ABSTRACT

While nanomaterials are found in a number of applications, much is still unknown about their properties. Therefore, there are concerns as to their potential health and environmental effects. As the first step to understanding the potential risks of nanomaterials, the California Environmental Protection Agency's Department of Toxic Substances Control (DTSC) requested information from manufacturers of certain nanomaterials. The Department was given the authority to make such requests under California's Health and Safety Code, sections 57018-57020. DTSC had requested information to manufacturers of CNTs in 2009 and expanded the call-in to include nanometal oxides (TiO$_2$, CeO$_2$, ZnO), nanometals (Ag, nano zero valent Fe), and quantum dots in late 2010. DTSC asked information to manufacturers regarding analytical test methods, fate and transport in the environment, and other relevant data.

This article reviews potential impacts of nanomaterials and the status of California nanoindustry, and addresses efforts and processes to facilitate data call-in, and finally, expectations and benefits of data call-in by DTSC are evaluated.

KEYWORDS: nanomaterials, data gap, information call-in, environment, potential risks.

1. INTRODUCTION

Nanotechnology is a rapidly emerging technology with vast potential and unique properties of nanomaterials. Many nanotechnology-based products that take advantage of these unique properties are already available in the marketplace[2][3]. In many fields, nanomaterials improve existing function; furthermore their unique properties are creating new areas of application. For example, cosmetics companies use the term 'nanotechnology' in their product marketing, and there is a dramatic increase in registered trademarks in personal care products that include the term 'nano'[4]. It is expected that the use of nanomaterials will increase with technology development and market demand.

However, there are knowledge gaps in what we know about the properties of nanomaterials. More information is needed on the toxicity, fate and transport of nanomaterials, and characterization methods need to be further developed to better understand their characteristics [5][6]. Due to their small size and unique properties, nanomaterials might have the potential to adversely affect human health and the environment; thus a safe and responsible approach for nanotechnology is necessary [7][8].

The small particle size can induce adverse effects such as oxidative stress and pulmonary inflammation [9]. Another result of the small size is that a large proportion of atoms in nanomaterials lies on the surface [10]. The high ratio of surface area to volume can result in different properties from the same material in bulk form. With high surface area, nanomaterials tend to be very reactive, and therefore nanomaterials are often used as catalysts [11]. This suggests that some nanomaterials could have as-yet unknown effects on human health and the environment.

In order to carefully examine the impacts of nanomaterials and make the findings widely available, DTSC has initiated a mandatory information call-in, conducted under authority contained in the California's Health and Safety Code, sections 57018-57020 [12]. The purpose of this program is to review the current state of the California nanoindustry and to use that information to help guide potential future nanoindustry practices in California and elsewhere. By working
cooperatively with interested parties, DTSC will make information available for safe nanotechnology and promote sustainable development of this rapidly expanding industry.

2. CHARACTERIZATION OF IMPACTS BY NANOMATERIALS

To understand potential impacts of nanomaterials, the reactions of materials in each life cycle stage must be evaluated. Raw materials, production methods, use, and end-of-life stages must be considered. Figure 1 shows a schematic flow-model of one nanomaterial, TiO$_2$, based on the life cycle concept.

The raw materials used to make nanomaterials show a diverse range of properties and forms. Some raw materials are very toxic, but others are benign. For example, TiCl$_4$, which has liquid form used in production of TiO$_2$ nanomaterial in chloride process, is toxic. On the other hand, CO$_2$, used in synthesis of CNTs, is nontoxic. From a safety standpoint, the production stage of nanomaterials is one of the most critical steps. Among the major potential risks, worker safety and health and environmental pollution are issues. Workers have a greater chance of exposure to nanomaterials by accident or without their knowledge during the manufacturing processes than during other stages such as use or end of life [13]. Also, the possibility of release of nanomaterials to the environment during the manufacturing processes is higher than for other stages. Technologies for monitoring and detection for nanomaterials are still under development, and exposure and transport mechanisms into human body is one of the most critical issues surrounding nanotechnology [13] [14].

Many consumers use products containing nanomaterials (sunscreens (TiO$_2$, ZnO), sporting goods (carbon nanotubes), socks (Ag), etc.). In the use stage, nanomaterials can be released by wear or breakage, or they can be directly applied to skin like a sunscreen. However, consumers likely do not recognize the nanomaterials inside the products and their potential effects on humans and the environment because many manufacturers fail to clearly disclose their products' composition, especially the size of nanomaterials and the risks they might pose. In addition, some commercial advertisements for nanomaterials, such as nano silver for antibacterial function, might promote a misleading concept, suggesting to consumers that all nanomaterials are inherently beneficial [15] [16].

In the end-of-life stage, there are potential emissions of nanomaterials to the environment. It is reported that the concentration of flame retardants is higher at electronic waste recycling facilities than at other places such as assembly factories or computer repair shops [17], and lead (Pb), a heavy metal, is leached out above the toxicity characteristic levels at electronic waste landfill sites [18]. Similar end-of-life phenomena may be associated with products containing nanomaterials. During the end-of-life treatments of nanomaterial-containing products, nanomaterials can be released into the environment depending on disposal practices.

If more information about fate and transport, and detection in the environment is available, it is likely that much of the potential threats could be avoided. To prevent unintended consequences from nanomaterials in the future, it is necessary to develop best practices to control release and adequate monitoring methods for nanomaterials. Unfortunately, progress in this area is slow. The research resources for nano-related environmental safety and health remain small compared to other research related to products and materials development. Less than 7% of total research funding for nanotechnology in the United States has been allocated for environmental safety and health for 2011 [19].

3. CALIFORNIA AND NANOINDUSTRY

3.1 Distribution of nanotechnology industry sectors in California

Figure 2 shows the distribution of nanoindustry in California for each industry sector (in terms of numbers of entities). These industry sectors include:

![Value chain of TiO$_2$ nanomaterial based on concept of life cycle stage.](image)
3.2 Practices of California nanoindustry

The State of California is a nanoindustry leader, with more than 20% of the U.S.-based nano companies located in California [21]. One concern in the nanoindustry is the size of individual companies. Although there are large companies that typically have enough resources to address safety and environmental concerns, many are small startup businesses with fewer than 10 employees; they may not have enough resources to invest for worker safety and health or for pollution prevention during manufacturing processes. This poses a challenge regarding safety and health for workers, and for addressing the unknown public health and environmental impacts of nanomaterials.

Another issue for California's nanoindustry is that although some companies have their headquarters or sales offices located in the state, the actual manufacturing facilities are overseas. Generally, the manufacturing facilities are in developing countries mainly because of lower manufacturing costs and relatively modest burden in terms of safety and health and/or environmental pollution. California has more research organizations than any other state for providing technical support for development and application of nanomaterials. The ten campuses of the University of California system, private universities, national research laboratories, and private research centers provide excellent resources and support for nano-related research and development. Typically California has been a crucible for high-tech industry and many innovative companies. Such resources and high-tech infrastructure uniquely position California to become a leader in nanotechnology, much as it was for the high-tech industry.

3.3 Concerns about nanomaterials and California

Data on human health, ecotoxicity or other adverse effects of nanomaterials are limited, but it is reported that toxicological behavior of nanomaterials depends on properties such as surface area, quantity, solubility, and shape [9] [22]. Several possible adverse effects of nanomaterials, such as oxidative stress by titanium dioxide (TiO₂), penetration of zinc oxide (ZnO) particles into animal skin, and structural resemblance of carbon nanotubes to asbestos, have been reported [23] [24] [25] [26]. Because of similar shapes, CNTs and asbestos might have same adverse impacts to human. Additionally, the end-of-life impacts of nanomaterials to humans and the environment are largely unknown.

The study of the fate and transport of nanomaterials is concerned with determining how their properties and behavior change over time, particularly after release into the environment. Information on the fate and transport of nanomaterials in aqueous matrices indicates that the behaviors of nanomaterials vary in different media [27]. At present, too little is known about nanomaterials' fate and transport in the environment.

Experience has shown that information on fate and transport, detection, and characterization of the chemicals all play an important role in determining the ultimate safety of the chemicals. In the case of nanomaterials, a more proactive approach is imperative before widespread use of materials leads to unintended consequences. Careful examination of risks during a development or design stage could afford the opportunity to avoid future environmental and health issues. In the past, important technical revolutions like nuclear power or the silicon chip industry have moved forward before an
understanding was developed about how to deal with wastes, or about the effects of the chemicals on workers or the environment. For example, the Silicon Valley's solvent pollution of groundwater by silicon chip industry has necessitated hundreds of million dollars of cleanup at more than 20 Superfund sites over the past several decades [28].

Because of its position as a nanoindustry leader and its large technical workforce already in place, California wants to assure that nanomaterials and the nanoindustry evolve in a manner that anticipates threats and avoids unnecessary risk. Due to those unique situations, California has an interest in nanomaterials and nanotechnologies, and started nanomaterials information call-in program.

4. RECENT EFFORTS TO ADDRESS THE DATA GAPS BY OTHERS

In October 2008, the U.S. Environmental Protection Agency (EPA) issued a Federal Register notice regarding carbon nanotubes. The notice reminds manufacturers and importers that they must notify EPA 90 days prior to the manufacture or import of new chemical CNTs for commercial purposes, in accordance with Toxic Substances Control Act (TSCA) Section 5 regulations for new chemicals at 40 C.F.R. 720.22. Also, USEPA started a voluntary 2-year program, the Nanoscale Materials Stewardship Program (NMSP), to help a firmer scientific foundation for regulatory decision and development of information for nanomaterials [29] [30]. Several states such as Massachusetts, New Jersey, and Wisconsin are considering addressing the data gaps in nanomaterials. Berkeley, California and Cambridge, Massachusetts have proactive reporting programs regarding nanotechnology. [31] [32].

More recently, France, Norway, Australia and Canada have announced plans to require reporting about nanomaterials. In Europe, there is no current plan to introduce reporting additional to Registration, Evaluation, Authorization and Restriction of Chemicals (REACH), but the European Union (EU) has implemented the first product-specific regulation of cosmetic products [33]. The Organization for Economic Co-operation and Development’s (OECD) Working Party on Manufactured Nanomaterials (WPMN) and the Safety for Risk Analysis (SRA) are working on nanomaterials risk assessment [34] [35].

5. CALIFORNIA DEPARTMENT OF TOXIC SUBSTANCES CONTROL (DTSC) APPROACHES FOR SAFE NANOTECHNOLOGY

5.1 Information call-in by DTSC

DTSC's mandatory information call-in program is different from those mentioned above. It includes both commercial and research entities, and it does not have an exemption for any threshold amount of production. California's Health and Safety Code, sections 57018-57020 authorizes a state agency to request a manufacturer of a chemical to provide the state agency with specified information regarding the chemical. In 2009, DTSC selected CNTs as the first information call-in material because they are new and because of their widespread commercial application. Twenty-six official information request letters were sent to producers and importers in California. Of those, DTSC received information from 23 companies and other organizations; the information received is under review. DTSC continued to select materials of interest for second call-in and started the second official call-in in late 2010 [36]. The selected materials for second call-in are TiO₂, CeO₂, ZnO, Ag, nano zero valent Fe, and quantum dots (QDs). The reasons these materials selected by DTSC are because, while there is a lack of information on their impact on human health and the environment, they are currently used in many available commercial products. DTSC believes the marketplace should have data on analytical methods, toxicity, physical-chemical properties, fate and transport, and other necessary information.

5.2 Process for information call-in by DTSC

In an effort to identify chemicals of concern, DTSC has been searching all known public sources, including electronically searchable databases maintained by all levels of governments, published academic journal papers, and reports from governments and/or industrial associations. Manufacturers worldwide who produce or import nanomaterials of interest into California have been identified. As part of its outreach efforts, DTSC has been meeting with individual manufacturers of nanomaterials in California and has sponsored a series of symposia and workshop on various topics relating to nanomaterials. Through these meetings and workshops, DTSC explains the call-in process, the laws, and why DTSC is interested in the nanomaterials [36] [37].
During the information call-in processes, confidential business information (CBI) will be protected. If a manufacturer believes that information provided to DTSC involves the release of a trade secret, a manufacturer can request protection of that information by notifying the DTSC in writing [12]. If that information is not a public record, DTSC will protect the CBI during the entire call-in process. All other information collected and process steps will be posted on the DTSC Web site in a timely manner.

Figure 3 details the chemical information call-in process. Throughout the call-in process, DTSC cooperates with numerous entities that have an interest in nanomaterials and seeks to develop an equitable and resource-efficient approach to filling key information gaps. DTSC is collaborating with manufacturers throughout the process to identify and prioritize information gaps and to develop strategies to address those gaps.

Furthermore, DTSC is deeply involved with the federal government, industrial associations, state governments, and academia to promote better information gathering and sharing of useful data or ideas. Partnership agreements between DTSC and several other government offices are in place or being developed to facilitate collaboration and information sharing [37].

5.3 What information is requested?

DTSC sends an official information request letter to manufacturers who produce or import nanomaterials into California or who may import nanomaterials into the State. Based on California's Health and Safety Code, sections 57018-57020, a state agency request can include, but is not limited to, an analytical test method, bioconcentration factor for humans for the chemical and other information relevant to the fate and transport of the chemical into the environment.

The CNT call-in letter (first call-in) included six categories of questions to manufactures regarding analytical test methods, fate and transport, and other information on nanomaterials. The questions posed for the first CNT call-in included [38]:

1. What is the value chain for your company? For example, in what products are your nanomaterials used by others? In what quantities? Who are your major customers?
2. What sampling, detection and measurement methods are you using to monitor (detect and measure) the presence of your chemical in the workplace and the environment? Provide a full description of all required sampling, detection, measurement and verification methodologies.
3. What is your knowledge about the current and projected presence of your chemical in the environment that results from manufacturing, distribution, use, and end-of-life disposal?
4. What is your knowledge about the safety of your chemical in terms of occupational safety, public health and the environment?
5. What methods are you using to protect workers in the research, development and manufacturing environment?
6. When released, does your material constitute a hazardous waste under California Health & Safety Code provisions? Are discarded off-spec materials a hazardous waste? Once discarded, are the nanomaterials you produce a hazardous waste? What are your waste handling practices for the nanomaterials?

Question 1 addresses the value chain of nanomaterials. Providing the value chain helps DTSC better understand the types of products that contain the chemical of interest. Who makes the nanomaterials, the production capacity? Who uses the nanomaterials and where they are located are all critical factors for understanding the general value chain of nanomaterials? The applications and products that use the materials should also be identified. It is expected that the number of applications will increase with innovations in technology. The value chain will be background information that DTSC can use to estimate the production capacity of each nanomaterial, the flow of materials of interest, and the potential release amounts of nanomaterials into the environment. Value chain information, also helps DTSC discern what types of materials are used in what products.

Question 2 covers one of the nanomaterials’ challenging issues: detection and monitoring. Although there are existing protocols for monitoring and testing of particles, most of them are based on the existing materials, i.e., at least micron scale, and have not been proven effective for nanomaterials. Before engineered nanomaterials were used widely, naturally or incidentally generated nanomaterials already existed in the environment. So, it may not be an easy task to separate engineered nanomaterials from background nanomaterials or from other interferences in environmental media such as sediment or wastewater. To date, there is no single comprehensive method to identify engineered nanomaterials. Several combined methods for characterizing nanomaterials in the environment are needed because of their small size and great variation of composition, structure, and morphology. DTSC recognizes that detection and monitoring of nanomaterials and the development of technology and instruments is absolutely necessary and fundamental to further understand fate and transport and toxicity of nanomaterials.

Questions 3 and 4 are about the properties and the fate and transport of nanomaterials. The properties of nanomaterials, such as toxicity, reactivity, and physical forms are different from their bulk materials. It is critical to understand nanomaterials’ behaviors in air, water, and soil in order to understand their impact on the health of ecosystems. Proper treatment of nanomaterials or nanomaterial-containing products in every life cycle stage is necessary to prevent adverse effects. Although knowledge of fate and transport of nanomaterials is in its infant stage, some studies have addressed the release of nanomaterials into the environment. These studies show that engineered nanomaterials already exist in the environment, and the amount is expected to increase because of increased usage.

Question 5 addresses environmental health and safety for workers who directly manipulate nanomaterials. Such workers can be exposed during the synthesis processes and during cleaning of equipment after synthesis or manufacturing of the products. Personal protective equipment and worker protection protocols currently exist for bulk materials. However, these conventional protocols may not be suitable for nanomaterials because it has not been demonstrated that they are appropriate for nanomaterials. Nanomaterial-specific worker protection protocols are under development but are not fully utilized. In addition, recent research indicates that about 24% of nanomaterials researchers in the lab did not use any type of general laboratory protection equipment such as a local extraction bench or a fume hood to prevent exposure from the nanomaterials being handled.

Another issue is the disposal of nanomaterials. Question 6 is about nanomaterials waste handling and disposal methods. Currently, nanomaterials are not categorized as hazardous waste. But because of the lack of clarity in regard to their toxicity to humans and the environment, their proper handling and disposal remain important. Interim guidelines for disposal of nanomaterials are based on the worst-case assumption that all nanomaterials-related wastes are potentially hazardous. Although many researchers know that nanomaterials should be treated as hazardous waste unless they are classified as non-toxic waste, about 85% of researchers dispose of nanomaterials without using special procedures. Thus, guidelines or standard disposal processes that take into consideration the hazardous nature of the material, the quantity involved, and physical form (pure solid, liquid suspension, or solid matrix with nanomaterial) are necessary for nanomaterials or products containing nanomaterials.

The second call-in is focused on analytical test methods and properties of nanomaterial in environmental matrices. DTSC is seeking information about the chemical and physical properties, fate and transport of nanomaterials in the environment, and sampling and test methods of nanomaterial. Proper characterization is essential to understand the impacts of nanomaterials in terms of toxicity, fate and transport, and exposure. Analytical test methods to characterize the properties of nanomaterial are the basic tools for risk assessment as well as development of nanomaterials. Without proper characterization, the possibility to understand the behaviors of nanomaterials in various matrices is very limited. Detecting and analyzing the nanomaterial in the various matrices are one of the rudimentary steps for further processes and these steps are also critical in the development of nanomaterial. From the viewpoint of material engineering, characterization of underdeveloped materials is an essential process because the internal structure, shape, and size determine the properties of materials. Thus,
historically, the development of materials goes side by side with the development of characterization methods and/or tools. Currently, only a few technologies are available to characterize nanomaterials. However, each method has its own limitations so that no single technology can be used in all fields. Some tools are useful for measuring the particle size, but the same tools cannot be used under other situations. Also, there are concerns regarding which properties should be analyzed and what methods should be used to understand and access the impacts from nanosized materials. However, many of the methods that access these impacts are still under development; some methods that are originally applied to analyze bulk material can be used for nanomaterials as well.

With the lack of proper instrumentations and methods, efforts to fill in the gaps of information are being carried out by manufacturers and researchers. The basic information will include toxicity, physicochemical property, and fate and transport of nanomaterials in the environment. There are several critical prerequisites should be developed before fully understanding the properties of nanomaterials, such as methods of detection in biological matrices, environment, and workplace; methods for standardizing assessment of particle size, size distribution, shape, and surface area; reference materials for chemical and physical characterization of nanomaterials, and methods to characterize chemical composition and purity [49].

Based on these prerequisites, there are several parameters, at minimum, that should be analyzed to address the impacts of nanomaterials. A study by Oberdorster et al and a report by the Minimum Information for Nanomaterial Characterization Initiative in 2008 selected a set of parameters to be characterized to better understand the properties of nanomaterials [50] [51]. The United Nations also established the Globally Harmonized System (GHS) of classification and labeling of general chemicals to define a set of parameters that address the health and hazard of chemicals, and the Safety Data Sheet (SDS) [52].

Even though there is limited information about analytical methods and data, DTSC has asked manufacturers to fill in these gaps since basic information on producing nanomaterials is critical. Below are some sample parameters asked by DTSC in the second information call-in.

Physical properties of nanomaterial
- Shape
- Density
- Size distribution
- Size of surface area

Chemical properties of nanomaterial
- Composition
- Purity
- Surface modification
- Solubility

Analytical methods used to measure above parameters

5.4 Time line for information call-in

Figure 4 below shows the proposed time line for the chemical information call-in. The information call-in process will take two years to accomplish. Prior to the formal call-in, DTSC has met with producers and importers of nanomaterials in California and discussed the needs, benefits, and burdens of the information call-in. DTSC will then send official letters requesting the information it seeks to producers and importers in California.
5.5 Share the data gaps and knowledge with other organizations

Nanotechnology encompasses many diverse fields, and thus multidisciplinary frameworks are needed to address the complex spectrum of issues. Nanotechnology includes fabrication of materials, detection and characterization of materials, applications and products, and health and safety issues. Because of data gaps in nanomaterials properties and their potential impacts on human health and the environment, it is absolutely necessary to collaborate with other organizations to better understand nanomaterials-related risk. To cover and understand better all these areas, and to collect high-quality and reliable information, DTSC is working with many domestic and international partners while it concurrently collects call-in information from manufacturers. While industry is its major partner, DTSC also has been collaborating with the U.S. Environmental Protection Agency (EPA), the California Department of Pesticide Regulation, the California Department of Public Health, academia, industrial associations and non-government organizations to share and develop information. The specialized functions and authorities of each organization should promote a more efficient and transparent processes and will ultimately provide a more comprehensive understanding of the properties of nanomaterials.

6. CONSEQUENCES OF INFORMATION CALL-IN BY DTSC

6.1 What does DTSC expect from chemical information call-in?

Through these information call-in processes, DTSC expects to develop an in-depth understanding of the nature of nanomaterials and their fate and transport in the environment. Protection of public health, the workforce, and the environment from adverse impacts is critical to success of the industry. The information call-in will help identify and fill data gaps and thus help develop a more comprehensive knowledge and more sustainable development of nanomaterials.

6.2 Benefits to industry from information call-in

Evaluating the potential impacts of engineered nanomaterials prior to their mass production is essential to address environmental and human health concerns and to develop sustainable nanomaterials. By recognizing the potential risks and developing safe nanomaterials, industry can avoid expensive cleanup costs and other future liability. Identification, prioritization, and the filling of information gaps will lead to more sustainable practices in this rapidly growing industrial sector.
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