Nanotechnology offers vast promise and potential. New benefits for health, the environment, industry, and commerce through application of nanotechnology are being discovered on a daily basis in arenas as varied as pollution control, food, pharmaceuticals, and engineering and construction. Yet, the study and understanding of the health and environmental risks associated with use of nanomaterials lag behind research into new applications. Research demonstrates that some nanomaterials may pose significant health and environmental concerns. As scientists conduct further studies into these concerns, regulators, manufacturers, insurers, and attorneys must keep apprised of potential risks. Although claims of personal injury related to exposure to nanomaterials have not yet resulted in litigation, it may be just a matter of time. This article focuses on recent studies into potential health effects of exposure to nanomaterials and governmental regulatory reaction.

What Is Nanotechnology?
Chemical substances that have structures with dimensions at the nanoscale are commonly referred to as nanoscale materials or nanoscale substances. The term “nanoscale” applies to any structure with at least one dimension measured from 1 to 100 nanometers. A nanometer is one-billionth of a meter. To provide perspective, the thickness of a single sheet of paper is about 100,000 nanometers. At the nanoscale, the physical, chemical, electrical, and biological properties of matter differ in fundamental ways from the properties of the same matter in its “macro” or bulk form. Below 50 nanometers, Newtonian physics gives way to quantum physics, so that the chemical, electrical, physical, mobility, solubility, magnetic, and optical properties of matter are altered. For example, at the nanoscale, it is reported that carbon becomes stronger than steel, aluminum becomes highly explosive, and silver assumes biological properties and becomes a biocide.
Increasingly, engineers are applying nanoscience to take advantage of these unusual properties. The projected applications of nanotechnology are almost limitless and are incorporated into appliances, coatings, electronics, food, beverages, toys, games, clothing, cosmetics, paint, homes, pharmaceuticals, electronics, and textiles. Incorporation of nanomaterials is expected to affect scientific advancement in engineering technologies, space exploration, pollution control, and national security. Since its inception in 2001, through and including amounts it has budgeted for 2017, the National Nanotechnology Initiative has invested $23 billion in nanotechnology. One research group has estimated that by 2018, investment in nanotechnology will reach $4 trillion worldwide.

**What Are the Concerns and What Do Recent Studies Indicate?**

There is a growing body of scientific evidence confirming the difference that exists between some chemical substances manufactured at the nanoscale and their macro counterparts. Nanoscale materials may have different or enhanced properties that raise new questions, such as whether the material in the smaller form presents hazards to humans and the environment. While research into the potential impacts on human health from exposure to nanomaterials has been under way for years, the results are inconclusive but worrisome. Recent studies have done little to alleviate concerns.

Carbon nanotubes (CNTs) are a cornerstone of nanoengineering. Their needle-like fiber shape has long been compared to the shape of asbestos fibers, raising concerns that widespread use of CNTs may lead to mesothelioma, a cancer linked to exposure to asbestos. In 2008, a study involving the introduction of multi-walled carbon nanotubes (MWCNTs) into the mesothelial lining of the abdominal cavity of mice resulted in asbestos-like pathogenic reactions, including inflammation and the formation of granulomas. See Craig Poland et al., “Carbon Nanotubes Introduced into the Abdominal Cavity of Mice Show Asbestos-Like Pathogenicity in a Pilot Study,” *3 Nature Nanotechnology* 423–28 (2008). Of more concern was another 2008 study in which researchers were able to induce mesotheliomas in mice through intraperitoneal exposure to a well-defined dose of CNTs. Atsuya Takagi et al., “Induction of Mesothelioma in p53+-/- Mouse by Intraperitoneal Application of Multi-Wall Carbon Nanotube,” *33 J. Toxicol. Sci.* 105–16 (Feb. 2008). In 2009, another murine study demonstrated that MWCNTs reach the sub-pleura after a single inhalation exposure of 30 milligrams per cubic meter for six hours. Upon examination, nanotubes were found embedded in the sub-pleural wall and within sub-pleural macrophages. Jessica Ryman-Rasmussen et al., “Inhaled Carbon Nanotubes Reach the Sub-Pleural Tissue in Mice,” *4 Nature Nanotechnology* 747–51 (Nov. 2009).
One of the most significant studies was conducted by Nagai et al. in 2011. This study showed that the deleterious effects of multi-walled carbon nanotubes on human mesothelial cells were associated with their diameter-dependent piercing of the cell membrane. Thin MWCNTs with high crystallinity showed mesothelial cell membrane piercing and cytotoxicity in vitro and subsequent inflammogenicity and mesotheliomagenicity in vivo.”

Hirotaka Nagai et al., “Diameter and Rigidity of Multiwalled Carbon Nanotubes Are Critical Factors in Mesothelial Injury and Carcinogenesis,” 108 Proc. of the Nat’l Acad. of Scis. E1330–E1338 (Dec. 6, 2011). In contrast, thick MWCNTs were less toxic, inflammagenic, and carcinogenic. The study found that mesotheliomas induced by MWCNTs were characterized by deletion of Cdkn2a/2b tumor suppressor genes, similar to mesotheliomas induced by asbestos, suggesting that different degrees of direct mesothelial injury by thin and thick MWCNTs are responsible for the extent of inflammogenicity and carcinogenicity. The authors concluded that their work suggests that the control of the diameter of MWCNTs could reduce the potential hazard to human health.

A 2012 in vitro study of human airway epithelial cells exposed to single-walled carbon nanotubes (SWCNTs) showed “significant disruption” of cellular mitosis at occupationally relevant doses and disruption of centrosomes. L.M. Sargent et al., “Single-Walled Carbon Nanotube-Induced Mitotic Disruption,” 745 Mutation Research 28–37 (2012). Disruption of the centrosome is common in many solid tumors, including lung cancer, and the resulting aneuploidy is an early event in the progression of many cancers, suggesting that it may play a role in both tumorigenesis and tumor progression. Id.

A 2015 study found that MWCNTs that were environmentally introduced to mice rapidly entered and disseminated throughout their bodies, initially accumulating in the lungs and brain and later reaching the liver and kidneys via the bloodstream. Adriana Albini et al., “Environmental Impact of Multi-Wall Carbon Nanotubes in a Novel Model of Exposure: Systemic Distribution, Macrophage Accumulation, and Amyloid Deposition,” 10 Int’l J. Nanomedicine 6133–45 (2015). The data from this study highlight the conclusion that, at least in a rodent model of exposure, MWCNTs may induce macrophage recruitment, activation, and amyloid deposition, causing potential damage to several organs.

In 2016, an in vivo mice study into the potential genotoxicity of MWCNTs demonstrated a significant increase in the level of DNA lesions measured within the first 24 hours of exposure. Gellért Gerencsér et al., “In Vivo Induction of Primary DNA Lesions upon Subchronic Oral Exposure to Multi-Walled Carbon Nanotubes,” 30 In Vivo 863–67 (Nov.–Dec. 2016). The study concluded that there were significant differences in sensitivities of the varied rat strains tested, which suggested human relevance as populations with
diverse genetic characteristics might present higher or lower susceptibility to the effects of exposure to ingested nanoparticles.

In 2014, a working group of the International Agency for Research on Cancer (IARC), the Working Group on the Evaluation of Carcinogenic Risks to Humans, met in Lyon, France, to assess the carcinogenicity of CNTs. In 2017, this group issued IARC Monograph 111, Some Nanomaterials and Some Fibres (May 2017). The monograph concluded that a lack of epidemiological data indicated inadequate evidence to find that CNTs were a carcinogen in humans. However, it did ultimately classify a particular type of multi-walled carbon nanotube (MWCNT-7) as possibly carcinogenic to humans based on the animal data. Based on its review of available studies, the working group determined that this type of CNT caused peritoneal mesotheliomas under various exposure methods and that the evidence was sufficient to conclude that MWCNT-7 was carcinogenic in experimental animals. There was also limited evidence for other types of MWCNTs with dimensions similar to those of MWCNT-7 and inadequate evidence for SWCNTs. The impact of the working group’s classification of these CNTs has significant implications and warrants further research.

**What Is the Government Doing?**

As production of nanoscale chemicals and other materials continues to outpace the scientific testing of these products, the federal government under the Obama administration stepped up efforts to “get its arms around” the extent of any serious problem before it develops. Although the National Institute of Occupational Safety and Health (NIOSH) has stated that it is unaware of any reports of adverse health effects on workers using or producing CNTs or carbon nanofibers (CNFs), it is aware of studies of animals exposed to these substances that are informative in predicting potential human health effects, including inflammation, granulomas, and pulmonary fibrosis.

Recent Current Intelligence Bulletins (CIBs) issued by NIOSH have been reviewing and assessing data on the potential nonmalignant adverse respiratory effects of CNTs and CNFs. NIOSH has provided a quantitative risk assessment based on animal dose-response data and proposed a recommended exposure limit (REL) of 1 microgram per cubic meter as a respirable mass over an eight-hour time-weighted average. U.S. Dep’t of Health & Human Servs., NIOSH, Current Intelligence Bull. 65, DHHS (NIOSH) No. 2013-145, Occupational Exposure to Carbon Nanotubes and Nanofibers (Apr. 2013). This particular CIB describes strategies for controlling workplace exposures and implementing a medical surveillance program. An earlier CIB on titanium dioxide set a recommended exposure limit of .3 milligram per cubic meter over an eight-hour time-weighted average. U.S. Dep’t of Health & Human Servs., NIOSH, Current Intelligence Bull. 63, DHHS (NIOSH) No. 2011-
160. Occupational Exposure to Titanium Dioxide (Apr. 2011). The Occupational Safety and Health Administration has adopted these same recommended exposure limits.

Those efforts continue to some extent. The U.S. Environmental Protection Agency (EPA) in May 2017 issued its Draft Guidance on EPA’s Section 8(a) Information Gathering Rule on Nanomaterials in Commerce. See 82 Fed. Reg. 2452 (May 16, 2017). The document requests public comment on the draft guidance, the deadline for which was June 15, 2017. The draft guidance relates to the EPA’s recently issued final rule on nanomaterial reporting and record keeping under section 8(a) of the Toxic Substances Control Act (TSCA). The rule, entitled Chemical Substances When Manufactured or Processed as Nanoscale Materials: TSCA Reporting and Recordkeeping Requirements, was finalized on January 12, 2017. See 82 Fed. Reg. 3641. The rule was set to become effective on May 12, 2017, but the EPA delayed implementation until August 2017 to allow for review of its draft guidance and comments from stakeholders. If adopted, the regulation would require electronic reporting and record keeping of certain chemical substances manufactured or processed at nanoscale. Specifically, the rule requires one-time reporting of certain information, including identity, production volume, methods of manufacture and processing, use, exposure and release information, and available health and safety information, as well as keeping records of this information for three years. This rule will not only require reporting for existing discrete forms of certain nanoscale materials but also will impose a standing one-time reporting requirement for new discrete forms of certain nanoscale materials before those new forms are manufactured or processed.

The EPA explained that the new rule is not intended to conclude that nanoscale materials as a class or specific uses of nanoscale materials are likely to cause harm to people or the environment. Rather, the EPA intends to use the information gathered through this reporting rule to determine whether any further action under the TSCA, including additional information collection, is needed. The EPA believes this regulatory approach under the TSCA will aid in ensuring that nanoscale materials are manufactured and used in a manner that protects against unreasonable risks to human health and the environment. The EPA has long followed nanotechnology developments with an eye toward potential hazards to human health and the environment. As far back as 2007, the EPA issued a white paper that surveyed current information on risks associated with nanomaterials. EPA, EPA No. 100/B-07/001, Nanotechnology White Paper (Feb. 2007). At that time, the EPA concluded that more research was required to perform proper risk assessment of health and environmental impacts, noting “[t]here is a significant gap in our knowledge of the environmental, health, and ecological implications associated with nanotechnology.” Id. at 52. This assessment largely holds true a decade later. However, as
discussed above, ongoing research strongly suggests that exposures to certain nanomaterials in some doses may pose significant health risks.

**What Next?**
The commercial applications of nanotechnologies are far outpacing our understanding of the potential risks of nanomaterials to human health. Recent studies have done little to alleviate those concerns and have raised additional questions. At the very least, it is generally accepted that some forms of nanomaterials are possible carcinogens, but a variety of other health conditions may also be connected to exposures. Of note to practitioners involved in asbestos litigation is the possibility of nanomaterials as a cause of mesothelioma. Although there is no nanomaterial personal injury litigation to date, it may only be a matter of time. For now, counsel must keep up-to-date on research developments because the indicators of a major toxic mass tort are present and building.

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