Report of second joint Science Council of Japan-Royal Society workshop on the potential health, environmental and societal impacts of nanotechnologies

Summary

The specific subjects that were discussed at the workshop are summarised in main body of this report. The general issues that emerged from these discussions are:

- The uncertainties around the potential health and environmental impacts of nanoparticles and nanotubes must be reduced. Government and industry should make funding available to support the research required to ensure the safe and responsible development of nanotechnologies.
- There are reasonably adequate instruments available for atmospheric and aquatic sampling and characterisation of nanoparticles, and newer instruments for directly measuring surface area are being developed. However, smaller, cheaper and more compact measuring instruments are needed for routine monitoring in both the workplace and the environment.
- Given the number of new engineered nanomaterials that are being produced, assessing the potential for exposure is a priority. Exposure must be considered throughout the life cycle of products containing nanomaterials.
- There remains an urgent need for international standard protocols for testing nanoparticles. However, some participants felt that more fundamental research on the adsorption, distribution, metabolism and excretion of nanoparticles is required before appropriate protocols can be agreed. It was suggested that research on specific high production volume nanomaterials and on model compounds designed to elucidate underlying mechanisms should be undertaken simultaneously.
- Standardised certified reference materials (CRMs) of nanoparticles with well characterised size, surface chemistry and other properties would enable better comparison of research from different laboratories. Further discussion between toxicologists, ecotoxicologists and nanotechnologists is required to enable a better understanding of how to address the challenges associated with achieving this.
- Further research on the life cycle of products containing fixed nanoparticles is required to assess whether nanoparticles might be released and present a significant source of exposure.
- Scientists researching the risks posed by nanoparticles and those researching their use in the treatment of disease would benefit from a greater exchange of information and ideas.

1 Overview

1.1 This report summarises the second joint Science Council of Japan - Royal Society workshop, held at the Tokyo Big Sight on 23 February 2006 during the Nanotech 2006 exhibition and conference. The British Embassy, Tokyo, provided some support for the workshop. This report has been produced to reflect the key issues that emerged during the meeting and is not necessarily an expression of the views of the Royal Society or the Science Council of Japan.

1.2 The first joint workshop was held at the Royal Society in London on 11 - 12 July 2005. The potential health, environmental and societal impacts of nanotechnologies were discussed and a report of this workshop is available on the Royal Society and Science Council of Japan's websites (Royal Society- Science Council of Japan 2005).

1.3 This second workshop focussed on the potential health and environmental impacts of nanotechnologies, as well as potential measurement technologies. Round table discussions followed presentations given by British and Japanese experts in the toxicology, ecotoxicology, fate and behaviour and the measurement of nanomaterials. Much of the discussion centred on human toxicology, and particularly exposure and risk assessment in the workplace.

2 Measurement of nanomaterials

2.1 A variety of parameters are likely to influence the toxicity of nanoparticles, including specific surface area, chemical composition, impurity, surface characteristics, size distribution, shape and 'active' surface area (amount of active material present on the surface). Measurement and characterisation techniques and instrumentation need to be developed to measure some, or all, of these parameters.

2.2. A challenge in developing characterisation instrumentation for nanoparticles is the need for it to take into account their dynamic nature. Reaction kinetics (the rate and mechanism of chemical reactions) will vary with many parameters including nanoparticle type. Aggregation kinetics (the rate and mechanisms by which particles aggregate) are very important to fate, behaviour, toxicology and ecotoxicology.

2.3 Nanoparticles under 50nm are rarely spherical particles and often have very rough surfaces. Examining shape using electron microscopy is expensive and laborious; however, measurement of shape is important and should be conducted alongside other measurements.

2.4 In environmental systems, measurement of mass, surface area and particle number are equally important and relate to processes of sedimentation, pollutant uptake and aggregation. In terms of fate and behaviour, it is likely that particle number may be a key parameter.

2.5 There are reasonably adeduate instruments available for atmospheric sampling and newer instruments for directly measuring surface area are being developed. Current research is exploring the use of photo-ionisation of the outermost layer of particles as they pass through a gas stream, which gives a measure of total surface area and some analytical information. This has the potential to distinguish the surface area of engineered nanoparticles from the background of other nanoparticles. Other techniques used for measuring nanoparticles, which were not discussed at the meeting, include force and electron microscopes and quartz microbalances. However, smaller, cheaper, and more compact instruments are needed to facilitate routine monitoring. There is often a gap between the initial funding for novel techniques and producing practical bench top instruments.

2.7 An example of the measurement of ambient nanoparticles in factories producing fullerenes and multi-walled carbon nanotubes in Japan was presented. Morphology, volume-size distribution and number of nanoparticles were measured using a Scanning Electron Microscope, scanning mobility particle sizer and an optical particle counter; and a particle mass monitor and low-volume air sampler were used. Both nanotubes and fullerene particles were found to be agglomerated and remained so when agitated. More studies on exposure assessment in various workplaces are required, along with development of the measuring instruments to enable this.

2.8 Measurement techniques need to be standardised otherwise research data is not comparable. The techniques used to measure nanoparticles during research into their impacts should be documented as different techniques can give different values.

2.9 It was suggested that greater collaboration is needed between those developing measurement technologies and scientists working in occupational medicine and toxicology to develop appropriate instrumentation to measure exposure in the workplace. There is a need to measure physical parameters such as size, aggregation and solubility that will directly feed into the necessary calculations related to dose and response required by toxicologists and ecotoxicologists.

3 Research on potential risks to health from nanoparticles

3.1 Given the number of new engineered nanomaterials that are being produced and the different methodologies and metrics for investigating the risks associated with them, there are a large number of possibilities for research. Assessing the potential for exposure is a priority and this requires development of measurement instrumentation and methodologies, as discussed above. Exposure must be considered throughout the life cycle of products containing nanomaterials. Determining the efficacy of preventative measures in the workplace is also necessary.

3.2 Nanoparticles in production now or close to market should be a priority for research. Some participants urged that carbon nanotubes should be prioritised because their fibrous shape are similar to that of disease causing fibres, such as asbestos, and they have great potential for industrial applications. Others suggested that collaborative research should start with metallic and ceramic nanoparticles, especially nickel, because of the availability of existing data and the rising level of production. Nickel is also a known allergen. Understanding fundamental mechanisms of fate and behaviour may require using model examples rather than specific, close to market nanomaterials. Following this debate it was suggested that research on specific high production volume nanomaterials and on model compounds designed to elucidate underlying mechanisms should be undertaken simultaneously. There remains an urgent need for international standard protocols for *in vitro* and *in vivo* testing of nanoparticles.

3.3 Research into the toxicology of asbestos, alpha quartz and PM10 (particulate matter up to 10 micrometres in size in the atmosphere) suggests that oxidative stress and inflammation drive disease. These seem appropriate targets to measure when assessing particle toxicology. Research presented revealed that when testing carbon black, titanium dioxide and polystyrene beads, smaller particles always generated more reactive oxygen species than the larger particles both in a cell-free system and in cells (all other parameters being equal).

3.4 Research presented at the meeting demonstrated how imaging techniques could be used to establish the distribution of fullerene and carbon nanotubes in human macrophage cells exposed to these nanoparticles. The images provided evidence of fullerenes and single walled carbon nanotubes penetrating the nucleus of the cell. Previous research on the genotoxicity of air pollution particles has revealed that if particles penetrate the nucleus and are able to produce reactive oxygen species, then they can introduce specific hydroxyl radical DNA lesions that are pre-mutagenic and pre-cancerous.

3.5 Another key issue in toxicological testing is that dispersing agents and solvents may themselves have biological influence or could mask the biological activity of nanoparticles. For example, polyvinylpyrrolidone and gamma-cyclodextrin, used as dispersing agents for fullerene, can cover its surface and may distort the results of research on the bioactivity of fullerene.

3.6 There was considerable discussion around the issue of standard reference materials. It was noted that making standard certified references materials widely available would enable better comparison between toxicology test results from different laboratories. However, nanotechnologists explained that 'standard' nanoparticles can be difficult to produce and nanoparticles within a batch can differ significantly. It was suggested that specifications that allow certain variability could be agreed. Further discussion between toxicologists, ecotoxicologists and nanotechnologist is required to enable a better understanding of how to address these challenges.

3.7 Scientists researching the risks posed by nanoparticles and those researching their use in the treatment of disease would benefit from a greater exchange of information and ideas. Particularly as the pharmaceutical industry has been investigating methodologies for characterisation of nanoparticles and has validated models for examining bioavailability across monolayers, the gastro-intestinal trap, the blood-brain barrier and particle transport.

4 Research on potential risks to the environment from nanoparticles

4.1 Fixed forms of nanoparticles could prove an important source of free nanoparticles in the environment, particularly in natural waters. Further research on the life cycle of products containing fixed nanoparticles is required to assess whether nanoparticles might be released and present a significant source of exposure.

4.2 The relationship between natural and engineered nanoparticles in natural waters is important, especially when considering transport processes and bioavailability. Natural waters are made up of very complex mixtures of a wide range of different types of materials, with a size range between 0.1 nanometers and 10 microns and over. Natural aquatic nanoparticles include humic and fulvic acids, degradation products from plants in fresh water and polysaccharides directly produced by bacteria. Research results presented during the meeting suggest that humic substances reduce the aggregation of engineered nanoparticles and prevent sedimentation process occurring. Other results show that carbon nanotubes increase aggregation in natural waters. Increased and decreased aggregation will affect the transport and fate of nanoparticles in water. Aggregation and sedimentation are not processes which will remove nanomaterials from the aquatic environment, but they will affect the distribution and partitioning of nanoparticles in aquatic and terrestrial environments. Further research is required to determine the wider impact free nanoparticles could have on the environment.

5 Developments in frameworks relating to risk assessment of nanomaterials

The following developments in national and international frameworks for the risk assessment of nanomaterials since the first workshop in July 2005 were reviewed:

5.1 The International Standards Organisation (ISO) has established Technical Committee 229 (TC229) to consider terminology, nomenclature, metrology, instrumentation, test methods, modelling and simulation, and product standards, which will include health, safety and environmental practices. There are other ISO technical committees relating to nanomaterials, such as the Surface Chemical Analysis Technical Committee 201, which has generated standards in measuring the chemistry of surfaces of particles.

5.2 In Japan, the first roadmap for the risk assessment of nanomaterials has been published by the National Institute of Advanced Industrial Science and Technology (AIST). It provides a five-year schedule for the analysis of hazard and exposure, followed by risk assessment. The Nanotechnology Business Creation Initiative (NBCI), a consortium of 320 private companies, has established a working group for societal impacts and standardisation of nanocarbon materials (particularly carbon nanotubes). A classified list of manufacturing methods and a flow chart for classification of their qualities is being prepared. They will also be studying risk assessment.

5.3 In the United Kingdom, the Nanotechnology Research Coordination Group (NRCG) was set up by the government in response to the Royal Society and Royal Academy of Engineering report *Nanoscience and nanotechnologies: opportunities and uncertainties* (HM Government 2005)*.* It has published a report outlining the research objectives for characterising the potential risks posed by engineered nanoparticles. These objectives are being taken forward by small taskforces. Since the meeting the Natural Environmental Research Council, Department for Environment Food and Rural Affairs and the Environment Agency have announced funding for an Environmental Nanotechnology Initiative.

6 Public engagement

In the United Kingdom, there have been a number of public engagement activities around nanotechnologies. One of these, a citizens' jury organised by Greenpeace, the University of Cambridge, the Guardian newspaper and the University of Newcastle, was discussed. The jury made a range of recommendations after listening to witnesses, including scientists, industrialists and NGOs. This included the recommendation that the governance of science and technology should be a more open and democratic and there should be greater public involvement in science policy making. They felt that publicly funded nanotechnologies research should focus on long term problems that would not be addressed by business. The jurors also hoped that new technologies would create new, high value jobs. The full report of the workshop can be accessed at http://www.nanojury.org/

7 Next steps

The two joint workshops have highlighted that research into the health, environmental and societal impacts of nanotechnologies should be a priority for international Governments. The Science Council of Japan and the Royal Society encourage bilateral and international academic collaboration on these issues and urge Government and industry to make funding available to support the research required to ensure the safe and responsible development of nanotechnologies. It was agreed that it should be considered whether it would be useful to hold another joint workshop on these issues in 2008.

References and related web links

HM Government (2005) Characterising the risks posed by engineered nanoparticles: a first UK Government research report Defra: London
http://www.defra.gov.uk/environment/nanotech/research/pdf/nanoparticles-riskreport.pdf

Micro and Nanotechnology Manufacturing Initiative
http://www.microandnanotech.info/mnt_network.html

Ministry of Economy, Trade and Industry, Japanese Government http://www.meti.go.jp/english/

Ministry of Education, Culture, Sports, Science and Technology, Japanese Government
http://www.mext.go.jp/english/

National Institute of Advanced Industrial Science and Technology (AIST)
http://www.aist.go.jp/index_en.html

Nanotechnology Research Coordination Group, Office of Science and Technology, UK Government http://www.ost.gov.uk/policy/issues/nrcg.htm

Nanojury http://www.nanojury.org/index.html

Nanosafenet http://www.nanosafenet.co.uk/

Nanosafe2 http://www.nanosafe.org/node/15

Nanotechnology Environmental and Health Implications (NEHI) Working Group
http://www.nano.gov/html/society/EHS.htm

Nanotechnology Researchers Network of Japan http://www.nanonet.go.jp/english/

National Institute for Environmental Studies (NIES) http://www.nies.go.jp/index.html

National Institute of Health Science (NIHS) http://www.nihs.go.jp/index.html

National Institute of Materials Science (NIMS) http://www.nims.go.jp/eng/index.html

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Safety of nanomaterials Integrated Research Centre www.snirc.org