% of the probability factors scoring.

Addressing expert opinion

Surface area

There was some professional consideration given as to whether total surface area should be considered an exposure characteristic or a severity characteristic. Total surface area was not included as a severity characteristic because all the other severity characteristics pertained to properties inherent to a given NM or PM and did not consider dosage or exposure. However, since particle size and particle shape are characteristics inherent to NM that would result in a greater total surface area, at the same mass concentration, these were included as severity parameters. Surface area relating to exposure characteristics is captured in the dustiness/mistiness scoring factor and is accounted for in its greater weighting for probability of exposure. Elevated dustiness/mistiness levels for a given activity will have a higher concentration of airborne nanoparticulate and a much higher surface area concentration than lower dustiness/mistiness levels. With dustiness/mistiness as such a heavily weighted scoring factor, especially with the potential for a lack of visual evidence to appropriately characterize this aspect, it is recommended for the evaluator to create their own decision matrix to decide whether they should make this a qualitative judgment or perhaps investing in a quantitative assessment specific to this input factor.

Dermal exposure

There were a few experts that questioned how dermal considerations were addressed in the design of the CB Nanotool. One issue was that the dustiness/mistiness input factor includes a design feature that defaults to "Extremely Unlikely" if there is no potential for airborne NM during a given process. It was mentioned during a third-party review of the CB Nanotool that this default appears to discount the potential for the dermal exposure route and therefore its relevancy (Ryman-Rasmussen et al. 2006). In actuality, the potential for dermal exposure and uptake through various external uptake routes (e.g., ocular, hair follicle) can be considered entirely influenced by highly dispersible nanoparticulate, affecting dermal exposure through both airborne routes as well as its deposition on working surfaces. If there is no airborne exposure, then dermal exposure is isolated to the source term, which can be controlled with gloves while handling the product. Another point of discussion was the weighting of the dermal toxicity parameters overall. As the research is indeterminate for the potential of dermal penetration of NM through intact skin, in question was the consideration of this route as an equivalent severity consideration. The equal weight of NM dermal toxicity was given to not only address this one aspect, but also in consideration of the other factors that encompass cutaneous toxicity in a manner that also includes the potential for absorption as well as penetration.

Frequency and duration

Some analysis was given toward the inclusion and weighting of the duration and frequency of a given task in determining the potential for exposure. As a primary reference in support of this CB approach for NM, Maynard (2007) considered dustiness and amount as the only factors to be considered within the exposure index. The weight to these two factors is given in protecting the employee first, regardless of the frequency and duration of a given task. In the CB Nanotool, the greatest weighting in the probability scoring is given to the dynamics of the source term—dustiness and amount—as these are the focus of the controls that are derived from the toolkits' application. However, the consideration of frequency and duration, in addition to number of employees potentially exposed, gives a practicality counterweight to the probability of exposure. Consideration of these additional factors was not seen as conflicting with the two primary factors, but rather supplementing them. That is, if a task takes a few minutes and is performed a couple of times in a year, this must also be given consideration in affecting the overall potential for exposure.

OEL of PM

Giving only 10% of the severity weight to a well researched, professionally derived, and science-based OEL for the PM was considered by some to be insufficient. In consideration of the relative value of the PM OEL, the authors of the CB Nanotool felt that its 10 points did not stand in isolation. The toxicological and epidemiological aspects that drive a PM's

OEL to lower and more conservative values are often the same as the identified critical effects (e.g., carcinogenicity, reproductive toxicity, mutagenicity, and dermal) which would each add an additional 5% to the severity weighting up to a theoretical maximum of 30%.

Number of employees

Experts at the ICOH Congress' fifth International CB Workshop questioned the 15% weighting given to the number of employees as part of the probability of exposure. The value of this weighting was agreed upon by the expert working group at LLNL, as there is a large working population at this national research laboratory. At LLNL, there can be a significant number of researchers working with NM as part of numerous projects, phases, and tasks at any given time that it deserved a comparable weighting to frequency and duration. It was decided that even with engineering controls potentially in place, the variability of individual working habits and approaches to NM research applications with a large research population supported this weighting. It should be noted that no risk assessment approach, especially those with a qualitative basis, should be adopted prima facie. The CB Nanotool was developed for the NM working parameters at LLNL and, although adopted by many organizations and even as a best practice (IRSST 2009), it should not be put directly into practice without consideration and evaluation given to the weighting of factors that may be pertinent to individual facilities. Therefore, this weighting factor may not be appropriate for research organization with only a few workers, and this weighting value may be distributed into other probability factors as deemed appropriate.

Uncertainty

One of the experts commented on the fact that through his numerous discussions with companies using NM in their processes, it appeared that the most common approach that is currently applied in The Netherlands is that no exposure to NM is accepted because of the uncertainty associated with NM. Similar sentiments were expressed during presentations of the CB Nanotool during the two aforementioned professional conferences. While the CB Nanotool, by assigning different levels of engineering controls based on RL, potentially allows some level of exposure for certain types of activities, the assignment of 75% of the rating score of high for "unknown" factors appeared to satisfy most experts in terms of erring on the safe side for relatively unknown materials and operations.

Validation

Appropriately, many experts have questioned the ability to develop the parameters to truly validate the pilot CB Nanotool. The problem is that there is a lack of a gold standard to accomplish this for NM. In practice, this question remains a major topic of discussion for chemical control CB strategies; however, publications have begun to fill this research need that is building confidence in the approach in the face of uncertainties (Zalk and Nelson 2008; Marquart et al. 2008; Tielemans et al. 2008). This question is more appropriately compared to the scarcity of validation publication for CB schemes utilized in the pharmacological industries. CB has been an accepted practice for the risk assessment and control of new and more potent pharmaceutical components and has been successfully in place within the industry for over a decade, though very little validation data has been presented in research publications (Farris et al. 2006; Naumann et al. 1996). Often in this industry, it is the recommended control that has been put in place that is monitored for its containment effectiveness using standardized, mock particulate (e.g., lactose) that have established analytical detection methods. In a similar manner, quantitative particle counters have been used in selected screening opportunities to compare rogue NM particle counts as compared to background levels. During the implementation and evaluation of the pilot CB Nanotool, this approach was used to facilitate the assignment of the appropriate dustiness/mistiness level to specific operations. The scenarios presented as case studies in Paik et al. (2008) focused on a sampling of representative and existing research and development (R&D) activities within the LLNL institutional safety document database. Prior to the existence of the CB Nanotool, expert IH advice was used to select the most appropriate controls for a given activity with NM. The IH would also utilize best practices such as the NIOSH "Approaches to Safe Nanotechnology" publication. Therefore, outcomes were directly compared with existing IH expertise which as close as we can come to a validating method without the existence of a gold standard. We provided this validation within the Paik et al. (2008) article and a good agreement was found at the time between the IH and the CB Nanotool. Since that time, many more applications were reviewed, and a much larger database for comparison has been developed and is presented below in Table 1. In addition, many more research articles in publication have been consulted, to make a formalized decision on our "pilot" determination, the validity of the findings, and parameters for refinement for the CB Nanotool in practice.

Further applications of the CB Nanotool

Despite the limitations presented, the CB Nanotool is a transparent and logical method. Although much research has been performed within the sciences relating to NM since the first publication of the tool (Paik et al. 2008), data on NM health effects is still limited and it is expected that this stream of information will continue to expand rapidly (Yang et al. 2008; Warheit et al. 2008; Hallock et al. 2008). Therefore, as specific studies are published, severity parameter scores that where once "unknown" can now be more accurately portrayed, and users of the tool can adjust their input and affect the severity score. More importantly, as one cannot control the pace of science, users of the CB Nanotool can immediately seek to address some of the parameters relating to the probability of exposure to reduce the final overall RL. For experts in the IH field, this is a common activity; however, for CB Nanotool users new to the exposure sciences, this is an essential learning opportunity in a simple and practical format. An additional 27 risk assessments with the CB Nanotool have been performed since the initial publication of the CB Nanotool, and the results and discussion are briefly discussed below.

Out of the 27 additional activities that were characterized, the CB Nanotool recommendation was equivalent to the existing controls for 16 of them, a higher level of control for eight of them, and a lower level of control for three of them. These data suggest that the CB Nanotool produced control recommendations that were generally equal to or in some cases more conservative than the existing controls that were implemented through expert IH judgment. The results were consistent with what the authors hoped to achieve through the tool, which was to develop a consistent approach that would generally err on the safe side, in light of the uncertainty associated with the health effects related to NMs.

Due to the novelty of the CB Nanotool, all the risk assessments with the CB Nanotool that are presented in Table 1 were completed by field IHs in conjunction with the Nanotechnology Safety SME. In reviewing an operation for the first time to collect information required for the risk assessment, the Nanotechnology SME accompanied the field IH in interviewing the workers and touring the work location. A "Nanomaterial Information Form" was developed soon after the CB Nanotool was developed to facilitate consistency in collecting the required information for entry into the CB Nanotool. The data inputs for the specific activities were resolved through face-to-face discussions between the field IH and Nanotechnology Safety SME. It was apparent from this process that while some questions did come up (e.g., is the duration of the activity based on the duration of direct worker interaction with the exposed NM or is it based on the duration of the activity itself, contained or otherwise?), the CB Nanotool was fairly easy to use and thorough instructions were included in LLNL's institutional NM safety document. Therefore, taken holistically, the entire process was considered valuable, not just in the utility of the CB Nanotool, but in the logical, cooperative, and educational process behind the creation of the qualitative risk assessment.

The process of implementing the CB Nanotool has been an excellent educational opportunity for the IH as well as the user. Both groups can benefit in that the individual parameters to be considered when scoring a task or procedure during its risk assessment are effective bases for risk communication by the IH and user alike. One application of the CB Nanotool was the evaluation of the grinding and shaping of a NM product where the RL outcome presented a control that was too expensive to implement, given the facility's limitations. The employee assisting the IH in filling out the CB Nanotool's score parameters immediately began considering which of the probability factors he could adjust for the task to lower the RL to the existing controls in place. Although it was possible to consider reducing the amount of NM used during the task, as well as the frequency of the operation, the discussion of risk pointed the IH to

Table 1 Additional activities assessed by the CB Nanotool

Activity number	Scenario description	Name or description of nanomaterial	Current engineering control recommended by IH expert	Severity band	Probability band	Overall risk level without controls	Recommended engineering control based on CB Nanotool risk level	Upgrade engineering control?
1	Synthesis of metal oxide nanowires on substrates within a tube furnace	ZnO, SnO_2, TiO_2, $PBZrTiO_3$, $BaTiO_3$, and $SrTiO_3$ nanowires	Containment	High	Extremely unlikely	RL2	Fume hood or local exhaust ventilation	No
2	Synthesis of silver and copper oxide nanoparticles	Ag oxide nanoparticles, Cu oxide nanoparticles	Fume hood or local exhaust ventilation	High	Less likely	RL2	Fume hood or local exhaust ventilation	No
3	Activities related to operating and maintaining a vertical tube quench furnace and horizontal tube furnace	Ag, Cu, Ni, brass, Au and Pt nanoparticles	Containment	High	Likely	RL3	Containment	No
4	Deposition of liquid-suspended nanoparticles onto surfaces using low voltage electric fields	Polymer latex, gold, platinum, palladium nanoparticles	General ventilation	Medium	Extremely unlikely	RL1	General ventilation	No
5	Preparation of samples. Activities include cutting, slicing, grinding, lapping, polishing, chemical etching, electrochemical polishing and ion etching	Carbon black, Al oxide, Mg oxide, polycrystalline diamond suspension, colloidal silica, Pd powder, carbon nanotubes	Fume hood or local exhaust ventilation	Medium	Extremely unlikely	RL1	General ventilation	No
6	Water is poured into container with liquid-suspended carbon nanotubes	Carbon nanotubes	Fume hood or local exhaust ventilation	High	Extremely unlikely	RL2	Fume hood or local exhaust ventilation	No
7	Gold nanoparticles used to test carbon nanotube filter	Gold nanoparticles	General ventilation	Medium	Extremely unlikely	RL1	General ventilation	No
8	Mixing polystyrene spheres with buffer, etching nanostructures onto semiconductors	Polystyrene spheres, nanostructures	General ventilation	Medium	Extremely unlikely	RL1	General ventilation	No
9	Addition of quantum dots onto porous glass	Cadmium selenide, lead sulfide	Fume hood or local exhaust ventilation	High	Extremely unlikely	RL2	Fume hood or local exhaust ventilation	No
10	Growth of palladium nanocatalyst	Palladium nanocatalyst	Fume hood or local exhaust ventilation	High	Less likely	RL2	Fume hood or local exhaust ventilation	No
11	Sample preparation and characterization	Gold, silver nanoparticles	General ventilation	Medium	Less likely	RL1	General ventilation	No

Table 1 continued

Activity number	Scenario description	Name or description of nanomaterial	Current engineering control recommended by IH expert	Severity band	Probability band	Overall risk level without controls	Recommended engineering control based on CB Nanotool risk level	Upgrade engineering control?
12	Sample preparation and characterization	Iron oxide, silicon dioxide, aluminum oxide, carbon, ceramic aerogels and nanopowders	Fume hood or local exhaust ventilation	Medium	Less likely	RL1	General ventilation	No
13	Synthesis of aerogel	Zinc, titanium nanoparticles	General ventilation	Medium	Extremely unlikely	RL1	General ventilation	No
14	Synthesis of aerogel	Silica, iron, chromium, copper, zinc nanoparticles	General ventilation	Medium	Extremely unlikely	RL1	General ventilation	No
15	Synthesis and optical characterization of nanoparticles	CdSe quantum dots, germanium quantum dots, iron oxide, gold, lead sulfide nanoparticles	General ventilation	High	Less likely	RL2	Fume hood or local exhaust ventilation	Yes
16	Sample preparation and characterization of CdSe nanodots	CdSe quantum dots	Fume hood or local exhaust ventilation	High	Less likely	RL2	Fume hood or local exhaust ventilation	No
17	Sample preparation and characterization of carbon diamonoids	Carbon diamonoids	Fume hood or local exhaust ventilation	High	Less likely	RL2	Fume hood or local exhaust ventilation	No
18	Sample preparation and characterization using laser microscopy	Gold, silver nanoparticles	General ventilation	High	Less likely	RL2	Fume hood or local exhaust ventilation	Yes
19	Preparation of nanofoam sample for microscopy	Gold, copper, aluminum, nickel nanoparticles	General ventilation	High	Extremely unlikely	RL2	Fume hood or local exhaust ventilation	Yes
20	Preparation of carbon nanotubes sample for microscopy	Carbon nanotubes	General ventilation	High	Extremely unlikely	RL2	Fume hood or local exhaust ventilation	Yes
21	Machining (e.g., turning, milling) of aerogels and nanofoams for target assembly	Silica aerogels, tantulum aerogels, metal nanofoams (copper, gold), carbon nanofoams	Fume hood or local exhaust ventilation	High	Less likely	RL2	Fume hood or local exhaust ventilation	No
22	Site wide waste sampling activities	Various	General ventilation	High	Less likely	RL2	Fume hood or local exhaust ventilation	Yes
23	Waste accumulation area activities, including waste management, waste packaging, etc.	Various	General ventilation	High	Less likely	RL2	Fume hood or local exhaust ventilation	Yes

Table 1 continued

Activity number	Scenario description	Name or description of nanomaterial	Current engineering control recommended by IH expert	Severity band	Probability band	Overall risk level without controls	Recommended engineering control based on CB Nanotool risk level	Upgrade engineering control?
24	Analysis of nanomaterial waste samples in the laboratory	Various	General ventilation	High	Less likely	RL2	Fume hood or local exhaust ventilation	Yes
25	Radioactive and Hazardous Waste Management field tech activities, including waste management, waste packaging, waste sampling, etc.	Various	General ventilation	High	Less likely	RL2	Fume hood or local exhaust ventilation	Yes
26	Purification and functionalization of carbon nanotubes	Carbon nanotubes	Fume hood or local exhaust ventilation	High	Less likely	RL2	Fume hood or local exhaust ventilation	No
27	Purification and functionalization of carbon nanotubes	Carbon nanotubes	Fume hood or local exhaust ventilation	High	Extremely unlikely	RL2	Fume hood or local exhaust ventilation	No

offer an alternative reduction factor. The weighting of the dustiness/mistiness was seen as an opportunity to offer a more quantitative evaluation rather then the qualitative one at the time. A condensation nuclei counter (P-trak, TSI, Inc) was used for this operation to determine if any particles in the 20–1,000 nm range were created in excess of background levels. This selective use of a quantitative measuring device was the most appropriate investment in this task's evaluation from the IH's point of view and the results determined that the existing controls were indeed appropriate in limiting employee exposures to background levels. More importantly, this standardized language for the discussion of risk between experts and non-experts opened the door for a greater understanding of the potential hazards during this activity and the employees were very grateful to receive this information.

Discussion

The CB Nanotool was not intended to be a static tool for a given task or procedure. This can be seen both in the valuation and utility of working with unknown aspects of risk factors as well as the relative values of each component within the CB Nanotool. This begins with an individual, task-specific risk assessment that was designed in a way that allows the user to have the opportunity to revisit their evaluation once more knowledge is obtained on any or all of the components deemed "unknown" in the initial qualitative evaluation. In the same manner, it is explicitly noted in the original manuscript that the tool itself can be updated in terms of any and all of its individual components as research and process knowledge is further developed. It was for this reason that the CB Nanotool was considered a "pilot" toolkit in its initial form as the relative importance of each of the implicit factors and their relative values may change as more research on the adverse effects of NM becomes more standardized in publications. Within this discussion, an effort was made to take the latest information available into account and offer opinions on what the next version of the CB Nanotool might look like as part of an overall risk management approach.

Risk management of operations involving nanoparticles primarily is managing exposure scenarios to these particles. Managing means that these scenarios are known and effective barriers are installed to control exposures. Slowly, as information becomes available on exposure scenarios, the quality of barriers and the population at risk will vary, both in production and research facilities (see for instance Bałazy et al. 2006; Borm et al. 2008; Paik et al. 2008; Schulte et al. 2008). The importance of a sound risk management approach is obvious. It is not only the public's attention serving as a driver, but also the necessity to provide adequate protection to workers in laboratories and production environments. The CB Nanotool is an instrument that can facilitate risk management, but there are obvious limitations to the tool. One of them is the relevant factors and the scores of these factors, determining the severity and probability, and hence, overall risk level. These factors and scores refer to the present state-of-the-art in characterizing risks from nanoparticle exposure. However, the relative importance of one factor compared to another may change, as more knowledge on the adverse effects of nanoparticles becomes available. Another limitation of CB in general is the inability to address process changes, such as automation, elimination of transport routes, etc. These process changes are dominant factors in the observed decline of exposure levels throughout the industry (Kromhout and Vermeulen 2000).

size, and surface characteristics including surface electrostatic charge on inhalation leading to higher deposition rates (Yang et al. 2008). Additional research has shown when the exposed mass of selected NM of the same size are held constant, it is the structure (e.g. anatase > rutile) that is the toxic differential and that surface area alone is not enough to address pulmonary exposure (Liao et al. 2008; Warheit et al. 2007b). It can be noted that there is no evidence on ingestion as a route of exposure and dermal penetration remains in study (Warheit et al. 2007a). A toxicological characteristic for NM that has been noticed in the recent research, in addition to those already mentioned in the original CB Nanotool publication, is the potential for NM be considered asthmagenic (Hallock et al. 2008; Orthen 2008). As the asthmagenic potential of the PM is also well researched, it was decided that "asthmagen" should be added to the toxicity scoring of the CB Nanotool for both NM and PM; however, the scoring would be divided amongst these toxicity factors equally and no additional weighting would be given (see Table 2) to the overall weighting for toxicity. In addition, as research on NM as a whole appears to create more questions than it answers, it seemed appropriate that the weighting for PM OELs should be adjusted as follows with two orders of magnitude given between the scoring factors:

$<10\ \mu g\ m^{-3} = 10$ points

$10\ \mu g\ m^{-3} - 100\ \mu g\ m^{-3} = 5$ points

$101\ \mu g\ m^{-3} - 1\ mg\ m^{-3} = 2.5$ points

$> 1\ mg\ m^{-3} = 0$ points

Unknown = 7.5 points

Severity factors

In consideration of the health effects potentially related to NM and the environmental safety and health (ES&H) protocol necessary to perform appropriate risk assessments, the majority of the physicochemical aspects appear to have received a further confirmation (Warheit et al. 2008; Yang et al. 2008). There remains a strong emphasis on the particle surface chemistry, surface area, solubility, particle number, shape, and its biological availability for translocation (Yang et al. 2008; Warheit et al. 2007a). Extrapulmonary translocation varies in degree of toxicological consequence due to differences in chemical composition, particle

Other than these moderate changes, the current research studies have served to confirm not only the CB Nanotool's risk assessment approach, but also its intent to provide a broad characterization of potential NM toxicological considerations. Warheit et al. (2008) have emphasized that as more and more studies are being conducted, there is further confirmation that enhanced toxicity is found for NM as had been earlier postulated and an increasing variation of physiochemical effects from the growing number of nanoparticulate materials is being observed. This points to an even greater need for standardization for toxicological characterization studies. The CB Nanotool would fit well within

Table 2 Severity and probability factors and maximum points per factor

Severity factor	Maximum pts (pilot)	Maximum pts (revised)	Maximum severity score
Surface chemistry (NM)	10	10	100
Particle shape (NM)	10	10	
Particle diameter (NM)	10	10	
Solubility (NM)	10	10	
Carcinogenicity (NM)	7.5	**6**	
Reproductive toxicity (NM)	7.5	**6**	
Mutagenicity (NM)	7.5	**6**	
Dermal toxicity (NM)	7.5	**6**	
Asthmagen (NM)	N/A	**6**	
Toxicity (PM)	10	10	
Carcinogenicity (PM)	5	**4**	
Reproductive toxicity (PM)	5	**4**	
Mutagenicity (PM)	5	**4**	
Dermal hazard (PM)	5	**4**	
Asthmagen (PM)	N/A	**4**	

Probability factor	Maximum pts (pilot)	Maximum pts (revised)	Maximum probability score
Estimated amount of nanomaterial	25	25	100
Dustiness/mistiness	30	30	
Number of employees with similar exposure	15	15	
Frequency of operation	15	15	
Duration of operation	15	15	

NM Nanomaterial, *PM* Parent Material

Bold values indicate Pilot Nanotool revisions resulting from this article's evaluation

the framework of a database that would result from such standardization.

Probability factors

All the research presented above confirms the importance given to the CB Nanotool's weighting of both dustiness/mistiness and estimated amount of chemical used. The same logic for offering a higher score relating to the NM's ability to become airborne has been given even greater emphasis in the more recent publications. The physicochemical focus remains on the biologically available surface area and its ability to translocate systemically. The unique properties of a given NM, inherent in its design and aiding its intended utility, also seem to afford an elevated, persistent, and comprehensive ES&H risk potential. Therefore, the CB Nanotool's conservative approach to capture and weight the factors that reflect the probability for a NM to become airborne and persist in the work environment relative to a given task's exposure potential appear to remain consistent with the pervasive expert call for a precautionary approach in implementing controls and worker protection (Yang et al. 2008; Warheit et al. 2008; Hallock et al. 2008; Orthen 2008; Stern and McNeil 2008).

Validation

A high level of consistency has been found when comparing the CB Nanotool RL outcomes to expert IH recommendations. It can be seen that there is a tendency for the CB Nanotool's qualitative risk assessment approach to err toward the conservative at times; however, IH experts also agree that it is better to err toward over-control rather than under-control (Zalk and Nelson 2008). An important question in testing the validity of the toolkit is to ascertain the most appropriate comparison to the tool's RL outcomes. For each of the examples given, there is an existing control in place as recommended by an expert IH. In all of the examples given, quantitative measurements were not taken to determine the initial control in place, just professional evaluation and expert judgment. It can be argued that as the CB Nanotool gives a research derived scoring parameter in a comprehensive and structured manner, the broad-based qualitative input is more valuable then an expert's judgmental opinion in the absence of an OEL for comparison. If for no other reason, this non-quantitative expert opinion is at best subjective and therefore highly dependent on the IH's NM expertise in particular. Perhaps, the best comparison is for an IH review of tasks using chemicals that have no OEL, which experts tend to agree is the most appropriate application of CB toolkits (ACGIH 2008; Zalk and Nelson 2008).

Controls

Although the control outcomes themselves do not require adjustment, further research has shown an optimum face velocity for work with dry NM within hoods. The use of a local enclosure within a hood can minimize powder dispersion during handling processes. It should be recommended to avoid higher face velocities when working in hoods with dry powder forms of NM, with an optimum face velocity range of 100 fpm, as some light density NM during transfer operations has been seen to escape at low or high face velocities (Hallock et al. 2008).

NM in industry

Consideration is now being given for a CB Nanotool approach for NM within industry as opposed to R&D. In good part, this scaling production volume can also find a counterpart in the pharmaceutical industry which also utilizes an analogous CB approach. For larger scale processes with NM in manufacturing, with such a relatively uncertain toxicological footing, the input factors would require a more appropriate relative value and the control options are potentially more robust and that may lead to additional expense. First and foremost, the mass utilized will more likely be orders of magnitude greater than the mass typically used in R&D applications and therefore the primary factor affecting variations in the probability of exposure among the different activities will be dustiness/mistiness. In order to aid in consistency for the scoring inputs of an industrial CB Nanotool strategy, there should be process-specific information that is uniform to manufacturing. As proposed in research, there should be task-based "airborne" factors derived by industry for standardization (Schneider 2008). The utility of "dustiness" within a set range is already a uniform application in many CB strategies and exposure models (Tielemans et al. 2008; Zalk and Nelson 2008). In addition, quantitative evaluations of control effectiveness should be considered an essential part of the validation effort. However, perhaps in a manufacturing process, there should also be the expectation of Material Safety Data Sheets (MSDSs) for the product used and that the MSDSs would be designed to communicate both NM and PM parameters that could be directly transferred into an industrial CB Nanotool.

MSDS improvement

The majority of MSDSs for NM, if they are available, provide most of their ES&H information based on the bulk PM. The opportunity for MSDSs to become an integral part of NM risk assessment, exposure prevention, and risk management needs to be addressed. The majority of chemical control CB strategies utilize R-phrases as inputs to the toolkit to derive appropriate controls and reduction of work-related exposures (Zalk and Nelson 2008). The majority of NM experts agree that research parameters affording comparisons and sharing of findings is a primary requirement for controlling exposures (Warheit et al. 2008; Yang et al. 2008, Liao et al. 2008). In practice, the toxicological information available on nanoparticulates is minimal and will require deference toward "unknown" for an individual NM property until this standardization occurs. The real question is not when will this information be put forward, but whether it will be put forth in a consistent manner that will be useful and interpretable for future users of the CB Nanotool. At present, the research publications that are in circulation seem to be more appropriate for expert dissemination and not necessarily for health and safety professionals in general, let alone managers and technicians. The request for uniformity of descriptive information about NM, captured in a database of set research parameters, should also be listed on MSDSs, which would afford users of the CB Nanotool the latest and most accurate input factors for product appropriate hazard information that would lead to a process specific risk assessment.

Conclusion

The fact that the majority of NM users in industry are not performing even the most basic risk assessment of their product in use, as indicated in the aforementioned recent survey, is unconscionable and must come to an end. CB strategies are known over decades to offer a simplified control of worker exposures when there is an absence of firm toxicological and exposure information and the nanotechnology industry fits this classification perfectly. The overwhelming uncertainties of work-related health risks posed by NM have appropriately led many experts to suggest CB as a solution for these issues. The CB Nanotool was created to fulfill this request. In order to do this, an expert group of IH professionals, NM and aerosol specialists, and an excellent depth of CB experience have sought to bring this request into the hands of practitioners. As presented, the CB Nanotool has been developed, implemented, and been proven to afford a qualitative risk assessment toward the control of nanoparticle exposures. The international use of the CB Nanotool reflects on its need and its possibilities, but the expansion of its use will assist in ensuring that risk assessments by NM users are both accessible and affordable. While minor changes considered necessary to adapt the CB Nanotool to the growing research publications have been presented, these changes are not expected to result in risk levels that are significantly different from those produced by the CB Nanotool in its original form.

The need for standardization of toxicological parameters has also been emphasized by nanotoxicological researchers. This is to afford better utility and consistency of research with NM as their use and exponential growth in application continue. A standardized database of toxicological research findings should be harnessed and presented in a format, preferably captured in MSDSs, feeding directly into the CB Nanotool severity and probability risk matrix. Making the latest research available for experts and practitioners alike will play an important role in the protection of workers in the nanotechnology industries. This study's evaluation of the CB Nanotool, its structure, weighting of risks, utility for exposure mitigation, and improvements place the CB Nanotool in the middle of directing the research still to come, maximizing its effectiveness for all those involved in the nanotechnology industries. It should be recognized that CB toolkits must always be used with some degree of caution. The different factors considered, weighted, and influencing the overall risk levels and control bands are determined as educated "guesses" as to factor importance and range delineation. Any CB toolkit requires frequent use, validation, and evaluation of recommended control effectiveness. The authors, therefore, strongly encourage an active dialog within the IH community and further utilization of this or other similar tools for a wide range of applications, as these efforts will undoubtedly improve and refine the tool.

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