California's Approach for Safe Nanotechnologies: Second Information Call-in from Manufacturers

Sho Takatori and Hai-Yong Kang

Department of Toxic Substances Control
California Environmental Protection Agency
1001 I Street, Sacramento, CA 95814. USA
hkang@dtsc.ca.gov

ABSTRACT

The Department of Toxic Substances Control (DTSC), within the California Environmental Protection Agency (Cal/EPA), initiated a chemical information call-in on nanometal oxides (titanium dioxide, cerium oxide, and zinc oxide), nanometals (silver and zero valent iron), and quantum dots in late 2010. DTSC sent a formal information request letter to manufacturers (including research institutions) who produce the six nanomaterials in California or import them into California for sale. DTSC seeks information about these nanomaterials because their commercial uses and applications are growing; yet, information about their analytical test methods, physicochemical properties, toxicity, and fate and transport are generally limited. The chemical information call-in is a mandatory program for nanomaterial data collection with no exemptions at any production threshold.

Keywords: nanomaterials, governance, information call-in, environment, regulation

1 INTRODUCTION

Realizing the promised benefits of nanotechnology requires a better understanding of potential risks and appropriate means to assess, reduce, or avoid such risks. Potential hazards and risks for human health and the environment posed by engineered nanomaterials have been reported for some time now.[1-8]

The unique phenomena associated with chemicals and materials engineered at the atomic and molecular level are precisely what enable novel uses and applications of nanotechnology, as well as pose potentially serious risks to public health and our environment. Whereas some information on toxicity to humans, animals, and the environment are documented, significantly less information is available on their analytical detection methodologies and end-of-life exposures. An example of this is quantum dots (QDs), which are increasingly being used in electronics and biological applications. A number of studies suggests that QD toxicity depends on the interaction of size, concentration, surface charge, and outer coating bioactivity,[9-13] and that toxicity may be reduced or increased by surface modifications.[14-17]

Whereas QD toxicity[9-11, 15, 18-23] and limited biological fate[20, 24-27] data are available, there is a paucity of information on its detection and quantification methods. Analytical detection is just as important as inherent toxicity in achieving a safe and sustainable development of nanotechnology-based products.

Major data gaps on analytical detection methodologies exist not only for QD but for most nanomaterials. Exposure and end-of-life impacts of nanomaterials also remain largely unknown, although bioaccumulation and magnification are reported to occur.[26, 27] The European Commission Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR)[28] laid out a number of major knowledge gaps that are needed to conduct a full risk assessment. Recently, Oberdorster[5] and Maynard et al.[4] have reviewed and extended the current state of knowledge on potential health risks of nanomaterials. The overwhelming consensus is that the health and safety risks are largely unknown or unavailable, which calls for an urgent comprehensive and systematic approach for a sustainable growth of nanotechnology.

Accordingly, DTSC initiated its chemical information call-in for nanomaterials. DTSC completed its first call-in in 2009, which focused on carbon nanotube toxicity, physical-chemical properties, fate and transport, and other necessary information.[29] In late 2010, DTSC launched its second chemical information call-in,[30] which is intended to collect information related to analytical test methods for nano titanium dioxide (TiO_2), cerium oxide (CeO_2), zinc oxide (ZnO), silver (Ag), zero valent iron (Fe), and quantum dots (QD) in environmental matrices, including water, air, soil, sludge, and chemical waste. DTSC is exercising its authority under California Health and Safety Code, Sections 57018 – 57020. The purpose of the call-in is to collect information so industry and interested stakeholders—working in partnership with state government agencies—can develop and use appropriate analytical test methods to ascertain how these chemicals may affect public health and our environment. DTSC's information call-in is a mandatory program for nanomaterial data collection with no exemptions at any production threshold.

2 INFORMATION CALL-IN

2.1 Methods

A flowsheet of the information call-in process is shown in Fig. 1. Briefly, the call-in begins with the identification of chemicals of concern based on their commercial use and data gaps on toxicity, physicochemical properties, fate and transport, or other key environmental and/or health parameters. DTSC conducts extensive literature searches on public databases and collaborates with the National Institute for Occupational Safety and Health (NIOSH), U.S. Environmental Protection Agency, and several academic institutions in identifying the key information needs of the specified chemical. An announcement is then made on the Internet Web site of Cal/EPA and DTSC of the chemical for which DTSC seeks information, the type of information it is seeking, and the reason for seeking the information. Manufacturers of these chemicals are identified and contacted to discuss the call-in program and evaluate key information needs. A formal information request letter is then sent to the manufacturers of the specified chemicals. It is important to note that throughout the call-in process, DTSC conducts extensive research on the specified chemicals and maintains a collaborative dialogue with manufacturers through public outreach workshops, symposia, and site visits. Manufacturers are encouraged to seek accredited independent laboratories, universities, national laboratories, and reference laboratories in formulating the comprehensive responses. Manufacturers must provide the requested information in writing to DTSC no later than one year from the date of the formal call-in letter. All collected information is posted on the DTSC Internet Web, unless a manufacturer claims certain "trade secret" protections set forth in Health and Safety Code section 57020.

2.2 Information Requested

Manufacturers, researchers, product developers, governments, and consumers will consider the collected information to advance science and safety in chemical practices. An information data request sheet was appended with the formal letter to manufacturers. Basic chemical and physical properties of the nanomaterial were listed, such as shape, density, particle size distribution in different media, surface modification and charge, reactivity, solubility, and octanol-water partition coefficient. Manufacturers must report the analytical detection method(s) used for each parameter and provide relevant references of each method. Manufacturers must further describe the analytical test method(s) used to sample, prepare, and analyze a specific matrix to determine the identity and concentration of each specified nanomaterial. References of the complete method or its procedure must be reported for each, individual matrix, which must include water, air, soil, sediment, sludge, chemical waste, fish, blood, adipose tissue, and urine.

Although analytical detection is the focus of the second call-in, DTSC also seeks information regarding safe nanomaterial handling, worker protection, and fate and transport. For the carbon nanotube call-in, DTSC asked manufacturers about the presence of their chemical in the environment from manufacturing, distribution, and end-of-life disposal. Manufacturers were further requested to document how they protect their workers, if their material constitute a hazardous waste, and how they handle the waste products. These are just a few knowledge gaps that apply not only to carbon nanotubes but to second round chemicals as well.

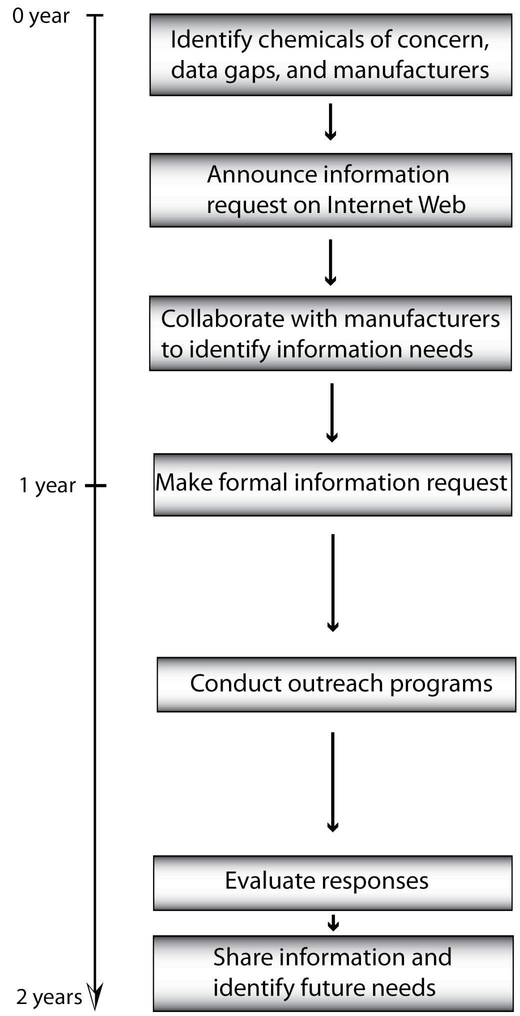

Figure 1: Flowsheet of information call-in process.

2.3 Timeline

A single phase of information call-in spans approximately two years (see Fig. 1). DTSC spends about one year to conduct literature searches and facilitate a collaborative dialogue with manufacturers and industry stakeholders. Upon submitting the formal request letters, manufacturers have 365 days to provide the information to DTSC. After reviewing the responses, all information except those identified as "trade secret" are posted on the DTSC Internet Web. Manufacturers who fail to respond by the deadline receive a follow-up letter.

3 DEFINITION OF NANO-

In a regulatory framework, it is critical to have a compatible, complete, and unequivocal definition of a "nanomaterial" based on scientific principles and processes. Thus far, the international and national communities have struggled to formulate a globally harmonized definition. Governmental entities, non-normative consensus standards organizations, and industry have each developed various definitions.[31-33] A common feature of many definitions is the establishment of "nano-" terminologies as having a single upper size limit of 100 nm.[31-33] Current evidence suggests that this value is arbitrary and has no scientific basis to support its appropriateness or of any single threshold. The unique phenomena associated with chemicals and materials engineered at the atomic and molecular level do not abruptly disappear at 101 nm.[34] In fact, nano-reinforced polymers have novel properties at ~ 200-300 nm because of the local bridges or bonds between the nanoparticles and the polymer.[35] Most size-based definitions, accordingly, include qualifier terms like "approximately" or "of the order of 100 nm" to form a flexible upper limit, which is difficult to enforce.[31] Some have thus formulated a different upper limit or questioned the appropriateness of this value.[31-40] A solely size-based definition must clearly address considerations of particle size distribution and aggregates or agglomerates, which may result in dimensions greater than the upper threshold but yet retain novel properties.[32]

Moreover, a significant number of articles published in legal and policy journals reiterate the almost universal absence of legal definitions of "nano-" terminologies in enacted local, state, or federal statutes. Non-normative, non-governmental consensus standards organizations have begun drafting various definitions, but mostly for commercial labeling purposes only. A workable and meaningful definition for nanotechnology must be consistent with current statutory definitions of "chemical," "chemical substance," "product," "drug," "material," and others. Various qualitative aspects must also be clearly defined, like "naturally occuring" versus "man-made," "manufactured" or "engineered," functionality, phenomenon, and various other classifications established by the Organization for Economic Co-operation and Development (OECD) and International Organization for Standardization (ISO)/ European Committee for Standardization (CEN).

4 CONCLUSION

DTSC's information call-in is a mandatory program that includes both commercial and research entities with no exemptions at any production threshold. The effort is intended to make information on the fate and transport, detection and analysis, and other information on chemicals more available. Manufacturers, researchers, product developers, governments, and consumers will then consider the collected information to foster a sustainable growth of nanotechnology.

DISCLAIMER: The ideas and opinions expressed herein are those of the authors and do not necessarily reflect the official position of the California Department of Toxic Substances Control.

REFERENCES

[1] Aitken RJ, Hankin SM, Ross B, et al. EMERGNANO: A review of completed and near completed environment, health and safety research on nanomaterials and nanotechnology. Edinburgh, UK: Institute of Occupational Medicine; 2009.
[2] Balbus JM, Maynard AD, Colvin VL, et al., "Meeting Report: Hazard Assessment for Nanoparticles--Report from an Interdisciplinary Workshop," Environ Health Perspect, 115, 1654-1659, 2007.
[3] International Council on Nanotechnology (ICON). Towards Predicting Nano-Biointeractions: An International Assessment of Nanotechnology Environment, Health and Safety Research Needs. Houston, TX; 2008.
[4] Maynard AD, Warheit DB, Philbert MA, "The New Toxicology of Sophisticated Materials: Nanotoxicology and Beyond," Toxicological Sciences, 120, S109-S129, 2010.
[5] Oberdorster G, "Safety assessment for nanotechnology and nanomedicine: concepts of nanotoxicology," Journal of Internal Medicine, 267, 89-105, 2010.
[6] Oberdorster G, Oberdorster E, Oberdorster J, "Nanotoxicology: An Emerging Discipline Evolving from Studies of Ultrafine Particles," Environ Health Perspect, 113, 823–839, 2005.
[7] Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR). Risk Assessment of Products of Nanotechnologies. Brussels, Belgium: European Commission; 2009.
[8] Warheit DB, Borm PJ, Hennes C, Lademann J, "Testing strategies to establish the safety of nanomaterials: conclusions of an ECETOC workshop," Inhal Toxicol, 19, 631-643, 2007.
[9] Farre M, Gajda-Schrantz K, Kantiani L, Barcelo D, "Ecotoxicity and analysis of nanomaterials in the aquatic environment," Anal Bioanal Chem, 393, 81-95, 2009.
[10] Hoshino A, Fujioka K, Oku T, et al., "Physicochemical Properties and Cellular Toxicity of Nanocrystal Quantum Dots Depend on Their Surface Modification," Nano Letters, 4, 2163-2169, 2004.
[11] Derfus AM, Chan WCW, Bhatia SN, "Probing the Cytotoxicity of Semiconductor Quantum Dots," Nano Lett, 4, 8-18, 2004.
[12] Geys J, Nemmar A, Verbeken E, et al., "Acute toxicity and prothrombotic effects of quantum dots: impact of

surface charge," Environ Health Perspect, 116, 1607-1613, 2008.
[13] Hardman R, "A Toxicologic Review of Quantum Dots: Toxicity Depends on Physicochemical and Environmental Factors," Environmental Health Perspectives, 114, 165-172, 2006.
[14] Cho SJ, Maysinger D, Jain M, Roder B, Hackbarth S, Winnik FM, "Long-Term Exposure to CdTe Quantum Dots Causes Functional Impairments in Live Cells," Langmuir, 23, 1974-1980, 2007.
[15] Su Y, He Y, Lu H, et al., "The cytotoxicity of cadmium based, aqueous phase - Synthesized, quantum dots and its modulation by surface coating," Biomaterials, 30, 19-25, 2009.
[16] Ryman-Rasmussen JP, Riviere JE, Monteiro-Riviere NA, "Surface Coatings Determine Cytotoxicity and Irritation Potential of Quantum Dot Nanoparticles in Epidermal Keratinocytes," J Invest Dermatol, 127, 143-153, 2006.
[17] Guo G, Liu W, Liang J, He Z, Xu H, Yang X, "Probing the cytotoxicity of CdSe quantum dots with surface modification," Materials Letters, 61, 1641-1644, 2007.
[18] Stern ST, Zolnik BS, McLeland CB, Clogston J, Zheng J, McNeil SE, "Induction of autophagy in porcine kidney cells by quantum dots: a common cellular response to nanomaterials?," Toxicol Sci, 106, 140-152, 2008.
[19] Lee J, Ji K, Kim J, et al., "Acute toxicity of two CdSe/ZnSe quantum dots with different surface coating in Daphnia magna under various light conditions," Environmental Toxicology, 25, 593-600, 2009.
[20] Pelley JL, Daar AS, Saner MA, "State of academic knowledge on toxicity and biological fate of quantum dots," Toxicol Sci, 112, 276-296, 2009.
[21] Gagne F, Auclair J, Turcotte P, et al., "Ecotoxicity of CdTe quantum dots to freshwater mussels: impacts on immune system, oxidative stress and genotoxicity," Aquat Toxicol, 86, 333-340, 2008.
[22] Moore MN, "Do nanoparticles present ecotoxicological risks for the health of the aquatic environment?," Environment International, 32, 967-976, 2006.
[23] Bouldin JL, Ingle TM, Sengupta A, Alexander R, Hannigan RE, Buchanan RA, "Aqueous toxicity and food chain transfer of quantum dots™ in freshwater algae and Ceriodaphnia dubia," Environmental Toxicology and Chemistry, 27, 1958-1963, 2008.
[24] Maysinger D, Lovric J, Eisenberg A, Savic R, "Fate of micelles and quantum dots in cells," Eur J Pharm Biopharm, 65, 270-281, 2007.
[25] Klaine SJ, Alvarez PJ, Batley GE, et al., "Nanomaterials in the environment: behavior, fate, bioavailability, and effects," Environ Toxicol Chem, 27, 1825-1851, 2008.
[26] Peyrot C, Gagnon C, Gagne F, Willkinson KJ, Turcotte P, Sauve S, "Effects of cadmium telluride quantum dots on cadmium bioaccumulation and metallothionein production to the freshwater mussel, Elliptio complanata," Comp Biochem Physiol C Toxicol Pharmacol, 150, 246-251, 2009.
[27] Werlin R, Priester JH, Mielke RE, et al., "Biomagnification of cadmium selenide quantum dots in a simple experimental microbial food chain," Nat Nano, 6, 65-71, 2010.
[28] Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR). The Appropriateness of Existing Methodologies to Assess the Potential Risks Associated with Engineered and Adventitious Products of Nanotechnologies. 2005.
[29] Department of Toxic Substances Control (DTSC). Carbon Nanotube Information Call-in, http://www.dtsc.ca.gov/TechnologyDevelopment/Nanotechnology/CNTcallin.cfm. Accessed March 31, 2011.
[30] Department of Toxic Substances Control (DTSC). Chemical Information Call-In: Nano Metals, Nano Metal Oxides, and Quantum Dots, http://www.dtsc.ca.gov/TechnologyDevelopment/Nanotechnology/nanometalcallin.cfm. Accessed March 31, 2011.
[31] Lövestam G, Rauscher H, Roebben G, et al. Considerations on a Definition of Nanomaterial for Regulatory Purposes. Joint Research Center, European Commission; 2010.
[32] Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR). Scientific Basis for the Definition of the Term “Nanomaterial”. 2010.
[33] Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR). Opinion on the Scientific Aspects of the Existing and Proposed Definitions Relating to Products of Nanoscience and Nanotechnologies. 2008.
[34] Stone D, Harper BJ, Lynch I, Dawson K, Harper SL, "Exposure Assessment: Recommendations for Nanotechnology-Based Pesticides," International Journal of Occupational and Environmental Health, 16, 467-474, 2010.
[35] Schmid G, Decker M, Ernst H, et al. Small Dimensions and Material Properties: A Definition of Nanotechnology. 2003.
[36] Auffan M, Rose J, Bottero J-Y, Lowry GV, Jolivet J-P, Wiesner MR, "Towards a definition of inorganic nanoparticles from an environmental, health and safety perspective," Nat Nano, 4, 634-641, 2009.
[37] Belinsky Z, "Nanoanagement: Synergizing Regulation with Common Law in Light of Nanotechnology," Nanotechnology Law & Business, 7, 165-179, 2010.
[38] Brouwer N, Weda M, Van Riet-Nales D, De Kaste D, "Nanopharmaceuticals: Implications for the European Pharmacopoeia," Pharmeuropa, 22, 5-7, 2010.
[39] Food and Drug Administration (FDA). Reporting Format for Nanotechnology-Related Information in CMC Review. Center for Drug Evaluation and Research (CDER) Office of Pharmaceutical Science. Manual of Policies and Procedures (MAPP) 50159; 2010.
[40] Kreyling WG, Semmler-Behnke M, Chaudhry Q, "A complementary definition of nanomaterial," Nano Today, 5, 165-168, 2010.