

## 8 Regulatory issues

### 8.1 Introduction

1 In this chapter we discuss the impact on regulation of the issues raised in earlier chapters. It is clear from the preceding chapters that nanosciences and nanotechnologies span a wide array of research institutions, industrial sectors and applications. Thus it is likely that several regulators will need to consider the impacts that nanotechnologies may have on each of their areas of coverage.

2 It is timely to consider the effect of regulations on the prudent development of nanotechnologies. Currently, applications are incremental in nature but if the broad range of nanotechnologies fulfil expectations it is likely that progress will accelerate in the coming years. We strongly believe that flexible and proportionate regulatory measures informed by scientific evidence are beneficial to everybody; the public, consumers and employees are protected from harm while industry is able to participate in developing standards and preparing guidance to ensure a level playing field and reduced risk of liability.

3 As we outline in section 5.1, many nanosciences and nanotechnologies present no unique risks to health, safety or the environment. In this chapter we focus primarily on the management of the potentially adverse health, safety and environmental impacts of the production, use and disposal of nanoparticles and nanotubes because these (particularly in a free rather than fixed form) were the main area of concern identified during the study (see Chapter 5). We stress that exposure of humans and the environment to nanoparticles and nanotubes is currently extremely low. However, nanoparticles and nanotubes are generating interest within industry, several products containing them being either in the market (for example cosmetics, anti-static packaging, self cleaning surfaces) or close to it (for example fuel cells, display screens). In section 5.6 we recommended the establishment of a new research centre as a way of addressing the uncertainties relating to the toxicity of and exposure to nanoparticles and nanotubes.

4 As part of our evidence-gathering process, we held a workshop with regulators in February 2004, at which it became apparent that existing regulations may need to be adapted to accommodate the particular characteristics of nanomaterials. We were encouraged to find, however, that most regulators were aware of nanotechnologies, and some (such as the Health Safety Executive (HSE)) had already taken initial steps towards this end.

### 8.2 Approaches to regulation

5 In general terms, regulation requires assessment of hazard (the intrinsic harmfulness of the material) and assessment of the likelihood or duration of exposure, these factors combining to produce the risk to any exposed biological or human population. The overall aim is to determine the risk management measures needed to eliminate risks or (in practice) reduce them to acceptable levels. Where possible this process is informed by factual evidence, usually obtained from toxicological, environmental or epidemiological studies. The precautionary principle comes into play when there is a lack of full scientific certainty about the threat of harm from the substance. An assumption then has to be made about the potential hazard on the basis of such evidence as is available (for example by analogy with materials of known toxicity) and the best available judgements about the hazard-inducing properties of the substance. There must then be an assessment of the risk of exposure, for example in the workplace or to the general public from the use of products.

6 The need to control the use of hazardous substances to prevent harm to people or the environment is not new. Only those substances that imply the most serious risks to health or to the environment, for example certain carcinogens, are banned. There is already extensive national and European legislation covering different aspects of hazardous substance use. In addition, several international agreements have been developed that are aimed at controlling global aspects of the issue. Where it is judged that controls are necessary, several regulatory options are available. For example:

- workplace controls;
- classification and labelling measures;
- control of emissions to air, water and land;
- waste disposal restrictions;
- marketing and use restrictions;
- prohibition.

All these options can be written into legislation. In Europe, this may take the form of a new directive or regulation or an amendment to existing legislation. Regulatory measures are not static; the regulator collaborates with industry in seeking to identify further measures that are reasonably practicable to reduce risks.

7 Regulation within the EU and the UK operates under a broad framework. Current frameworks already in place cover a wide range of products and processes, such as chemicals, cosmetics and medicines, which represent some of the major areas that nanomaterials are likely to impact. At least for the foreseeable future we believe that the present frameworks are sufficiently

broad to encompass nanotechnologies and hence a separate regulator or regulatory framework is unnecessary. Given the hazards outlined in Chapter 5, we believe however that specific aspects of these frameworks such as requirements or triggers for testing will require consideration by regulators, with the collaboration of scientists and toxicologists. We illustrate this in the case studies presented below.

### 8.3 Case studies

8 In this section we present several case studies from various stages in the lifecycle of products, from manufacture and use through to disposal. These examples encompass several concerns raised with us during the evidence-gathering process. In most cases they relate to situations where there is currently the potential for exposure to nanoparticles or nanotubes, such as in the workplace.

#### 8.3.1 Workplace (including research laboratories)

9 Currently, the most likely place of exposure to nanoparticles and nanotubes is the workplace, including academic research laboratories. The Health and Safety at Work etc. Act (1974) sets out the responsibilities for health and safety that employers have towards employees and members of the public, and employees have to themselves and to each other. Detailed regulations that build on this Act allow these general responsibilities to be expanded and adapted in the light of technological developments and the identification of new risks. Responsibility for health and safety rests primarily with the employer whereas the HSE is responsible for developing detailed standards and ensuring compliance.

10 The regulations particularly relevant to nanotechnologies are the Control of Substances Hazardous to Health (COSHH) regulations, which set the broad requirements of reducing occupational ill health by setting out a simple framework for controlling hazardous substances in the workplace. Concern has been expressed about the potential risk (particularly through inhalation) to workers involved in the production and use of manufactured nanoparticles and nanotubes. Personal exposure (through inhalation) is regulated by requiring compliance with occupational exposure limits (OELs) for individual substances. The OELs are separately specified and are reviewed and adapted in the light of new knowledge through a process that involves the regulator, industry, employees and the public interest.

11 Some materials, such as carbon black and titanium dioxide, are being produced by industry either as micrometre-sized or as nano-sized particles. These materials, previously regarded as harmless in their larger forms, may present different toxicological characteristics

in their nanoparticulate forms. At present, the regulatory standards are based on the mass of inhaled particles and are derived from a consideration of larger size distributions. If these mass-based standards were to be applied to materials in nanoparticle form, this would imply the relative safety of inhaling vast numbers of nanoparticles. As discussed above and in section 5.3, there is now experimental toxicological evidence that toxicity of these nanoparticles is related to their size. **We therefore recommend that the HSE reviews the adequacy of its regulation of exposure to nanoparticles, and in particular consider the relative advantages of measurement on the basis of mass and number. In the meantime, we recommend that it considers setting lower occupational exposure levels for manufactured nanoparticles.**

12 In many cases it is expected that high standards of containment will be used to prevent the release in workplaces of nanoparticles and that high standards of occupational hygiene will be in place. However, releases can and do occur, both because of leakage from containment in normal use and because of isolated events arising from human error or equipment failure. Minimising these possibilities is an essential part of risk management. **Given the greater hazard posed by some chemicals in the form of nanoparticles we recommend that the HSE, DEFRA and the EA review their current procedures for the management of accidental releases within and outside the workplace.**

13 The single current example of exposure to nanoparticles in the workplace that is regulated by number and not mass is that of fibres, including asbestos. Many (but not all) such fibres are visible by light microscopy, being above the nanometre range in at least one dimension, and regulation is based on counting by phase-contrast optical microscopy, using a specially designed eyepiece graticule. This is a time-consuming process with potential for inter- and intra-laboratory variability and, as a result, is covered by UK and international quality-control schemes. Future developments in nanotechnologies may result in the introduction into the workplace of much finer fibrous materials such as nanotubes that are well below 100 nm in diameter yet may be longer than 10 µm, and may not be visible by existing methods. We have highlighted our concerns about the similarity between nanotubes and asbestos, and the need to control exposure of those working with them until more is known about their toxicity (see sections 5.3.1b and 5.3.2a). Therefore **we recommend that the HSE consider whether current methods are adequate to assess and control the exposures of individuals in laboratories and workplaces where nanotubes and other nanofibres may become airborne, and whether regulation based on electron microscopy rather than phase-contrast optical microscopy is necessary.**

14 Until the reviews recommended above have been undertaken, and appropriate regulation and control measures are in place, there will be a need for interim guidance to ensure as far as possible the safety of workers in academic laboratories and industry. In this respect, we welcome the publication of a preliminary information note from the HSE on the current understanding of the health and safety issues surrounding nanomaterials (HSE 2004). In addition to the health risks resulting from inhalation, we have identified in section 5.5 the need to avoid large quantities of combustible nanoparticles becoming airborne until more information about the explosion hazard has been quantified.

### 8.3.2 Marketing and use of chemicals

15 The chemicals industry is likely to be the major producer of nanomaterials, currently in the form of bulk nanoparticles such as titanium dioxide and eventually more advanced functional materials as research and development progresses. Although nanomaterials currently account for only a tiny fraction of the total quantity of chemicals manufactured, production is expected to increase over the coming years, albeit probably not reaching the levels of larger particulate chemicals currently produced.

16 From the discussions in preceding chapters, it will be clear that nanoparticles (particularly at the smaller end of the scale) often have different or enhanced properties compared with those of the same chemical in a larger form. It is not yet known to what extent the new or enhanced properties of nanomaterials will be associated with differences in their toxicity but, as we have seen in section 5.3, there is evidence that some substances are more toxic when in nanoparticulate form, probably caused in part by their greater surface area. Whether this increased toxicity poses a risk to human health will depend on the mode of exposure and whether the particles are coated.

17 The regulation of the marketing or use of chemicals in the UK (which reflects European legislation) is outlined in Box 8.1. Neither of the triggers that are used to determine the need for and extent of testing of chemicals take account of particle size. Existing substances that are produced in the form of nanoparticles are not defined as new chemicals and the threshold levels do not recognise the fact that substances in nanoparticle form may have different health and environmental impacts per unit mass. These different properties of nanoparticles are also not considered in the latest version of REACH, currently under negotiation. Thus present chemical regulation, and that being negotiated under REACH, implicitly assume that toxicity will be unaffected by particle size.

#### Box 8.1 Regulation of the marketing and use of chemicals

Regulation begins with a determination of whether a chemical is a new or existing substance. The EC defines 'existing substances' as chemicals declared on the market in September 1981, and 'new substances' as those placed on the market since that date. New substances have to undergo much stricter testing and assessment than existing chemicals even though existing chemicals account for more than 99% of all substances on the market. At present this takes place under the Notification of New Substances (NONS) regulations. The EC is currently negotiating a new single system called REACH (Registration, Evaluation, Authorisation of Chemicals) designed to help clear the backlog of untested chemicals. Aside from any possible implications that nanotechnologies may have, the testing of existing industrial chemicals is already lagging far behind what is already in the marketplace.

The triggers currently used to determine the need for testing and to decide the number and types of test required under NONS are:

- *New chemicals.* A new chemical is defined as one that does not appear on the EINECS (European Inventory of Existing Commercial Substances) inventory. When a new chemical is produced, before introduction to the market, the producer of that chemical is required to conduct testing, and in the meantime take such precautions as are practicable. The level of testing required is determined by the mass produced, with the lowest mass trigger currently set at 10kg per annum. Only changes in chemical structure constitute a new substance, whereas changes in form (for example size or shape) do not. An exception is made for polymers: those produced entirely from EINECS-listed monomers are exempt from notification.
- *Mass (tonnage) triggers.* Essentially, the more of an existing substance that is produced, the more data on its properties are required by regulators.

18 We see this as a regulatory gap and **we recommend that chemicals in the form of nanoparticles or nanotubes be treated as new substances under the existing Notification of New Substances (NONS) regulations and in the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) (which is currently under negotiation at EU level and will eventually supersede NONS).** To comply with this recommendation Directorate General (DG) Enterprise and DG Environment will need to ensure that the final

version of REACH is sufficiently flexible to take account of the enhanced or different properties that some nanoparticles (and nanotubes) may have compared with larger particles of the same chemical species. Experts convened to produce a preliminary risk analysis for the EC reached a similar conclusion and recommended that a new Chemical Abstract Service (CAS) Registry number be assigned to manufactured nanoparticles (European Commission 2004b).

19 The type of research that we outline in section 5.6 (and Boxes 5.6 and 5.7) will provide more information about the types and sizes of nanoparticulate that have an increased toxicity. It will also determine the tests that are most appropriate for various types of nanoparticle. For example, are existing tests for persistence and bioaccumulation appropriate for nanoparticulates? **As more information about the toxicity of nanoparticles and nanotubes becomes available, we recommend that the relevant regulatory bodies consider whether the annual production thresholds that trigger testing and the testing methodologies relating to substances in these forms should be revised under NONS and REACH.**

20 Since we began our study, the EC has recognised

the need to revisit the mass thresholds that trigger testing (European Commission 2004b) and we understand that the US Environmental Protection Agency is assessing whether nanomaterials should best be regulated as new chemicals. International co-operation in developing regulation in this area would be beneficial.

### **8.3.3 Consumer products incorporating free nanoparticles, particularly skin preparations**

21 As we have seen in earlier chapters, some manufacturers of consumer products, particularly cosmetics, and perhaps in the future foodstuffs, may utilise the advantages derived from including nanoparticulate materials in these products to give improved or additional functionality. Here the nanoparticles will essentially be free rather than fixed, although their reactivity (and thus toxicity) may be influenced by coatings. In this section we concentrate on cosmetics because this is an area where nanoparticles of oxides of zinc, titanium and iron are being used, and where there are concerns (outlined in section 5.3.2b) that they might penetrate through the protective layers of the skin and cause reactions with UV light that result in damage to DNA in cells. Regulation of cosmetics in the UK and EU is outlined in Box 8.2.

#### *Box 8.2 Regulation of cosmetics in the UK and EU and the role of the scientific advisory committee*

Cosmetics include hair and skincare products, colour cosmetics and toiletries. Under the EU Cosmetics Directive (and the UK's Cosmetic Products (Safety) Regulations 2003), the manufacturer (or the person responsible for placing the product on the market in the European Community) is primarily responsible for ensuring that cosmetic products do not cause damage to human health when applied under normal or reasonably foreseeable conditions of use. The definition of normal use takes into account the product's presentation, its labelling and any instructions for its use and disposal. In assessing safety the manufacturer must take into consideration the general toxicological profile of the ingredients, their chemical structure and its level of exposure.

Two annexes of the Cosmetics Directive list substances that must not be used in cosmetics or that have restrictions on their use. Three additional annexes list the substances that are permitted for use as colourants, preservatives and UV filters. Unless listed in the various annexes, any substance can be included in a cosmetic providing the manufacturer declares the final preparation safe.

The safety of cosmetics and non-food products intended for consumers is assessed for the European Commission by the Scientific Committee on Cosmetic Products and Non-food Products intended for consumers (SCCNFP), which comprises independent scientific experts from across the EU. One of its roles is to assess dossiers of evidence submitted by industry on the safety of substances used in their products and to produce an opinion on safety. It does not conduct its own testing, but can request that further evidence be supplied by industry. The Opinions of the SCCNFP are publicly available. Based on these Opinions, the EC's DG Enterprise makes recommendations to the Expert Group on Cosmetics, which comprises representatives from all member states of the European Union. This group votes on whether an amendment to the Cosmetics Directive is required (for example, to add a substance to an annex). Once an amendment has been adopted, it is the obligation of the competent authorities within member states (DTI in the UK) to transpose it into national legislation. Member states can bring any issues of concern to the attention of the EC. The Scientific Committee on Consumer Products will shortly replace the SCCNFP.

In the UK the DH reviews the safety dossiers from the SCCNFP and can highlight any issues of concern to the DTI. Although cosmetics legislation is harmonised at EU level, the DTI can introduce temporary legislation in the UK if it identifies a serious and immediate risk to consumers.

22 At the request of industry, the SCCNFP considered separate requests to include both titanium dioxide and zinc oxide (including the nanoparticulate form) on the list of approved UV filters. As outlined in section 5.3.2b, titanium dioxide has been approved for use at all sizes by the SCCNFP (2000), but further evidence was requested in June 2003 about microfine zinc oxide (200nm and below). In its opinion concerning zinc oxide, the SCCNFP requested clarification as to whether the damage caused to DNA by microfine zinc oxide during tests on cell cultures (*in vitro*) would be seen in living animals (*in vivo*) and if zinc oxide could pass through the skin (a necessary precursor to harm occurring) (SCCNFP 2003a). Without a favourable safety Opinion microfine zinc oxide cannot be used as a UV filter but there are no restrictions on its use in cosmetics (including sun protection products) for other purposes providing the manufacturer is assured of its safety. It is our understanding that nanoparticles of zinc oxide are not much used in sun protection products in Europe.

23 **We recommend that industry submit the additional information on microfine zinc oxide that is required by the SCCNFP as soon as reasonably practicable so that the SCCNFP can deliver an opinion on its safety.** The uncertainties about the safety of nanoparticles of zinc oxide are not just applicable to its use as a UV filter. Titanium dioxide in nanoparticle form was judged by the SCCNFP not to pose a risk, based on observations that it does not penetrate the skin and that coatings reduced its reactivity. Further information from industry may demonstrate that microfine zinc oxide does not penetrate the skin or that the activity seen *in vitro* does not occur *in vivo*, in which case the SCCNFP will be able to deliver a positive opinion on its safety. However, until the safety dossier is provided to the SCCNFP the uncertainties remain.

24 Based on the evidence that some chemicals have different properties when in their nanoparticulate form, safety assessments based on the testing of a larger form of a chemical cannot be used to infer the safety of nanoparticulate forms of the same chemical (as outlined in section 8.3.2). Therefore, **we recommend that ingredients in the form of nanoparticles undergo a full safety assessment by the relevant scientific advisory body before they are permitted for use in products.** One way to implement this recommendation in the Cosmetics industry would be to add as an annex to the Cosmetics Directive a list of ingredients permitted in nanoparticulate form. Only those ingredients that have been assessed by the SCCNFP (or its equivalent) would be considered for addition to this list. If this approach is taken, titanium dioxide could be included in the new annex (as it has received a favourable assessment) while the nanoparticulate form of zinc oxide would await the SCCNFP's assessment before a decision was made about its inclusion on the new annex. We understand that particles iron oxide below

100 nm are not used as an ingredient in cosmetics in Europe. Were it to be used in Europe in the future we would expect it to be assessed by the SCCNFP. The assessments should pay particular attention to our concerns about the penetration of damaged skin; these are of particular relevance to sun protection products as they are used for a preventative purpose and may be used on skin already damaged by the sun. The SCCNFP should also consider whether the tests introduced as alternatives to animal testing are appropriate for testing nanoparticles. Our recommendation from section 5.3.2b, that committees considering the safety of ingredients for which there is incomplete toxicological information in the peer-reviewed literature should insist that the data submitted to them by industry is placed in the public domain, would apply here.

25 Except for a few categories of uses (such as UV filters), responsibility for the assessment of the safety of the inclusion of free nanoparticles in products rests with the manufacturer or supplier. The Cosmetic Directive does not specify the type of safety studies that must be performed. So manufacturers must ensure that the toxicological tests that they use recognise that nanoparticles of a given chemical will often have different properties to the larger forms and may have greater toxicity. In the UK, details of the safety assessments must be made available to Trading Standards, but they are not publicly available. The guidelines on the testing of cosmetics produced by the SCCNFP (2003b) do not specifically refer to the use of microfine ingredients or those in nanoparticulate form. Because of uncertainties about the safety of nanoparticles in cosmetics, and while they are awaiting a safety assessment by the SCCNFP, **we recommend that manufacturers publish details of the methodologies they have used in assessing the safety of their products containing nanoparticles that demonstrate how they have taken account that properties of nanoparticles may be different from larger forms.** Based on our understanding that the use of nanoparticles in the European Cosmetics sector is not extensive we do not believe that this recommendation will apply to many manufacturers.

26 Although the current use of free nanoparticles in consumer products is limited to a few cosmetic products, it is probable that in the future they will be used in other consumer areas such as food and pharmaceuticals. Because we believe that chemicals in the form of nanoparticles should be treated as new chemicals, **we recommend that the ingredients lists of consumer products should identify the fact that manufactured nanoparticulate material has been added.** There is an additional case in favour of labelling based on a desire for transparency of information about consumer products.

27 The three EC non-food safety advisory committees, including the SCCNFP, are being replaced shortly. One of the new committees, the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR)

will examine the risks of new technologies, including nanotechnologies. Given that nanoparticles are expected to be used increasingly in consumer products in the future, with various coatings (some of which may alter their toxicity), **we recommend that the new EC SCENIHR gives a high priority to the consideration of the safety of nanoparticles in consumer products**. It should also liaise with equivalent safety advisory bodies relating to food and those related to medicines and medical products in the EU and internationally to share expertise in this area.

28 Because of the regulatory gaps that we identify **we recommend that the EC (supported by the UK) review the adequacy of the current regulatory regime for the introduction of nanoparticles into consumer products**. In undertaking this review, they should be informed by the relevant scientific safety advisory committees in the way that we outline above. Attention should also be given to the question that we posed in section 5.3.2b about whether all sun protection products (not just those containing ingredients in nanoparticle form) should be regulated as medicines rather than cosmetics because they are used for a preventative purpose and may be used on skin already damaged by the sun.

#### **8.3.4 Medicines and medical devices**

29 Research is being undertaken to introduce nanomaterials into medical diagnosis and treatment. Although such materials would be subject to the stringent regulatory regime that governs all new interventions in medicine, the particular properties of nanoparticles suggest the possibility of unforeseen toxicity if introduced into the body in large numbers. Therefore, **we recommend that the DH review its regulations for new devices and medicines to ensure that particle size and chemistry are taken into account in investigating possible adverse side effects of medicines**.

#### **8.3.5 Consumer products incorporating fixed nanoparticles: end-of-life issues**

30 In contrast to products such as cosmetics that contain free nanoparticles, those that contain nanomaterials in which nanoparticles or tubes are fixed or embedded (for example in plastics) will present a much lower likelihood of exposure. In section 5.4 we have outlined the requirement for industry to quantify the likelihood of release of nanoparticles or nanotubes during the lifecycle of the product. The processes involved in disposal, destruction or recycling may pose an increased risk of exposure to workers in recycling and disposal industries and to the environment. We consider this in more detail in the context of end-of-life legislation.

31 In Europe and Japan (but to a lesser extent in the USA), management of products at the end of their service life is regarded as an aspect of extended producer responsibility; in effect, waste management is seen as part of the product life cycle. In the EU extended producer responsibility is mandated through Directives of which those applying to Waste Electrical and Electronic Equipment (WEEE) and End-of-Life Vehicles (ELVs) already cover two of the leading potential engineering applications of nanotechnologies. Take-back Directives require the industry – ideally, but not always, the manufacturer – to take responsibility for recovering used products and for recycling materials or re-using components. In addition to ensuring that such products do not enter the waste stream, the take-back principle is intended to encourage design for disassembly, re-use and recycling.

32 **We recommend 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**. The EC's approach to Integrated Product Policy (European Commission 2003) seeks to extend producer liability for end-of-life to other product classes. This recommendation applies equally to product classes that fall under extended producer responsibility regulations in the future. As more information becomes available about the hazard and risk presented by releases at end of life, regulators will need to consider whether end-of-life regulation need to be modified to set out how such materials should be managed.

33 The objective of minimising human and environmental exposure to free nanoparticles and nanotubes at all stages of the life cycle should also form an integral part of the innovation and design process.

### **8.4 Knowledge gaps**

34 In the following section we discuss the main knowledge gaps that must be addressed to support the development of appropriate regulation. These relate to hazard, exposure and measurement.

#### **8.4.1 Hazard**

35 In this report we have emphasised possible toxic and explosion hazards associated with nanoparticles and nanotubes. These hazards should be viewed in the light of two important facts. First, such materials are currently being produced in very low volumes and, aside from their use in cosmetics, involve as yet little or no exposure to populations outside the workplace. Second, the well-

publicised adverse effects of particulate air pollution are related to exposures of very high concentrations of particles, usually in susceptible individuals. Thus any assessment of risk needs to take account not just of toxic potential but also likely exposures of workers, of individuals and of organisms.

36 At present, very few studies have been published on the potential adverse effects that nanoparticles or nanotubes may have on humans, and only one to our knowledge on environmental effects. A detailed discussion of the current knowledge gaps relating to the hazards (and exposure) of nanoparticles and nanotubes is given in section 5.6 where we identify the need for the development of internationally agreed protocols and models for investigating the routes of exposure and toxicology to human and non-human organisms of nanoparticles and nanotubes in the indoor and outdoor environment, including investigation of bioaccumulation. As it will not be possible to test the toxicity of all sizes of nanoparticles with all possible coatings, there is a need for models to be developed so that results can be extrapolated and the amount of testing reduced. In section 5.6 we recommend the establishment of a centre to undertake research to address these knowledge gaps and to provide advice to regulators.

#### **8.4.2 Exposure**

37 Even when, as at present, the magnitude and mechanisms of risks associated with the production, use and disposal of nanoparticles and nanotubes remain uncertain, it should nevertheless be possible to manage the overall level of risk through careful control of exposure. Indeed, the history of the regulatory process shows that delays have in the past occurred from a desire to understand detailed mechanisms of toxicity before firm action to reduce exposures is taken. As will be seen from the preceding case studies, we are of the view that sensible, pragmatic steps can be taken now by regulators to control possible risks from new manufactured nanoparticles without the need for a cessation of development activity, and that such steps should be taken alongside action to understand further the possible mechanisms of toxicity.

38 Roughly spherical nanoparticles present a regulatory problem that is far removed from the high technology of laboratory nanoscience. Such particles are not only present in urban air but are also generated in very large numbers by such day-to-day activities as cooking. In industry, welding, soldering and burning operations also generate nanoparticles, and these are currently regulated on a mass basis. The specific production of useful, rather than polluting, nanoparticles of titanium and zinc oxides for paints, cosmetics and colourants involves rather few occupationally exposed individuals compared with these. Nevertheless, workers are exposed to such materials and it is questionable whether regulation by

mass or by another metric reflecting surface area or number is the more appropriate. A decision on this can only be made on the basis of good epidemiological studies, comparing different measurement metrics in relation to health outcomes, combined with toxicology studies. The lack of quantitative epidemiology prevented the Expert Panel on Air Quality Standards from recommending a standard based on a metric other than mass for ambient air particles in the United Kingdom in 2000, and no suitable epidemiology has been performed so far in industrial situations where nanoparticle exposure may occur.

39 There are difficulties in identifying the relevance of particles of different sizes in causing disease in industrial situations. A programme of research that we outline in section 5.6 will address this knowledge gap and is urgently needed as a basis for regulatory exposure limits. However, all studies would have to take account of the background, complex mixture of nanoparticles normally found in outdoor and indoor air; these background levels are likely to obscure any small escapes of manufactured particles from production or other processes save when using pollution-free clean room technology. There is a need for the development of practical instruments to measure the size and surface area of industrial and ambient aerosols in the nanometre range, where particles may have aggregated into irregular shapes and there may be a background of nanoparticles.

40 In section 5.3.1c, we discussed research into the adverse effects of ambient air pollution on human health, and the hypothesis that the nanoparticle constituents may play a role. This has led to work by DEFRA, Department for Transport (DfT) and others into the measurement of airborne nanoparticles in the environment. This includes research into vehicle emissions, which are currently also regulated by mass (DfT 2003). Important issues arise for the best metric for measuring the toxic potential of emissions, as discussed in the report on Airborne Particles (DEFRA 2001). For example, manufacturers might reduce mass emissions from an engine by a process that inadvertently led to greater emission of nanoparticle numbers. If the toxicity of the aerosol were due to the numbers of nanoparticles, this could have paradoxically adverse consequences. Because these issues are the subject of active research in the air pollution scientific community, **we recommend that researchers and regulators looking to develop methods to measure and monitor airborne manufactured nanoparticulates liaise with those who are working on the measurement of pollutant nanoparticles from sources such as vehicle emissions.**

#### **8.4.3 Measurement**

41 Because of the small size of manufactured nanoparticles and nanotubes, there are several technical challenges surrounding measurement of their physical

and chemical properties. These challenges become particularly problematic when measurement is required in 'real-world' situations, as opposed to carefully controllable laboratory conditions (as might be used for quality control or toxicity experiments). Such measurement problems arise in the field as fluctuating environmental conditions (for example wind speed, temperature, humidity) can modify readings, and background nanoparticles already present in the environment (for example from pollution) may mask the manufactured nanoparticles of interest.

#### a) Measurement in the workplace

42 As outlined in Table 4.1, production rates of nanoparticles are currently estimated to be relatively low. Nevertheless, there is a need for standard validated methods of nanoparticle measurement and monitoring to control exposure to workers and to assess the suitability of protective equipment. As highlighted in section 5.6 the most relevant metric for nanoparticles is unlikely to be mass, although this may be an adequate surrogate for the time being. It is likely that particle size, surface area, chemical reactivity and shape may all play a role, and research should be directed at investigating this.

43 Several instruments currently exist that, at least in combination, are capable of measuring all the potentially relevant metrics for nanoparticles. These instruments are large, expensive, non-portable and require highly trained operators, and are thus likely to be economically justifiable only in a few laboratories. However, a similar though perhaps less demanding requirement applies to workplace measurement of toxic dusts such as asbestos and quartz. The normal procedure is to collect samples under closely defined conditions for subsequent analysis in specialised laboratories. The extension of these procedures will require investigation of sampling technology that is capable of capturing and retaining a representative sample in a manner that matches the measuring capabilities of the laboratory instruments. The development of a quality assurance scheme to regulate the performance of the laboratories will also be needed.

44 We see the main technical challenges associated with measurement of exposure to nanoparticles as follows:

- *Geometry*: measuring irregularly shaped particles and tubes.
- *Simultaneous measurement of different metrics*: can information about size, surface area, chemical species etc be measured at the same time?
- *Specificity*: the ability to differentiate (and quantify) particles of interest, from the background.
- *Portability and robustness*: can the apparatus be used in workplaces?
- *Validity*: are the results of measurements a valid representation of the exposure conditions?

#### b) Measurement for toxicological studies

45 Toxicology requires measurement of dose given to the target, be it a cell, an animal or a human being. In most initial toxicological studies relatively large doses are given just once or over a short period, and adequate methods are available for measuring particle mass and number and for calculating surface area in these circumstances. In special circumstances, such as studies of skin penetration and of distribution of particles around the body, validated and accurate methods need to be developed, but we do not see particular problems in developing instrumentation.

#### c) Measurement standards

46 In addition to the development of measurement techniques for regulatory purposes, there is a growing need for international measurement standards for nanoscale metrics. These will include but not be limited to dimension, chemical composition, force and electrical quanta. Monitoring of nanoparticles in the workplace will also require a high level of traceability to ensure that any future agreed exposure levels are accurately adhered to. We have considered the requirement for internationally agreed standards in detail in section 3.3 and recommended that the DTI ensure that work in this area is adequately funded.

## 8.5 Conclusions

47 The research, development and commercialisation of nanotechnologies will have an impact on a diverse range of regulatory frameworks, including those relating to health and safety at work, environmental protection, licensing of medicines and management of the end-of-life of products. We believe that for the foreseeable future, the present regulatory frameworks for protecting humans and the environment are sufficiently broad to encompass nanotechnologies and that a separate regulator or regulatory framework is unnecessary. However, our very limited set of case studies has demonstrated that it will be necessary to modify individual regulations within existing frameworks or their supporting standards, to reflect the fact that materials have new and enhanced properties at the nanoscale that in some cases may be associated with a greater toxicity than is seen in the same materials in the larger size ranges. There is also a role for industry to provide information about how they are accommodating the properties of nanoparticles and nanotubes in their safety assessments.

48 Regulators need to consider the new or enhanced properties that nanoparticles may have compared with larger particles of the same chemical. These may affect, but not be limited to: toxicity; chemical or photo-reactivity; persistence; bio-accumulation; explosion. We have provided examples of some of the regulatory

bodies that will need to be aware of the potential for nanoparticles and nanotubes to present hazards not present in materials at the larger scale. In section 5.4 we identified a specific need for the EA to prohibit releases of nanoparticles for use in remediation applications until further research into their environmental impacts has been undertaken but the responsibilities of the EA will go much wider than this. In the future, nanoparticles may be produced for use in food; and regulators such as the UK Food Standards Agency will need to investigate the potential risks posed by ingestion and consider the need for regulation. **We recommend that all relevant regulatory bodies consider whether existing regulations are appropriate to protect humans and the environment from the hazards outlined in this report, and publish their review and details of how they will address any regulatory gaps.**

49 It will be clear from preceding chapters that in the medium- and long-term, nanotechnologies are expected to have a much greater impact in many sectors of industry. There is a need for regulators to be aware of developments and the implications for regulation at an early stage. For example, nanotechnologies may enable the development of new forms of sensing and surveillance, which may raise concerns about privacy (as discussed in section 6.4). Although the widespread use of nano-enabled sensors is not yet a reality, this potential raises questions about whether the current regulatory frameworks and mechanisms for ensuring compliance provide appropriate safeguards for individuals and groups in society, which the UK's Information Commissioner's Office should be aware of.

50 It is not possible at this stage to predict all the possible applications of nanotechnologies. Therefore, **we recommend that regulatory bodies and their respective advisory committees include future applications of nanotechnologies in their horizon scanning programmes to ensure that any regulatory gaps are identified at an appropriate stage.** The identification of nanotechnologies as an issue for the new EC SCENIHR indicates an awareness of this requirement at European level. From our meeting with UK regulators, it is clear that they are also becoming aware of the potential issues raised by nanotechnologies. In Chapter 9 we consider a mechanism by which they might be alerted to significant developments in all new and emerging technologies.

51 A call has been made for a moratorium on the on laboratory use of synthetic nanoparticles by the ETC group (2003b), and Greenpeace (2004) has called for a moratorium on the release of nanoparticles to the environment until evidence that it is safe (for the environment and human health) is clear. We have carefully considered these positions, but do not believe it to be an appropriate response to the challenge posed by the emergence of new nanotechnologies and their applications.

52 For a moratorium to be justified, there would need to be either: (i) a sufficiently robust body of scientific evidence already available to politicians and regulators to warrant such a major intervention; or (ii) some kind of consensus among key protagonists that a moratorium should be imposed on a precautionary basis, given legitimate and cogently argued concerns about the risk of severe or irreversible damage to human health or the environment as a direct consequence of the continuing development of nanomaterials.

53 Moreover, we do not believe that the body of evidence outlined in (i) exists. Throughout this report, we have referred to such scientific studies as are already in the public domain, and have carefully reviewed their findings. They do not provide any incontrovertible demonstration of negative impacts on human health or the environment, although there are some indications (which require further study) that substances in the form of nanoparticles may be more toxic than larger forms. Almost all our witnesses have commented on the paucity of good data; the overriding imperative is therefore to fill those 'knowledge gaps'. We have outlined how this might be achieved through the establishment of a new centre to investigate the toxicity and exposure of nanoparticles.

54 We do not think a consensus for a moratorium on a precautionary basis exists either. As this report demonstrates, there are indeed many legitimate and cogently argued concerns about nanotechnologies in general (and specific applications in particular), but the risks of severe or irreversible damage from those technologies or applications (either already on the market or near-market) seem to us to be small, if a rigorous and comprehensive regulatory regime can be secured covering impacts of these new technologies and their applications.

55 It must, however, be acknowledged that this judgement is based on current knowledge, which we have already pointed out is far from sufficient. Some have argued that the current level of knowledge is so poor that no regulatory approach whether based on new regulations or the adaptation of existing regulations could possibly provide the levels of protection and assurance that the public seeks and deserves. Hence the need for a moratorium. Although accepting that there will be a need to modify individual regulations within existing frameworks or their supporting standards, we have concluded that the regulatory gaps that we have addressed in our recommendations above are neither insurmountable nor permanent.

56 Our rejection of a moratorium is based on the assumption that governments will be minded to secure an appropriate regulatory regime as rapidly and effectively as possible. Therefore we have focused on precautionary recommendations to ensure that

regulations reflect the fact that nanoparticulate material may have greater toxicity than material in the larger size range, and have also recommended that all relevant regulators review regulations within their remit and ensure that they keep pace with future developments. Part of the remit of the new research centre that we recommend in section 5.6 is to provide information to allow prompt and appropriate revision of regulation.

57 The combined effect of these measures will not entirely eliminate the risk of adverse impacts on human health or the environment. But it will reduce those risks to the point where research into and commercial development of new nanotechnologies, with all the prospective economic and social benefits that may flow from this development, can be authorised by governments and society.