Nanotechnology And Asbestos: Informing Industry's Approach To Carbon Nanotubes, Nanoscale Titanium Dioxide, And Nanosilver

With greater knowledge comes greater responsibility, and greater liability. When it comes to nanotechnology, our ability to understand the potential risks is unprecedented, thanks in part to the asbestos mass tort experience. If the nanotechnology industry wants to avoid a similar catastrophe, the lessons of the asbestos litigation should be heeded now.

Although there are many types of nanoparticles, three in particular have become the subject of increasing discussion: (1) carbon nanotubes (CNTs); (2) nano-sized titanium dioxide (TiO₂); and (3) nanosilver [1, 2]. Like asbestos years ago, these nanomaterials are considered a critical industrial resource with immense potential, and they are already present in hundreds of products that we use every day [3, 4].

However, apprehension about the <u>potential</u> (though not established) effects of these materials on human health and the environment is growing. For example, certain physical properties of long, thin CNTs are similar to the most hazardous forms of asbestos, which raises the specter of mesothelioma – an incurable cancer of the pleura and peritoneum that is caused by asbestos exposure. [5]. As a result of such concerns, at least one insurer has specifically excluded CNTs from coverage [6] [7]. Recent agency statements regarding the potential health effects of occupational exposure to nano-scale TiO₂ have spurred inquiry into the use of this material in finished products [8]. And environmental groups have petitioned the EPA to stop the proliferation of products that use nanosilver in the absence of further research [9] [10]. Meanwhile, public awareness of the use of nanomaterials remains low: In a survey conducted by the Project for Emerging Nanotechnologies, 70 percent of respondents had heard little or nothing about nanotechnology [11].

Against the backdrop of the asbestos experience and issues of regulatory inefficacy, this paper addresses the existing studies involving CNTs, nano-scale TiO₂, and nanosilver; potential litigation scenarios; and strategies for mitigating litigation risk. Litigation relating to one or more of these nanomaterials is likely; the question is when and in what form [2]. Companies that are implementing this technology without also investing in product stewardship and risk prevention could become prime targets for the "Plaintiffs' Bar" -- the lawyers who represent individual plaintiffs against corporations.

ASBESTOS 101

For the better part of a century, asbestos was revered by industry for its amazing chemical and heat resistance, flexibility, and tensile strength. Because of these properties, asbestos was used in innumerable commercial and industrial products, including: insulation, fireproofing, asbestos cement pipes, transite panels, brakes, gaskets, valves, pumps, joint compound, welding blankets, and so on. But by the 1940s, it was reported that very high doses of asbestos could cause scarring of the lungs known as asbestosis. By the 1960s, it had been reported that similarly high doses could also cause lung cancer. Still, these diseases had been seen principally in individuals

who worked with raw asbestos in manufacturing or mining situations, not end users of asbestoscontaining products.

The late 1960s brought with it three important revelations about asbestos: (1) certain forms of asbestos known as amphiboles may cause a deadly and previously unreported form of cancer of the pleura (lining of the lung) and peritoneum (lining of the abdomen) called mesothelioma; (2) mesothelioma was appearing in insulators who worked with highly friable asbestos-containing insulation products, not raw asbestos; and (3) mesothelioma has an extremely long latency period -- it typically takes more than 20 years from first exposure to manifest. Nevertheless, Dr. Irving Selikoff, a pioneer in mesothelioma research and author of the groundbreaking insulator studies, believed asbestos was far too important and valuable a resource to remove from industrial use [3]. Instead, he advocated the use of industrial hygiene measures to control dust. The first mandatory industrial hygiene practices and warnings for asbestos-containing products took effect in 1972. The litigation avalanche began in the 1970s as well, but it took another decade for asbestos to balloon into the bankruptcy-inducing mass tort we know today.

When it comes to assessing the state of scientific knowledge at the relevant time ("state of the art"), jurors in the modern era can find it difficult to turn back the clock. Thus, state of the art can be a difficult defense in asbestos litigation. Some companies that used small amounts of asbestos in finished products and complied with all applicable regulations have found themselves subject to punitive damages claims. Actual ignorance of the state of the science generally provides no shield against liability.

NANOTECH STATE OF THE ART

"It's like you shrink a cat and keep shrinking it, and then at some point, all at once, it turns into a dog." [13]

This quote aptly describes the nanotechnology phenomenon. When reduced to nano form, familiar, inert materials – like carbon -- can exhibit very different properties. While these differences account for the amazing industrial potential of nanotechnology, they also can lead to disturbing toxicological effects. Reducing the size of the particles vastly increases the surface area for each mass dose, which can lead to greater biological reactivity [12, 14]. Some nanoscale materials are more easily absorbed than their standard-sized counterparts and may bypass some of the human body's natural defense mechanisms [12, 14]. For all these reasons and more, the toxicological properties of nanomaterials cannot be extrapolated from the behavior of the same chemical at a larger size [12, 15]

A. Carbon Nanotubes

"Carbon nanotubes are made of graphene sheets in which carbon atoms form a perfect ensemble very similar in structure to a chicken wire" [16]. CNTs may be long or short, tangled or straight, multi-walled or single-walled. [5, 16]. CNTs are typically about 1-3 nm in diameter, but may be hundreds to thousands of nanometers long [17]. "As individual molecules, nanotubes are 100 times stronger-than-steel and one-sixth its weight." [17].

The potential applications of CNTs are numerous and varied. CNTs have been proposed for use as an interconnective material in electrical circuits; as a strength and performance enhancer in fabrics, sports equipment, and building materials; and as a biological, gas, and chemical sensor [16]. Because of their sensor capabilities, it has been suggested that CNTs could be incorporated into "smart packaging" that detects harmful bacteria in food [18]. CNTs also can enhance drug delivery, an application that introduces them directly into the human body at the cellular level [19].

A growing body of evidence suggests that some CNTs may pose health risks. *In vivo* studies have demonstrated that certain CNTs can cause inflammation, scarring (fibrosis), and granulomas when injected into the lungs of mice [20–23]. In an animal inhalation study, lung discoloration and concentration-dependant lesions (inflammation and granulomas) were observed in the lungs of rodents exposed to relatively low mass doses of multiwall CNTs [20]. Oxidative stress on the pulmonary and cardiovascular systems of rodents exposed to CNTs has been reported as well [24].

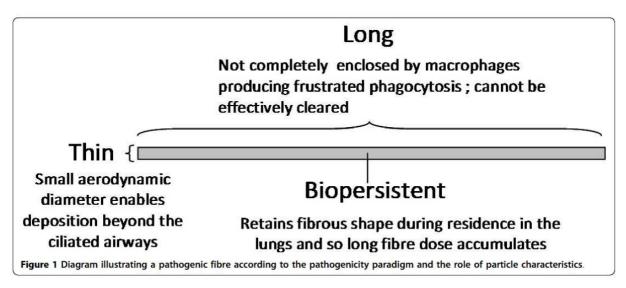
CNTs top the list of potential mass tort catalysts because certain forms – specifically long, thin CNTs – possess the same physical characteristics as the most hazardous types of asbestos known as amphiboles. The physical similarities between CNTs and amphibole asbestos have lead some researchers to suggest that long, thin CNTs may be capable of inducing mesothelioma. Although mesothelioma cases are very unusual in the general public, they are not uncommon in populations who are exposed to the amphibole forms of asbestos [25].

When injected into the peritoneal cavity of mice, long CNTs have induced a mesothelioma response [26, 27]. Animal research also indicates that CNTs may be able to translocate within the body and penetrate the pleura in the same way as amphibole asbestos [14, 28].

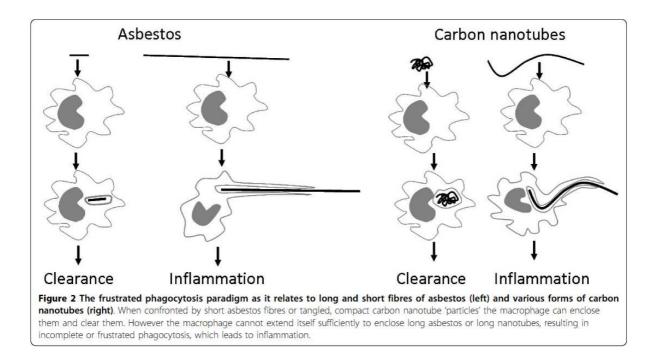
Recent studies also have described a potential biological process by which long, thin CNTs -and long fiber asbestos -- could be retained by the body and induce mesothelioma. According to this research, the ability of any fiber to cause mesothelioma is directly related to its length, diameter, and ability to remain in the body for long periods of time ("biopersistence"). See Figure 1 [5].¹ This paradigm is consistent with the epidemiological studies regarding asbestos, which show that long, thin, highly biopersistent forms of asbestos fibers – the amphiboles -- are the most potent for inducing mesothelioma [5]. Graphene – the main component of CNTs – is very strong and, therefore, likely to exhibit a high degree of biopersistence [5].

¹ Figures 1 and 2, including the text contained therein, were reproduced in full from 2010 Donaldson et. al. [5], an Open Access article. These figures were reproduced pursuant to the applicable Creative Commons Attribution License (<u>http://creativecommons.org/licenses/by/2.0/</u>), which allows unrestricted use, distribution, and reproduction with appropriate citation to the original work. The authors of 2010 Donaldson, et. al. [5] have not reviewed or endorsed this article.





When applied to CNTs, the fiber paradigm suggests that long, thin CNTs are a potential mesothelioma hazard because of their dimensions. By contrast, short or tangled CNTs are more likely to be cleared by the body's defenses, specifically the macrophage cells that can engulf short fibers and remove them from the body. See Figure 2 [5].



While troubling, the existing studies do not establish that CNTs cause disease in humans. The lack of human or chronic exposure studies makes it difficult to extrapolate human effects from existing data [1]. Animal injection studies deliver an artificially high dose to the deposition site

and do not mimic the process by which humans would be exposed [26]. Innocuous substances that do not cause mesothelioma in humans can induce mesotheliomas in animal injection studies [29]. *In vitro* testing (e.g., cellular research) is similarly limited because such studies do not account for the complex mechanisms and interactions that occur in the body [1].

Furthermore, there are significant questions about what the expected doses and modes of exposure to CNTs would be, particularly in non-occupational settings [6]. While workers who manufacture CNT-containing products could inhale CNTs if strict protective measures are not employed, consumer exposure scenarios are less apparent. Most nanotechnology research has focused on the toxicology effect of the raw materials themselves; thus, little is known about the potential routes of exposure or health effects from products that incorporate CNTs [1].

Although unanswered questions persist, studies regarding possible health risks associated with CNTs are multiplying at an exponential rate [6]. At this point, more research is being done into the potential effects of CNTs than almost any other nanomaterial [1, 6]. The insurance industry now views CNTs as a serious risk, and one insurer has specifically excluded them from coverage [6, 7]. The response from manufacturers or users of CNTs is more difficult to gauge, in part because the absence of nano-specific labeling requirements makes it hard to determine exactly which products implement this technology.

B. Ultrafine Titanium Dioxide

Nanoparticles of titanium dioxide (TiO₂) are widely used in paint, coatings, varnishes, sunscreens, and cosmetics [8]. In its standard form, TiO₂ has not been associated with cancer in humans [8].

So far, studies indicate that the nano-scale TiO_2 is not absorbed through healthy skin [30]. However, some commentators have observed that absorption may be possible through skin that is sunburned, cut, or otherwise abraded [6]. One study suggests that ultraviolet radiation damage (i.e., sunburn) may increase the potential for dermal absorption of nanoparticles [31]. Nevertheless, the present weight of evidence does not indicate that dermal absorption poses a significant health risk.

While dermal absorption of nano-scale TiO_2 used in products currently does not appear to present appreciable risk, the National Institute of Occupational Safety and Health (NIOSH) recently expressed concern about the potential effects of inhaled TiO_2 nanoparticles in occupational settings. In April 2011, NIOSH issued Current Intelligence Bulletin 63 regarding Occupational Exposure to Titanium Dioxide [8]. In it, NIOSH concludes that inhaled "ultrafine" TiO_2 is a potential occupational carcinogen. NIOSH defined "ultrafine" particles as those with a primary particle diameter < 100 nm, including engineered nanoparticles [8].

According to NIOSH, the available animal data shows higher lung cancer potency for inhaled ultrafine or nano-sized TiO₂ than for "fine" (non-nano) particles [8]. NIOSH also noted that the appropriate dose consideration in risk assessment is surface area, not mass dose. NIOSH has recommended a time weighted average airborne exposure limit of 2.4 mg/m³ for fine TiO₂ versus .3 mg/m³ for ultrafine (including engineered nanoscale) TiO₂ [8].

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Concerns about occupational inhalation of ultrafine TiO_2 do not mean that exposure to finished products that incorporate these particles is harmful to humans. The NIOSH report only addresses *occupational* exposure by inhalation, and NIOSH cautions that, "conclusions derived herein should not be inferred to pertain to nonoccupational exposures." [8 at p.11]. Occupational exposures involve far greater doses than would be expected from the use of finished products, even in aerosolized form [32]. In addition, NIOSH's conclusions regarding ultrafine TiO_2 are based on animal models. Physiological differences between rodents and humans limit the power of animal models to predict human response, and the animal models generally do not simulate human exposure situations, particularly exposure to finished products.

Although there is currently no scientific evidence of harm from inhaled ultrafine TiO_2 at nonoccupational levels, in June 2011 the Food and Drug Administration (FDA) began evaluating the possibility of a mandatory warning against inhaling spray sunscreens [33]. None of the warnings under consideration mention nanotechnology; however, the FDA's advance notice of proposed rulemaking included a request for information pertaining to the particle size distributions for spray sunscreen products [33]. This request suggests concerns over use of ultrafine TiO_2 in spray products played a role in the FDA's notice [34].

FDA research on the matter continues, and no mandatory warning has issued to date. However, if approved, a mandatory warning will substantially increase the likelihood of litigation, as agency actions carry great weight with both judges and juries [32, 34]. In the interim, some consumer groups are advising the public not use spray sunscreens on children or vulnerable populations until the FDA investigation is completed [35].

C. Nanosilver

Nanosilver's antibacterial and antimicrobial properties have made it extremely appealing to industry. As a result, nanosilver is ubiquitous. Hundreds of products consumers use every day contain nanosilver, and the number is growing [37]. Because labeling is not required, the complete universe of products that contain nanosilver is unknown [10].

Nanosilver is commonly used as an ingredient in polymer coatings that have been incorporated into a wide variety of products, such as bandages, medical devices, food storage containers, household appliances, and feminine hygiene products. Nanosilver can be used in swimming pools as a replacement for chlorine. Nanosilver also has been integrated into fabrics used to make sheets and clothing. Nanosilver suspended in water, known as "colloidal silver," can be used in solutions, including some that are recommended for daily consumption [37].

Concentrations of nanosilver used in products are highly variable and difficult to discern with any degree of accuracy [37]. Nevertheless, because it has been reported that antibacterial effectiveness requires concentrations of 10 ppm silver, it is reasonable to assume that this is the minimum concentration found in most products that use nanosilver [37].

Very little is currently known about the effects of nanosilver on human health. However, because of its antibacterial properties, it is possible that use of nanosilver could increase bacterial resistance or adversely affect the human immune system [6, 9, 10]. Generalized concerns

regarding the unknown properties and effects of nano-scale materials have been raised in the context of nanosilver as well [9].

While the effects of nanosilver on human health, if any, are unclear; nanosilver is viewed by many as a potential environmental hazard. In macro form, silver is highly toxic to aquatic life. In its nanoform, these effects may multiply [9]. Nanosilver also may destroy useful, harmless bacteria [9]. While nanosilver may be released from products into water supplies through washing or other processes, preliminary EPA information indicates that oxidants in the wash water would limit such release [37].

Because nanosilver is an antibacterial and anti-microbial agent, it meets the definition of a pesticide under the Federal Instecticide, Fungicide and Rodenticide Act (FIFRA), which is administered the EPA [6, 9-10]. Currently, only products that claim to have antibacterial properties are subject to the FIFRA requirements. To avoid the extensive registration regulations that apply to pesticides under FIFRA, companies can eliminate the antibacterial marketing and labeling from their products [6].

In 2008, the International Center for Technology Assessment (ICTA) petitioned the EPA for a change in the regulations pertaining to nanosilver [9]. The ICTA Petition calls on the EPA to: (1) close the loophole that allows manufacturers to avoid FIFRA registration by removing antibacterial labeling; (2) identify and ban unregistered products containing nanosilver as illegal pesticides; (3) increase the warning, research and disclosure obligations for products that contain nanosilver; and (4) conduct further research before approving nanosilver pesticide registrations under FIFRA [9]. ICTA also contends that the levels of nanosilver in products approved under FIFRA are too high because the EPA did not properly consider aggregate exposure [9-10]. According to ICTA, the EPA has not responded to its petition [10].

In December 2011, the Office of the Inspector General (OIG) published a scathing report on the EPA's approach to nanomaterials entitled: "EPA Needs To Manage Nanomaterial Risks More Effectively" [12]. Among the various deficiencies OIG identified was the EPA's "failure to communicate," both internally and externally, about nanomaterial hazards. The OIG report also indicates that further study on the effects of nanomaterials is sorely needed [12]. The OIG ultimately concluded that the EPA, "does not currently have sufficient information or processes to effectively manage the human health and environmental risks of nanomaterials." [12].

The principle complaint of environmental groups and the OIG is this: the EPA needs to do more research into the effects of nanosilver <u>before</u> products that use it are allowed to hit the shelves. Nevertheless, the number of products that incorporate nanosilver continues to expand [10]. But a new era may be coming. EPA's response to the OIG report indicates that efforts to identify unregistered nano-containing products and step-up research and regulation are in the works [12]. Such efforts could adversely impact industry's bottom-line and lead to consumer, environmental, or securities actions.

LITIGATION SCENARIOS

Nanotechnology litigation scenarios include consumer and environmental complaints; securities claims; and tort suits. Although not specifically addressed below, insurance disputes are a likely follow-on to any nanotechnology litigation.

A. Consumer and Environmental Cases

The first wave of nano-litigation could come in the form of consumer or environmental complaints that allege nuisance, breach of implied warranty, fraud, or other theories of liability. In connection with these cases, plaintiffs may seek remediation, injunctive relieve, medical monitoring, and/or monetary damages [38].

A recent decision on bisphenol-A (BPA) consumer class action suggests that such consumer litigation against manufacturers who use nanotechnology in their products could be viable. In the BPA decision, the court allowed the class action to continue despite defendants' efforts to characterize it as an impermissible "no injury" products liability case. The court reasoned that consumers who learned about BPA's risks when they had the products and later disposed of them did not obtain the benefit of their bargain [39].

By contrast, where agencies have concluded no health risk exists (e.g., the FDA conclusion that there is no risk from lead used in lipsticks), courts have been more willing to dismiss consumer complaints [39]. Thus, agency decisions could play a central role in any consumer class actions based on undisclosed potential health risks from nanoparticles.

B. Securities cases

Investors have been pouring money into nanotechnology, and with good reason. The EPA predicts that, by 2015, "consumer products with nanotechnology applications will value \$1 trillion on the world market." [40].

While nanotechnology has become big business, some corporate disclosure documents disseminated to investors have not kept up with the science. A report published by the Investor Environmental Health Network describes an epic failure to inform investors of the risks associated with certain nanotechnology products, including CNTs, nanosilver, and nano scale TiO_2 [6]. The report also highlights the possibility that nanotechnology risks may not be insured, which may need to be addressed in disclosure statements as well [6].

Companies that sustain liabilities or stock price drops based on undisclosed nanotechnology risks or activities are susceptible to securities actions [38]. It does not matter if the nanotech at issue actually causes disease; the failure to properly disclose the various risks associated with the nanomaterial use is enough if those facts would be material to the investor community.

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C. Tort Suits

Manufacturers, distributors, and employers that use nanoparticles or nano-enabled products may be subject to tort suits for property damages and personal injury caused by exposure to nanomaterials. Personal injury claims may be based on theories of negligence or strict liability for defective product design and/or failure to warn. These claims also carry with them the threat of punitive damages.

Given the widespread use of nanomaterials in our daily lives, if tort litigation relating to nanotechnology occurs, it is likely to become a mass tort scenario. Mass torts involve large numbers of scientifically complex, hotly-disputed claims in numerous federal and state courts across the country.

General and case-specific causation are elements of every tort claim. Causation is the principle barrier to mass tort litigation because most – but not all -- courts recognize that animal and in vitro studies do not always translate to the human experience. However, definitive proof of causation in humans (e.g., epidemiology) is not a necessary prerequisite to litigation or to adverse jury verdicts. Some courts are reluctant to exclude even highly-speculative causation evidence, and tort claims based solely on animal data have reached a jury [41]. Agency statements or actions may also be used by plaintiffs to bolster their causation arguments.

Because epidemiological evidence is not needed to establish causation in many jurisdictions, we may be a few case reports away from a tort explosion. Such reports -- if they occur -- will most likely appear first in worker populations. Although they lack scientific controls, case reports are the principal form of human causation evidence used to support peritoneal mesothelioma cases against chrysotile (non-amphibole) asbestos defendants. These peritoneal mesothelioma cases often make it to the jury, and adverse verdicts are not uncommon.

The causation studies are further advanced for CNTs than most other nanomaterials. If any reports of lung disease (particularly mesothelioma) eventually emerge in individuals who work with and around CNTs, they could easily ignite the first wave of nanotort filings. And if plaintiffs are permitted to "borrow" from the asbestos studies the asbestos-like properties of CNTs, then CNT cases truly could become the next asbestos.

RISK MITIGATION

There are at least four risk mitigation strategies that every company using nanotechnology should employ: (1) monitor and comply with the evolving regulations that apply to nanomaterials; (2) audit insurance policies; (3) reduce human and environmental exposure to the greatest extent possible; and (4) engage in product stewardship.

A. Compliance With Regulations

Compliance with government regulations is imperative for all businesses, but it will not prevent private litigation. The law generally views regulatory compliance as a *minimum* level of action; however, the public may be entitled to more protection than existing regulations require.

Numerous companies that followed OSHA's 1972 requirements have nevertheless been bankrupted by asbestos litigation.

It is widely recognized that regulatory agencies have not done enough to address nanomaterial risks or to communicate those risks to the public. According to the OIG's report on the EPA, "the Agency as a whole has not provided a transparent overall message about nanomaterials to the general public." [12]. Commentary on other agencies' efforts to police nano-risks has been similarly critical [42].

Given the ineffective response of government agencies to these emerging technologies, it is reasonable to assume that juries – and consumers -- will expect companies to do more than comply with regulations. This is particularly true where the government has acknowledged its own inability to properly address nanomaterial risks [12].

B. Insurance Review

The insurance industry is carefully monitoring nanotechnology developments and can be expected to craft exclusions accordingly [6, 38]. Some insurance companies have explicitly excluded certain nanomaterials from policy coverage already [6 -7]. Every company that uses, manufactures, or invests in nanotechnology should review the applicable insurance policies to determine whether the risks associated with those products are covered. If they are not, this fact may need to be disclosed to investors [6].

C. <u>Reduce Exposure</u>

Reducing exposure reduces risk. Accordingly, a product design that prevents release of, or exposure to, nanomaterial components can reduce litigation risk. Notably, the most resilient asbestos defendants manufactured products with very low potential for fiber release.

Manufacturers of nanotechnology also need to reduce exposure for workers. This means industrial hygiene measures must be implemented. NIOSH has recommended that companies using ultrafine TiO_2 employ well-known, standard industrial hygiene practices, including source enclosure (isolation) and local exhaust ventilation. Local ventilation systems should use high efficiency particulate (HEPA) filters, and the systems should be tested routinely to ensure efficacy [8]. Workers should be equipped with the most effective, least permeable respirators possible [43]. Notably, in 1972 OSHA required employers to engage in similar industrial hygiene practices in order to limit asbestos exposure.

In addition to industrial hygiene practices, material safety data sheets for "macro" forms of nanomaterials should be revised to incorporate lower exposure limits for nanoparticles [43]. Worker education is another effective and low-cost method of reducing exposure [43]. Industry, researchers and government agencies should also identify and track nanomaterial worker populations to monitor health effects and advance epidemiological research on the health effects of nanoparticles [24].

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D. Stewardship

The definition of product stewardship developed by Kodak is appropriate here:

Product Stewardship is an integrated business process for identifying, managing and minimizing the health, safety and environmental risks throughout all stages of a product's life in the best interest of society and our key stakeholders; customers, employees and shareholders [44].

Unfortunately, the OIG reports that participation in voluntary reporting and stewardship programs initiated by the private sector and government has been weak [12]. While trade publications are awash in reports regarding the toxicological potential of nanoparticles, the general public knows little about these materials or their potential risks [12]. In short, nanotechnology is becoming a plaintiff lawyer's dream.

The failure of many companies to engage in product stewardship was the worst mistake of the asbestos experience. We now know better. Responsible corporate behavior has proven critical to consumers and juries alike. Companies – particularly those who use the three nanomaterials discussed herein – are best served by promptly incorporating product stewardship into their business plans.

CONCLUSION

Nanotechnology – including nanosilver, ultrafine TiO_2 and CNTs – may be the most exciting and important technological development of the past century. But it is not without risk. The question of whether, and under what circumstances, these materials may cause disease in humans is still very much open; however, enough is known about the potential dangers that all stakeholders – and juries – will expect industry to mitigate risk and engage in product stewardship right now. If a mass tort scenario comes to pass, companies that are not affirmatively acting to assess and limit risk today could face punitive damages claims in the future.

Furthermore, industry cannot assume that the Plaintiffs Bar will continue to wait for the science to develop further. While some courts -- particularly in the federal system -- demand definitive proof of causation in humans, that is not true everywhere. Personal injury cases involving scientifically-suspect causation evidence are not uncommon, and some courts will allow such cases to proceed to verdict. Moreover, *perceived* risk alone may be sufficient to support certain claims.

Finally, industry should assess the risk of exposure for nanomaterial workers and take steps to protect them. If nanomaterials cause diseases in humans, industry is likely to see it in unprotected worker populations first. Once this happens, the floodgates will open.

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