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A CONSTRUCTIVE CONTRIBUTION TO THE RESPONSIBLE DEVELOPMENT AND USE OF ENGINEERED NANOMATERIALS

nanoRISK

OPTIMIZING THE BENEFITS OF NANOTECHNOLOGY WHILE MINIMIZING AND CONTROLLING THE RISKS

Insider Report

The EPA moves to quicken the pace of its regulatory efforts.

THE EPA SHARPENS ITS FOCUS ON NANOTECHNOLOGY

For most of the last decade, the Environmental Protection Agency (EPA) has proceeded cautiously in exercising its regulatory authority over nanoscale materials. This caution was largely a reflection of EPA's conclusion that the agency lacked sufficient information to assess whether regulations specifically directed at nanoscale materials were necessary (1). Accordingly, much of EPA's focus over the past several years has been aimed at filling information gaps and gathering more data regarding the potential risks associated with nanomaterials, mostly through voluntary programs and agency-funded research (2).

Recently, EPA has moved to quicken the pace of its regulatory efforts, through a series of actions taken under the authority of the Toxic Substances Control Act (TSCA) (3). The agency has also fired a clear shot across the bow of the nanotechnology industry, warning producers and importers of nanoscale materials that the agency intends to pursue enforcement actions against companies that fail to heed EPA's new focus on regulating nanomaterials under TSCA. In light of these developments, companies with an interest in nanotechnology may want to reexamine the agency's recent regulatory initiatives, in order to gain a better understanding of how those actions might affect them.

TSCA's Scope Key to Future Regulation

As indicated, EPA's recent regulatory initiatives aimed at nanomaterials have been pursued primarily under the Toxic Substances Control Act. While most other environmental statutes regulate "pollution" in one form or another (e.g., air emissions, hazardous wastes, etc.), TSCA provides the EPA with unique authority to regulate chemical substances in commerce and prior to entering commerce.

Central to the TSCA regulatory program is the "Chemical Substances Inventory," which is a list maintained by the agency of all chemical substances known to be in commerce in the United States. The TSCA provides EPA with broad authority to regulate both "new" substances (substances not listed on the Chemical Substances Inventory) as well as "existing" substances. Thus, under section 5(a)(1) of TSCA, a company may not manufacture or import a "new" chemical substance without first completing a pre manufacture notification (PMN) review by EPA (4). Based on its PMN review, EPA may permit the new substance to be placed on the Inventory – allowing it to be manufactured, processed, distributed, or imported without restriction – or the Agency may issue an administrative order under TSCA section 5(e) to impose restrictions on the manufacture, use and/or distribution of the substance, or to require the submission of more data on the substance, or to ban the chemical outright (5).

In contrast to "new" substances, which are automatically subject to PMN review when they are first manufactured or imported into the US, the process for regulating "existing" chemicals under TSCA is more cumbersome. Specifically, section 5(a)(2) of TSCA provides EPA with authority to regulate "significant new uses" of an existing chemical substance, through the promulgation of a "significant new use rule" ("SNUR"). The SNUR process allows EPA to impose restrictions on manufacture, distribution and use of a substance – similar to the restrictions that can be imposed on "new" substances under section 5(e) orders. However, in order to designate the use of a substance as being a "significant new use," which is a necessary predicate for promulgating a SNUR, EPA must engage in a rulemaking process that includes public notice and an opportunity to comment. This is typically a more time consuming and more burdensome process for EPA, as

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New results provide powerful evidences that the biocompatibility and toxicity of nanoparticles is highly dependent on their chemical properties.

NANOPARTICLES' RANDOM WALK HAS IMPLICATIONS FOR NANOTOXICOLOGY

The interest in exploring the use of noble metal nanoparticles for diagnostic and therapeutic imaging stems from the drawbacks of current *in vivo* probes. Fluorescent probes, such as fluorescent dyes and proteins, are not photostable and are useful only for a limited time during the probing event. Besides imaging agents, especially gold nanoparticles are also intensely researched as target-specific vehicles for drug delivery.

Due to its inert chemical properties, gold has been widely considered as one of the most stable and biocompatible materials. But, as X. Nancy Xu explains, "studies of the biocompatibility and toxicity of gold nanoparticles in various types of cells, have yielded inconclusive results: some studies show a toxic effect and high-dependence of toxicity on nanoparticle size and surface functional groups, while other studies report no significant cytotoxicity. Many of these studies did not use purified gold nanoparticles, or examine any other chemicals present in the gold nanoparticle solutions, or well characterize the physical properties (e.g., possible size change and aggregation) of gold nanoparticles in buffer solution and cell culture media during the experiments, leading to these inconclusive results. Furthermore, study of the biocompatibility and toxicity of gold nanoparticles in living animals is yet to be fully explored."

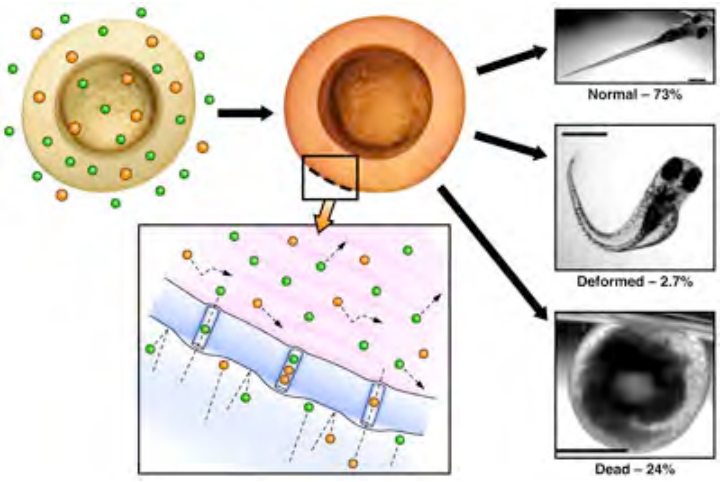
Xu is a professor in chemistry and biochemistry at Old Dominion University. In her latest work, she and her group have synthesized and characterized stable (photostable, non-aggregating), nearly monodisperse, and highly purified gold nanoparticles, and utilized them to study cleavage-stage embryos in real-time and to probe their effects on embryonic development at the single-nanoparticle level in real time.

The team has reported their findings in a recent paper in *Nanoscale* ("Random walk of single gold nanoparticles in zebrafish embryos leading to stochastic toxic effects on embryonic developments").

"We found that single gold nanoparticles passively diffused into chorionic space of the embryos via their chorionic pores and continued their random-walk into inner mass of embryos," says Xu. "Diffusion coefficients of single nanoparticles vary dramatically as nanoparticles diffuse through various parts of embryos, suggesting highly diverse transport barriers and viscosity gradients of the embryos."

The researchers also found that the amount of gold nanoparticles accumulated in embryos increases with increased nanoparticle concentration. "Interestingly," says Xu, "their effects on embryonic development show random dependence on concentration – they are not proportionally related to their concentration."

The team found that the majority of embryos (73% on average) chronically incubated with 0.025–1.2 nM gold nanoparticles for 120 hours developed to normal zebrafish, with some (24%) being dead and a few (3%) deformed. This result is in stark contrast with what they reported previously for silver nanoparticles, showing that gold nanoparticles are much more biocompatible with the embryos than silver nanoparticles. This also suggests that the biocompatibility and toxicity of nanoparticles depends on their chemical properties.



It is well known that the physical and chemical properties of nanoparticles are highly dependent upon a range of parameters – their size, shape, surface properties, embedded solvents, and the way that they were prepared and purified.

As Xu points out, their chemical and physical properties will surely affect their interactions with living organisms, and define their biocompatibility and toxicity in given living organisms. "Therefore, it will be misleading if one tries to compare the study of one type of nanoparticles in one living organism with other types of nanoparticles in other living organisms" she says.

To overcome the limitations of current nanotoxicity studies, Xu's team have developed three important components for such studies: 1) New methods to prepare stable (non-aggregated) and purified model nanoparticles (e.g., different sizes and surface functional groups of gold and silver nanoparticles); 2) Real-time imaging tools (e.g., DFOMS) for characterizing the size of individual nanoparticles in vivo in real-time; and 3) Effective in vivo assays (zebrafish embryos) for screening and probing the biocompatibility and toxicity of model nanoparticles, aiming to depict the dependence of biocompatibility and toxicity of nanoparticles on their physical and chemical properties, and their underlying mechanisms.

"We found gold nanoparticles in various parts of normally developed zebrafish," says Xu. "Together with the strong variations in diffusion coefficients, these interesting findings suggest that the random diffusion of gold nanoparticles in embryos during their development might have led to uncertain effects on embryonic development."

The team is already working on further probing what causes the embryos to become normally developed, deformed or dead zebrafish, as they are incubated with nanoparticles.

Article Reviews Landscape Of Current Nanoparticle Risk And Regulation

Nanotechnology continues to be forecast to reap massive global benefits across multiple sectors. Increasing public awareness of nanotechnologies, linked to non-specifically regulated introduction of products containing nanomaterials into the market, and the increasing use of 'Health & Safety' as an easy excuse for the prevention of desirable or beneficial activities by those unable or unwilling to understand them, makes heeding advice laid out by UK Government in 2005 via the Royal Society / Royal Academy of Engineering ever important to their responsible development.

Taking these issues into account, an article published this month within the *Journal of the Royal Society 'Interface',* presents an objective review of the current landscape of nanoparticle risk research and regulation. The paper, entitled "Nanoparticles, human health hazard and regulation", is authored by nanotechnology & occupational health expert Professor Anthony Seaton CBE, and co-scientists from the Safety of Nanoparticles Interdisciplinary Research Centre (SnIRC).

Researchers Pinpoint Neural Nanoblockers in Carbon Nanotubes

Carbon nanotubes hold many exciting possibilities, some of them in the realm of the human nervous system. Recent research has shown that carbon nanotubes may help regrow nerve tissue or ferry drugs used to repair damaged neurons associated with disorders such as epilepsy, Parkinson's disease and perhaps even paralysis. Yet some studies have shown that carbon nanotubes appear to interfere with a critical signaling transaction in neurons, throwing doubt on the tubes' value in treating neurological disorders. No one knew why the tubes were causing a problem.

Now a team of Brown University researchers has found that it's not the tubes that are to blame. Writing in the journal *Biomaterials* ("The inhibition of neuronal calcium ion channels by trace levels of yttrium released from carbon nanotubes"), the scientists report that the metal catalysts used to form the tubes are the culprits, and that minute amounts of one metal — yttrium — could impede neuronal activity. The findings mean that carbon nanotubes without metal catalysts may be able to treat human neurological disorders, although other possible biological effects still need to be studied.

In experiments using cloned calcium ion channels in embryonic kidney cells, the scientists discovered that nickel and yttrium, two metal catalysts used to form the single-walled carbon nanotubes, were interfering with the ion channel's ability to absorb the calcium.

Researchers In China Link Nanoparticle Exposure to Lung Failure Deaths

A study published in the *European Respiratory Journal* (ERJ), ("Exposure to nanoparticles is related to pleural effusion, pulmonary fibrosis and granuloma") has for the first time claimed a concrete link between exposure to nanoparticles in adhesive paint and development of severe pulmonary fibrosis in a group of young female workers; two of whom went on to suffer fatal lung failure. Toxicity from nanoparticulates has been the topic of increasing research effort for several years. For some nanoparticles and nanomaterials, toxicity has already been established in animals. For example, mice were found to develop symptoms of inflammation and pulmonary fibrosis following application of carbon nanoparticles to the trachea ("A Review of Carbon Nanotube Toxicity and Assessment of Potential Occupational and Environmental Health Risks"). However, until now no cases have been reported in humans. The work of a Beijing-based group of scientists to be published in the ERJ this week linking exposure to nanoparticles in adhesive paint to severe pulmonary fibrosis in a group of young female workers therefore breaks new ground in the area, providing fascinating new evidence for consideration in the debate on the dangers of nanotechnologies. The study, by a team led by Yuguo Song, of the Occupational Disease and Clinical Toxicology Department at Chaoyang Hospital in Beijing, involved seven healthy young women employed in a print plant. Over the course of a few months, all of the women were hospitalized for respiratory problems, accompanied by itchy eruptions of the skin on the face and arms. On examination, the patients were found to have liquid effusion around the heart and lungs, which proved resistant to all treatments. Comprehensive investigation led to a diagnosis, in all cases, of pulmonary fibrosis with consequent impairment of lung function.

The Chinese team's link between the symptoms and nanoparticle exposure was based on the results from electron microscopy of the chemical used, lung biopsy tissue and pleural effusion liquid, all three of which were found to contain round nanoparticles with a diameter of approximately 30 nanometres. Yuguo Song, the lead scientist, claims that these particles were likely to originate in the polyacrylate-based adhesive paints used by the women daily in the course of their work. However, he emphasizes that despite repeated efforts, the group has not at this stage been able to obtain precise data on the composition of the paint in question. Likewise, the researchers have not been able to determine the workers' level of exposure through measurement of airborne particles, since the workshop was closed down several months before their investigation began.

Despite the unfavorable working conditions, the authors of the ERJ article maintain that this was not simply a case of intoxication by paint vapor as a result of poor ventilation; but rather that the illness was caused by the inherent toxicity of the nanoparticles, which entered the body either through the airways or through the skin, or perhaps through both.

EPA Focus On Nanotechnology…

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compared to regulating a "new" substance under section 5(e).

In this context, a pivotal and controversial question for industry has been whether nanoscale versions of conventional-sized substances already listed on the TSCA Inventory should be regulated as "new" chemical substances and required to undergo PMN review prior to being manufactured or imported into the US. That question was largely resolved late last year.

EPA: Size (and Space) Matters in Determining Molecular Identity

In the summer of 2007, EPA gave its first clear indication that the agency might regulate nanoscale materials as "new substances" under TSCA, even if conventional-scale versions of those substances are *already listed* on the TSCA Inventory. This interpretation was outlined in a guidance document entitled "TSCA Inventory Status of Nanoscale Substances – General Approach" (the "*General Approach*") (6). A casual reader of the EPA's *General Approach* might have been misled by the document's prominent statement that:

In determining whether a nanoscale substance is a new or existing chemical, the Agency intends to continue to apply its current Inventory approaches based on molecular identity, rather than focus on physical attributes such as particle size. (7)

The agency's guidance appears to say that nanoscale versions of substances on the Inventory will *not* be subject to regulation as "new substances" under TSCA (since the agency purports not to distinguish between "new" and "existing" substances on the basis of particle size). However, EPA's interpretation was actually much more nuanced. Elsewhere in the *General Approach* document, the agency explains that two substances will be considered to have different "molecular identities" for purposes of TSCA, and therefore will be considered different substances, if the *spatial arrangements* of the atoms within the molecules are different (even if the composition and chemical bonding are identical). Thus, for example, EPA explains that molecules consisting of the same atoms arranged in different crystal lattices are considered to have different molecular identities and therefore are different "substances" under TSCA, as are allotropes of the same element. (8)

Any lingering questions EPA's *General Approach* may have left any regarding the agency's intent to regulate nanomaterials as "new" substances under TSCA questions were largely answered in October 2008, when EPA published a notice in the Federal Register announcing its determination that carbon nanotubes are, in fact, "new" chemical substances for purposes of TSCA, and are therefore subject to the PMN reporting requirements. (9) Drawing upon the logic described in the *General Approach*, EPA explained that it considers carbon nanotubes to be distinct from graphite and other allotropes of carbon listed on the TSCA Inventory and therefore subject to PMN review. In addition, the agency alerted corporations that sometime after Spring 2009 it would begin "focusing its compliance monitoring efforts to determine if companies are complying with TSCA section 5 requirements for carbon nanotubes." (10) This was (and is) a clear warning to companies that manufacture or import nanomaterials that they must pay close attention to their newly explained TSCA obligations or they risk facing an enforcement response. (11)

Carbon Nanotube Restrictions give Insight to Stakeholders

Following publication of the *General Approach*, EPA received a number of PMNs for nanoscale materials. Within the past year, at least five of those PMNs (for single-walled and multi-walled carbon nanotubes) have resulted in the issuance of section 5(e) orders. As with all section 5(e) orders, these are substance-specific (in other words, they only pertain to the specific nanotube materials that were the subject of the PMNs). In addition, the orders were predicated on EPA's finding that: (i) information available to the agency is "insufficient to permit a reasoned evaluation of the human health effects" of the nanotube materials and (ii) uncontrolled manufacture, import, processing, distribution in commerce, use, and disposal of those materials "may present an unreasonable risk of injury to human health." (12)

Although the section 5(e) nanotube orders are substance-specific, they all contain a number of common elements. In particular, all of the orders impose restrictions on the types of applications in which the nanotubes may be used. In addition, each order includes the following requirements:

- The manufacturer (or importer) must provide EPA with a sample of material, along with certain material characterization data;
- The manufacturer (or importer) must conduct a 90-day rat inhalation toxicity study on their material;
- The manufacturer (or importer) must employ specified types of personal protective equipment at facilities under its control; and
- The manufacturer (or importer) may only distribute the material to persons who agree to comply with all of the restrictions of the 5(e) order. (13)

In addition, at least one of the orders prohibits any manufacture of the subject nanotube within the United States. Interestingly, all of the orders also contain language supporting the use of a consortium approach to developing inhalation toxicity data. (14) As noted earlier, section 5(e) of TSCA provides EPA with expansive authority to prohibit or restrict the manufacture, processing, distribution and/or use of substances for which the agency has risk concerns. The multiple section 5(e) orders that the Agency has issued over the past year for carbon nanotube materials demonstrate unequivocally that the agency intends to use its expansive authority under TSCA section 5(e) to impose restrictions on nanoscale materials that, in EPA's view, present unresolved risk concerns. Violations of section 5(e) orders are subject to civil penalties of up to $37,500 per violation as well as possible criminal penalties for "knowing" violations. (15)

New Regulations on the Horizon

Regulatory momentum at EPA regarding nanoscale materials is unlikely to abate anytime soon. One need only look at the agency's most recent "regulatory agenda," to draw

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the conclusion that we are likely to see new proposed regulations under TSCA specifically directed at nanoscale materials in the not-too-distant future. (16) In particular, one of the "long term" regulatory actions the agenda identifies is the issuance of a test rule under TSCA section 4, requiring manufacturers and importers to generate needed health and safety data on multi wall carbon nanotubes. (17) Moreover, EPA might feel compelled to proceed with this type of rulemaking if it were to conclude that its voluntary data collection efforts have failed to generate an adequate response. (For example, in a recent report on the Nanoscale Materials Stewardship Program (NMSP), the agency notes that: "a number of the environmental health and safety data gaps the Agency hoped to fill through the NMSP still exist. *The EPA is considering how to best use testing and information gathering authorities under the Toxic Substances Control Act to help address those gaps.*") (18)

In addition, as manufacturers and importers of nanoscale materials heed EPA's warnings and submit more PMNs to the agency for review, we are likely to see additional section 5(e) orders for those materials, as well as additional SNURs.

Conclusions

After a long period of relative inaction, EPA has recently intensified its focus on the regulation of nanoscale materials. The agency has sent a clear signal to industry that nanoscale materials are likely to require PMN review before they lawfully can be manufactured or imported into the United States. It is clear from EPA's recent actions that the agency intends to use its expansive authority under TSCA, including section 5(e), to impose restrictions and limitations on the manufacture, processing, distribution or use of nanoscale materials in instances when the agency has unresolved risk concerns regarding those materials. Companies that manufacture or import nanomaterials into the US would do well to heed the agency's warnings, pay close attention to their TSCA obligations – and to watch out for new regulations that may soon be heading our way.

Footnotes

1) Thus, in a 2007 White Paper, the EPA repeatedly emphasized the need to gather more data about nanoscale materials. See "U.S. Environmental Protection Agency Nanotechnology White Paper" (February 2007). Specifically, the White Paper identified critical information gaps in the areas of: chemical identification and characterization; environmental fate, including how nanomaterials are transported through environmental media and how they transform and react with other chemicals in the environment; environmental detection methods; human exposure; human health effects; ecological effects; and risk assessment approaches. Id at 70-81. See www.epa.gov/OSA/pdfs/nanotech/epa-nanotechnology-whitepaper-0207.pdf

2) In addition to the EPA laboratories conducting their own research, as of 2007 the agency had also funded more than $17 million in Science to Achieve Results (STAR) grants to research the environmental fate of nanomaterials and monitoring and detection of nanomaterials. Also, in 2008 the EPA launched a voluntary "Nanoscale Materials Stewardship Program" in order to encourage companies to provide the EPA with data on material characterization, hazards, potential uses, potential exposures, and risk management practices associated with nanoscale materials. See www.epa.gov/oppt/nano/stewardship.htm

3) 15 U.S.C. § 2601 et seq.

4) See 15 U.S.C. § 2604(a)(1). The PMN must provide certain information pertaining to the chemical identity of the substances, as well as any health and environmental effects data in the PMN submitter's possession. See 40 C.F.R. §§ 720.45 and 720.50

5) Because they are issued pursuant to Section 5(e) of TSCA, these administrative orders are commonly referred to as "section 5(e) orders."

6) U.S. EPA, TSCA Inventory Status of Nanoscale Substances – General Approach (July 12, 2007), available at: http://www.epa.gov/oppt/nano/nmspfr.htm

7) General Approach at 5.

8) Id. at 3.

9) See 73 Fed. Reg. 64,946 (Oct. 31, 2008).

10) Id. at 64,947.

11) In this regard it is worth noting that the EPA has already pursued enforcement actions against products that incorporate nanoscale materials, especially nano-silver, to impart anti-microbial properties. For example, last year, the EPA fined ATEN Technology, the manufacturer of IOGEAR equipment, over $200,000 for selling keyboards and other computer peripherals that purported to incorporate nano-scale silver for anti-microbial benefits, without first obtaining agency approval. See Press Release, *U.S. EPA fines Southern California Technology Company $208,000 for "Nano Coating" Pesticide Claims on Computer Peripherals* (March 5, 2008), available at yosemite.epa.gov/opa/admpress.nsf/0/16a190492f2f25d585257403005c2851

12) See, e.g., Consent Order and Determinations Supporting Consent Order, Premanufacture Notice Number: P 08 0328 (Sep. 12, 2008); see also 15 U.S.C. § 2604(e) (statutory findings required for issuance of a section 5(e) order).

13) Id. See also Consent Order and Determinations Supporting Consent Order, Premanufacture Notice Number: P 08 0733/0734 (Feb. 13, 2009); Consent Order and Determinations Supporting Consent Order, Premanufacture Notice Number: P 08 0177 (Aug. 11, 2008); Consent Order and Determinations Supporting Consent Order, Premanufacture Notice Number: P 08 0392 (date unavailable).

14) On June 24, 2009 the EPA published a notice in the

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Federal Register that would have established a significant new use rule for two of the nanotube materials that were the subject of section 5(e) orders: P-08-177 and P-08-328. The purpose for issuing the SNURs (which were subsequently withdrawn for additional notice and comment -- see 74 Fed. Reg. 42,177) was to extend the section 5(e) order restrictions to any person manufacturing or importing the nanotube materials. See 74 Fed. Reg. 29,982 (June 24, 2009). The agency can only accomplish this via a SNUR because the section 5(e) order itself is only effective with respect to the original PMN submitter.

15) See 15 U.S.C. § 2615; 74 Fed. Reg. 626 (Jan. 7, 2009) (Civil Monetary Penalty Inflation Adjustment Rule).

16) EPA, *Semiannual Regulatory Agenda* (Spring 2009) available at http://www.the EPA.gov/regulations/search/regagenda.html. The semiannual regulatory agenda, which previously had been published in the Federal Register, is now only available online.

17) Id. at 105.

18) EPA, *Nanoscale Materials Stewardship Program Interim Report* (January 2009) at 3.

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EPA ANNOUNCES RESEARCH STRATEGY TO STUDY NANO-MATERIALS

On September 29, 2009, the U.S. Environmental Protection Agency today outlined a new research strategy to better understand how manufactured nanomaterials may harm human health and the environment. Nanomaterials are materials that are between approximately one and 100 nanometers. These materials are currently used in hundreds of consumer products, including sunscreen, cosmetics and sports equipment.

The strategy outlines what research EPA will support over the next several years to generate information about the safe use of nanotechnology and products that contain nano-scale materials. The strategy also includes research into ways nanotechnology can be used to clean up toxic chemicals in the environment.

EPA's research is conducted using a multidisciplinary approach that examines all aspects of nanomaterials in the environment, from their manufacture and use to their disposal or recycling. EPA's new nanotechnology Web site provides more details about the research and offers news and publications.

UPCOMING EVENTS
LOOKING AT THE RISKY SIDE OF NANO

NanoImpactNet 2009
October 5-7, 2009, Bilthoven (The Netherlands)
Workshops on Exposure Measurements, Environmental Fate and Behavior, and Risk Assessment

Nanomaterials and the Environment & Instrumentation, Metrology, and Analytical Methods
October 6-7, 2009, Arlington, VA (USA)
An active discussion on the state-of-the-art in the two overarching research need tracks: 1) Nanomaterials & The Environment and 2) Instrumentation, Metrology & Analytical Methods.

Rusnanotech 09
October 6-8, 2009, Moscow (Russia)
The conference will include a track on "Certification, metrology, standardization and technical regulation for safety and quality in nanoindustry."

Nanomaterials on the Market. What Regulators Need to Know
October 9, 2009, Brussels (Belgium)
The conference will provide a forum for informed discussion of the key issues surrounding the existing knowledge gaps as well as options for gathering the additional information needed to ensure that any significant risks to health and the environment are adequately addressed.

BioNanoTox
October 21-22, 2009, Little Rock, AK (USA)
BioNanoTox lies at the interface of a variety of disciplines ranging from biology to chemistry, toxicology, computational sciences, mathematics, engineering, nanotechnology and biotechnology.

3rd Nano Safety for Success Dialogue: Building Trust in Nanotechnologies
November 3-4, 2009, Brussels (Belgium)
This workshop will again bring together scientists, risk assessors, public authorities, industry, and consumer and environmental NGOs to examine and discuss issues related to the use of nanotechnologies, and to identify appropriate means to strengthen guidance in support of the safe, integrated, and responsible development of nanotechnologies.

First Nanosafety Autumn School
November 16-20, 2009, Venice (Italy)
This event will provide the "state-of-the-art" on scientific knowledge and technical tools available for an integrated assessment of nanotechnology products. The school will offer an interactive learning environment in which participants will use a combination of approaches to update their skills and to discuss current issues pertaining to human and environmental nanotechnology issues.

IN SHORT – PAPERS, INITIATIVES & UPDATES

GUIDELINES: OECD Adds New Publications to its Series on the Safety of Manufactured Nanomaterials

The purpose of the OECD Series on the Safety of Manufactured Nanomaterials is to provide up-to-date information on the diverse activities at OECD related to human health and environmental safety. The latest publications are available for download on the OECD website.

PAPER: Carbon Nanoparticles Toxic to Older Fruitflies, Not To Young

In a series of experiments, researchers at Brown University sought to determine how carbon nanoparticles would affect fruit flies — from the very young to adults. The scientists found that larval *Drosophila melanogaster* showed no physical or reproductive effects from consuming carbon nanoparticles in their food. Yet adult *Drosophila* experienced a different fate. Tests showed adults immersed in tiny pits containing two varieties of carbon nanoparticles died within hours. Analyses of the dead flies revealed the carbon nanoparticles stuck to their bodies, covered their breathing holes, and coated their compound eyes. Scientists are unsure whether any of these afflictions led directly to the flies' death. The findings, published online in *Environmental Science & Technology* ("Differential Toxicity of Carbon Nanomaterials in Drosophila: Larval Dietary Uptake Is Benign, but Adult Exposure Causes Locomotor Impairment and Mortality"), help to show the risks of carbon nanoparticles in the environment.

PROJECT: Regulating Nanomaterials – A Transatlantic Agenda

Regulating Nanotechnologies in the EU and US is a collaborative research project involving researchers from Chatham House, the London School of Economics, the Environmental Law Institute and the Project on Emerging Nanotechnologies at the Woodrow Wilson International Center for Scholars. Its goal is to investigate the regulatory challenges posed by nanotechnologies and to assess the effectiveness of existing approaches on both sides of the Atlantic. The project is innovative in taking a comparative perspective and in contributing to the early identification of regulatory methodologies and best practices that promote regulatory convergence between the EU and US. The project has now published a Briefing Paper that summarizes its findings.

REPORT: New Report Demands Public's Involvement In Nanotechnology Policy Debate

Decision-making on science – especially nanotechnology – must become more democratic, a new report on science policy released today argues. The group of leading European academics behind the 'Reconfiguring Responsibility' report argue forcefully that current governance activities are limiting public debate and may repeat mistakes made in managing GM. The DEEPEN report comes in the wake of a move within UK and European science policy-making to govern 'upstream' in a technology's development, before its impacts become irreversible, and to involve the public in decision-making. Analysing this move in the context of nanotechnology, the 'Reconfiguring Responsibility' report argues that these developments do not go nearly far enough.

PAPER: Decreasing Uncertainties in Assessing Environmental Exposure, Risk, and Ecological Implications of Nanomaterials

Determining the fate and interactions of nanomaterials in complex environmental contexts is required to assess exposure and possible harm as well as to inform regulation.. In this Viewpoint, the authors highlight research issues whose overarching objective is to develop the tools necessary to identify and mitigate the negative impacts of manufactured nanomaterials in the environment. This research agenda is premised on the need to understand the hazards of nanomaterials (e.g., toxicity, mutagenicity, impacts on ecosystem services) and underlying mechanisms as a basis for focusing study of the processes controlling exposure. doi: 10.1021/es803621k

PAPER: Fullerene Exposure With Oysters

Oysters are an ecologically important group of filter-feeders, and a valuable toxicology model for characterizing the potential impacts of nanoparticles to marine organisms. Fullerene (C_{60}) exposure studies with oysters, *Crassostrea virginica*, were conducted with a variety of biological levels, e.g., developmental studies with embryos, whole organism exposures with adults, and isolated hepatopancreas cells. Significant effects on embryonic development and lysosomal destabilization were observed at concentrations as low as 10 ppb. doi: 10.1021/es900621j

PAPER: Titanium Nanomaterial Removal And Release From Wastewater Treatment Plants

This study is the first to provide evidence of the quantities, physical characteristics, and fate of Ti in a municipal Waste Water Treatment Plant (WWTP). Given that TiO_2 has been used by the industry for decades, is currently one of the most utilized nanomaterials in consumer products, and is relatively easy to measure and image in complex biological matrices, TiO_2 is a prime candidate to serve as a sentinel, or tracer, for other nanomaterials, especially those of similar size and aggregation behavior, by indicating the possible fate of nanomaterials in a WWTP. doi: 10.1021/es901102n

REVIEW: Quantitative Analysis of Fullerene Nanomaterials in Environmental Systems

Conclusions of this review are: (1) Analytical procedures are needed to account for the potentially transitory nature of fullerenes in natural environments through the use of approaches that provide chemically explicit information including molecular weight and the number and identity of surface functional groups. (2) Sensitive and mass-selective detection, such as that offered by mass spectrometry when combined with optimized extraction procedures, offers the greatest potential to achieve this goal. (3) Significant improvements in analytical rigor would result from an increased availability of well characterized authentic standards, reference materials, and isotopically labeled internal standards. Finally, the benefits of quantitative and validated analytical methods for advancing the knowledge on fullerene occurrence, fate, and behavior are indicated. doi: 10.1021/es900692e

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