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ABSTRACT

Nanotechnology – the use of particulate material at such a small scale that its properties are determined by size and surface condition as well as bulk properties – has been heralded as offering the potential to revolutionise many industrial sectors and medical practices. Nanotechnology also presents problems in managing risks to human health and the environment which are explored here, drawing on the report of a Working Group set up by the Royal Society and the Royal Academy of Engineering. Taking an anticipatory approach to assessing the benefits and regulating the risks from an emerging technology is itself novel. Very little is known about the risks to human health and the environment from nanomaterials, so that a precautionary approach is advocated. Stopping short of the moratorium on production and use of nanomaterials advocated by some NGO's, restrictions on the technology are recommended including regulating nanomaterials as new chemicals, planning end-of-life management of products containing nanomaterials and a presumption against release of manufactured nanomaterials into the environment. Conclusions are drawn for the regulation of other emerging technologies in future.

INTRODUCTION – TECHNOLOGY AND RISK MANAGEMENT

It is now accepted that *the conventional separation (in engineering decisions involving risk) between the technical (the province of engineers) and the social (the province of managers, politicians and the public) cannot survive scrutiny* (Royal Academy of Engineering, 2002). Failure to recognise the need to manage all aspects of risk including the societal aspects has led to obvious "difficulties" for certain technologies. The nuclear industry is well-known example, as are some forms of biotechnology including attempts to introduce Genetically Modified (GM) crops. Without passing comment on whether these technologies should have achieved public acceptance, it is clear that failure to engage in broad-based debate has introduced problems in achieving satisfactory regulatory bases for the introduction of new technologies, and that once opposition develops it is difficult to overcome (e.g. Mayer, 2002; Mehta, 2004). Once a climate of suspicion starts to develop it may be amplified, for example by media reporting, into a "crisis of trust" (O'Neill, 2002). The Royal Commission on Environmental Pollution went so far as to advocate a deliberative approach to involve public values in setting environmental standards, and proposed a model for the kind of process needed (RCEP, 1998).

It is probably fair to say that, while "deliberative stakeholder engagement" is widely advocated, experience has not shown that any particular type of process is especially effective. In particular, it is not clear how a successful public debate can be conducted over an emerging technology, to develop an anticipatory approach to assessing its likely benefits and regulating its possible risks. Nanotechnology is an example for which such an approach is needed, given the emergence of public concerns ahead of (and arguably unrelated to) introduction of the technology.

In June 2003, the UK Government commissioned the two principal academies of science and engineering, the Royal Society and the Royal Academy of Engineering, to carry out an *independent study into current and future developments in nanoscience and nanotechnologies and their impacts.* However, the study was carried out independently of Government, by a Working Group whose 14 members included engineers and scientists, a philosopher, a social scientist, a consumer champion and an environmentalist. The terms of reference included to *identify what environmental, health and safety, ethical or societal implications or uncertainties may arise from the use of the technology, both current and future* and to *identify areas where regulation needs to be considered.* The Report of the Working Group was published in July 2004 (Royal Society and Royal Academy of Engineering, 2004). This paper draws largely on the Report of the Working Group, of which the author was a member, concentrating on the risk management aspects covered under the above two terms of reference.

Although embodying current thinking in risk management, this approach to examining and planning to manage the risks associated with an emerging technology is itself new. The Royal Society/Royal Academy study has been hailed (Wilsdon and Willis, 2004) as *a change in the scientific community's approach to the risks, uncertainties and wider social implications of new and emerging technologies – in many ways, it redefines the genre.* The present author is as sceptical of this enthusiasm as of the promises made for nanotechnology. However, the questions of whether nanotechnology and the prospective approach to risk management will turn out to be paradigm shifts provide the context for this paper.

NANOTECHNOLOGY – HOPES, DOUBTS AND FEARS

The Royal Society report defies nanoscience as *the study of phenomena and manipulation of materials at atomic, molecular and macromolecular scales, where properties differ significantly from those at a larger scale.* Nanotechnologies are *the design, characterisation, production and application of structures, devices and systems by controlling shape and size at nanometre scale.* In essence, nanotechnology is an emerging technology based on solid particles in the size range where their properties are determined by size and surface condition as well as bulk properties[1.] The principal dimension of a nanoparticle – e.g. the diameter in the case of a fibre – is typically a few tens of nanometers; i.e. an order of magnitude larger than a DNA strand but of the same order as a virus.

Recognition of the potential for using nanoscale materials and operations is usually dated to a lecture by Richard Feynman (1959) while the term *nanotechnology* was coined later (Taniguchi, 1974) to describe precision engineering of materials at the nanometre scale. Nanomaterials are already in use in some consumer products, specifically cosmetics and sun-screens. But nanotechnology has been held up as offering the potential to revolutionise a wide range of economic activities; see Table 1. Several of the more immediate possible applications lie in the process and energy sectors. The potential developments in manufacturing arise from the convergence of "top-down" processes such as ultraprecision machining and lithography with"bottom-up" processes based on chemicals and biochemicals (Whatmore, 2001); i.e. through a materials revolution combining synthesis and smart fabrication. In the longer term, many of the more interesting possible applications lie in bio-nanotechnology and nanomedicine: implants and prosthetics, improved diagnostics, targeted drug delivery and radiological treatment.

[1] Some Applications may also use the properties of nanopores in materials of larger scale (e.g. Zhao et al, 2004). However, the focus of this paper is nanoparticles rather than nanopores.

Table 1: Some possible applications of nanotechnology

Evolutionary:	• catalysts and separation membranes • batteries and fuel cells • paints and coatings • electronics and displays • "smart" packaging and labelling • environmental clean-up
Longer term:	• composites • lubricants • components and prosthetics • diagnosis and targeted drug delivery • environmental monitoring

Other claims for nanotechnology are more fanciful. A report by the US National Science Foundation and Department of Commerce (NSF, 2003) is cited in the Royal Society/Royal Academy report as *a very good example of the difficulty some commentators find in drawing an appropriate line between hope and hype.* In support of the US National Nanotechnology Initiative, Roco (2004) has claimed *it is conceivable that by 2015, our ability to detect and treat tumours in their first year of occurrence might totally eliminate suffering and death from cancer.* The Royal Society/Royal Academy Working Group considered that *such a claim demonstrates an over-simplistic view of the detection and treatment of cancer.* Concern over damage rather than benefit has been raised by the idea of molecular assemblers, nanoscale machines or "nanobots" able to select and position atoms to assemble an object and thus to replicate themselves. Uncontrolled self-replication, leading to massive pollution of the biosphere by "grey goo", has been the subject of novelistic interest (and certain statements by public figures). The Royal Society/Royal Academy study considered self-replicating devices to be too fanciful to merit immediate attention. Even Eric Drexler, who originated the idea of nano-scale machines, has since changed his position (Phoenix and Drexler, 2004).

Effective selling of the potential developments has led to major R and D investment in the USA in particular (Roco, 2004) and somewhat lower activity in Japan and Europe (European Commission, 2004a). UK Government interest has been criticised as *too little, too late* (House of Commons Science and Technology Committee, 2004).

Amongst the many questions over the realism of the claims made for nanotechnology is whether the benefits from using nanomaterials are really much larger than the resource use and environmental impacts associated with producing nanomaterials. This would clearly require systematic Life Cycle Assessment of some typical nanotechnology products and applications, but no such study yet appears to have been reported. The Royal Society/Royal Academy Working Group recognised this as a clear research need.

Distinct from alarmism over "grey goo", the public view of nanotechnology appears to be undeveloped. A web-based survey in the USA (Bainbridge, 2002) found that most respondents were favourably disposed towards the potential of nanotechnology, but the value and representativity of such samples is questionable (Royal Society and Royal Academy of Engineering, 2004). A survey promoted by the Working Group found, not surprisingly, widespread ignorance of nanotechnology in the general public in the UK. This can be interpreted to mean that the time is good to promote public debate on the development and regulation of nanotechnology; the Working Group made specific recommendations on how a dialogue should be taken forward. However, in view of the very considerable uncertainty over human and environmental risks posed by nanomaterials, discussed below, some Non-Governmental Organisations have argued for a precautionary moratorium. ETC (2003) has called for a complete moratorium on the production and use of synthetic nanoparticles. Greenpeace (2004) has called for a moratorium on release of nanoparticles into the environment. The Working Group did not consider such moratoria to be justified; their analysis of the risks and the appropriate regulatory approach is discussed in the following sections of this paper.

At a different level, concerns have also been expressed over the possible social impacts of nanotechnology (e.g. NSF, 2001; Wood *et al.*, 2003): whether it could constitute a "disruptive" technology, causing the demise or total restructuring of existing industries; whether by "convergence" with other new technologies, nanotechnology could have major social impacts (including enabling increased surveillance, and widening the disparity between privileged and relatively deprived individuals, groups and countries).[2] Such concerns, of course, arise over any nascent technology. The Royal Society/Royal Academy Report recommends establishment of a group to identify potential *health, safety, environmental, social, ethical and regulatory issues* raised by new technologies. However, the issue of social impacts is not explored in this paper.

ENVIRONMENTAL SAFETY AND HUMAN HEALTH: HAZARDS AND RISKS

The current approach to risk assessment contains the scientific elements summarised in Table 2; note that this assessment should form only part of the process of risk management which must incorporate public values (see Introduction). The hazard posed by a substance depends on its inherent properties, while risk assessment also accounts for the probability of exposure of humans and non-human beings to a hazardous substance. The discussion here follows the stages in Table 2.

Table 2: ***The elements of current risk assessment***
After Worth and Balls (2002) and RCEP (2003)

Hazard Assessment: *Hazard identification: identification of the inherent capacity of a substance to cause adverse effects, without regard to the likelihood or severity of such effects.* *Hazard characterisation: quantitative evaluation of adverse effects following exposure to a chemical.*
Exposure Assessment: *Quantitative evaluation of the likely exposure of humans and the environment to the substance.*
Risk Characterisation: *Quantitative estimation of the probability that an adverse effect will occur, and of its severity and duration under defined exposure conditions.*

Humans and other beings are routinely exposed to nanoparticles, particularly in the atmosphere originating from natural events (such as volcanic eruptions) and from anthropic activities (particularly combustion processes, including vehicle engines). To some extent, living organisms have developed defences against such particles (including viruses). However, particles can still penetrate into the body. For humans, the principle entry routes are via the lungs by respiration, via the skin by dermal exposure and via the gut by ingestion of food and drink. There is some evidence that exposure to nano-sized particles can cause human health impacts, particularly by respiration. The principal evidence derives from epidemiological studies which have indicated an association between particulate air pollution and health, particularly cardiovascular and respiratory disorders (e.g. Brook *et al.*, 2004). Largely by analogy with the known

[2] The author raised, but the Working Group did not address, the question of whether "smart labelling" using nanotechnology could show the existence or otherwise of Weapons of Mass Destruction, thereby obviating the need to invade a country to establish their absence.

effects of asbestos fibres, monofibres are particularly implicated as health hazards. However, their impact will depend at least on their dimensions (including surface area) and on their surface composition and reactivity; i.e. on their properties as nanomaterials. This underlines the conclusion that the health impacts of nanomaterials, along with the other properties that define them as nanomaterials, depend on their size and surface condition.

People using skin preparations such as cosmetics and sun-screens are subject to dermal exposure. Some sun-screens contain titanium dioxide nanoparticles. It is by no means firmly established that they do reduce risks of skin cancer. Furthermore, while there is evidence that nanoparticles cannot penetrate healthy skin, it is not certain that they cannot penetrate lesions (such as areas of skin already damaged by sunburn). The likely impact of ingested nanomaterials is unknown, but likely to be less serious than respiratory exposure and probably less of a concern than dermal exposure. Once in the body, it is possible that nanoparticles can cause damage at the neural and cellular level, possibly even penetrating into the brain (see Royal Society and Royal Academy of Engineering, 2004).

The potential impacts of nanomaterials on the environment and non-human species are even more uncertain. The conventional toxicological approach to assessing ecotoxicity involves exposing organisms – usually daphnia, fish and rats – to the substance in question and observing the dose or concentration at which measurable morbidity results. The results from such tests are then scaled up to give a rough prediction of human toxicity. For nanomaterials, no way of adapting animal exposure tests to show the effect of particle dimensions has been proposed, beyond the obvious approach of testing with particles of different sizes and thereby multiplying the number of tests needed. Only one study appears to have been reported, on the effect of carbon-60 particles on a species of fish (Oberdörster, 2004), and that study is limited and unsatisfactory. An alternative approach, still at an explanatory stage, is to observe the effect of a pollutant on cells in culture. Such "in vitro" tests do not appear to have been carried out for nanomaterials, and no protocol has been proposed to examine the effect of particle dimensions. A further approach, sometimes known as "in silico" testing, aims to assess the toxicological potential of chemicals by computer calculation of Quantitative Structure - Activity Relationships (QSARs). QSARs are central to the US approach to risk assessment of chemicals (see below), but the approach does not appear yet to have been developed for nanomaterials although in principle it might be possible to adapt QSAR calculations to allow for particle dimensions. In spite of the general level of ignorance, there are reasons to expect that nanoparticles could interfere with the action of microorganisms, including those in soils.

In the presence of this level of uncertainty, chemical pollutants are conventionally classified according to their persistence in the environment and their propensity to bioaccumulate and hence affect organisms, such as humans, in the higher levels of the food chain (RCEP, 2003). The tests conventionally applied do not immediately apply to nanomaterials. Given that their properties depend on their surface condition, it is likely that nanomaterials will have limited persistence but this inference remains speculative.

PRECAUTIONARY RISK MANAGEMENT AND REGULATION

From the preceding discussion, it is clear that the current state of understanding of the risks to human health and the environment from nanomaterials is one of almost complete ignorance: there area reasons to think that there could be harmful impacts, but the nature and extent of the hazards and risks are essentially unknown. Nanomaterials therefore present a case for adopting a precautionary approach, as appropriate in situations where there is a lack of scientific certainty. The Rio Declaration on Environment and Development (UN 1992) includes the precautionary approach and has subsequently been addressed by various Multilateral Environment Agreements (MEAs) such as the Framework Convention on Climate Change, the Convention on Biological Diversity and its Protocol on Biosafety, the Convention on POPs, etc.

As for conventional chemicals, the objectives of risk management and regulation are to eliminate risks to humans and the environment or at least to reduce them to "acceptable levels"[3]. Risk results from possible exposure to a hazard (see Table 2). If the hazards associated with exposure and the exposure pathways are unknown for nanoparticles, then risk can only be confined if release is avoided. For regulatory purposes, this places nanomaterials into essentially the same category as new chemicals. In the EU, new chemicals are at present covered by regulations on the Notification of New Substances (NONS), which require provision of a base data set from which a substance is assigned to a category determining its permitted use before it can be "placed on the market"; i.e. traded or incorporated into products. The data set is placed on a register maintained by the European Chemicals Bureau. Full risk assessment can be required for chemicals identified as priorities from the base data, but fewer than 30 complete risk assessments have yet been published. Partly in an attempt to improve the rate at which new chemicals are given full assessment, a new approach to Registration, Evaluation and Authorisation of CHemicals (REACH) has been proposed (European Commission, 2001). However, REACH has been widely criticised, *inter alia* for being too cumbersome, and it is not clear when it might be implemented. An approach broadly similar to NONS is followed in Japan, although the classification is made before the substance can be manufactured. The US Toxic Substances Control Act requires the Environmental Protection Agency (EPA) to keep an inventory of all substances regulated under the act, and requires new substances to be notified to the EPA before manufacture or importation.

Existing substances produced as nanoparticles are not currently defined as new chemicals. The Royal Society/Royal Academy Working Group recommended that *nanoparticles or nanotubes be treated as new substances.* However, two differences from conventional chemicals were highlighted. One concerns the requirement, noted above, to include the effect of particle size in hazard assessment. The other concerns the "triggers" applied to determine the need for and extent of testing. At present the triggers are determined by the mass of a new substance produced. It was recommended that the relevant regulatory bodies should consider "trigger levels" based on some property which reflects particle size.

A precautionary approach implies that the use of nanomaterials requires a high level of risk management unless sufficient information is available to justify a lower level approach. The Working Group recommended *that factories and research laboratories treat manufactured nanoparticles and nanotubes as if they were hazardous and seek to reduce or remove them from waste streams* and that *as an integral part of the innovation and design process of products and materials containing nanoparticles or nanotubes, industry should assess the risk of release of these components throughout the life cycle of the product and make this information available to the relevant regulatory authorities.* Taken together, these recommendations would cover regulation of the supply chain and require protection from exposure to nanomaterials in the workplace. The pressure to avoid risk of releases would have a further implication: it would favour production of nanomaterials at the point where they are incorporated into a finished material or product. This would represent further pressure towards small-scale distributed production of high value chemicals and materials.

The explicit mention of the life cycle also leads to the important conclusion that products containing nanomaterials must be managed after use to ensure that none of these materials can escape into the environment. The specific recommendation is that *manufacturers of products that incorporate nanoparticles and nanotubes and which fall under extended producer responsibility regimes such as end-of-life regulations be required to publish procedures outlining how these materials will be managed to minimise human and environmental exposure.* This recommendation represents an extension of one of the stated objectives of "takeback" legislation such as the EU Waste Electrical and Electronic Equipment

[3] The concept of "acceptable risk" is embedded in risk management and regulation but is being questioned, for example in a current enquiry by the Royal Commission on Environmental Pollution into "bystander" exposure to sprayed pesticides: acceptable to whom? On the basis of what kind of evidence and assessment?

(WEEE) and End-of-Life Vehicles (ELV) Directives: to require manufacturers to design systems for recovery and management of products at the end of their service lives. It has been argued that the way these Directives have been implemented has failed to have this effect (e.g. Castell *et al*., 2004). Thus, if the recommendation is implemented seriously, it could actually improve management of material cycles and promote the development of industrial ecology.

Other recommendations are likely to be more contentious. With products such as cosmetics, sun screens and food additives in mind, the Working Group recommended that *ingredients in the form of nanoparticles undergo a full safety assessment… before they are permitted for use in products;* that *manufacturers publish details of the methodologies… used in assessing the safety of … products containing nanoparticles;* and that *the ingredients lists of consumer products should identify the fact that manufactured nanoparticulate material has been added.* This obviously supports the EU's general approach to regulation and disclosure rather than that used in the USA. But it would go further and put regulation of cosmetics on a basis approaching that applied to pharmaceuticals.

Pursuing the logic further, the Working Group recommended that *until more is known about environmental impacts of nanoparticles and nanotubes… release of manufactured nanoparticles and nanotubes into the environment be avoided as far as possible.* If implemented, this recommendation would immediately prevent any activity which deliberately involves unconfined release of nanomaterials, including the use of nanoparticles to improve combustion of hydrocarbons in engines and of iron nanoparticles for soil remediation by injecting them into groundwater (Zhang, 2003). It was specifically recommended that *the use of free manufactured nanoparticles in environmental applications such as remediation be prohibited until appropriate research has been undertaken and it can be demonstrated that the potential benefits outweigh the potential risks.* This conclusion stops short of the complete moratorium advocated by ETC (2003) but is similar to the approach advocated by Greenpeace (2004).

POSTSCRIPT – UNCERTAINTY AND ASPIRATION

Both technologies using nanoscale materials and the anticipatory approach to assessing the benefits and regulating the risks from an emerging technology are at an early stage: nanotechnology has yet to make a serious economic impact outside the R and D community, and the Royal Society/Royal Academy report should be only the starting point for a wider public debate. It is therefore important to avoid the uncritical over-enthusiasm which has characterised some of the advocates of nanotechnology. However, the need to manage and regulate risks in the face of uncertainty is a general problem. New technologies involving new materials will continue to present the kind of difficulty raised by nanoscale materials: lack of epidemiological evidence, lack of systematic toxicological evidence and possibly lack of suitable testing protocols. A precautionary approach is intended to avoid the impacts on human health and the environment which are the topic of epidemiological studies, so that effective regulation should ensure that epidemiological evidence never does become available. Risk management will therefore increasingly depend on limiting exposure rather than substituting materials with lower inherent hazards. It remains to be seen whether the kinds of general measures recommended by the Royal Society/ Royal Academy Working Group will be implemented and will succeed in preventing impacts on humans and the environment.

It also remains to be seen whether the experiment of adopting an anticipatory approach to risk management represented by the Royal Society/Royal Academy study really proves to be a paradigm shift. In commenting on the report of the Working group, Wilsdon and Willis (2004) argue that R and D companies should open up their innovations to public debate at an early stage; that NGOs should engage in debate early in development of a new technology rather than campaigning later; and that the media should concentrate on the "public interest" in reporting on science and technology. It remains to be seen whether these hopes are as fanciful as some of the claims which have been made for nanotechnology.

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