Editorial

Nanotechnology Health and Safety —What Can Occupational Health Professionals Do?

The nanotechnology industry is growing in size and economic importance worldwide. Yet, despite recent progress in research, the potential adverse health effects from exposure to engineered nanomaterials are still inadequately understood. Regulation of the nanotechnology industry is also still in its infancy. We outline here the present situation, how occupational health professionals could contribute, and follow with an example of what is being done in the National University of Singapore.

Since it was first envisioned by Feynman in his 1959 speech¹), nanotechnology has grown into a vast, diverse industry in many developed nations as well as newly industrializing countries. Annually, over US\$18 billion is invested in nanotechnology research and development by public and private sectors around the world²⁾. By 2014, over a tenth of the global manufacturing sector workforce could be employed in nanotechnology-related work processes. Experts have predicted that as many as 10 million people could be working in processes involving nanotechnology by the year 2014^{3} . In 2005, there were just over 50 consumer products on the market known to contain nanomaterials. By early 2011 there were over 1,300 such consumer products being sold, many of which are for personal care. For instance, there are at present over 30 types of nanomaterial-containing sunscreens being marketed for consumer use⁴).

High-tech industries are now no longer the sole territory of developed countries — they are increasingly to be found in newly industrializing countries, with nanotechnology being no exception. For example, in China there were over 1,000 enterprises involved in nanotechnology-related business and an estimated 3,000 people employed in nanotechnology industries in Shanghai alone as of June 2010⁵). In recent years, the nanotechnology industry in Thailand has also grown tremendously⁶ and the government is actively putting in measures to grow the industry further.

What impact could all this have on human health and the environment? It now well-recognised that some nanomaterials have the potential to adversely affect health. Nanomaterials can enter the body via inhalation of airborne particles, through dermal absorption or by ingestion^{7, 8)}, and numerous in-vitro and animalmodel studies in recent years have documented adverse biological effects such as oxidative stress, inflammatory response following exposure to various nanomaterials. Some of these studies report that nanomaterials display greater toxic effects compared to the bulk form of the same material. For example, Shvedova and colleagues demonstrated in 2005 that carbon nanotubes introduced via pharyngeal aspiration (at levels that were chosen to reflect actual human occupational exposure situations) induced significantly greater levels of pulmonary inflammation in mice compared to the same doses of ultrafine carbon administered via the same route⁹⁾. Such results highlight the need for further investigation of the factors influencing toxicity of nanomaterials, especially those intended for medical use or widespread consumer product application. Indeed, in Oberdorster's 2010 nanotoxicology review paper, he cautions that "until we know better it should be made mandatory to prevent exposure by appropriate precautionary measures/regulations and by practicing best industrial hygiene to avoid future horror scenarios¹⁰)".

In contrast to when nanotechnology research and development first became popular, interest in health and safety risk research has gradually increased in recent vears. Efforts have been made to identify, understand and address potential human health and environmental risks¹¹⁾. To this purpose, a number of collaborative research and information-exchange bodies have been formed. For example, the Regulation for Registration, Evaluation, Authorisation of Chemicals (REACH) was launched by the European Commission in June 2007. The objectives of REACH include improvement of human health and environment protection from risks that can be posed by chemicals and the promotion of alternative methods for assessment of hazards of substances. Nanomaterials are among the substances covered under REACH¹²). Another such example is the Working Party on Manufactured Nanomaterials (WPMN) formed by the Organisation for Economic Cooperation and Development (OECD) in 2006. The focus of the WPMN is on improving the testing and assessment methods for studying the human and environmental health and safety impact of nanomaterials use¹³⁾.

Early progress has been made in terms of regulation of nanotechnology in industries. Some countries such as France have developed mandatory reporting systems for nanotechnology industries¹⁴⁾. In the United States, the Nanotechnology Safety Act of 2010 empowered the Food and Drug Administration to launch scientific studies on the safety of nanotechnology-based medical and health products¹⁵⁾.

However, research into the occupational and environmental health and safety aspects nanotechnology stills lags behind discovery and applications research²). Despite recent progress in research, understanding of the potential health effects of engineered nanomaterials is still incomplete and in particular the long-term effects are as yet still unknown. Many products incorporating nanomaterials progress from bench to consumer without thorough or adequate health and safety evaluation. Assessment of the potential health risks of nanomaterials is still limited by many factors, a major one being insufficient human and environmental exposure data of adequate quality. While the societal benefits of nanotechnology may be great, health and environmental safety issues must be given due attention, in order to avoid repeating the tragedies that have taken place in the past such as with asbestos.

Occupational health professionals have an important role to play in practice, education as well as research. As exhorted by Oberdorster, we need to ensure that "best industrial hygiene¹⁰)" is practiced in order to minimize employee exposure to nanomaterials. This can be done in part through the investigation of work practices and control measures in research institutions and companies handling nanomaterials.

Occupational health professionals can contribute to raising awareness among employers and their workers about the potential health risks of exposure to nanomaterials and how these can be mitigated based on best available evidence. This requires us to stay updated on the toxicological and health and safety developments in this growing industry. In the United States, public awareness on nanotechnology is gradually increasing¹⁶⁾ and in Japan, over half of people surveyed in 2004 had heard about nanotechnology¹⁷⁾. However, figures can be expected to be lower in many other countries, especially the less developed. There is therefore a need for occupational health professionals to look beyond the factory fence¹⁸⁾ and contribute to consumer safety and the education of the general public.

Last but definitely not least, there is great need for further research into the various aspects of occupational health and safety in nanotechnology, such as the adequacy of current control measures. Here we illustrate what can be done despite continued uncertainty about how best to capture exposure data:

The National University of Singapore (NUS) recently launched a collaborative surveillance project that aims

to characterize typical exposures in its nanomaterialhandling laboratories and to develop a health surveillance protocol for persons working with nanomaterials. This is a multidisciplinary, collaborative effort with occupational health, environmental monitoring and laboratory safety specialists from the Department of Epidemiology and Public Health, Department of Civil & Environmental Engineering and the Office of Safety, Health and Environment respectively.

Firstly, a database for laboratories handling nanomaterials will be built from existing infrastructure. The university requires all principal investigators involved in laboratory-based research projects are required to submit risk assessment details via an online project risk assessment system for approval by the Office of Safety, Health and Environment (OSHE) before commencement of work. Thus, information on laboratories handling nanomaterials will be drawn from this existing database.

Second, environmental monitoring will be conducted in all laboratories handling nanomaterials. This will encompass the measurement of airborne nanomaterial concentrations associated with typical processes occurring in the laboratories, characterization of chemical and physical properties of the airborne nanomaterials as well as assessment of dermal exposure potential and significance.

Next, a health surveillance program will be developed. In order to streamline the implementation process, this will initially follow the occupational health program that is already in place. The existing program comprises statutory medical examinations for researchers handling materials containing chemicals on the Singapore Manpower Ministry's prescribed list, such as cadmium, arsenic or mercury, regardless of particle size. Researchers handling nanomaterials containing any of the chemicals on the prescribed list will already be under regular statutory medical surveillance, such as those working with cadmium-containing quantum dots. The next group of researchers to be offered health surveillance will be those handling nanomaterials that have high suspicion of adverse health effects, such as carbon nanotubes. Eventually, health surveillance will be made available to all researchers working on nanomaterials, regardless of chemical composition.

Through the accumulation of detailed exposure information and documentation of baseline health status, it is hoped that in years to come there will be adequate prospective data that could provide valuable insights on the exposure characteristics and health outcomes of nanomaterials-exposed persons. This would be further strengthened by collaboration both at the local and international level.

References

- Feynman RP (1959) There's Plenty of Room at the Bottom. Speech given at the annual meeting of the American Physical Society at the California Institute of Technology, originally published in the February 1960 issue of Caltech's Engineering and Science Magazine. http://media.wiley.com/product_data/excerpt/ 53/07803108/0780310853.pdf Accessed March 11, 2011
- 2) Maynard A, Rejeski D (2009) Too small to overlook. Nature **460**, 174.
- 3) Lux Research (2004) Sizing Nanotechnology's value chain. Lux Research Inc., New York.
- Project on Emerging Nanotechnologies: Inventories. Available at http://www.nanotechproject.org/inventories/ consumer/browse/categories/health_fitness/sunscreen/ page4/ Accessed March 9, 2011.
- 5) Scott A, Zhou E (2010) The Increased Use Of Nanotechnology In China's Biotech Industry. Life Science Leader, Jameson Publishing Inc. http://www. lifescienceleader.com/index.php?option=com_jambozine &layout=article&view=page&aid=4059 Accessed March 11, 2011.
- 6) Pratchaya W (2010) Thailand nanotech plan moves ahead. http://www.scidev.net/en/news/thailand-nanotechplan-moves-ahead.html Accessed March 11, 2011.
- 7) Gulson B, McCall M, Korsch M, Gomez L, Casey P,Oytam Y, Taylor A, McCulloch M, Trotter J, Kinsley L, Greenoakkj G (2010) Small Amounts of Zinc from Zinc Oxide Particles in Sunscreens Applied Outdoors Are Absorbed through Human Skin. Tox Sci 118, 140–9.
- Crosera M, Bovenzi M, Maina G, Adami G, Zanette C, Florio C, Larese FL (2009) Nanoparticle dermal absorption and toxicity: a review of the literature. Int Arch Occup Environ Health 82, 1043–55.
- 9) Shvedova AA, Kisin ER, Mercer R, et al. (2005) Unusual inflammatory and fibrogenic pulmonary

responses to single-walled carbon nanotubes in mice. Am J Physiol Lung Cell Mol Physiol **289**, L698–L708.

- Oberdorster G (2010) Safety assessment for nanotechnology and nanomedicine: concepts of nanotoxicology. J Int Med 267, 89–105.
- 11) Maynard A, Warheit DB, Philbert MA (2011) The new toxicology of sophisticated materials: Nanotoxicology and beyond. Tox Sci **120**, S109–S29.
- 12) European Chemicals Agency. REACH guidance. http:// ec.europa.eu/environment/chemicals/reach/reach_intro. htm Accessed 1 March 2011.
- 13) Organisation for Economic Co-operation and Development. Safety of Manufactured Nanomaterials. http://www.oecd.org/about/0,3347,en_2649_37015404_ 1_11_1_37465,00.html Accessed March 9, 2011.
- 14) Nanotechnology Industries Association (2010) Nanotech 2010: Mandatory Reporting, Nano-Regulation & -Legislation, 'applied' Risk Assessment. http://www.nanotechia.org/global-news/nanotech-2010mandatory-reporting-nano-regulatio Accessed March 9, 2011.
- 15) Oszakiewski R (2010) Nanotechnology Law Report. Porter Wright Morris & Arthur LLP, Washington, DC. http://www.nanolawreport.com/2010/01/articles/thenanotechnology-safety-act-of-2010/ Accessed March 9, 2011.
- 16) Hart Research Associates (2009) Nanotechnology, Synthetic Biology, & Public Opinion. http://www. nanotechproject.org/process/assets/files/8286/ nano_synbio.pdf Accessed March 11, 2011.
- 17) Fujita Y (2006) Perception of Nanotechnology among general public in Japan. Asia Pacific Nanotech Weekly. http://www.nanoworld.jp/apnw/articles/library4/pdf/4-6. pdf Accessed March 11, 2011.
- Seaton A (2006) Nanotechnology and the occupational physician. Occup Med (Lond) 56, 312–6.

Judy SNG, MBBS, MMed (OM), MS (Epidemiology) Department of Epidemiology and Public Health, Yong Loo Lin School of Medicine, National University of Singapore

Sin-Eng CHIA, MBBS, MSc, MD, FAMS, FFOM Department of Epidemiology and Public Health, Yong Loo Lin School of Medicine, National University of Singapore