



SAFENANO's Review of 2009

Rob Aitken & Bryony Ross, January 2010

The New Year always brings an avalanche of lists, reviews and retrospectives for all to digest. The nano-world is no exception, and SAFENANO is pleased to bring you its review of events, news and views of 2009. Of course, this account is by no means an exhaustive one and represents only our personal views, so apologies to those we have missed from these reflections (and occasionally to those we have mentioned!).

Five years of RS/RAE

For many people in this field, the starting point of all of our work was the publication of the RS/RAEng report, for which the 5 year anniversary took place in July '09. This anniversary provided the opportunity for a considered reflection on the issues and what progress had been made since publication of that seminal document. SAFENANO provided commentary and a guest blog from Anthony Seaton, one of the authors of the original report. We also contributed to a [publication](#) by the Responsible Nano Forum which featured 25 contributions from a range of stakeholder groups in the UK and internationally.

Our view was that whilst in the UK there has been greatly increased co-ordination at government level, increased knowledge sharing through a series of state of the art reviews published by DEFRA and others, activities such as SAFENANO as well as increased research funding opportunities, many fundamental questions remain unanswered and are likely to remain so for some time. There is an undoubtedly an enormous increase in research being carried out internationally and interesting studies are beginning to emerge, yet few of the key issues relating to exposure, toxicology and risk of nanoparticles and nanotubes have yet been answered in a satisfactory way. We still require, for example, basic information about relationships between dose and effect, distribution kinetics of nanoparticles which enter the body, safe levels of exposure, measurement methods and agreed protocols for nanotubes. This SAFENANO view was broadly shared by the other stakeholders. Key reasons identified included poor co-ordination within and between research programmes, a situation which is beginning to be addressed at European level.

New studies and reviews

In this challenging new area of research, the efforts of those working across the field is now beginning to be rewarded with some fascinating results. Amongst the many papers appearing in 2009 we highlight three which were of particular interest.

Han et. al. – Inhalation Toxicity of MWCNT in Rats Exposed for 3 Months

The first paper which really caught our attention was a 90-day inhalation toxicity study which demonstrated the potential for multi-walled carbon nanotubes (MWCNTs) to induce lung toxicity in exposed rats. This is one of only a handful of CNT inhalation studies published thus far. Published in August in the journal [Toxicological Sciences](#), the study was performed according to OECD test guidelines with the overall aim of providing data to support risk assessment for workplaces. Led by Robert Landsiedel, a toxicologist from BASF SE in Germany, the study not only demonstrated the potential for MWCNTs to induce lung toxicity following inhalation exposure at what (in mass terms) are low concentrations, but also incorporated numerous advances in methodology, representing a significant step forward in



terms of generating suitable data to support workplace risk assessments. The paper was discussed extensively in our [August Feature article](#).

Wijnhoen et. al. - Nano-silver: a review of available data and knowledge gaps in human and environmental risk assessment

A second noteworthy paper was the review and gap analysis of nano-silver, conducted by researchers at the [RIVM \(NL\)](#) and published in the journal [Nanotoxicology](#). The review, which had primary aims to assess whether the toxic effects of nano-silver are due to a combination of the specific properties of silver nanoparticles and/or silver ions released from them, and whether or to what extent, nano-silver particles are able to enter the body, presented the most comprehensive collation and analysis of data on the topic the SAFENANO team has seen on this multi-faceted but contentious nanoparticle in 2009.

Bhabra et. al. - 'Nanoparticles can cause DNA damage across a cellular barrier'

In the last quarter of 2009 a controversial paper was published in the journal [Nature Nanotechnology](#). This particular study suggested that cobalt-chromium nanoparticles (CoCr NPs) used in many medical devices may damage DNA without crossing cellular barriers such as the placenta or blood-brain-barrier. The implied association sparked much debate amongst experts in the field, the crux of which was that although the study itself was elegantly conducted, the results were not necessarily of any relevance to actual human exposure risk. Although it received less news coverage than other controversial papers in the year such as [Song et al.](#) (which is discussed later), the paper nonetheless still caused a stir for nano's public image. As a result, the reporting of the results and potentially emotive association between a medical product and adverse health effects was criticised as irresponsible reporting by some in the field.

New threats?

Hand in hand with the discovery of new and beneficial applications for any technology always comes the potential for hazard. In August, the nano-networks were in a state of high anxiety following leak of a paper which was about to be published in the [European Respiratory Journal](#) and purported to demonstrate a link between occupational exposure to nanoparticles and serious clinical symptoms. The case study, led by [Yuguo Song](#) of Chaoyang Hospital in Beijing, involved seven healthy young women employed in a print plant who, over the course of a few months, were all hospitalised for severe respiratory problems. A diagnosis was reached in all cases of pulmonary fibrosis with consequent impairment of lung function, which proved fatal for two of the women.

At face value, the paper's findings seemed set to have a huge impact on the nanotoxicology field, and potentially on the public acceptance of nano in general. However, there were a number of issues with the evidence presented in the paper (highlighted in our August '09 feature article), which led many nanotoxicologists to question the causal link implicated between the nanoparticle exposures and the consequent illness. In addition, this paper served to highlight the need for clarity and impartiality in reporting of results within studies of such potentially great impact.

In response to this paper, a group of leading scientists working on nanotechnology risk issues published a memorandum in the journal [Nanotoxicology](#) at the close of 2009 warning of the dangers from misusing the term 'nanoparticles'. With a focus on liaison with media bodies and wording of journal titles, the group (which included SAFENANO's [Lang Tran](#) and [Rob Aitken](#) as co-authors) stressed the importance of clearly communicating the nature of the nanoparticle being investigated. While the reporting of controversial findings such as that of [Song et al.](#) are important and appropriate in line with a long history of publishing clinical



studies in the peer-reviewed literature, it is key that the manner in which the paper is reported does not serve to "promulgate the myth of generic nanoparticle toxicity, and potentially misled the public and the media into believing there is some reason to fear 'nanoparticles'", a conclusion which is clearly undesirable.

What about consumers?

A key requirement of nano safety research is not only to protect people working with nanomaterials but also those consumers who come into contact with the technology throughout its lifecycle. In keeping with this, consumer safety issues continued to provide a strong platform for debate throughout the year. In June, NGOs Friends of the Earth, the Consumers Union, and the International Center for Technology Assessment (ICTA) released a report entitled 'Manufactured Nanomaterials and Sunscreens: Top Reasons for Precaution'. The report argued that adding nanoparticles to sunscreens presented an "unnecessary potential risk to our health and to the environment, with no significant gain", and attracted much attention in the press. Later in the year, Friends of the Earth (FoE) Australia released a second report which claimed that nanomaterials are abundant in many 'big-name' cosmetics. FoE stated that in an independent study they identified nanoparticulate materials in 10/10 randomly selected foundations, which included names such as The Body Shop, Max Factor and Christian Dior. Although the group did not properly quantify or characterise the nanoparticles identified in the cosmetics, the study once again highlighted nano to the consumer world in less than a glowing light.

Respite from this negative publicity came in the summer from another NGO, the Environmental Working Group, when their annually published safe sunscreen guide (which claims to be "the only place concerned consumers can go to identify which sunscreens, lip balms and moisturizers are the safest, most protective for themselves and their families") came up trumps for nano.

Despite stating in previous years that a lack of definitive safety data and consumer information on these common new ingredients make it very hard to support the use of nano, the group's 2009 report states that zinc and titanium-based formulations "are among the safest, most effective sunscreens on the market based on available evidence".

"When we began our sunscreen investigation at the Environmental Working Group, our researchers thought we would ultimately recommend against micronized and nano-sized zinc oxide and titanium dioxide sunscreen" the group stated "...But many months and nearly 400 peer-reviewed studies later, we find ourselves drawing a different conclusion, and recommending some sunscreens that may contain nano-sized ingredients". The group's approach was commended by the nano world, and proved that the divide between industry and NGOs isn't as great as it at times may seem.

Even more data

2009 has seen a number of excellent resources and tools emerge. Below are a few of our favourites:

OECD Database on the Safety of Manufactured Nanomaterials

In April 2009, the OECD launched a global database on research into the safety of manufactured nanomaterials. Holding details of completed, current and planned research projects on safety, the database will help identify research gaps and assist researchers in future collaborative efforts. To access the database, [click here](#).



The Project on Emerging Nanotechnologies NanoInventories

The NanoInventories were launched in March 2006, at the time containing only 212 products. In August of this year, three and a half years into the Inventories' lifespan, the Project on Emerging Nanotechnologies announced that the number of nano-enabled consumer products on sale had reached the 1,000 mark. To access the PEN NanoInventories, [click here](#) .

findNANO – putting nanotech in your pocket

Also from the Project on Emerging Nanotechnologies and based on their NanoInventories, findNANO is an application for Apple's iPhone and iPod Touch that lets users discover and determine whether consumer products are nano-enabled. The app, which was released in November 2009, is free to download and well worth having to hand – [click here](#) to find out how to get your own copy.

LST Nanotech Regulation Database

In December 2009, Arizona State University announced the launch of a global database of government documents on nanotechnology. The first of its kind, the [Nanotech Regulatory Document Archive](#) , is a free resource which promises to be valuable to stakeholders interested in all areas of nanotechnologies.

New guidance

The year of 2009 saw the publication of several new guidance documents by standards organisations, government agencies and the OECD as well as the development of a guidance website, the GoodNanoGuide. The majority of these concerned occupational hygiene and workplace practices, addressing the issues of control and minimisation of exposure. In January, the International Standards Organisation ISO published a technical report ISO/TR 12885:2008 "[Health and safety practices in occupational settings relevant to nanotechnologies](#)". The report provides a general background the nanoparticle risk issues and describes in some detail current practices for risk assessment, exposure measurement and control which are appropriate for use with engineered nanoparticles. This report takes an encyclopaedic view but stops short of recommending which practices are appropriate for which materials under which circumstances, leading to disappointment for some users. This report is commercially available from ISO.

This was closely followed by a report from Canada published by Institut de recherche Robert-Sauvé en santé et en sécurité du travail (IRSST), in collaboration with CSST and NanoQuébec. The document "[Best Practices Guide to Synthetic Nanoparticle Risk Management, Report R599](#)", covered much of the same ground as the ISO document but in less detail. This document also introduced the idea of using a "control banding" approach based on that [described by Paik](#) and recommends that this approach is used where there is insufficient information for a quantitative risk assessment. Control banding is based on a matrix comprising the toxicity of the material (severity) and likelihood of exposure (probability) to choose an appropriate control method. The document provides a scoring system in order to assess both of these variables. The method benefits from being simple to use and providing a reproducible decision making process. However it is difficult to judge, given the current lack of knowledge about both toxicity and exposure issues, how appropriate the scoring system is and how protective the final method is. A useful contribution though and one which can be downloaded free from the [IRSST website](#) .

A more direct approach was provided by the UK's [Health and Safety Executive \(HSE\)](#) who published their information sheet on the "[Risk Management of Carbon Nanotubes](#)". The document outlines in brief some of the key evidence linking CNTs to the fibre paradigm of toxicity, in particular referencing the 2008 Nature Nanotechnology paper from Poland et al. It



emphasised the legal responsibility which falls on people who create risk through work activities, stressing that there is "a legal duty to understand those risks, and make sure they are kept as low as reasonably practicable". The document affirms HSE's consideration of CNTs as substances of very high concern, stating that "a precautionary approach should be taken to the risk management of all CNTs, unless sound documented evidence is available on the hazards from breathing in CNTs". It provides specific advice including to reduce the number of employees exposed, and to minimise the level and duration of exposure; the quantities used; and CNT handling. The document also recommends all tasks, including packaging for disposal, should be carried out in a ducted fume cupboard with a HEPA filter, or by using other suitable effective local exhaust ventilation (LEV) with a HEPA filter, quite a challenging requirement for some process.

Taking a different approach is the [Goodnanoguide](#). This goal of this innovative project has been to develop web-based, expert led and written guidance following an Wikipedia type model. The project was led by the ICON group at RICE University. They assembled an international group of experts, including SAFENANO's Steve Hankin, to map out the basic ideas, to develop the structure and produce the first content. Even in its initial form the outcome is impressive and will surely become more so as the content develops further. The web-based approach is not for everyone and the international nature of this can sometimes generate inappropriate advice in specific national circumstances (for example for CNTs in the UK), but with appropriate support this is sure to develop into a major recourse. Over the next year we will be looking at further ways in which SAFENANO can synergise with GoodNanoGuide to provide the best possible guidance to our users.

Government activities

Significant activity at a governmental level occurred in 2009. In the UK, February saw the UK House of Lords Science and Technology Select Committee consider nanotechnologies in the food sector. Amongst those who gave [evidence](#) at the Committee's hearing on the topic were SAFENANO colleagues Prof Ken Donaldson and Dr Qasim Chaudhry. The [final report](#), which was published on the 8th January 2010, accused the food industry of being too 'secretive' about nanotechnologies in food products, and highlighted the need for increased transparency in the area. They also called for a public register of food products and packaging containing nanomaterials, and more Government-funded research into possible health hazards, particularly those relating to ingestion risks. For SAFENANO it was gratifying to see the extensive use made of our EMERGNANO report by the Committee.

In June, the UK Government published its [official response](#) to the Royal Commission on Environmental Pollution (RCEP) Report "Novel Materials in the Environment: The Case of Nanotechnology" which was published in November 2008. Much of what the RCEP report had contained was reflective of what had been in the RS report 5 years earlier. The Government response included statement of a commitment to "develop an approach that has the protection of human and environmental health at the heart of its agenda", but was in truth short on detail on how this would be achieved. The report also stated the Government's intention to develop a UK Strategy for nanotechnologies, building on previous and existing activities and review the UK's priorities and strategic direction. Consultation on this strategy was launched in the summer, and we await the outcome with interest.

There was also significant activity at the European level with both the European Parliament and the European Commission active. The year began with publication and adoption of a key opinion on the most recent developments in the risk assessment of nanomaterials from the European Commission's independent Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR). Building on earlier opinions from 2006 and 2007, the [2009](#)



opinion highlighted that methodologies to assess exposure to manufactured nanomaterials to humans and the environment and the identification of potential hazards require further development, and SCENIHR maintains its earlier recommendation to perform risk assessment case-by-case for each nanomaterial in the absence of a general approach.

In April, the European Commission launched a public nanotechnology consultation . Using themes for discussion based on the influential SCENIHR opinion on the Risk Assessment of Nanomaterials, the consultation culminated in a scientific hearing held in September 2009.

Also in April the European Parliament's Environment Committee adopted a 'no data, no market' principle for nanotechnology products in line with the principle contained within the REACH chemicals Regulation. The report conflicted with the EC position that nanomaterials are in principle covered by existing legislation and called for products containing nanotechnology which are already on the market to be withdrawn until safety assessments can be made.

Following the summer break, late 2009 saw a flurry of activity from the EC, including:

- a pledge to review all relevant legislation within two years to ensure safety for all applications of nanomaterials in products with potential health, environmental or safety impacts over their life cycle,
- publication of the EC's second nanotechnology implementation report (2007-09) outlining key developments, challenges and conclusions from various relevant policy areas, and
- provision of insight into the future state-of-the-art NMP research for Europe from the Framework Programme's Expert Advisory Panel (of which Rob Aitken is a member), in the form of a position paper on the future research and technological development activities of the programme 2010-15.

Regulation

Hand in hand with increasing availability of data, 2009 saw some of the first real developments within the regulatory landscape announced by regulatory bodies worldwide. Amongst changes announced from the UK, EU, Australasia and the US, one of the most interesting stories from 2009 was that of the EPA and carbon nanotubes.

Early in 2009, the EPA's only involvement with nanomaterials was through its voluntary reporting approach , a system which even the EPA were forced to admit was yielding little useful information on nanomaterials. This passive stance ended in June 2009 when the EPA announced that it was promulgating further significant new use rules (SNUR) under section 5(a)(2) of the Toxic Substances Control Act (TSCA) for 23 chemical substances, including different modifications of single-walled and multi-walled carbon nanotubes, carbon black, and (mixed) metal oxide containing film coating additives.

Stating concerns regarding potential lung effects of the nanomaterials specified as justification, the EPA included recommendation within the SNUR that a 90-day inhalation toxicity test, in some cases including a post-observation period of up to 3 months, would help characterise the human health effects of the substances. In addition, the SNUR required manufacturers of specific carbon nanotubes to ensure that their workers are wearing protective clothing and masks that comply with National Institute for Occupational Safety and Health (NIOSH) requirements.



Among the first regulations designed to protect workers dealing with carbon nanotubes, the SNURs attracted much attention from consumers and regulators worldwide and in July, and the EPA stated that similar SNURs were expected to be issued for other types of carbon nanotubes. However the following month, the SNURs for single and multi-walled CNTs were withdrawn. The reason appeared to be a legal technicality - whilst the direct final rulemaking procedures that the EPA used to issue the SNURs meant that the new rules applied immediately when issued (thus bypassing lengthy notice-and-comment rulemaking), US law states that these must be withdrawn if a notice of intent to submit adverse or critical comments is received within 30 days. One such notice was received, and the SNURs were removed.

Within the Federal Register, the EPA has stated that it now 'intends to publish in the Federal Register, under separate notice and comment rulemaking procedures, proposed SNURs' for single- and multi-walled carbon nanotubes. However, this process will take considerably longer than the original route, interpreted by many as a rather disappointing outcome. To read the Federal Register notice released on the 6th November 2009, [click here](#).

A Nano-Headache for REACH

Another area in which nanomaterials have proved tricky to handle was that of the REACH Regulation for chemicals. In April, members of the European Parliament called for a review of the way in which nanomaterials are handled within REACH following concerns that nano was not specifically accounted for within the regulation. In June, Chemistry World reported that confusion over classification of nanomaterials had led to two groups of companies using different criteria to submit data on carbon nanotubes to the European Chemicals Agency (ECHA). One group set up its own SIEF for carbon nanotubes to register them as distinct chemicals with their own safety profile, whilst another much larger collection of CNT producers and importers planned to register the nanomaterials as a form of bulk graphite so that they will not require their own registration dossier.

In response, ECHA Executive Director Geert Dancet, said that special regulation of nanomaterials would be considered when the Commission produces a review of the scope of REACH, which it must do by June 2012, adding that he was sure that following the review, "...nanomaterials will be covered in a more systematic way".

Exclusively, we can now announce that arrangements are now in place to tackle this review in the form of two projects on behalf of the European Commission, under management of the SAFENANO team! More information will be made available on these important new contracts very shortly.

What's new for SAFENANO?

Closer to home, 2009 has also been a busy year for the SAFENANO team. Our year began with publication of two new reports – HARN examining toxicity of high aspect ratio nanomaterials, & CELL PEN, both of which were authored by a consortium of UK scientists led by the Institute of Occupational Medicine (IOM; SAFENANO's parent institution), and attracted critical acclaim from the nano community.

This summer, we announced publication of another key report led by the SAFENANO team. The EMERGNANO report, a first global review of environment, health and safety research into nanomaterials, was authored by a SAFENANO-led team, and published by Defra, the UK Government Department for Food & Rural Affairs. Since its publication, the



report has received acclaim internationally, and has received specific mention in several policy documents within the EU and further afield.

In addition, 2009 also saw expansion to our staff as we welcomed three new team members – Steve Hankin, Julia Varet and Sheona Peters. As Director of Operations, Steve took on the task of shaping our consultancy tier SAFENANO Scientific Services. Steve was joined in this by Julia Varet who now works as our dedicated toxicologist. Finally, Sheona Peters joined the team providing input from her role as an Associate Editor on our Information Service.

The close of the year brought good news for SAFENANO, with the announcement of secured continuation and development funding for our information service. Following three successful years, SAFENANO is now recognised internationally as a key resource for the nanotechnology environment, health & safety (EHS) information. Over the coming year we hope that the funding will be used to streamline SAFENANO's current provision, and develop additional resources to enable improved access to the latest developments in nano EHS. We will of course keep you updated on improvements and expansions to SAFENANO as they happen!

Nanosafety community

In addition to their work with SAFENANO, all of our team are involved many other nano EHS activities including outreach activities, collaboration and European Research.

At the beginning of the year, the FP7 project ENRHES (Engineered Nanoparticles, Review of Health and Environmental Safety) was progressing an extensive review of four major types of nanomaterials (fullerenes, metals, metal oxides and nanotubes). It involved all of the SAFENANO team plus several other experts and was led from Edinburgh Napier University. The final report provides a detailed evaluation of the knowledge base for these materials and a set of prioritised recommendations to inform policy makers in the development of methods to assess risk, and in the development of appropriate regulation. As of the beginning of January 2010, the final report is free to download – to access it [click here](#).

At the start of summer came the launch of a major new FP7 project – ENPRA (Engineered Nanoparticles, Proactive Risk Assessment). Led by SAFENANO team member Dr Lang Tran, the project aims to develop and implement a novel integrated approach for engineered nanoparticle (ENP) risk assessment and will utilise the latest advances within in vitro, in vivo and in silico approaches. The project's inaugural meeting was held at the University of Paris 'Diderot', and in recognition of its expected impact, ENPRA consortium members were honoured to receive an invite to the British Embassy in Paris for a reception to celebrate the project's launch.

In July, following the successful completion of its first of four years, the EC FP7 project NanoImpactNet published its second Major Information Package and Stakeholder report. Many of the SAFENANO team are all consortium members on this project, and it was great to reach the end of NanoImpactNet's first year having established the project as a EU-wide network of nanotechnologists, and achieved all deliverables successfully.

In all, there are now around 25 European FP6 and FP7 projects dealing with nanoparticle risk issues. These are major projects, some of them with funding up to 4M Euro with often 10-20 partner organisations. Most of them deal with toxicology but an increasing number are dealing with exposure or risk issues. Up to this year (when another six had been added to the list) these projects had been working largely independently from each other with little or no attempt to co-ordinate inputs or outputs. In early 2009 a "clustering" process was initiated by the Commission, in which the project leaders met informally to discuss their work and to



look for synergies between them. This process grew substantially through the year and significant progress has been made on sharing of information, materials, data storage and protocols. One of the outcomes was a bid for infrastructure support for which we should know the outcome in a couple of months. This clustering activity is at present a bottom-up process but, encouraged by the Commission, will become increasingly relevant over the next 12 months and will surely accelerate the rate of progress in the field.

What did it all mean?

While it is challenging to digest everything from the last year, it's clear from even this brief run-through that there is no sign of a let up in the activity underway in this field. Most of the current work is considering the toxicology of nanoparticles, for a diverse range of endpoints. This work is mostly in vitro, and whilst it may not be fashionable to say this, there is a great shortage of in vivo data. Without this data, progress on assuring the safety of nanoparticles within the context of healthy human populations and compromised sub-populations, and in providing necessary evidence for regulatory approval of nanomaterials use across a number of sectors is likely to be slow.

Exposure to workers is an area in which there clearly remains a major lack of information - we need to address this urgently. Some studies are ongoing, including our new NANEX project under FP7, and more are planned. However, without better information on exposure, trying to interpret risk will continue to be problematic. Toxicity information on its own is not enough. Lack of evidence should not be an excuse for lack of action and there remains a need for everyone to implement high levels of care in order to prevent unnecessary exposure. It is undeniable that if occupational hygiene practises are poor, workers health (and at times lives) will be put at risk, and the current lack of hard evidence to date for health effects in exposed human populations should not lead us to complacency in this respect.

Outside of the occupational setting, 2009 saw growing evidence of consumer exposure the nanomaterials from products already on the market. However, this mainly seems to be to relatively well known materials such as zinc oxide or titanium dioxide in, for example, sunscreen products and dermal absorption & toxicity studies are currently inconclusive as to the realistic probability of these products causing actual harm.

Reflection on 2009's key nano stories also highlights the importance of responsible reporting of nano EHS findings; poorly reported cases mean that the focus is wrongly assigned. Integrity of scientific design, and responsible reporting of the findings are not difficult to achieve, and should be a key consideration when working toward publishing results – public opinion is ultimately what will judge the success or otherwise of the nanotechnology industry.

Clearly 2010 offers great possibilities of significant progress. SAFENANO will continue to strive to bring the best of it to you in order to support the development of nanotechnology in a safe and responsible manner. Thank you all for your continued support.

Rob Aitken & Bryony Ross
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