Occupational Risk Assessment of Engineered Nanomaterials by Control Banding Method in Chemistry Laboratories

Rasoul Yarahmadi[1], Reza Abbaszadeh Dizaji[2*], Ali Asgar Farshad[3], Fatemeh Teimuri[4],Mohammad soleimani[5]

[1]Assistant Professor of Occupational Health, Faculty of Health, Tehran University of Medical Sciences, occupational health research center, Tehran, Iran
[2*]MPH,Faculty of Health, Tehran University of Medical Sciencies,Tehran,Iran,Tel:09141476720,
[3]Professor of Occupational Health, Faculty of Health, Tehran University of Medical Sciences, occupational health research center, Tehran, Iran
[4]Biotechnology Expert, Faculty of Chemical Engineering Modares University,Tehran, Iran
[5]Mohammad soleimani, PhD Student in Environment, Urmia University of medical Sciences, Jahad Ave., Urmia, Iran
*Corresponding author: popsreza@yahoo.com

Abstract: The field of nanotechnology is one of the fastest growing areas of research and technology and numerous workers currently are potentially exposed to engineered nanomaterials (ENMs) in research and industrial sitting. furthermore. initial studies show that toxicity of ENMs is significantly interrelated with emerging physicochemical characteristics of these materials, and may be adverse affects on human health. **Aims:** Evaluation of physicochemical properties and toxicology and exposure of employees to determine the level of risk by control banding(CB) method. **Methods:** This research is a descriptive and cross-sectional study of exposure to ENMs in 20 staff members and students involved in five different activities of production and consumption of ENMs. The level of risk factors was determined by a checklist as qualitative assessment of risk based on CB method. Data analysis was performed using Excel software. **Results:** The study show that highest level of severity index and probability score of risk factors about the process of identifying functional groups of carbon nanotubes are 60 and 67.5, respectively, while the lowest scores for producing silver nanoparticles are 50, 41.25 out of 100. **Conclusions :** Application of CB method showed that to reduce risk level of exposed to, ENMs, control measures focus on reducing probability score. Thus, some mechanisms, such as engineering controls, replacing hazardous processes and materials with safer ones, and administrative controls may be offered to reduce amount of generated dust and number of workers exposed to ENMs**.**

[Rasoul Yarahmadi, Reza Abbaszadeh Dizaji, Ali Asgar Farshad, Fatemeh Teimuri, Mohammad soleimani. **Occupational Risk Assessment of Engineered Nanomaterials by Control Banding Method in Chemistry Laboratories.** *J Am Sci* 2013;9(6s):42-47]. (ISSN: 1545-1003). http://www.jofamericanscience.org. 5

Key Words: engineered nanomaterials ; occupational Risk Assessment;Control Banding

Introduction

Nanotechnology is leading to the development in many field, of new materials and devices in many fields that demonstrate nanostructure-dependent properties. and development of new products containing engineered nanomaterials (ENMs), is an emerging multidisciplinary technology that involves the synthesies of molecules in the nanoscale size range. ENMs are materials with structural features having at least one dimension in a size range between one and a hundred nanometers. However, concern has been expressed that these same properties may present unique challenges to addressing potential health impact[1,2,3]. Studies show a significant relationship among toxicity of ENMs and their emerging physicochemical properties (i.e., size and shape, aggregation status, surface coating and solubility, etc). These nano-scale properties bring about new behaviors and lead to chemical and physical changes in these materials and make them act differently in biological systems, which may inflict undesirable affects on human health[3,4]. Experimental studies in rodents and cell cultures have shown that the toxicity of nanoparticles(NPs) is greater than that of the same mass of larger paticles of similar chemical composition[5]. Studies show that Discrete NPs (35-37 nm median diameter) that deposit in the nasal region may be able to enter the brain by translocation along the olfactory nerve, as was observed in rates [6]. The researchers reported in an in vitro study that single wall carbon nanotubes (SWCNT) cause dose-response and decrease cellular viability. They also induce oxidative stress in biomarkers and lead to significant increase of peroxide lipid in keratin epithelial cells. The authors revealed that exposure to gross SWCNT can increase pulmonary toxicity in workers exposed to oxidative stress [7,8,9]. At present, numerous workers currently are potentially exposed to ENMs in research and manufacturing operations[10]. Therefore Risk assessment is an important component in the development of effective risk management strategies in nanotechnology field. Toxicology, epidemiology, and workplace exposure data are very limited for ENMs [11]. The lack of information on the toxicity of many NPs as well as on the exposure level, together with a lack of specific standards, often makes us unable to quantify the risk in a situation involving many uncertainties[12]. Therefore Control Banding (CB) strategies offer simplified processes for controlling worker exposures in the absence of firm toxicology and exposure information.The CB Nanotool used internationally, was developed to conduct qualitative risk assessment to control NPs 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 Nanotools severity and probability risk matrix, therefore enhancing the protection of nanotechnology industry workers[13].

The researchers presented a conceptual of CB model using impact and exposure indices. The proposed model is a combination of physical and chemical structures, toxicology of NPs (shape, size, surface activity, solubility, toxicity and carcinogenicity of NPs and nanoparents) with exposure availability (dustiness, and estimated amount of NPs used during the task). These indices are linked to bands with corresponding control approaches. The control approaches are a grouping of three levels of engineering controls, based on sound Industrial Hygienist (IH) principal; general ventilation, fume hoods or local exhaust ventilation, and containment. The fourth level is seek specialist advice referring to specialist IH expertise. Therefore Special controlling devices approved by industrial hygiene was used for the 4th level. CB is basically used for determining total levels of risk for applicable assessments in workplaces[13].

Currently, most guidance documents and exposure studies to date have focused primarily on industrial settings, but academic research settings present their own challenges that also need to be addressed. Much of the initial research and development (R&D) in nanotechnology is still performed in academic research laboratories. In academic laboratories, the quantity of ENMs used tends to be less than those used in industry, but the variety of ENMs used tends to be more diverse. As a result, the potential hazards are also more diverse and exposure monitoring is more challenging. Furthermore, academic practices tend to be less standardized and to vary more from lab to lab and from day to day than typical industrial processes. This means that engineering controls which are commonly used in industry may not be practical to apply in academic laboratory research settings. The nature of research and training in academic institutions dictates that new students and employees with various backgrounds and levels of training are regularly being introduced into the many diverse laboratory settings. Undergraduate student researchers, graduate students and other laboratory personnel often have minimal formal safety training or are lacking the latest hazard information about such new technological developments. All of these factors make a simple adoption or application of risk assessment and standardized industrial best practices for working with ENMs in laboratories[14].

Thus, the present study undertakes to collect data about physicochemical and toxicological characteristics of NPs and nanoparents and conditions of exposure in laboratories so that it can perform a Occupational risk assessment on ENMs by CB method based on a controlling approach.

Methods

This research is a descriptive and cross-sectional study of exposure to ENMs in 20 staff members and students involved in five different activities of ENMs production and consumption in a Faculty of Chemical Engineering. For this purpose, a checklist of qualitative risk assessment of ENMs with CB method was used in biotechnology, isolation and instrumental analysis laboratories.

Risk assessment team included two staff members in charge of laboratories and an occupational health specialist. An introductory session about the concepts of risk, risk assessment and CB method was hold to familiarize the team with risk assessment method. Then, it was arranged by the agreement of team members to perform the assessment and evaluation. The existing valid checklists and scientific resources were used for preparing the checklist [12,13,14,15,16]. Using the checklist, tables designed for recording risk factors data related to severity and probability of ENMs for any one task of Table 1 and Table 2, were divided and numbered[12,13]. Based on the total scores resulting from risk factors severity and probability, total level of risk was obtained and presented in Figure 1(13). Based on existing grading system, using raw forms and tables for the five selected activities, the above method was completed in the laboratories of the Faculty of Chemical Engineering and was analyzed and classified using Excel.

Results

As seen in Table 3, results of risk assessment with CB method provide initial description of activities in chemistry laboratories, including description of the activity, name and characteristics of ENMs, class of activity, and current controls. Based on our analysis, the highest score of risk factor severity was 60, which was associated with the process of identifying functional groups of fiber-type carbon nanotubes which ranging in size between 1-10 nm by Fourier transform infrared spectroscopy(FTIR). Activities performed in this process include handling, grinding the particles into powder and making tablets (Table 4).

The lowest score of risk factor severity was found to be 50 and was associated with production of spherical silver NPs with the size of 45 nm which are generated through chemical renewal of silver nitrate in liquid phase in suspension (Table 4). Results of toxicity of nanoparents, as presented in Table 5, show that larger particles (carbons, sulfate calcium, and silver) possess some sort of occupational exposure level. However, this amount of occupational exposure level varies between them, with silver having the lowest (10 mg/m3) and sulfate calcium having the highest (10000 mg/m3), while it is 2000 mg/m3 for carbon nanoparents. Also, results of toxicological studies and material safety data sheet reveal that only silver and sulfate calcium nanoparents induce risks of skin toxicity, while they impose no risks of toxicity in terms of carcinogens, mutagenesis and Reproductive. The above risks were not observed for carbon nanoparents (Table 5). The lowest and the highest scores of probability for production of silver NPs through chemical renewal of silver nitrate and the process of identifying functional groups of carbon nanotubes were obtained to be 41.25 and 67.5, respectively (Table 6). Results also show that the amount of generated dust (dustiness), scoring 30, is the most influential factor on determining risk level of probability score. Nevertheless, powder and gas phase NPs generate more amount of dustiness, as compared to liquid and suspension phase. Risk level is very high for the former, while it is medium for the latter. The second most influential factor on probability score is the synthesis of sulfate calcium NPs and PS/caso4 nanocomposite with consumption level of 100 mg and it scores 25 (Table 6). This leads to higher risk level of probability score as compared to activities 1 and 2. From among scores of severity indices, the highest unknown risk level score was obtained for toxicological characteristics and information of NPs throughout production and consumption processes of these NPs, entailing carcinogens, Reproductive risks, mutagenesis, and skin hazards(Table 4). The score of one of physiochemical characteristics, i.e., chemical surface of NPs, for generating free radicals was found to be unknown. Number of unknown risk severity score for each activity and process were 5. The score obtained for unknown cases for each activity and process were 30.

The highest severity score for physiochemical characteristics was associated with the process of identifying functional groups of carbon nanotubes, which had the form of a fiber, insoluble and sized among 1-10 nanometer. Compared to other larger and spherical processes considered for NPs, this process causes higher risks (Table 6). As can be seen in Table 6 results of evaluating the four activities demonstrate that risk level of activities 1,3,4,5 is high (RL3), while it is low for activity 2 (RL1). Control methods applied in the study includes general ventilation, three cases of laboratory chemical hood, and a case of bio-safety cabinet for the whole process. From among these control methods, four activities need to be promoted in terms of engineering controls.

Probability Score

Severity score	Extremely Unlikely (0-25)	Less Likely (26-50)	Likely (51-75)	Probable (76-100)
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. RL matrix as a function of severity and probability. Control bands are based on overall RL
Control bands:
RL1: General Ventilation
RL2: Fume hoods or local exhaust ventilation
RL3: Containment
RL4: Seek specialist advice

Discussion

A comparison of scores of risk factors severity in the activities under study shows the highest score of 60 for activity 4, which includes fiber-type carbon nanotubes (1-10 nm), and the lowest score of 50 for activity 2, including spherical silver NPs (45 nm). This signifies that shape and size of NPs (Table 4), as compared to toxicity characteristics of nanoparents (Table 5), are more influential in classifying level of severity. The results are in agreement with findings of other studies on effective role of size, shape, solubility and surface area of NPs on toxicity level of NPs [17,18]. From among scores of severity indices, the highest unknown risk level score was obtained for toxicological characteristics and information of NPs throughout production and consumption processes of these NPs, entailing carcinogenesis, Reproductive risks, mutagenesis, and skin hazards. The score of one of physiochemical characteristics, i.e. chemical surface of NPs, for generating free radicals was found to be unknown. Number of unknown risk severity score for each activity and process were 5. The score obtained for unknown cases for each activity and process were 30. This is in agreement with findings of other studies who performed a risk assessment of NPs with CB method on 5 activities concerned with NPs in laboratories and research centers. Similarly, toxicological score obtained in their study was unknown(15). It implies that toxicological information and findings and effects of ENMs in humans and biological systems are not as abundant as physiochemical information. However, the trend to conduct toxicological studies is on the increase. The highest risk factor of probability score of 67.5 was obtained for activity 4, including carbon nanotubes, and the lowest risk level of probability score of 41.25 was obtained for activity 2, which includes silver NPs generated by chemical renewal method (Table 6). Amount generated dust (dustiness), number of operations, operating time in shift duration had effects to increase probability score in activity 4.

Table 1: Severity index of NPs based on assessment

	Low	Medium	Unknown	High
Surface chemistry, reactivity and capacity to induce free radicals	0	5	7.5	10
Shape of the NPs	0 if spherical or compact	5 if different shapes	7.5	10 if tubular or fibrous
Diameter of the NPs	0 if 40 à 100 nm	5 if 11-40 nm	7.5	10 if 1 à 10 nm
Solubility of the NPs		5 NP soluble	7.5	10 NP insoluble
Carcinogenicity of the NPs	0 not carcinogen		5.625	7.5 potential
Reproductive toxicity of the NPs	0 no risk		5.625	7.5 with risk
Mutagenicity of the NPs	0 no		5.625	7.5 yes
Dermal toxicity of the NPs	0 non toxic		5.625	7.5 toxic to the skin
Toxicity of the parent material *	2.5 if TWA from 11 to 100 μg/m3	5 If TWA from 2 to 10 μg/m3	7.5	10 if TWA from 0 to 1 μg/m3
Carcinogenicity of the parent material	0 not carcinogen		3.75	5 carcinogen
Reproductive toxicity of the parent material	0 non toxic		3.75	5 toxic
Mutagenicity of the parent material	0 no		3.75	5 yes
Dermal toxicity of the parent material	0 no		3.75	5 yes

* The parent product refers to the product of the same chemical composition but of larger size for which standards often exist. The score is 0 if the time-weighted average exposure value (TWA) is greater than 100 μg/m3.

Table 2: the probability score based on assessment

	Low	Medium	*Unknown*	High
Estimated amount of ENMs used during the task	6.25 if < 10 mg	12,5 if 11 to 100 mg	18.75	25 when > 100 mg
Dustiness/mistiness *	7.5	15	22.5	30
Number of employees with similar exposure **	5 if 6-10	10 if 11-15	11.25	15 if >15
Frequency of operations	5 less than monthly	10 weekly	11.25	15 daily
Duration of operations ***	5 30 to 60 minutes	10 1 to 4 hours	11.25	15 if > 4 hours

* The dust level can be more easily determined by using a condensation particle counter, by knowing about the process, by observing the work surface contamination and the state of the NPs (powders or suspensions).** A score of 0 is given for 5 employees or less. *** A score of 0 is given for less than 30 minutes.

Dustiness was found to be the most influential factor in increasing probability score in activity 4 throughout all activities, except activity 5(Table 6).

Conclusion

The present study show that qualitative risk assessment with CB method is a simple, affordable and comprehensive way for assessment risk. The most important risk factors of NPs in determining risk level (nano processes) were found to be amount of generated dust and the amount of materials used in the processes, respectively. Risk mitigation in NPs and potential control measures (engineering and administrative) focus on reducing the level of probability. As regards the inherent potential of NPs (impracticality of reducing severity), there are some factors that covertly contribute to durability of risks (residual risks) in laboratories, though controlling measures are always at place. Thus, some mechanisms, such as engineering control methods, replacing hazardous processes and materials with safer ones, and reducing time and number of workers exposed to ENMs, a shift from dry processing to wet processing, physical transformation of ENMs from powder and aerosol to suspended state in liquid, paste or composite, administrative controls and use of personal protective equipment may be offered in order to reduce amount of dustiness and number of workers

Table 3: results of Nanotechnology activity description

Activity number	Scenario description(free text)	Name or description of ENMs	CAS#	Activity classification	Current engineering control
1	Extra-cellular production of silver NPs by Fusarium oxysporum fungus	Spherical silver NPs with an average diameter of 20 nm	7440-22-4	Production of NPs in the liquid phase and Suspension	BIOSAFETY CABINET
2	Synthesis of silver NPs with revival of Chemical (silver nitrate)in the presence of methyl trimethoxy silane (MTMs), metallic tin powder as reducing agent in water at room temperature	Spherical silver NPs with an average diameter of 45 nm	7440-22-4	Synthesis of NPs in the liquid phase and Suspension	Laboratory Chemical Hood
3	Synthesis of NPsof calcium sulfate using chemical reaction between the two sources of sulfate and calcium in the presence of stabilizer	Synthesis of calcium sulfate NPs and nanocomposites PS/caso4 to cubic form	7778-18-9	Synthesis of NPs in the liquid phase and Suspension	Laboratory Chemical Hood
4	First grinding of carbon nanotubes and then nano powder was mixed with potassium bromide pellet to form tablets for FTIR measurements	Carbon nanotubes	N/A	Transporting and grinding of carbo nanotubes to form nano powder and	General Ventilation
5	Thermal analysis of the behavior of carbon nanotubes for the simultaneous measurement of changes in weight and temperature of carbon nanotubes under a controlled temperature (700 to 900 °) C)	Carbon nanotubes	N/A	Transporting and grinding of carbo nanotubes to form a gas phase	Laboratory Chemical Hood

N/A, non- applicant

Table 4: Severity factors of the NPs based on assessment

Activity Number	Surface reactivity	Particle shape	Particle diameter(nm)	Solubility	Carcinogen?	Reproductive hazard?	Mutagen?	Dermal hazard?	Severity score	Severity band
1	Unknown	Spherical	11-40	Insoluble	Unknown	Unknown	Unknown	Unknown	55	High
2	Unknown	Spherical	40-100	Insoluble	Unknown	Unknown	Unknown	Unknown	50	Medium
3	Unknown	Different shapes	11-40	Insoluble	Unknown	Unknown	Unknown	Unknown	55	High
4	Unknown	Fibrous	1-10	Insoluble	Unknown	Unknown	Unknown	Unknown	60	High
5	Unknown	Fibrous	11-40	Insoluble	Unknown	Unknown	Unknown	Unknown	55	High

Table 5: Severity factors of the nanoparent material based on assessment

Activity Number	Lowest OEL(mcg m3)	Carcinogen?	Reproductive hazard?	Mutagen?	Dermal hazard?
1	10	No	No	No	Yes
2	10	No	No	No	Yes
3	10000	No	No	No	Yes
4	2000	No	No	No	No
5	2000	No	No	No	No

Table 6: Probability factors, RL and recommended engineering control

Activity Number	Estimated maximum amount of chemical used in 1 day (mg)	Dustiness	Number of employees with similar exposure	Frequency of operation (annual)	Operation duration (pershift, h)	Probability score	Probability score	Overall risk level without controls	Recommended engineering control based on risk level	Upgrade engineering control?	Overal risk level with controls
1	11-100	Medium	3	Weekly	8	52.5	Likely	RL3	Containment (glove box)	Yes	RL2
2	0-10	Medium	6	Weekly	1	41.25	Less Likely	RL1	Current control (Laboratory Chemical Hood)	No	RL1
3	> 100	Medium	3	Weekly	2 to3	60	Likely	RL3	Containment (glove box)	Yes	RL2
4	11-100	High	4	Daily	2	67.5	Likely	RL3	Containment (glove box)	Yes	RL2
5	0-10	High	4	Weekly	6	61.25	Likely	RL3	Containment (glove box)	Yes	RL2

exposed to ENMs.

Key points:

- The most important risk factors of NPs in determining risk level were found to be amount of generated dust and the amount of materials used in the processes.
- Risk mitigation in NPs and potential control measures focus on reducing the level of probability.
- Some mechanisms, such as engineering controls, safer ones, and administrative controls may be offered to reduce amount of generated dust and number of workers exposed to ENMs.

References

1. Maynard AD, Kuempel ED. Airborne nanostructured particles and occupational health. Journal of Nanoparticle Research 2005 April 25; 7:587-614.
2. Warheit DB. Assessing health risks of inhaled nanomaterials: development of pulmonary bioassay hazard studies. Anal Bioanal Chem 2010 July1; 398:607-612
3. Sayes CM, Warheit DB. Characterization of nanomaterials for toxicity assessment. Sons Inc.Wires Nanomedicine Nanobiotechnology 2009 November; 1:660-670.
4. Seaton A. Nanotechnology and the occupational physician. Occupational Medicine 2006; 56: 312- 316
5. Duffin R, Tran L, Brown D, Stone V, Donaldson K. Proinflammogenic effects of low-toxicity and metal nanoparticles in vivo and in vitro: highlighting the role of particle surface area and surface reactivity. Inhal Toxicol, 2007; *19*(10):849–856.
6. Oberdorster G, Sharp Z, Atudorei V, Elder A,Gelein R, Kreyling W, Cox C. Translocation of inhaled ultrafine particles to the brain Inhal Toxicol 2004; 16: 437-445.
7. Shvedova AA, Castranova V, Kisin E, Schwegler-Berry D, Murray AR, Gandelsman VZ, Maynard A, Baron P. Exposure to carbon nanotube material: assessment of nanotube cytotoxicity using human keratinocyte cells. *J Toxicol Environ Health* A 2003; 66 : 1909-1926.
8. Shvedova AA, Kisin E, Murray AR, Schwegler-Berry D, Gandelsman VZ, Baron P *et al.* Exposure of human bronchial cells to carbon nanotubes caused oxidative stress and cytotoxicity. *In*: Proceedings of the Meeting of the SFRR Europe 2003, Ioannina, Grèce., 2004b;91-103.
9. Ostiguy C, Soucy B, Lapointe G, Woods C,Ménard L, Trottier M. Health Effects of Nanoparticles - Second Edition, Studies and Research Projects / Report R-589, Montréal, IRSST, 2008, 114 pages.Available at: URL: http://www.irsst.qc.ca/. Accessed October, 2008
10. Schulte P, Geraci C, Zumwalde R, Hoover M, Kuempel E. Occupational risk management of engineered nanoparticles. Journal of Occupational and Environmental Hygine,2008; 5: 239-249.
11.,Kuempel ED, Geracl CL, Schulte PA. Nanotechnology-Toxicological Issues and Environmental Safety and Environmental Safety. Springer Netherlands, pp 119-145;2007
12. Ostiguy C.,Roberge B, Ménard L, Anica Endo C. Best Practices Guide to Synthetic Nanoparticle Risk Management- Second Edition, Studies and Research Projects / Report R-599, Montréal, IRSST, 2009, 67 pages.Available at: URL: http:// www.irsst.qc.ca/. Accessed January, 2009
13. David M. Zalk, Samuel Y.Paik, Paul Swuste, Evaluating the control banding nanotool: a qualitative risk assessment method for controlling nanoparticle exposures, J Nanopart, 2009; Res 11:1685 – 1704.
14. Scislowicz C, Geraci C, Parr F, DeRose G, Saebfar H, Godwin H, et al. Working Safety With Engineered Nanomaterials In Academic Research Settings. California Nanosafety Consortium of Higher Education. 2011, Available at: URL: http:// luskin.ucla.edu/content/ Nanotoolkit/. Accessed Nov 2011.
15. David M. Zalk, Samuel Y.Paik, Paul Swuste, Application of a pilot control banding tool for risk level assessment and control of nanoparticle exposures, Ann. Occupational hygine,2008;419-428.
16. General Safe Practices for Working with Engineered Nanomaterials in Research Laboratories.2012. Available at: URL: http:// www.cdc.gov/niosh/. Accessed May 2012
17. Donaldson K, Aitken R, Tran L, Stone V, Duffin R, Forrest G, Alexander A. Carbon nanotubes: a review of their properties in relation to pulmo- nary toxicology and workplace safety. Toxicol Sci, 2006; *92*(1):5–22.
18. Maynard AM, Kuempel ED. Airborne nano-structured particles and occupational health. J Nanoparticle Research 2005;*7*(6):587–61.

5/29/2013