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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 exposure to CNTs, especially by factory workers, will increase substantially over the next few years. Since the jury is still out as to the toxicity of nanotubes it appears prudent to at least develop suitable sensor technology to detect CNTs, especially in the workplace.

THE DETECTION OF CARBON NANOTUBES AND WORKPLACE SAFETY

More and more carbon nanotube (CNT) applications are moving from the research lab into commercial products. For example, CNTs can be found already in tennis rackets and bicycles, displays and TV screens, and numerous resins used by aerospace, defense, health care, and electronics companies. Not surprisingly, CNT production is growing by hundreds of metric tons a year. One of the large suppliers alone, Bayer, is talking about having 3,000 metric tons of production capacity in place by 2012. As a result of the increasing supply, prices are dropping fast. While a kilogram of multi-walled CNTs (MWCNTs) sold for tens of thousands of dollars just a few years ago (and single-walled CNTs still do), the price for some types of MWCNTs has fallen to hundreds of dollars per kg. Recent market analyses forecast sales of all nanotubes to reach $1 billion to $2 billion annually within the next four to seven years. In terms of dollar value, electronics devices will be the largest end-use category, although composite materials in automotive applications may account for greater volumes. These volumes are expected to approach several thousand metric tons per year. This means that the exposure to CNTs, especially by factory workers, will increase substantially over the next few years. Since the jury is still out as to the toxicity of nanotubes it appears prudent to at least develop suitable sensor technology to detect CNTs, especially in the workplace.

The confusing and by now familiar "yes, they are toxic!" – "no, they are not!" tug of war with regard to the toxicity of carbon nanotubes was evident just last week again: While one study reported good news ("New nanotube findings give boost to potential biomedical applications") another did the opposite ("Single-Walled Carbon Nanotubes Can Induce Pulmonary Injury in Mouse Model"). We have written about this dilemma in a recent Nanowerk Spotlight article ("Nanotechnology risk assessment could benefit from nanoparticle categorization framework").

Over recent years, the rapidly emerging applications of CNTs have made the CNT community increasingly aware of the need for more toxicological studies on the material they were working with. A recent review paper in Nanotoxicology ("The detection of airborne carbon nanotubes in relation to toxicology and workplace safety") introduces a new paradigm in that the community should not only be interested in production, applications and toxicological effects but also to recognize flaws with current tools for detection and emphasize the need to develop an efficient sensor platform.

"In our review paper we have raised the need for a better detection platform in the CNT-affected workplace" Dr. Peter Cumpson tells Nanowerk. "The quickly rising industrial production of carbon nanotubes highlights the ever-increasing need to have an efficient and effective tool for the detection of nanotubes – because right now we don't. This new tool must be improved compared to the general purpose airborne particle counters that are currently employed, to allow better sensitivity and specificity to CNTs."

According to Cumpson, a researcher at the National Physical Laboratory (NPL) and a Visiting Professor at the University of Newcastle-upon-Tyne in the UK, such a platform ideally would allow single strand sensitivity with sufficient selectivity for nanotube detection amongst (other airborne) impurities. "The general consensus is that the sampling and detection combination should be capable of monitoring the

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The Institute of Occupational Medicine (IOM) based in Edinburgh has launched a range of new services to help companies minimise the environmental and health risks of working with nanomaterials.

SAFENANO LAUNCHES SCIENTIFIC SERVICES

The Safenano Initiative is a venture by the Institute of Occupational Medicine (IOM). The initiative was designed to help industrial and academic communities to quantify and control the risks to their workforce, as well as to consumers, the general population collage and the environment, through both information provision and consultancy services.

Complementing the IOM's SAFENANO Information Service and Community Portal, SAFENANO Scientific Services will provide companies operating in the nanotechnology industry with a multidisciplinary range of solutions to ensure they can offer employees a safe and healthy working environment and end products that are safe for customers.

The development of nanotechnology is expected to drive major advances in medicine, drug discovery, security and defense. At a scale 10,000 times smaller than the thickness of a human hair, nanoparticles have unique properties that hold promise for the fabrication and assembly of ground-breaking new products in many industry sectors. However, there is currently little known about the long term consequences of working with nanomaterials.

SAFENANO Scientific Services, which is part-funded by Scottish Enterprise Edinburgh and Lothian and the Technology Strategy Board, aims to provide greater insight into potential hazards of working with nanotechnology by offering companies expert advice and support to help ensure they meet regulatory duties, achieve effective product stewardship and manage potential liabilities towards users, customers and the environment.

SAFENANO Scientific Services offers laboratory services and testing, workplace occupational hygiene, toxicology reports and reviews, as well as related training for staff and management to aid companies in the development of effective nanotechnology risk management programs.

"SAFENANO Scientific Services builds on the IOM's international reputation as a leading provider of nanotechnology risk research and consultancy. Through provision of proactive risk assessment, these services will enable UK companies to access the best available support to ensure safe and responsible development of nanotechnology." said Dr Rob Aitken, Director of the SAFENANO initiative. SAFENANO Scientific Services is managed by the Institute of Occupational Medicine, in partnership with Napier University, who are recognized as a leading institution in nanoparticle toxicity assessment.

Professor Vicki Stone, Nanoparticle Toxicologist and Director of the Biomedicine and Sport Science Research Group at Napier University, said: "I am delighted to be part of this latest innovative project from SAFENANO – it is a great opportunity to start to address the real needs of industry in terms of assessing the safety of nanomaterials now and in future development, and is reflective of Napier's commitment to working with industry and business."

Neil Francis, Director of Growing Business at Scottish Enterprise Edinburgh and Lothian, added: "Nanotechnology is widely believed to offer great potential for the development of new materials, products, processes and economic growth over the coming years.

"It is, however, recognized that there are still some uncertainties concerning the risks that some of these new materials may pose to the health of those working with them, the wider public and to the general environment. Having an organization like IOM and the services of SAFENANO in Scotland gives us a significant advantage and reinforces our expertise in this area, which companies working with this technology will be able to benefit from."

The SAFENANO initiative is one of the Technology Strategy Board's Micro and Nanotechnology Network's UK Nanotechnology Centres of Excellence. Phase 1 of this initiative was officially launched in August 2007.

The launch of SAFENANO Scientific Services represents the latest stage in IOM and SAFENANO's nanotechnology program which aims to understand, quantify and control risks posed by nanomaterials to the workforce, consumers, the general population and the environment through research, consultancy and service work for industry and government.

The European Union has released a publication on nanotechnology research funding addressing in particular the health and environmental impact of nanoparticles

EU Research In The Field Of Health And Environmental Impact Of Nanoparticles

Following its commitment of addressing upfront the potential risks, the European Commission has boosted support for specific collaborative research into the potential impact of nanoparticles on human health and the environment since the Framework Programme 5 (FP5). These activities have been continued and reinforced in FP6 and in FP7 where several topics were launched specifically addressing the safety of nanomaterials. At the same time, the EU Members States have also been funding research in that field, but a consolidated overview of these ongoing or finished projects was not yet available so the magnitude of these national efforts was difficult to evaluate.

The new compilation aims at gathering the most complete overview of past and ongoing research projects funded by the FPs, EU Member States, Candidate Countries and Countries associated to FP6 or FP7 in the area of possible impacts in health, environment and safety of nanoparticles. Being the first of its kind, this compilation has information of 106 projects, 14 of them are from the FPs which give around €32 million in grants. The others 92 projects are from the EU Members States which spend around €47 million in grants. This makes a total of some €79 million.

This information may well be incomplete. All interested parties are kindly requested to send additional information on research projects funded through national funding schemes to the email address pilar.aguar@ec.europa.eu. Several projects are currently in negotiation for funding under FP7; information will be added as soon as possible. It is the intention to regularly update this information and make it available through the European Commission dedicated websites.

It is foreseen that past research activities in the area of impact assessment of nanoparticles will continue and be reinforced within the Seventh Framework Programme for Research (2007-2013), with the first call already containing topics in the area of the health, safety and environmental impact of nanoparticles. FP7 will be the main initiative for implementing the Action Plan on Nanosciences and Nano-technologies.

Of particular relevance is the topic **NMP-2007-1.3-2 Risk assessment of engineered nanoparticles on health and the environment,** which strives to reinforce the international cooperation, in particular with USA research teams. This call is the result of particular efforts to address point 7 of the Action plan (on International Cooperation).

Document: EU nanotechnology R&D in the field of health and environmental impact of nanoparticles (pdf down-load, 400 KB).

Upcoming Events
Looking At The Risky Side Of Nano

nanoECO
March 2-7, 2008, Monte Verità (Switzerland)
It is the aim of this conference to gather researchers working at the forefront of nanoparticles in the environment to present, discuss and review the data existing on applications and behavior of nanoparticles in the environent. In addition it is the aim to use these data for a foresight approach on future nanoscale materials, uses and impacts.

Greener Nano 2008
March 10-11, 2008, Corvallis, OR (USA)
As nanotechnology advances, many questions arise regarding putative effects of nascent nanomaterials on the environment and health. How do we make the right decisions in the face of these uncertainties? This conference focuses on cutting edge research in sustainable nanomaterials design, the latest developments in nanoscience and nanotechnology, and potential biological impacts of nanomaterials.

Risk, Uncertainty and Decision Analysis for Nanomaterials: Environmental Risks and Benefits and Emerging Consumer Products
April 27-30, 2008, tba (Portugal)
It is The NATO workshop will focus on recent advances in nanotechnology that may have environmental and health implications (e.g., benefits, risks and costs).

Nanotechnology – A Contributor to Reducing Animal Experiments?
May 28-29, 2008, London (UK)
The application of nanotechnology is currently revolutionizing medicine and this two-day conference, the first of its kind in Europe, will examine the role nanotechnology could also play in improving or refining the development of alternatives to animal testing whilst maintaining safety.

2nd World Congress on Risk – Risk and Governance
June 8-11, 2008, Guadalajara (Mexico)
This is the second of a series of World Congresses on Risk that are important, logical steps to further develop the field of risk analysis and its applications.

11th International Inhalation Symposium – Benefits and Risks of Inhaled Engineered Nanoparticles
June 11-14, 2008, Hannover (Germany)
The symposium will cover the main areas of current concern and active research in the context of inhaled engineered nanoparticles: Relevant physico-chemical characteristics; Measuring methods for airborne particles; Emerging biological test systems; Bioavailability; Pulmonary and systemic toxicity; Mechanisms of toxicity; Use in therapy and diagnosis; Potential sources of human exposure; Potential risks.

THE DETECTION OF CARBON NANOTUBES …

Continued from page 1

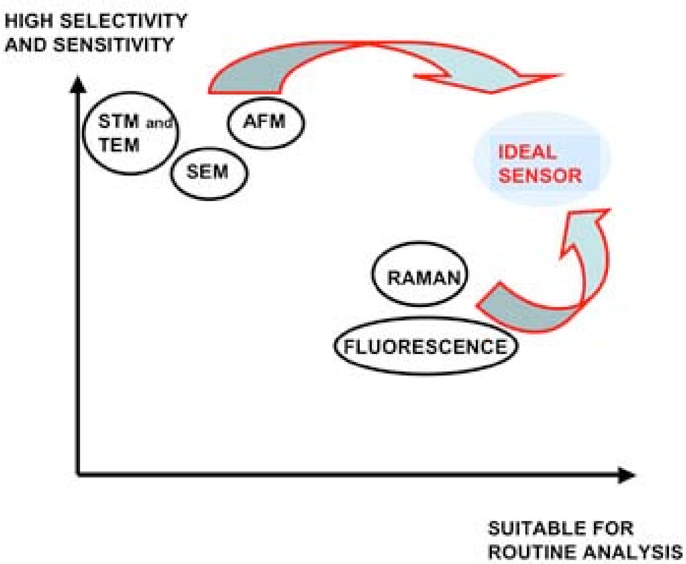
concentration of airborne nanotubes and that the detection platform should have sufficient sensitivity to measure exposure well below levels where there is a risk to health" he says.

The paper, first-authored by Ratna Tantra, a researcher at the NPL, is an assessment of current commercial instruments that have the potential to meet certain criteria identified as key components in a CNT detection platform in the workplace.

The tools reviewed are based on instruments that have been previously used as characterization techniques to examine CNTs' quality (diameter, purity, etc) after production. The focus of the paper is evaluating their suitability as an effective detection platform.

"Besides sensitivity and selectivity issues, we have assessed other criteria including the potential for automation, the ability of detecting the different forms of CNTs (aggregates, bundles and individual strands) and the ability to give some indication of CNT concentration" Ratna explains to Nanowerk. "Our review has shown that no single perfect method exists i.e. one that meets all of the requirements against the key criteria identified."

Various technologies that could potentially used to detect airborne CNTs in the workplace



Raman spectroscopy, a tool capable of generating a chemical fingerprint (as displayed in the spectrum of that molecule) was considered as having the most potential. Although the tool provides the basis for single strand detection, it only shows high selectivity to certain types of carbon nanotubes, particularly single-walled CNTs. In addition, the need to incorporate multiple laser lines in the instrument so as to detect nanotubes with different diameters, may prove to be expensive.

"In the past, scientists have likened some nanotubes to resemble the shape of asbestos fibers, which have been linked to cancer" Ratna says. "This has triggered new concerns about airborne exposure to CNTs. However, it is important to stress that the toxicology of CNTs is largely an unexplored field, particularly with regards to the different levels of toxicological complexity and diversity associated with the many different types of nanotubes. In addition, there is also the issue of exposure frequency and concentration levels."

The two UK scientists stress that their biggest concern is the limited knowledge that exists with regard to CNTs' toxicity and they argue that the minimum criteria regarding detection issues for CNTs, until the facts have been established, should be based on the assumption that all CNTs are hazardous to health.

"Until we are able to fully extract and unravel all the relevant information an immediate implementation of preventive measures should be carried out and having an early detection platform is vital" says Cumpson. "Quite simply put: CNTs are a next generation material and there is a need to develop next generation detection technologies to go with that."

Ratna notes that, with regard to evaluation criteria in relation to sampling, this will follow a similar trend for general nanoparticle sampling: "In the past, a number of key issues have been highlighted, which are related to the general properties of nanoparticles. For example, nanoparticles will not stay localized and have tendency to move rapidly away from the source, potentially exposing many individuals; this poses questions regarding sampling location and frequency. From a workplace safety point of view, this would suggest the need to monitor CNTs from personal rather than fixed workstations on a routine basis. Furthermore, like all nanoparticles, CNTs are prone to aggregation; aggregates can bond to each other to form agglomerates and the speed at which they agglomerate will depend on their numerical concentration and mobility. Careful considerations in choosing how to sample are required so as to ensure that analysis will give a true representation of the different forms of CNTs in which the workers are exposed to. Correspondingly, it is best to implement 'direct' sampling activities, which would involve the collection of airborne CNTs on to a suitable substrate. For example, an adhesive coated substrate would be suitable supporting substrate, as the adhesive layer will promote entrapment and fix CNTs."

Cumpson says that this review article marks the starting point of the NPL scientists' research into this subject. In the future they would very much like to be involved in a 'community-based' research, which would require more communication with different players of the nanotube community e.g. toxicologists, instrument manufacturers, nanotube factories, users, etc.

"Certainly this in itself is challenging – with different people having different vested interests – but it is important for specialists to work together on an international level" he says. "Through the collection and dissemination of knowledge, this will enable us to firstly further develop the criteria for evaluating an effective detection platform, which will then pave the way to further developing technologies to render them as 'suitable'; this will be done either through using new technology or through the novel integration of existing platforms."

An understanding of the relationship between the physical and chemical properties of nanostructures and their in vivo behavior would provide a basis for assessing toxic response and could lead to predictive models for assessing toxicity

NANOTOXICITY: THE GROWING NEED FOR *IN VIVO* STUDY

Toxicology is an interdisciplinary research field concerned with the study of the adverse effects of chemicals on living organisms. It applies knowledge, methods and techniques from such fields as chemistry, physics, material sciences, pharmacy, medicine and molecular biology. Toxicology established itself in the last 25-30 years as a testing science in the course of efforts of industrial nations to regulate toxic chemicals. Particle toxicology, as a subdiscipline, developed in the context of lung disease arising from inhalation exposure to dust particles of workers in the mining industry. It later expanded to the area of air pollution. With the rapid development of nanotechnology applications and materials, nanotoxicology is emerging as an important subdiscipline of nanotechnology as well as toxicology. Most, if not all, toxicological studies on nanoparticles rely on current methods, practices and terminology as gained and applied in the analysis of micro- and ultrafine particles and mineral fibers. Together with recent studies on nanoparticles, this has provided an initial basis for evaluating the primary issues in a risk assessment framework for nanomaterials. However, current toxicological knowledge about engineered nanoparticles is extremely limited and traditional toxicology does not allow for a complete understanding of the size, shape, composition and aggregation-dependent interactions of nanostructures with biological systems. An understanding of the relationship between the physical and chemical properties of nanostructures and their *in vivo* behavior would provide a basis for assessing toxic response and more importantly could lead to predictive models for assessing toxicity.

"Nanotoxicology is important for the advancement of nanotechnology in a wide-array of applications" Dr. Warren Chan tells Nanowerk. " Studies in this area could lead to the required information to make responsible regulatory decisions. Thus far, most reported nanotoxicity studies have focused on in vitro cell culture studies, however, data obtained from such studies may not correspond to *in vivo* results. In the future, a full *in vivo* life cycle characterization framework needs to be formulated wherein systematic evaluation of the size, shape, and surface chemistry of nanostructures, and their correlation to in vivo behavior, is obtained."

Chan is an Assistant Professor at the University of Toronto's Institute of Biomaterials and Biomedical Engineering. Together with Hans Fischer, a PhD student in his group, he published a review article in the December 2007 issue of Current Opinion in Biotechnology in which he describes the assumptions and challenges in the nanotoxicity field and provide a rationale for *in vivo* animal studies to assess nanotoxicity ("Nanotoxicity: the growing need for in vivo study").

The two scientists argue that the development of predictive models of nanostructure toxicity requires a systematic mapping of the fate, kinetics, clearance, metabolism, protein coating, immune response and toxicity of nanostructures to the nanostructure's physical properties within a life cycle model.

The focus of Chan's article is to provide a review of the in vivo activities of nanostructures and define the link between these studies and a better toxicological understanding of nanostructures. He also provides a brief description of nanostructures, their interactions with cells in *in vitro* cell culture systems, and their potential molecular effects (e.g. inflammation).

"Currently, there is a common assumption that the small size of nanostructures allows them to easily enter tissues, cells, organelles, and functional biomolecular structures (i.e. DNA, ribosomes) since the actual physical size of an engineered nanostructure is similar to many biological molecules (e.g. antibodies, proteins) and structures (e.g. viruses)" explains Chan. "A corollary is that the entry of the nanostructures into vital biological systems could cause damage, which could subsequently cause harm to human health. However, a number of recent studies have demonstrated that despite the size of the nanostructures they do not freely go into all biological systems but are instead governed by the functional molecules added to their surfaces."

Although researchers can now engineer nanostructures to direct the intracellular or in vivo biodistribution but the final metabolic fate is still unknown, and strategies for avoiding secondary unintentional behaviors are lacking.

Progression of studies required to fully assessing the impact of nanostructures

"Overall the relationship between size, shape, and surface chemistry of nanostructures and their correlation to intracellular and *in vivo* bio-distribution is unknown" says Chan. "By contrast, pharmaceutical strategies have developed this sort of relationship for a number of drugs and carriers and thus, they have created predictive categorization which will need to be emulated with nanostructures. Systematically, one cannot predict the movements and location of nanostructures after intracellular or *in vivo* exposure based on nanostructure properties at this time, and such studies must be done before one can assess the toxicity of nanostructures in a systematic format."

With a systematic and thorough quantitative analysis of the pharmacokinetics – absorption, distribution, metabolism, and excretion – of nanoparticles is missing, the overall behavior of nanostructures can be summed only in general terms:

(1) nanostructures can enter the body via six principle routes: intra venous, dermal, subcutaneous, inhalation, intraperitoneal, and oral;

(2) absorption can occur where the nanostructures first interact with biological components (proteins, cells);

(3) afterward they can distribute to various organs in the

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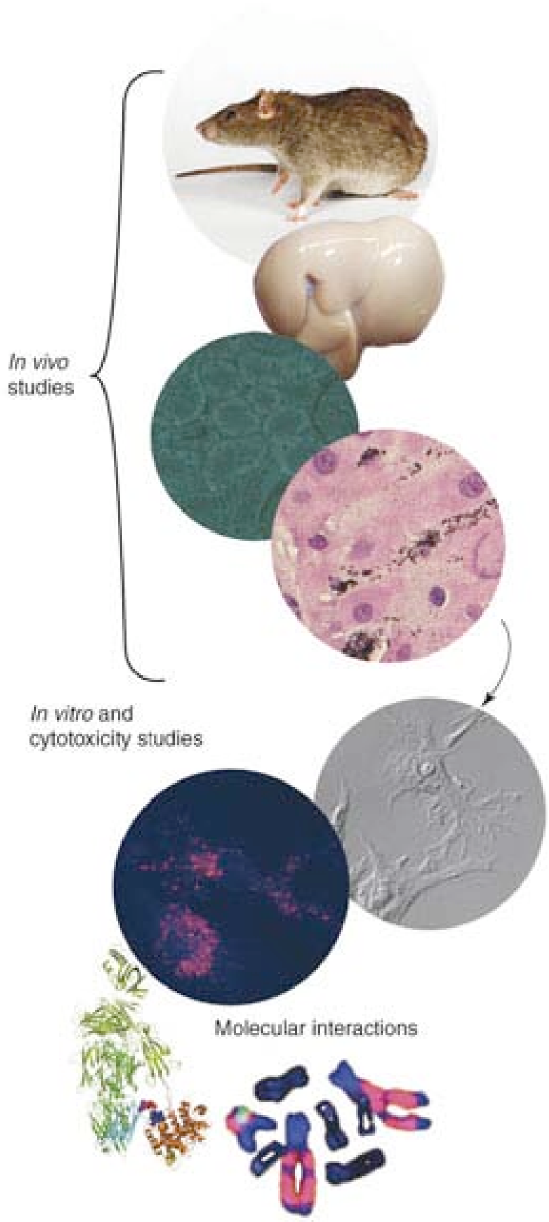
body and may remain the same structurally, be modified, or metabolized or excreted;

(4) they enter the cells of the organ and reside in the cells for an unknown amount of time before leaving to move to other organs or to be excreted. of engineered nanostructures.



Progression of studies required to fully assessing the impact of physicochemical nanostructure properties. Studies in animal models will identify the organs of interest, in turn leading to identifying the best cell types for studies, and to focused studies on how these cells molecularly respond to the nanostructures. A number of the images were adapted with reprint permission from the Public Division of the Massachusetts Medical Association and the American Association for Cancer Research. (Reprinted with permission from Elsevier)

"In our view there is an urgent need for conducting pharmacokinetics studies as a first route for assessing nanotoxicity" says Chan. "The information obtained from such studies identifies the cells that take them up, which could logically lead to more focused studies. These specific studies will identify the organ that could potentially be stressed by exposure to nanostructures and will provide a molecular basis of the stress. If one can associate these responses to specific types, surface chemistry, size, shape, aggregation and composition, then we would be able to correlate the toxic responses to the properties of the nanostructures."

Chan notes that it will require a progression of studies to fully assessing the impact of physicochemical nanostructure properties. Once the specific organs and cells are identified in connection with a toxic response, further focused studies using in vitro models (e.g. cell culture) would complement the in vivo studies. "Currently, most studies in this area of research utilize cell culture models, in which the results could only be considered as exploratory" he says. "The combined results from multiple studies of different cells in vitro cannot be assumed to capture the same behavior as the same cells arranged *in situ* in an organ."

Chan and Fischer point out that in vivo studies of nanostructures provide new challenges to how pharmaceutical sciences traditionally conduct pharmacokinetics research. They emphasize that detection strategies must be capable of quantifying all of the major parts of a nanostructure in tissues and organs since many modern nanostructures are engineered with multiple components. "Techniques must be flexible and tailored to the specific nanostructure being investigated, and the investigators be cognoscente of the correlation between chosen metric and actual interpreted quantity. Multi-indicator techniques, in which each of the three components listed above would incorporate distinct markers, would provide a complete picture of metabolic processes but this has not been applied to nanostructures."

Another considerable challenge is the variability in manufacturing methods, associated raw materials, and reaction scaling necessary to produce adequate volumes of uniform nanostructures.

"Consistent particle properties and a classification scheme to support it are necessary to be able to make cross comparisons between the results obtained from different research groups" says Chan. "Once the detection and synthetic challenges are overcome, significant infill of data is required to construct an accurate picture of what variables influence nanostructure pharmacokinetics and whether toxicity will be observed."

Finally, the authors stress that another major challenge with nanostructure in vivo studies is understanding how proteins interact with nanostructure surfaces: "In order to qualify observed in vivo results, an understanding of the nanostructure protein-interface is vital, since this can potentially dictate behavior *in vivo*."

In Short – Papers, Initiatives & Updates

PAPER: Toxicity of single-walled carbon nanohorns

Researchers at JST/SORST in Japan extensively investigated in vitro and in vivo the toxicities of as-grown single-walled carbon nanohorns (SWNHs), a tubular nanocarbon containing no metal impurity. The SWNHs were found to be a nonirritant and a nondermal sensitizer through skin primary and conjunctival irritation tests and skin sensitization test. Negative mutagenic and clastogenic potentials suggest that SWNHs are not carcinogenic. The acute peroral toxicity of SWNHs was found to be quite low—the lethal dosage for rats was more than 2000 mg/kg of body weight. Intratracheal instillation tests revealed that SWNHs rarely damaged rat lung tissue for a 90-day test period, although black pigmentation due to accumulated nanohorns was observed. While further toxicological assessments, including chronic (repeated dose), reproductive, and developmental toxicity studies, are still needed, yet the present results strongly suggest that as-grown SWNHs have low acute toxicities.

GOVERNMENT: UK government releases second nanotechnology risk report

The UK government has now published its second research report Characterising the Potential Risks posed by Engineered Nanoparticles (pdf download, 1.2 MB). This report builds on the 2005 report and 2006 progress report, providing an update on the Defra's (the UK's Department for Environment, Food and Rural Affairs) Nanotechnology Research Co-ordination Group's objectives and associated program of work.frame. The report provides a detailed update of progress on the 19 research objectives which were set out in 2005, it reviews research funding opportunities for nanotechnology, places the UK work program in an international context and responds to recommendations from the Council for Science and Technology's review of March 2007 of the Government's research agenda on nanotechnology environment, health and safety issues and the activities of the Nanotechnology Research Coordination Group (NRCG).

GOVERNMENT: EU call for scientific data on nanotechnology applications in food and feed

The European Commission has requested an initial scientific opinion from the European Food Safety Authority (EFSA) relating to the risks arising from nanoscience and nanotechnologies on food and feed safety and the environment. The request also asks to identify the nature of the possible hazards associated with actual and foreseen applications in the food and feed area and to provide general guidance on data needed for the risk assessment of such technologies and applications. The request is handled by the EFSA Scientific Committee who in November 2007 appointed an expert working group to prepare a draft opinion. A draft of the opinion is scheduled to be published for public consultation in July 2008, which is reflected in the short deadline for submission of data testing,

PAPER: Toxicity studies of fullerenes and derivatives

Due to their unique properties, fullerenes, a model of carbon-based nanoparticles, have attracted considerable interest in many fields of research including material science and biomedical applications. The potential and the growing use of fullerenes and their mass production have raised several questions about their safety and environmental impact. Available data clearly shows that pristine C60 has no acute or sub-acute toxicity in a large variety of living organisms, from bacteria and fungal to human leukocytes, and also in drosophila, mice, rats and guinea pigs. In contrast to chemically--either covalently or noncovalently--modified fullerenes, some C60 derivatives can be highly toxic. Furthermore, under light exposure, C60 is an efficient singlet oxygen sensitizer. Therefore, if pristine C60 is absolutely nontoxic under dark conditions, this is not the case under UV-Visible irradiation and in the presence of O2 where fullerene solutions can be highly toxic through 1O2 formation.

INITIATIVE: EPA seeks data about nanoscale materials

EPA launched the Nanoscale Materials Stewardship Program (NMSP). The NMSP will help provide a firmer scientific foundation for regulatory decisions by encouraging submission and development of information including risk management practices for nanoscale materials. The NMSP contains a basic and an in-depth program: Under the Basic Program participants are invited to voluntarily report available information on the engineered nanoscale materials they manufacture, import, process or use. Under the In-Depth Program participants will voluntarily develop data, including testing, over a longer time frame.

PAPER: Single-walled carbon nanotubes can induce pulmonary injury in mouse model

The potential health risk of chronic carbon nanotubes exposure has been raised as of great public concern. Scientists at National Chung Cheng University in Taiwan have demonstrated that intratracheal instillation of 0.5 mg of single-walled carbon nanotubes (SWCNT) into male mice (8 weeks old) induced alveolar macrophage activation, various chronic inflammatory responses, and severe pulmonary granuloma formation. They then used Affymetrix microarrays to investigate the molecular effects on the macrophages when exposed to SWCNT. A biological pathway analysis, a literature survey, and experimental validation suggest that the uptake of SWCNT into the macrophages is able to activate various transcription factors and this leads to oxidative stress, the release of pro-inflammatory cytokines, the recruitment of leukocytes, the induction of protective and antiapoptotic gene expression, and the activation of T cells. The resulting innate and adaptive immune responses may explain the chronic pulmonary inflammation and granuloma formation *in vivo* caused by SWCNT.

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