June 8, 2005

Re: EPA proposal to regulate nanomaterials through a voluntary pilot program

These comments are presented to the EPA in response to the following notice and request for comments:

ENVIRONMENTAL PROTECTION AGENCY [OPPT–2004–0122; FRL–7700–7]
Federal Register / Vol. 70, No. 89 / Tuesday, May 10, 2005

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These comments are respectfully submitted by:
?? The Natural Resources Defense Council (NRDC)
?? Greenpeace
?? Science and Environmental Health Network
?? Beyond Pesticides/NCAMP
?? Environmental Health Project, Ecology Center
?? Rachel Carson Council, Inc.
?? ScienceCorps
?? The Endocrine Disruption Exchange, Inc (TEDX)
?? Institute for Agriculture & Trade Policy
?? Sierra Club
?? Environmental Health Fund
?? Maryland Pesticide Network

SUMMARY OF EPA ACTION (as written in the FR notice): "EPA will conduct a public meeting on nanoscale materials to discuss a potential voluntary pilot program for certain nanoscale materials and the information needed to adequately inform the conduct of the pilot program. Nanoscale materials are chemical substances containing structures in the length scale of approximately 1 to 100 nanometers, and may have different molecular organizations and properties than the same chemical substances in a larger size. Some of the nanoscale materials are new chemical substances subject to notification requirements under section 5 of the Toxic Substances Control Act (TSCA) and, therefore, are subject to review for potential human health and environmental risks before they are manufactured and enter commerce. Other nanoscale materials are existing chemical substances that may enter commerce without notification to EPA. EPA is considering a potential voluntary pilot program for such nanoscale materials. To that end, EPA is requesting comments at the public meeting on: (1) The scope and purpose of a voluntary pilot program for nanoscale materials that are existing chemical substances, (2) kinds of information that are relevant to the evaluation of potential risks from exposure to nanoscale materials, (3) chemical characterization and nomenclature of nanoscale materials for regulatory purposes, and (4) identification of interested stakeholders. These comments will inform EPA on possible approaches to protect human health and the environment from exposure to such chemical substances. DATES**:** The meeting will be held on June 23, 2005, from 9 a.m. to 5 p.m."[1]

[1] Federal Register / Vol. 70, No. 89 / Tuesday, May 10, 2005 / Notices

SUMMARY OF RECOMMENDATIONS:

We appreciate the opportunity to comment on the EPA proposed voluntary initiative to develop information on nanomaterials, and to discuss approaches for the regulation of nanomaterials that may enter commerce. We appreciate the efforts of EPA to reach out to diverse stakeholders and interested groups, and look forward to a continued dialogue with EPA and other stakeholders on these important issues.

We would like all individuals and organizations that have endorsed these comments to be considered as stakeholders by EPA, and included in all future discussions of the regulation of nanomaterials.

I. The EPA proposed voluntary program is inadequate and inappropriate

While we appreciate EPA's recognition that something must be done to protect the public and the environment from potential adverse effects from nanomaterials, the voluntary initiative proposed by EPA[2] is both inadequate and inappropriate for the regulation of nanomaterials for commercial use. We conclude that *all* engineered nanomaterials are "new chemical substances" under TSCA because they are new "organic or inorganic substance[s] of a particular molecular identity," TSCA §3(2)(A), 42 U.S.C. §2602(2)(A), and that therefore the pre-manufacture notice (PMN) reporting requirements under TSCA section 5 42 U.S.C. §2604, are triggered prior to their commercial manufacture or import.

In addition, while we believe that the PMN and other requirements under TSCA (including test rules under TSCA section 4, and regulations under section 6) must be applied to nanomaterials under the Act, we also note that there are fundamental problems with TSCA as it has been interpreted by a court (the Fifth Circuit's *Corrosion Proof Fittings v. EPA*, 947 F.2d 1201 (1991) decision). If the *Corrosion Proof Fittings* court's decision (and subsequent problematic EPA interpretations of that decision) govern the agency's actions under TSCA on nanomaterials, it will be extraordinarily difficult for EPA to sufficiently regulate these materials under TSCA section 6. Thus, while requiring PMNs, issuing test rules, and promulgating regulations under TSCA are *necessary* steps for nanomaterials, such actions will be *insufficient* to protect public health and the environment. Ultimately, additional legislative action by Congress, the states, and potentially the courts will be necessary to ensure that nanomaterials are adequately addressed.

II. Immediate Regulatory Objectives

EPA should use its authority under the Toxics Substances Control Act (TSCA) section 4 and other authorities to require adequate toxicity testing of engineered[3] nanomaterials and to evaluate these materials so as to prevent unreasonable risk to the population, by preventing the release of potentially harmful nanomaterials into commerce.

III. Adequate Information

All testing on nanomaterials should be performed in a transparent manner by a credible independent agent, and all findings made public as required by, *inter alia*, TSCA sections 4, 8(e), and 14(b)(1).

IV. Long-term regulatory objectives

[2] Federal Register / Vol. 70, No. 89 / Tuesday, May 10, 2005 / Notices

[3] In these comments we use the words "engineered", "synthetic", and "manufactured" nanomaterials interchangeably. We refer to those nanomaterials generated intentionally and by design.

We recommend that EPA conclude *ab initio* that because of their inherent properties, engineered nanomaterials "may present an unreasonable risk of injury to health or the environment," until it is demonstrated by their manufacturers otherwise. We further recommend that those lacking demonstrated safety be prevented from entering commerce unless they can be used in a safe manner so as to prevent human exposures or releases to the environment. We recommend that multi-stakeholder discussions be initiated and continued.

INTRODUCTION

How small is "nano"?

Nano comes from the Greek word meaning "dwarf", and is used by scientists to indicate 10^{-9}, or one billionth. Nanometer-sized materials are one-billionth of a meter in size; larger than atoms, but much smaller than a cell. Earth is approximately one hundred million times larger than the soccer ball. This same ratio describes the difference in size between the soccer ball and a nanoparticle of carbon (C_{60}), approximately 0.7 nanometers (nm) in diameter. Molecules in the range of 1-100 nm are considered nano-sized.

Width of human hair	80 µm (micrometer)	80,000 nm (nanometer)
Width of a red blood cell	7 µm	7,000 nm
Width of a double-stranded DNA molecule		2 nm

What are Nanotechnologies?

Nanotechnology describes the design, production, and application of engineered nano-sized materials (nanoparticles and nanotubes) from known chemicals such as carbon, iron, or titanium. The term "nanotechnology" was coined in 1974, when nanomaterials advanced the miniaturization of electronic devices on silicon chips. Since that time, many chemicals and chemical processes have incorporated nanoscale materials, such as the fabrication of polymers like plastics, and components of computer chips. While nanoscale technologies are not new, our ability to investigate and manipulate nanoscale materials has become more sophisticated within the last decade.

Nano-sized chemicals have different properties compared with their bulk-sized counterparts. The two main reasons for this difference are an increased relative surface area per unit mass, and the dominance of quantum effects at the nanometer size. The increased surface area results in an increase in strength and chemical reactivity. Quantum effects can change a material's optical, magnetic, or electrical properties. These manufactured nanomaterials serve as the raw materials, ingredients, or additives in new and existing products. When manipulated at the nanoscale, substances can take on new properties. What was opaque may become transparent, what was stable may become reactive, what was an insulator may become a conductor. Nano materials are also able, due to their very small size, to be integrated with biological materials, producing new structures that have properties of both types of materials. Knowing the properties of a substance in bulk tells you nothing about its properties at the nano scale, so all nano materials' characteristics -- including hazardous traits -- must be learned anew by direct experiment.

The Potential for Good

Nanotechnologies have been hailed by many as the next industrial revolution, likely to change everything from the cars we drive to the clothes we wear to the medical treatments our doctors can offer. From new cancer therapies to pollution-eating compounds, from more durable consumer products to detectors for biohazards like anthrax, nanotechnologies are changing the way people think about the future. The pressure for rapid development of nanotech is enormous. The surprising properties of materials at the nano scale have opened up a new universe of industrial applications and entrepreneurial

dreams. Largely unnoticed, hundreds of products containing nano-sized particles have already reached the market -- metal surfaces and paints so slick they clean themselves when it rains; organic light-emitting diodes for computer screens, digital cameras and cell phones; sub- miniature data storage devices (aiming to hold the Library of Congress in a computer the size of a sugar cube); specialty lubricants; nano-reinforced plastics for stronger automobile fenders; light-weight military armor; anti-reflective and scratch-resistant sun glasses; super-slippery ski wax; powerful tennis rackets and long-lasting tennis balls; inkjet photographic paper intended to hold an image for 100 years; high-contrast MRI scanners for medical diagnosis; efficient drug and vaccine delivery systems; vitamins in a spray; invisible sunscreen ointments containing nano particles of titanium or zinc; anti-wrinkle cosmetic creams; very thin films and surface coatings that are so smooth they prevent dirt and moisture from adhering to glass; cotton and synthetic fibers modified at a nanoscale level to repel oil and liquids; tires strengthened with special nanocomposites to improve skid resistance and reduce wear. In 2001 the first engineered nanomaterial was cleared for medical use by the FDA, a synthetic bone nanomaterial (pure, dense hydroxyapatite) that is expected to integrate with natural bone when used as a repair and re-building material. (some overviews of research on nanotechnology can be found in the PCAST report[4], the CBEN website[5], and the NNI website[6]).

The "nano-visionaries" predict applications for nano-sized materials will enable new technologies to: create tougher, stronger cutting tools with nanocrystalline molecules of carbon, tungsten carbide, or titanium carbide; neutralize toxic chemicals in groundwater and soil with iron nanoparticles; improve the fuel economy of diesel with nanoparticles of cerium oxide; create stronger, longer-lasting medical implants such as artificial heart valves with nanocrystalline silicon carbide; improve water purification with nano-engineered filtration membranes; enhance drug delivery with nanoparticles capable of targeting specific diseased cells or genes, such as in cancer treatment; build data storage devices based on molecular electronics with nanomaterials that can store more computer information in far less space.

Worldwide investment in nanotechnology is currently between $5 and $6 billion dollars annually, and includes investment by virtually all the Fortune 500 companies. U.S. federal funding for nanotech research and development expanded from $116 million in 1997 to about $961 million in 2004 under the National Nanotechnology Initiative, with the Defense Department getting the bulk of this money. The President's FY 2006 budget includes over $1 billion for nanotechnology research across 11 federal agencies[7]. This represents approximately one-quarter of the global investment by all nations.

The Potential for Harm

The properties that make engineered nanomaterials exciting for science also present unique regulatory challenges, huge potential impacts on human and environmental integrity, and fears of product liability and litigation. While such new nanotechnologies promise advances in human health and environmental clean-up, almost nothing is known about the risks these nano-sized chemicals may pose to exposed workers, consumers, and wildlife. Animal studies suggest that nanoparticles can trigger a variety

[4] President's Council of Advisors on Science and Technology (PCAST). The National Nanotechnology Initiative at Five Years: Assessment and Recommendations of the National Nanotechnology Advisory Panel. May, 2005. Report available online at http://www.ostp.gov/PCAST/pcast.html

[5] Center for Biological and Environmental Nanotechnology, Rice University. http://cohesion.rice.edu/centersandinst/cben/index.cfm

[6] National Nanotechnology Initiative. www.nano.gov

[7] President's Council of Advisors on Science and Technology (PCAST). The National Nanotechnology Initiative at Five Years: Assessment and Recommendations of the National Nanotechnology Advisory Panel. May, 2005. Report available online at http://www.ostp.gov/PCAST/pcast.html

of inflammatory and immune responses that would not be predicted by current toxicity models based solely on particle mass and composition. [8] Early research also has highlighted the unique ability of tiny nanoparticles to move from one area of the body to another: from the lungs to the blood stream and beyond, from the GI tract to other organs, and from the nose via olfactory nerves into the brain. A nanoparticle may easily penetrate into a cell, while the bulk form of the same chemical may be unable to enter. When used as a therapeutic device, a nanoparticle may enter a cancerous cell to deliver a cancer-fighting drug, but when it contaminates food, drinking water, or consumer products, the same nanoparticle may also enter healthy cells to cause cancer or other adverse effects. Just as the minute size of nanomaterials gives them unusual properties of strength and reactivity, we anticipate that this would give them unpredicted properties of toxicity. Scientists thus anticipate that many otherwise relatively inert and stable chemicals, such as carbon, might pose toxic risk in their nano-scale form. Many unknowns remain, especially regarding the long-term impacts of exposure and the possible effects of nano-engineered materials on the environment and ecosystems. It is also difficult to predict which of these new materials may bioaccumulate and persist in the environment because of their unique physiochemical characteristics that are largely unknown with respect to either environmental or physiological implications. (reviewed in Oberdorster et al, 2005[9])

Fears of Future Liabilities and Litigation

The insurance industry has expressed concern about, the potential health and environmental hazards of tiny particles. In May of 2004, Swiss Re[10], the world's second-largest reinsurance firm, issued a report calling for the Precautionary Principle to guide nanotech development, and itemized a host of potential problems that it says need to be resolved before nanotech products are fully deployed. As a

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[8] Raloff, J. Science News Online. Nano Hazards: Exposure to minute particles harms lungs, circulatory system. Week of March 19, 2005; Vol 167, No. 12. This article reports on numerous research abstracts presented at the Society of Toxicology Annual Meeting, 2005. It cites the following research abstracts:

> James, J.T., and C. Lam. 2005. Pulmonary toxicity of carbon nanotubes in mice and implications for human risk assessment. Society of Toxicology 44th Annual Meeting and ToxExpo. March 6-10. New Orleans.
>
> Li, Z. . . . and P.P. Simeonova. 2005. Pulmonary exposure to carbon nanotubes induces vascular toxicity. Society of Toxicology 44th Annual Meeting and ToxExpo. March 6-10. New Orleans.
>
> Rodricks, J.V., and A. Seaton. 2005. SOT/Eurotox debate. Society of Toxicology 44th Annual Meeting and ToxExpo. March 6-10. New Orleans.
>
> Shimada, A., et al. 2005. Electron microscopic study on the translocation of ultrafine carbon black particles at the airway-capillary barrier in lung. Society of Toxicology 44th Annual Meeting and ToxExpo. March 6-10. New Orleans.
>
> Silva, V.M. . . . A. Elder, et al. 2005. Exposure to ultrafine elemental carbon particles (UCP) significantly increase thrombogenesis. Society of Toxicology 44th Annual Meeting and ToxExpo. March 6-10. New Orleans.

[9] Oberdorster G, Oberdorster E, Oberdorster J. 2005. Nanotoxicology: An emerging discipline evolving from studies of ultrafine particles. Env Health Perspect, available online March 22 at http://dx.doi.org/

[10] Swiss Re. Nanotechnology: Small matter, many unknowns. http://www.swissre.com/

major risk carrier, the insurance industry can only responsibly support the introduction of a new technology if it can evaluate and calculate its inherent risks. A risk needs to be identified before its consequences can be measured and a decision can be reached on the optimal risk management approach. This is why an open risk dialogue is required involving all stakeholders – industry, scientists, regulators and the insurance sector.

One of the new properties of nano-sized particles is their extreme mobility. In contrast to larger particles, they have "almost unrestricted access to the human body," Swiss Re points out, because they can enter the blood stream through the lungs and possibly through the skin, and seem to enter the brain directly via olfactory nerves. Once in the blood stream, nano particles can "move practically unhindered through the entire body," unlike larger particles that are trapped and removed by various protective mechanisms.

If they become airborne, nano particles can float for very long periods because -- unlike larger particles -- they do not readily settle onto surfaces. In water, nano particles spread unhindered and pass through most available filters. So, for example, current drinking water filters will not effectively remove nano particles. Even in soil, nano particles may move in unexpected ways, perhaps penetrating the roots of plants and thus entering the food chains of humans and animals.

One of the most useful features of nano particles is their huge surface area. The smaller the particle, the larger its surface is in relation to its mass. A gram of nano particles has a surface area of a thousand square meters. Their large surfaces give nano particles some of their most desirable characteristics. For example, drug-coated nano particles may one day transport pharmaceuticals directly to specific sites within the human body. Unfortunately, their large surface also means that nano particles may collect and transport pollutants. Furthermore, their large surface means nano particles are highly reactive in a chemical sense. As Swiss Re noted, "As size decreases and reactivity increases, harmful effects may be intensified, and normally harmless substances may assume hazardous characteristics." Nano particles may harm living tissue, such as lungs, in at least two ways -- through normal effects of chemical reactivity, or by damaging phagocytes, which are scavenger cells that normally remove foreign substances. Phagocytes can become "overloaded" by nano particles and cease functioning. Worse, overloaded phagocytes retreat into deeper layers and so become unavailable to protect against foreign pathogens and bodily invaders. Successive particles are then able to do their full reactive damage, and other invaders, such as bacteria, may penetrate unhindered. The surface reactivity of nano particles gives rise to "free radicals," which are atoms containing an "unsatisfactory" number of electrons (either too few or too many for stability). Free radicals swap electrons with nearby atoms, creating further instabilities and setting off a cascade of effects. Free radicals give rise to inflammation and tissue damage, and may initiate serious harm, such as growth of tumors. On the other hand, some free radicals are beneficial, destroying invaders. So the role of nano particles in producing free radicals remains to be clarified.

Nano particles would normally tend to clump together, forming larger, less dangerous particles -- but nanotechnologists take pains to prevent clumping by adding special coatings. As a result, nano particles in many commercial products, sprays and powders remain reactive and highly mobile. Whether nano particles can pass through the skin into the blood stream is the subject of intense debate. Different experiments have yielded conflicting results, presumably because test protocols have not been standardized. Some believe that nano particles may slip between the layers of outer skin and penetrate through to the blood below. Others believe that hair follicles offer a direct route for nano particles to penetrate from skin to blood. No one knows for sure. Despite this knowledge gap, sun screens, skin lotions and baby products containing nano particles are already on the market. Clearly this is a problem for insurance firms providing liability coverage. Swiss Re says, "Considering the wide variety of products already on the market, the need for a solution is urgent."

Swiss Re expresses concern that ingested nano particles can be absorbed through "Peyer's patches," part of the immune system lining the intestines, and from there may enter the blood stream, be transported throughout the body, and behave in ways that may be detrimental to the organism. While in the blood stream, nano particles have been observed entering the blood cells themselves. Once in the body, nano particles may be able to enter the heart, bone marrow, ovaries, muscles, brain, liver, spleen

and lymph nodes. During pregnancy, nano particles would likely cross the placenta and enter the fetus. The specific effects in any given organ would depend upon the surface chemistry of particular particles, which in turn would be determined by their size and surface coating. "It is likely that in the course of its entire evolution, humankind has never been exposed to such a wide variety of substances that can penetrate the human body apparently unhindered," Swiss Re says.

The brain is one of the best-protected of all human organs. A guardian "blood-brain barrier" prevents most substances in the blood from entering the brain (alcohol and caffeine being two well-known exceptions). However, nano particles have repeatedly been shown in animal studies to pass into the brain, where their effects are unknown. Will they accumulate and, if so, to what effect?

Nano particles may disrupt the immune system, cause allergic reactions, interfere with essential signals sent between neighboring cells, or disrupt exchanges between enzymes, Swiss Re says. Some of these characteristics may be harnessed for benefit -- for example, in experiments a carbon nano crystal has been able to disrupt one of the processes that allow the AIDS virus to multiply.

Nano particles in disposable products will eventually enter the environment. In the environment, nano particles represent an entirely new class of pollutants with which scientists (and nature) have no experience. Swiss Re speculates that, "Via the water cycle, nano particles could spread rapidly all over the globe, possibly also promoting the transport of pollutants." Swiss Re asks, "What would happen if certain nanoparticles did exert a harmful influence on the environment? Would it be possible to withdraw them from circulation? Would there be any way of removing nanoparticles from the water, earth, or air?"

Turning to workplace hazards, Swiss Re asks whether nano particles will become the next asbestos. To protect workers, effective face masks are "not a very realistic prospect at present, since the requisite design would render normal breathing impossible." New designs may be possible but remain unproven.

The Need for Caution

What would precaution look like in a rapidly developing field like nanotech? The British Royal Society and the Royal Academy of Engineering[11] issued a nanotech report in July 2004 recommending a series of precautionary actions, with the following chain of reasoning:

?? "The evidence we have reviewed suggests that some manufactured nanoparticles and nanotubes are likely to be more toxic per unit mass than particles of the same chemicals at larger size and will therefore present a greater hazard."

?? "There is virtually no evidence available to allow the potential environmental impacts of nanoparticles and nanotubes to be evaluated."

?? Therefore, "the release of nanoparticles to the environment [should be] minimized until these uncertainties are reduced."

?? And, "until there is evidence to the contrary, factories and research laboratories should treat manufactured nanoparticles and nanotubes as if they were hazardous and seek to reduce them as far as possible from waste streams."

We support these recommendations as rational and practical. They reverse the traditional approach to industrial materials, which have historically been assumed benign until shown otherwise. The Royal Society puts the burden of producing information about safety on industry, not on the public: "A wide range of uses for nanotubes and nanoparticles is envisaged that will fix them within products.... We

[11] U.K. Royal Society of Engineers: Nanoscience and Nanotechnologies: Opportunities and Uncertainties. The U.K. Royal Society report on nanotechnologies - 'Nanoscience and nanotechnologies: opportunities and uncertainties' - was published on 29 July 2004. The report illustrates the fact that nanotechnologies offer many benefits both now and in the future but that public debate is needed about their development. It also highlights the immediate need for research to address uncertainties about the health and environmental effects of nanoparticles – one small area of nanotechnologies. It also makes recommendations about regulation to control exposure to nanoparticles. http://www.nanotec.org.uk/finalReport.htm

believe that the onus should be on industry to assess ... releases [of nano particles from products] throughout a product's lifetime (including at the end-of-life) and to make that information available to the regulator." From such a recommendation, it is a very short step to the European Union's precautionary proposal for industrial chemicals, called REACH (Registration, Evaluation and Authorization of Chemicals), which is often summarized as, "No data, no market." The Royal Society recommended that the use of zinc oxide nano particles and iron oxide nano particles in cosmetics should "await a safety assessment" -- in other words a moratorium on these products is recommended. Likewise, "the release of free manufactured nanoparticles into the environment for [pollution] remediation (which has been piloted in the USA) should be prohibited until there is sufficient information to allow the potential risks to be evaluated as well as the benefits.

The President's Council of Advisors on Science and Technology (PCAST) issued their review of the National Nanotechnology Initiative at Five Years this spring (May, 2005).[12] Although the text of the report is 46 pages long, the section addressing "Environmental, Health and Safety" concerns doesn't appear until page 35 (Chapter 3), and is less than one page long. In that short section the Report states that only 4% of the total FY2006 budget for nanotechnology is, "aimed primarily at understanding and addressing the potential risks posed by nanotechnology to health and environment." The report weakly adds that there is also research in other areas that "would likely" include health and environmental effects. In any case, the roughly $40 million earmarked for health and environmental effects research is paltry and inadequate to keep pace with the $1 billion budget driving nanotechnology R&D. An equally paltry sum is earmarked for "societal concerns", suggesting that readying the market for nanomaterials will require equal efforts at understanding the health impacts and allaying the public's fears. This "fuzzy thinking" neglects to acknowledge that the public's fears would be best allayed if the potential hazardous health and environmental impacts of nanomaterials were thoroughly researched in an independent and transparent manner by credible institutions, and made available to the public.

As currently allocated, the budget for evaluation of potential health and environmental impacts is following a familiar precedent we observed with genetically modified foods and other biotechnology developments. The results of this serious oversight in addressing public safety issues for these products has been a very widespread public concern regarding safety, rejection of many products, and the barring of some products from large international markets. The lack of adequate information has also led to considerable concerns regarding health impacts of the genetically-modified products among scientists and the medical community who still do not have adequate information to evaluate the risks their hazards. The lack of adequate funding and regulatory requirements for testing are responsible for causing these problems. By ignoring public health and environmental concerns, a public response was generated against genetically-modified foods that resulted in the loss of potential benefits to society, as well as justifiable anger, suspicion, and discrediting of the agencies and institutions charged with the protection of public health. The current budget allocation for evaluation of nanotechnology is so woefully insufficient that it is clear that the same path is being followed for this class of materials, likely leading to the same outcomes we have observed in biotechnology. In fact, the emphasis on health and safety testing, having lagged for years behind the product development and applications efforts, needs a disproportionately large emphasis for some time in order to "catch up" with the R&D that has already been carried out as well as ongoing new developments.

While there is no turning back from nanotechnologies-- and, indeed, we are optimistic about their potential benefits if they are developed in a prudent fashion-- in the face of such large unknowns, proceeding with extreme caution is recommended by all who are monitoring wide-scale use of these new advances. The need for caution draws in part on the experience with the discovery of radiation a century ago. Radiation-based technologies, such as diagnostic X-rays, have saved millions of lives and enhanced

[12] President's Council of Advisors on Science and Technology (PCAST). The National Nanotechnology Initiative at Five Years: Assessment and Recommendations of the National Nanotechnology Advisory Panel. May, 2005. Report available online at http://www.ostp.gov/PCAST/pcast.html

the quality of medical and dental care dramatically. But these advances came at an unnecessarily high cost. Early researchers did not consider the possible dangers of radiation, and many research workers died young from radiation sickness. Many others were harmed by radiation-based patent medicines that were brought to market before the biophysics of radiation was understood. The potential hazards of widespread nanotechnology could be far greater than those of radiation. Until we can demonstrate the safety of particular nanomaterials, research and application on them must proceed with great caution.

RECOMMENDATIONS:

These recommendations are generally consistent with the Report of the U.K. Royal Society of Engineers[13] (Spring, 2004); a Report by Swiss Re insurance company[14] (Spring 2004); and by participants in a diverse multi-stakeholder meeting co-hosted by the Environmental Law Institute and the Woodrow Wilson Center for International Studies[15], Washington DC (May 25, 26, 2005).

I. The EPA Proposed Voluntary Program is Inadequate

The voluntary initiative proposed by EPA[16] is both inadequate and inappropriate for the regulation of nanomaterials for commercial use. Whereas the High Production Volume (HPV) voluntary initiative was designed to leverage existent data (primarily from the regulated industry) on a pre-defined subset of chemicals used commercially at over 1 million pounds annually, the regulation of nanomaterials will require the generation of new data, and must include all engineered nanomaterials and not a subset. Further, we recommend that all nanomaterials be considered "new" chemical substances under TSCA, and TSCA Section 5 requires EPA to review activities associated with the manufacture, processing, use, distribution in commerce, and disposal of any new chemical substance before it enters commerce, and requires pre-manufacture notice (PMN) reporting prior to commercial manufacture or import. Therefore, the legal requirements under TSCA for new materials preclude the need for a voluntary program.

II. Immediate Regulatory Objectives

We recommend that EPA use its authority under TSCA section 4 and other authorities to require adequate toxicity testing of nanomaterials and to prevent or limit the release of potentially harmful nanomaterials into commerce that may create an unreasonable risk to human or ecological health.

A. Prevent release of engineered nanomaterials

Until more is known about environmental impacts of nanomaterials (nanoparticles and nanotubes), we recommend that the release of manufactured nanomaterials into the environment be prevented. TSCA Section 6 *requires* EPA to prohibit or limit the manufacture, import, processing,

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[13] U.K. Royal Society of Engineers: Nanoscience and Nanotechnologies: Opportunities and Uncertainties. The U.K. Royal Society report on nanotechnologies - 'Nanoscience and nanotechnologies: opportunities and uncertainties' - was published on 29 July 2004. The report illustrates the fact that nanotechnologies offer many benefits both now and in the future but that public debate is needed about their development. It also highlights the immediate need for research to address uncertainties about the health and environmental effects of nanoparticles – one small area of nanotechnologies. It also makes recommendations about regulation to control exposure to nanoparticles. http://www.nanotec.org.uk/finalReport.htm

[14] Swiss Re. Nanotechnology: Small matter, many unknowns. http://www.swissre.com/

[15] Environmental Law Institute. Securing the promise of nanotechnology: Is US environmental law up to the job? http://www2.eli.org/research/events/nanotech5.25.05.cfm

[16] Federal Register / Vol. 70, No. 89 / Tuesday, May 10, 2005 / Notices

distribution in commerce, use, or disposal of a chemical if there is a reasonable basis to conclude the chemical presents or will present an "unreasonable risk of injury to health or the environment"[17]. This recommendation is consistent with those of the Swiss Re insurance company, and of the U.K. Royal Society of Engineers report discussed in these comments. We believe that this is both reasonable and feasible.

B. Declare engineered nanomaterials to be "new" chemical substances

We recommend that EPA declare all engineered nanomaterials to be "new" chemical substances having new physical properties and a "particular molecular identity" under TSCA section 3(2)(A). Indeed, the novel properties of nano-engineered materials make them different, for all purposes relevant to EPA's mandate, from existing materials with the same chemical composition. Classification of nanomaterials under TSCA as "new" requires clarification by EPA, to inform and alert manufacturers of their obligations under TSCA. All chemical substances not already listed on the TSCA inventory are considered to be "new" chemical substances under TSCA. TSCA Section 5 authorizes EPA to review activities associated with the manufacture, processing, use, distribution in commerce, and disposal of any new chemical substance before it enters commerce, and requires pre-manufacture notice (PMN) reporting prior to commercial manufacture or import. No exemptions should be given for nanomaterials; no exemptions for nanomaterials generated for research and development; no exemptions for nanomaterials identified as inerts, by-products, impurities, or intermediates of processes; no exemptions for nanomaterials produced in low volume; no exemptions for low release materials; no exemptions for high molecular weight or polymerized nanomaterials.

Engineered nanomaterials are sufficiently different from existing materials that they are being patented, supporting their classification as "new" materials under TSCA. The PCAST report (May, 2005)[18] reported that by searching a list of nanotechnology-related keywords, the US Patent and Trademark Office has issued over 8,600 nanotechnology-related patents in 2003. This represents an increase of about 50% over the number issued in 2000. Not only the U.S. is considering these materials to be sufficiently innovative as to be patentable; according to the PCAST report, nanotechnology-related patents in 2003 were also issued in Japan (926), Germany (684), Canada (244), France (183), and other countries to a lesser degree.

C. Require adequate toxicity testing for engineered nanomaterials intended to be commercially available

We recommend that adequate toxicity testing be required under TSCA section 4 and other authorities of all engineered nanomaterials before they are released into commerce, and that the "substantial quantity" threshold built into TSCA be automatically waived for all nanomaterials, since by design even single molecules of nanoparticles can have significant effects. We recognize that the definition of "adequate" toxicity testing regarding nanomaterials will develop in the context of both National and International regulatory needs. We do not here propose to pre-define or limit that determination.

TSCA Section 4(a) provides that EPA "*shall*" require manufacturers and/or processors of chemical substances to develop new data on health and environmental effects that are needed to assess potential risks from chemicals if: A. The manufacture, distribution, use, and disposal practices may

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[17] However, as noted above, we are concerned that "unreasonable risk" findings under TSCA have been construed by a court in a manner that establishes substantial hurdles for EPA action under the Act. Corrosion Proof Fittings v. EPA, 947 F.2d 1201 (5th Cir. 1991)).

[18] President's Council of Advisors on Science and Technology (PCAST). The National Nanotechnology Initiative at Five Years: Assessment and Recommendations of the National Nanotechnology Advisory Panel. May, 2005. Report available online at http://www.ostp.gov/PCAST/pcast.html

present an unreasonable risk of injury [Section 4(a)(1)(A)(i)]; or, B. The chemical may be produced in substantial quantities and it enters or may be anticipated to enter the environment in substantial quantities or there may be significant or substantial human exposure to the substance [Section 4(a)(1)(B)(i)], and there are insufficient data to assess the effects of the manufacture, distribution, etc. of such activities, and testing is necessary to develop such data. Clearly, the production volume threshold under this section must be waived for all nanomaterials. For an engineered nanochemical or nanomaterial to remain on or be placed on the market manufacturers must be required to provide publicly available safety data sufficient to permit a reasonable evaluation of the safety of the chemical for human health and the environment, including hazard, use and exposure information, no matter how little volume of nanomaterials they are producing, under TSCA Section 4(a); no exemptions for volume thresholds, and no exemptions for processors.

It is necessary to approach these materials as fundamentally different from their bulk counterparts with respect to quantification, and develop a health or damage based metric for establishing reporting and control policies. This is analogous to our approach to gamma emitting radioisotopes, or other materials with unique physiochemical properties such as asbestos fibers. The quantification in those cases is tailored to the behavior and risk management needs of the materials. Because the specific characteristics of nanomaterials vary widely and do not share common characteristics (as, for example, all beta emitting radioisotopes do), it is essential to rapidly identify the critical characteristics that require monitoring and control. The need for this information is fundamental and requires immediate and substantial investment in testing and evaluation in order to establish appropriate regulatory strategies.

D. Develop an inventory for all engineered nanomaterials

We recommend that EPA develop an inventory for all engineered nanomaterials. EPA maintains under TSCA Section 8(b) an information Inventory that enables EPA to identify chemicals in commerce. It is important that all engineered nanomaterials be included on an inventory as distinct nano-scale materials, with distinct properties. The inventory should be made publicly available in a transparent database or repository that is accessible to both the US and International community.

E. Develop an export notification and tracking system

We recommend that EPA develop an export notification and tracking system for all engineered nanomaterials. TSCA Section 12(b) requires exporters to notify EPA, in writing, if they export, or intend to export, chemical substances or mixtures that are subject to certain TSCA rules or orders. EPA, in turn, notifies those foreign governments of hazards that may be associated with a chemical substance or mixture absent requirements in the importing country. Without some type of export notification and tracking system, nanomaterials could be exported for use, distribution, processing, or disposal to anywhere in the world with no way of tracking its/their movement. The tracking results should be made publicly available in a transparent database/repository that is accessible to both the US and International community.

III. Adequate Information

We recognize that the definition of "adequate" information regarding nanomaterials will develop in the context of both national and international regulatory needs. We do not here propose to pre-define or limit that determination, but rather to propose basic elements that we feel are necessary but not sufficient elements of an adequate information database to regulate the commercial use of nanomaterials.

We recommend that government require comprehensive safety data for all engineered nanomaterials: For an engineered nanochemical or nanomaterial to remain on or be placed on the market we recommend that manufacturers be required to provide publicly available safety information about that chemical. The information must be sufficient to permit a reasonable evaluation of the safety of the chemical for human health and the environment, including hazard, use and exposure information. This is the principle of "No Data, No Market."

Basic information required of all engineered nanomaterials should include: a full life cycle analysis including fate and effects information; solubility; bioavailability; basic physical/chemical properties such as electrical conductivity, particle size, configuration, mass/surface area ratio. Importantly, the availability of screening and detection methods must be demonstrated so that tracking of nanomaterials in the ecosystem and as a body burden in human populations can be performed.

All toxicity testing should be done in a publicly-accessible and transparent manner by a credible independent authoritative body, conducted according to generally accepted laboratory practices. All results should be made publicly available in a transparent database/repository that is accessible to both the US and International community, as envisioned by, *inter alia,*TSCA sections 4, 8(e), and 14(b)(1).

The public and workers must be provided with the opportunity to know and participate in the evaluation and regulation of nanomaterials. Information disclosed to the public and workers must include quantities of nanomaterials produced, used, released, and exported, hazard, use and exposure information.

To date we have no experience with the impacts of aging, degradation, or interaction on most nanomaterials. The potential hazards posed by interaction or breakdown products is essential and must be addressed in the above described toxicity testing. Mechanisms for safe disposal or destruction of nanomaterials must be described so that cradle-to-grave safety can be assured.

As a precautionary measure to address inevitable shortcomings and uncertainty in any testing regimen, there must be a protocol prescribed for initial tracking of materials that do enter the market with respect to impacts on the health of those involved in production, use, and disposal, of products. As we have learned recently from FDA's experience with extensively tested pharmaceuticals on the market, there are many impacts on human health which are not fully characterized and predicted by pre-market testing, no matter how extensive. Even with ostensibly "safe" products, post-market monitoring is essential.

IV. Long-term regulatory objectives

- We recommend that nanomaterials be regarded as hazardous until demonstrated to be safe, based on an established set of reasonable criteria.
- We recommend that workers in research laboratories and manufacturing settings where nanomaterials are used should be protected by stringent safeguards against inhalation, ingestion, and dermal exposure and accidental release into the environment.
- We recommend that the Federal inter-agency *National Nanotechnology Initiative*[19] increase federal funding for the toxicity, epidemiology, persistence and bioaccumulation of manufactured nanomaterials as well as their exposure pathways, and develop methodologies and instrumentation for monitoring them in the built and natural environment. A key role would be to liaise with the regulated industry, regulators, community groups, labor and union groups, health and medical professionals, and regulatory watchdog groups. We recommend that the research center maintain a publicly accessible database of its results and that it interact with those collecting similar information in Europe and internationally. Plans for response to accidental releases of products in development or any hazardous feedstock must be made available and all stakeholders must be involved in their development and approval to insure adequate protection of public safety

[19] The National Nanotechnology Initiative (NNI) is a federal R&D program established to coordinate the multi-agency efforts in nanoscale science, engineering, and technology. http://www.nano.gov/html/about/home_about.html

- ?? We recommend that the ingredients lists of consumer products identify when manufactured nanomaterial has been added.
- ?? We recommend that all nanomaterials be considered hazardous until demonstrated otherwise, and we recommend that those lacking demonstrated safety be prevented from entering commerce unless they can be used in a safe manner so as to prevent human exposures or releases to the environment.
- ?? We recommend that the Government initiate adequately funded public dialogue around the development of nanotechnologies. We recognize that a number of bodies are appropriate in taking this dialogue forward, including labor unions, public interest groups, the health and medical community, nanotechnology manufacturers, nanotechnology users, nanotechnology regulators, and academic nanoscience researchers.
- ?? Inequalities within and between nations may be exacerbated if individuals and corporations gain monopoly control of nanotech by patenting the building blocks of the universe[20] -- a precedent set in
- ?? 1964 when Glenn T. Seaborg was issued a patent on an element he discovered and named Americium. The US needs to work in concert with the International regulatory community to ensure equitable impact of nanotechnologies.

CONCLUSION:

Nanotechnology affords the corporate and regulatory bodies an opportunity to "get it right". We've been here before. The hazards of asbestos, lead, and mercury were known many decades before they were used and released in large quantities into commercial markets. Public suspicion and rejection of genetically-modified foods taught us that empty assurances of safety will not win over consumers. We urge the federal government, state regulators, and corporate leaders to develop this new technology with transparency, credibility, public oversight and participation. The public includes all of us, our children, and our grandchildren. We look forward to working together with all stakeholders to advance technology safely.

[20]ETC Group. The Little Big Down: A Small Introduction to Nano-scale Technologies. ETC Group is a public interest group whose position is a moratorium on nanomaterials being used in commerce, until we have a better understanding of the toxicity of these materials, and government regulations to adequately protect human health and the environment. http://www.etcgroup.org/search.asp?theme=11

Respectfully,

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Suggested Further Reading on Nanotechnology

The Center for Biological and Environmental Nanotechnology, Rice University
http://www.ruf.rice.edu/~cben/
The Center for Biological and Environmental Nanotechnology will foster the development of this field through an integrated set of programs that aim to address the scientific, technological, environmental, human resource, commercialization, and societal barriers that hinder the transition from nanoscience to nanotechnology.

Institute of Medicine: Technology and Environmental Health: Implications of Nanotechnology
http://www.iom.edu/subpage.asp?id=19612

Nanotechnology Grand Challenge in the Environment
http://es.epa.gov/ncer/publications/nano/nanotechnology4-20-04.pdf

Nanotechnology and the Environment: Applications and Implications
http://es.epa.gov/ncer/publications/nano/index.html

ETC Group
Down on the Farm: The impact of nano-scale technologies on food and agriculture
http://www.etcgroup.org/search.asp?theme=11

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Raloff, J. 2003. Air sickness. *Science News* 164(Aug. 2):72-74. Available at http://www.sciencenews.org/articles/20030802/bob8.asp.

The National Nanotechnology Initiative has a Web site devoted to "nanotech facts" at http://www.nano.gov/html/facts/home_facts.html.