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## Nanomaterials: Applying the Precautionary Principle

### Nanodimensions – New discoveries about familiar materials

The 2016 Nobel Prize in Chemistry was awarded to Jean-Pierre Sauvage, Sir J. Fraser Stoddart and Bernard L. Feringa for their three decades of learning to design and synthesize molecular machines, demonstrated by a four-nanometre-long 'car' with four wheels operated by molecular motors.<sup>1</sup> Scientists have continued to push the boundaries and explore new technologies, in this case for innovations beyond physical limitations that realize the potential for countless applications in everyday life. The recent advances in nanotechnology and nanoscience have introduced nanoscale materials with emergent physical and chemical properties to transform the world.<sup>2,3,4</sup>

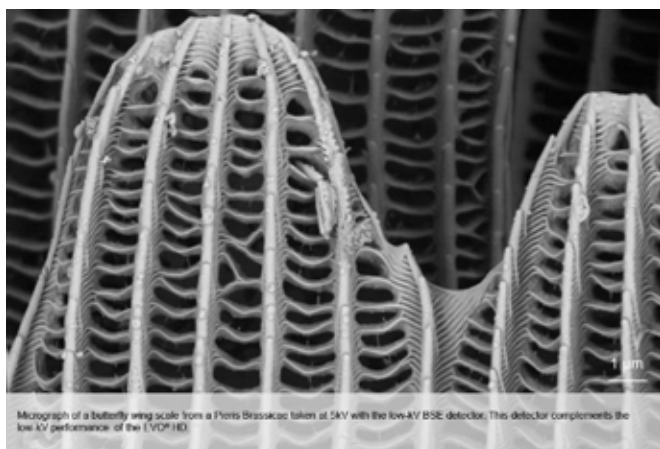
Nanomaterials are composed of nanosized particles, measuring less than 100 nanometres in at least one dimension: a nanometre is one-billionth of a metre, or roughly 80 000 times smaller than a human hair. Nanomaterials are not new and they are not all synthetic; they do occur naturally and they are everywhere. What is new is our ability to engineer them from common materials for a functional purpose.

In the natural world, nanomaterials appear in the skeletons of marine plankton and corals; bird beaks and feathers; animals' hair and bone matrix, including the human variety; spider webs; scales and wings; even in paper, silk and cotton. There are also naturally occurring inorganic nanomaterials, such as some clays, volcanic ash, soot, interstellar dust, and certain minerals. Natural nanomaterials are fundamentally a result of chemical, photochemical, mechanical, thermal and biological processes.<sup>5,6</sup>



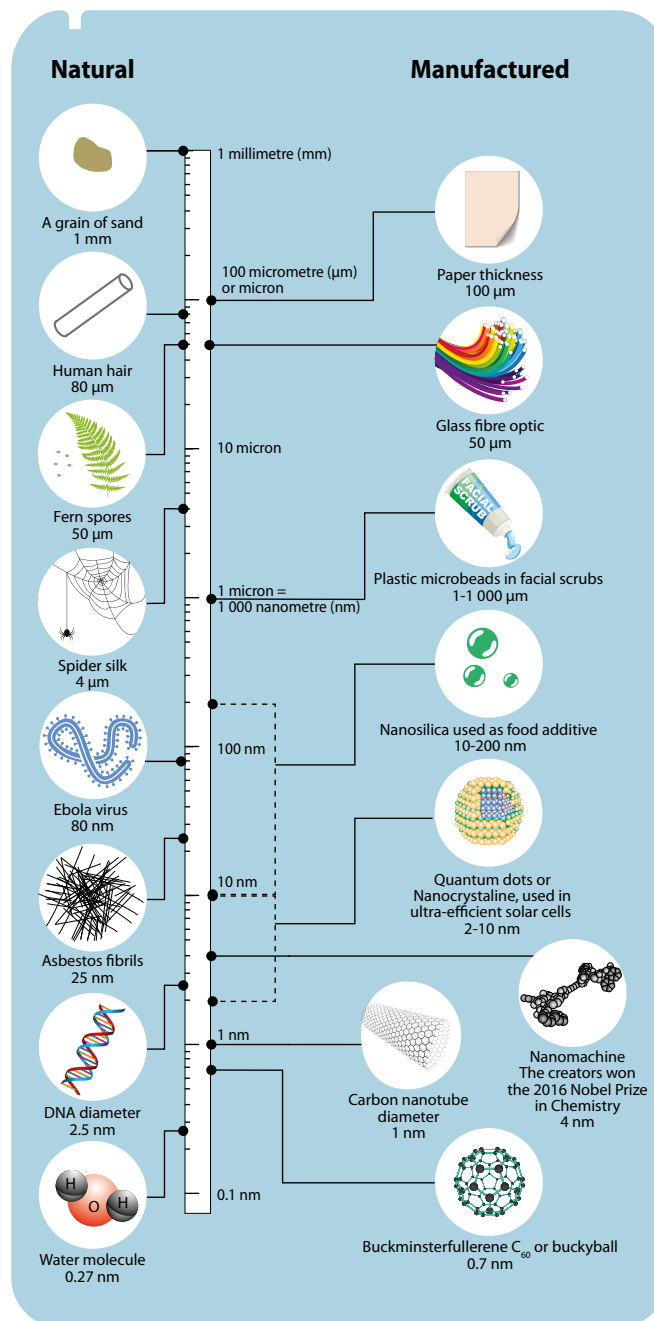
Research suggests that some preparation methods used in traditional medicine, such as calcination, inadvertently produce nanomaterials and their particular attributes.<sup>7,8</sup> As well, researchers are examining medieval weapons, such as Damascus steel blades, to test the theory that specific and ritualized forging and annealing techniques exploited production of nanomaterials to enhance strength and suppleness of the steel.<sup>9,10</sup>

In the engineered world, nanomaterials are deliberately designed and synthesized for specific optical, electronic, mechanical, medical and enzymatic applications using a range of micro-fabrication techniques. Today, nanomaterials are widely used in a variety of products, such as food, cosmetics, personal care products, antimicrobial agents and disinfectants, clothing and electronic devices. Along with the excitement about opportunities the engineered nanomaterials could present, questions have emerged about the environmental safety of nanomaterials, as well as their production and applications. There are still significant gaps in our knowledge about what nanomaterials could do and what effects they might have. Despite many more nanomaterials being developed, there is a serious risk that we do not know enough about the long-term effects of these materials on human health or the environment to use them without greater safeguards in place.



Nanosized wing scale of Cabbage White Butterfly, *Pieris brassicae*

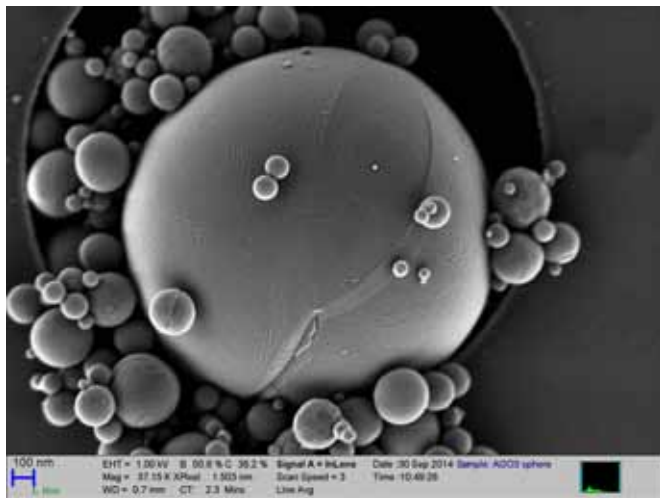
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## Specific forms, applications and effects

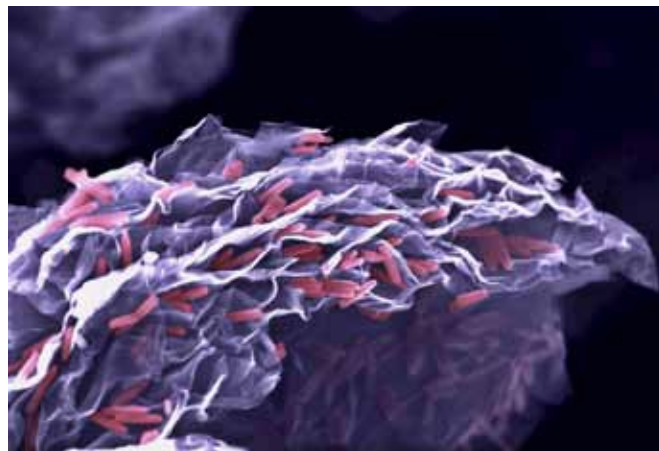
In Lewis Carroll's story of *Alice's Adventures in Wonderland*, young Alice swallows a potion that makes her very small. In her new size, she is able to enter a world of animals and characters that have extraordinary behaviours quite unlike their larger world versions. At nanoscale, the physical, chemical, optical, magnetic and electrical properties and behaviours of the materials change significantly compared to the same materials at larger sizes. This happens because of the dramatic increase in the surface-to-volume ratio and the appearance of quantum effects as a material gets smaller. Rendering a nanosized version of a material can produce capabilities in materials that are otherwise inert. For example, bulk gold is diamagnetic—it responds very weakly to magnetic field—but gold nanoparticles possess unusual magnetic properties.<sup>11</sup>

Like their bulk counterparts, nanoforms of metals, such as silver, titanium and zinc and their oxides, are used in sunscreen, toothpaste, cosmetics, food, paints, and clothing.<sup>12</sup> Due to its antimicrobial properties, nanosilver is widely incorporated into many consumer products such as sports textiles, shoes, deodorants, personal care items, washing powder and washing machines.



Aluminium oxide ( $\text{Al}_2\text{O}_3$ ) nanospheres

Photo credit: ZEISS Microscopy licensed under CC BY-NC-ND 2.0



Iron (III) oxide ( $\text{Fe}_2\text{O}_3$ ) nanorods, grown on reduced graphene oxide for supercapacitors

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Nanodiamonds demonstrate functional characteristics that enable them to penetrate through the blood-brain barrier, and allow targeted delivery of remedies to multiple types of cancerous tumours.<sup>13,14</sup> Because of their fluorescence, optical and electrochemical properties, nanodiamonds are used in advanced bioimaging techniques, and promising materials for transmitting signals that indicate the health of brain function.<sup>15,16</sup>

Nanozymes are nanomaterials with intrinsic enzyme-like properties developed for biosensing, bioimaging, tumour diagnosis and therapy.<sup>17</sup> They also find applications in marine anti-fouling, pollutant removal and environmental monitoring.

Carbon nanomaterials can present themselves in various shapes and forms. Graphene is a single-atom-thick sheet of carbon. Carbon nanotubes are essentially graphene sheets rolled into seamless hollow cylinders with diameters of the order of a nanometre.<sup>18</sup> Discovered in 1985, buckminsterfullerene, or buckyball, is a spherical structure of 60 carbon atoms, named after R. Buckminster Fuller, famous for his design of geodesic domes.

# Nanomaterials

## What is a Nanomaterial?

**Nanomaterials** can be **naturally occurring**, or **fabricated** by scaling commonly used materials to nanosize, such as carbon, metal oxides and precious metals

At nanoscale, the **properties and behaviours** of a material change significantly compared to the bulk forms of the same material. This is due to the increase in the **surface-to-volume ratio** and the **quantum effects**.

Changing the properties of a material by nanosizing it can **intensify its health and environmental impacts**

## Adverse Effects

**Nanomaterial** is a material with any external dimension measured **less than 100 nanometres**—one nanometre is one-billionth of a metre

**Global Nanomaterials market**  
**20.7% Annual Growth**  
Projected to reach **US\$ 55 billion** by 2022

**Bulk material**      **Nano-sized material**

As material size decreases, surface area-to-volume ratio increases, making the material more chemically reactive to its surrounding environment

The minuscule dimensions and high surface-to-volume ratio that give engineered nanomaterials remarkable properties also **alter how they interact** with and accumulate in biological systems, ranging from the environment, living organisms, organs, cells, down to the DNA level

For example, carbon nanotubes look and behave like asbestos fibres. Their long and pointy structure can pierce through tissue, and cause inflammation and fibrosis much like the effects of asbestos exposure. Nanosilver can disturb the immune system, and cause abnormality in gene expression

If we want to realise the full potential of engineered nanomaterials, we must also **anticipate their impacts**, otherwise we risk exposing ourselves to far greater impacts in the future

## Nanosilver

is widespread in products, such as textiles, toys, personal and health care products, medical devices and food, owing to its **antimicrobial properties**

## Nanodiamond

is used in biomedical imaging applications due to its luminescent properties, high chemical stability and biocompatibility

The unique **mechanical, magnetic, electrical and optical** properties of nanomaterials provide endless applications in pharmaceutical, biomedical, electronic and material engineering

Because of its magnetic properties, **iron oxide nanoparticles** have great potentials for targeted drug delivery in cancer treatment, medical imaging techniques, and removal of arsenic from water

A football-like cage of 60 carbon atoms, known as **Buckminsterfullerene** (C<sub>60</sub>) or buckyball, has potentials for the treatment of bone and cartilage degeneration, and musculoskeletal and bone marrow disorders

**Carbon nanotube** is a one-atom thick layer of carbon rolled up into a seamless cylinder. It is 117 times stronger than steel of the same diameter and a better conductor than copper.

Iterative and responsive regulatory frameworks that **apply the precautionary principle** are needed to minimize the risks and ensure human health and environmental safety

Carbon nanotubes are widely used in lithium ion batteries, lightweight wind turbine blades and data cables. Potential applications include tissue engineering and regeneration, and cancer biomarker.

## Applications

Engineered nanomaterials are present in **diverse consumer items**, e.g. food products, cosmetics, disinfectants, kitchenware, baby goods, clothing, fabrics, electronics and appliances

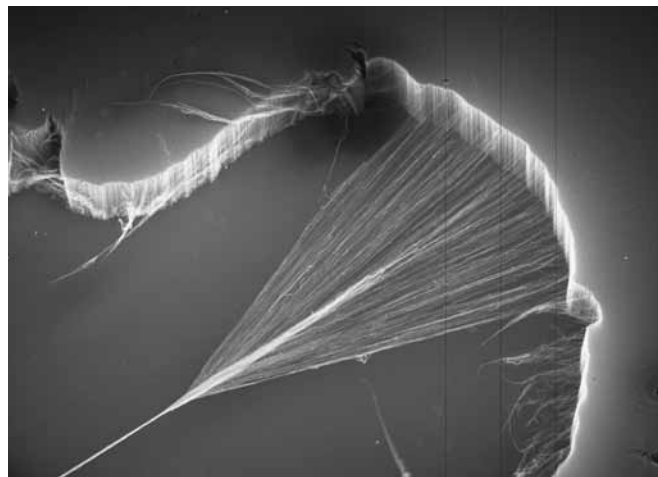
**Graphene** is a single-atom-thick sheet of carbon atoms. Potential applications include drug delivery systems, molecular transporters, tissue engineering and implants.

Carbon nanotubes have amazing properties. They are stronger than steel, are better conductors than copper, and have higher thermal conductivity than diamonds. Carbon nanotubes are widely used in lithium ion batteries for notebook computers and mobile phones, lightweight wind turbine blades, boat hulls, data cables, and biosensors and medical devices.<sup>19</sup> The worldwide commercial production capacity of carbon nanotubes now exceeds several thousand tons per year.

As engineered nanomaterials replace more conventional materials in everyday products, it is vital that we know the adverse effects of such materials. If we want to realise the full potential of nanomaterials, we must also anticipate their environmental and human health impacts; otherwise we risk exposing ourselves to far greater risks in the future.<sup>20</sup>

Changing the properties of a material by nanosizing it can intensify its environmental and health impacts. In the case of nanosilver, its toxicity can cause argyria, which turns the skin permanently into a metallic blue colour; pulmonary inflammation; alterations in organ functions and disturbances to the immune system and gene expression.<sup>12,21,22</sup> Exposure to silver nanoparticles can produce a stress response and genomic changes in bacteria, which may contribute to the development of antimicrobial resistance genes.<sup>12,23</sup> Silicon and titanium dioxides can cause pulmonary inflammation.<sup>24</sup>

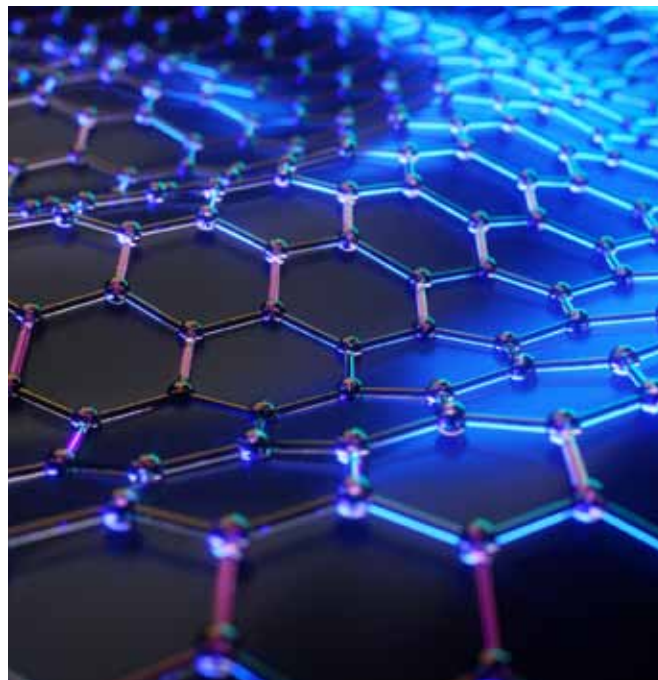
In parallel to the continuing discoveries of novel biomedical and therapeutic applications of fullerenes, including  $C_{60}$  buckyballs, these incredible nanomaterials are also under investigation for their potential effects on cells, gene expression, immune function, metabolism and fertility.<sup>25</sup> Carbon nanotubes and carbon nanofibres demonstrate their ability to cause damage to skin, eye, lung and brain tissues, and accumulate in the body.<sup>26,27</sup>



Carbon nanotubes being spun to form a yarn

Photo credit: Commonwealth Scientific and Industrial Research Organisation (CSIRO)

 **Video: Graphene - the material of the future**



Video link: <https://www.youtube.com/watch?v=TFo2xShvtj0>

Photo credit: Olive Tree/Shutterstock.com

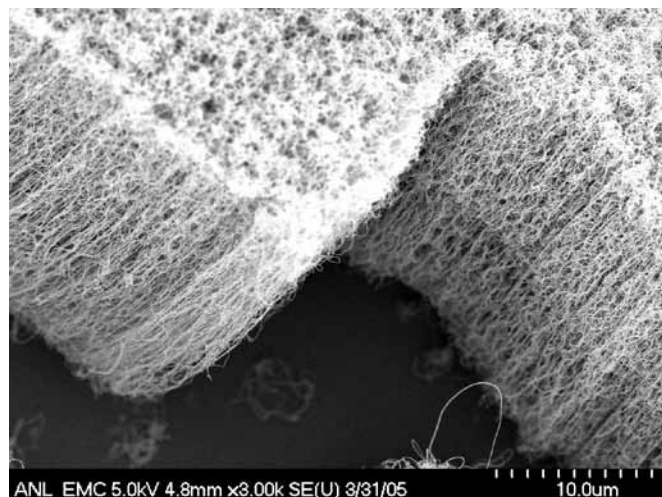
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## Environmental and health exposure to engineered nanomaterials

The global nanotechnology market is projected to grow roughly 18 per cent per year and be worth nearly US\$174 billion by 2025.<sup>28</sup> The increased production and use of engineered nanomaterials by diverse industries will likely result in their unintentional release into the environment at any point along the product's lifecycle.<sup>29</sup> For example, nanosilver from clothing and fabric is released during washing; titanium dioxide nanoparticles in paint and building materials are emitted to the air and water due to weathering; and carbon nanotubes become airborne during production or leach from discarded lithium-ion batteries into soil and groundwater.<sup>19,30,31</sup>

To assess the potential human health and environmental risk, it is critical to understand the exposure and adverse effects of engineered nanomaterials.<sup>32</sup> At present, a limited number of studies are available to explain the fate of engineered nanomaterials once released into the atmosphere, soil, sediment, water and biota, including their behaviour, concentration, transport, distribution, transformations, bioavailability, bioaccumulation in food chains, and biochemical interactions with ecological communities.<sup>29,33-36</sup>



Aligned carbon nanotubes

Photo credit: Junbing Yang/Argonne National Laboratory, licensed under CC BY-NC-SA 2.0

In contrast, knowledge and evidence of the toxicity effects of nanomaterials is expanding. Results suggest that nanomaterials can cause a wide range of adverse health effects. Comparative toxicity studies of familiar materials, particles and fibres with shape and chemical characteristics similar to those of nanomaterials, such as asbestos, ultra-fine particles and diesel exhaust fumes, provide insights into the potential health threats from being exposed to nanomaterials.<sup>37</sup> Further, what we have learned from managing these well-known hazardous substances could also help us to better prepare for the less understood nanomaterials.

Carbon nanotubes are found to share similar characteristics with asbestos fibres.<sup>38</sup> They have needle-like shape, and both are biopersistent. They can pierce through lung tissue and cause inflammation.<sup>39</sup> Evidence of the health hazard of working with asbestos came as early as 1898 from Lucy Deane, one of the first women Inspectors of Factories in the UK.<sup>40</sup> She noted that asbestos work was a 'demonstrated danger to the health of workers ... because of ascertained cases of injury to bronchial tubes and lungs medically attributed to the employment of the sufferer'.



Asbestos fibres magnified 1500 times under scanning electron microscope

Photo credit: US Centers for Disease Control and Prevention/ John Wheeler/ Janice Haney Carr



Female workers lie on the asbestos mattresses they have produced at a Lancashire factory, United Kingdom, September 1918

Photo credit: © Imperial War Museum (Q 28250)

In 1982, a TV documentary, *Alice, a Fight for Life*, featured Alice Jefferson, a 47-year-old woman who contracted mesothelioma, a fatal form of cancer, from working for a few months at a local asbestos plant in the United Kingdom.<sup>20</sup> The story of this Alice had an immediate impact on British public opinion. The government responded by introducing asbestos licensing regulations that lowered asbestos exposure limits. A voluntary labelling scheme soon followed. Pressure continued to build, and so did scientific evidence on the mesothelioma epidemic due to past exposure to asbestos.<sup>41</sup>

It took until 1999 for all types of asbestos to be banned in the United Kingdom: 101 years after evidence of harm had begun to accumulate and thousands of people had died of asbestosis or related cancers. Today efforts are still made to minimize the risk of asbestos exposure to workers engaged in renovation and maintenance of buildings containing asbestos.<sup>42</sup>

The question is, “What lessons can we learn from the century of struggle to understand and address the deadly dangers posed by exposure to asbestos when managing and assuring the safety of nanomaterials in the future?”

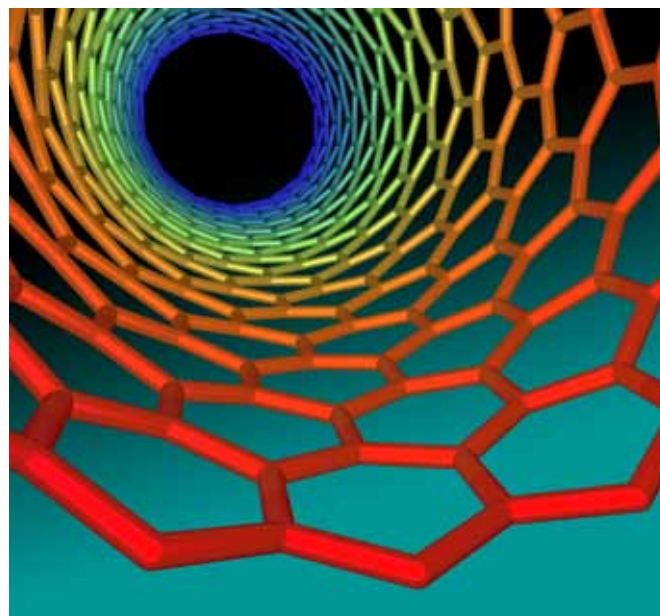
## Appropriate regulations for health and environmental safety

From our experience with asbestos and other hazardous materials, we know the list of potential threats is long. Environmental exposure of engineered nanomaterials is inevitable. Their adverse effects and persistence could have significant consequences on organisms, ecosystems and food chains.<sup>32,35,43,44</sup> Oral, dermal and pulmonary exposure could lead to inflammation and fibrosis, disrupt metabolism and organ’s function, and induce DNA damage and genetic instability.<sup>22,26,45,46</sup>

The speed of industrial development is far out-stripping the pace of regulatory development. In the absence of long-term monitoring and scientific information of the many aspects of nanomaterial toxicity and toxicology, specific regulations have been slow to emerge, despite mounting indications of potential exposure and risks.<sup>47</sup>



**Video:** Are carbon nanotubes the next asbestos?



Video link: <https://www.youtube.com/watch?v=6L7xXgWcbrQ>  
Photo credit: Geoff Hutchison, licensed under CC BY 2.0

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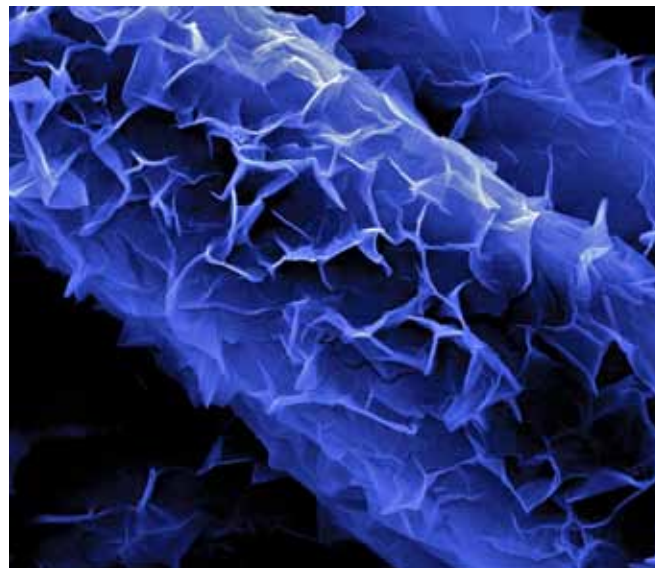
As in the case for asbestos, the first people exposed to nanomaterials are workers. The first few studies conducted in the late 1990s and early 2000s to assess occupational exposure to carbon nanotubes paved the way for further workplace investigations, and later the establishment of a first ISO-guideline on characterizing occupational nanoaerosol exposures in 2007.<sup>48,49</sup>

Based on studies of animals exposed to carbon nanotubes and carbon nanofibres, the US National Institute for Occupational Safety and Health considers findings such as lung inflammation, granulomas and fibrosis in subject animals to be significant enough to warrant action to set a recommended exposure limit.<sup>22</sup> The Organisation for Economic Co-operation and Development undertook multi-year programmes to generate toxicological data on a variety of nanomaterials to amend existing test guidelines for manufacturers.<sup>50</sup>

Because of the breadth of applications, regulatory bodies need to rely on existing regulations governing the areas of chemicals, pharmaceuticals, cosmetics, food, pollution, wastes and labelling to seek provisions for nanomaterials.<sup>51</sup> However, there are also challenges in applying existing regulatory frameworks to nanosized materials.<sup>47</sup> For instance, the reduction in size of a material may not initiate any need to revise the existing regulations or legislation if the nanosized and bulk materials are of the same chemical substance. Or, some consumer products are not subject to safety requirements and can enter the market without being tested.

In the European Union, the Regulation on Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) is used to ensure the human health and environmental safety of any chemical substance to be manufactured and marketed in the EU. Companies need to register the chemical substances they intend to manufacture and trade, and, based on REACH's specific guidelines, demonstrate how the risks associated with the substances can be managed for human health and environmental safety.<sup>52,53</sup>

At the global level, under the policy framework of the Strategic Approach to International Chemicals Management (SAICM) administered by UN Environment, nanomaterials



Carbon-graphene hierarchical core shell nanofibres

*Photo credit: Ranjith Shanmugam/ZEISS Microscopy, licensed under CC BY-NC-ND 2.0*

are one of its emerging policy issues. It works with governments and international stakeholders to facilitate information exchange on nanotechnologies and engineered nanomaterials and to develop internationally applicable technical and legal guidance for the sound management of manufactured nanomaterials.<sup>54</sup>

When working with new technologies, regulatory bodies are confronted with a combination of promise, risk and uncertainty.<sup>55</sup> Expanding the research, production and use of engineered nanomaterials across the world will need transformative policies to encourage innovation and industrial applications of green chemistry, and more critically, iterative and responsive regulatory frameworks that apply the precautionary principle to assure safety and non-polluting outcomes. The world cannot afford to ignore the lessons of the past about risks and damages to human health and the environment when responding to the promising opportunities created by new materials.



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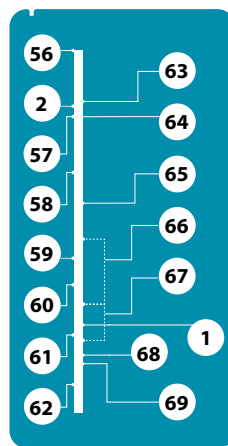
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