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Science Policy Section  
The Royal Society  
6–9 Carlton House Terrace  
London SW1Y 5AG  
email [nano@royalsoc.ac.uk](mailto:nano@royalsoc.ac.uk)

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# Nanoscience and nanotechnologies: opportunities and uncertainties

## Contents

|  | <i>page</i> |
|--|-------------|
| <b>Summary</b>   | <b>vii</b>  |
| <b>1 Introduction</b>  | <b>1</b>    |
| 1.1 Hopes and concerns about nanoscience and nanotechnologies                        | 1           |
| 1.2 Terms of reference and conduct of the study                                      | 2           |
| 1.3 Report overview  | 2           |
| 1.4 Next steps   | 3           |
| <b>2 What are nanoscience and nanotechnologies?</b>                                  | <b>5</b>    |
| <b>3 Science and applications</b>  | <b>7</b>    |
| 3.1 Introduction   | 7           |
| 3.2 Nanomaterials  | 7           |
| 3.2.1 Introduction to nanomaterials  | 7           |
| 3.2.2 Nanoscience in this area   | 8           |
| 3.2.3 Applications   | 10          |
| 3.3 Nanometrology  | 13          |
| 3.3.1 Introduction to nanometrology  | 13          |
| 3.3.2 Length measurement   | 13          |
| 3.3.3 Force measurement  | 14          |
| 3.3.4 Measurement of single molecules  | 14          |
| 3.3.5 Applications   | 14          |
| 3.4 Electronics, optoelectronics, and information and communication technology (ICT) | 17          |
| 3.4.1 Introduction to electronics, optoelectronics, and ICT                          | 17          |
| 3.4.2 Nanoscience in this area   | 17          |
| 3.4.3 Current applications   | 17          |
| 3.4.4 Applications anticipated in the future   | 18          |
| 3.5 Bio-nanotechnology and nanomedicine  | 19          |
| 3.5.1 Introduction to bio-nanotechnology and nanomedicine                            | 19          |
| 3.5.2 Nanoscience in this area   | 20          |
| 3.5.3 Current and future applications  | 20          |
| <b>4 Nanomanufacturing and the industrial application of nanotechnologies</b>        | <b>25</b>   |
| 4.1 Introduction   | 25          |
| 4.2 Characterisation   | 25          |
| 4.3 Fabrication techniques   | 25          |
| 4.3.1 Bottom-up manufacturing  | 26          |
| 4.3.2 Top-down manufacturing   | 28          |
| 4.3.3 Convergence of top-down and bottom-up techniques                               | 29          |
| 4.4 Visions for the future   | 30          |
| 4.4.1 Precision Engineering  | 30          |
| 4.4.2 The chemicals industry   | 31          |
| 4.4.3 The information and communication technology industry                          | 31          |
| 4.5 Resource management and environmental issues                                     | 32          |
| 4.6 Barriers to progress   | 32          |
| 4.7 Summary  | 33          |

|          |  |           |
|----------|--|-----------|
| <b>5</b> | <b>Possible adverse health, environmental and safety impacts</b>                         | <b>35</b> |
| 5.1      | Introduction   | 35        |
| 5.2      | Assessing and controlling risk   | 35        |
| 5.3      | Human health   | 36        |
|          | 5.3.1 Understanding the toxicity of nanoparticles and fibres                             | 36        |
|          | 5.3.2 Manufactured nanoparticles and nanotubes   | 41        |
| 5.4      | Effects on the environment and other species   | 45        |
| 5.5      | Risk of explosion  | 47        |
| 5.6      | Addressing the knowledge gaps  | 47        |
| 5.7      | Conclusions  | 49        |
| <b>6</b> | <b>Social and ethical issues</b>   | <b>51</b> |
| 6.1      | Introduction: framing social and ethical issues  | 51        |
| 6.2      | Economic impacts   | 52        |
| 6.3      | A 'nanodivide'?  | 52        |
| 6.4      | Information collection and the implications for civil liberties                          | 53        |
| 6.5      | Human enhancement  | 54        |
| 6.6      | Covergence   | 54        |
| 6.7      | Military uses  | 55        |
| 6.8      | Conclusions  | 56        |
| <b>7</b> | <b>Stakeholder and public dialogue</b>   | <b>59</b> |
| 7.1      | Introduction   | 59        |
| 7.2      | Current public awareness of nanotechnologies in Britain                                  | 59        |
|          | 7.2.1 Quantitative survey findings   | 59        |
|          | 7.2.2 Qualitative workshop findings  | 60        |
|          | 7.2.3 Interpreting the research into public attitudes                                    | 61        |
| 7.3      | Importance of promoting a wider dialogue   | 62        |
| 7.4      | Nanotechnologies as an 'upstream' issue  | 64        |
| 7.5      | Designing dialogue on nanotechnologies   | 64        |
|          | 7.5.1 Incorporating public values in decisions   | 66        |
|          | 7.5.2 Improving decision quality   | 66        |
|          | 7.5.3 Resolving conflict   | 66        |
|          | 7.5.4 Improving trust in institutions  | 66        |
|          | 7.5.5 Informing or educating people  | 66        |
| 7.6      | Conclusions  | 67        |
| <b>8</b> | <b>Regulatory issues</b>   | <b>69</b> |
| 8.1      | Introduction   | 69        |
| 8.2      | Approaches to regulation   | 69        |
| 8.3      | Case studies   | 70        |
|          | 8.3.1 Workplace (including research laboratories)  | 70        |
|          | 8.3.2 Marketing and use of chemicals   | 71        |
|          | 8.3.3 Consumer products incorporating free nanoparticles, particularly skin preparations | 72        |
|          | 8.3.4 Medicines and medical devices  | 74        |
|          | 8.3.5 Consumer products incorporating fixed nanoparticles: end-of-life issues            | 74        |
| 8.4      | Knowledge gaps   | 74        |
|          | 8.4.1 Hazard   | 74        |
|          | 8.4.2 Exposure   | 75        |
|          | 8.4.3 Measurement  | 75        |
| 8.5      | Conclusions  | 76        |

|                                   |   |            |
|-----------------------------------|---|------------|
| <b>9</b>                          | <b>Conclusions</b>  | <b>79</b>  |
| 9.1                               | Nanoscience and nanotechnologies and their industrial application | 79         |
| 9.2                               | Health, safety and environmental risks and hazards                | 79         |
| 9.3                               | Social and ethical impacts  | 81         |
| 9.4                               | Stakeholder and public dialogue                                   | 81         |
| 9.5                               | Regulation  | 82         |
| 9.6                               | Responsible development of nanotechnologies                       | 83         |
| 9.7                               | A mechanism for addressing future issues                          | 84         |
| <b>10</b>                         | <b>Recommendations</b>  | <b>85</b>  |
| <b>11</b>                         | <b>References</b>   | <b>89</b>  |
| <b>Annexes</b>                    |   |            |
| <b>A</b>                          | <b>Working Group, Review Group and Secretariat</b>                | <b>95</b>  |
| <b>B</b>                          | <b>Conduct of the study</b>                                       | <b>97</b>  |
| <b>C</b>                          | <b>List of those who submitted evidence</b>                       | <b>99</b>  |
| <b>D</b>                          | <b>Mechanical self-replicating nano-robots and 'Grey Goo'</b>     | <b>109</b> |
| <b>Acronyms and abbreviations</b> |   | <b>111</b> |



# Summary

## Overview

1 Nanoscience and nanotechnologies are widely seen as having huge potential to bring benefits to many areas of research and application, and are attracting rapidly increasing investments from Governments and from businesses in many parts of the world. At the same time, it is recognised that their application may raise new challenges in the safety, regulatory or ethical domains that will require societal debate. In June 2003 the UK Government therefore commissioned the Royal Society and the Royal Academy of Engineering to carry out this independent study into current and future developments in nanoscience and nanotechnologies and their impacts.

2 The remit of the study was to:

- define what is meant by nanoscience and nanotechnologies;
- summarise the current state of scientific knowledge about nanotechnologies;
- identify the specific applications of the new technologies, in particular where nanotechnologies are already in use;
- carry out a forward look to see how the technologies might be used in future, where possible estimating the likely timescales in which the most far-reaching applications of the technologies might become reality;
- identify what health and safety, environmental, ethical and societal implications or uncertainties may arise from the use of the technologies, both current and future; and
- identify areas where additional regulation needs to be considered.

3 In order to carry out the study, the two Academies set up a Working Group of experts from the relevant disciplines in science, engineering, social science and ethics and from two major public interest groups. The group consulted widely, through a call for written evidence and a series of oral evidence sessions and workshops with a range of stakeholders from both the UK and overseas. It also reviewed published literature and commissioned new research into public attitudes. Throughout the study, the Working Group has conducted its work as openly as possible and has published the evidence received on a dedicated website as it became available ([www.nanotec.org.uk](http://www.nanotec.org.uk)).

4 This report has been reviewed and endorsed by the Royal Society and the Royal Academy of Engineering.

## Significance of the nanoscale

5 A nanometre (nm) is one thousand millionth of a metre. For comparison, a single human hair is about 80,000 nm wide, a red blood cell is approximately 7,000 nm wide and a water molecule is almost 0.3nm across. People are interested in the nanoscale (which we define to be from 100nm down to the size of atoms (approximately 0.2nm)) because it is at this scale that the properties of materials can be very different from those at a larger scale. We define 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; and nanotechnologies as the design, characterisation, production and application of structures, devices and systems by controlling shape and size at the nanometre scale. In some senses, nanoscience and nanotechnologies are not new. Chemists have been making polymers, which are large molecules made up of nanoscale subunits, for many decades and nanotechnologies have been used to create the tiny features on computer chips for the past 20 years. However, advances in the tools that now allow atoms and molecules to be examined and probed with great precision have enabled the expansion and development of nanoscience and nanotechnologies.

6 The properties of materials can be different at the nanoscale for two main reasons. First, nanomaterials have a relatively larger surface area when compared to the same mass of material produced in a larger form. This can make materials more chemically reactive (in some cases materials that are inert in their larger form are reactive when produced in their nanoscale form), and affect their strength or electrical properties. Second, quantum effects can begin to dominate the behaviour of matter at the nanoscale - particularly at the lower end - affecting the optical, electrical and magnetic behaviour of materials. Materials can be produced that are nanoscale in one dimension (for example, very thin surface coatings), in two dimensions (for example, nanowires and nanotubes) or in all three dimensions (for example, nanoparticles).

7 Our wide-ranging definitions cut across many traditional scientific disciplines. The only feature common to the diverse activities characterised as 'nanotechnology' is the tiny dimensions on which they operate. We have therefore found it more appropriate to refer to 'nanotechnologies'.

## **Current and potential uses of nanoscience and nanotechnologies**

8 Our aim has been to provide an overview of current and potential future developments in nanoscience and nanotechnologies against which the health, safety, environmental, social and ethical implications can be considered. We did not set out to identify areas of nanoscience and nanotechnologies that should be prioritised for funding.

### *(i) Nanomaterials*

9 Much of nanoscience and many nanotechnologies are concerned with producing new or enhanced materials. Nanomaterials can be constructed by 'top down' techniques, producing very small structures from larger pieces of material, for example by etching to create circuits on the surface of a silicon microchip. They may also be constructed by 'bottom up' techniques, atom by atom or molecule by molecule. One way of doing this is self-assembly, in which the atoms or molecules arrange themselves into a structure due to their natural properties. Crystals grown for the semiconductor industry provide an example of self assembly, as does chemical synthesis of large molecules. A second way is to use tools to move each atom or molecule individually. Although this 'positional assembly' offers greater control over construction, it is currently very laborious and not suitable for industrial applications.

10 Current applications of nanoscale materials include very thin coatings used, for example, in electronics and active surfaces (for example, self-cleaning windows). In most applications the nanoscale components will be fixed or embedded but in some, such as those used in cosmetics and in some pilot environmental remediation applications, free nanoparticles are used. The ability to machine materials to very high precision and accuracy (better than 100nm) is leading to considerable benefits in a wide range of industrial sectors, for example in the production of components for the information and communication technology (ICT), automotive and aerospace industries.

11 It is rarely possible to predict accurately the timescale of developments, but we expect that in the next few years nanomaterials will provide ways of improving performance in a range of products including silicon-based electronics, displays, paints, batteries, micro-machined silicon sensors and catalysts. Further into the future we may see composites that exploit the properties of carbon nanotubes – rolls of carbon with one or more walls, measuring a few nanometres in diameter and up to a few centimetres in length – which are extremely strong and flexible and can conduct electricity. At the moment the applications of these tubes are limited by the difficulty of producing them in a uniform manner and separating them into individual nanotubes. We may also see lubricants based on

inorganic nanospheres; magnetic materials using nanocrystalline grains; nanoceramics used for more durable and better medical prosthetics; automotive components or high-temperature furnaces; and nano-engineered membranes for more energy-efficient water purification.

### *(ii) Metrology*

12 Metrology, the science of measurement, underpins all other nanoscience and nanotechnologies because it allows the characterisation of materials in terms of dimensions but also in terms of attributes such as electrical properties and mass. Greater precision in metrology will assist the development of nanoscience and nanotechnologies. However, this will require increased standardisation to allow calibration of equipment and we recommend that the Department of Trade and Industry ensure that this area is properly funded.

### *(iii) Electronics, optoelectronics and ICT*

13 The role of nanoscience and nanotechnologies in the development of information technology is anticipated in the International Technology Roadmap for Semiconductors, a worldwide consensus document that predicts the main trends in the semiconductor industry up to 2018. This roadmap defines a manufacturing standard for silicon chips in terms of the length of a particular feature in a memory cell. For 2004 the standard is 90 nm, but it is predicted that by 2016 this will be just 22 nm. Much of the miniaturisation of computer chips to date has involved nanoscience and nanotechnologies, and this is expected to continue in the short and medium term. The storage of data, using optical or magnetic properties to create memory, will also depend on advances in nanoscience and nanotechnologies.

14 Alternatives to silicon-based electronics are already being explored through nanoscience and nanotechnologies, for example plastic electronics for flexible display screens. Other nanoscale electronic devices currently being developed are sensors to detect chemicals in the environment, to check the edibility of foodstuffs, or to monitor the state of mechanical stresses within buildings. Much interest is also focused on quantum dots, semiconductor nanoparticles that can be 'tuned' to emit or absorb particular light colours for use in solar energy cells or fluorescent biological labels.

### *(iv) Bionanotechnology and nanomedicine*

15 Applications of nanotechnologies in medicine are especially promising, and areas such as disease diagnosis, drug delivery targeted at specific sites in the body and molecular imaging are being intensively investigated and some products are undergoing clinical trials. Nanocrystalline silver, which is known to have antimicrobial properties, is being used in wound dressings in the USA. Applications of nanoscience and nanotech-

nologies are also leading to the production of materials and devices such as scaffolds for cell and tissue engineering, and sensors that can be used for monitoring aspects of human health. Many of the applications may not be realised for ten years or more (owing partly to the rigorous testing and validation regimes that will be required). In the much longer term, the development of nanoelectronic systems that can detect and process information could lead to the development of an artificial retina or cochlea. Progress in the area of bionanotechnology will build on our understanding of natural biological structures on the molecular scale, such as proteins.

(v) *Industrial applications*

16 So far, the relatively small number of applications of nanotechnologies that have made it through to industrial application represent evolutionary rather than revolutionary advances. Current applications are mainly in the areas of determining the properties of materials, the production of chemicals, precision manufacturing and computing. In mobile phones for instance, materials involving nanotechnologies are being developed for use in advanced batteries, electronic packaging and in displays. The total weight of these materials will constitute a very small fraction of the whole product but be responsible for most of the functions that the devices offer. In the longer term, many more areas may be influenced by nanotechnologies but there will be significant challenges in scaling up production from the research laboratory to mass manufacturing.

17 In the longer term it is hoped that nanotechnologies will enable more efficient approaches to manufacturing which will produce a host of multi-functional materials in a cost-effective manner, with reduced resource use and waste. However, it is important that claims of likely environmental benefits are assessed for the entire lifecycle of a material or product, from its manufacture through its use to its eventual disposal. We recommend that lifecycle assessments be undertaken for applications of nanotechnologies.

18 Hopes have been expressed for the development and use of mechanical nano-machines which would be capable of producing materials (and themselves) atom-by-atom (however this issue was not raised by the industrial representatives to whom we spoke). Alongside such hopes for self-replicating machines, fears have been raised about the potential for these (as yet unrealised) machines to go out of control, produce unlimited copies of themselves, and consume all available material on the planet in the process (the so called 'grey goo' scenario). We have concluded that there is no evidence to suggest that mechanical self-replicating nanomachines will be developed in the foreseeable future.

## Health and environmental impacts

19 Concerns have been expressed that the very properties of nanoscale particles being exploited in certain applications (such as high surface reactivity and the ability to cross cell membranes) might also have negative health and environmental impacts. Many nanotechnologies pose no new risks to health and almost all the concerns relate to the potential impacts of deliberately manufactured nanoparticles and nanotubes that are free rather than fixed to or within a material. Only a few chemicals are being manufactured in nanoparticulate form on an industrial scale and exposure to free manufactured nanoparticles and nanotubes is currently limited to some workplaces (including academic research laboratories) and a small number of cosmetic uses. We expect the likelihood of nanoparticles or nanotubes being released from products in which they have been fixed or embedded (such as composites) to be low but have recommended that manufacturers assess this potential exposure risk for the lifecycle of the product and make their findings available to the relevant regulatory bodies.

20 Few studies have been published on the effects of inhaling free manufactured nanoparticles and we have had to rely mainly on analogies with results from studies on exposure to other small particles – such as the pollutant nanoparticles known to be present in large numbers in urban air, and the mineral dusts in some workplaces. The evidence suggests that at least some manufactured nanoparticles will be more toxic per unit of mass than larger particles of the same chemical. This toxicity is related to the surface area of nanoparticles (which is greater for a given mass than that of larger particles) and the chemical reactivity of the surface (which could be increased or decreased by the use of surface coatings). It also seems likely that nanoparticles will penetrate cells more readily than larger particles.

21 It is very unlikely that new manufactured nanoparticles could be introduced into humans in doses sufficient to cause the health effects that have been associated with the nanoparticles in polluted air. However, some may be inhaled in certain workplaces in significant amounts and steps should be taken to minimise exposure. Toxicological studies have investigated nanoparticles of low solubility and low surface activity. Newer nanoparticles with characteristics that differ substantially from these should be treated with particular caution. The physical characteristics of carbon and other nanotubes mean that they may have toxic properties similar to those of asbestos fibres, although preliminary studies suggest that they may not readily escape into the air as individual fibres. Until further toxicological studies have been undertaken, human exposure to airborne nanotubes in laboratories and workplaces should be restricted.

22 If nanoparticles penetrate the skin they might facilitate the production of reactive molecules that could lead to cell damage. There is some evidence to show that nanoparticles of titanium dioxide (used in some sun protection products) do not penetrate the skin but it is not clear whether the same conclusion holds for individuals whose skin has been damaged by sun or by common diseases such as eczema. There is insufficient information about whether other nanoparticles used in cosmetics (such as zinc oxide) penetrate the skin and there is a need for more research into this. Much of the information relating to the safety of these ingredients has been carried out by industry and is not published in the open scientific literature. We therefore recommend that the terms of reference of safety advisory committees that consider information on the toxicology of ingredients such as nanoparticles include a requirement for relevant data, and the methodologies used to obtain them, to be placed in the public domain.

23 Important information about the fate and behaviour of nanoparticles that penetrate the body's defences can be gained from researchers developing nanoparticles for targeted drug delivery. We recommend collaboration between these researchers and those investigating the toxicity of other nanoparticles and nanotubes. In addition, the safety testing of these novel drug delivery methods must consider the toxic properties specific to such particles, including their ability to affect cells and organs distant from the intended target of the drug.

24 There is virtually no information available about the effect of nanoparticles on species other than humans or about how they behave in the air, water or soil, or about their ability to accumulate in food chains. Until more is known about their environmental impact we are keen that the release of nanoparticles and nanotubes to the environment is avoided as far as possible. Specifically, we recommend as a precautionary measure that factories and research laboratories treat manufactured nanoparticles and nanotubes as if they were hazardous and reduce them from waste streams and that the use of free nanoparticles in environmental applications such as remediation of groundwater be prohibited.

25 There is some evidence to suggest that combustible nanoparticles might cause an increased risk of explosion because of their increased surface area and potential for enhanced reaction. Until this hazard has been properly evaluated this risk should be managed by taking steps to avoid large quantities of these nanoparticles becoming airborne.

26 Research into the hazards and exposure pathways of nanoparticles and nanotubes is required to reduce the many uncertainties related to their potential impacts on health, safety and the environment. This research must keep pace with the future development

of nanomaterials. We recommend that the UK Research Councils assemble an interdisciplinary centre (perhaps from existing research institutions) to undertake research into the toxicity, epidemiology, persistence and bioaccumulation of manufactured nanoparticles and nanotubes, to work on exposure pathways and to develop measurement methods. The centre should liaise closely with regulators and with other researchers in the UK, Europe and internationally. We estimate that funding of £5-6M pa for 10 years will be required. Core funding should come from the Government but the centre would also take part in European and internationally funded projects.

## Social and ethical impacts

27 If it is difficult to predict the future direction of nanoscience and nanotechnologies and the timescale over which particular developments will occur, it is even harder to predict what will trigger social and ethical concerns. In the short to medium term concerns are expected to focus on two basic questions: 'Who controls uses of nanotechnologies?' and 'Who benefits from uses of nanotechnologies?'. These questions are not unique to nanotechnologies but past experience with other technologies demonstrates that they will need to be addressed.

28 The perceived opportunities and threats of nanotechnologies often stem from the same characteristics. For example, the convergence of nanotechnologies with information technology, linking complex networks of remote sensing devices with significant computational power, could be used to achieve greater personal safety, security and individualised healthcare and to allow businesses to track and monitor their products. It could equally be used for covert surveillance, or for the collection and distribution of information without adequate consent. As new forms of surveillance and sensing are developed, further research and expert legal analysis might be necessary to establish whether current regulatory frameworks and institutions provide appropriate safeguards to individuals and groups in society. In the military context, too, nanotechnologies hold potential for both defence and offence and will therefore raise a number of social and ethical issues.

29 There is speculation that a possible future convergence of nanotechnologies with biotechnology, information and cognitive sciences could be used for radical human enhancement. If these possibilities were ever realised they would raise profound ethical questions.

30 A number of the social and ethical issues that might be generated by developments in nanoscience and nanotechnologies should be investigated further and we recommend that the research councils and the

Arts and Humanities Research Board fund a multidisciplinary research programme to do this. We also recommend that the ethical and social implications of advanced technologies form part of the formal training of all research students and staff working in these areas.

## Stakeholder and public dialogue

31 Public attitudes can play a crucial role in realising the potential of technological advances. Public awareness of nanotechnologies is low in Great Britain. In the survey of public opinion that we commissioned, only 29% said they had heard of 'nanotechnology' and only 19% could offer any form of definition. Of those who could offer a definition, 68% felt that it would improve life in the future, compared to only 4% who thought it would make life worse.

32 In two in-depth workshops involving small groups of the general public, participants identified both positive and negative potentials in nanotechnologies. Positive views were expressed about new advances in an exciting field; potential applications particularly in medicine; the creation of new materials; a sense that the developments were part of natural progress and the hope that they would improve the quality of life. Concerns were about financial implications; impacts on society; the reliability of new applications; long-term side-effects and whether the technologies could be controlled. The issue of the governance of nanotechnologies was also raised. Which institutions could be trusted to ensure that the trajectories of development of nanotechnologies are socially beneficial? Comparisons were made with genetically modified organisms and nuclear power.

33 We recommend that the research councils build upon our preliminary research into public attitudes by funding a more sustained and extensive programme involving members of the general public and members of interested sections of society.

34 We believe that a constructive and proactive debate about the future of nanotechnologies should be undertaken now – at a stage when it can inform key decisions about their development and before deeply entrenched or polarised positions appear. We recommend that the Government initiate adequately funded public dialogue around the development of nanotechnologies. The precise method of dialogue and choice of sponsors should be designed around the agreed objectives of the dialogue. Our public attitudes work suggests that governance would be an appropriate subject for initial dialogue and given that the Research Councils are currently funding research into nanotechnologies they should consider taking this forward.

## Regulation

35 A key issue arising from our discussions with the various stakeholders was how society can control the development and deployment of nanotechnologies to maximise desirable outcomes and keep undesirable outcomes to an acceptable minimum – in other words, how nanotechnologies should be regulated. The evidence suggests that at present regulatory frameworks at EU and UK level are sufficiently broad and flexible to handle nanotechnologies at their current stage of development. However some regulations will need to be modified on a precautionary basis to reflect the fact that the toxicity of chemicals in the form of free nanoparticles and nanotubes cannot be predicted from their toxicity in a larger form and that in some cases they will be more toxic than the same mass of the same chemical in larger form. We looked at a small number of areas of regulation that cover situations where exposure to nanoparticles or nanotubes is likely currently or in the near future.

36 Currently the main source of inhalation exposure to manufactured nanoparticles and nanotubes is in laboratories and a few other workplaces. We recommend that the Health and Safety Executive carry out a review of the adequacy of existing regulation to assess and control workplace exposure to nanoparticles and nanotubes including those relating to accidental release. In the meantime they should consider setting lower occupational exposure levels for chemicals when produced in this size range.

37 Under current UK chemical regulation (Notification of New Substances) and its proposed replacement being negotiated at European level (Registration, Evaluation and Authorisation of Chemicals) the production of an existing substance in nanoparticulate form does not trigger additional testing. We recommend that chemicals produced in the form of nanoparticles and nanotubes be treated as new chemicals under these regulatory frameworks. The annual production thresholds that trigger testing and the testing methodologies relating to substances in these sizes, should be reviewed as more toxicological evidence becomes available.

38 Under cosmetics regulations in the European Union, ingredients (including those in the form of nanoparticles) can be used for most purposes without prior approval, provided they are not on the list of banned or restricted use chemicals and that manufacturers declare the final product to be safe. Given our concerns about the toxicity of any nanoparticles penetrating the skin we recommend that their use in products be dependent on a favourable opinion by the relevant European Commission scientific safety advisory committee. A favourable opinion has been given for the nanoparticulate form of titanium dioxide (because chemicals used as UV filters must

undergo an assessment by the advisory committee before they can be used) but insufficient information has been provided to allow an assessment of zinc oxide. In the meantime 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. We do not expect this to apply to many manufacturers since our understanding is that nanoparticles of zinc oxide are not used extensively in cosmetics in Europe. Based on our recommendation that chemicals produced in the form of nanoparticles should be treated as new chemicals, we believe that the ingredients lists for consumer products should identify the fact that manufactured nanoparticles have been added. Nanoparticles may be included in more consumer products in the future, and we recommend that the European Commission, with the support of the UK, review the adequacy of the current regulatory regime with respect to the introduction of nanoparticles into any consumer products.

39 Although we think it unlikely that nanoparticles or nanotubes will be released from most materials in which they have been fixed, we see any risk of such release being greatest during disposal, destruction or recycling. We therefore recommend that manufacturers of products that fall under extended producer responsibility regimes such as end-of-life regulations publish procedures outlining how these materials will be managed to minimise possible human and environmental exposure.

40 Our review of regulation has not been exhaustive and we recommend that all relevant regulatory bodies consider whether existing regulations are appropriate to protect humans and the environment from the hazards we have identified, publish their reviews and explain how they will address any regulatory gaps. Future applications of nanotechnologies may have an impact on other areas of regulation as, for example, developments in sensor technology may have implications for legislation relating to privacy. It is therefore important that regulatory bodies include future applications of nanotechnologies in their horizon-scanning programmes to ensure that any regulatory gaps are identified at an appropriate stage.

41 Overall, given appropriate regulation and research along the lines just indicated, we see no case for the moratorium which some have advocated on the laboratory or commercial production of manufactured nanomaterials.

## **Ensuring the responsible development of new and emerging technologies**

42 Nanoscience and nanotechnologies are evolving rapidly, and the pressures of international competition will ensure that this will continue. The UK Government's Chief Scientific Adviser should therefore commission an independent group in two years time, and again in five years time, to review what action has been taken as a result of our recommendations, to assess how nanoscience and nanotechnologies have developed in the interim, and to consider the ethical, social, health, environmental, safety and regulatory implications of these developments. This group should include representatives of, and consult with, the relevant stakeholder groups.

43 More generally, this study has highlighted again the value of identifying as early as possible new areas of science and technology that have the potential to impact strongly on society. The Chief Scientific Adviser should therefore establish a group that brings together representatives of a wide range of stakeholders to meet bi-annually to review new and emerging technologies, to identify at the earliest possible stage areas where issues needing Government attention may arise, and to advise on how these might be addressed. The work of this group should be made public and all stakeholders should be encouraged to engage with the emerging issues. We expect this group to draw upon the work of the other bodies across Government with horizon-scanning roles rather than to duplicate their work.

44 We look forward to the response to this report from the UK Government and from the other parties at whom the recommendations are targeted. This study has generated a great deal of interest among a wide range of stakeholders, both within the UK and internationally. As far as we are aware it is the first study of its kind, and we expect its findings to contribute to the responsible development of nanoscience and nanotechnology globally.

# 1 Introduction

## 1.1 Hopes and concerns about nanoscience and nanotechnologies

1 Nanoscience and nanotechnologies are widely seen as having huge potential to bring benefits in areas as diverse as drug development, water decontamination, information and communication technologies, and the production of stronger, lighter materials. They are attracting rapidly increasing investments from governments and from businesses in many parts of the world; it has been estimated that total global investment in nanotechnologies is currently around €5 billion, €2 billion of which comes from private sources (European Commission 2004a) (see also Table 1.1). The number of published patents in nanotechnology increased fourfold from 1995 (531 parents) to 2001 (1976 patents) (3i 2002). Although it is too early to produce reliable figures for the global market, one widely quoted estimate puts the annual value for all nanotechnologies-related products (including information and communication technologies) at \$1 trillion by 2011–2015 (NSF 2001). Although many people believe that nanotechnologies will have an impact across a wide range of sectors, a survey of experts in nanotechnologies across the world identified hype ('misguided promises that nanotechnology can fix everything') as the factor most likely to result in a backlash against it (3i 2002).

2 Against this background of increased research funding and interest from industry, several non-governmental organizations (NGOs) and some nanotechnologists have expressed concerns about current and potential future developments of nanotechnology. These include uncertainties about the impact of new nanomaterials on human health,

questions about the type of applications that could arise from the expected convergence, in the longer term, of nanotechnologies with technologies such as biotechnology, information technology (IT) and artificial intelligence, and suggestions that future developments might bring self-replicating nano-robots that might devastate the world (Joy 2000; ETC 2003a). Others have questioned the adequacy of current regulatory frameworks to deal with these new developments, and whether applications will benefit or disenfranchise developing countries (Arnall 2003).

3 The media has reflected the hopes and concerns about nanoscience and nanotechnology.

4 In January 2003 the Better Regulation Task Force (BRTF) published its report *Scientific Research: Innovation with Controls* (Better Regulation Task Force 2003), which included a consideration of nanotechnologies. Its first recommendation was that the UK Government should enable the public, through debate, to consider the risks of nanotechnologies for themselves. Other recommendations advocated openness in decision making, involving the public in the decision-making process, developing two-way communication channels and taking a strong lead over the handling of any issues of risk to emerge from nanotechnologies. In its response to the first recommendation, the Government stated that there was currently no obvious focus for an informed debate, but that it was initiating work that would 'examine whether there were any areas of nanotechnology which raise or will raise specific safety, environmental or ethical issues' that would warrant further study (UK Government 2003).

Table 1.1 Examples of public funding for research and development (R&D) in nanoscience and nanotechnology (source: European Commission 2004a).

| Country | Expenditure on nanoscience and nanotechnologies   |
|---------|---|
| Europe  | Current funding for nanotechnology R&D is about 1 billion euros, two-thirds of which comes from national and regional programmes.   |
| Japan   | Funding rose from \$400M in 2001 to \$800M in 2003 and is expected to rise by a further 20% in 2004.  |
| USA     | The USA's 21st Century Nanotechnology Research and Development Act (passed in 2003) allocated nearly \$3.7 billion to nanotechnology from 2005 to 2008 (which excludes a substantial defence-related expenditure). This compares with \$750M in 2003. |
| UK      | With the launch of its nanotechnology strategy in 2003, the UK Government pledged £45M per year from 2003 to 2009.  |

## **1.2 Terms of reference and conduct of the study**

5 In June 2003, following its response to the BRTF, the UK Government commissioned the Royal Society and the Royal Academy of Engineering (the UK's national academies of science and of engineering, respectively) to conduct an independent study on nanotechnology. The terms of reference of our study, jointly agreed by the Office of Science and Technology and the two Academies, were as follows:

- define what is meant by nanoscience and nanotechnology;
- summarise the current state of scientific knowledge about nanotechnology;
- identify the specific applications of the new technologies, in particular where nanotechnology is already in use;
- carry out a forward look to see how the technology might be used in future, where possible estimating the likely time-scales in which the most far-reaching applications of the technology might become reality;
- identify what environmental, health and safety, ethical or societal implications or uncertainties may arise from the use of the technology, both current and future;
- identify areas where regulation needs to be considered.

6 The two academies convened a multidisciplinary working group of experts in science and engineering, medicine, social science, consumer affairs, ethical issues and the environment to conduct this study (see Annex A for a list of Working Group members). The study was conducted independently of Government, which was not involved in the selection of the working group members or its methods of working, and which did not view the report before it was printed. We received much written evidence, and we held a series of oral evidence sessions and workshops with a range of stakeholders from the UK and overseas. The volume of evidence that was sent in for the Working Group to consider and follow up extended the time taken to complete this project beyond that originally anticipated. At the outset of the study it was agreed that the report should include public concerns and that data should be collected about public awareness of nanotechnology, which could form important baseline data. The market research company BMRB International was commissioned to research public attitudes to nanotechnology, which took the form of two workshops and a short market survey. The evidence was published as the project progressed and comments were invited through a dedicated website ([www.nanotec.org.uk](http://www.nanotec.org.uk)). A detailed description of the

conduct of the study can be found in Annex B. We are extremely grateful to all those organisations and individuals who contributed to the study; they are listed in Annex C. Their contributions can be found on our website and are available on the CD at the back of the hardcopy version of this report. In the report these contributions have been referred to as evidence. The report was peer reviewed by a small group of Fellows from the two academies (listed in Annex A) before being considered by the two academies. It has been endorsed by the Council of the Royal Society and approved for publication by the Royal Academy of Engineering.

## **1.3 Report overview**

7 In Chapter 2 we introduce nanoscience and nanotechnologies, and explain the definitions of each that we used during the study. In Chapter 3 we give examples of key current research, and current and potential future advances in: nanomaterials; nanometrology; electronics, optoelectronics and ICT; and bio-nanotechnology. We also look at the benefits they are currently providing and might provide in the short, medium and longer term. In Chapter 4 we look at current and possible future industrial applications of nanotechnology, and examine some of the barriers to its take-up by industry. In Chapters 3 and 4 we have provided an overview (rather than a detailed assessment) of current and potential future developments in, and applications of, nanoscience and nanotechnologies, against which health, safety, environmental, social and ethical implications (addressed later in the report) could be considered. The Taylor report (DTI 2002) reviewed the state of nanotechnology applications in industry in the UK and proposed a series of actions to accelerate and support increased industrial investment in the exploitation of nanotechnology in the UK. It was not our intention to critique or update the Taylor report or to identify research priorities for nanoscience and nanotechnology. The House of Commons Science and Technology Committee has recently evaluated the implementation of the recommendations of the Taylor report (House of Commons 2004a).

8 In Chapter 5 we evaluate the potential health, safety and environmental implications of nanotechnologies, and in Chapter 6 we consider the potential social and ethical implications. In both chapters we identify the main gaps in knowledge related to the potential impacts of nanotechnologies. Chapter 7 outlines the results of our commissioned research into public attitudes to nanotechnology in Great Britain, and considers the role of multi-stakeholder dialogue in the future development of nanotechnologies. The implications of our conclusions for the current regulatory framework are

outlined in Chapter 8. Finally, Chapters 9 and 10 contain our overall conclusions and list our recommendations.

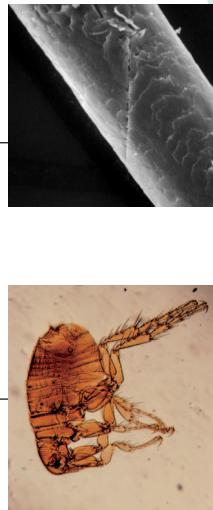
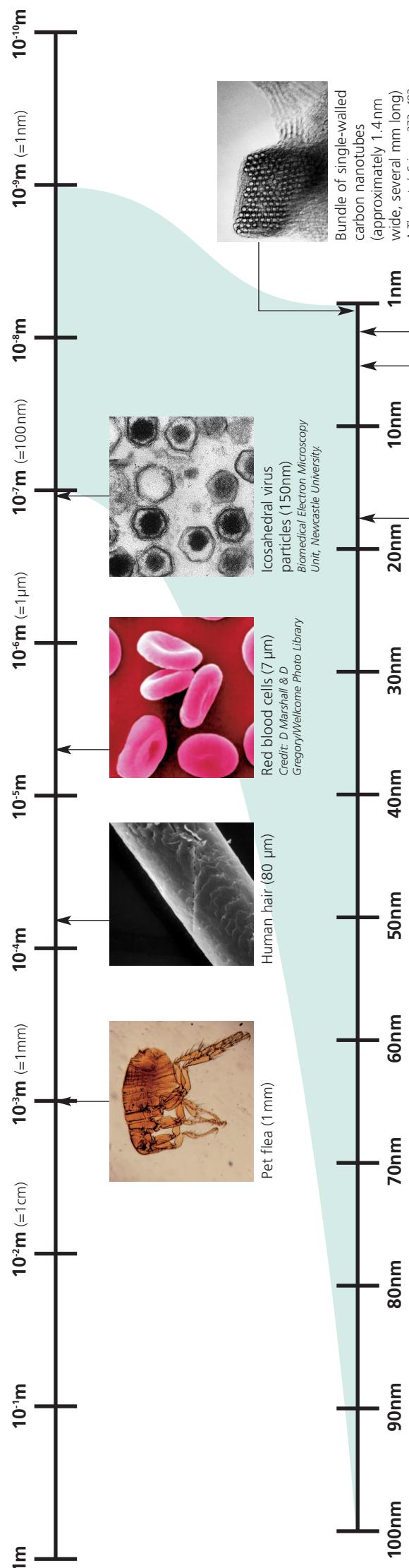
#### **1.4 Next steps**

9 We look forward to the response to this report from the UK Government and from the other parties at whom the recommendations are targeted. This study has generated a great deal of interest among a wide range of stakeholders, both within the UK and

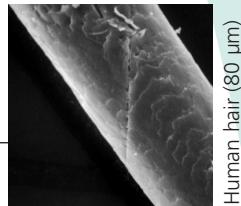
internationally. As far as we are aware it is the first study of its kind, and we expect its findings to contribute to the responsible development of nanoscience and nanotechnology globally. The two academies will continue to participate in this important area. The issues raised and conclusions reached in this report can be debated through the discussion section of the dedicated website ([www.nanotec.org.uk](http://www.nanotec.org.uk)). We will hold an open meeting in London to discuss the report's findings shortly after its publication.



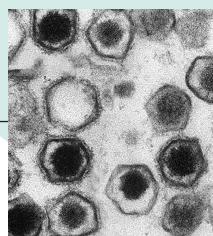
Football (approximately 22 cm)



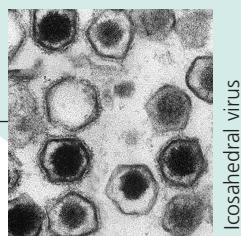
Pet flea (1 mm)



Human hair (80  $\mu$ m)

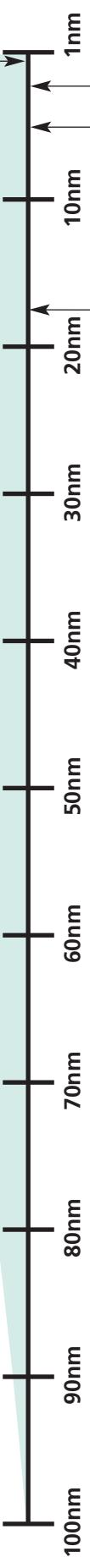


Red blood cells (7  $\mu$ m)  
Credit: D Marshall & D Gregory/Welcome Photo Library



Icosahedral virus  
particles (150nm)

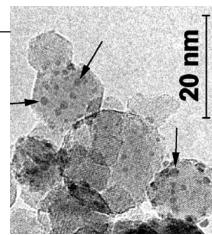
Biomedical Electron Microscopy  
Unit, Newcastle University



Bundle of single-walled  
carbon nanotubes  
(approximately 1.4nm  
wide, several nm long)  
A Thess et al., Science 273, 483,  
1996



Strand of DNA  
(approximately 2nm wide)



Each letter in the logo  
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to bottom.  
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Unauthorized use not permitted.

Platinum/Titanium  
dioxide particles  
(Platinum particles less  
than 3 nm in diameter  
are indicated by arrows  
on titanium dioxide)  
R Strober et al., J Catal 222, 296,  
2003

Figure 2.1. Length scale showing the nanometre in context. The length scale at the top ranges from 1m to 10<sup>-10</sup>m, and illustrates the size of a football compared to a carbon 60 ( $C_{60}$ ) molecule, also known as a buckyball. For comparison the world is approximately one hundred million times larger than a football, which is in turn one hundred million times larger than a buckyball. The section from 10<sup>-7</sup>m (100 nm) to 10<sup>-9</sup>m (1 nm) is expanded below. The lengthscale of interest for nanoscience and nanotechnologies is from 100 nm down to the atomic scale - approximately 0.2 nm.

## 2 What are nanoscience and nanotechnologies?

1 The first term of reference of this study was to define what is meant by nanoscience and nanotechnology. However, as the term 'nanotechnology' encompasses such a wide range of tools, techniques and potential applications, we have found it more appropriate to refer to 'nanotechnologies'. Our definitions were developed through consultation at our workshop meeting with scientists and engineers and through comments received through the study website.

2 Although there is no sharp distinction between them, in this report we differentiate between nanoscience and nanotechnologies as follows.

### *Box 2.1 Definitions of nanoscience and nanotechnologies*

**Nanoscience** is 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.

3 The prefix 'nano' is derived from the Greek word for dwarf. One nanometre (nm) is equal to one-billionth of a metre,  $10^{-9}$ m. A human hair is approximately 80,000nm wide, and a red blood cell approximately 7000 nm wide. Figure 2.1 shows the nanometre in context. Atoms are below a nanometre in size, whereas many molecules, including some proteins, range from a nanometre upwards.

4 The conceptual underpinnings of nanotechnologies were first laid out in 1959 by the physicist Richard Feynman, in his lecture 'There's plenty of room at the bottom' (Feynman 1959). Feynman explored the possibility of manipulating material at the scale of individual atoms and molecules, imagining the whole of the Encyclopaedia Britannica written on the head of a pin and foreseeing the increasing ability to examine and control matter at the nanoscale.

5 The term 'nanotechnology' was not used until 1974, when Norio Taniguchi, a researcher at the University of Tokyo, Japan used it to refer to the ability to engineer materials precisely at the nanometre level (Taniguchi 1974). The primary driving force for miniaturisation at that time came from the electronics industry, which aimed to develop tools to create smaller (and therefore faster and more complex) electronic devices on silicon chips. Indeed, at IBM in the USA a

technique called electron beam lithography was used to create nanostructures and devices as small as 40–70nm in the early 1970s.

6. The size range that holds so much interest is typically from 100 nm down to the atomic level (approximately 0.2 nm), because it is in this range (particularly at the lower end) that materials can have different or enhanced properties compared with the same materials at a larger size. The two main reasons for this change in behaviour are an increased relative surface area, and the dominance of quantum effects. An increase in surface area (per unit mass) will result in a corresponding increase in chemical reactivity, making some nanomaterials useful as catalysts to improve the efficiency of fuel cells and batteries. As the size of matter is reduced to tens of nanometres or less, quantum effects can begin to play a role, and these can significantly change a material's optical, magnetic or electrical properties. In some cases, size-dependent properties have been exploited for centuries. For example, gold and silver nanoparticles (particles of diameter less than 100 nm; see section 3.2) have been used as coloured pigments in stained glass and ceramics since the 10th century AD (Erhardt 2003). Depending on their size, gold particles can appear red, blue or gold in colour. The challenge for the ancient (al)chemists was to make all nanoparticles the same size (and hence the same colour), and the production of single-size nanoparticles is still a challenge today.

7. At the larger end of our size range, other effects such as surface tension or 'stickiness' are important, which also affect physical and chemical properties. For liquid or gaseous environments Brownian motion, which describes the random movement of larger particles or molecules owing to their bombardment by smaller molecules and atoms, is also important. This effect makes control of individual atoms or molecules in these environments extremely difficult.

8. Nanoscience is concerned with understanding these effects and their influence on the properties of material. Nanotechnologies aim to exploit these effects to create structures, devices and systems with novel properties and functions due to their size.

9. In some senses, nanoscience and nanotechnologies are not new. Many chemicals and chemical processes have nanoscale features – for example, chemists have been making polymers, large molecules made up of tiny nanoscalar subunits, for many decades. Nanotechnologies have been used to create the tiny features on computer chips for the past 20 years. The natural world also contains many examples of nanoscale structures, from milk (a nanoscale colloid) to sophisticated nanosized and nanostructured proteins

that control a range of biological activities, such as flexing muscles, releasing energy and repairing cells. Nanoparticles occur naturally, and have been created for thousands of years as the products of combustion and food cooking.

10 However, it is only in recent years that sophisticated tools have been developed to investigate and manipulate matter at the nanoscale, which have greatly affected our understanding of the nanoscale world. A major step in this direction was the invention of the scanning tunnelling microscope (STM) in 1982, and the atomic force microscope (AFM) in 1986. These tools use nanoscale probes to image a surface with atomic resolution, and are also capable of picking up, sliding or dragging atoms or molecules around on surfaces to build rudimentary nanostructures. These tools are further described in Box 3.1. In a now famous experiment in 1990, Don Eigler and Erhard Schweizer at IBM moved xenon atoms around on a nickel surface to write the company logo (Eigler and Schweizer 1990) (see Figure 2.1), a laborious process which took a whole day under well-controlled conditions. The use of these tools is not restricted to engineering, but has been adopted across a range of disciplines. AFM, for example, is routinely used to study biological molecules such as proteins.

11 The technique used by Eigler and Schweizer is only one in the range of ways used to manipulate and produce nanomaterials, commonly categorised as either ‘top-down’ or ‘bottom-up’. ‘Top-down’ techniques involve starting with a block of material, and etching or milling it down to the desired shape, whereas ‘bottom-

up’ involves the assembly of smaller sub-units (atoms or molecules) to make a larger structure. The main challenge for top-down manufacture is the creation of increasingly small structures with sufficient accuracy, whereas for bottom-up manufacture, it is to make structures large enough, and of sufficient quality, to be of use as materials. These two methods have evolved separately and have now reached the point where the best achievable feature size for each technique is approximately the same, leading to novel hybrid ways of manufacture.

12 Nanotechnologies can be regarded as genuinely interdisciplinary, and have prompted the collaboration between researchers in previously disparate areas to share knowledge, tools and techniques. An understanding of the physics and chemistry of matter and processes at the nanoscale is relevant to all scientific disciplines, from chemistry and physics to biology, engineering and medicine. Indeed, it could be argued that evolutionary developments in each of these fields towards investigating matter at increasingly small size scales has now come to be known as ‘nanotechnology’.

13 It will be seen in Chapters 3 and 4 that nanoscience and nanotechnologies encompass a broad and varied range of materials, tools and approaches. Apart from a characteristic size scale, it is difficult to find commonalities between them. We should not therefore expect them to have the same health, environmental, safety, social or ethical implications or require the same approach to regulation; these issues are dealt with in Chapters 5 – 8.

### 3 Science and applications

#### 3.1 Introduction

1 In this chapter we provide an overview of some key current developments in nanoscience and nanotechnologies, and highlight some possible future applications. The chapter is informed by evidence from scientists and engineers in academia and industry. It illustrates the wide-ranging interest in these areas and provides a background to the later chapters, which address health, environmental, social, ethical and regulatory implications of nanotechnologies. It does not consider in detail the developments in nanoscience and nanotechnologies in all scientific and engineering fields.

2 As nanoscience and nanotechnologies cover such a wide range of fields (from chemistry, physics and biology, to medicine, engineering and electronics), we have considered them in four broad categories: nanomaterials; nanometrology; electronics, optoelectronics and information and communication technology; and bio-nanotechnology and nanomedicine. This division helps to distinguish between developments in different fields, but there is naturally some overlap.

3 Where possible, we define the development of future applications as short term (under 5 years), medium term (5–15 years), and long term (over 20 years). It may be that some of the potential applications that we identify are never realised, whereas others that are currently unforeseen could have a major impact. We also identify potential in environmental, health and safety, ethical or societal implications or uncertainties that are discussed further in later chapters.

4 Current industrial applications of nanotechnologies are dealt with in Chapter 4, as are the factors that will influence their application in the future.

#### 3.2 Nanomaterials

##### 3.2.1 Introduction to nanomaterials

5 A key driver in the development of new and improved materials, from the steels of the 19th century to the advanced materials of today, has been the ability to control their structure at smaller and smaller scales. The overall properties of materials as diverse as paints and silicon chips are determined by their structure at the micro- and nanoscales. As our understanding of materials at the nanoscale and our ability to control their structure improves, there will be great potential to create a range of materials with novel characteristics, functions and applications.

6 Although a broad definition, we categorise nanomaterials as those which have structured components with at least one dimension less than 100 nm. Materials that have one dimension in the nanoscale (and are extended in the other two dimensions) are layers, such as a thin films or surface coatings. Some of the features on computer chips come in this category. Materials that are nanoscale in two dimensions (and extended in one dimension) include nanowires and nanotubes. Materials that are nanoscale in three dimensions are particles, for example precipitates, colloids and quantum dots (tiny particles of semiconductor materials). Nanocrystalline materials, made up of nanometre-sized grains, also fall into this category. Some of these materials have been available for some time; others are genuinely new. The aim of this chapter is to give an overview of the properties, and the significant foreseeable applications of some key nanomaterials.

7 Two principal factors cause the properties of nanomaterials to differ significantly from other materials: increased relative surface area, and quantum effects. These factors can change or enhance properties such as reactivity, strength and electrical characteristics. As a particle decreases in size, a greater proportion of atoms are found at the surface compared to those inside. For example, a particle of size 30 nm has 5% of its atoms on its surface, at 10 nm 20% of its atoms, and at 3 nm 50% of its atoms. Thus nanoparticles have a much greater surface area per unit mass compared with larger particles. As growth and catalytic chemical reactions occur at surfaces, this means that a given mass of material in nanoparticulate form will be much more reactive than the same mass of material made up of larger particles.

8 In tandem with surface-area effects, quantum effects can begin to dominate the properties of matter as size is reduced to the nanoscale. These can affect the optical, electrical and magnetic behaviour of materials, particularly as the structure or particle size approaches the smaller end of the nanoscale. Materials that exploit these effects include quantum dots, and quantum well lasers for optoelectronics.

9 For other materials such as crystalline solids, as the size of their structural components decreases, there is much greater interface area within the material; this can greatly affect both mechanical and electrical properties. For example, most metals are made up of small crystalline grains; the boundaries between the grain slow down or arrest the propagation of defects when the material is stressed, thus giving it strength. If these grains can be made very small, or even nanoscale in size, the interface area within the material greatly

increases, which enhances its strength. For example, nanocrystalline nickel is as strong as hardened steel. Understanding surfaces and interfaces is a key challenge for those working on nanomaterials, and one where new imaging and analysis instruments are vital.

10 Nanomaterials are not simply another step in the miniaturization of materials. They often require very different production approaches. As introduced in Chapter 2, and discussed further in Chapter 4, there are several processes to create nanomaterials, classified as 'top-down' and 'bottom-up'. Although many nanomaterials are currently at the laboratory stage of manufacture, a few of them are being commercialised.

### 3.2.2 Nanoscience in this area

11 Below we outline some examples of nanomaterials and the range of nanoscience that is aimed at understanding their properties. As will be seen, the behaviour of some nanomaterials is well understood, whereas others present greater challenges.

#### a) Nanoscale in one dimension

##### *Thin films, layers and surfaces*

12 One-dimensional nanomaterials, such as thin films and engineered surfaces, have been developed and used for decades in fields such as electronic device manufacture, chemistry and engineering. In the silicon integrated-circuit industry, for example, many devices rely on thin films for their operation, and control of film thicknesses approaching the atomic level is routine. Monolayers (layers that are one atom or molecule deep) are also routinely made and used in chemistry. The formation and properties of these layers are reasonably well understood from the atomic level upwards, even in quite complex layers (such as lubricants). Advances are being made in the control of the composition and smoothness of surfaces, and the growth of films.

13 Engineered surfaces with tailored properties such as large surface area or specific reactivity are used routinely in a range of applications such as in fuel cells and catalysts (see section 3.2.3b). The large surface area provided by nanoparticles, together with their ability to self assemble on a support surface, could be of use in all of these applications.

14 Although they represent incremental developments, surfaces with enhanced properties should find applications throughout the chemicals and energy sectors. The benefits could surpass the obvious economic and resource savings achieved by higher activity and greater selectivity in reactors and separation processes, to enabling small-scale distributed processing (making chemicals as close as possible to the point of use). There is already a move in the chemical industry towards this. Another use could be the small-scale, on-site production of high value chemicals such as pharmaceuticals.

#### b) Nanoscale in two dimensions

15 Two dimensional nanomaterials such as tubes and wires have generated considerable interest among the scientific community in recent years. In particular, their novel electrical and mechanical properties are the subject of intense research.

##### *Carbon nanotubes*

16 Carbon nanotubes (CNTs) were first observed by Sumio Iijima in 1991 (Iijima 1991). CNTs are extended tubes of rolled graphene sheets. There are two types of CNT: single-walled (one tube) or multi-walled (several concentric tubes) (Figure 3.1). Both of these are typically a few nanometres in diameter and several micrometres ( $10^{-6}\text{m}$ ) to centimetres long. CNTs have assumed an important role in the context of nanomaterials, because of their novel chemical and physical properties. They are mechanically very strong (their Young's modulus is over 1 terapascal, making CNTs as stiff as diamond), flexible (about their axis), and can conduct electricity extremely well (the helicity of the graphene sheet determines whether the CNT is a semiconductor or metallic). All of these remarkable properties give CNTs a range of potential applications: for example, in reinforced composites, sensors, nanoelectronics and display devices.

Figure 3.1a Schematic of a single-walled carbon nanotube (SWNT)

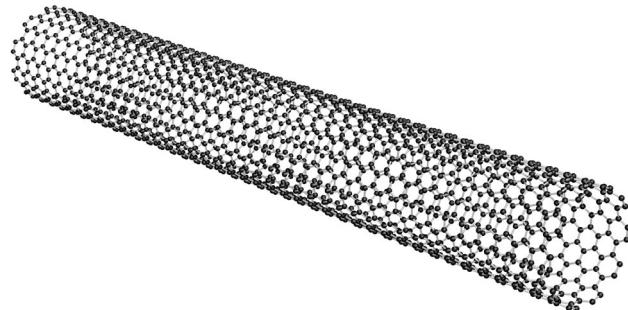
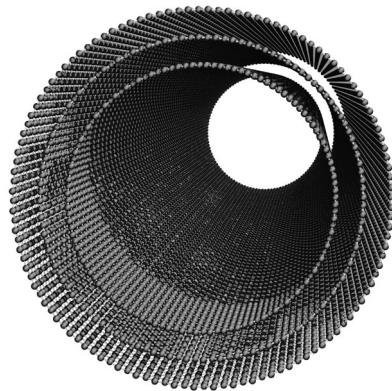


Figure 3.1b Schematic of a multi-walled carbon nanotube (MWNT)



17 CNTs are now available commercially in limited quantities. They can be grown by several techniques, which are discussed in section 4.3.1b. However, the selective and uniform production of CNTs with specific dimensions and physical properties is yet to be achieved. The potential similarity in size and shape between CNTs and asbestos fibres has led to concerns about their safety, which we address in detail in sections 5.3.1b and 5.3.2a.

#### *Inorganic nanotubes*

18 Inorganic nanotubes and inorganic fullerene-like materials based on layered compounds such as molybdenum disulphide were discovered shortly after CNTs. They have excellent tribological (lubricating) properties, resistance to shockwave impact, catalytic reactivity, and high capacity for hydrogen and lithium storage, which suggest a range of promising applications. Oxide-based nanotubes (such as titanium dioxide) are being explored for their applications in catalysis, photo-catalysis and energy storage.

#### *Nanowires*

19 Nanowires are ultrafine wires or linear arrays of dots, formed by self-assembly. They can be made from a wide range of materials. Semiconductor nanowires made of silicon, gallium nitride and indium phosphide have demonstrated remarkable optical, electronic and magnetic characteristics (for example, silica nanowires can bend light around very tight corners). Nanowires have potential applications in high-density data storage, either as magnetic read heads or as patterned storage media, and electronic and opto-electronic nanodevices, for metallic interconnects of quantum devices and nanodevices. The preparation of these nanowires relies on sophisticated growth techniques, which include self-assembly processes, where atoms arrange themselves naturally on stepped surfaces, chemical vapour deposition (CVD) onto patterned substrates, electroplating or molecular beam epitaxy (MBE). The 'molecular beams' are typically from thermally evaporated elemental sources.

#### *Biopolymers*

20 The variability and site recognition of biopolymers, such as DNA molecules, offer a wide range of opportunities for the self-organization of wire nanostructures into much more complex patterns. The DNA backbones may then, for example, be coated in metal. They also offer opportunities to link nano- and biotechnology in, for example, biocompatible sensors and small, simple motors. Such self-assembly of organic backbone nanostructures is often controlled by weak interactions, such as hydrogen bonds, hydrophobic, or van der Waals interactions (generally in aqueous environments) and hence requires quite different synthesis strategies to CNTs, for example. The combination of one-dimensional nanostructures consisting of biopolymers and inorganic compounds opens up a number of scientific and technological opportunities.

#### c) Nanoscale in three dimensions

##### *Nanoparticles*

21 Nanoparticles are often defined as particles of less than 100 nm in diameter. In line with our definitions of nanoscience and nanotechnologies (see Box 2.1), we classify nanoparticles to be particles less than 100 nm in diameter that exhibit new or enhanced size-dependent properties compared with larger particles of the same material. Nanoparticles exist widely in the natural world: for example as the products of photochemical and volcanic activity, and created by plants and algae. They have also been created for thousands of years as products of combustion and food cooking, and more recently from vehicle exhausts. Deliberately manufactured nanoparticles, such as metal oxides, are by comparison in the minority. In this report we will refer to these as natural, pollutant and manufactured nanoparticles, respectively.

22 As described in Chapter 2, nanoparticles are of interest because of the new properties (such as chemical reactivity and optical behaviour) that they exhibit compared with larger particles of the same materials. For example, titanium dioxide and zinc oxide become transparent at the nanoscale, however are able to absorb and reflect UV light, and have found application in sunscreens. Nanoparticles have a range of potential applications: in the short-term in new cosmetics, textiles and paints; in the longer term, in methods of targeted drug delivery where they could be used to deliver drugs to a specific site in the body. Nanoparticles can also be arranged into layers on surfaces, providing a large surface area and hence enhanced activity, relevant to a range of potential applications such as catalysts.

23 Manufactured nanoparticles are typically not products in their own right, but generally serve as raw materials, ingredients or additives in existing products. Although their production is currently low compared with other nanomaterials we have given them a considerable amount of attention in this report. This is because they are currently in a small number of consumer products such as cosmetics and their enhanced or novel properties may have implications for their toxicity. The evidence submitted during the course of our study indicates that for most applications, nanoparticles will be fixed (for example, attached to a surface or within a composite) although in others they will be free or suspended in fluid. Whether they are fixed or free will have a significant affect on their potential health, safety and environmental impacts. We address these issues in detail in Chapter 5.

##### *Fullerenes (carbon 60)*

24 In the mid-1980s a new class of carbon material was discovered called carbon 60 ( $C_{60}$ ) (Kroto et al 1985). A diagram of carbon 60 can be found in Figure 2.1. These are spherical molecules about 1 nm in diameter, comprising 60 carbon atoms arranged as 20 hexagons

and 12 pentagons: the configuration of a football. The C<sub>60</sub> species was named ‘Buckminsterfullerene’ in recognition of the architect Buckminster Fuller, who was well-known for building geodesic domes, and the term fullerenes was then given to any closed carbon cage. In 1990, a technique to produce larger quantities of C<sub>60</sub> was developed by resistively heating graphite rods in a helium atmosphere (Krätschmer et al 1990). Several applications are envisaged for fullerenes, such as miniature ‘ball bearings’ to lubricate surfaces, drug delivery vehicles and in electronic circuits.

#### Dendrimers

25 Dendrimers are spherical polymeric molecules, formed through a nanoscale hierarchical self-assembly process. There are many types of dendrimer; the smallest is several nanometres in size. Dendrimers are used in conventional applications such as coatings and inks, but they also have a range of interesting properties which could lead to useful applications. For example, dendrimers can act as nanoscale carrier molecules and as such could be used in drug delivery. Environmental clean-up could be assisted by dendrimers as they can trap metal ions, which could then be filtered out of water with ultra-filtration techniques.

#### Quantum dots

26 Nanoparticles of semiconductors (quantum dots) were theorized in the 1970s and initially created in the early 1980s. If semiconductor particles are made small enough, quantum effects come into play, which limit the energies at which electrons and holes (the absence of an electron) can exist in the particles. As energy is related to wavelength (or colour), this means that the optical properties of the particle can be finely tuned depending on its size. Thus, particles can be made to emit or absorb specific wavelengths (colours) of light, merely by controlling their size. Recently, quantum dots have found applications in composites, solar cells (Grätzel cells) and fluorescent biological labels (for example to trace a biological molecule) which use both the small particle size and tuneable energy levels. Recent advances in chemistry have resulted in the preparation of monolayer-protected, high-quality, monodispersed, crystalline quantum dots as small as 2 nm in diameter, which can be conveniently treated and processed as a typical chemical reagent.

### 3.2.3 Applications

27 Below we list some key current and potential short- and long-term applications of nanomaterials. Most current applications represent evolutionary developments of existing technologies: for example, the reduction in size of electronics devices.

#### a) Current

##### Sunscreens and cosmetics

28 Nanosized titanium dioxide and zinc oxide are

currently used in some sunscreens, as they absorb and reflect ultraviolet (UV) rays and yet are transparent to visible light and so are more appealing to the consumer. Nanosized iron oxide is present in some lipsticks as a pigment but it is our understanding that it is not used by the European cosmetics sector. The use of nanoparticles in cosmetics has raised a number of concerns about consumer safety; we evaluate the evidence relating to these concerns in section 5.3.2b.

#### Composites

29 An important use of nanoparticles and nanotubes is in composites, materials that combine one or more separate components and which are designed to exhibit overall the best properties of each component. This multi-functionality applies not only to mechanical properties, but extends to optical, electrical and magnetic ones. Currently, carbon fibres and bundles of multi-walled CNTs are used in polymers to control or enhance conductivity, with applications such as anti-static packaging. The use of individual CNTs in composites is a potential long-term application (see section 3.2.3c). A particular type of nanocomposite is where nanoparticles act as fillers in a matrix; for example, carbon black used as a filler to reinforce car tyres. However, particles of carbon black can range from tens to hundreds of nanometres in size, so not all carbon black falls within our definition of nanoparticles.

#### Clays

30 Clays containing naturally occurring nanoparticles have long been important as construction materials and are undergoing continuous improvement. Clay particle based composites – containing plastics and nano-sized flakes of clay – are also finding applications such as use in car bumpers.

#### Coatings and surfaces

31 Coatings with thickness controlled at the nano- or atomic scale have been in routine production for some time, for example in MBE or metal oxide CVD for optoelectronic devices, or in catalytically active and chemically functionalized surfaces. Recently developed applications include the self-cleaning window, which is coated in highly activated titanium dioxide, engineered to be highly hydrophobic (water repellent) and antibacterial, and coatings based on nanoparticulate oxides that catalytically destroy chemical agents (Royal Society 2004a). Wear and scratch-resistant hard coatings are significantly improved by nanoscale intermediate layers (or multilayers) between the hard outer layer and the substrate material. The intermediate layers give good bonding and graded matching of elastic and thermal properties, thus improving adhesion. A range of enhanced textiles, such as breathable, waterproof and stain-resistant fabrics, have been enabled by the improved control of porosity at the nanoscale and surface roughness in a variety of polymers and inorganics.

### *Tougher and harder cutting tools*

32 Cutting tools made of nanocrystalline materials, such as tungsten carbide, tantalum carbide and titanium carbide, are more wear and erosion-resistant, and last longer than their conventional (large-grained) counterparts. They are finding applications in the drills used to bore holes in circuit boards.

### b) Short-term

#### *Paints*

33 Incorporating nanoparticles in paints could improve their performance, for example by making them lighter and giving them different properties. Thinner paint coatings ('lightweighting'), used for example on aircraft, would reduce their weight, which could be beneficial to the environment. However, the whole life cycle of the aircraft needs to be considered before overall benefits can be claimed (see section 4.5). It may also be possible to substantially reduce solvent content of paints, with resulting environmental benefits. New types of fouling-resistant marine paint could be developed and are urgently needed as alternatives to tributyl tin (TBT), now that the ecological impacts of TBT have been recognised. Anti-fouling surface treatment is also valuable in process applications such as heat exchange, where it could lead to energy savings. If they can be produced at sufficiently low cost, fouling-resistant coatings could be used in routine duties such as piping for domestic and industrial water systems. It remains speculation whether very effective anti-fouling coatings could reduce the use of biocides, including chlorine. Other novel, and more long-term, applications for nanoparticles might lie in paints that change colour in response to change in temperature or chemical environment, or paints that have reduced infra-red absorptivity and so reduce heat loss.

34 Concerns about the health and environmental impacts of nanoparticles (which we address in detail in Chapter 5) may require the need for the durability and abrasion behaviour of nano-engineered paints and coatings to be addressed, so that abrasion products take the form of coarse or microscopic agglomerates rather than individual nanoparticles.

#### *Remediation*

35 The potential of nanoparticles to react with pollutants in soil and groundwater and transform them into harmless compounds is being researched. In one pilot study the large surface area and high surface reactivity of iron nanoparticles were exploited to transform chlorinated hydrocarbons (some of which are believed to be carcinogens) into less harmful end products in groundwater (Zhang 2003). It is also hoped that they could be used to transform heavy metals such as lead and mercury from bioavailable forms into insoluble forms. Serious concerns have been raised over the uncontrolled release of nanoparticles into the environment; these are discussed in section 5.4.

### *Fuel Cells*

36 Engineered surfaces are essential in fuel cells, where the external surface properties and the pore structure affect performance. The hydrogen used as the immediate fuel in fuel cells may be generated from hydrocarbons by catalytic reforming, usually in a reactor module associated directly with the fuel cell. The potential use of nano-engineered membranes to intensify catalytic processes could enable higher-efficiency, small-scale fuel cells. These could act as distributed sources of electrical power. It may eventually be possible to produce hydrogen locally from sources other than hydrocarbons, which are the feedstocks of current attention.

### *Displays*

37 The huge market for large area, high brightness, flat-panel displays, as used in television screens and computer monitors, is driving the development of some nanomaterials. Nanocrystalline zinc selenide, zinc sulphide, cadmium sulphide and lead telluride synthesized by sol-gel techniques (a process for making ceramic and glass materials, involving the transition from a liquid 'sol' phase to a solid 'gel' phase) are candidates for the next generation of light-emitting phosphors. CNTs are being investigated for low voltage field-emission displays; their strength, sharpness, conductivity and inertness make them potentially very efficient and long-lasting emitters.

### *Batteries*

38 With the growth in portable electronic equipment (mobile phones, navigation devices, laptop computers, remote sensors), there is great demand for lightweight, high-energy density batteries. Nanocrystalline materials synthesized by sol-gel techniques are candidates for separator plates in batteries because of their foam-like (aerogel) structure, which can hold considerably more energy than conventional ones. Nickel–metal hydride batteries made of nanocrystalline nickel and metal hydrides are envisioned to require less frequent recharging and to last longer because of their large grain boundary (surface) area.

### *Fuel additives*

39 Research is underway into the addition of nanoparticulate ceria (cerium oxide) to diesel fuel to improve fuel economy by reducing the degradation of fuel consumption over time (Oxonica 2003).

### *Catalysts*

40 In general, nanoparticles have a high surface area, and hence provide higher catalytic activity. Nanotechnologies are enabling changes in the degree of control in the production of nanoparticles, and the support structure on which they reside. It is possible to synthesise metal nanoparticles in solution in the presence of a surfactant to form highly ordered monodisperse films of the catalyst nanoparticles on a surface. This allows more uniformity in the size and chemical structure of the catalyst, which in turn leads to

greater catalytic activity and the production of fewer by-products. It may also be possible to engineer specific or selective activity. These more active and durable catalysts could find early application in cleaning up waste streams. This will be particularly beneficial if it reduces the demand for platinum-group metals, whose use in standard catalytic units is starting to emerge as a problem, given the limited availability of these metals.

### c) Longer-term applications

#### *Carbon nanotube composites*

41 CNTs have exceptional mechanical properties, particularly high tensile strength and light weight. An obvious area of application would be in nanotube-reinforced composites, with performance beyond current carbon-fibre composites. One current limit to the introduction of CNTs in composites is the problem of structuring the tangle of nanotubes in a well-ordered manner so that use can be made of their strength. Another challenge is generating strong bonding between CNTs and the matrix, to give good overall composite performance and retention during wear or erosion of composites. The surfaces of CNTs are smooth and relatively unreactive, and so tend to slip through the matrix when it is stressed. One approach that is being explored to prevent this slippage is the attachment of chemical side-groups to CNTs, effectively to form 'anchors'. Another limiting factor is the cost of production of CNTs. However, the potential benefits of such light, high strength material in numerous applications for transportation are such that significant further research is likely.

#### *Lubricants*

42 Nanospheres of inorganic materials could be used as lubricants, in essence by acting as nanosized 'ball bearings'. The controlled shape is claimed to make them more durable than conventional solid lubricants and wear additives. Whether the increased financial and resource cost of producing them is offset by the longer service life of lubricants and parts remains to be investigated (along the lines of the methodology outlined in section 4.5). It is also claimed that these nanoparticles reduce friction between metal surfaces, particularly at high normal loads. If so, they should find their first applications in high-performance engines and drivers; this could include the energy sector as well as transport. There is a further claim that this type of lubricant is effective even if the metal surfaces are not highly smooth. Again, the benefits of reduced cost and resource input for machining must be compared against production of nanolubricants. In all these applications, the particles would be dispersed in a conventional liquid lubricant; design of the lubricant system must therefore include measures to contain and manage waste.

#### *Magnetic materials*

43 It has been shown that magnets made of nanocrystalline yttrium-samarium-cobalt grains possess

unusual magnetic properties due to their extremely large grain interface area (high coercivity can be obtained because magnetization flips cannot easily propagate past the grain boundaries). This could lead to applications in motors, analytical instruments like magnetic resonance imaging (MRI), used widely in hospitals, and microsensors. Overall magnetisation, however, is currently limited by the ability to align the grains' direction of magnetisation.

44 Nanoscale-fabricated magnetic materials also have applications in data storage. Devices such as computer hard disks depend on the ability to magnetize small areas of a spinning disk to record information. If the area required to record one piece of information can be shrunk in the nanoscale (and can be written and read reliably), the storage capacity of the disk can be improved dramatically. In the future, the devices on computer chips which currently operate using flows of electrons could use the magnetic properties of these electrons, called spin, with numerous advantages. Recent advances in novel magnetic materials and their nanofabrication are encouraging in this respect.

#### *Medical implants*

45 Current medical implants, such as orthopaedic implants and heart valves, are made of titanium and stainless steel alloys, primarily because they are bio-compatible. Unfortunately, in some cases these metal alloys may wear out within the lifetime of the patient. Nanocrystalline zirconium oxide (zirconia) is hard, wear-resistant, bio-corrosion resistant and bio-compatible. It therefore presents an attractive alternative material for implants. It and other nanoceramics can also be made as strong, light aerogels by sol-gel techniques. Nanocrystalline silicon carbide is a candidate material for artificial heart valves primarily because of its low weight, high strength and inertness.

#### *Machinable ceramics*

46 Ceramics are hard, brittle and difficult to machine. However, with a reduction in grain size to the nanoscale, ceramic ductility can be increased. Zirconia, normally a hard, brittle ceramic, has even been rendered superplastic (for example, able to be deformed up to 300% of its original length). Nanocrystalline ceramics, such as silicon nitride and silicon carbide, have been used in such automotive applications as high-strength springs, ball bearings and valve lifters, because they can be easily formed and machined, as well as exhibiting excellent chemical and high-temperature properties. They are also used as components in high-temperature furnaces. Nanocrystalline ceramics can be pressed into complex net shapes and sintered at significantly lower temperatures than conventional ceramics.

#### *Water purification*

47 Nano-engineered membranes could potentially lead to more energy-efficient water purification processes, notably in desalination by reverse osmosis. Again, these

applications would represent incremental improvements in technologies that are already available. They would use fixed nanoparticles, and are therefore distinct from applications that propose to use free nanoparticles.

#### *Military battle suits*

48 Enhanced nanomaterials form the basis of a state-of-the-art ‘battle suit’ that is being developed by the Institute of Soldier Nanotechnologies at Massachusetts Institute of Technology, USA (MIT 2004). A short-term development is likely to be energy-absorbing materials that will withstand blast waves; longer-term are those that incorporate sensors to detect or respond to chemical and biological weapons (for example, responsive nanopores that ‘close’ upon detection of a biological agent). There is speculation that developments could include materials which monitor physiology while a soldier is still on the battlefield, and uniforms with potential medical applications, such as splints for broken bones. In section 6.7 we consider the possible social implications of the exploitation of nanotechnologies for military purposes.

### **3.3 Nanometrology**

#### **3.3.1 Introduction to nanometrology**

49 The science of measurement at the nanoscale is called nanometrology. Its application underpins all of nanoscience and nanotechnologies. The ability to measure and characterise materials (determine their size, shape and physical properties) at the nanoscale is vital if nanomaterials and devices are to be produced to a high degree of accuracy and reliability and the applications of nanotechnologies are to be realised. Nanometrology includes length or size measurements (where dimensions are typically given in nanometres and the measurement uncertainty is often less than 1nm) as well as measurement of force, mass, electrical and other properties. As techniques for making these measurements advance, so too does the understanding of nanoscale behaviour and therefore the possibility of improving materials, industrial processes and reliability of manufacture. The instruments for making such measurements are many and varied; a description of some key instruments is given in Box 3.1. The characterisation of materials, particularly in the industrial context, is discussed further in Chapter 4.

50 As with all measurement, nanometrology is essentially an enabling technology. Nanotechnologies, however defined, cannot progress independently of progress in nanometrology. Apart from their direct influence on scientific research and its application, the solutions developed for nanometrology problems can often be exploited elsewhere. For example, the concept of the AFM, a key nanometrology tool, has had a direct influence on lithographic processes and techniques for molecular manipulation. Conversely, it is likely that

continuing research into nanodevices will suggest new measurement methods.

51 Making measurements with nanoscale precision poses several major difficulties. Environmental fluctuations such as vibration or temperature change have a large effect at the nanoscale. For example, any external change to the large machines used in manufacturing microelectronics components will affect the creation of nanoscale features and their crucially important alignment to each other. The ability to measure these influences, and thereafter to minimise them, is therefore vital.

52 Currently, instruments are available that can make sufficiently precise measurements to support laboratory research. There are a number of sensor technologies and instruments with nanometre, or better, sensitivity for measuring length that repeat well if used carefully, including the scanning probe and electron microscopes and some optical devices (see Box 3.1). However, universal measurement standards have not yet been established. Data published recently from the Physikalisch-Technische Bundesanstalt in Germany (Breil et al 2002) shows that even apparently sophisticated users of atomic force microscopes can produce large variations in their measurements of the same artefacts. Without agreed standards, tools or machines cannot be calibrated at the nanometre scale. It is therefore not yet possible for laboratories and manufacturing plants to exchange or compare data or physical components. Also, health and safety standards cannot be set for legal requirements. Nanoparticle characterization for size, size distribution and shape is also lacking formal methods.

53 Evidence presented at our industry workshop highlighted that good comparative metrology is proving difficult to develop. There is no particular difficulty with working at the nanoscale within a single laboratory or organization in the sense artifacts (either universal or in-house ‘gold standards’ such as the spacing of the silicon lattice) can be used to calibrate instruments so that there is self-consistency across a set of measurements. In doing this there must naturally be levels of protection against vibration, thermal changes, etc that are becoming increasingly stringent. However, the determination of absolute measurements of length at the nanometer scale and below is very difficult and expensive.

#### **3.3.2 Length measurement**

54 Although there is not currently an international standard that can be applied to them, calibration artefacts are becoming available for AFMs for length measurement calibration in each of the three dimensions. Such artefacts can also be used for tip characterization, as the exact shape of the fine tip which scans across the surface can strongly influence length measurements, particularly when the tip

becomes blunt. The National Physical Laboratory (NPL) in the UK has a considerable reputation in formal metrology and has done much to develop measurement capability as well as to take responsibility for the UK's national standards. It also has excellent realisations of the metre, mainly through optical and x-ray interferometry, that can calibrate transfer standards with uncertainties of the order of nanometres when working with sufficiently large wave-fronts. However, comparative methods (akin to the interferometric measurement of optical lenses and mirrors) become ineffective when working with very small objects comparable to the wavelength of the photons being used. Hence, it is not yet possible to accurately determine dimensions or shape in all axes. Many surface characterization methods (especially for the electronics industries) directly exploit comparison via x-ray (occasionally optical) reflection or diffraction. It is likely that the practice of length metrology would be improved through better, more easily-used calibration systems and improved instrument design, relative to the current commercial versions. Undoubtedly, better education in best practice for nanometrology would also partly address this issue.

### 3.3.3 Force measurement

55 Along with length measurement, force measurement (measured in Newtons (N)) is likely to become an important area of nanometrology. The control of probe stiffness and geometry will need to improve if truly quantitative measurements of surface mechanical properties can be made, particularly when measuring biological and other soft materials. There is also likely to be an increasing need to accurately measure the elasticity of protein and nucleotide molecules, to determine bond strength and other properties of the molecules. Currently, there is a large capability gap in this field. There is a large, and growing, need for force characterisation in the pico- to micronewton ( $10^{-12}$ – $10^{-6}$ N) range. Currently, no fully satisfactory techniques are available either for secondary standards or transfer artefacts, although a few research projects are in progress (NPL and the National Institute for Standards and Technology (NIST), USA, are both looking at methods based on electrostatic forces). Several groups, mainly within or sponsored by national laboratories (such as NPL and Warwick University in the UK, and NIST in the USA), are investigating systems that relate force to electrical properties and so to quantum standards. However, so far all of them remain experimental and a great deal more work is urgently needed into fundamental and transfer standards for forces much smaller than millinewtons. Unlike length measurement, there is also a lack of readily available and applicable force or mass instrumentation with sensitivity adequate for engineering on the nanometre scale. AFM cantilevers have nanonewton force sensitivity, but their calibration tends to be through indirect calculation from their dimensions, and batch-to-

batch repeatability may be poor. Some nano-indentation instruments for hardness measurement use micro-electromechanical systems (MEMS), with broadly similar questions over traceability. Thus there is urgent need for research into basic laboratory and industrial nanoforce instrumentation alongside that for standards.

### 3.3.4 Measurement of single molecules

56 In the longer term, development in measurement at the scale of the single molecule is expected. Measurements of single organic molecules and of structures such as single-wall nanotubes are already made, providing the molecules can be anchored to a substrate. Electron microscope and AFM/STM determinations of shape are relatively routine in many research laboratories. Increasingly, there is interest in molecule stiffness, in effect producing a tensile test curve in which jumps indicate the breaking and by inference the location of various types of bond in folded proteins and nucleotides. AFM manufacturers are starting to offer options that can do this without the need for the skills of a large research team.

### 3.3.5 Applications

57 Metrology forms the basis of the semiconductor industry and as such is enormously advanced. The International Technology Roadmap for Semiconductors (ITRS) roadmap (see also section 3.4) highlights a series of challenges for nanometrology if it is to keep pace with the reduction in feature size of semiconductor devices. Shrinking feature sizes, tighter control of device electrical parameters and new interconnect materials will provide the main challenges for physical metrology methods. To achieve desired device scaling, metrology tools must be capable of measurement of properties at atomic distances. Compounding these is the uncertain nature of the development of device design, making it difficult to predict metrology needs in the long term and in particular the necessary metrology for manufacturing to ensure reliability. A major need is to integrate metrology data into the manufacturing process.

58 The developing capabilities of semiconductor processing, particularly the ever-reducing dimensions that can be defined using lithographic tools, are being combined with the techniques developed for MEMS device fabrication to enable the manufacture of electro-mechanical components with sub-100nm dimensions. The exploitation of these structures in nano-electromechanical systems (NEMS) devices has produced some interesting and exciting developments in the field of nanometrology. For example, Schwab et al (2000) have made a NEMS device that has enabled the measurement of the quantum of thermal conductance.

59 Another group has made ultra-thin silicon cantilevers with attonewton ( $10^{-18}$ N) sensitivity. These devices have potential applications in the

characterisation of single molecule properties and are examples of how the field of NEMS is increasing the capabilities of nanometrology.

60 The role of nanometrology and in particular the need for the standardisation of measurement at the nanometre scale is explored further in section 8.4.3. There is a need to develop agreed standards that can be used to calibrate equipment that will be used by both industry and regulators. We believe that this can best be addressed through existing programmes such as the Department of Trade and Industry (DTI) National Measurement System Programme and should be undertaken in collaboration with industry.

**We recommend that the DTI supports the standardisation of measurement at the nanometre scale required by regulators and for quality control in industry through the adequate funding of initiatives under its National Measurement System Programme, and that it ensures that the UK is in the forefront of any international initiatives for the standardisation of measurement.**

61 We are pleased to learn that initial steps in this area are being undertaken by the British Standards Institution, as part of the European Committee for Standardisation Technical Board working group on nanotechnology.

### *Box 3.1 Instruments used in nanometrology*

#### *a) Electron beam techniques*

Transmission electron microscopy (TEM) is used to investigate the internal structure of micro- and nanostructures. It works by passing electrons through the sample and using magnetic lenses to focus the image of the structure, much like light is transmitted through materials in conventional light microscopes. Because the wavelength of the electrons is much shorter than that of light, much higher spatial resolution is attainable for TEM images than for a light microscope. TEM can reveal the finest details of internal structure, in some cases individual atoms. The samples used for TEM must be very thin (usually less than 100nm), so that many electrons can be transmitted across the specimen. However, some materials, such as nanotubes, nanocrystalline powders or small clusters, can be directly analysed by deposition on a TEM grid with a carbon support film. TEM and high-resolution transmission electron microscopy (HRTEM) are among the most important tools used to image the internal structure of a sample. Furthermore, if the HRTEM is adequately equipped, chemical analysis can be performed by exploiting the interactions of the electrons with the atoms in the sample.

The scanning electron microscope (SEM) uses many of the basic technology developed for the TEM to provide images of surface features associated with a sample. Here, a beam of electrons is focused to a diameter spot of approximately 1nm in diameter on the surface of the specimen and scanned back and forth across the surface. The surface topography of a specimen is revealed either by the reflected (backscattered) electrons generated or by electrons ejected from the specimen as the incident electrons decelerate secondary electrons. A visual image, corresponding to the signal produced by the interaction between the beam spot and the specimen at each point along each scan line, is simultaneously built up on the face of a cathode ray tube similar to the way that a television picture is generated. The best spatial resolution currently achieved is of the order of 1nm.

#### *b) Scanning probe techniques*

Scanning probe microscopy (SPM) uses the interaction between a sharp tip and a surface to obtain an image. The sharp tip is held very close to the surface to be examined and is scanned back-and-forth. The scanning tunnelling microscope (STM) was invented in 1981 by Gerd Binnig and Heinrich Rohrer, who went on to collect the Nobel Prize for Physics in 1986. Here, a sharp conducting tip is held sufficiently close to a surface (typically about 0.5nm) that electrons can 'tunnel' across the gap. The method provides surface structural and electronic information with atomic resolution. The invention of the STM led directly to the development of other 'scanning probe' microscopes, such as the atomic force microscope. The atomic force microscope (AFM) uses a sharp tip on the end of a flexible beam or cantilever. As the tip is scanned across the sample, the displacement of the end of the cantilever is measured, usually a laser beam. Unlike the STM, where the sample has to be conductive, an AFM can image insulating materials simply because the signal corresponds to the force between the tip and sample, which reflects the topography being scanned across.

There are several different modes for AFM. In contact mode, the tip touches the sample; this is simple to implement but can lead to sample damage from the dragging tip on soft materials. Tapping mode mitigates this difficulty: the tip is oscillated and only touches intermittently, so that dragging during scanning is minimized. Non-contact mode is where the tip senses only the attractive forces with the surface, and causes no damage. It is technically more difficult to implement since these forces are weak compared with contact forces. In non-contact mode at larger tip-surface separation, the imaging resolution is poor, and the technique not often used. However, at small separation, which requires specialized AFM apparatus to maintain, true atomic resolution can be achieved in non-contact mode AFM.

#### *c) Optical tweezers (single beam gradient trap)*

Optical tweezers use a single laser beam (focused by a high-quality microscope objective) to a spot on a specimen plane. The radiation pressure and gradient forces from the spot creates an 'optical trap' which is able to hold a particle at its centre. Small interatomic forces and displacements can then be measured. Samples that can be analysed range from single atoms and micrometre-sized spheres to strands of DNA and living cells. Optical tweezers are now a standard method of manipulation and measurement. Numerous traps can be used simultaneously with other optical techniques, such as laser scalpels, which can cut the particle being studied.

## **3.4 Electronics, optoelectronics and information and communication technology (ICT)**

### **3.4.1 Introduction to electronics, optoelectronics and ICT**

62 The past 30 years has seen a revolution in information technology (IT) that has impacted the lives of many people around the world. At the heart of this revolution is the desire to share information, whether the printed word, images or sounds. This requires a technology that can absorb and process information on one side of the planet and deliver it almost instantaneously to the other in a form that is immediately accessible. Such a technology places enormous pressure on advances in processing and storing information, and on transmitting it and converting it from and to a human readable form. It also increasingly requires secure encryption of information so that access to information can ultimately be restricted to particular individuals.

63 The market size of the IT industry is currently around \$1000 billion, the order of \$150 for every human being on the planet, with an expectation that it will reach \$3000 billion in 2020. In no other industry sector is the trend for miniaturisation so apparent. This is perhaps most obvious by charting the number of transistors, the building blocks of computer chips, over the past 30 years. In 1971 there were just 2300 transistors on Intel's 4004, their first computer chip, with a clock speed (a measure of how fast the chip could operate) of 0.8 million cycles per second. By 2003 the Intel Xeon processor had 108 million transistors operating at clock speeds in excess of 3,000 million cycles per second. Remarkably, the physical size of the computer chip has remained virtually unchanged over this time; it is the transistor and all the circuitry associated with it that has shrunk dramatically. The increase in the number of transistors on a chip coupled with increased speed have fuelled the economics of the IT industry; in 1971 the fabrication of a single transistor cost about 10 cents; it is currently less than one-thousandth of a cent. This evolutionary progression of technology is charted and anticipated in the ITRS roadmap, a worldwide consensus-based document that predicts the main trends in the semiconductor industry 15 years into the future (ITRS 2003). The roadmap which defines in detail all elements of technology that have to be realised for each step change improvement in manufacturing process. This roadmap is used by all industries that are directly or indirectly involved in the manufacture of silicon chips. It identifies material, architecture, metrology and process challenges as well as addressing environmental and health issues in manufacturing.

### **3.4.2 Nanoscience in this area**

64 Nanoscience research in ICT shares many of the same goals as for other applications of nanotechnologies: an improved understanding of nanoscale properties of

materials and devices, advances in fabrication and process technology to satisfy increasingly stringent dimensional tolerances, and exploration of alternative technologies that may offer economic or performance benefit. There is no doubt that the ICT sector has effectively driven a large proportion of nanoscience. Indeed, the first use of the word nanotechnology was in relation to ultra thin layers of relevance to the then up-and-coming semiconductor industry. Since then, the research into all aspects of semiconductor device fabrication, from fundamental physics to process technology, has dominated the nanoscience landscape and will continue so to do. Decreasing device scales will add further impetus to the truly nanoscalar aspects of this global research activity. The ICT sector is, and for historical and economic reasons is likely to remain, heavily silicon-based for the foreseeable future. However, the end of the ITRS roadmap, currently set at 2018 (commonly referred to as the end of Moore's Law) has prompted intensive research into alternative or hybrid technologies for electronics such as conducting polymers, which are discussed further below.

### **3.4.3 Current applications**

#### *Computer chips*

65 The dominant role of miniaturisation in the evolution of the computer chip is reflected in the fact that the ITRS roadmap defines a manufacturing process standard – a technology node – in terms of a length. The current 130 nm technology node that produces the Intel Xeon processor defines the size of the DRAM (dynamic random access memory) half-pitch (half the distance between two adjacent metal wires in a memory cell). This in turn places a requirement on the lithography, process technology and metrology required to manufacture a working device to this tolerance. As a comparison, the 1971 Intel 4004 chip used 10,000 nm technology; the chips of 2007 and 2013 will require 65 nm and 32 nm technology, respectively. In the broadest sense, computer chips in current manufacture are therefore already using nanotechnologies and have been so doing for over 20 years. Furthermore, it is not simply the DRAM half-pitch that is on the nanometre scale. All the technology that goes into the research, metrology and production of chips has been working, in some cases, at the sub-nanometre atomic level. The variety of tools that support the IT industry includes computer modelling of advanced devices and materials atom by atom, microscopies that can image single atoms, metrologies that can define the absolute position of a single atomic defect over a 30 cm diameter wafer (the substrate used for computer chips), thin-film growth processes that can produce layers of material with atomic precision, and lithographies that can 'write' features, such as the DRAM cell, with an accuracy of sub-10 nm.

#### *Information storage*

66 A technology that has necessarily developed in tandem with IT is that of memory for data storage. This

can be divided into two quite different types: solid-state memory such as DRAM that a processor chip would use or flash memory for storing images in a digital camera; and disk-based memory such as the magnetic hard drives as found in all computers. Solid-state memory essentially uses the same processes and technology as the computer chip, with very similar design rules and a similar emphasis on packing more memory into a given area to increase total memory per device. The development of the hard disk drive, however, has taken a quite different route in evolution as it is based on reading and writing information magnetically to a spinning disk. It is therefore primarily mechanical, or more strictly electro-mechanical, and presents quite different technical challenges. Once again, however, the importance of length scales is paramount as the ideal disk drive is one that has the minimal physical size with a massive ability to store data. This is reflected in the evolution of the disk drive over the past 50 years. The first magnetic hard drive was developed by IBM in 1956 and required fifty 24 inch disks to store five megabytes (million bytes) of data. In 1999 IBM introduced a 73 gigabyte (thousand million bytes) drive that could fit inside a personal computer; that is, over 14,000 times the available data storage in a device less than one-thousandth the size of the 1956 drive. Although the individual bits of magnetic information that are written onto the disk drive to give it the high-density storage are currently smaller than 100 nm, the constraints related to this nanotechnology on other aspects of the drive require fabrication of components with even greater precision. The importance of this nanotechnology in the related compact disk (CD) and digital versatile disk (DVD) drives that are now commonplace is equally ubiquitous.

#### *Optoelectronics*

67 The other crucial element of the IT revolution, optoelectronics, relates to devices that rely on converting electrical signals to and from light for data transmission, for displays for optical-based sensing and, in the future, for optical-based computing. Technology in this sector is strongly associated with those described above, and relies substantially on the tools developed there. Although some optoelectronic devices do not depend so critically on miniaturisation as computer chips do, there is nevertheless a similar trend towards miniaturisation, with some existing components, such as quantum-well lasers and liquid crystal displays, requiring nanometre precision in their fabrication.

#### **3.4.4 Applications anticipated in the future**

68 The future development of hardware for the IT industry can be conveniently separated into two paths: a path that is following the well-established ITRS roadmap (which projects out to 2018); and a path that explores alternative technologies and materials that may supersede the roadmap.

69 For the roadmap, miniaturisation remains a key driving force, so that a 22 nm technology node is envisaged for manufacture in 2016. Having set this technology target, it is possible to anticipate all the challenges associated with realising it. Such challenges are detailed extensively in the roadmap but include enhancing performance by introducing new materials such as low dielectrics and higher-conductivity interconnects (wiring), developing lithographies capable of fabricating structures in the sub-50 nm range, and integrating advanced metrology tools into the manufacturing process capable of detecting and sizing defects down to the nanometre size. As such, nanoscience and nanotechnologies will continue to have a pivotal role in developing new generations of chips. Related technology such as flash memory will evolve in a similar fashion, with the aim of maximising memory capacity in the smallest possible device.

70 Hard disk technologies, although not explicitly part of the ITRS roadmap, will continue to increase in memory density. However, there are prospects for some step changes in technology that may significantly change the data storage industry. One obvious potential trend is for solid-state memory to replace disk-based memory. This is already obvious in, for example, personal music players where, as solid-state memory increases in density, hard-disk-based storage is competing with the jog-proof solid-state players. It is likely that the hard disk, whether magnetic or optical, will still be the choice for large volume data storage for the foreseeable future, especially as the bit size shrinks even further. This is an active area of nanoscience research.

71 Optoelectronics, although not as dependent upon length-scale tolerances as computer chips and data storage, will nevertheless have challenges of its own. Integration of optical components into silicon devices has started and can be expected to evolve further. Some of the challenges where nanotechnologies will have an impact will be in the area of photonic band-gap materials, where the propagation of light through a device can be controlled with the aim of computing with light. Photonic crystals, fabricated either through a lithographic process or through a self-assembly technique, confine light into precisely controlled pathways in a device structure so that both transmission and functionality can be combined into a single structure. A typical photonic crystal would consist of an array of holes in a dielectric material, fabricated with sub-10 nm accuracy, so that the periodicity of the holes determines the ability of the material to transmit the light at any given wavelength. The development of photonic crystals could mean that optical integrated circuits are shrunk further, making a significant impact in areas such as communications and optical computing.

72 Quantum computing and quantum cryptography will also benefit from advances in optoelectronics. Both technologies rely on the fact that discrete energy

(quantum) levels increasingly dominate as electromagnetic energy is confined into smaller and smaller structures. Assuming that the considerable technological challenges of making nanostructures from complex materials can be solved, in some cases by designing at the level of the single atom, then on a 10 year time-scale quantum cryptography (a much more secure encryption technology) will replace current encryption methods. On a similar time-scale, quantum computing will start to provide solutions to complex problems that are difficult or impossible to solve by conventional computing.

73 Once controlling where, how and when light interacts is possible by the advances in technology alluded to above, there is the potential for developing new types of optical spectroscopy at the level of the single molecule, assembling nanostructures by arrays of optical tweezers placing objects into patterns on surfaces, new optical lithographic methods for fabricating computer chips, and optical devices that act as biosensors with detection of single molecules. The last type of sensor, able to detect the presence of a single molecule in, say, a drop of blood, represents one of the greatest challenges for nanotechnologies. Not only does it require precision in manufacture, but it also requires a unique mixture of electronics, optics, chemistry, biochemistry and medicine to make devices that can be used routinely, cheaply and reliably to monitor the state of human health. An example of this is in point-of-care health screening where a single drop of blood placed on a sensor chip would be almost instantaneously analysed to provide data to aid a diagnosis. This will require the processing power of a silicon chip with biochemical sensitivity to identify many blood components. This type of monitoring could also begin to be incorporated within the body to provide constant monitoring of health, such as in the control of diabetes or in critical care. There are many other potential applications of such devices in medicine, making this an area of increasing investment.

74 Alternative, 'off-roadmap' technology will have a similar reliance on nanoscience and nanotechnologies as that of the IT sector described above, but with far greater freedom to explore materials and architectures that may have little resemblance to existing technology. Plastic-based electronics is an example of an alternative technology. It does not directly compete with silicon-based devices but, because of its vastly cheaper fabrication, offers a far cheaper alternative. For inexpensive electronic and optoelectronic applications where speed and high memory density are less important, such as smart cards, plastic offers a new approach to building electronics. Plastic-based electronics is already moving into the commercial sector with potential for considerable growth. Similarly, the use of single molecules as functional elements in future circuits will continue to be an important element of nanoscience where the size of the molecule, typically less than 1 nm, offers the ultimate in miniaturisation. In fact, the goal of shrinking function down to single molecules and atoms, foreseen

by Richard Feynman in 1959, is the only way to go beyond the currently foreseen evolutionary limit of the ITRS roadmap; conventional silicon transistors have a size limit of the order of tens of nanometres. Nanoscience is still pursuing the concept of storing and processing information at the atomic scale with the hope of, for example, quantum computing and atomic memory where each bit of data is stored on a single atom.

#### Sensors

75 Nanotechnologies play several important roles in developing sensor technology. First, the ideal sensor will be minimally invasive and therefore as small as possible. This includes the power supply, the sensing action, whereby the detected property is converted into an electrical signal, and the transmission of the sensing signal to a remote detector. Combining these actions into a device that is smaller than 1 mm<sup>2</sup> will certainly require nanofabrication techniques, similar to those employed by the IT industry. The second role for nanotechnologies will be in designing the sensing element to be as specific and accurate as possible; as the sensor dimension decreases the area of the sensor available to effect detection will also decrease, making increasing demands on sensitivity. In the limit of, say, chemical detection this may require detection at the single molecule level; close to the bottom end of the nanotechnology length scale and a significant technical challenge.

76 Nanotechnologies are therefore expected to enable the production of smaller, cheaper sensors with increasing selectivity, which can be used in a wide range of applications. These include monitoring the quality of drinking water, measuring mechanical stresses in buildings or vehicles to monitor for structural damage, detecting and tracking pollutants in the environment, checking food for edibility, or continuously monitoring health. Developments could also be used to achieve greater safety, security, and individualised healthcare, and could offer advantages to business (for example in tracking and other monitoring of materials and products). However, there are concerns that the same devices that are used to deliver these benefits might also be used in ways that limit privacy of groups or individuals; these are considered further in section 6.4. Other potential applications vary from monitoring the state and performance of products and materials to give early warning of the need for repair or replacement to enhancing human capabilities by extending physical performance.

### 3.5 Bio-nanotechnology and nanomedicine

#### 3.5.1 Introduction to bio-nanotechnology and nanomedicine

77 Without doubt the most complex and highly functional nanoscale machines we know are the naturally occurring molecular assemblies that regulate and control biological systems. Proteins, for example,

are molecular structures that possess highly specific functions and participate in virtually all biological sensory, metabolic, information and molecular transport processes. The volume of a single molecule bio-nanodevice such as a protein is between one-millionth and one-billionth of the volume of an individual cell. In this respect the biological world contains many of the nanoscale devices and machines that nanotechnologists might wish to emulate.

78 Bio-nanotechnology is concerned with molecular-scale properties and applications of biological nanostructures and as such it sits at the interface between the chemical, biological and the physical sciences. It does not concern the large-scale production of biological material such as proteins or the specific genetic modification of plants, organisms or animals to give enhanced properties. By using nanofabrication techniques and processes of molecular self-assembly, bio-nanotechnology allows the production of materials and devices including tissue and cellular engineering scaffolds, molecular motors, and biomolecules for sensor, drug delivery and mechanical applications. Bio-nanotechnology can be used in medicine to provide a systematic, as well as a screening, approach to drug discovery, to enhance both diagnostic and therapeutic techniques and to image at the cellular and sub-cellular levels, at a much higher resolution than that of magnetic resonance imaging (MRI).

### **3.5.2 Nanoscience in this area**

79 The primary aim of much current research is to obtain a detailed understanding of basic biochemical and biophysical mechanisms at the level of individual molecules. This knowledge will allow the design rules of naturally occurring molecular machines to be determined, which may lead to new technological applications. As we saw in section 3.3, several tools have developed in recent years, such as SPM, that allow the direct observation of the behaviour of single molecules within biological systems. Examples range from the relatively large (45 nm) rotary molecular motors that power bacterial flagella 'propellers' to the tiny enzymes such as ATP-synthase (9 nm) that catalyse energy conversion in biological processes. The intricate sequence of changes in molecular structure that forms the basis of such biomolecular machines can now be measured directly by using AFM and 'optical tweezers'. The recent development of high-speed AFM has enabled real-time molecular movement within a molecular motor to be observed directly. Future bio-nanotechnology and nanomedicine devices may exploit many classes of functional biological materials. One particular group of proteins that is attracting attention are the membrane proteins; these are another class of protein-based machine that regulate many physiological processes. They include ion channels that enable rapid yet selective flux of ions across the cell membrane, hormone receptors that behave as molecular triggers, and photoreceptors that switch between

different conformational states by the absorption of a single photon of light, the process that is the basis of vision and photosynthesis. That approximately one-quarter of all genes code for membrane proteins provides evidence of their immense biological importance; it is estimated that they will be the target of up to 80% of all new drugs. Single molecule techniques for both observation and manipulation are now being used routinely to study the selectivity and gating mechanisms of ion channels, and their response to drugs.

### **3.5.3 Current and future applications**

80 Bio-nanotechnology is regarded by many experts as a longer-term prospect: much fundamental science must first be investigated, and many applications, especially in the medical field, will by necessity have to undergo strict testing and validation procedures. The time-scale for such applications is 10 years and beyond. In the shorter term it may be possible to use proteins, DNA and other bio-polymers directly in nanoelectronics and biosensor applications, but factors such as biocompatibility and robustness may prove to be serious obstacles. Alternatively, bio-mimetic structures may be devised that are based on naturally occurring machines: examples include catenanes and rotaxanes, compounds that behave as rotary or linear molecular motors, respectively.

81 Applications in the field of medicine are especially promising. Areas such as disease diagnosis, drug delivery and molecular imaging are being intensively researched. Medical-related products containing nanoparticles are currently on the market in the USA. Examples that exploit the known antimicrobial properties of silver include wound dressings containing nanocrystalline silver, which release ionic silver over a sustained period of time to provide a claimed extensive antimicrobial spectrum of 150 different pathogens.

#### a) Array technologies

82 The enormously powerful array technologies, which use relatively large biological samples at the micrometre scale, are continuously being enhanced for sensitivity, size and data analysis. The original DNA chip approach, which carries an array of DNA molecules on an inert carrier, is now routinely used in gene and protein analysis. The push towards higher resolution and smaller sample volume makes this an emerging nanotechnology. Lab-on-a-chip technologies, which are used for sensing and supporting disease diagnosis, are also currently in the micrometre range, but progress in nanofluidic systems will potentially lead to integrated nanoscale systems becoming available. These could have a range of applications, for example in improved devices for detection of biological and chemical agents in the field (Royal Society 2004a).

b) Electronics and information and communication technology

83 One of the objectives of bio-nanotechnology research is to use the highly specialised functionality of proteins in devices such as molecular sensors. One of the greatest challenges is to understand the fundamental electronic properties of such molecules and the mechanisms by which electronic charge is transferred between them and metals, semiconductors and novel nanoelectronic components such as CNTs. Progress in this area could allow these 'smart' molecules to be integrated into devices and networks for specific or indeed ICT applications: the realisation of a protein-based transistor is a major scientific challenge. DNA itself may turn out to be a useful electronic material, although the weight of experimental evidence indicates that it is not a good electrical conductor; however, used as a template, gold or silver 'coated' DNA nanowires can be produced, and integrated circuits using DNA interconnects have already been realised which use the information coded in the DNA.

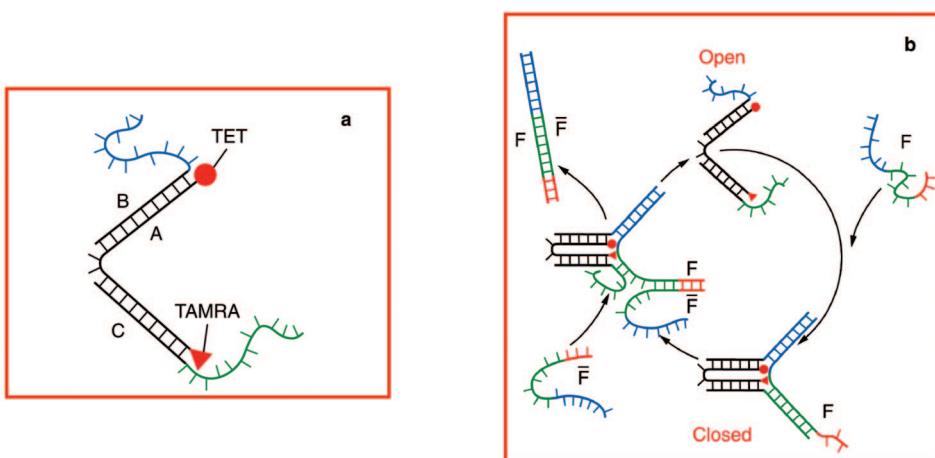
84 Thin films and crystals of the membrane protein bacteriorhodopsin have already been demonstrated to have potential photonics applications such as optically addressable spatial light modulators, holographic

memories and sensors. The photosynthetic reaction centre in this protein, which is only 5 nm in size, behaves as a nanometre diode and so it may be useful in single molecule optoelectronic devices. For example, its integration with electrically conducting CNTs and nanometre electrodes could lead to logic devices, transducers, photovoltaic cells, memories and sensors.

c) Self-assembly

85 The top-down approach to nanofabrication has the advantage that almost any pre-determined structure can be produced. However, much attention is now being focused on processes that involve some degree of molecular self-assembly, and in this respect biological materials have remarkable advantages over inorganic materials in the diversity of self-assembled structures that they can produce. Evolution in the natural world has produced an astonishing variety of biomolecular devices, and compared with conventional technologies, many natural molecular devices display enormous functionality. Among the most outstanding examples of synthetic structures now being fabricated are DNA-based geometrical structures (including artificial crystals) and functioning DNA-based nanomachines (and example of which can be seen in Figure 3.2).

Figure 3.2 DNA nanomachine (a) A simple device composed of three short single strands of DNA can be made to operate as a tweezer that opens and closes on the addition of another strand. The base sequences are chosen to make parts of A and B and parts of A and C complementary with each other so that double strands form; this produces the tweezer that is initially in the open state. (b) The addition of a strand F that is complementary to the unpaired sections of B and C causes the tweezer to close when pairing occurs. The tweezer opens again when a strand Fbar is added that is complementary to F: Fbar pairs with F to form a doubled stranded DNA by-product. The energy source for the machine is the hybridisation energy of the FFbar by-product. (Yurke et al 2000).



86 Hybrid nanomachines, composed of biological material with inorganic components, have been suggested as posing a threat if they are able to replicate. There are ongoing investigations into the application of biological machines that involve incorporation or transport of non-biological components or material, but these are basic molecular constructions compared with even a simple cell. Although they have the ability to move when chemical fuel is added, the working group found no convincing evidence that self-replication, a characteristic of a living organism, is possible.

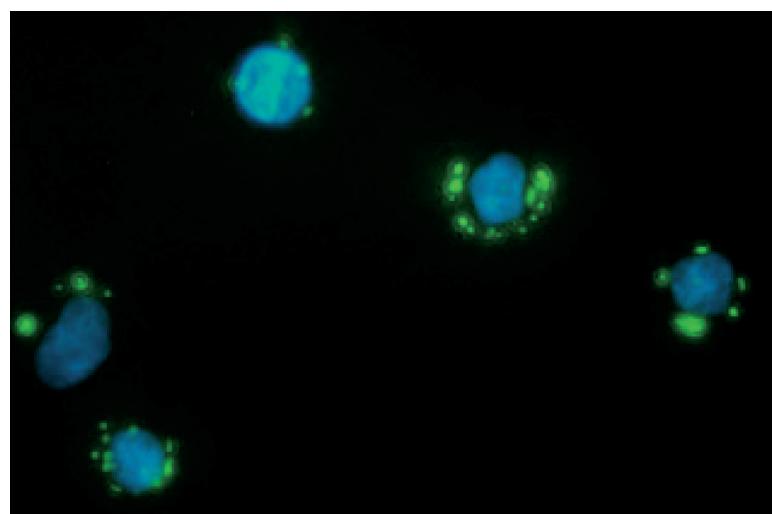
d) Drug delivery

87 There is enormous potential for nanotechnology to be applied to gene and drug delivery. The vehicle might be a functionalised nanoparticle capable of targeting specific diseased cells, which contains both therapeutic agents that are released into the cell and an on-board sensor that regulates the release. Different stages of this approach have already been demonstrated, but the combined targeting and controlled release have yet to be accomplished. In this event the way will be opened up for initial trials, and the eventual approval of such techniques will be fully regulated as for any new pharmaceutical.

88 A related approach already in use is that of polymer-based drug therapies: they include polymeric drugs,

polymer-drug conjugates, polymer-protein conjugates, polymeric micelles to which the drug is covalently bound, and multi-component complexes being developed as non-viral vectors for gene therapy. An illustration of how nanoparticles target cells for drug or gene delivery can be seen in Figure 3.3. Many of these materials are now undergoing clinical trials for a variety of disease states. Gene therapy, where the DNA has been packaged into a nanometre-scale particle, holds much promise for the treatment of genetic defects such as cystic fibrosis and immune deficiencies. Gene therapy using viral vectors has been successfully used to treat ten children with severe combined immunodeficiencies. These are life threatening diseases for which there is no alternative treatment. Unfortunately two of the children subsequently developed leukaemia leading to a temporary moratorium on all gene therapy trials in 2003. After intensive risk assessments most trials have now resumed. Alternative non-viral approaches bio-nanotechnology approaches are being actively researched although none has reached clinical trials. Advantages of these approaches include the versatility of synthetic chemistry, which allows tailoring of molecular weight, addition of biomimetic features to the man-made construct and even the possibility to include bio-responsive elements. The safety implications of nanoparticles in the body are discussed in section 5.3.

*Fig 3.3 An illustration of how nanoparticles target cells for drug or gene delivery. Liver cells (stained blue) surrounded by 200nm semiconductor nanoparticles that have been coated with the outermost protein (E2) of the hepatitis C virus (HCV) which is believed to be the main binding protein. The nanoparticle is the same size as the virus and so it targets cells in the same way as the HCV. (Reproduced by permission James F Leary, University of Texas Medical Branch).*



### e) Drug discovery

89. Nanotechnology techniques offer the possibility of studying drug–receptor interactions at the single molecule level, for example by using optical tweezers and AFM, so that a more direct approach to drug discovery becomes feasible. This approach might also allow, for example, the discovery of disease at the single cell level, long before physical symptoms are manifested. This has been achieved by monitoring changes in atomic forces or ion conductance of a single receptor or ion channel when a drug molecule attaches. However, the industrial process will require the development of large arrays of such instruments working in parallel to create a high-throughput screening capability.

### f) Medical Imaging

90. Non-invasive imaging techniques have had a major impact in medicine over the past 25 years or so. The current drive in developing techniques such as functional MRI is to enhance spatial resolution and contrast agents. Nanotechnologies already afford the possibility of intracellular imaging through attachment of quantum dots or synthetic chromophores to selected molecules, for example proteins, or by the incorporation of naturally occurring fluorescent proteins which, with optical techniques such as confocal microscopy and correlation imaging, allow intracellular biochemical processes to be investigated directly.

### g) Nanotechnologies and cancer treatment

91. In the USA the National Nanotechnology Initiative has claimed that nanotechnology has potential in the treatment of cancer. It has been stated that ‘It is conceivable that by 2015, our ability to detect and treat tumors in their first year of occurrence might totally eliminate suffering and death from cancer’ (Roco 2004). We have, however, seen no evidence to support the notion that nanotechnologies will eliminate cancer in the short- to medium term, and feel that such a claim demonstrates an over-simplistic view of the detection and treatment of cancer. Although it is reasonable to

hope that some measures based on nanotechnologies may make contributions to detection and treatment of some forms of cancer, other factors such as a greater understanding of environmental causes of cancer, public health measures, and advances in surgical, pharmacological and radiological management are important in the reduction of incidence of and death from cancer.

### h) Implants and prosthetics

92. As discussed in section 3.2, some nanomaterials such as nanocrystalline ceramics have certain properties – such as hardness, wear resistance and biocompatibility – that may make them of use as implants in the long term. The development of nanoelectronic systems with high detector densities and data processing capability might allow the development of an artificial retina or cochlea. Important progress is already being made in this area, but many issues must be resolved before they can become viable treatments. Similarly, the introduction of nanoelectronics will allow biological neural processing to be investigated at much enhanced spatial resolution. Neurons of rodents have already been grown on nanofabricated surfaces to form elementary neural networks in which electrical signalling can be measured. By sending and receiving electrical impulses from the network, it might begin to be possible to understand how neurons create memory by their responses to different patterns of stimuli.

93. It is hoped that this research might help some visually impaired people regain their sight, or that muscle function might be restored to sufferers of Parkinson’s disease. However, these developments raise potential ethical concerns about human enhancement and the convergence of technologies, in particular whether the availability of body alterations that enhance human performance might diminish the role of disabled people in society, and whether progress in information processing and data storage technologies combined with developments in neurophysiology could lead to the possibility of non-therapeutic enhancement of human performance. These concerns are explored in section 6.5.



# 4 Nanomanufacturing and the industrial application of nanotechnologies

## 4.1 Introduction

1 In the previous chapter, we saw many examples of nanoscience and some current and potential applications of nanotechnologies. Current industrial applications of nanotechnologies are mainly in the characterisation of materials, the production of chemicals and materials, precision manufacturing and ICT. In general, these applications represent incremental rather than truly disruptive advances; however, in the longer term it is likely that many manufacturing processes will be influenced by nanotechnologies, just as they are today by ICT.

2 In this chapter we outline how nanotechnologies are being realised in industry, focusing on the generic methods of nanomaterial manufacture, production rates and applications in some key industry areas. We indicate how nanoscience and nanotechnologies might impact on industry in the longer term, and highlight some of the factors that will affect the commercialisation of nanotechnologies. A detailed consideration of these issues for the UK can be found in the Taylor report (DTI 2002). Our aim, in particular, is to provide an appropriate background for Chapter 5, in which we discuss the health, environmental and safety impacts of nanotechnologies. We have focused disproportionately on the manufacture and use of nanoparticles and nanotubes, because they raise particular concerns, but it should be noted that nanoparticles and nanotubes only account for a small fraction of the predicted global market for nanotechnologies.

## 4.2 Characterisation

3 The characterisation of materials – the determination of their shape, size, distribution, mechanical and chemical properties – is an important

part of the industrial process. It serves two broad purposes: as quality control, and as part of the research and development of new processes, materials and products. Evidence taken during our industry workshop suggested that many areas of industry did not consider nanotechnologies to be new (for example, nanoscale structures have been important to the catalyst industry for over 100 years). However, the industrialists believed that a nanotechnology ‘breakthrough’ had occurred in the tools used to observe and measure properties and processes at the nanoscale level. Sophisticated tools, such as the STM, AFM and TEM (see Box 3.1), enable surface and interfacial characterisation of materials at the nanoscale, allowing individual atoms to be observed and analysed. This is leading to greater understanding of the relationship between form and material properties, and enabling the control of processes at the nanoscale and the design materials with specific properties. However, the commercialisation of such advanced functional materials requires that they can be made in a predictable, reliable way, and in sufficient quantities. Until that is achieved production will be limited to academia and R&D departments within industry.

## 4.3 Fabrication techniques

4 There are a wide variety of techniques that are capable of creating nanostructures with various degrees of quality, speed and cost. These manufacturing approaches fall under two categories (first introduced in Chapter 2): ‘bottom-up’, and ‘top-down’. In recent years the limits of each approach, in terms of feature size and quality that can be achieved, have started to converge. A diagram illustrating some of the types of materials and products that these two approaches are used for is shown below in Figure 4.1.

Figure 4.1 The use of bottom-up and top-down techniques in manufacturing

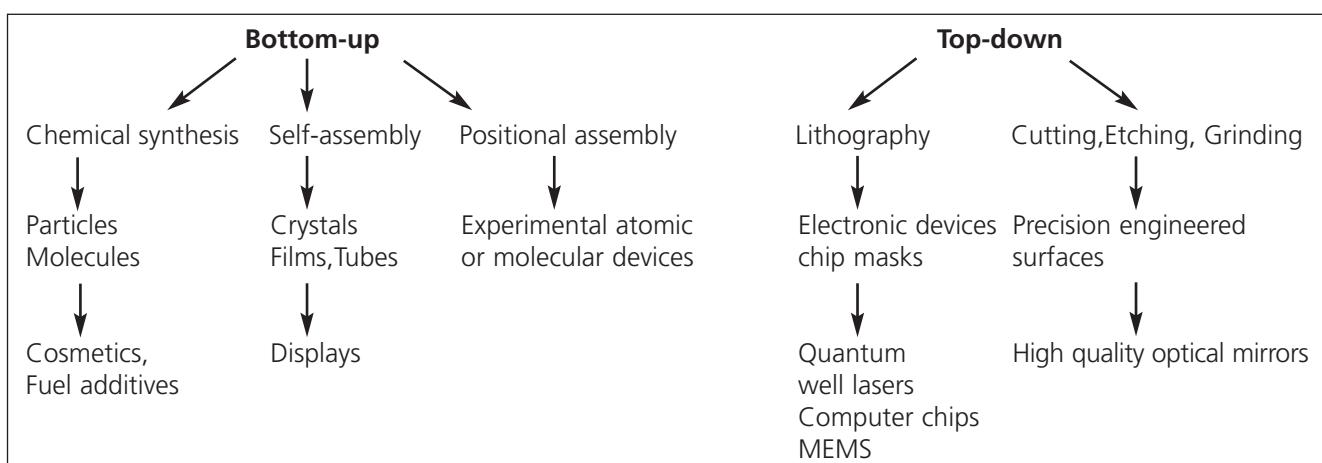
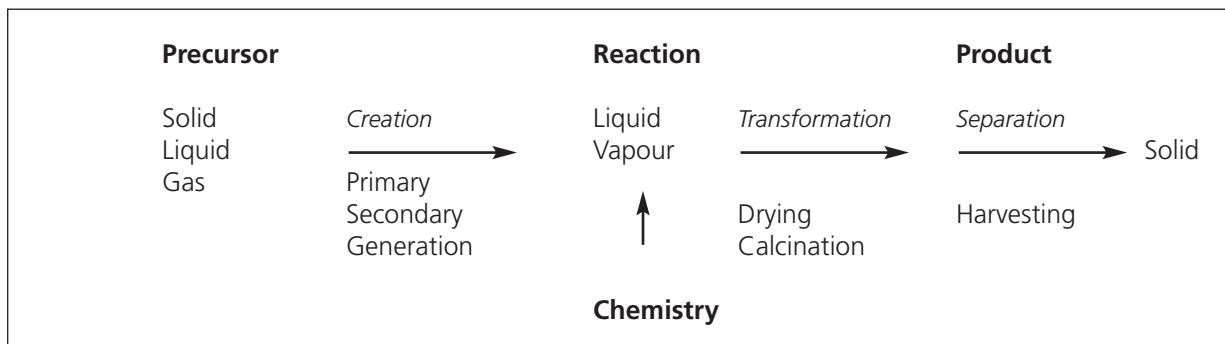


Figure 4.2 The generic processes that are involved in the production of nanoparticles



#### 4.3.1 Bottom-up manufacturing

5 Bottom-up manufacturing involves the building of structures, atom-by-atom or molecule-by-molecule. The wide variety of approaches towards achieving this goal can be split into three categories: chemical synthesis, self-assembly, and positional assembly. As discussed below, positional assembly (with its many practical drawbacks as a manufacturing tool) is the only technique in which single atoms or molecules can be placed deliberately one-by-one. More typically, large numbers of atoms, molecules or particles are used or created by chemical synthesis, and then arranged through naturally occurring processes into a desired structure.

##### a) Chemical synthesis

6 Chemical synthesis is a method of producing raw materials, such as molecules or particles, which can then be used either directly in products in their bulk disordered form, or as the building blocks of more advanced ordered materials, produced using the techniques outlined in sections (b) and (c) below.

7 A generic process by which nanoparticles may be produced by chemical synthesis is shown in Figure 4.2.

8 The precursor phase is the starting point, and the material can be in any physical state (or multiphase) or spatial arrangement to other components. The first step is the creation of a new phase or state where the nanoparticles either form or can be formed by a chemical step. In other words, the phase change itself could bring about nanoparticle formation (rare but possible) although generally the circumstances are created whereby nanoparticles can be made, for example vaporisation of a precursor mixture. Once in a state where nanoparticles can be made, usually a chemical reaction of some description is performed to generate the desired material. A further phase transformation or even solid-state reaction may be necessary to produce the final product.

9 Potential exposure of the workforce to nanoparticles is likely to be greatest when these materials are processed

in a gaseous environment; in such cases worker exposure will need to be monitored closely. However, nanoparticles have a tendency to agglomerate, and are therefore often manufactured from a liquid phase as this enables surface energies to be better controlled, reducing agglomeration. This also reduces the potential exposure level of workers. The expected health impacts of nanoparticles and the implications for regulation in the workplace are discussed in sections 5.3 and 8.3, respectively. Processing and handling ability is very important for nanomaterials: mixing nanoscale particles together before agglomerating and (for example) sintering can generate wholly new complex nanophase materials which could not be made by any other method. Most genuinely nanoscale and nanostructured materials, however, are still at the laboratory scale of synthesis (kilograms per day scale of operation or even less).

10 Table 4.1 gives our estimates of current and future production of nanomaterials. Metal oxides, such as titanium dioxide, zinc oxide, silicon dioxide, aluminium oxide, zirconia and iron oxide, are currently the most commercially important nanoparticles. They are available as dry powders or liquid suspensions. The quantities currently used in the skincare market sectors (titanium dioxide etc.) amount to 1,000–2,000 tonnes per annum worldwide, with the nanoscalar component materials worth approximately \$10 to \$100,000 per tonne. Although the world market for nanoparticles is expected to increase during the next few years, to provide perspective, it is worth noting that the global production rate of all chemicals is around 400M tonnes per annum (European Commission 2001), and so chemicals in nanoparticulate form account for only a tiny fraction of the total (around 0.01%) currently produced. Nanoscalar inorganic, metallic or semiconductor material often will have multifunctionality, which enables it to be used across many industry sectors. Zinc oxide, for example, will have more commercial use as an optoelectronic material (for displays or advanced solar and photovoltaic cells) where it will be fixed in the final product, than as an ingredient for skincare products, where particles will be free.

*Table 4.1 Estimated global production rates for various nanomaterials and devices based on international chemical journals and reviews (2003–2004), and market research (BCC 2001). These rates are intended for guidance only, as validated numbers are commercially confidential.*

| <b>Application</b>                     | <b>Material/device</b>  | <b>Estimated production rates (tonnes/annum)</b> |                  |                  |
|--|---|--|------------------|------------------|
|  |   | <b>Present</b>                                   | <b>2005–2010</b> | <b>2011–2020</b> |
| Structural applications                | Ceramics, catalysts, composites, coatings, thin films, powders, metals  | 10   | $10^3$           | $10^4$ – $10^5$  |
| Skincare products                      | Metal oxides (titanium dioxide, zinc oxide, iron oxide)   | $10^3$   | $10^3$           | $10^3$ or less   |
| ICT                                    | Single wall nanotubes, nano electronics, opto-electro materials (titanium dioxide, zinc oxide, iron oxide), organic light-emitting diodes (OLEDs) | 10   | $10^2$           | $10^3$ or more   |
| Biotechnology                          | Nanoencapsulates, targeted drug delivery, bio-compatible, quantum dots, composites, biosensors  | less than 1                                      | 1                | 10               |
| Instruments, sensors, characterisation | MEMS, NEMS, SPM, dip-pen lithography, direct write tools  | 10   | $10^2$           | $10^2$ – $10^3$  |
| Environmental                          | Nanofiltration, membranes   | 10   | $10^2$           | $10^3$ – $10^4$  |

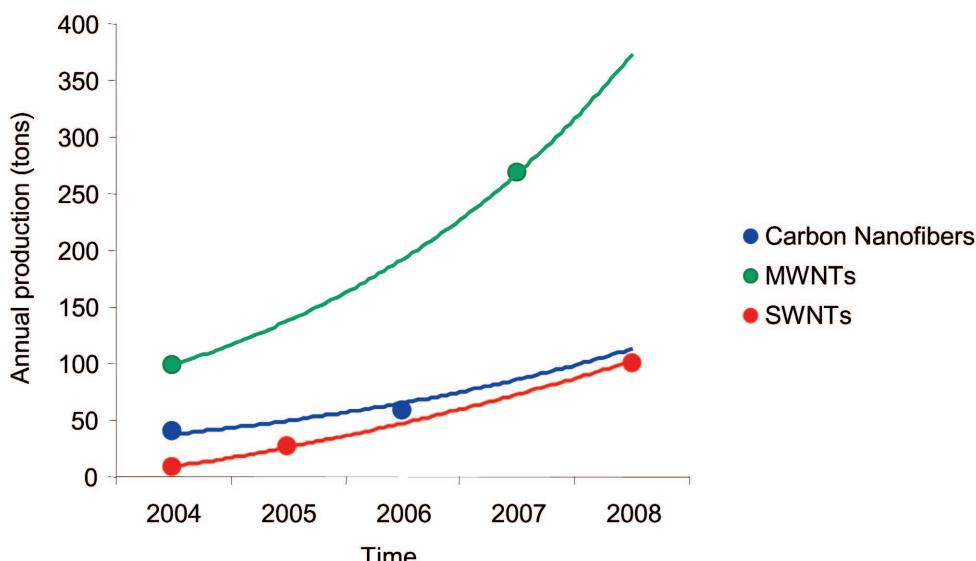
### b) Self assembly

11 Self assembly is a bottom-up production technique in which atoms or molecules arrange themselves into ordered nanoscale structures by physical or chemical interactions between the units (see Chapter 2). The formation of salt crystals and snowflakes, with their intricate structure, are examples of self-assembly processes. Although self assembly has occurred in nature for thousands of years, the use of self assembly in industry is relatively new. There is an economic and environmental interest in processes through which materials or product components essentially form themselves, creating less waste and using less energy. However, current understanding extends only to the creation of fairly rudimentary systems. Improved understanding of thermodynamic and kinetic processes at the nanoscale, enabled through advances in the characterisation techniques described in section 4.2 and Box 3.1, and improved computer modelling, are

expected to aid the development of more complex systems. One potential processing technique involves the use of an external force or field (for example, electric or magnetic) to accelerate the often slow self-assembly process, which is attractive in an industrial context. This is known as directed self assembly.

12 As we saw in section 3.2.3, CNTs are generating interest within industry because of their remarkable properties. Potential applications include composites, conductive plastics, sensors, batteries and fuel cells. CNTs can be grown by several techniques, such as the laser ablation of metal-doped graphite targets, carbon arc discharge, and the pyrolysis of hydrocarbons over metal catalysts. However, because of a lack of understanding of the growth mechanism, the selective and uniform production of CNTs with specific dimensions and physical properties has yet to be achieved (as, indeed, has an industrial process for separation of the spaghetti-like bundles that are

Figure 4.3 Estimated future global production of nanotubes (Cientifica 2004)



currently produced). This is an area of intense research. Current production capacity for CNTs is estimated to be around 100 tonnes per annum (Cientifica 2004); the actual production output remains commercially confidential, but is expected to be lower. Most of the capacity is estimated to be multi-walled tubes, with single-wall tubes accounting for about 9 tonnes of capacity. Estimated future global production of nanotubes is outlined in Figure 4.3.

#### c) Positional assembly

13 The final bottom-up technique is positional assembly, whereby atoms, molecules or clusters are deliberately manipulated and positioned one-by-one (see Chapter 2). Techniques such as SPM for work on surfaces, or optical tweezers in free space, are used for this. Positional assembly is extremely laborious and is currently not suitable as an atomic-scale industrial process. As described in Chapters 2 and 3, the utility and strength of SPM in industry lie in their ability to characterise and measure surfaces with atomic-level precision, rather than as fabrication tools.

14 The fact that (albeit very rudimentary) structures can be fabricated atom-by-atom has led to speculation that tiny nanoscale machines could be made which could be used in parallel to manufacture materials atom-by-atom. The idea is to fabricate one or a few machines (or assemblers) that would first make copies of themselves, and then go on to make materials in parallel, in principle solving the problem of slow production speed. This speculation has led some individuals to voice fears of uncontrollable self-replication, known as 'grey goo', which are discussed in Annex D. Such concerns currently belong in the realm of science fiction. We have seen no evidence of the

possibility of such nanoscale machines in the peer-reviewed literature, or interest in their development from the mainstream scientific community or industry. Indeed, the originator of concerns over grey goo, Eric Drexler, has since retracted his position (Phoenix and Drexler 2004).

#### **4.3.2 Top-down manufacturing**

15 Top-down manufacturing involves starting with a larger piece of material and etching, milling or machining a nanostructure from it by removing material (as, for example, in circuits on microchips). This can be done by using techniques such as precision engineering and lithography, and has been developed and refined by the semiconductor industry over the past 30 years. Top-down methods offer reliability and device complexity, although they are generally higher in energy usage, and produce more waste than bottom-up methods. The production of computer chips, for example, is not yet possible through bottom-up (or hybrid top-down/bottom-up) methods are under exploration (see sections 3.4.4 and 4.3.3).

#### a) Precision engineering

16 In general, ultra-precision engineering and manufacture underpin much of the micro-electronics industry in everything from the production of the flat low-damage semiconductor wafers used as substrates for computer chips, to the mechanical stages used to position the wafers, to the manufacture of the precision optics used to print the patterns on the wafers. In addition, the techniques of ultra-precision engineering are used in a variety of consumer products such as computer hard disks, CD and DVD players.

17 Ultra-precision machine tools can now achieve very high performance in terms of both the accuracy with which form can be defined (up to 1 part in  $10^7$ , or better than 100 nm over distances of tens of centimetres) and the surface finishes that can be achieved (0.5–1 nm root mean square surface roughness), although these are currently on simple shape surfaces and with low output levels. This capability, which is bringing benefits in several areas (see (b) below), has been achieved through a combination of advances. These include: the use of advanced materials for cutting tools, based on diamond or cubic boron nitride; very stiff, precise machine tool structures; new linear and rotary bearing designs employing fluid films; and sensors for size control combined with numerical control and advanced servo-drive technologies. Very precise process and temperature control is needed to achieve this performance (the latter being of the order of  $\pm 0.01^\circ\text{C}$ ).

#### b) Lithography

18 As discussed in section 3.4, manufacturing in the ICT sector predominantly involves lithographic processes that pattern a semiconductor wafer in a sequence of fabrication steps. Lithography involves the patterning of a surface through exposure to light, ions or electrons, and then subsequent etching and/or deposition of material on to that surface to produce the desired device. The ability to pattern features in the nanometre range is fundamental to the success of the IT industry and the ITRS roadmap. The main lithographic tools can be conveniently separated into methods that use a focused beam of electrons or ions to write patterns, and those that rely on the projection of light through a mask to define a pattern over a complete semiconductor wafer. Electron- and ion-based methods are both capable of making sub-10 nm structures (with electron beam lithography having the greatest routine resolution), but they are too slow to be used directly in production. Optical lithography is used for production of semiconductor devices. Although it does not have the resolution of the beam-based techniques, it provides rapid throughput and cost-effective manufacture. Electron beam lithography is primarily used to fabricate the masks used for optical lithography, and ion beam techniques are mostly used to repair masks and for specialist device applications.

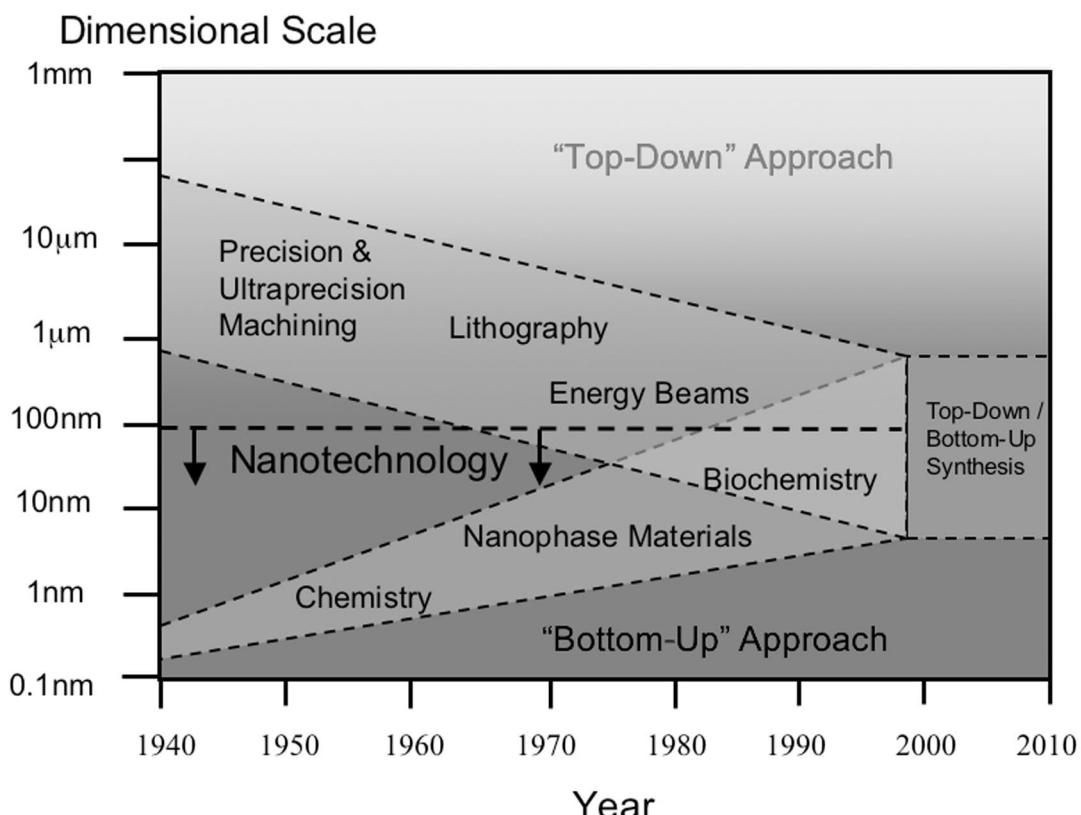
19 The requirement for ever-shrinking device structures has placed enormous technical demands on optical lithographic process, as the nanostructures have length scales similar to or less than the wavelength of the illuminating light (ultraviolet). Despite these difficulties, the ITRS roadmap implicitly expects optical lithography to keep track of future device dimensions until 2016 when the target critical device dimension reaches 22 nm.

20 Techniques developed in the microelectronics industry have also enabled the miniaturisation of small mechanical moving devices (MEMS), which in turn have led to research into NEMS. MEMS technology seeks to exploit and extend the capabilities that have been provided by silicon integrated circuit manufacturing from one of making chips for electronic signal processing to the provision of on-chip sensing and/or actuation through the use of moving mechanical parts. Some MEMS technologies are starting to attain maturity in manufacture (for example, MEMS accelerometers are used widely in air-bag sensors). However, there are currently difficulties in the reproducible large-scale manufacture of more complex MEMS systems. Although not strictly a ‘nanotechnology’ as defined in this report, MEMS, NEMS and the technologies used to make them are used extensively in techniques that can access and exploit the nanoscale (such as SPMs or lab-on-a-chip and biosensing). The reducing dimensional tolerances (less than 100 nm) being provided by modern lithographic patterning techniques are now enabling the production of structures of such small dimensions that they are becoming a legitimate part of nanotechnologies in their own right.

#### **4.3.3 Convergence of top-down and bottom-up techniques**

21 The relationship between top-down and bottom-up manufacturing is illustrated in Figure 4.4. The ‘top-down’ section is an updated version of the diagram produced by Norio Taniguchi, which showed the development in the accuracy of artefact definition from the early 20th century to 1974, extrapolated to the end of the century. The ‘bottom up’ section illustrates how bottom-up processes have evolved to control ever-larger structures through advances in chemical processing. Now the dimensions that can be controlled by either approach are of a similar order, and this is leading to exciting new hybrid methods of manufacture.

Figure 4.4 The convergence of top-down and bottom-up production techniques (Whatmore 2001)



## 4.4 Visions for the future

### 4.4.1 Precision Engineering

22 There are strong drivers to reduce tolerances in engineering, including miniaturisation, improved wear and reliability characteristics, automated assembly and greater interchangeability, reduced waste and requirement for re-work. As the trend towards miniaturisation continues, research and the industrial application of energy beam processing methods will increase, driven in particular by the electronics and computer industries. Techniques such as electron beam lithography (EBL), focused ion beam (FIB), reactive ion etching (RIE) and femtosecond pulsed laser ablation are becoming more accurate and cheaper to apply in a production context. Some examples of future applications of high-precision engineering are given below.

- ICT: the machines used to fabricate chips depend fundamentally upon the use of ultra-high precision techniques for their manufacture and nanometrology techniques for their operation. The manufacture of larger-diameter semiconductor wafers with improved flatness and reduced sub-surface damage should lead to improved device yields and reduced costs.
- Optics: innovative ductile-mode grinding processes, together with electrolytic in-process dressing (ELID),

should result in the elimination of polishing in the production of high-quality optical devices. This is likely to be of particular importance in the production of the optics for extra-large astronomical telescopes such as the proposed 50 m and 100 m systems (Euro50 and OWL), which will consist of many individually figured segments (Shore et al 2003).

- Transport: precision-machined parts should be more reliable, because of reduced wear, requiring fewer replacement parts and less energy consumption. For example, the ability to produce surfaces with controlled textures through finishing to 10 nm average roughness followed by laser surface treatment is expected to lead to improved power transmission trains with losses through slip reduced by up to 50%. Precision manufacturing is predicted to lead to weight reductions in airframe wings and to improve the performance of internal combustion chambers.
- Medical: it is hoped that the use of ultra-precision machining techniques to produce improved surface finishes on prosthetic implants should lead to lower wear and better reliability.

23 It is hoped that advances in precision engineering will enable the reduction of environmental impacts by, for example, reducing the use of lubricants. However, for any particular product, the whole life cycle needs to be taken into account before it can be established

whether there is a net environmental benefit. This is discussed further in section 4.5.

#### **4.4.2 The chemicals industry**

24 The long-term goal within the chemicals industry is to use nanoscale ‘building blocks’ to assemble organised nanostructures, that can in turn be manufactured into commercially useful products. From an understanding of the chemistry and physics of nanoscale materials, and top-down/bottom-up modelling and measurement, industry will concentrate on processes that use manufacturing at the nanoscale in a way that preserves the desired effect and function as nanoscale components are combined into macroscale materials and products. This will involve the development of technologies based on self-assembling materials, or more probably on directed-assembly methods, which allow for some form of massively parallel production, along with modelling and measuring tools. The vision is the manufacture of reproducible, accurate and designable nanomaterials.

25 The time-scale for the commercial exploitation of these types of highly organised structures or quantum materials is approximately 2020 and beyond, for use in the biotechnology and IT sectors. These materials will be extremely valuable, in excess of \$1,000,000 per tonne, with the production rates of the order of 10–10,000 tonnes a year. The price is expected to remain relatively high because, though the effect of the nanomaterial will be to add value to consumer products, it will only form a tiny fraction of the final product as sold.

26 The desired functionality is created through exploiting structure – property relationships. Measurement, modelling and simulation are essential for the characterisation and subsequent control of property and functional performance and therefore the production of desirable materials. The development of measurement tools for use at the nanoscale will move from laboratory-based characterisation to in-line and on-line methods of monitoring and controlling accuracy at the 6-sigma level (99.9997% accurate) in terms of reproducible structure, texture and surface properties. The use of computer simulation based on advanced structure – property – process predictor codes will become the key technology for manufacture-by-design, where the characteristics of the material are effectively ‘dialled up’ through morphology, texture, structure and reactivity based on the interaction of materials across molecular- and nano-length scales. The structure or form of the material then dictates the processing options for economic, reliable and reproducible operation. The combination of measurement, modelling and manufacturing technologies will be the basis for intelligent material systems. It is also hoped that it will be possible to produce materials with less waste.

27 The synthesis and control of micro- and nano-scale

structures may yield unprecedented control of meso- and macro-scale properties in functional materials for use in applications of direct relevance to industry. It has been predicted (Chemical Industry 2003) that over the course of the century, many of the needs of commerce and society may be satisfied through a materials revolution involving synthesis and smart fabrication. Because of some of the barriers outlined in section 4.6 it is difficult to predict when these developments might occur, but we provide some estimated timeframes in Box 4.1.

*Box 4.1 Estimated timeframes for developments in nanomanufacturing*

Short term (next 5 years): opportunities will arrive through the exploitation of equipment capable of imaging, analysing and fabricating simple materials and devices at the nanoscale.

Medium term (5–15 years): nanoscience and technology will give rise to nanomanufacture-by-design, using self-assembly and directed assembly methodologies to create a sustainable knowledge-based industry capable of addressing simple bio–info–nano material needs.

Longer term: it is hoped that the idea of nanomanufacturing will encompass genuine ‘green’ concepts of zero waste and little or no solvent use incorporating life cycle (sometimes referred to as ‘cradle to grave’) concepts of responsible products coupling biology with inorganic materials.

#### **4.4.3 The information and communication technology industry**

28 Although the future of device fabrication is still centred around the lithographic processes described in section 4.3.2, there are other techniques that are increasingly being applied both to on-roadmap developments and to alternative approaches to device materials. Soft lithography techniques where a flexible master is used to stamp out patterns on a range of surfaces have been available for several years. The accuracy demands imposed by the silicon-based industry have, until now, prohibited the use of soft lithographies as the elastic nature of the stamp can cause small, but still unacceptable, physical distortions across a wafer surface. However, for small-area device fabrication and for applications where spatial tolerances are less restrictive, they offer a real alternative to conventional methods, although the fabrication of the master still requires optical or electron beam methods. Soft lithographies can be used for plastic electronics, as can alternative ink-jet based methods which use essentially the same technology as desk-top printers. Although plastic electronics are not truly in the nano-range in terms of critical dimensions, a relatively simple

manufacturing technique that can deal with wet chemistries will enable cheap electronic and photonic devices. Such developments, combined with advances in directed self-assembly, may bring the semiconductor, materials and chemical industries closer together, in order to create novel alternative methods for chip production as the end of the roadmap approaches.

#### 4.5 Resource management and environmental issues

29 It has been claimed that several nanotechnology-based applications and processes will bring environmental benefits, for example through fewer resources required in manufacture or improved energy efficiency in use. It is important to substantiate such claims by checking that there are indeed net benefits over the life of the material or product.

30 The potential benefits of nanotechnologies should be assessed in terms of life cycle assessment (LCA) (sometimes referred to as 'cradle-to-grave' analysis). LCA is the systematic analysis of the resource usages (for example, energy, water, raw materials) and emissions over the complete supply chain from the 'cradle' of primary resources to the 'grave' of recycling or disposal. For example, one of the areas of application foreseen for nanomaterials is in photovoltaic (PV) energy converters in order to increase efficiency. An LCA would investigate the extent to which the additional energy yield over the service life of a PV device would be offset by any additional energy used in manufacturing the device and in recovering or disposing of its material content at the end of its life.

31 To illustrate the importance and associated complexity of such analyses, an example can be taken from the possible use of nanotechnologies in the transport sector. As we have seen in section 3.2.3b, reducing the weight of aircraft is a foreseeable application, for example through use of CNT composites and thinner (that is, lighter) paints and coatings. Available LCA studies on aircraft show that the resource use and environmental impacts of aircraft in flight currently outweigh those from aircraft construction by several orders of magnitude (Energy Technology Support Group 1992). The first assumption has therefore been that technological developments towards 'lightweighting' are always beneficial. This assumption would need to be tested for nanoengineered materials where end-of-life disposal may have an adverse environmental impact. Also, the basis on which reducing aircraft weight is assessed needs to be defined carefully to avoid reaching simplistically optimistic conclusions. In practice, it is likely that reductions in aircraft weight will be exploited by increasing payload, i.e. carrying more passengers, which if the market were fixed would bring environmental benefits due to fewer flights. However, if this is used to decrease ticket costs, it could stimulate additional passenger movements, albeit using

less fuel per passenger-kilometre flown. The true trade-off to be considered is between the benefits of additional passenger movements rather than the environmental performance of the aircraft and the impacts of producing nano-engineered materials. Thus the superficially simple environmental assessment ends up involving social and ethical issues.

32 LCA is now a standardised and accepted tool, covered by a set of international standards (ISO 14040–14044) and is the basis of much European environmental policy including the End-of-Life Directives (see section 8.3.5). We are aware of only one study (in progress at Carnegie Mellon University, USA, funded by the US Environmental Protection Agency) applying LCA approaches to nanotechnology-enabled products and processes, and we welcome the inclusion of LCA in a recent Communication from the EC (European Commission 2004a). **We recommend that a series of life cycle assessments be undertaken for the applications and product groups arising from existing and expected developments in nanotechnologies, to ensure that savings in resource consumption during the use of the product are not offset by increased consumption during manufacture and disposal. To have public credibility these studies need to be carried out or reviewed by an independent body.**

33 **Where there is a requirement for research to establish methodologies for life cycle assessments in this area, we recommend that this should be funded by the research councils through the normal responsive mode.**

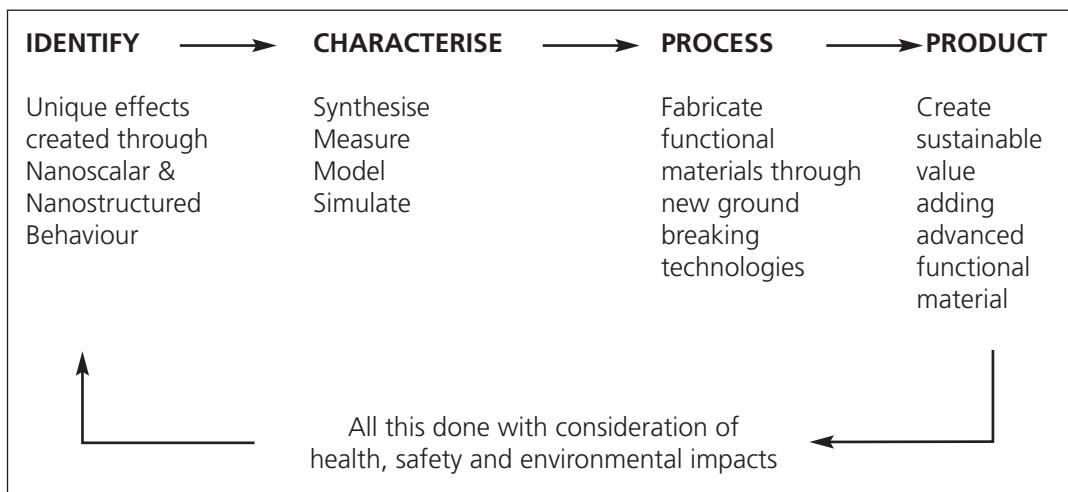
#### 4.6 Barriers to progress

34 There are several factors that will influence whether nanotechnologies will be used routinely within industrial processes. Some of these are economic or social, others are technical.

35 Any new process or technology must be able to exceed (in terms of economic value) what is already in place, and it must be of value (or perceived value) to the consumer, to be adopted by industry. As we have heard in evidence from Don Eigler and others, the technology used in current industrial processes is already generally very advanced, and so nanotechnologies will only be used where the benefits are high. This economic reality may well act to moderate their rate of introduction.

36 The technical barriers should not be underestimated: as well as the difficulty in scaling a process up from the laboratory to an industrial operation, more fundamental barriers stem from a lack of understanding of nanoscale properties and the techniques to characterise and engineer them to form useful materials and products. Figure 4.5 summarises the

*Figure 4.5 The generic steps that are undertaken to manufacture nanomaterials, from identification of properties through to production*



generic technical steps that needed to be undertaken to produce a material with designed functionality.

37 The current technical barriers to achieving the steps outlined in Figure 4.5 are as follows:

- Inadequate characterisation and measurement tools and capabilities to enable on-line and in-line monitoring and processing control based on nanoscalar features.
- Insufficient understanding to enable the design and production of desired material properties through the development of multi-phase, multiple length-scale mathematical models that are capable of linking effectively across structure–property–processing boundaries. This is crucial if we are to preserve functionality from the nanoscalar synthesis through to the creation of macroscopic functional materials.
- Insufficient knowledge to synthesize complex heterogeneous nanostructured large-scale, self-assembled monolayers (SAMs) and directed assembly of monolayers (DAMs). Of great practical interest are DAMs whereby scale-out (reliable replication of a process) will be key to the development of continuous nanomanufacturing processes (NSF 2001; DTI 2002).

38 Alongside purely technical barriers to progress are those relating to regulation such as classification and standardisation of nanomaterials and processes, and the management of any health, safety and environmental risks that may emerge. Appropriate regulation and guidance informed by scientific evidence will help to overcome some of these barriers, and there are already discussions between industry and regulators on the above issues. Until these regulatory measures are in place, industry will be vulnerable to reduced consumer confidence, uncertainty over appropriate insurance cover (Swiss Re 2004) and litigation should some

nanomaterials prove to be harmful. These issues will be of particular importance to the smaller, more innovative companies. Health, safety and environmental impacts of some nanomaterials are discussed in Chapter 5 and regulatory issues are discussed further in Chapter 8.

39 Naturally, the development and exploitation of new technologies or techniques cannot proceed without a sufficiently trained workforce. This point has been made strongly for the UK in the Taylor report (DTI 2002), by the EC in its recent communication on nanotechnology, and by the House of Commons Science and Technology Committee report on UK Government investment in nanotechnology (House of Commons Science and Technology Committee 2004a). However, it is not part of the remit of our study.

## 4.7 Summary

40 In their widest sense, nanotechnologies have been used by industries for decades (semiconductors), and in some cases considerably longer (chemicals). However, developments over the past 20 years in the tools used to characterise materials have led to an increased understanding of the behaviour and properties of matter at very small size scales. Increased knowledge of the relationship between the structure and properties of nanomaterials has enabled the production of materials and devices with higher performance and increased functionality. This progress has taken place steadily over several years; so, at least so far, the influence of nanotechnologies on industry can be described as evolutionary rather than revolutionary. This is also evident in the current production rates of nanoparticles and nanomaterials which, although increasing, are negligible compared with bulk chemicals and materials.

41 True nanomanufacturing is therefore very much in its infancy; however, there are strong economic, societal

and environmental reasons why its development is currently the focus of so much attention. At the same time, there are uncertainties about the direction the technology may take and about the hazards to humans

or the environment presented by certain aspects of nanotechnologies. The health, environmental and safety aspects of nanoparticles and nanotubes are discussed in Chapter 5.

# 5 Possible adverse health, environmental and safety impacts

## 5.1 Introduction

1 In Chapters 3 and 4 we have outlined the ways in which researchers and industry hope to exploit the unique properties of nanomaterials and the processes of nanomanufacturing for medical applications and to deliver environmental benefits. Current medical applications of nanotechnologies include anti-microbial wound dressings, and it is anticipated that future applications will include more durable and better prosthetics and new drug delivery mechanisms. Current research into applications of nanotechnology includes efforts to reduce the amount of solvents and other harmful chemicals in manufacturing, to improve energy efficiency and energy storage capabilities, and to remove persistent pollutants from soil and water supplies, all of which offer hope of benefiting the environment and increasing sustainability. In section 4.5 we highlighted the need to incorporate a life cycle assessment approach into the research and development of products and processes arising from nanotechnologies to ensure that they do not result in a net increase in resource use. In this chapter we consider potential adverse health, environmental and safety impacts of nanotechnologies.

2 Whereas the potential health and environmental benefits of nanotechnologies have been welcomed, concerns have been expressed that the very properties that are being exploited by researchers and industry (such as high surface reactivity and ability to cross cell membranes) might have negative health and environmental impacts and, particularly, that they might result in greater toxicity. The public who participated in the market research that we commissioned expressed worries about possible long-term side effects associated with medical applications and whether nanomaterials would be biodegradable. Analogies were made with plastics, which were once hailed as 'the future' but which have proved to have accompanying adverse effects on individuals and the environment (BMRB 2004).

3 Almost all the concerns expressed to us, in evidence and during our workshop on health and environmental impacts of nanotechnologies, related to the potential impacts of manufactured nanoparticles and nanotubes (in a free rather than fixed form) on the health and safety of humans, non-human biota and ecosystems. The fact that nanoparticles are on the same scale as cellular components and larger proteins has led to the suggestion that they might evade the natural defences of humans and other species and damage cells. It is important to set these concerns in context by noting that humans have always been exposed to some types of nanoparticles arising from natural sources such as atmospheric photochemistry and forest fires, and exposures to millions of pollutant nanoparticles per breath have been commonplace since the first use of fire.

4 Manufactured nanoparticles and nanotubes are important because they are among the first nanoscale technologies used in consumer products, but as Table 4.1 makes clear, the production rates of these materials is only a small fraction of the predicted potential for nanotechnologies. The IT industry also uses nanotechnologies, both in techniques used and the minimum feature size of devices; however, in contrast to manufactured nanoparticles and nanotubes, it does not present any unique hazards. There is an important distinction between applications that use nanoscalar active areas on larger objects (for example, nanometre-scale junction regions in transistors, which form part of a millimetre-sized chip and are therefore fixed), and chemicals or pharmaceuticals in which the nanometre-scale 'active area' is a discrete nanoparticle or nanotube. Although a computer chip with 100 million nanostructures presents a potential hazard for manufacture, disposal or recycling, these issues are related to the bulk materials, which make up the chips (for example, gallium), rather than to the nanostructures within them. Although nanoscience and nanotechnologies may involve individual scientists and other workers using or being exposed to a range of chemical reagents and physical processes that could imply harm to their health, such exposures to substances and materials other than nanoparticles are covered by existing understanding and regulation. They are not considered further in this report except in that they may be in the form of discrete particles incorporated into materials in the nanometre size range.

## 5.2 Assessing and controlling risk

5 The general approach to assessing and controlling risk involves identification of hazard (the potential of the substance in question to cause harm) and then a structured approach to determining the probability of exposure to the hazard and the associated consequences. Risk is usually controlled in practice by reducing the probability of exposure, although the first principle of risk management is to substitute less hazardous for more hazardous substances where possible. An appreciation of hazard (for example, toxicity or likelihood of explosion) is required to determine to what extent exposure should be controlled. Risk is controlled by limiting release of the material to air or water, and/or by interrupting the pathways by which the substance reaches the receptor where it could cause harm (for example an organ in the body), making an understanding of exposure pathways and likely quantities essential to risk management. In any new technology, foresight of possible risks depends on a consideration of the life cycle of the material being produced. This involves understanding the processes and materials used in manufacture, the likely interactions between the product and individuals or the environment during its manufacture and useful life, and the methods

used in its eventual disposal. Some of the definitions used in this chapter are outlined in Box 5.1.

#### Box 5.1 Definitions

**Hazard** is defined as the potential to cause harm: hazard is typically assessed by toxicology, for example testing harmful potential on cultured cells or isolated organs (*in vitro*) or directly on laboratory animals or humans (*in vivo*). Another hazard is the potential for clouds of combustible nanoparticles to explode.

**Exposure** is the concentration of the substance in the relevant medium (air, food, water) multiplied by the duration of contact.

**Dose** is defined here as the amount of a substance that will reach a specific biological system, and is a function of the amount to which the individual is exposed, namely the exposure, taking account of the fact that a proportion is eliminated by the body's natural defences and does not reach the target organ.

**Risk** is a quantification of the likelihood of such harm occurring: risk is assessed from consideration of the likelihood of exposure, the dose and the inherent toxicity of the substance to which people or other organisms may be exposed. Sometimes, in the case of materials to which exposure has already occurred, risk may be measured directly by the techniques of epidemiology.

6 Manufactured nanoparticles might be used in products where they are not fixed (such as sunscreens), be used to form composites from which they might later be released, be formed during the self-assembly of nanomaterials (again from which they might later be released), or be created if nanomaterials are damaged or break down. For physical harm to occur, humans or other organisms must come into contact with the materials or be involved in the processes in such a way that the material contacts or enters the body and takes part in reactions with cells, leading to tissue-damaging reactions. Any such damage might be anticipated if the material has toxic properties and reaches the target organ in sufficient dose (defined in Box 5.1). Some of the possible routes by which exposure might occur now and in the future after release of a nanoparticle are illustrated in Figure 5.1. If the material is released into the air, it may be inhaled directly. This is the dominant pathway for humans exposed to manufactured nanoparticles released in the workplace, and for all organisms exposed to nanoparticles from sources such as combustion. In addition to inhalation by air-breathing organisms, exposure to nanoparticles could occur from surface contact (for example in cosmetic skin preparations) or from ingestion (if nanoparticles are to

be added to food or drink in the future). In the future, medicinal applications may result in particles being injected into the body. Other organisms such as bacteria and protozoa may take in nanoparticles through their cell membranes, and thus allow the particles to enter a biological food chain.

7 In this chapter we examine the possible hazards from nanoparticles before going on to consider the exposure pathways, any current exposure levels and how these might be managed to reduce the risk from manufactured nanoparticles and nanotubes. We address the important gaps in scientific understanding of possible interactions between nanoparticles, the environment and people, and outline the areas of research necessary to reduce these uncertainties. Ways in which regulation might be used to manage any risks presented by free nanoparticles or nanotubes are discussed in Chapter 8.

### 5.3 Human health

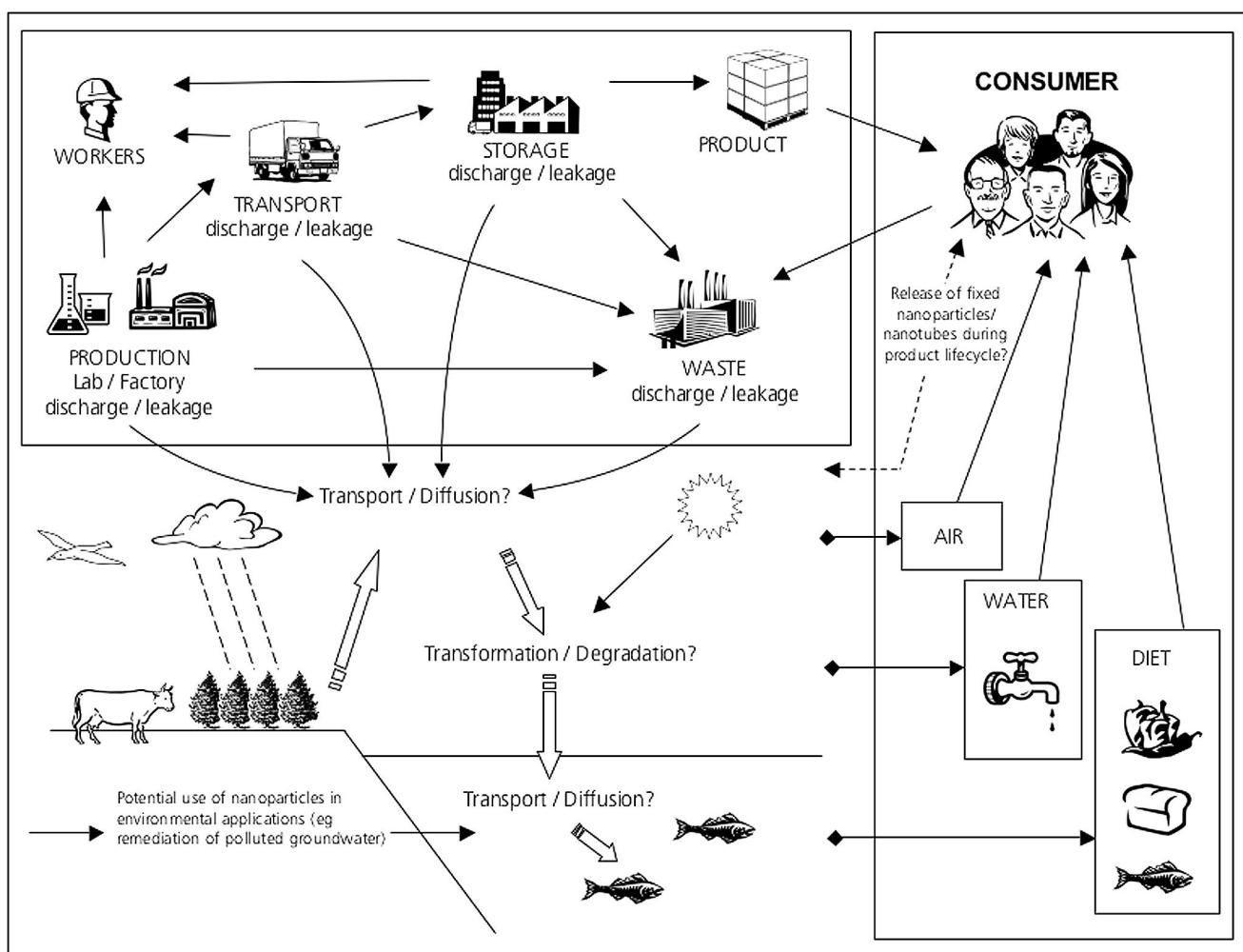
#### 5.3.1 Understanding the toxicity of nanoparticles and fibres

8 To understand the potential risks to humans from nanoparticles, it is necessary first to consider briefly the body's defences against particles in general and the properties that particles require to overcome these defences. Throughout much of their evolutionary history, humans have been exposed to small particles, often in very high concentration, and the mechanisms evolved for defence against micro-organisms are also used to defend the body against such particles. Access to the human body can occur through the lungs, the skin or the intestinal tract. Each organ presents a barrier to penetration by micro-organisms or other particles. Nevertheless, despite the defence mechanisms outlined in Box 5.2, certain particles have proved to have toxic effects on humans, just as have certain micro-organisms. In general this is a consequence of properties that either allow them to evade or cause damage to defensive mechanisms. An understanding of these mechanisms is of importance to estimate the possible toxic effects of nanoparticles or nanotubes. Three types of particle in particular have provided relevant information: the minerals quartz and asbestos, and the particles associated with air pollution.

##### a) Evidence from exposure to quartz

9 Quartz is a mineral to which many millions of workers have been exposed, for example in mining and stone working. Exposure for a few years to micrometre-sized particles, in concentrations of the order of a milligram per cubic metre of air, leads to a potentially fatal form of lung fibrosis (Seaton 1995). Toxicological studies have shown that relatively low exposure to micrometre-sized particles of quartz causes severe lung

Figure 5.1 Some possible exposure routes for nanoparticles and nanotubes based on current and potential future applications. Very little is known about exposure routes for nanoparticles and nanotubes and this figure should be considered with this in mind (Adapted from National Institute for Resources and Environment, Japan [http://www.nire.go.jp/eco\\_tec\\_e/hyouka\\_e.htm](http://www.nire.go.jp/eco_tec_e/hyouka_e.htm)).



inflammation, cell death, fibrosis and tumours in rats (Vallyathan 1994). This has been demonstrated to be related to the surface of the quartz crystal, which is highly reactive and generates free radicals (reactive atoms or molecules), leading to oxidative damage to the defensive cells that take up the particles. It is likely that this surface activity is a fundamental aspect of the toxicity of particles but one that varies considerably between different types of particle. Other mineral particles encountered in industry, such as coal and various silicates, are less toxic but are still capable of causing similar diseases when inhaled in higher doses. It is now believed that inhaled particles in general, even when they have a low intrinsic toxicity to cells, may cause disease of the lungs if the dose is sufficiently high by overloading the lung defences, and that this property relates to the total surface area of the particles inhaled (Faux et al 2003). Thus studies of mineral particles have demonstrated that the toxic hazard is related to the surface area of inhaled particles and their surface activity. The risk relates to the dose inhaled.

#### b) Evidence from exposure to asbestos

10 The effects of asbestos have also been studied in great detail (Mossman et al 1990). Inhalation by workers of this natural fibrous mineral is known to cause several different diseases of the lung and its lining (the pleura), most of which prove fatal. Fibres are defined as particles with a length at least three times their diameter. Fibres narrower than about  $3\mu\text{m}$  have aerodynamic properties that allow them to reach the gas-exchanging part of the lung when inhaled, whereas those longer than about  $15\mu\text{m}$  are too long to be readily removed by macrophages (Figure 5.2). Once lodged in the deep lung, their toxicity depends upon an ability to initiate an inflammatory reaction, involving attraction of macrophages and other defensive cells, which, if sufficiently widespread, may eventually lead to scarring (asbestosis) and lung cancer. Over decades, migration of fibres through the lung to the pleura in sufficient numbers leads to the development of mesothelioma, a fatal tumour. Studies in rats have shown that the likelihood of a fibre, be it asbestos or some other natural or man-made fibre, to cause these

## *Box 5.2 Human defences against particles*

### Lungs

In the lung, small particles may be filtered out of the inhaled air by deposition on the airway wall and removal to the throat by the rhythmical beating action of microscopic protrusions (cilia) from the lining cells of the airways, or they may reach the gas-exchanging tissues and be engulfed by phagocytic cells called macrophages. These cells then carry the particles up the airways or through the lungs to lymphatic vessels and thence to lymph nodes. Both mechanisms tend to remove the particles from areas where they have the potential to cause harm and to neutralise their toxicity. However, an overwhelming dose may lead to excessive inflammation, scarring and destruction of lung tissue, as exemplified by bacterial pneumonia or industrial lung diseases such as asbestosis.

### Skin

The skin is protected by a layer of dead cells (the epidermis or stratum corneum), covered by a hydrophobic (water-repelling) lipid layer. Beneath the epidermis is a layer of living cells supplied by nerves and blood vessels, the dermis. Within the dermis are glands that produce sweat and the protective secretion, sebum. The blood supply of the dermis allows recruitment of inflammatory cells when the skin is attacked by bacteria or otherwise damaged, enabling protective inflammation and tissue repair. Prolonged or repeated inflammation, such as may be induced by certain chemicals or by sunlight, may lead to skin damage and cancer. The epidermis is normally impermeable to particles and micro-organisms but is readily damaged (for example, by cuts and abrasions) or perforated (for example, by specialised insects or by therapeutic injections). Several skin diseases such as allergies can also impair its ability to withstand toxic agents.

### Gut

The epithelium of the gut differs from the other external epithelia in that its primary function is to allow absorption of substances into the body. However, unless diseased, it is impermeable to large molecules such as proteins (the largest of which are tens of nanometres in size), which it needs to break down before absorption, and to particles and micro-organisms. The high acidity of the stomach has an important microbial function, as well as a digestive one, and may dissolve some particles and affect toxins in various ways. The lower gut has a highly specialised secretory and absorptive epithelium that produces mucus and digestive enzymes and is richly supplied with blood and lymphatic vessels, allowing it to recruit defensive cells and remove penetrating micro-organisms if necessary. Research into better formulations for drug delivery has shown that some nanoparticles may be taken up by gut lymphatic vessels (Hussain et al 2001). Much disease of the gut relates to infections and to adverse reactions to foods. Environmental and occupational causes of diseases of the gut, other than these, are uncommon.

diseases depends critically on its solubility. Fibres that dissolve readily are likely to break into shorter particles that are easily removed by macrophages, and so are unlikely to persist long enough to cause such diseases (Mossman et al 1990). This has been supported by studies of human lungs, which have shown differential persistence of different fibre types in exposed workers with asbestos-related diseases (Wagner et al 1982). Asbestos is present in the fabric of many buildings and in cities, and all of us have some in our lungs. In contrast, those who develop asbestos-related diseases usually prove to have millions of fibres in every gram of lung tissue as a consequence of cumulative exposure to concentrations of several hundred fibres in every breath when they are exposed to the mineral at work over months or, more often, years (Wagner et al 1982). Thus, studies of asbestos and other fibres have shown that their toxicity depends on the two physical factors, length and diameter, and two chemical factors, surface activity and durability (ability to resist degradation). Again, the risk relates to the dose reaching the target organ.

### c) Evidence from exposure to air pollution

11 Whereas studies of mineral dusts and asbestos have shown the importance of particle size, surface reactivity and dose in the causation of lung disease, the most direct evidence on nanoparticles comes from studies of air pollution. Any combustion process produces nanoparticles in vast numbers from condensation of gases. Initially only about 10nm in diameter, these rapidly coalesce to produce somewhat larger aggregates of up to about 100nm, which may remain suspended in the air for days or weeks (Figure 5.3). The sources of such combustion nanoparticles range from volcanic activity and forest fires, to the use of fires for heating and cooking, and more recently industrial and traffic pollution (Dennekamp et al 2002). Modern scientific interest in air pollution started after the disastrous London smog episode in December 1952, when some 4000 excess deaths occurred over a two-week period. Particle concentrations were as high as several milligrams per cubic metre, and most of these particles were in the nanometre size range. Reductions in pollution as a result of legislation to restrict coal burning have prevented such serious episodes from occurring

Figure 5.2 Four macrophages attempting to ingest an asbestos fibre (approximately 80 µm long). (Reproduced by permission of Professor Ken Donaldson, University of Edinburgh).



subsequently in UK cities. Nevertheless, from the 1980s, a series of epidemiological studies has provided evidence that exposure to the particulate fraction of air pollution is associated with both heart and lung disease and is still responsible for measurable morbidity and mortality in urban areas as outlined in Box 5.3 (Brook et al 2004). This seems to be the case despite the fact that concentrations in western cities are now measured in concentrations of only a few tens of micrograms per cubic metre.

*Box 5.3 Observed epidemiological associations between particulate air pollution and health*

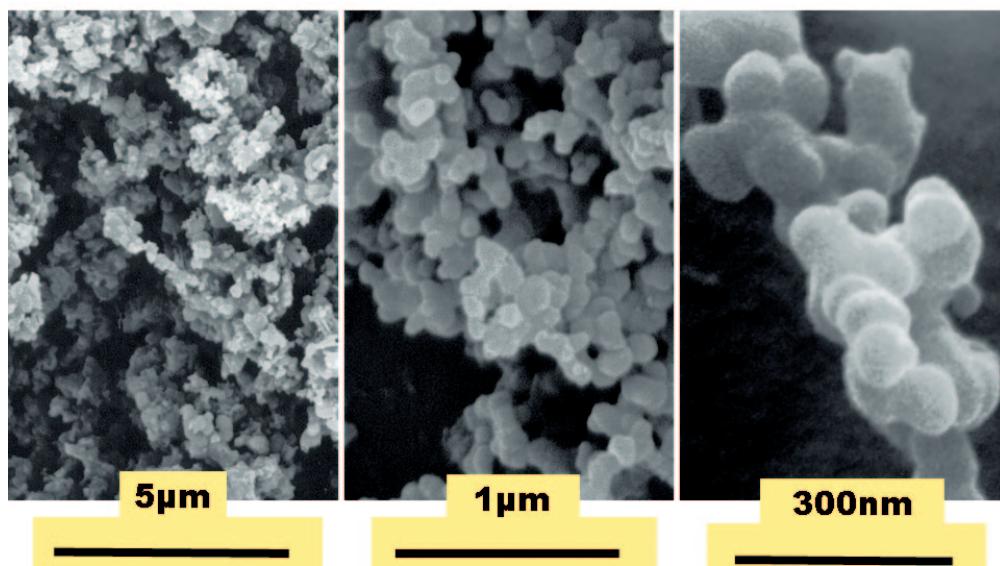
- Death from and exacerbation of heart disease in vulnerable people.
- Death from and exacerbation of chronic lung disease in vulnerable people.
- Exacerbations of asthma.
- Long-term increase in risk of death from heart attack and lung cancer.
- Possibly, precipitation of cot death and stroke in vulnerable individuals.

12 Air pollution is caused by a complex mix of particles and gases. However, there appear to be consistent associations between exposure to the particulate fraction and adverse health effects. In seeking to explain these, two difficult facts have had to be considered. First, the concentrations associated with measurable effects on health in populations are extraordinarily low – for example, rises of only 10 µg/m<sup>3</sup> are consistently associated with an increase in cardiac deaths of about 1%. Secondly, the particles comprise chemicals generally believed to be non-toxic, mostly carbon and simple ammonium salts. It seemed unlikely that inhalation of less than a milligram of non-toxic particles over 24 hours (a human breathes about 20 m<sup>3</sup> per day and urban concentrations average about 20–30 µg/m<sup>3</sup>) could cause a heart attack. Consideration of this problem led to the hypothesis that the adverse heart and lung effects are due to the action

of the nanoparticulate component of the pollution on susceptible individuals, reflecting the point made above for quartz: that the total surface area and the surface activity hold the key to toxicity (Seaton et al 1995). Although the mass concentration of nanoparticles is low, it still amounts to some tens of thousands of nanoparticles per millilitre of urban particle counts (Figure 5.4). This concentration implies that one inhalation of 300 ml will contain several million such particles, over half of which will be retained within the lungs. Activities such as cooking, driving in traffic or being in the presence of smokers entail breathing much higher concentrations. Since all are exposed yet few suffer adverse effects, it is generally believed that air pollution exerts its adverse effects on a minority of individuals who, because of prior illness, are particularly susceptible.

13 These studies of air pollution have therefore shown that although we are all exposed to very many, very small, apparently non-toxic particles on a regular basis, only relatively few of us succumb to their effects, but such effects may occur at very low mass concentrations. The concept that nanoparticles in air pollution might be responsible for the observed adverse health effects has promoted interest in their toxicology, and this interest is expanding rapidly. Review of *in vivo* animal studies supports the hypothesis that there may be a general effect of low-toxicity particles of all sizes that depends on the total surface area inhaled (Faux et al 2003); further investigation has shown that, weight for weight, finely divided particles of a material, such as titanium dioxide or carbon black, are more toxic than larger particles of the same material (Ferin et al 1990; Oberdörster 1996). This toxicity is largely explained by the presence of transition metals on the surfaces of some types of nanoparticle and their subsequent ability to promote release of free radicals in contact with body tissues (Donaldson et al 2001). However, other nanoparticles with no transition metals appear to achieve their effects by their large surface area and the ability of this surface to generate oxidative stress on cultured cells or isolated organs (*in vitro*) or directly on laboratory animals or humans (*in vivo*) by as yet

Figure 5.3 Soot nanoparticles viewed using Field Emission Scanning Electron Microscopy. (Reproduced by permission of Professor Roy Richards, University of Cardiff).



unknown mechanisms (Brown et al 2000). In both cases, nevertheless, the observed effects are related to the total surface area of inhaled particles and to the chemical reactivity of that surface, a sufficient dose to the lungs leading to inflammation and secondary effects on the blood that in turn lead to increased risk of lung and heart illness in susceptible individuals.

14 Owing to universal exposure to air pollution, and despite the defence mechanisms outlined in Box 5.2, many particles of all sizes do in fact enter the body mainly through the lungs, having been taken up by macrophages and transferred into the interstitial tissues. Some remain in the lung while some are removed through draining lymphatic vessels to lymph nodes and the blood stream. After death it is usually possible to find traces of the minerals to which workers have been exposed in their lungs (Seaton et al 1981), and very small amounts may be found in other tissues. Nanoparticles are probably removed from the lung more efficiently than somewhat larger ones, although inter-species differences are known to occur (Churg and Brauer 1997; Bermudez et al 2004). It is likely that a proportion of this removal is by the blood stream.

15 A few specifically designed epidemiological studies on human populations have investigated the cellular reactions demonstrated by *in vitro* and *in vivo* toxicology (Seaton et al 1999; Schwartz 2001). However, it is often difficult to attribute responsibility to one or other component of the air pollution (Seaton and Dennekamp 2003), and air pollution particles themselves are of differing chemistry and likely to include metallic atoms and molecules that will influence their toxicity. In general, epidemiological studies of air pollution point towards the finer particles rather than the coarser causing harm, although gases such as nitrogen oxides

(which correlate closely with particle number) also show associations with several negative health impacts (Seaton and Dennekamp 2003).

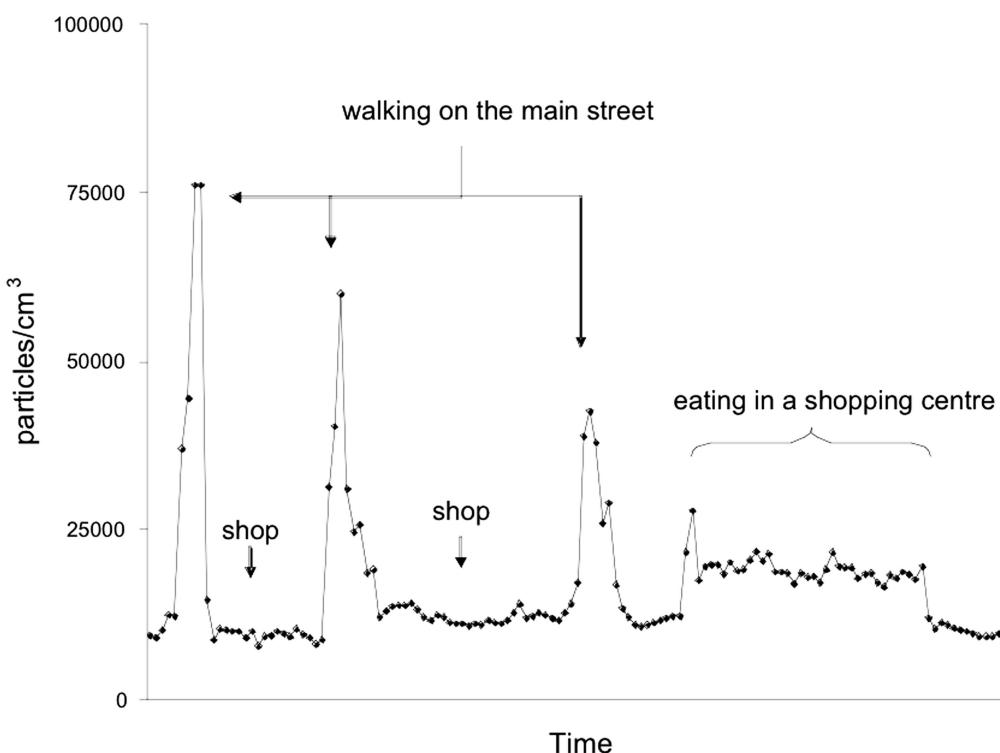
16 Observations linking air pollution episodes with cardiac responses (Peters et al 2000) and with changes in heart rhythm and sometimes blood pressure (Peters et al 1999) have led to suggestions that, as well as a humoral (or blood-borne) response, a short-term neural response to air pollution may occur. The mechanism for a response by the nervous system is not clear and is currently an area of active research. Nanoparticles would be a strong candidate (though not the only one: gases might have such an effect) for the role of initiator of the neural reflex; viruses may use nerves for transmission (Bodian and Howe 1941), and recent work has suggested that manufactured nanoparticles may penetrate and pass along nerve axons and into the brain (Oberdörster et al 2004b). There is also some evidence that metals characteristic of air pollutants may be found in the brains of urban dogs (Calderón-Garcidueñas et al 2003), and it is possible that transfer of particles along the nerves concerned with smell may provide a transport mechanism. More research on the neurotransmission of nanoparticles is needed.

17 The most significant finding from research into air pollution particles for the hazard of nanoparticles is that cells and organs may demonstrate toxic responses even to apparently non-toxic substances when they are exposed to a sufficient dose in the nanometre size range.

d) Evidence from medical applications of nanoparticles

18 Further information on the effects of nanoparticles on the human organism comes from the pharmaceutical

*Figure 5.4 Exposure to particles over the course of a four hours spent in Aberdeen City centre. Measurements were taken using a PTrak continuous particle counter which counts all particles below 500nm, though in ambient air the very large majority are below 100nm. (Data collected by Martine Dennekamp, University of Aberdeen)*



industry. For many years pharmaceutical scientists have studied the fate of nanometre-scale particles with the aim of developing novel drug delivery systems for pharmaceutical compounds (see section 3.5). These studies have been undertaken on spherical particles and have explored different routes of delivery including inhalation, ingestion, injection and transdermal delivery. Given the barriers to uptake of particles in the lungs, gut and skin, much of the knowledge on the fate of nanoparticles has been derived from studies of drug delivery by injection. It is known that after such administration the nanoparticles are taken up by macrophages in the liver and spleen. Ultimately, depending on their solubility and surface coating, they may be excreted by the kidneys (Borm and Kreyling 2004). In general, the options for removal of all foreign matter are excretion in urine or breath, through the gut by bile excretion, or in dead cells shed from the body. The use of surface coatings has enabled some particles to influence these disposal mechanisms and allowed them to be selectively deposited in particular organs or cells (Illum et al 1987). This suggests that surface coating might allow some nanoscale material to be directed to specific organs and that tests for toxicity need to take account of these coatings. It also implies the possibility that less desirable nanoparticles may penetrate into cells or cross natural barriers, such as those between the blood and the brain, that serve as important defences against harm.

### 5.3.2 Manufactured nanoparticles and nanotubes

19 In this section we consider the health impacts of manufactured nanoparticles and nanotubes, current and potential exposure routes and levels, and discuss ways of managing any potential risks.

20 The understanding derived from studies of air pollution, mineral dusts and pharmaceuticals has led to the general conclusion that the principal determinants of the toxicity of nanoparticles are:

- the total surface area presented to the target organ;
- the chemical reactivity of the surface (including any surface components such as transition metals and coatings), and particularly its ability to take part in reactions that release free radicals;
- the physical dimensions of the particle that allow it to penetrate to the organ or into cells or that prevent its removal;
- possibly, its solubility, in that soluble particles such as salts may disperse before initiating a toxic reaction.

### a) Inhalation

21 The small size of nanoparticles ensures that a high proportion inhaled from the air reaches and is deposited in the deep lung. The size of nanoparticles appears to influence their uptake into cells. Specialised phagocytic cells such as tissue macrophages and leukocytes in the blood generally take up larger particles. This is a mechanism evolved in higher animals for removal of potentially harmful bacteria, and is analogous to the feeding method of unicellular organisms. Nanoparticles in contrast, because of their small size, may pass into cells directly through the cell membrane with the possibility of interfering with important cell functions such as motility and ability to remove bacteria (Renwick et al 2001).

22 Small size alone is not the critical factor in the toxicity of nanoparticles; the overall number and thus the total surface area (essentially the dose) are also important. Based on the evidence we have reviewed it follows that, although nanoparticles may imply a toxic threat because of their small size and therefore large surface area per unit mass, any toxicity would be expected to be dependent upon inhalation or absorption into the body of a very large number. For nanoparticles with low surface reactivity, potential toxicity to humans and, presumably, other animals, should be considered in relation to the likely dose and route of exposure. From the point of view of the lung, inhalation of small numbers of particles is unlikely to represent a significant risk. Inhalation of very large numbers, as may occur in a manufacturing process, should be controlled by regulation. For specific types of nanoparticle that may be expected to have a more reactive surface, perhaps because of a higher proportion or different combination of transition metals, greater caution would be advised and exposure should be minimised. Toxicological studies, both *in vitro* and *in vivo*, will be required for the investigation of any such substances to which people might be exposed.

23 Only a few types of manufactured nanoparticle, such as titanium dioxide, carbon black, zinc oxide and iron oxide are currently in industrial production (see Chapter 4). There is, however, a realistic prospect of industrial production of other nanoparticles for therapeutic or diagnostic use, often based on metals with chemical coatings that confer particular properties with respect to uptake into the body, across natural tissue barriers, and into cells (Borm and Kreyling 2004). There is also considerable interest in the possible production of nanotubes: some pilot manufacturing plants exist for CNTs, and nanotubes made of carbon and other elements are being extensively investigated in research laboratories. The greatest potential for exposure therefore over the next few years will be in the workplace, both in industry and in universities.

24 Workplace exposure will depend on production techniques (outlined in Chapter 4): for example, production and storage in liquid will reduce the risks of airborne exposure but fugitive emissions as vapour or wet aerosol may occur. Manufacturers must take account of the differences in toxic potential between larger and nano-sized particles and until the toxicology of the nanoparticles is better known, they should be assumed to be harmful and such workers seek protection by the usual methods of industrial hygiene, including provision of personal respiratory protection and appropriate hazard information, together with appropriate procedures for cleaning up accidental emissions and for making repairs to machinery. Several issues require further research. In particular, standard, validated methods of measurement and monitoring will be required to control airborne concentrations of nanoparticles in industry and academic laboratories, and the efficiency of various filter materials and respirator cartridges with respect to nanoparticles requires investigation. Toxicological research should be directed at assessing the hazard of new manufactured nanoparticles, particularly investigating the surface properties that alter toxicity.

25 As outlined in Chapter 3.2, nanotubes are of interest because they are mechanically strong, flexible and can conduct electricity. So far, most research has focused on CNTs but nanotubes made from other elements and molecules are also being developed. Perceived similarities with asbestos and other disease-causing fibres have led to concern about their safety. Technology exists that allows production of nanotubes that can have remarkable predicted dimensions of a few nanometres in diameter and micrometres in length (although currently they can only be produced as agglomerates, not as single nanotubes). These could represent a hazard because of their combination of fibrous shape and nanometre dimensions. It is also likely that such tubes are sufficiently robust to resist dissolution in the lung, and their dimensions suggest that they could reach the deep lung if inhaled as individual fibres. The presence of iron or other metals within them from its use as a catalyst in their production suggests that they may also have free-radical-releasing, pro-inflammatory properties. This has been borne out by one study that has investigated the effects of what must have been heavy doses in terms of numbers (60–240 $\mu$ g, dimensions unspecified) of single-wall nanotubes on cultured skin epithelial cells (Shvedova et al 2003). In this case the effects were probably due to the iron, and the tubes are likely to have been relatively short and clumped into masses. It is unlikely that such structures would remain as individual fibres in the air; rather, electrostatic forces probably cause them to clump into masses that are less easily inhaled to the deep lung. However, little is known of their aerodynamic properties and indeed whether they can be present in the air in sufficient numbers to constitute a risk.

26 If nanotubes were to intertwine and become airborne as 'ropes', these might pose a risk equivalent to a conventional fibre. If they combined as 'balls of wool' their aerodynamic diameter would be critical: greater than 10 µm diameter they would not be inhalable, whereas less than that they would act like larger particles. It is recognised, however, that one objective of current research is to find structures or coatings that enable the nanotubes to remain separate. In whatever final format, if they are inhalable, their toxicity is likely to be determined, at least in part, by their surface activity. The published mammalian studies relating to lung toxicity cannot be easily extrapolated, as of necessity the tubes were instilled (injected as a mass into the trachea rather than inhaled in a natural manner) as tangles rather than as individual fibres. The high masses instilled resulted in blockage of airways and intra-airway fibrosis - a not unexpected result in the circumstances (Maynard et al 2004). Preliminary studies in several workplaces suggest that single-wall nanotubes are difficult to disperse as an aerosol and tend to clump into large masses (Warheit et al 2004). Nevertheless, inhalation of small clumps may also imply problems for normal lung defences, with the possibility of them acting as large surface area, non-fibrous particles or being separated into single fibres by the action of lung surfactant.

27 If the barriers to producing single nanotubes (rather than clumps) are overcome, we would expect to see them used in many products such as electronic devices (as outlined in Chapters 3 and 4) and the potential exposure to manufacturing workers would increase. There are obvious difficulties in measuring aerosols of nanotubes against a background of normal laboratory or workplace air. The fact that they are currently difficult to disperse suggests that the escape of large numbers of individual fibres into the air is unlikely in normal processes. Given previous experience with asbestos, we believe that nanotubes deserve special toxicological attention; the types of studies that are required are listed in Box 5.4. The aim of such a programme would be to characterise as far as possible the potential for harm to occur by assessing possible human exposures in the laboratory and the workplace, and by performing simple tests of solubility and toxicity *in vitro*, assessing the validity of these tests by *in vivo* studies in small mammals. In the meantime, we believe that there is sufficient concern about possible hazards to those involved in the research and early industrial development of nanotubes to control their exposure. The role of regulation in controlling the exposure to nanoparticles and nanotubes in the workplace is discussed in Chapter 8.

b) Dermal contact

28 Currently, dermal exposure is limited to people applying skin preparations that use nanoparticles. Before and during this study, concerns were raised

*Box 5.4 Assessment of likely risks to health of novel fibres such as nanotubes*

Exposure studies

- Occupational hygiene study of production and use/disposal to determine the sizes and concentrations of fibres likely to be present in the workplace
- Are fibres longer than about 15 µm (preventing their removal by macropahges)?
- Can fibres reach the part of the lung responsible for gas-exchange (ie are they narrower than 3 µm)?

In vitro studies

- Are fibres durable (an indication that they might persist in the lung)?
- Do fibres kill cells, provoke inflammation and release free radicals?
- What is the effect of removal of metals on their toxicity?

Small mammal (*in vivo*) studies

- Do fibres persist in rat lung during following inhalation or instillation?
- Do fibres cause an inflammatory response following inhalation or instillation?
- Do fibres cause fibrosis and/or cancer after long-term inhalation?
- Do fibres cause mesothelioma (a cancer) after injection into rat pleura/peritoneum (membranes of the lung and abdominal cavity, respectively)?

about the use of nanoparticles (particularly of titanium dioxide) for cosmetic purposes. Nanoparticles of titanium dioxide are used in some sunscreens, as they are transparent to visible light while acting as absorbers and reflectors of ultraviolet. Iron oxide is used as a base in some products, including lipsticks, although we understand that in Europe only sizes greater than 100 nm are used. It is clear that nanoparticles have different properties to the same chemical at a larger scale, and the implications of these different properties for long-term toxicity to the skin require rigorous investigation on a case-by-case basis.

29 Although the use of sunscreens reduces the risk of acute sunburn, the evidence that it prevents skin cancer in humans is far from established. There have even been suggestions that, perhaps by changing patterns of behaviour, the use of sunscreens may actually increase risks (IARC 2001). Some of the preparations used in sunscreens, including organic chemicals and particles, may themselves be photoactive in some conditions, so particular care is necessary in assessing their effects on the human skin. We have examined the concerns expressed to us that nanoparticles might penetrate the skin, that titanium dioxide is photoactive and that if it is

able to penetrate the skin it has the potential to generate free radicals that are known to cause damage to DNA. Limited toxicology so far on animal and human skin appears to indicate that the nanoparticles of titanium dioxide used currently in sunscreens do not penetrate beyond the epidermis (SCCNFP 2000) and that organic components of sunscreens are more likely to penetrate the skin than are the nanoparticles. The Scientific Committee on Cosmetic and Non-food Products (SCCNFP), which advises the European Commission, considered the safety of nanoparticles of titanium dioxide when used as a UV filter. They declared it safe for use at any size, uncoated or coated (SCCNFP 2000).

30 One of the concerns expressed to us was that the safety dossier submitted to the SCCNFP remains confidential to the industries supplying it, although the evidence supplied is referenced in the final opinion of the Committee. Although we recognise that industry has legitimate concerns about commercial confidentiality, we consider that this should not prevent data on the safety testing of cosmetic ingredients being accessible to the scientific community and other interested parties. We expect it to be possible for this to be done in a way that does not reveal proprietary information about the composition of individual products. Therefore, **we recommend that the terms of reference of scientific advisory committees (including the SCCNFP or its replacement) that consider the safety of ingredients that exploit new and emerging technologies like nanotechnologies, for which there is incomplete toxicological information in the peer-reviewed literature, should include the requirement for all relevant data related to safety assessments, and the methodologies used to obtain them, to be placed in the public domain.**

31 Cosmetics (including sunscreens) are intended for use on undamaged skin, and most skin penetration tests appear to have been designed with this in mind. Few reported studies indicate whether these particles penetrate skin that might have been damaged previously, for example by severe sunburn from sunlight exposure or by disease such as eczema. Uncoated nanoparticulate titanium dioxide is photoactive but the coatings used on titanium dioxide in sunscreens to prevent agglomeration also reduce the formation of free radicals (Bennat and Müller-Goymann 2000); so even if the titanium dioxide used in sunscreens were able to penetrate the skin it would probably not exacerbate free radical damage. Based on our concerns about sunscreens being used on damaged skin, our initial instinct was to recommend that all products containing sunscreens be regulated as medicines, as they are in the USA. However, we recognise that this poses challenges, including deciding how many and which types of product would fall into this category. We note that the UK has a total ban on the testing of cosmetic products

and ingredients on animals and that the EU is in the process of moving incrementally towards a complete ban on all animal testing effective from 2013. Although tests on human skin and on cells are available, it is not clear that suitable non-animal models will be available for testing nanoparticles by 2013.

32 The SCCNFP has also considered the safety of nanoparticulate zinc oxide for use as a UV filter in cosmetic products and issued an opinion that they require more information from manufacturers to enable a proper safety evaluation (SCCNFP 2003a). In doing so they highlight evidence that zinc oxide (200nm and below – referred to as microfine) has phototoxic effects on cultured mammalian cells and their DNA *in vitro*. They recommend that the relevance of these findings be clarified by appropriate investigations *in vivo*. In addition, they commented on the lack of reliable data on the absorption through the skin of zinc oxide and noted that the potential for absorption by inhalation had not been considered (SCCNFP 2003a). The US Food and Drug Administration (FDA) has approved zinc oxide for use in sunscreens without restrictions on the size that can be used, although it is not clear if specific consideration was given to whether its properties were different at the nanoscale (FDA 1999). The uncertainties raised by SCCNFP about microfine zinc oxide as a UV filter are also relevant to its use in cosmetics and other skin preparations. In Europe, whereas all cosmetics must undergo a safety assessment by the manufacturer, only some categories of ingredients (such as UV filters) must be assessed by the SCCNFP before they can be approved for use.

33 The regulatory implications of our concerns relating to skin preparations containing free nanoparticles are addressed in Chapter 8.

### c) Other exposure routes

34 Several therapeutic and investigative options for the use of nanoparticles are under development, with the broad aim of them being injectable and able to transport active chemicals to diseased cells. It is likely that such applications, when realised, will use relatively few particles that are biodegradable. As therapeutic substances, they should be subject to rigorous safety and toxicological testing before general release, and this testing will need to take account of their size as well as their chemistry. It is apparent that there has been little communication between pharmaceutical scientists investigating nanoparticles for their properties in evading cell defences to target disease and toxicologists investigating the properties of air pollution particles and the means by which they may cause adverse effects on organs distant from the lung. For example, nanoparticles are being investigated as carriers of proteins, such as antibodies, for pharmaceutical applications. This ability to conjugate implies that, once injected, a similar effect could occur with natural

proteins in vivo, interfering with the proteins' functions in the blood or within cells. It has been speculated that these interactions might alter a range of important cellular functions or indeed nullify the intended functions of the nanoparticles (Borm and Kreyling 2004). These possible hazards would most likely apply if nanoparticles intended for medical applications were injected or inhaled, and represent an area in which fundamental toxicological research is required.

35 There are two important implications of this lack of dialogue. First, research by pharmaceutical scientists will provide much useful information about the potential toxicity of nanoparticles being developed in other sectors and about means of reducing that toxicity. Secondly, when seeking novel applications of nanoparticles, pharmaceutical scientists need to be aware of the possible toxic properties of such particles, perhaps on organs or cells other than those targeted. It is important that the knowledge being gathered by each is shared with the other. Later in this chapter we consider how this might be facilitated.

#### 5.4 Effects on the environment and other species

36 Although there is a body of literature about the human impacts of pollutant nanoparticles, research on the impacts of particulate air pollution on the natural environment and on non-human species within it has primarily been concerned with the impact of pollutant gases such as sulphur dioxide and ozone rather than particles. So with the exception of studies on some laboratory mammals related to investigation of human toxicology, there is no equivalent body of literature on non-human animals that can be used to consider the impacts of nanoparticles. Similarly, there is a dearth of evidence about effects of pollution nanoparticles, if any, on plants or micro-organisms.

37 We are only aware of one small published study of the impact of manufactured nanoparticles on non-human species (other than laboratory mammals). In the study in question, small numbers of juvenile largemouth bass (between four and nine fish in the treatment levels) were exposed to carbon 60 ( $C_{60}$ ) nanoparticles (fullerenes) that had been treated to make them soluble (Oberdörster 2004a). A significant increase in lipid peroxidation (the oxidation of fats) was found in the brains of the fish after exposure for 48 hours to 0.5 parts per million (p.p.m.)  $C_{60}$ , but the increase was not significant at 1 p.p.m. The author noted clarification

of the water in the treated fish tanks, suggesting a possible effect of the nanoparticles on micro-organisms. There is a need to follow up this pilot study with a larger and more detailed investigation.

38 It is plausible that soil or water organisms could take up manufactured nanoparticles escaping into the natural environment and that these particles could, depending on their surface activity, interfere with vital functions. The evidence that nanoparticles may inhibit motility and phagocytosis of macrophages, for example, suggests that similar effects might be expected on simple soil organisms. As with human toxicology, the dose to which the organisms are exposed would be expected to be critical in determining toxicity.

39 In common with other chemicals, nanoparticles may reach humans and other organisms by a wide variety of environmental routes. For example, organisms may ingest materials that have entered the water system or been deposited on vegetation. The criteria used to identify chemicals that have intrinsic properties that give cause for concern about their potential to damage the environment (or human health through the environment) are based on persistence, bioaccumulation and toxicity. The criteria used by the UK Chemicals Stakeholder Forum, for example, are outlined in Box 5.5. Chemicals that score highly according to all three criteria are of particular concern. Once inhaled or ingested, materials may enter the food chain, leading to the possibility of bioaccumulation and ingestion by organisms higher up the chain. Exposure by ingestion therefore depends on the persistence of the material (that is, its longevity in the environment) and its potential to accumulate, usually in lipids. Measures of persistence and bioaccumulation indicate when levels of a chemical are likely to build up in the environment and how difficult it will be to return concentrations to background levels if a problem is identified with the chemical. Bioaccumulation will depend on the surface properties of nanoparticles, which will determine whether they are likely to be taken up by the fatty tissues, bone or proteins in the body. For example, the  $C_{60}$  particles used in the study on largemouth bass (Oberdörster 2004a) were lipophilic, indicating that they could be taken up by fatty tissues. Persistence will depend on whether the material decomposes, for example by oxidation, and on whether the particles are modified in the environment, for example by agglomerating or adhering to other materials so that they lose the particular properties that could make them hazardous as nanomaterials.

*Box 5.5 Criteria for concern of the UK Chemicals Stakeholder Forum*

**Persistence:** Chemicals that are persistent are those that either take a long time to decay once they are released into the environment, or do not decay at all. The Forum classes a substance as persistent if it does not decay to half of its original quantity within two months (if in water) or six months (if in soil or sediment).

**Bioaccumulation:** Chemicals that are bioaccumulative have a strong tendency to be taken from solution (for example, in the stomach or from the blood of organisms that they enter) into the fatty tissues of the body where they remain. A substance is classed as bioaccumulative if, in tests to determine its attraction to fatty tissue over water, the substance favours fatty tissue in a ratio (quantity-wise) of 10,000 to 1 or more. Any substance that favours fatty tissue with a ratio of at least 100,000 to 1 is consequently considered as cause for extreme concern. Chemicals that accumulate in bone or bind to proteins are also of concern.

**Toxicity:** Chemicals that are toxic cause direct damage to organisms that are exposed to them. The Forum's criteria for toxicity generally follow those outlined in the EU Directive on dangerous substances (67/548/EEC). In addition to the Directive, a substance is classed as being of concern if it is fatal to at least 50% of waterborne organisms in a given sample, where the concentration of the substance is 0.1mg per litre or less.

Adapted from Chemicals Stakeholder Forum (2003)

40 For animals, simple tests for persistence and bioaccumulation are available (Royal Commission on Environmental Pollution 2003), and can be used for preliminary screening to identify chemicals whose risks may give cause for concern. In addition, there are numerous tests for toxicity. Whether these simple tests can be adapted for nanoparticles and nanotubes needs to be established and, if not, alternatives need to be developed. More generally, there is a need to establish appropriate methodologies for testing the toxicity of substances in nanoparticulate form in the context of both the environment and human health. Currently, almost nothing is known about the behaviour of nanoparticles in the environment (for example, whether they agglomerate and how this affects their toxicity); the only information on how they are transported through environmental media such as soil and water comes from initial studies on their potential for remediation, which indicate that nanoparticles of iron can travel with the groundwater over a distance of 20 metres and remain

reactive for 4–8 weeks (Zhang 2003).

41 A current source of environmental exposure is in the waste streams from factories and research laboratories. Until more is known about the environmental impacts of nanoparticles and nanotubes, we are keen to manage any potential risk by avoiding their release into the environment as far as possible. Therefore, **we recommend 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.**

42 One of the difficulties in determining potential future exposure of the environment and humans to manufactured nanoparticles is the lack of information about both the extent to which they will be used in products and also the likelihood of such particles being released from nanomaterials such as composites in a form or quantity that might cause harm to humans or the environment. Although we expect that exposure from composites containing nanoparticles and nanotubes will be low – because they will typically make up a very small fraction of the final product and the functionality of the material will rely on them being retained – there is a need to test this assumption. We expect the ways of fixing nanoparticles and nanotubes will be proprietary. Therefore, **we recommend 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.**

43 Any widespread use of nanoparticles in products such as medicines (if the particles are excreted from the body rather than biodegraded) and cosmetics (that are washed off) will present a diffuse source of nanoparticles to the environment, for example through the sewage system. Whether this presents a risk to the environment will depend on the toxicity of nanoparticles to organisms, about which almost nothing is known, and the quantities that are discharged.

44 Perhaps the greatest potential source of concentrated environmental exposure in the near term comes from the application of nanoparticles to soil or waters for remediation (and possibly for soil stabilisation and to deliver fertilisers), as outlined in section 3.2. In some cases the nanoparticles used for remediation are confined in a matrix but, in pilot studies, slurries of iron nanoparticles have been pumped into contaminated groundwater in the USA (Zhang 2003). Given the many sites contaminated with chemicals and heavy metals, the potential for nanotechnologies to contribute to effective remediation is large. But this potential use also implies a question about eco-toxicity: what impact

might the high surface reactivity of nanoparticles that are being exploited for remediation have on plants, animals, microorganisms and ecosystem processes? It is of course possible that, in the concentrations used in remediation, any negative impacts on ecosystems will be outweighed by the benefits of the clean up of contaminated land and waters, but this needs to be evaluated by appropriate research and further pilot studies before deliberate release into the environment is allowed. In the UK, requests for use of nanoparticles in remediation of groundwater and other contaminated media are likely to be made to the Environment Agency.

**We recommend that the use of free (that is, not fixed in a matrix) 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.**

45 It has also been suggested to us that that nanoparticles might be used to increase the bioavailability of pollutants, allowing them to be broken down by bacteria, or that they might be used to disperse and dilute pollutants. As with the example above, the very properties that researchers hope to exploit could potentially lead to unintended consequences for the environment, for example increased bioavailability of pollutants to plants and animals, or the transport of pollutants to sensitive ecosystems. This is clearly another area where more research is required alongside the development of these remediation systems.

## 5.5 Risk of Explosion

46 The explosion of dust clouds is a potential hazard in industries such as food production (sugar, flour, custard powder), animal feed production and places handling sawdust, many organic chemicals, plastics, metal powders and coal. The increased production of nanopowders such as metals has led to questions about whether there is a greater risk of explosion in the clouds of these nanopowders that might form during their production, transport or storage. Any dry, fine and combustible powder poses an explosion or fire risk, either through spontaneous combustion or ignition. The increased surface area of nanoparticles might mean that they would be more likely to become self-charged, and be more easily ignited. In addition, because of their small size, nanoparticles may persist for longer in the air, may be harder to detect and may be invisible to the naked eye, making crude detection difficult.

47 The UK Health and Safety Laboratory (HSL) has recently reviewed research in this area and found that although there is a body of literature about the explosion risk of micrometre-scale powders, no information exists on nanopowders (HSL 2004). Research on micrometre-scale powders reveals that

explosion severity tends to increase with decreasing particle size, although for some substances this effect levels off. The report recognises that the changes in the physical and chemical properties of particles below 100nm mean that results from tests at the micrometre-scale cannot be extrapolated to the nanoscale, where the risk of explosion could be either greater or smaller. The HSL has identified the need for research to determine the explosion characteristics of a representative range of nanopowders; they believe that this research can be undertaken using standard apparatus and procedures already employed for assessing dust explosion hazards.

48 The risk of explosion can be avoided if combustible nanopowders are manufactured, handled and stored in liquid. By contrast, the drying of nanopowders in rotary driers is of particular concern. At present only a very few nanopowders are produced in the type of quantities that might present a dust explosion hazard (for example, carbon black). Other than these, specialist nanoparticles are currently produced or used in very small quantities (that is, grams) and do not pose this particular hazard. Until the explosion hazard has been properly evaluated, this potential risk can be managed by avoiding large quantities of combustible nanoparticles becoming airborne.

## 5.6 Addressing the knowledge gaps

49 Given the relatively small amounts of manufactured nanoparticles being produced, it is perhaps not surprising that there is a lack of information about their health, safety and environmental impacts. At present we have to rely by analogy on research results from air pollution and occupational research, the budget for which in the UK is very limited. Some research on the toxicity of new nanoparticles is underway, particularly in the USA (Service 2004). For example, the National Institute for Occupational Safety and Health in the USA is about to undertake a 5-year study into the toxicity and health risks associated with occupational nanoparticle and nanotube exposure, and is developing a dedicated centre to coordinate activities. Some work is also being funded by the European Commission.

50 With the exception of the research into air pollution by the Department of Health (DH) and the Department for Environment Food and Rural Affairs (DEFRA), no coordinated programme of research into the health and environmental risks of nanomaterials is being undertaken in the UK. We are pleased to hear that the UK research councils have committed to work together to address the issues raised in our report, and note that the Engineering and Physical Sciences Research Council (EPSRC) is assembling two 'thematic networks' in the area of nanosafety (House of Commons 2004b). In addition, the environmental impact of nanotechnologies is now on the agenda for the Environmental Funders'

Forum, which brings together the UK's major public sector sponsors of environmental science (including the research councils, DEFRA and the Environment Agency). As nanotechnologies advance, so environmental and human health hazard and risks should be investigated in tandem, priority being given to categories of products either in or near to the market.

51 The capacity for particle toxicology in the UK, based as it was on the need to protect workers in heavy industries such as those concerned with coal, steel and asbestos, has declined with the reduction in numbers of workers employed in such industries. However, a recent rise in interest in air pollution has allowed maintenance of a nucleus of expertise, particularly in Edinburgh and Cardiff. Traditionally, particle toxicologists have worked very closely with the relevant industries and the research councils. There is now an opportunity for a new collaboration between nanotechnologies, environmental science, pharmaceutical science and toxicology, building on the current expertise in air pollution and fibre research. Fundamental questions about the interactions of cells and their components and particle surfaces, and pragmatic questions about likely exposures and methods of their reduction, need to be addressed. We note the close relationship between toxic effects on cells such as macrophages derived from humans or other mammals and similar effects on organisms in the general environment. We also note the common interests of those concerned with research into possible beneficial effects of nanoparticles in the pharmaceutical industry and those concerned with toxicity. We believe that there is a strong case for a research dialogue between human toxicologists, pharmaceutical nanoscientists and eco-toxicologists.

52 A fundamental aspect of assessment of risk is the ability to quantify the hazard; this applies to all the above sections. Nanoparticles and nanotubes are too small to be measured by most standard instruments used, for example, in workplaces. Those instruments used for their quantification, electron microscopes and scanning mobility particle size analysers, are expensive and require a high level of expertise to use, although some cheaper, portable instruments are becoming available. Moreover, it is not known which physical property of nanoparticles is the one that correlates most closely with toxicity. The quantification of nanoparticles for regulatory purposes in mixtures such as cosmetics or in effluents would raise particular problems. There is an important need to develop, standardize and validate methods of measurement of nanoparticles and nanotubes in workplaces and the environment.

53 In Box 5.6, we summarise the research required to address some of the knowledge gaps highlighted in this chapter and to develop methodologies and instrumentation to support the regulation of

production, use and disposal of nanoparticles (discussed further in section 8.4.3).

54 Much of the necessary research by its nature requires an interdisciplinary approach. Some of the relevant research should be done by Government agencies or through international collaborations, but it is important for the UK to have its own centre of expertise, which would maintain a database of information, become the centre of a network to disseminate this information, and act as a source of advice for industry and regulators.

**55 We recommend that Research Councils UK (RCUK) establish an interdisciplinary centre (probably comprising several existing research institutions) to research the toxicity, epidemiology, persistence and bioaccumulation of manufactured nanoparticles and nanotubes as well as their exposure pathways, and to develop methodologies and instrumentation for monitoring them in the built and natural environment.** A key role would be to liaise with regulators. **We recommend that the research centre maintain a database of its results and that it interact with those collecting similar information in Europe and internationally.** The remit of the research centre is summarized in Box 5.7.

56 Initially, RCUK will need to build expertise and collaborations in the areas outlined in Box 5.6, and it should work with the community to assemble an appropriate centre (along the lines of EPSRC quantum information processing Interdisciplinary Research Collaboration) rather than invite competitive bids. Its advisory board should include industrialists and regulators as well as scientists from the UK and overseas to ensure the wider relevance of the research programmes. Funding for the centre should keep pace with the development of manufactured nanoparticles. We estimate that funding at the rate of £5-6 M per annum for 10 years is needed to perform the tasks that we have outlined. Although core funding would need to be provided by the UK Government, we would expect to see the centre participating in European and internationally funded projects. As methodologies become established, the centre might become the recognized place for the testing of nanoparticles and nanotubes and develop a sustainable funding base within approximately 10 years. **Because it will not be possible for the research centre to encompass all aspects of research relevant to nanoparticles and nanotubes, we recommend that a proportion of its funding be allocated to research groups outside the centre to address areas identified by the advisory board as of importance and not covered within the centre.**

#### *Box 5.6 Research areas to be addressed*

- Development of suitable and practical methods for measurement of manufactured nanoparticles and nanotubes in the air and other media, including those properties most likely to reflect their toxicity such as surface area and potential to release free radicals.
- Investigation of methods of measuring the exposures of workers to manufactured nanoparticles and nanotubes in current laboratories and manufacturing processes.
- Development of international agreement on measurement standards.
- Establishment of protocols for investigating the long-term fate of nanoparticles as products containing them approach the market, to determine whether, how and to what extent they might come into contact with the natural environment.
- In conjunction with research on environmental remediation, develop an understanding of the transport and behaviour of nanoparticles and tubes in air, water and soil, including their interactions with other chemicals.
- Epidemiological investigation of the inter-relations of exposure and health outcomes in those industrial processes, such as welding, carbon black and titanium dioxide manufacture, where nanoparticle exposure has been known to have occurred for some time.
- Development of internationally agreed protocols and models for investigating the routes of exposure and toxicology to humans and non-human organisms of nanoparticles and nanotubes in the indoor and outdoor environment, including investigation of bioaccumulation. This would include an understanding of the impact of different sizes of nanoparticles and different types of coating.
- In collaboration with pharmaceutical nanoscientists and air pollution toxicologists, fundamental studies of the mechanisms of interaction of nanoparticles with cells and their components, particularly the effects on blood vessels, the skin, heart and the nervous system.
- Development of protocols for *in vitro* and *in vivo* toxicological studies of any new nanoparticles and nanotubes likely to go into large-scale production and which could impact people or the natural environment.
- Further investigation of the absorption through skin of different commercial nanoparticles used in dermal preparations, in particular any changes that may occur if the skin is damaged before application.
- Determination of the risk of explosion associated with a representative range of nanopowders (assuming funding has not already been received by HSL for this research).

#### *Box 5.7 Remit of the proposed interdisciplinary research centre*

- To undertake the research programmes outlined in Box 5.6.
- To act as the UK centre for advice on the potential health, safety and environmental impacts of nanomaterials.
- To hold regular dialogue meetings with appropriate regulators to exchange information on the requirements of regulators and research findings.
- To maintain a network bringing together those researching into:
  - epidemiology, toxicology, persistence, bioaccumulation, exposure pathways and measurement of manufactured nanoparticles and nanotubes;
  - medical applications of nanoparticles and nanotubes;
  - epidemiology, toxicity, exposure pathways and measurement of nanoparticles in air pollution.
- To maintain an accessible database of results from publicly funded research within the centre on the toxicity of nanoparticles and nanotubes, and to interact with those collecting similar information in Europe and internationally.

## **5.7 Conclusions**

57 Many applications of nanotechnologies introduce no new health, environmental or safety aspects, for example where the nanotechnology is in the scale of a node on a computer chip or of nanometre thin films in data storage devices such as hard disks. Free particles in the nanometre size range do raise health, environmental and safety concerns and their toxicology cannot be inferred from that of particles of the same chemical at larger size. The difference comes largely from two size-dependent factors: the larger surface area of small particles compared with larger particles, given equal mass, and the probable ability of nanoparticles to penetrate cells more easily and in a different manner than larger ones. Exposure to natural and pollution nanoparticles in ambient and indoor air is universal, and most of the population and workers in many industries are exposed to high concentrations without significant harm. Nevertheless, in recent decades it has been suggested, though not proven, that such exposures may be responsible for the observed relationships between air pollution and several diseases, particularly of the heart and the lung, in susceptible individuals.

58 Toxicological investigations, based largely on low solubility, low surface-activity nanoparticles, have suggested that the ability of such particles to cause inflammation in the lung is a consequence of reactions

between cells and a large total particulate surface area (perhaps carrying reactive metals and other chemicals). Although it is very unlikely that new manufactured nanoparticles could be introduced into humans in sufficient doses to cause the effects associated with air pollution, nevertheless it is important that precautions are taken in the workplace in manufacturing and research laboratories to manage this potential risk by limiting exposure.

59 Moreover, it seems likely that the needs of industry will be met by development of a diverse range of nanoparticles with differing properties, and that these might lead to production of nanoparticles with surfaces that increase their reactivity and their ability to traverse cells, become blood-borne or cause injury to tissue. Therefore new nanoparticles that differ substantially from those with low solubility, low toxicity physico-chemistry should be treated with caution. If they are to be produced on a large scale they should be tested for their hazard and any likely human exposure assessed, so that risk can be minimised.

60 Exposure to fibres in industry, in the form of asbestos, is a well-recognised cause of serious illness, including cancer. The toxic properties of such fibres are dependent upon a diameter narrow enough to allow inhalation deep into the lung, a length that prevents their removal by macrophages, resistance to dissolution in tissue fluid, and a surface able to cause oxidative damage. However, the doses of asbestos associated with disease are substantial, of the order of several hundred per breath at work over months or years. Any new fibre with these properties would be expected to cause similar problems if inhaled in sufficient amounts to lead to similar lung burdens of long fibres. Carbon and other nanotubes have physical characteristics that raise the possibility of similar toxic properties, although preliminary studies suggest that they may not readily be able to escape into the air in fibrous form. Such materials require careful toxicological assessment and should be treated with particular caution in laboratories and industry.

61 Several nanoparticles are currently used in cosmetics and sunscreens. We believe the published evidence on toxic hazards from some such particles for skin penetration is incomplete, particularly in individuals using these preparations on skin that has been damaged by sun or by common diseases such as eczema. Further careful studies of skin penetration by nanoparticles being considered for use, and the propensity of such particles to potentiate free radical damage, are desirable.

62 The methods of quantifying nanoparticles and especially nanotubes pose serious problems at present. There is a need for more industrial hygiene and epidemiological evidence to guide regulation by different particle metrics; this requires research into appropriate instrumentation and standardisation of measurement.

63 Until research has been undertaken and published in the peer-reviewed literature, it is not possible to evaluate the potential environmental impact of nanoparticles and their behaviour in environmental media. **Until more is known about environmental impacts of nanoparticles and nanotubes, we recommend that the release of manufactured nanoparticles and nanotubes into the environment be avoided as far as possible.** In section 5.4 we make specific recommendations to reduce releases of nanoparticles and nanotubes in waste streams and those used for environmental applications in which nanoparticles are dispersed freely (for example, in remediation and soil stabilization).

64 Our conclusions have been based on incomplete information about the toxicology and epidemiology of nanoparticles and their behaviour in air, water and soil, including their explosion hazard. If nanotechnologies are to expand and nanomaterials become commonplace in the human and natural environment, it is important that research into health, safety and environmental impacts keeps pace with the predicted developments. In this chapter we recommend that RCUK establish an interdisciplinary centre (probably comprising several existing research institutions) to undertake research into the toxicity, epidemiology, biopersistence and bioaccumulation of manufactured nanoparticles, their exposure pathways, and methods and instrumentation for monitoring them in the environment. A key role would be to liaise with regulators. We recommend that the research centre maintain a database of its results and that it interact with those collecting similar information in Europe and internationally.

65 In this chapter we have identified several ways in which the risks of nanoparticles and nanotubes can be managed. In Chapter 8 we consider how this risk management can be incorporated into some of the relevant regulatory frameworks, such as those that relate to the safety of employees and consumers.

## 6 Social and ethical issues

### 6.1 Introduction: framing social and ethical issues

1 As recent debates in the UK and elsewhere demonstrate, developments in science and technology do not take place in a social and ethical vacuum. Widespread discussions of issues such as nuclear energy, agricultural biotechnology and embryonic stem cells illustrate this point only too clearly.

2 Given this backdrop, it seems highly likely that some nanotechnologies will raise significant social and ethical concerns. Such concerns seem most likely for developments envisaged for the medium (5–15 years) and much longer (more than 20 years) time horizons. However, such issues rarely become matters of concern merely as a result of the underlying science or engineering. More typically, they are associated with specific applications of a technology. For example, in Europe medical or 'red' uses of biotechnology have raised a very different set of concerns from those raised by agricultural or 'green' applications (Gaskell and Bauer 2001). As earlier chapters of this report illustrate, the term 'nanotechnologies' encompasses an even wider range of basic science, methods and engineering approaches than biotechnology, and so are likely to give rise to a highly diverse set of potential applications over very different time-scales. Predicting all but the near-market applications of such a diverse effort is a difficult enough task, as a recent report from the RAND Corporation points out (Anton et al 2001), but anticipating which applications are likely to raise significant long-term social or ethical issues sets an even bigger challenge. Some currently envisioned applications of nanotechnologies which are seen as technically feasible may never be realised on a significant scale, while unanticipated scientific breakthroughs may lead to rapid applications that are not currently foreseen.

3 Most of the social and ethical issues arising from applications of nanotechnologies will not be new or unique to nanotechnologies. However, throughout this chapter we take the view that effort will need to be spent whenever significant social and ethical issues arise, irrespective of whether they are genuinely new to nanotechnologies or not. Previous chapters have highlighted some of the possible short-term health and environmental implications of certain developments in nanotechnologies, each of which have their own social and ethical dimensions. Here we discuss some of the wider social and ethical issues that these new technologies raise. The list is not intended to be an exhaustive treatment but to highlight what seem to us to be significant issues. When discussing both the potential positive and negative impacts of nanotechnologies, we have tried to avoid an unbalanced discourse (present in some of the more speculative writings on the subject),

which implies that major positive benefits for society always be accredited to the 'new science of nanotechnology', while any negative social and ethical issues are 'just a problem of technology' or alternatively that the very newness of a technology is itself evidence against it. Nanotechnologies, whether singly or in convergence with other technologies, are likely to hold a range of both positive and (however unintended) negative outcomes.

4 Widespread acceptance and use of nanotechnologies will depend upon a range of social factors including: specific technical and investment factors; consumer choice and wider public acceptability; the political and macro-economic decisions that contribute to the development of major technologies and outcomes that are viewed as desirable; and legal and regulatory frameworks. Equally, just as the knowledge-base underpinning science and technology can change rapidly and unpredictably, so can society. Forecasting people's needs and values 20 years or more into the future is fraught with uncertainty. Accordingly, it is difficult to state with any confidence how nanotechnologies are likely develop in the future, in interaction with a changing society and its shifting social and ethical concerns. It may also be important to look beyond the perspective of Western industrialised societies, to take account of the ways in which people in developing societies might respond to developments in nanotechnologies and their impacts.

5 Precisely which social and ethical issues become a focus of concern will hinge upon the actual trajectories of change in particular nanotechnologies. In their recent report for the ESRC on the social and economic challenges of nanotechnology, Wood et al (2003) point out that current evaluations of the impacts of nanotechnologies can be located on a continuum whose extreme poles are on the one hand incremental progress (the view that nanotechnologies merely represent a basic evolution from well-established principles and procedures), and on the other a radical disjunction from current science and technology (for example, as represented by the vision of nanobots outlined in Annex D). According to the authors of the ESRC report, most current commentary on social, economic and ethical impacts, which ranges from the highly optimistic to the almost apocalyptic, occupies the centre ground of this continuum. What does seem clear is that genuinely new and/or unanticipated social or ethical issues are likely to be associated with radical disjunctions if they occur. Equally, much of what passes for incremental nanotechnologies (for example, powerful computers networked with cheaper small sensors) may still prove transformative in social terms. This is because the role of nanotechnologies is likely to be an enabling one, often in convergence with other

new technologies, bringing to fruition applications such as pervasive sensing which have been anticipated by commentators for many years, but are only now becoming a practical possibility. Much of the commentary provided to the working group also suggests that many of the social and ethical issues raised by incremental developments are unlikely to prove entirely new. For example, many concerns about the overall impact of a rapidly changing science on society, and the governance and regulation of the technology, are likely to echo some of those raised previously about other developments in science and technology that have proved controversial, such as nuclear energy, reproductive technologies or biotechnology (Mosterín 2002). That does not make these concerns any the less significant or worthy of the attention of policy-makers; indeed, past experience with controversial technologies should predispose policy-makers to pay timely and applied attention to these concerns rather than dismissing them as 'nothing new'.

6 This chapter provides selective comments on the significant claims and arguments that have been presented to the working group, alongside others that are found in the published literature, to highlight some of the more difficult issues that might potentially emerge. Some of the issues covered here were also raised in the group workshops on nanotechnologies with members of the public that were conducted as part of this study; findings from these are discussed in detail in section 7.2. For the reasons outlined above, this chapter cannot pretend to be a full-scale horizon scanning exercise for social and ethical impacts. This is one of the reasons why we recommend here that at least some form of ongoing evaluation, and in section 7.6 that continuing dialogue and engagement, be extended well beyond the lifetime of the Working Group.

## 6.2 Economic impacts

7 There is some disagreement about how much of an economic impact nanotechnologies will have. A range of views has been heard in evidence. Overall, it seems that effects will be incremental in the short term but, given the fact that nanotechnologies are likely to enable a great many products and processes, they may well have significant economic impact in the long-term. As argued above, much will depend upon which particular applications eventually come to market, and the order in which they are developed. Judging by experience, seemingly insignificant technological advances could have profound long-term economic impacts. Some commentators appear to assume that the potential economic results of nanotechnologies – greater gross domestic product (GDP), greater efficiency and less wastage in industrial processing – will be entirely positive across society or across the range of developed and developing nations. However, in general the introduction of new technologies creates both 'winners'

and 'losers'; for example, as employment is displaced from one sector to another.

8 At this stage, evidence does not suggest that nanotechnologies raise economic issues that differ significantly from other cases of technological innovation. However, it would contribute greatly to the wider societal debate and to decisions about the introduction of nanotechnologies if appropriate economic analysis of developments with widespread societal impacts, including an assessment of the advantages and disadvantages, is undertaken at an appropriate stage. Since this cannot be done on a systematic basis far ahead of the development of new technologies (for reasons given at the start of this chapter), such analysis would need to proceed on a case-by-case basis, as developments and applications come closer to market. Such analysis should also take full account of the uncertainties involved, of the case for relying on alternative technologies and of any economic shocks and surprises.

## 6.3 A 'nanodivide'?

9 Much of the 'visionary' literature at the radical disjunction end of the continuum described in the ESRC report (Wood et al 2003) contains repeated claims about the major long-term impacts of nanotechnologies upon global society: for example, that it will provide cheap sustainable energy, environmental remediation, radical advances in medical diagnosis and treatment, more powerful IT capabilities, and improved consumer products (see many of the contributions to two recent National Science Foundation (NSF) workshops (NSF 2001, 2003)). If even a few of these predictions prove true then the implications for global society and the economies of many nations are profound indeed. However, it is equally legitimate to ask who will benefit and, more crucially, who might lose out? The application of science, technology and engineering has undoubtedly improved life expectancy and quality of life for many in the long term. In the short-term, however, technological developments have not necessarily benefited all of humankind, and some have generated very definite 'winners' and 'losers'.

10 Concerns have been raised over the potential for nanotechnologies to intensify the gap between rich and poor countries because of their different capacities to develop and exploit nanotechnologies, leading to a so-called 'nanodivide'. If global economic progress in producing high-value products and services depends upon exploiting scientific knowledge, the high entry price for new procedures and skills (for example, in the medical domain) is very likely to exacerbate existing divisions between rich and poor (P Healey, written evidence). Equally, a parallel danger that could arise if the more radical 'visions' of the promise of nanotechnologies were realised, is that enthusiasm for developing a 'technical fix' to a range of global and

societal ills might obscure or divert investment from cheaper, more sustainable, or low-technology solutions to health and environmental problems.

11 A further concern that has been highlighted (ETC 2003a; GeneWatch UK written evidence) relates to patenting in the field of nanotechnologies. Appropriate ownership of intellectual property is generally considered advantageous. However, as experience in genetics shows (Nuffield 2002), patents that are too broad or that do not strictly meet the criteria of novelty and non-obviousness, can work against the public good. There is a concern that broad patents could be granted on nanotechnologies, for example on processes for manipulating or creating materials, which would stifle innovation and hinder access to information, not least by those in the developing world. As highlighted in the Royal Society report on intellectual property (Royal Society 2003), it is vital that patent offices monitor the complex and rapidly changing developments in science and technology so that any patents which are granted are appropriate and support rather than constrain research and innovation.

12 In evidence presented to the Working Group, Doug Parr of Greenpeace highlighted the potentially beneficial applications of nanotechnologies for the developing world and for the environment, for example by reducing carbon dioxide emissions through improving renewable energy technology, and expressed concern that nanotechnologies could become another 'opportunity lost' for developing countries. The Joint Centre for Bioethics (2004) also highlight applications such as using nanosized quantum dots for cheaper, quicker disease detection, and improved water purification technologies, which could have benefits for the poor. There have also been suggestions that nanotechnologies could offer new opportunities for some developing countries to participate more directly in global technology through their own initiatives – for example, through the development of plastic electronics facilities, which are one-hundredth of the cost of conventional silicon fabrication plants.

13 There are therefore significant risks that some short-term developments in nanotechnologies will be exclusive to those who already own wealth and power, to the detriment of wider society. Equally, opportunity to apply nanotechnologies in ways that will benefit the developing world should not be overlooked. Two fundamental questions arise in this context. First, can the future trajectories of nanotechnologies be steered towards wider social or environmental goals (for example, cheap sustainable energy generation and storage) rather than towards meeting short-term or developed world 'market' opportunities (for example, cosmetics)? Second, if a 'nanodivide' develops, what can governments do about it? For example, to the extent that the products of nanotechnologies become essential to normal participation in society, should public

authorities try to rectify the divide in an appropriate way? Where the products are luxury goods, can their demand and supply reasonably be left to the market? The governance of nanotechnologies must in some way be designed to incorporate the perspectives and objectives of governments, the market and civil society.

## 6.4 Information collection and the implications for civil liberties

14 As we saw in Chapter 3, nanotechnologies promise considerable advances in developing small and cheap sensing devices, enabling a range of features that will make smaller, longer-lasting sensors possible. The convergence of nanotechnologies with IT could provide the basis for linking complex networks of remote sensing devices to significant computational power. Some nanodevices may be widely incorporated in other products. Such developments could be used to achieve greater safety, security and individualised healthcare, and could offer advantages to business (for example in tracking and other monitoring of materials and products). However, the same devices might be used in ways that limit individual or group privacy by covert surveillance, by collecting and distributing personal information (such as health or genetic profiles) without adequate consent, and by concentrating information in the hands of those with the resources to develop and control such networks. The ETC Group claim that 'biosensors and chips...could become ubiquitous in daily life – monitoring every aspect of the economy and society' (ETC 2003a).

15 These kinds of development might reinforce existing consumer concerns about the use of radio frequency identification (RFID) technology to replace bar codes, currently being trialled by supermarkets and clothing retailers. A recent briefing on RFID from the National Consumer Council (2004) highlights concerns such as: the potential to link personal information (for example, credit card number) to a particular product, which may then allow individuals to be profiled and tracked in store and marketed to on an individual basis; the increased collection of data on an individual; and whether there is abuse if the technically unequipped cannot detect sensing devices. The Government's Foresight programme recently completed a project on cyber trust and crime prevention, which explored the application and implications of next generation information technologies (including developments in nanotechnologies) in areas such as identity and authenticity, surveillance and information assurance. One of the science reviews that contributed to this project (Raab 2004) highlighted the increased use of surveillance, with implications for policing, profiling and 'social sorting', all of which 'continually seek to identify, classify and evaluate individuals according to ever more refined and discriminating forms of personal data. Sorting is a highly potent set of techniques with political and social-control

implications'. These themes were also explored in the Royal Society's public dialogue on cybertrust and information security in March and April 2004.

16 This issue is clearly one where nanotechnologies play an enabling role in promoting societal changes that have both positive and (if the technology is abused) negative consequences. It seems unlikely that the underlying legal and ethical issues raised by such developments will be any different in principle from those society has faced in the past across a whole range of healthcare and consumer issues. However, as new forms of surveillance and sensing are developed, further research and expert legal analysis might be necessary to establish whether current regulatory frameworks and institutions provide appropriate safeguards to individuals and groups in society. We touch on this again in section 8.5.

## 6.5 Human enhancement

17 As noted in section 3.5.3h, nanotechnologies are contributing to the development of some 'enhancement' applications; the closest to development being improved cochlear and retinal implants, to improve or restore hearing and eyesight.

18 A few disability rights groups have objected to proposed interventions that enhance human capacities, on the grounds that this might lead to stigmatisation of those without enhanced capacities (see, for example, Wolbring 2003). The general concern is difficult to grasp without a clear account of the difference between enhancements and other interventions. The issue of specific human enhancements is also likely to fall, initially at least, squarely within the medical domain, where there is an established history of considering emergent ethical issues and the societal acceptability of particular procedures.

19 The general issues about stigmatisation of those who are different in various ways is a serious one, but it has little connection with ways in which differences between people may be brought about. All successful medical treatment of illness, including treatment of illness with a genetic basis, enhances the functioning and capacities of those who are treated. Even where an intervention – a drug, a prosthesis, a medical device, surgery – is not effective for all sufferers, it can hardly be withheld from those who could benefit on the grounds that some others cannot. There is no general case for resisting technologies or interventions that enhance human capacities. It would be wrong to deny appropriate treatment to patients whose impaired sight can be improved by glasses or surgery simply because others have sight impairments that cannot be improved.

20 What is important to note is that a purely 'technical fix' view of disability is not unproblematic. In evidence presented to the Working Group, Richard Light, director

of the DAART Centre for Disability and Human Rights, suggested that disabled people may prefer money to be allocated to, for example, anti-discrimination or human rights measures, rather than technology in general and nanotechnologies in specific as a cure. He also stated that medical technology is irrelevant unless people can afford and have access to it, and urged proper consideration of the claims that nanotechnologies will provide benefits to the disabled: 'any suggestion that nanotechnologies will have an impact on their lives must be assiduously tested; making such claims without a demonstrable basis in fact is immoral and does little to reassure those concerned by the commercialisation of science.'

21 However, certain types of enhancement may be more controversial, whether because those who lack them would be stigmatised or (more probably) for other reasons. For example, some have argued that all enhancement by gene therapy is an unacceptable form of eugenics, while others have argued that genetic enhancement of basic capacities such as intelligence or height would only be acceptable only if fairly distributed (Buchanan et al 2002). Yet others hold that if enhancement of capacities by education or training is acceptable, then enhancement of capacities by other means, such as cosmetic surgery or taking drugs with cognitive effects, is also acceptable. A parallel debate can be found between those who are concerned about the use of performance-enhancing drugs by athletes or others (usually on grounds of unfairness or risk to health)<sup>1</sup>, and those who think that if it is acceptable to enhance performance by exercise, then it is acceptable to do so by taking drugs<sup>2</sup>.

## 6.6 Convergence

22 Convergence refers to the multiple ways in which nanotechnologies will combine in the future with other developments in new technology (reflecting its genuinely interdisciplinary nature). Convergence probably presents some of the biggest uncertainties, with respect to what is genuinely plausible and when new technologies might actually come into use. We have noted above how convergence of nanotechnologies with information technologies could raise concerns about civil liberties. However, convergence is likely to generate a range of other social and ethical challenges, particularly in relation to longer-term applications within bio-nanotechnology that involve significant interface of material systems with, or internal modification of, the body. Some developments – although essentially physical interventions conducted primarily for medical benefits – might well raise a range of fundamental psychological and sociological questions centred around the issue of identity: that is, what we understand to be 'human', what is 'normal' and what is not. As stated in the recent report from the German Parliament Office of Technology Assessment (TAB 2004):

<sup>1</sup> For more on the medical consequences of taking performance-enhancing drugs in sport, see [http://www.bmjpg.com/chapters/0727916068\\_sample.pdf](http://www.bmjpg.com/chapters/0727916068_sample.pdf).

<sup>2</sup> For a bibliography of writing on human enhancement see <http://www.ucl.ac.uk/~ucbtdag/bioethics/biblio.html>.

'In visions of nanotechnology, we repeatedly see aspects which dissolve the boundaries between what constitutes a human being, and what they can create with the help of technological achievements and applications. Such aspects relate for example to the penetration and modification of the human body by attempts to supplement or replace its biological components by nanotechnology components, and to network it with external machines or other bodies or body parts'. Developments that in some way invade or intervene with the body in the manner described above are also likely to raise issues of control and choice and to be particularly sensitive in relation to public perceptions and concern. In evidence presented to the working group, Stephen Wood and Richard Jones highlighted that although these very extreme visions of the potential outcomes of nanotechnologies – including the possibility of greatly expanding lifespans, or even of the separation of human consciousness from the body and its relocation in a computer – may seem too far-fetched for many scientists, these visions do form a background for discussions of the impact of nanotechnologies by informed non-scientists.

23 An example of proposals for radical human enhancement appears in a recent publication jointly sponsored by the US NSF and the Department of Commerce, which maps out a possible future convergence of nanotechnologies with biotechnology, information and cognitive sciences for enhancing human performance. The editors of this report suggest that 'the integration of the four technologies (nano–bio–info–cognito) originates from the nanoscale, where the building blocks of matter are established' (NSF 2003). Although it is not entirely clear what is being said here, it appears that convergence is being used in two senses. In addition to the definition of convergence as interdisciplinary research and development, convergence is used to refer to matter 'converging' at the atomic level – ie to the fact that all matter is made of atoms.

24 This volume provides a very good example of the difficulty some commentators find in drawing an appropriate line between hope and hype. The authors contributing to this report are almost universally optimistic about the potential of convergence for the human condition, and provide very little critical discussion of potential drawbacks. The report also makes strong assumptions about the social acceptability of some of its implications (see Baird 2004). The book also places some very concrete and beneficial developments that converging technologies will shortly bring (non-invasive diagnostics for example) alongside more fanciful visions of the future (for example, of human society as one single interconnected 'brain'). Many of the papers also advocate a highly mechanistic view of people and society, where machines and biological systems are intersubstitutable, with very little consideration of some of the ethical challenges that the

more radical enhancement proposals (such as the development of direct neural-to-computer interfaces) might encounter. One would be forgiven, therefore, for dismissing many of the papers as being less about sound science and technology than they are about science fiction (for example, the volume talks extensively about the 'human genome project' but contains little by way of mainstream neuroscience). However, the volume does pose the question of whether society has appropriate mechanisms for anticipating and deliberating some of the more radical enhancement proposals, currently thought possible through convergence, if and when they were ever to become practical realities.

## 6.7 Military uses

25 Nanotechnologies are predicted to offer significant advances and advantages in defence capability. According to the UK Ministry of Defence (MOD 2001), nanotechnologies will present both new opportunities for defence and new external threats. Echoing the points made above about the prospects for the development of pervasive sensing, the main initial defence impact is predicted to be in information systems using large numbers new and cheap sensors, as well as in information processing and communications. These developments might enable pervasive nanosensors to contribute to national defence capability through early detection of chemical or biological releases, and increased surveillance capability. In addition, 'a whole range of military equipment including clothing, armour, weapons, personal communications will, thanks to low cost but powerful sensing and processing, be able to optimise their characteristics, operation and performance to meet changing conditions automatically'.

26 A current military example is provided by the US Institute for Soldier Nanotechnologies at Massachusetts Institute of Technology, which has been awarded a \$50 million budget from the US army to research new materials. Its ultimate goal is 'to create a 21st century battlesuit that combines high-tech capabilities with light weight and comfort', focusing on soldier protection, injury intervention and cure, and human performance improvement. Specific features of the battlesuit were described in section 3.2.3c. The Institute states that their research describes 'a long-range vision for how technology can make soldiers less vulnerable to enemy and environmental threats' but does not discuss a specific time-scale for realising that vision.

27 Military developments raise several obvious social and ethical issues, most of them once again not confined to nanotechnologies. Manipulation of biological and chemical agents using nanotechnologies could result in entirely new threats that might be hard to detect and counter. Some observers have suggested

that refinements of both existing and new weapons systems, through applications of nanotechnologies, might lead to a new form of arms race (see, for example, Gsponer 2002; Arnall 2003). One can also ask whether the use of arms control frameworks developed for existing categories of nuclear, chemical and biological weapon will be sufficient to control future developments involving nanotechnologies.

28 A related issue arises from the fact that much of the basic knowledge and technology needed to achieve military capabilities using applications of nanotechnologies will be produced within the civil sector, and hence is potentially available to a very wide range of parties, including non-state actors. Joy (2000) suggested that 'The 21st-century technologies – genetics, nanotechnology, and robotics (GNR) – are so powerful that they can spawn whole new classes of accidents and abuses. Most dangerously, for the first time, these accidents and abuses are widely within the reach of individuals or small groups. They will not require large facilities or rare raw materials. Knowledge alone will enable the use of them'. This factor also makes proliferation of weapons development programmes much harder to detect because the line between non-military and military industrial activity becomes blurred. In this way, nanotechnologies may increase the range of asymmetric power relations.

29 Those applications of nanotechnologies that attract military funding are likely to raise other concerns: for example considerations of secrecy will make the open peer review of findings in these areas much more difficult. An unintended consequence of secrecy in the development of some nanotechnologies could also be to fuel public distrust and concerns about non-military developments. This would be so particularly if the term 'nanotechnology' as a whole became to be closely associated with military ends (it is not currently: see the analysis of our research into public attitudes in section 7.2). The case of nuclear energy is instructive here. Flynn (2003) in the USA argues that one of the historical reasons for the stigmatisation of, and enduring hostile public attitudes towards, nuclear power was the inability of the civilian nuclear industry to separate itself from destructive uses of the atom. Government denials of this linkage – scarcely believed at the time – further served to undermine public trust in those regulating the technology. There seems to be a significant danger that public acceptance of a whole range of beneficial applications of nanotechnologies, particularly in the environmental domain, might be threatened by too close an association with military applications. However, individual perceptions of the role of the military will of course impact on the way that military development of nanotechnologies will be received.

## 6.8 Conclusions

30 Nanotechnologies will have an impact across many branches of science and technology and can be expected to influence a range of areas of human endeavour. Some applications of nanotechnologies are likely to raise significant social and ethical concerns, particularly those envisaged in the medium (5–15 years) and longer (longer than 20 years) time-scales. However, given the difficulty of predicting any but the most short-term applications of nanotechnologies, evaluating long-term social or ethical impacts is a huge challenge. Incremental advances in nanotechnologies may play a role in enabling a number of applications, often in convergence with other technologies, which may in the long term prove transformative to society.

31 In the near- to medium term, many of the social and ethical concerns that have been expressed in evidence are not unique to nanotechnologies. The fact that they are not necessarily unique does not make these concerns any less valid. Past experience with controversial technologies demonstrates that effort will need to be spent whenever significant social and ethical issues arise, irrespective of whether they are genuinely new to nanotechnologies or not. In this chapter we have identified a range of social and ethical issues relating to the development of nanotechnologies that would benefit from further study. These include concerns about who controls nanotechnologies and who will benefit from its exploitation in the short- and long term. The recent report to ESRC (Wood et al 2003) raised other relevant issues. Although not all these issues are necessarily research questions, some are and others may be in the future, presenting a unique opportunity for interdisciplinary research to be undertaken between scientists and social scientists. The cost would be small compared with the amount spent on research on nanotechnologies, the applications of which could have major social and ethical impacts. Therefore, **we recommend that the research councils and the Arts and Humanities Research Board (AHRB) fund an interdisciplinary research programme to investigate the social and ethical issues expected to arise from the development of some nanotechnologies.** This programme would include research grants and interdisciplinary research studentships, which would explicitly link normative and empirical inquiry. Research studentships could involve taught courses to familiarise students with the terms and approaches used by natural and social scientists, pooled or within institutions.

32 In the longer term we see civil liberties as a key ethical issue. The expected convergence between IT and nanotechnologies is likely to enable devices that can

increase personal security on the one hand but might be used in ways that limit individual or group privacy by covert surveillance, by collecting and distributing personal information (such as health or genetic profiles) without adequate consent, and by concentrating information in the hands of those with the resources to develop and control such networks. There is speculation that a possible future convergence of nanotechnologies with biotechnology, information and cognitive sciences could be used for the purposes of radical human enhancement. These currently fall into the far-future/science fiction category, but should they be realised are likely to raise fundamental and possibly unique social and ethical issues. There is a need to monitor future applications of nanotechnologies to determine whether they will raise social and ethical impacts that have not been anticipated in this report. Later in this report we consider how this might be facilitated for nanotechnologies (section 9.6) and for other new and emerging technologies (section 9.7).

33 On the whole, the scientists and engineers from whom we have collected evidence during this study indicated that they had considered, or were willing to consider, the ethical and social impacts of their work. Because nanotechnologies and other advanced technologies have the potential for significant and

diverse impacts, which bring both benefits and risks, all researchers engaged in these fields should give thought to the wider implications of their work. We note that the Joint Statement of the Research Councils'/AHRB's Skills Training Requirements for Research Students does specify that research students should be able to demonstrate awareness of the ethical issues associated with their research. However, the Statement does not require formal training of students to raise awareness in these areas, which in the case of advanced technologies such as nanotechnologies may not always be obvious, nor does the Statement apply to staff. **We recommend that the consideration of ethical and social implications of advanced technologies (such as nanotechnologies) should form part of the formal training of all research students and staff working in these areas and, specifically, that this type of formal training should be listed in the Joint Statement of the Research Councils'/AHRB's Skills Training Requirements for Research Students.** The research councils/AHRB should support and expand the provision of short courses, bringing together junior researchers and doctoral students in science, engineering and social science to address the ethical and societal implications of technological developments.



# 7 Stakeholder and public dialogue

## 7.1 Introduction

1 As has been seen for other technologies, such as genetically modified (GM) crops and food in the UK, public attitudes play a crucial role in the realisation of the potential of technological advances. A number of social and ethical issues have been outlined in Chapter 6 and, as will be seen below, through our research into public attitudes, which could valuably be addressed through stakeholder and public dialogue on nanotechnologies. In this chapter we consider current public awareness of nanotechnologies in Britain (based on market research commissioned for this study), discuss the value of public dialogue on new technologies, and examine possible mechanisms for future dialogue on nanotechnologies.

## 7.2 Current public awareness of nanotechnologies in Britain

2 There is currently very little research evidence available on public attitudes to nanotechnologies in the UK or elsewhere. A single quantitative item appeared on the 2002 Eurobarometer survey (Gaskell et al 2003), where over 50% of the sample answered 'don't know' when asked whether they thought that nanotechnologies would improve or make worse their way of life over the next 20 years. Of the remainder who did have an opinion, a clear majority felt that it would indeed improve their lives. However, the extremely high level of 'don't know' responses indicates very low general levels of awareness of the issue of nanotechnologies across Europe. A web-based survey conducted in 2001 in the USA jointly sponsored by the National Geographic Society and the National Science Foundation (Sims-Bainbridge 2002) found that 57% of respondents agreed with the statement that 'human beings will greatly benefit from nanotechnology, which works at the molecular level atom by atom to build new structures, materials and machines'. However, such a web-based sampling technique is inherently self-selecting in nature, drawing disproportionately from people who have ready internet access as well as those who are particularly interested in science and technology issues in the first place. Accordingly, it is impossible to extrapolate this result to attitudes among a sample of the general public. A further difficulty with both surveys is that we cannot know whether the responses obtained reflect genuinely considered beliefs about nanotechnologies, or a response to the questions based upon beliefs about the future impacts of technology more generally (where attitudes are known to be highly favourable). That is, neither survey gives us detailed information on how people might *interpret* a new development when it is described to them in some detail, something that is arguably more

important as an indicator of the way in which public attitudes to nanotechnologies might develop in the future. Accordingly, BMRB International Ltd was commissioned by the Working Group to carry out preliminary research into levels of awareness of and attitudes to nanotechnologies with samples drawn from the general public. This research was both quantitative and qualitative, and comprised two strands (see BMRB 2004): (a) a representative national survey using three items; and (b) two in-depth workshops. Sections 7.2.1 and 7.2.2 outline BMRB's findings, as presented in its report to the Working Group.

### 7.2.1 Quantitative survey findings

3 The first strand was a three-question survey with a representative sample of 1 005 people aged 15 or over in Great Britain. This was designed to give a basic measure of awareness of nanotechnologies among members of the general public, establish whether those who had heard of it could provide any definition, and whether they thought it would have a positive or negative effect on quality of life. The questions used are shown in Box 7.1.

#### Box 7.1 The BMRB survey questions

*The first question was asked of all 1 005 respondents*

Q1. Have you heard of nanotechnology? (n=1005)

*If the respondent answered yes at question 1 they were then asked*

Q2. What do you think nanotechnology is? (n=262)

*Finally, if a person said yes at question 1 and had not said don't know at question 2 they were asked*

Q3. Do you think nanotechnology will improve our way of life in the next 20 years, it will have no effect, or it will make things worse? (n=172)

4 As had been expected, there was limited awareness of nanotechnologies among the survey respondents.

5 In response to question 1, only 29%<sup>1</sup> of the survey respondents said they were aware of the term. Awareness was higher among men (40%) than women (19%), and was slightly lower for older respondents, falling from around one-third for those aged under 55, to one-fifth (20%) of those aged 65 or over. There was also a clear pattern by social grade, with awareness peaking at 42% of socio-economic group AB and falling to 16% of socio-economic group DE.

<sup>1</sup> 262 out of 1 005 respondents gave this response at the time of the interview, which is approximately 26%. However, the final data are weighted to the profile of all adults in Great Britain. This means that those 262 respondents represent more respondents (293) in the weighted data. In terms of the estimated percentage of all GB adults, this is 29%.

6 At question 2, just 19% (172) of the survey sample could offer any form of definition. The most common centred on miniaturisation, or technology on a very small scale. Another frequent response relied on a particular application such as computing, electronics or medicine.

7 At question 3, the majority (68%) of those who were able to give a definition of the word felt that it would improve life in the future, compared with only 4% who thought it would make things worse. Thirteen per cent said unprompted that whether nanotechnology would make things better or worse depended on how it was used (despite the fact that this was not presented as an option on the questionnaire). This last finding is consistent with views presented in the qualitative workshops (discussed next), which also showed that participants' decisions about whether a technology is 'good' or 'bad' depends on what it is used for.

### 7.2.2 Qualitative workshop findings

8 The second strand of research consisted of two in-depth qualitative workshops with members drawn from a broad spectrum of the general public: one held in London (23 participants) and one in Birmingham (27 participants). The aim was to explore participants' ideas about and attitudes towards nanotechnologies, the everyday concepts that people might use to understand and interpret the technology, and to identify and discuss areas for concern and questions they might have. As expected (and congruent with the survey findings discussed above) prior awareness and knowledge of nanotechnologies among most workshop participants was limited. In anticipation of this, the nature of nanotechnologies was described as the workshops progressed, and participants could subsequently ask questions of a member of the working group who attended in the capacity of expert scientist<sup>2</sup>. The workshops also aimed to discuss the issue of the control and regulation of nanotechnologies.

9 The more in-depth exploration of respondents' views that was possible in the qualitative workshops revealed that, although there were major concerns about nanotechnologies, as with any new technology, there was also much that respondents thought was positive, or potentially so. However, it was also felt that nanotechnologies were very much untried technologies,

and as such their potential benefits and drawbacks would only become clear over time.

10 The workshop participants were concerned about many aspects of nanotechnologies, including those outlined in Box 7.2. They felt that reassurances were necessary about the areas of concern, although the balance of concerns obviously varied from individual to individual.

#### *Box 7.2 Aspects of nanotechnologies that caused concern in workshops*

- Its financial implications: whether there would be an adequate return on any investment made by the UK; also whether the UK could afford not to invest; and who might make such an investment, and with what sort of hoped-for return;
- its impact on society: employment; social freedom and control; the position of the developing world in relation to industrialised nations; and the possibility of corporations gaining influence;
- whether or not nanotechnologies, and devices using it, would work: particularly for applications used within the human body;
- the long-term and side-effects of nanotechnologies: whether enough was being done to establish what these were, and whether or not lessons had been learned from the past (for example, from nuclear technology);
- whether nanotechnologies could be controlled: whether this could be done internationally as well as nationally; whether the public would be involved and whether they would be capable of making a contribution; also, whether the public's contribution to the debate would be listened to.

11 There was also much that participants in the workshops were positive towards. The key areas in which it was felt that nanotechnologies had a potential contribution to make, or which interested respondents, are listed in Box 7.3.

<sup>2</sup> The scientist's role was confined to providing basic information on what nanotechnologies were, scenarios of possible developments in nanotechnologies, and then to be on hand to answer any questions raised by the group. The scientist did not take part in any other aspect of the moderating or running of the groups. The full methodology is described in BMRC (2004).

**Box 7.3 Aspects of nanotechnologies that workshop participants were positive about**

- The exciting nature of nanotechnologies: the sense that it was untried and, as such, had untapped potential, and an unknown number of ways in which humankind and individuals could benefit;
- the possible applications of nanotechnologies: respondents were particularly positive towards medical and, to a lesser extent, cosmetic applications;
- the possible creation of new materials, potentially being more useful and creating less waste;
- a sense that nanotechnology was a natural technological progression and that, in the future, arguments against nanotechnology developments will appear to be ridiculous;
- a hope that nanotechnology would improve quality of life, both through the creation of new products and new medical treatments.

### **7.2.3 Interpreting the research into public attitudes**

12 In interpreting the findings from the survey and qualitative workshops, it should be borne in mind that both were exploratory exercises, conducted within the remit and financial resources available to the Working Group. They certainly should not be taken to represent a full exploration of current British attitudes to nanotechnologies. In addition, the findings should be interpreted in a British context only: no generalisations can be made from these data about public attitudes to nanotechnologies in other countries, particularly to cultural contexts outside Europe.

13 Several issues are, however, worthy of comment. The fact that awareness among the British population is currently very low (consistent with the 2002 Eurobarometer findings cited above) implies that much will hinge upon how attitudes to nanotechnologies are shaped over the next few years. In addition, when attempting to define this new development, the survey respondents made reference to other technologies with relatively positive associations (IT, medicines). This may well explain in part why the majority of those who could provide a definition also thought that nanotechnologies would improve the quality of life for people.

14 By contrast, in the qualitative workshops, where respondents deliberated the issues in greater depth, responses were more mixed and at times touched also upon issues with more negative connotations (such as

nuclear energy and GM organisms)<sup>3</sup>. Four issues arising from the qualitative workshops can be placed in relation to what is already known about public perceptions of risk.

15 First, the need for informed and accessible commentary on, and consideration of, any long-term uncertainties associated with nanotechnologies. Uncertainty has potentially both positive and negative outcomes, as the workshop participants fully recognised. However, it is known to be a significant driver of public concerns about technological risks, particularly where doubts exist over future safety or environmental impacts. Uncertainty was identified as a key factor in some of the very first research into risk perception on nuclear energy, and subsequent studies of a wide range of risk issues (Royal Society 1992; Slovic 2000).

16 Second, questions over governance of nanotechnologies. Like the concerns over long-term uncertainties, these issues are not specific to nanotechnologies, but arise in public discourse about many other technological issues. It can be helpful to separate governance issues into two strands. The first involves the role and behaviour of institutions, and their abilities to minimise unintended consequence and adequately regulate. Such questions are not, as Wynne (2003) points out, the product of a mis-informed or 'irrational' public. Rather, they are legitimate questions touching upon areas of very real potential risk, albeit ones that are inherent to the way organisations and regulation operate, and as a consequence sometimes difficult to represent in formal quantitative risk assessments. Nor should such questions be seen as the product of views that are anti-science or anti-technology. Many people, as the current workshop findings also indicate, remain highly enthusiastic about the general impacts that science will have on their future lives (see OST/Wellcome 2000). A second strand (highlighted in Chapter 6) concerns the possible trajectories that nanotechnologies will follow as they develop: who can be trusted to ensure that these trajectories will be socially beneficial? Can the public play a role in determining which trajectories are realised? Such questions express genuine doubts that people have about the ethics, social uncertainties and future governance of the technologies. Such concerns are likely to be key ones that will arise in any dialogue process involving nanotechnologies.

17 Third, the enthusiasm that many workshop participants expressed for the possible ways that nanotechnologies would benefit their and others' lives. Perhaps not surprisingly, benefits are an important part (if not the only part) of the evidence that people weigh up, alongside perceived risks, when making a judgement about the acceptability or otherwise of a hazard that might impact upon them (Royal Society 1992).

<sup>3</sup> It is important to recognise that the qualitative and quantitative research yield complementary findings, rather than one being in any sense more valid than the other. In addition, the total number of participants in the two workshops ( $n=50$ ) may at first sight seem small compared with that of the survey ( $n=1005$ ). However, this number is not untypical of qualitative social science research into risk attitudes, where the main objective is to explore the views of a group of people in depth, rather than gather a statistically representative sample of opinion. For example, the recent 'narrow-but-deep' component of the UK GM Nation? public debate (Public Debate Steering Board 2003) involved 77 participants, selected as here to represent a cross-section of lay views.

18 Fourth, BMRB (2004) also report that there was some mention in the workshops of ethical concerns over 'messing' with the building blocks of nature, in part in response to suggestions of scientists manipulating matter at the atomic level to create entirely new materials. An analogy was also drawn here by some workshop participants between nanotechnologies and GM. We know from both quantitative and qualitative risk perception research that this issue is one determinant of uneasiness over biotechnology (Grove White et al 1997; Gaskell et al 2000; Marris et al 2002) and other issues such as radioactive waste and nuclear energy (Sjöberg 2000). It follows that, not only does the potential exist for nanotechnologies to be stigmatised by such general association, but also some specific applications (as in the production of entirely new materials or properties, material/biological systems or organisms) are likely to raise significant ethical dilemmas.

19 In summary, awareness of nanotechnologies is currently low among the British population. In addition, the workshops reported here represent the first in-depth qualitative research on attitudes to nanotechnologies in the published literature, as far as we are aware. Their findings, although limited, provide a valuable indication of some of the wider social and ethical questions that ordinary people might wish to raise about nanotechnologies both now and in the future.

Accordingly, **we recommend that the research councils build on the research into public attitudes undertaken as part of our study by funding a more sustained and extensive programme of research into public attitudes to nanotechnologies. This should involve more comprehensive qualitative work involving members of the general public as well as members of interested sections of society, such as the disabled, and might repeat the awareness survey to track any changes as public knowledge about nanotechnologies develops.**

### 7.3 Importance of promoting a wider dialogue

20 It would be easy to argue that the assessment and control of the impacts of nanotechnologies – as a highly technical and complex subject – should be an expert-led process, restricted primarily to the peer community of scientists and engineers within academia, industry and government. However, the discussion in Chapter 6, as well as the results of the public attitudes research described above, indicates that some of the social and ethical concerns that certain applications of nanotechnologies are likely to raise stretch well beyond the basic science or engineering of the matter. In this respect, we are in broad agreement with the Better Regulation Taskforce (2003), which has recommended that the government communicate with, and involve as far as possible, the public in the decision-making

process in the area of nanotechnologies. This view is also in line with that of the European Commission, set out in their Communication 'Towards a European Strategy for Nanotechnology' (EC 2004a), in which coherent action 'to integrate societal considerations into the R&D process at an early stage' is endorsed.

21 In addition, several recent UK reports have recommended that scientists and policy makers engage in dialogue with interested parties about science and technology issues (House of Lords 2000; POST 2001), risk (Cabinet Office 2002; National Consumer Council 2003) and the environment (Royal Commission on Environmental Pollution 1998; Environment Agency 2004). In this respect, the events surrounding the bovine spongiform encephalopathy (BSE) crisis in the 1990s marked a turning point in the way UK science policy and risk assessment practice is viewed. The House of Lords Science and Technology Committee in particular, in its report on Science and Society, recommended 'That direct dialogue with the public should move from being an optional add-on to science-based policy-making and to the activities of research organisations and learned institutions, and should become a normal and integral part of the process.' (House of Lords 2000). Its rationale was that a crisis of trust had arisen in certain areas of UK science policy-making. To regain public trust, it recommended greater openness and transparency about science policy and scientific uncertainties. This assertion did not go unchallenged. O'Neill (2002) has argued that the evidence is not clear that the so-called crisis of trust is a response to greater untrustworthiness of officials in the UK: rather, many statements of mistrust might actually reflect a climate of suspicion, partly fed by media reporting of issues.

22 Dialogue with a range of stakeholders about risks also holds an increasingly important place in the work of many of the new advisory and regulatory bodies set up in the UK in the wake of BSE, such as the Food Standards Agency, the Agriculture and Environmental Biotechnology Commission, and the Human Genomics Commission. Dialogue-based processes have also been extensively used for addressing environmental and risk decision-making across Europe (Renn et al 1995) and the USA (Beierle and Cayford 2002). The Royal Society is undertaking its own dialogue initiatives through its 5-year Science in Society programme (see Royal Society 2004b). The aims of this programme are captured by the President of the Royal Society, in his 2001 Anniversary Address: 'Society needs to do a better job of asking what kind of tomorrow we create with the possibilities that science offers. Such decisions are governed by values, beliefs, feelings; science has no special voice in such democratic debates about values. But science does serve a crucial function in painting the landscape of facts and uncertainties against which such societal debates take place'.

23 The general case for wider societal dialogue about novel technologies, and with it greater openness about science policy, rests upon three broad sets of argument. Fiorino (1990) characterises these as normative, instrumental and substantive. The normative argument proposes that dialogue is a good thing in and of itself and as such forms a part of the wider democratic processes through which controversial decisions are made. The normative argument suggests, in particular, that it is important to make decisions sensitive, as far as is possible, to the ethical and value concerns of directly affected groups or populations. The instrumental argument suggests that dialogue, as one means of rendering decision-making more open and transparent, will increase the legitimacy of decisions and through this generate secondary effects such as greater trust in the policy-making process. Many of the arguments in the 2000 House of Lords Science and Society report focus upon the issue of the legitimacy of risk regulation and science. Finally, the substantive argument is that dialogue will help to generate better quality outcomes. In the field of environmental risk, non-technical assessments and knowledge have been shown to provide useful commentary on the validity or otherwise of the assumptions made in expert assessments (Wynne 1996; Yearley 2000). For upstream issues, where high levels of uncertainty exist, there may be particular benefits to opening up the risk characterisation process to a wide range of differing perspectives (Funtowicz and Ravetz 1992; Stirling 2004). The aim here is to avoid an overly narrow framing of the problem, through giving consideration to as full a range of impacts as possible, including potential 'shocks and surprises', many of which may not, initially at least, be open to formal quantitative analysis.

24 A US National Research Council report on Understanding Risk (Stern and Fineberg 1996) develops a detailed set of proposals for risk characterisation. They define the resultant analytic-deliberative process as combining sound science and systematic uncertainty analysis with deliberation by an appropriate representation of affected parties, policy makers and specialists in risk analysis. According to the authors, dialogue and deliberation should occur throughout the process of risk characterisation, from problem framing through to detailed risk assessment and then on to risk management and decision implementation. Likewise, the Royal Society's report on risk (Royal Society 1992) argued that the evaluation of whether a risk is tolerable or not involves judgements both about basic statements of fact (what types of harm might we run, and with what likelihood) as well as values (what level of a particular harm should we run). Even the basic statements of fact used in a risk assessment can be critically sensitive to 'framing' assumptions (that is, decisions about what factors to include or exclude, as necessary, to structure a risk assessment model). For example, probabilistic risk

assessments have particular difficulty in accommodating the human and organisational causes of major technological accidents and failures, even though evidence from case histories shows that these are the principal determinants of major failures in complex engineered systems (Blockley 1980; Vaughan 1996; Turner and Pidgeon 1997). The National Research Council report argues here that failure to attend to dialogue at the early stages of framing the problem can be particularly costly, for if a key concern is missed in subsequent analysis the danger is that the whole process may be invalidated. As we argue below, the issue of framing is particularly relevant to the upstream nature of the debate on nanotechnologies, and the case for stakeholder dialogue at the present time.

25 Although there is clearly a considerable momentum in the UK and elsewhere to engage in dialogue over science and technology issues, this should not be viewed uncritically. A first challenge concerns defining who might be involved. A useful distinction in this regard can be made between 'stakeholders' and 'the public' as follows: 'the term, stakeholder refers to organized, official and defined interested parties in any decision, such as NGOs, environmental groups, industry, regulators. The term public refers to individuals and communities who have an interest or stake in an issue but who may be less organized and less easily defined and identified' (Petts 2004).

26 This distinction is particularly important when designing engagement processes, for who needs to be involved will depend upon the objectives of dialogue, and in turn will have a direct bearing upon the expected outcomes, their efficacy and legitimacy. For many issues even the category 'the public' should not be viewed as a single undifferentiated entity, particularly in terms of attitudes towards risk (Royal Society 1992). And as noted in Chapter 6 of the current report, with nanotechnologies special interests might lie with very specific groups in society such as those who suffer from particular disabilities or health problems.

27 Other difficulties with dialogue processes arise because, as Okrent (1998) points out, we do not yet know enough about the practicalities and impacts of using analytic-deliberative processes. One reason for this is that systematic evaluation of dialogue processes and their outcomes remains relatively uncommon, being difficult and expensive to do properly, and often not recognised as important by sponsors at the outset of the process of dialogue. In addition, a number of technical and institutional/cultural barriers, such as regulatory fragmentation (which may preclude discussion of all relevant issues if these fall outside the sponsor's legal remit), may thwart effective implementation of an otherwise well-intentioned and planned dialogue process (Petts 2004).

## **7.4 Nanotechnologies as an 'upstream' issue**

28 Most developments in nanotechnologies, as viewed in 2004, are clearly 'upstream' in nature. There are at least three senses in which this is so: regarding current decisions, impacts and public acceptance, respectively.

29 First, many of the significant decisions that will affect the future trajectory of the technology, concerning research funding and R&D infrastructure, have yet to be made. As discussed in sections 6.3 and 7.2.3, one driver of the current concerns among NGOs (Arnall 2003; ETC 2003a) is a scepticism over whether the technology will be shaped in such a way that its outcomes will genuinely benefit society, the environment and people (particularly in the developing world) as is sometimes claimed. A timely and very broad-based debate might therefore focus upon which trajectories are more or less desirable, and who should be the ultimate beneficiaries of public sector investment in R&D, before deeply entrenched or polarised positions appear. Mehta (2004) argues that in the Canadian context the failure to consult the public early over biotechnology has led to several difficulties in the regulatory process, while Mayer (2002) also points out that the problematic issues that heralded the advent of biotechnology in the 1970s and 1980s did not go away, and that the participative technology assessment methods only now being developed for biotechnology might be usefully deployed in the upstream phase of nanotechnologies.

30 Second, as also noted in Chapter 6, many of the social and ethical impacts of nanotechnologies are yet to be envisioned, remain hypothetical, or will depend upon nanotechnologies' convergence with other technologies. Only over the medium (5–15 years) or far longer (more than 20 years) term will its precise outcomes and associated ethical implications become clear. Achieving meaningful dialogue today will therefore set several difficult challenges: to separate current hype from what is realistically achievable with the technology; to provide good-quality information on likely impacts; and to scope fully the potential sources of uncertainty. In turn, very specific applications might raise unanticipated social or ethical questions only well into the future or when the technology has reached a mature stage of development.

31 Finally, in terms of public acceptance, the research presented above illustrates that nanotechnologies have yet to gain any major place in public discourse in Britain, with awareness of the technology among the general population being extremely low. Although this has the potential to change rapidly, research on the factors that lead to risk issues becoming amplified or attenuated in public discourse shows that this rarely depends upon any single factor operating alone. Rather, this depends upon the combined impacts of a range of factors accumulating over time. These include: the balance of perceived benefits between individuals, private and the

public sectors; analogies drawn with other (both stigmatised or accepted) technologies; patterns of media coverage; position of campaigning groups; the existence of significant scientific dispute; and attribution of blame for prominent 'accidents' were these to occur (Pidgeon et al 2003).

32 Viewing nanotechnologies in upstream terms suggests that lessons can and should be learned from the history of other similar technological innovations. Mayer (Mayer 2002) argues that the development of all major technologies should be viewed as social processes, and that framed in this way there are clear parallels to be drawn between nanotechnologies today and the position that biotechnology faced in the 1980s. Similarities include the levels of excitement and hype, a promise to control the future without critical consideration first of which futures are desirable and who might ultimately control them, and narrowly framed debates about risk issues not encompassing wider social and ethical issues. One can also draw parallels between nanotechnologies today and the nuclear energy industry in the 1950s. Wynne (2003) argues that a particular difficulty with the early history of that industry, unanticipated at the time, was that the over-optimistic early claims made for the technology laid the foundations for the deep public scepticism and opposition that was to emerge much later in the 1970s.

33 Ultimately, it is difficult at this stage to judge whether, and which, applications of nanotechnologies will necessarily prove more or less difficult than nuclear power, GM or any other controversial technology (although Chapter 6 and the research into public attitudes discussed above outlines some of the potentially sensitive issues). One can make the argument that with many of these more mature technologies public dialogue has typically arrived too little too late, only being seen as an optional 'add-on' when the decision-making surrounding an issue (for example, radioactive waste siting) has become pressing, difficult or uncomfortable for regulators or governments. Under such circumstances the existence of highly polarised positions can make it very difficult, if not impossible, to take any real dialogue forward.

## **7.5 Designing dialogue on nanotechnologies**

34 We have reviewed, and are in broad agreement with, a number of submissions and papers that have argued for wider public dialogue and debate about the social and ethical impacts of nanotechnologies. However, the evidence presented to us also suggests that specifying the precise forms of such dialogue will be no simple matter. The objectives of dialogue, alongside who needs to take part, are likely to vary over time as the issues with nanotechnologies evolve. Equally, the methodologies available to meet dialogue objectives vary widely. Given that nanotechnologies are

likely to pose a wide range of issues (for example, regarding strategic direction and investment, specific applications, or convergence with other technologies) there is no single method to draw upon. Rather, dialogue methods must be designed specifically around the objectives at hand at any point in time.

35 Renn et al (1995) distinguish between three broad classes of citizen participation: genuine deliberative methods which allow for fair and competent debate and discussion between all parties, such as consensus conferences, citizens' juries and planning cells; traditional consultation methods, including public meetings, surveys, focus groups, and mediation, where there is little or no extended debate; and referenda, in which people do have democratic power but which are not generally deliberative in nature.

#### *Box 7.4 Possible Approaches to dialogue*

- Participatory and/or constructive technology assessment with stakeholders, particularly that which takes account of the dynamic interrelations between society and the development of nanotechnologies (see, for example, Rip et al 1995).
- Scenario analysis with stakeholders to identify significant uncertainties that might emerge with nanotechnologies. For example, the GM 'shocks and surprises' seminar organised by the Cabinet Office (2003).
- Direct public engagement such as citizen juries or panels for identifying at an early stage broad 'desired futures' for nanotechnologies, significant ethical concerns, or the acceptability of key applications and options. The quality of scientific and other input to such public engagement activities is critical to their success.
- Decision analytic methods draw upon more formal approaches for framing problems, as well as for identifying preferred options and their attributes (see, for example, Stirling and Mayer 1999; Arvai et al 2001)
- Multi-stage methods, which combine different approaches to framing, option appraisal and final choice in a sequence of linked activities, often with different groups of stakeholders and the public at various stages (see, for example, Renn 1999)
- Research into public attitudes, both qualitative and quantitative, to generate good quality 'social intelligence' (Grove White et al 2000) about nanotechnologies and public concerns.

36 Although referenda are not a typical engagement mechanism in the UK (unlike some other European countries such as Switzerland), government and other organisations have used various forms of traditional consultation on science and technology issues in the past, while consensus conferences occurred in the UK in 1994 for plant biotechnology (POST 1995) and in 1999 for radioactive waste management (UKCEED 1999). A useful summary of dialogue processes has been produced by the Parliamentary Office of Science and Technology (POST 2001); Box 7.4 lists some possible approaches.

37 Often dialogue processes need to be multi-stage (Renn 1999): that is, involving different participants and methodologies at different points in time. The GM Nation? public debate on the commercialisation of agricultural biotechnology, held in the UK in 2003, is a case in point in multi-stage design. GM Nation? had three main engagement components: initial issue framing (or foundation) workshops with randomly selected members of the general public were followed by a series of open activities (public meetings, interactive website) to which anybody could contribute, and finally a set of closed 'narrow-but-deep' groups, again comprising randomly selected members of the public (Public Debate Steering Board 2003).

38 Experience with GM Nation? (Horlick-Jones et al 2004) and deliberative processes elsewhere highlights several key requirements that any dialogue process involving nanotechnologies must meet and which we recommend. First, dialogue and engagement should occur early, and before critical decisions about the technology become irreversible or 'locked in'. Second, dialogue is not useful in and of itself, but has to be designed around specific objectives. Accordingly, clarity at an early stage about the objectives for dialogue is essential. Third, at least some form of commitment from the sponsor (typically government or some other agency) to take account of outcomes is required when commissioning dialogue processes: otherwise why should organisers and participants bother? Fourth, stakeholder and public dialogue should be properly integrated with other processes of technology assessment for nanotechnologies, as and when they occur. For example, the 2003 GM Nation? public debate was conducted in parallel with, and in part provided inputs to, both a science review of GM agriculture and an economic analysis of its costs, benefits and associated uncertainties. Finally, and not least, any dialogue process should be properly resourced, including the means for systematic evaluation (see also Petts 2004). Providing proper resources for dialogue processes is not a trivial matter, and one that Government should consider very seriously. The 1999 UK nuclear waste consensus conference costs were in the order of £100,000 (POST 2001), while the overall costs for the GM Nation? public debate totalled

£650,000 (Public Debate Steering Board 2003). Such costs, although at first sight large, must be viewed in relation to the far greater potential economic and social costs of getting decisions about investments in major areas of nanotechnologies wrong at this stage.

39 As discussed above, many of the issues currently surrounding nanotechnologies are 'upstream' in nature, providing a real opportunity for engagement to be designed in early. However, it seems likely that the precise requirements and objectives for such forms of engagement are much more difficult to specify, compared with the 'downstream' issues with which the UK has more experience. Accordingly, at the moment, we believe that we can only indicate generic areas of need. In the sections below we have applied the five generic objectives of dialogue and public participation mechanisms that have been proposed by Beierle and Cayford (2002) to nanotechnologies.

### **7.5.1 Incorporating public values in decisions**

40 For nanotechnologies, decisions will need to be sensitive to public values where significant ethical issues arise. For example, the concerns raised in Chapter 6 about the nano-divide and the future trajectory of the technology suggest such a need. Similarly, some of the issues associated with the convergence of nanotechnologies with other technologies, and in particular developments in bio-nanotechnologies, are likely to raise novel ethical questions in the future requiring wide public debate. This in turn suggests a requirement for periodic reflection on possible emerging ethical questions, and initiating appropriate forms of dialogue with stakeholders or the public as appropriate, as the technology matures and its tangible applications become clearer.

### **7.5.2 Improving decision quality**

41 The arguments above suggest that for upstream issues such as nanotechnologies the quality, as well as the acceptability, of initial decisions will depend heavily upon achieving appropriate framings for risk and technology assessments at an early stage. In particular, framing needs to incorporate both social as well as technical outcomes and concerns. Two important issues here, suggested by the research into public attitudes, would appear to be first the governance of nanotechnologies (who is to control and regulate nanotechnologies, and ensure that socially desirable goals can be identified and delivered), and second the long-term uncertainties. At a more operational level one could envisage the introduction of specific applications being accompanied by forms of stakeholder engagement on a case-by-case basis: one obvious issue would be to explore labelling requirements that people wish to see for specific classes for products, another the privacy implications of developments in sensing devices.

### **7.5.3 Resolving conflict**

42 Unlike with some other issues of more mature technologies, nanotechnologies have so far not generated significant levels of conflict between stakeholders. However, as applications emerge and decisions are made, this situation might well change. The hope expressed in evidence submitted to the group is that methods for upstream deliberation may help society to find appropriate resolutions for potential conflicts in advance, by better anticipation of sensitive issues.

### **7.5.4 Improving trust in institutions**

43 Although we note above some of the difficulties surrounding current discourses about openness and trust, a process of early debate and dialogue would signal to people a commitment by the UK Government, with the science and technology community, to a measure of transparency in the future development of nanotechnologies.

### **7.5.5 Informing or educating people**

44 This is a particularly critical objective, given the upstream nature of most nanotechnologies. At a broad societal level there is a need for a mature debate that can discriminate between the many (and we note sometimes exaggerated) claims for the technology. However, information provision has to aim at more than just 'educating' the public as a presumed means of avoiding controversy, a view embedded in the so-called 'deficit model' of much traditional public understanding of science and science communication practice (Irwin 1995). Meeting such an objective has proven unrealistic time and again: in particular because people resent or resist attempts at direct manipulation, greater knowledge does not necessarily bring greater acceptance of risks, and one-way communication without genuine dialogue about science issues may not address people's wider concerns (see Wynne 2003). The ESRC report on nanotechnology (Wood et al 2003) makes clear that some current commentary on social science and nanotechnologies runs a similar risk of assuming an unproblematic relationship between the role of communication and technology acceptance. Moving beyond the deficit model will require more innovative approaches to information provision, ones that involve a genuine two-way engagement between scientists, stakeholders and the public. The development and incorporation of good-quality, independent scientific information will also be central to the success of any analytic-deliberative process, such as a citizens' jury or public debate, that is adopted for nanotechnologies, as well as the design of appropriate health communications for individuals potentially exposed to nanoparticles and other materials in the workplace (see Cox et al 2003).

## 7.6 Conclusions

45 As has been seen with GM crops and food in the UK, public attitudes can play a crucial role in the realisation of the potential of technological advances. The research into public attitudes that we commissioned indicated that awareness of nanotechnologies among the British population is currently very low, which implies that much will depend on how attitudes to nanotechnologies are shaped over the next few years. Many of the participants in the qualitative workshops were enthusiastic about the possible ways that nanotechnologies might benefit their lives and those of others. However, reassurances were sought for long-term uncertainties about the possible impact of nanotechnologies, and analogies were made with issues such as nuclear power and genetic modification. Concerns were also raised about the role and behaviour of institutions, specifically about who can be trusted to ultimately control and regulate nanotechnologies.

46 The qualitative workshops reported here represent the first in-depth qualitative research on attitudes to nanotechnologies in the published literature, as far as we are aware. They provide a valuable indication of the wider social and ethical questions that ordinary people might wish to raise about nanotechnologies, but they were by necessity limited. We have therefore recommended that the research councils fund further and ongoing research into public attitudes to nanotechnologies that will in turn inform future dialogue work.

47 The upstream nature of most nanotechnologies means that there is an opportunity to generate a constructive and proactive debate about the future of the technology now, before deeply entrenched or polarised positions appear. Our research into public attitudes highlighted questions around the governance of nanotechnologies as an appropriate area for early public dialogue.

48 We recognize that dialogue on nanotechnologies is likely to be taken forward over the next few years in a

diversity of ways, and by a number of parties (not only Government). We welcome this and the opportunity that diverse activities are likely to present to identify best practice in public dialogue, and not just as applied to nanotechnologies.

49 We see an additional and important role for Government in supporting early stakeholder and public dialogue about nanotechnologies. A current particular strategic need is to ensure that the framing for subsequent public debate and technology assessments is drawn as widely as possible. This is particularly true for some of the governance questions highlighted in the research into public attitudes and in wider evidence, which would be appropriate for early public dialogue. Therefore, **we recommend that the Government initiates adequately funded public dialogue around the development of nanotechnologies. We recognise that a number of bodies could be appropriate in taking this dialogue forward.** For example, were issues about governance of nanotechnologies to be the subject of initial dialogue, as we suggest in this report, the research councils might be asked to take this forward as they are currently funding research into nanotechnologies. Others that could be appropriate to take forward, or co-sponsor, such dialogue include organisations such as the British Association for the Advancement of Science, the national academies, and major charities with experience of public engagement processes. Industry should also be encouraged to sponsor public dialogue. An example of this from 2003 was the citizens' jury on GM crops jointly convened by Unilever, Greenpeace, the Consumers Association and the Co-op in 2003. As noted above, the precise means of dialogue would need to be designed around specific objectives to be agreed by an independent steering board comprising a range of relevant stakeholders and experts in public engagement. Dialogue must be adequately funded (for example, a properly conducted citizens' jury or consensus conference would require minimum funding of the order of £100,000–£200,000) and properly evaluated, so that good public dialogue practice can be built on.



# 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 (200 nm 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 nanoscalar 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 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.

## 9 Conclusions

### 9.1 Nanoscience and nanotechnologies and their industrial application

1 Nanoscience and nanotechnologies incorporate exciting areas of research and development at the interface between biology, chemistry and physics. They are widely seen as having huge potential, and are attracting substantial and increasing investments from governments and from industrial companies in many parts of the world. We have defined nanoscience as the study of phenomena and manipulation of materials at atomic, molecular and macromolecular scales, where properties of matter differ significantly from those at a larger scale; and nanotechnologies as the design, characterisation, production and application of structures, devices and systems by controlling shape and size at nanometre scale. As the term 'nanotechnology' encompasses such a wide range of tools, techniques and potential applications, we have referred to 'nanotechnologies' in the plural throughout the report.

2 Much of nanoscience is concerned with understanding the properties of materials at the nanoscale and the effects of decreasing the size of materials or the structured components of materials. Nanoscale particles can exhibit, for example, different electrical, optical or magnetic properties from larger particles of the same material. Nanoscience is truly interdisciplinary, with an understanding of the physics and chemistry of matter and processes at the nanoscale being relevant to all scientific disciplines, from chemistry and physics to biology, engineering and medicine. Collaborations between researchers in different areas have enabled the sharing of knowledge, tools and techniques. Some of the benefits of this research are near realisation – for example in improved catalysis – but most are longer-term.

3 Current examples of nanotechnologies are predominately in the areas of characterisation, precision manufacturing, chemicals and materials. At this early stage, these represent predominantly incremental advances, and in some cases, a re-labelling of existing technologies. However, it is clear to us that nanotechnologies have the potential to substantially affect manufacturing processes across a wide range of industries over the medium- to long term. Most products currently enabled by nanotechnologies utilise fixed or embedded nanomaterials, or nanoscale regions of larger objects (for example, electronic components), which form a small percentage of the final product. Other applications use free (but sometimes coated) nanoparticles, which in contrast may have the capability to come into contact with humans and the environment. Of the chemicals produced in the form of nanoparticles, metallic oxides (for example, titanium dioxide, zinc oxide and iron oxide) – whose uses include skincare, electrical

storage, and catalysis – dominate. Small quantities of CNTs are being manufactured and used. For example, their electrical conductivity is being exploited in anti-static packaging. Although it is predicted that the demand for nanoparticles and nanotubes will continue to grow, the longer-term focus of industry is expected to be materials with specific properties for applications whose properties will be designed for use in a wide range of electronics, chemicals, communication and consumer products. However, this type of nanomanufacturing has not yet begun in any substantial way and will take decades to mature.

4 Wherever possible we have indicated the time by which we expect certain nanotechnologies to be realised. However it is difficult to give a detailed timescale, because most are at such an early stage of development. Moreover, potential products and applications will not be realised unless there is a market for them. Nor will nanotechnologies be incorporated into products and devices without the development of scalable, cost-effective manufacturing techniques that retain and preserve the properties of the nanoscalar material in the final product. Thus, realising the applications envisaged in this report will require advances in R&D and nanomanufacturing, and the supply of scientists and engineers with the appropriate multidisciplinary skills. Some applications may never be realised, whereas unanticipated scientific breakthroughs may lead rapidly to developments not foreseen at the time of our study.

5 Nanotechnologies have the potential to impact on a wide range of applications in many industries in the medium- and long term. However, some people exaggerate potential benefits whereas others exaggerate the risks. Overstated claims about benefits and risks, neither of them based on sound science, are doing a disservice to these emerging fields. In this report we have tried to separate hype from realistic hopes and concerns. For example, significant benefits to the environment are being claimed from the application of nanotechnologies. We recommend that a life cycle approach be taken to evaluate these claims and to ensure that savings in resource consumption during the use of the product are not offset by increased consumption during other stages.

### 9.2 Health, safety and environmental risks and hazards

6 Many applications of nanotechnologies pose no new health or safety risks – computer chips exploiting nanoscalar active areas, for example. Currently we see the health, safety and environmental hazards of nanotechnologies as being restricted to discrete manufactured nanoparticles and nanotubes in a free

rather than embedded form. Industry is beginning to exploit these because their physical and chemical properties differ from those of the same chemical at larger size; although it should be stressed that free nanoparticles and tubes represents only a small subset of nanotechnologies and there is currently very little exposure outside the workplace. In assessing and managing any risk it is necessary to understand both the hazard and the exposure pathways.

7 The evidence that we have reviewed suggests that some manufactured nanoparticles and nanotubes are likely to be more toxic per unit mass than particles of the same chemicals at larger size and will therefore present a greater hazard. The fundamental mechanisms of toxicity of nanoparticulates may not be very different: the capacity to induce inflammation by release of free radicals in response to a dose that is adequate to overcome the body's natural defences. However, the difference comes largely from two size-dependent factors: the relatively greater surface area of nanoparticles, given equal mass, and their probable ability to penetrate cells more easily and in a different way. To pose a risk, these nanoparticles must come into contact with humans or the environment in a form and quantity that can cause harm. Currently, the main risk of human exposure to manufactured nanoparticles and nanotubes is in a few workplaces (including academic research laboratories) and through the use of a small number of skin preparations that contain free nanoparticles. However the current lack of available research means that the scale of this risk cannot be fully determined.

8 Humans inhale very many pollutant nanoparticles (millions per breath) produced as the products of combustion. In recent decades it has been suggested, but not proven, that such exposures may be responsible for the observed relationships between air pollution and several diseases, particularly of the heart and the lung. Industrial exposure to fibres such as asbestos is a well-recognised cause of serious illness such as cancer. Nanotubes have physical properties that raise the possibility of similar toxic properties although preliminary studies suggest that they do not readily escape into the air in fibrous form. Sufficient toxicological information has been obtained, on both asbestos and air pollution nanoparticles, to allow reasonable estimates of the likely effects of any new manufactured nanomaterials so long as they are composed of low-toxicity and low-solubility materials. Shape and surface coatings of nanoparticles and nanotubes will also influence toxicity. It is very unlikely that manufactured nanoparticulates of low-toxicity and low-solubility materials (the characteristics of the materials that we have assessed in this report) would be introduced into humans in sufficient doses to cause the effects associated with air pollution or asbestos. Nevertheless (depending on the way in which they are manufactured, stored, transported or incorporated into products), there is the potential for some nanopowders to

be inhaled in certain workplaces in significant amounts.

9 Currently, dermal exposure is predominately through the use of cosmetics such as sunscreens that contain nanoparticles of titanium dioxide. Here the issue is whether they can penetrate the protective layers of the skin and then cause damage through the production of free radicals that can damage cells. There is little evidence in the public domain about penetration of the skin by the nanoparticles most commonly used in cosmetics. The toxicological evidence to date indicates that nanoparticles of titanium dioxide do not penetrate through the skin, although there is insufficient evidence available for the relevant scientific advisory committee to provide a judgement about the likelihood of skin penetration by zinc oxide. It is not clear whether skin penetration will be enhanced if these preparations are used on skin that has been damaged by sun (as might be expected in the case of sunscreens) or by common diseases such as eczema. We have recommended further studies of skin penetration by manufactured nanoparticles and that existing information collected by industry is placed in the public domain.

10 There is virtually no evidence available to allow the potential environmental impacts of nanoparticles and nanotubes to be evaluated. With the exception of some experiments on laboratory animals (designed to evaluate human toxicity) and one small study on one species of fish, little information is available about the toxicity of nanoparticulates to non-human species. In addition, the scarcity of published research into how nanoparticulates behave in the air, water, soil and other environmental media makes an assessment of environmental exposure pathways difficult. Nanoparticles and nanotubes that persist in the environment or bioaccumulate will present an increased risk and should be investigated. We have recommended that the release of nanoparticulates to the environment be minimised until these uncertainties are reduced. We have focused on the largest potential sources of manufactured nanoparticles and nanotubes and recommended that until there is evidence to the contrary, factories and research laboratories should treat manufactured nanoparticles and nanotubes as if they were hazardous and seek to reduce them as far as possible from waste streams. In addition, we have recommended that the release of free manufactured nanoparticles into the environment for remediation (which has been piloted in the USA) be prohibited until there is sufficient information to allow the potential risks to be evaluated as well as the benefits.

11 A wide range of uses for nanotubes and nanoparticles is envisaged that will fix them within products. It is impossible to assess whether this will be a significant source of exposure to nanoparticles and nanotubes without information about the rate at which such particles might be released. Because ways of fixing nanoparticles and nanotubes will be proprietary, we believe that the onus should be on industry to assess

such releases throughout a product's lifetime (including at the end-of-life) and to make that information available to the regulator.

12 The explosion of dust clouds of combustible material is a potential hazard in several industries. There is some evidence to suggest that combustible nanoparticles might cause an increased risk of explosion because of their increased surface area and potential for enhanced reaction. Until this hazard has been properly evaluated this risk should be managed by taking steps to avoid large quantities of nanoparticles becoming airborne.

13 Our conclusions about health, safety and environmental impacts have by necessity been based on incomplete information about the toxicology and epidemiology of nanoparticulates and their behaviour in air, water and soil, including their explosion hazard. There are uncertainties about the risk of nanoparticulates currently in production that need to be addressed immediately to safeguard workers and consumers and support regulatory decisions. In Chapters 5 and 8 we have identified a series of research objectives aimed at reducing the uncertainties relating to the toxicology and exposure pathways of nanoparticulates, as well as developing methodologies and instrumentation for monitoring them in the built and natural environment. We think that they can best be addressed by the establishment of a dedicated research centre that would probably be based on one or more existing research groups or centres. Our preliminary assessment of the toxicity of nanoparticles is based on those formed from low-toxicity and low-solubility chemicals. In the future, nanoparticles may be manufactured with surface chemistry that renders them more toxic or more able to overcome the body's natural defences. The research centre would ensure that the understanding of the health, safety and environmental risks of nanoparticulates keeps pace with developments in the field and might in time become a self-funded centre for the safety testing of nanomaterials.

### 9.3 Social and ethical impacts

14 In contrast to the health, safety and environmental concerns that have focused almost solely on a small part of nanotechnology, the social and ethical concerns range across the breadth of nanoscience and nanotechnologies, from concerns about the strategic direction of (and investment in) research into nanotechnologies through to those relating to specific applications. We expect some developments in nanoscience and nanotechnologies to raise significant social and ethical concerns, particularly those envisaged in the medium (5–15 years) and long (more than 20 years) term. Depending on the economic and political impacts of nanotechnologies (as yet unknown), some of these will relate to the governance of nanotechnologies, with concerns about who will decide

and control developments and who will benefit from their exploitation. Some facets of nanotechnologies, including their potential to manipulate the fundamental building blocks of materials, have raised concerns similar to those encountered in biotechnology.

15 Given that nanotechnologies are primarily enabling technologies, it is not surprising that, at least in the short- to medium term, the social and ethical concerns that have been expressed about it are similar to those encountered for other technologies as the applications will be similar. Past experience with controversial technologies demonstrates that these issues should be taken seriously even though they are not unique to nanotechnologies. We have therefore recommended that the research councils and the AHRB commission research into the potential social and ethical issues identified in this report. There is also need for researchers working in new technologies to consider the social and ethical implications of their work, and we have recommended that this form part of their training.

16 In the longer term, we expect increased information collection (for example, where sensors incorporate developments in nanotechnologies) to have implications for civil liberties. The expected convergence between IT and nanotechnologies could enable devices that can increase personal security but might also be used in ways that limit privacy. There is speculation that a possible future convergence of nanotechnologies with biotechnology, information and cognitive sciences could be used for radical human enhancement. This currently falls into the category of the far future or science fiction, but should some of the more speculative suggestions ever be realised they would raise fundamental and possibly unique social and ethical issues. We see a need to monitor future developments of nanotechnologies to determine whether they will raise social and ethical impacts that have not been anticipated in this report. Later in this chapter we consider how this might be facilitated, both for nanotechnologies (section 9.6) and for other new and emerging technologies (section 9.7).

### 9.4 Stakeholder and public dialogue

17 As has been seen with GM crops and food in the UK, public attitudes play a crucial role in the realization of the potential of technological advances. The research into public attitudes that we commissioned indicated that awareness of nanotechnologies among the British population is currently very low, which implies that much will depend on how attitudes to nanotechnologies are shaped over the next few years. Many of the participants in the qualitative workshops were enthusiastic about the possible ways that nanotechnologies might benefit their lives and those of others. However, questions were asked about their health, safety and environmental impact in the long term, and analogies were made with issues such as

nuclear power and genetic modification. Concerns were also raised about the role and behaviour of institutions, specifically about who can be trusted to ultimately control and regulate nanotechnologies.

18 The qualitative workshops reported here represent the first in-depth qualitative research on attitudes to nanotechnologies in the published literature, as far as we are aware. They provide a valuable indication of the wider social and ethical questions that ordinary people might wish to raise about nanotechnologies, but were by necessity limited. We have therefore recommended that the research councils fund a more sustained and extensive programme of research into public attitudes to nanotechnologies that will in turn inform future dialogue.

19 The upstream nature of most nanotechnologies means that there is an opportunity to generate a constructive and proactive debate about the future of the technology now, before deeply entrenched or polarized positions appear. We broadly agree with those who have argued for wider public dialogue and debate about the social and ethical impacts of nanotechnologies, and we have therefore recommended that the Government initiate adequately funded public dialogue around the development of nanotechnologies. Several bodies could be asked to take this forward, including organisations such as the British Association for the Advancement of Science, the national academies, and major charities with experience of public engagement processes. Industry should be encouraged to sponsor public dialogue. Our research into public attitudes highlighted questions around the governance as an appropriate area for early public dialogue, with questions being raised about who can be trusted to ensure that nanotechnologies will develop in a socially beneficial way. Given that the research councils are currently funding research into nanotechnologies, they might be asked to take forward dialogue on this issue.

20 Nanotechnologies are likely to pose a wide range of issues, so it would be inappropriate to identify a single method of public dialogue. Instead, the precise means of dialogue would need to be designed around specific objectives and should be agreed by an independent steering board comprising a range of relevant stakeholders and experts in public engagement. Finally, dialogue must be properly evaluated, so that good practice in public dialogue can be built on.

## 9.5 Regulation

21 Proportionate and flexible regulation (informed by scientific evidence) benefits and protects consumers, workers, industry and the environment, and also generates public confidence in new technologies. We expect the research, development and industrial application of nanotechnologies to impact on a diverse

range of regulations, including those relating to health and safety at work, environmental protection, licensing of medicines and the management of products at the end of their life. We believe that for the foreseeable future, the present regulatory frameworks are sufficiently broad to encompass nanotechnologies, and that a separate regulator or regulatory framework is unnecessary. Although many nanotechnologies are accommodated within existing regulations, it will be necessary to modify some regulations within existing frameworks to reflect the hazard presented by free nanoparticles and nanotubes. Our case studies were selected to illustrate how regulation will need to be adapted to reflect the fact that the safety of substances in the form of nanoparticles cannot be inferred from knowledge of their hazard in larger form. The examples were selected because of concerns raised during the study, and in most cases they relate to situations where there is potential for exposure in the short- or medium term.

22 We believe that chemicals in the form of nanoparticles and nanotubes should be treated separately to those produced in a larger form. Given the evidence that increased surface area can lead to greater toxicity per unit mass, regulation of exposure on a mass basis to nanoparticles and nanotubes may not be appropriate. Currently, the main source of exposure to nanoparticles and nanotubes is inhalation in the workplace. While HSE performs a wider review of the adequacy of current regulation to assess and control workplace exposure to nanoparticles and nanotubes, we have recommended that it consider setting lower occupational exposure levels for chemicals in this form. In addition, there is a need to review procedures relating to accidental exposure.

23 Under current UK chemical regulation (NONS) and its proposed replacement under negotiation at European level (REACH), the production of an existing substance in nanoparticulate form does not trigger additional testing. We have recommended that this regulatory gap be addressed by treating nanoparticulates as new substances, thus requiring additional testing, under both NONS and REACH. As more information about the toxicity of nanoparticles becomes available, a review should be undertaken of whether the toxicological tests required under NONS and REACH, and the production amounts that trigger these tests, are appropriate to nanoparticles and nanotubes.

24 Under EU cosmetics regulations, ingredients (including those in the form of nanoparticles) can be used for most purposes without prior approval, provided they are not on the list of banned or restricted use chemicals. Given our concerns about the toxicity of nanoparticles if they penetrate the skin, we have recommended that their use in products is dependent on a favourable assessment by the relevant EC scientific safety advisory committee. Thus, nanoparticles of titanium dioxide could be permitted for use (as its safety

has been assessed in the context of their use as a UV filter) but nanoparticles of chemicals such as zinc oxide and iron oxide (should manufacturers wish to use in Europe) would await a safety assessment. In addition to taking into account our concerns about the potential for nanoparticles to penetrate damaged skin, the safety advisory committee should consider whether the tests introduced as alternatives to tests on animals are appropriate for the testing of the safety of nanoparticles. In the light of the regulatory gaps that we identify, we have also recommended that the EC (encouraged and supported by the UK Government and informed by its scientific advisory committees) review the adequacy of the current regulatory regime for the introduction of nanoparticles into all consumer products, not just cosmetics. We have recommended a similar regulatory review be performed about the use of nanoparticles in medicines and medical devices.

25 Although we expect nanoparticles or nanotubes to have a low likelihood of being released from materials in which they have been fixed, we see the risk of exposure being greatest during disposal, destruction or recycling. Under the European Take-back Directives, industry is responsible for recovering used products and recycling materials or re-using components from vehicles and electrical and electronic equipment, two sectors that are expected to use materials containing fixed nanoparticles. We have recommended that these sectors publish procedures outlining how these materials will be managed to minimise human and environmental exposure to free nanoparticles and nanotubes. Avoiding end-of-life release should form an integral part of the innovation and design process of all components using embedded nanoparticles and nanotubes.

26 In many cases, decisions about how regulations should be modified to address particular risks of nanoparticles and nanotubes will require more information than is currently available about hazard to humans and the environment, and a better understanding of exposure pathways. The enforcement of regulations will require appropriate measurement techniques to monitor exposure. The research centre on toxicology and epidemiology of nanoparticles and nanotubes that we recommended will address these knowledge gaps, and one of its functions will be to advise regulators who will also have an opportunity to influence its research programme. We have also identified the need for adequate funding of a programme to develop agreed standards of measurement at the nanometre scale that can be used to calibrate equipment, which is a requirement for regulators and for quality assurance by industry.

27 Transparency of safety assessments is important in areas of new and emerging risks to human health and the environment. Because the responsibility for assessing the safety of a consumer product often rests with the manufacturer, some information may not be in

the public domain. We have therefore recommended that the terms of reference of scientific advisory committees considering the safety of ingredients should make provision for them to place all relevant data related to safety assessments in the public domain. In the meantime we have recommended that manufacturers that are including nanoparticles in their cosmetic products publish information about how they are taking account of the new properties of ingredients in nanoparticulate form in the methodologies used in their safety assessments. Because we believe that nanoparticles should be treated as new chemicals we have recommended that where ingredients are in the form of nanoparticles, they should be identified on the lists of ingredients in consumer products and preparations. There is an additional case for labelling based on transparency.

28 During this study we examined the appropriateness of some of the regulations in several key areas. Consequently, we have recommended that all relevant regulatory bodies review the implications of developments in nanotechnologies for the existing regulations within their remit and make the results of this review publicly available. Our consideration of regulation has focused primarily on current or near-term applications of nanotechnologies, and particularly on nanoparticles and nanotubes. Future applications of nanotechnologies may impact on other areas of regulation. For example, advanced sensors enabled by nanotechnologies may present challenges to regulation relating to privacy. We have also recommended that regulators and their respective advisory committees should include future applications of nanotechnologies into their horizon-scanning programmes. We are pleased to learn that one of the new EC scientific safety advisory committees for consumer products will examine the risks from new technologies, including nanotechnologies.

29 We have considered the calls for a moratorium on the development and release of new nanomaterials. We do not think that there is either the body of scientific evidence to warrant this intervention or a consensus that this is necessary on a precautionary basis. We have recommended measures that will minimise exposure while the uncertainties about the hazards posed by nanoparticles and nanotubes are being addressed, without the need for such a moratorium.

## 9.6 Responsible development of nanotechnologies

30 Nanoscience and nanotechnologies have huge potential. It is recognised that nanotechnologies and the uses to which they might be put may raise new challenges in the safety, regulatory or ethical domains, which will require societal debate if they are to fulfil this potential. The implementation of our recommendations

will address many of the potential ethical, social, health, environmental, safety and regulatory impacts, and help to ensure that nanotechnologies develop in a safe and socially desirable way. As part of the Government's commitment to the responsible development of nanotechnologies, **we recommend that the Office of Science and Technology commission an independent group in two and five years' time to review what action has been taken on our recommendations, and to assess how science and engineering has developed in the interim and what ethical, social, health, environmental, safety and regulatory implications these developments may have.** This group should comprise representatives of, and consult with, the relevant stakeholder groups. Its reports should be publicly available. The academies will also monitor the implementation of these recommendations and would of course be willing to participate in this review.

31 The Working Group gave consideration to the creation of a Nanotechnologies Commission, analogous to UK's Agriculture and Environment Biotechnology Commission, which would continuously monitor emerging nanotechnologies and advise on their implications. However, most of the Working Group believed that, on balance, a commission would not be appropriate at this time. We believe that our recommendations, if implemented, will deal adequately with short- and medium-term developments. It is not clear when, if ever, some of the longer-term possibilities discussed in this report will be feasible. In addition, nanotechnologies cover such a diverse range of techniques and applications with little commonality that it is not clear that a single body would be appropriate to oversee them all. The 2- and 5-year reviews recommended above should reconsider whether there is a need for a nanotechnologies commission.

## 9.7 A mechanism for addressing future issues

32 Our study has identified important issues that need to be addressed with some urgency. Given the potential impacts that other new and emerging technologies (including nanotechnologies) may have on society, we see it as essential that the Government establishes a systematic approach to identifying health, safety, environmental, social, ethical and regulatory issues of new technologies at the earliest possible stage. Therefore, **we recommend that the Chief Scientific Advisor should establish a group that brings together representatives of a wide range of stakeholders to look at new and emerging technologies and identify at the earliest possible stage areas where potential health, safety, environmental, social, ethical and regulatory issues may arise and advise on how these might be addressed.** As a minimum, we would envisage such a group meeting bi-annually. We appreciate that there are several bodies across Government with horizon-scanning roles; we do not see this group as duplicating their work but drawing on them to fulfil the following remit:

- Undertaking horizon scanning for new and emerging technologies and considering their potential health, safety, environmental, social and ethical implications.
- Commissioning wide-ranging evaluations of issues as they think appropriate to identify areas where there is lack of knowledge about impacts.
- Providing an early warning of areas where regulation may be inadequate for specific applications of these technologies.

33 The work of this group should be made public so that all stakeholders can be encouraged to engage with the emerging issues. This group would be separate to, but may contribute to, the periodic reviews of nanoscience and nanotechnologies that we outline in section 9.6.

# 10 Recommendations

## The industrial application of nanotechnologies

- R1 We recommend that a series of life cycle assessments be undertaken for the applications and product groups arising from existing and expected developments in nanotechnologies, to ensure that savings in resource consumption during the use of the product are not offset by increased consumption during manufacture and disposal. To have public credibility these studies need to be carried out or reviewed by an independent body. (Section 4.5: paragraph 32).
- R2 Where there is a requirement for research to establish methodologies for life cycle assessments in this area, we recommend that this should be funded by the research councils through the normal responsive mode. (Section 4.5: paragraph 33)

## Possible adverse health, safety and environmental impacts

*The lack of evidence about the risk posed by manufactured nanoparticles and nanotubes is resulting in considerable uncertainty.*

- R3 We recommend that Research Councils UK establish an interdisciplinary centre (probably comprising several existing research institutions) to research the toxicity, epidemiology, persistence and bioaccumulation of manufactured nanoparticles and nanotubes as well as their exposure pathways, and to develop methodologies and instrumentation for monitoring them in the built and natural environment. A key role would be to liaise with regulators. We recommend that the research centre maintain a database of its results and that it interact with those collecting similar information in Europe and internationally. Because it will not be possible for the research centre to encompass all aspects of research relevant to nanoparticles and nanotubes, we recommend that a proportion of its funding be allocated to research groups outside the centre to address areas identified by the advisory board as of importance and not covered within the centre. (Section 5.6: paragraphs 55 & 56)
- R4 Until more is known about environmental impacts of nanoparticles and nanotubes, we recommend that the release of manufactured nanoparticles and nanotubes into the environment be avoided as far as possible. (Section 5.7: paragraph 63)

- R5 Specifically, in relation to two main sources of current and potential releases of free nanoparticles and nanotubes to the environment, we recommend:
- (i) 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. (Section 5.4: paragraph 41)
  - (ii) that the use of free (that is, not fixed in a matrix) 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. (Section 5.4: paragraph 44)
- R6 We recommend 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 lifecycle of the product and make this information available to the relevant regulatory authorities. (Section 5.4: paragraph 42)
- R7 We recommend that the terms of reference of scientific advisory committees (including the European Commission's Scientific Committee on Cosmetic and Non-food Products or its replacement) that consider the safety of ingredients that exploit new and emerging technologies like nanotechnologies, for which there is incomplete toxicological information in the peer-reviewed literature, should include the requirement for all relevant data related to safety assessments, and the methodologies used to obtain them, to be placed in the public domain. (Section 5.3.2b: paragraph 30)

## Regulatory issues

- R8 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. (Section 8.5: paragraph 48)
- R9 We recommend that regulatory bodies and their respective advisory committees include future applications of nanotechnologies in their horizon scanning programmes to ensure any regulatory gaps are identified at an appropriate stage. (Section 8.5: paragraph 50)

*Recommendations R10 to R14 are based on applying our conclusions - that some chemicals are more toxic when in the form of nanoparticles or nanotubes and that safety assessments based on the testing of a larger form of a chemical cannot be used to infer the safety of chemicals in the form of nanoparticles - to a series of regulatory case studies:*

R10 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). As more information regarding 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. (Section 8.3.2: paragraphs 18 & 19)

R11 Workplace:

- (i) We recommend that the Health & Safety Executive (HSE) review the adequacy of its regulation of exposure to nanoparticles, and in particular considers 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. (Section 8.3.1: paragraph 11)
- (ii) We recommend that the HSE, Department for Environment Food and Rural Affairs and the Environment Agency review their current procedures relating to the management of accidental releases both within and outside the workplace. (Section 8.3.1: paragraph 12)
- (iii) 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. (Section 8.3.1: paragraph 13)

R12 Consumer products:

- (i) 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. Specifically: 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 it can deliver an opinion on its safety. (Section 8.3.3: paragraph 24 & 23)

- (ii) 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. (Section 8.3.3: paragraph 25)
- (iii) We recommend that the ingredients lists of consumer products should identify the fact that manufactured nanoparticulate material has been added. (Section 8.3.3: paragraph 26)
- (iv) We recommend that the EC's new Scientific Committee on Emerging and Newly Identified Health risks gives a high priority to the consideration of the safety of nanoparticles in consumer products. (Section 8.3.3: paragraph 27)
- (v) In the light of the regulatory gaps that we identify we recommend that the EC (supported by the UK) review the adequacy of the current regulatory regime with respect to the introduction of nanoparticles into consumer products. In undertaking this review they should be informed by the relevant scientific safety advisory committees. (Section 8.3.3: paragraph 28)

R13 We recommend that the Department of Health review its regulations for new medical devices and medicines to ensure that particle size and chemistry are taken into account in investigating possible adverse side effects of medicines. (Section 8.3.4: paragraph 29)

R14 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. (Section 8.3.5: paragraph 32)

R15 Measurement:

- (i) 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. (Section 8.4.2: paragraph 40)

- (ii) We recommend that the Department of Trade and Industry supports the standardisation of measurement at the nanometre scale required by regulators and for quality control in industry through the adequate funding of initiatives under its National Measurement System Programme and that it ensures that the UK is in the forefront of any international initiatives for the standardisation of measurement. (Section 3.3.5: paragraph 60)

comprehensive qualitative work involving members of the general public as well as members of interested sections of society, such as the disabled, and might repeat the awareness survey to track any changes as public knowledge about nanotechnologies develops. (Section 7.2.3: paragraph 19)

- R19 We recommend that the Government initiates adequately funded public dialogue around the development of nanotechnologies. We recognise that a number of bodies could be appropriate in taking this dialogue forward. (Section 7.6: paragraph 49)

## Social and ethical issues

- R16 We recommend that the research councils and the Arts and Humanities Research Board (AHRB) fund an interdisciplinary research programme to investigate the social and ethical issues expected to arise from the development of some nanotechnologies. (Section 6.8: paragraph 31)

- R17 We recommend that the consideration of ethical and social implications of advanced technologies (such as nanotechnologies) should form part of the formal training of all research students and staff working in these areas and, specifically, that this type of formal training should be listed in the Joint Statement of the Research Councils/AHRB's Skills Training Requirements for Research Students. (Section 6.8: paragraph 33)

## Ensuring the responsible development of nanotechnologies

- R20 We recommend that the OST commission an independent group in two and five years' time to review what action has been taken on our recommendations, and to assess how science and engineering has developed in the interim and what ethical, social, health, environmental, safety and regulatory implications these developments may have. This group should comprise representatives of, and consult with, the relevant stakeholder groups. Its reports should be publicly available. (Section 9.6: paragraph 30)

- R21 We recommend that the Chief Scientific Advisor should establish a group that brings together representatives of a wide range of stakeholders to look at new and emerging technologies and identify at the earliest possible stage areas where potential health, safety, environmental, social, ethical and regulatory issues may arise and advise on how these might be addressed. (Section 9.7: paragraph 32)

## Stakeholder and public dialogue

- R18 We recommend that the research councils build on the research into public attitudes undertaken as part of our study by funding a more sustained and extensive programme of research into public attitudes to nanotechnologies. This should involve more



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# **Annex A Working Group, Review Group and Secretariat members**

## **Working Group**

*The two Academies are extremely grateful to the Working Group for their hard work.*

|  |   |
|--|---|
| Prof Ann Dowling CBE FREng FRS (Chair) | Professor of Mechanical Engineering, University of Cambridge  |
| Prof Roland Clift OBE FREng            | Director of the Centre for Environmental Strategy, University of Surrey   |
| Dr Nicole Grobert                      | Royal Society Dorothy Hodgkin Research Fellow, University of Oxford   |
| Dame Deirdre Hutton CBE                | Chair of the National Consumer Council  |
| Dr Ray Oliver FREng                    | Senior Science and Technology Associate in the Strategic Technology Group, ICI plc  |
| Baroness Onora O'Neill CBE FBA FMedSci | Newnham College, University of Cambridge  |
| Prof John Pethica FRS                  | SFI Research Professor, Department of Physics, Trinity College Dublin and Visiting Professor, Department of Materials, University of Oxford                         |
| Prof Nick Pidgeon                      | Director of the Centre for Environmental Risk, University of East Anglia  |
| Jonathon Porritt                       | Chair of the UK Sustainable Development Commission and Programme Director of Forum for the Future   |
| Prof John Ryan                         | Director of the Interdisciplinary Research Collaboration on Bionanotechnology. Based at the University of Oxford  |
| Prof Anthony Seaton CBE FMedSci        | Emeritus Professor of Environmental and Occupational Medicine, University of Aberdeen and Honorary Senior Consultant, Institute of Occupational Medicine, Edinburgh |
| Prof Saul Tendler                      | Head of the School of Pharmacy and Professor of Biophysical Chemistry, University of Nottingham   |
| Prof Mark Welland FREng FRS            | Director of the Interdisciplinary Research Collaboration in Nanotechnology. Based at the University of Cambridge  |
| Prof Roger Whatmore FREng              | Head of the Advanced Materials Department, Cranfield University   |

## **Review Group**

*The two academies gratefully acknowledge the contribution of the reviewers. With the exception of Sir John Enderby and Mr Philip Ruffles, they were not asked to endorse the conclusions or recommendations, nor did they see the final draft of the report before its release.*

|  |   |
|--|---|
| Sir John Enderby CBE FRS (Chair)             | Physical Secretary and Vice-President of the Royal Society  |
| Mr Philip Ruffles CBE FRS FREng (Vice-Chair) | Vice-President of the Royal Academy of Engineering and Chair of its Standing Committee on Engineering |
| Sir Richard Friend FRS FREng                 | Cavendish Professor of Physics, Cambridge University  |
| Prof Nigel Gilbert FREng                     | Pro Vice-Chancellor and Professor of Sociology, University of Surrey                                  |
| Dr James McQuaid CB FREng                    | Previously Chief Scientist, Health and Safety Executive   |
| Prof Anthony Segal FRS                       | Department of Medicine, University College London   |

## **Secretariat**

The core secretariat was: Sara Al-Bader, Dr Jofey Craig (June 2003 - September 2003), Dr Andrew Dunn (October 2003 – August 2004) and Dr Rachel Quinn at the Royal Society and Richard Ploszek at the Royal Academy of Engineering. Valuable administrative and web support was provided by Karen Scott-Jupp (Royal Society). The secretariat is grateful to the many other staff at the two Academies who contributed to the successful completion of this study.



# Annex B Conduct of Study

## Overview

The Working Group sought a wide range of views in the ways outlined below. Written evidence, and summary reports of workshops, meetings and other oral evidence sessions were posted on the dedicated website ([www.nanotec.org.uk](http://www.nanotec.org.uk)) as they became available, and comments on evidence was requested. The report has been prepared by the Working Group (listed in Annex A) on the basis of evidence collected and their own expertise. The report has undergone a rigorous peer review process by a review group comprising Fellows of both Academies (also listed in Annex A). It has been endorsed by the Council of the Royal Society and approved for publication by the Royal Academy of Engineering.

## Evidence gathering elements

### *Initial call for views (June 2003)*

The study was launched with an initial call for views that invited individuals and organisations to register their interest in this study and to identify the key issues that they thought should be considered by the Working Group. Over 90 responses were received.

### *Scientists/engineers workshop (30 September 2003)*

The Working Group used this meeting to gather evidence from the scientific community (including industry) about the current state of research in nanotechnologies and both current and future applications of nanotechnologies.

### *Civil Societies workshop (30 October 2003 & 24 February 2004)*

At this small workshop the Working Group consulted and discussed issues with a range of civil society organisations. The Working Group prepared questions or issues they wanted to discuss and participants had the opportunity to help set the meeting's agenda. The Working Group met with additional representatives on 24 February 2004.

### *Health and environmental impacts meeting (8 December 2003)*

At this meeting the Working Group met with health and environment experts to consider the environmental applications of nanotechnologies as well as whether nanotechnologies might have a negative impact on human health or the environment.

### *Public consultation (December 2003 - March 2004)*

To explore public attitudes to nanotechnology, the market research company BMRB International was commissioned to research public attitudes to nanotechnology. This involved two strands:

- Two in-depth workshops with members of the public were held in December 2003 to explore their ideas about nanotechnology, and to identify and discuss any potential concerns or questions that might arise.
- Three questions, designed to establish public awareness of nanotechnology were included in an Access omnibus survey in early January. The survey sought the views of 1,000 people in Great Britain aged 15+.

### *Workshop on regulation (11 February 2004)*

The Working Group met with regulators and others with expertise in regulatory issues to discuss whether or not existing legislation is appropriate to nanosciences and nanotechnologies.

### *Industry meeting (3 March 2004)*

This half-day meeting offered the Working Group an opportunity to further explore the issues covered in the terms of reference with industry representatives.

### *Dedicated website ([www.nanotec.org.uk](http://www.nanotec.org.uk))*

All interested parties (including the public) were able to comment via the website on any of the information posted on the website or raise issues relating to nanotechnologies in general or the about the study itself.

## Independence

The study was conducted independently of Government, which was not involved in the selection of the Working Group members or its methods of working, and which did not view the report before it was printed.



## Annex C List of those who submitted evidence

On 11 June 2003, the Royal Society and Royal Academy of Engineering issued a call for written evidence for the nanotechnology study. This was followed by a number of oral evidence sessions, meetings and workshops. Reports of these were posted on the website as they became available, and comments requested on them.

The following is a list of the individuals and organisations that gave evidence to the study in writing and/or orally. For ease of reference, evidence is listed according by individual and by organisation. The views of individuals do not necessarily represent those of their organisations.

The Royal Society and Royal Academy of Engineering are most grateful to those who assisted the study by providing evidence, and have made every endeavour to list them all here. If any individuals or organisations have been omitted we offer our apologies and will ensure that the web version of the evidence list is updated.

W = provided written evidence

O = attended oral evidence session

M = attended meeting or workshop

### Individuals

#### A

|                       |   |
|-----------------------|---|
| Adams, Michael        | Unilever (M)                                      |
| Aeppli, Gabriel       | London Centre for Nanotechnology (W &O)           |
| Alakeson, Vidhya      | Forum for the Future (W)                          |
| Albertario, Fabio (W) |   |
| Aldrich, Tim          | Forum for the Future (M)                          |
| Allen, Geoffrey       | University of East Anglia (M)                     |
| Allen, Ray            | University of Sheffield (M)                       |
| Alsop, Adrian         | Economic and Social Research Council (W)          |
| Altmann, Juergen      | Experimentelle Physik II, Dortmund University (W) |
| Andrews, Arlan (W)    |   |
| Arnall, Alexander     |   |
| Ayres, John           | Imperial College London (W)                       |
|                       | University of Aberdeen (W)                        |

#### B

|                            |  |
|----------------------------|--|
| Bachmann, Gerd             | Co-worker of a German Governmental nanotechnology funding agency (O) |
| Ball, Philip (W)           |  |
| Balmer, Richard            | Association of Liberal Democrat Engineers and Scientists (W)         |
| Barbur, Vicki              | Eastman Kodak Company, USA (W)                                       |
| Batchelor FREng, Keith (W) |  |
| Besenbacher, Flemming      | University of Aarhus, Denmark (O)                                    |
| Biggs FREng, Simon         | University of Leeds (W)  |
| Binks, Peter               | Nanotechnology Victoria (W)  |
| Bosch, Wolfgang            | Filtronic (M)  |
| Bott, David                | ICI (M)  |
| Brazil, Rachel             | Royal Society of Chemistry (W & M)                                   |
| Briscoe, Brian             | Imperial College London (M)  |
| Broughton, Duncan (W)      |  |
| Brown, Mike                | Boots (M)  |
| Burgess, Doug              | MOD (O)  |
| Burgess, Jacquie           | University College London (O)  |

#### C

|                            |   |
|----------------------------|---|
| Calladine FRS FREng, Chris | University of Cambridge (W)                                   |
| Carroll, John              | University of Cambridge (W)                                   |
| Carson, Dave (W)           |   |
| Cass, Tony                 | Imperial College London (M)                                   |
| Chadwick, Derek            | The Novartis Foundation (W)                                   |
| Chetwynd, Derek            | University of Warwick (M)                                     |
| Church, Colin              | Department for environment food and rural affairs (DEFRA) (M) |
| Clarke, Andrew             | Kodak (M)   |

Colbeck, Ian  
Collis, Amanda  
Cumpson, Peter  
  
**D**  
University of Essex (M)  
The Biotechnology and Biological Sciences Research Council (W)  
National Physical Laboratory (M)

Davey, Roger J (W)  
Davies, Graham J  
Davies FREng, Stewart  
Delic, Julian  
Dent, Benjamin  
Depledge, Mike  
Devine, Steve (W)  
Dibb, Sue  
Dimmock, John  
Dobson, Peter  
Donaldson, Ken  
Dowding, Peter  
Downing, Steve  
Dransfield, Graham  
Drexler, Eric  
Duncan, Ruth  
  
University of Birmingham (M) (W)  
CEO BT Exact (W)  
Health and Safety Executive (M)  
Department for environment food and rural affairs (DEFRA) (M)  
Environment Agency, Head of Science (M)  
  
National Consumer Council (W&O)  
Media Services Sussex Ltd (W)  
University of Oxford, Begbroke Science Park (W & M)  
MRC Centre for Inflammation Research, University of Edinburgh (W &M)  
Infinaeum (M)  
ICI (M)  
Uniqema (M)  
Foresight Institute (W&O)  
Welsh School of Pharmacy (W)

**E**  
Eigler, Don  
Ellis, John  
Evans, Barry  
  
IBM (O)  
X-FAB UK Ltd (M)  
University of Surrey (W)

**F**  
Fenton, Gary (W)  
Festing, Michael  
Fisher, Andrew  
Fitzmaurice, Donald  
Fletcher, Amy L (W)  
Flodstrom, Anders  
Florence, Sandy  
Foo, Joyce  
Fox-Male, Nick  
Fullam, Brian  
  
Animal Procedures Committee (M)  
University College London (M)  
University College Dublin (M)  
  
Royal Institute of Technology, Stockholm, Sweden (O)  
The London School of Pharmacy (M)  
FCO Singapore (W)  
Eric Potter Clarkson IP Services (W)  
HSE (M)

**G**  
Gallop, John  
Gann, David  
Garnett, Martin  
Gimzewski FREng,  
James  
Gittins, David  
Glover, Anne  
Golunski, Stan  
Grant, Malcolm  
Greisch, Edward R  
Griffiths, Glynis  
Grimshaw, David  
Gubrud, Mark Avrum  
  
National Physical Laboratory (M)  
Imperial College London (W)  
University of Nottingham (W)  
Chemistry Dept, University of  
California, Los Angeles (W)  
Imerys (M)  
University of Aberdeen (M)  
Johnson Matthey (W)  
Agriculture and Environment Biotechnology Commission (O)  
US Military (W)  
Food Standards Agency (M)  
ITDG (M)  
Center for Superconductivity Research, Physics Dept, University of Maryland (W)

**H**  
Hanson, Robin  
Harper, Tim  
Harrison, Robert  
Hawkesworth, Stuart  
Hayes, Emma  
  
George Mason University, Fairfax, USA (W)  
Cientifica Ltd (W & O)  
Rouse Patents (O)  
HSE (M)  
Environment Agency (M)

Healey, Peter  
Higgins, Rob  
Hilsum, Cyril  
Hinde, Julia  
Hitchcock, Julian  
Holister, Paul  
Holtum, Dave  
Hook, David  
Hossain, Kamal  
Howard, Vyvyan  
Howorth, Dave (W)  
Howse, Mike (W)  
Humphreys, Colin (W)  
Hurley, Fintan  
Hyde, Vic

Institute of Occupational Medicine, Edinburgh (M)  
Cosmetics Toiletry and Perfumery Association (M)

## I

Iden, Ruediger  
Illsley, Derek  
Ion, Sue  
Irwin, Alan

BASF (M)  
Sun Chemical Co (M)  
BNFL (W)  
Brunel University (O)

## J

James FREng, Jim (W)  
Janzen, William  
Jones, Richard  
Juniper, Tony

Amphora Discovery Corporation (O)  
University of Sheffield (W & O)  
Friends of the Earth (W)

## K

Karn, Barbara  
Kelly, Mike  
Khandelwal, Amit  
Knowland, John  
Krauss, Thomas  
Kroto FRS, Harry (O)  
Kulinowski, Kristen M  
Kumar, Dinesh

US Environmental Protection Agency (W)  
University of Cambridge (M)  
Chemical Industries Association (M)  
University of Oxford (M)  
University of St Andrews (M)

Center for Biological and Environmental Nanotechnology USA (O)  
ION IT Ltd (W)

## L

Leigh, Beatrice  
Light, Richard  
Loveridge, Denis

GlaxoSmithKline (M)  
DAART Centre for Disability and Human Rights (W)  
Honorary Visiting Professor – PREST (W)

## M

Macaskie, Lynne  
Martin, Philippe  
Matthews, Kevin  
Maynard, Andrew  
McKeown FREng, PA (W)  
McLeod, Alistair  
McQuaid, Jim (W)  
Mehta, Michael D.  
Meldrum, Maureen  
Merrifield, David  
Mesquida, Patrick  
Miles, Glenn (W)  
Miles, Mervyn  
Milner, Robin  
Molyneaux, Andrea  
Mooney, Pat

University of Birmingham (M) (W)  
EC Health and Consumer Protection (M)  
Oxonica (M)  
National Institute for Occupational Safety and Health (W)

Imperial College London (M)

University of Saskatchewan (W)  
HSE (M)  
GSK (M)  
London Centre for Nanotechnology (M)

University of Bristol (M)  
UK Computing Research Committee (W)  
Medicines and Healthcare products Regulatory Agency (M)  
Etc Group (O)

Moore, Julia  
Morris, Vic  
Murray, Mike  
Murrer, Barry  
  
National Science Foundation (M)  
Institute of Food Research (M)  
ABPI (M)  
Johnson Matthey (M)

**N**  
Northage, Christine  
Health and Safety Executive (M)

**O**  
Ozorio de Almeida  
FCO, Brazil (W)

**P**  
Pacholak, Anna  
Palmer, Richard E  
Palmer, SB  
Parkinson, Stuart  
Parr, Douglas  
Parry, Vivienne (O)  
Pethrick, RA  
Pham FREng, DUC  
Phillips, Ian  
Phoenix, Chris  
Pick, Martin (W)  
Pilkington, Ian  
Poirier, Natalie  
Polak, Julia  
  
FCO, Poland (W)  
University of Birmingham (W & M)  
Warwick Nanosystems Group, UK (W)  
Scientists for Global Responsibility (W)  
Greenpeace (W&O)  
  
University of Strathclyde (W)  
University of Cardiff (W)  
ARM  
Center for Responsible Nanotechnology (W)  
  
Ilford (M)  
FCO, The Netherlands (W)  
Imperial College London (M)

**Q**  
Quinn, Francis  
L'Oreal (M)

**R**  
Rajan, Bob  
Rayner, Steve  
Richards, David  
Rickerby, David  
Reip, Paul  
Rip, Arie  
Rix, Sam  
Roco, Mike  
Roos, Ursula  
  
HSE (M)  
Saïd Business School, Oxford University (O)  
Technopreneur limited (W)  
Advisory Cell for Science and Technology, European Joint Commission Centre (W)  
Qinetiq Nanomaterials Ltd. (O)  
University of Twente, The Netherlands (O)  
ex pupil of Hills Road Sixth Form College (W)  
National Science Foundation, USA, Senior advisor for nanotechnology also Chair  
US Nanoscale Science and Engineering (W & O)  
FCO, Germany (W)

**S**  
Santoli, Salvatore  
Savage, Nora  
Schneemilch, Matthew  
Scott, Andrew  
Semple, Sean  
Sloan, Jeremy  
Smalley, Richard  
Smith, George  
Snape, Julian (W)  
Snowdon, Ken  
Southerland, David  
Stark FREng, Jim (W)  
Stepney, Susan UK  
Stewart FREng, Will (W)  
Stone, Vicki  
Sutherland Olsen, Dorothy (W)  
Sutton, David  
  
International Nanobiological Testbed Ltd (W)  
Environmental Protection Agency, USA (W)  
Imperial College London (M)  
Intermediate Technology Development Group (W)  
University of Aberdeen (M)  
University of Oxford (M)  
Rice University (O)  
University of Oxford (M)  
  
University of Newcastle (M)  
Department of trade and industry (M)  
  
Computing Research Committee (W)  
  
Napier University (M)  
  
ICI (M)

Swan, Harry  
Symons, Rex  
Syms, Richard

Thomas Swan & Co Ltd (M)  
Better Regulation Taskforce (M)  
Imperial College London (M)

## T

Tran, Lang  
Thomas, Jim  
Tolfree, David  
Tomlinson, Geoffrey (W)  
Treder, Mike  
Tsavalos, Alexander  
Tuppen, Chris

Institute of Occupational Medicine, Edinburgh (M)  
Action Group on Erosion, Technology and Concentration (W & M)  
Technopreneur limited (W)  
  
Center for Responsible Nanotechnology, USA (W)  
Health and Safety Executive (W & M)  
BT (M)

## V

Vadgama, Pankaj  
Vaughan-Lee, David  
Vest, Charles  
Visser, Germ W

Editor, Asia Pacific Coatings Journal (W)  
Massachusetts Institute of Technology (O)  
DSM, The Netherlands (W)

## W

Wadey, Rita  
Wakeford, Tom  
Wang, Brian  
Ward, Professor IM  
Warheit, David B.  
Weiss, Tilo  
Wells FRS FREng, PNT  
Whitby, Raymond  
White, Ian  
Whitesides, George  
Wiggins, Jason  
Wilkinson, Chris  
Willett, Steve (W)  
Williams, Gary (W)  
Williams, Martin  
Williams FREng, Richard  
Williams, Simon  
Wilsdon, James  
Wilson, Neil  
Windle, Alan  
Winkler, Stefan  
Wood, Stephen

OST (M)  
PEALS (M)  
Owner of a software company, Silicon Valley (W)  
University of Leeds (W)  
DuPont (W)  
Sustech (M)  
University of Bristol (W)  
University of Sussex (W)  
Chairman, scientific committee on cosmetic and non-food products (O)  
Harvard University, Department of chemistry and chemical biology (O)  
University of Oxford, Begbrooke Science Park (W)  
University of Glasgow (M)  
  
Department for environment food and rural affairs (DEFRA) (M)  
Institute of Particle Science & Engineering (W)  
The Patients Association (M)  
Demos (M)  
University of Warwick (M)  
University of Cambridge (M)  
FCO, USA (W)  
University of Sheffield (W & O)

## Y

Yeates, Steve (W)  
Young, Anthony R

St Johns Institute of Dermatology, Kings College London

## Organisations

### A

Action Group on Erosion, Technology and Concentration (W & M)  
Advisory Cell for Science and Technology, European Joint Commission Centre  
Agriculture and Environment Biotechnology Commission  
Amphora Discovery Corporation  
Animal Procedures Committee  
Asia Pacific Coatings Journal  
Association of Liberal Democrat Engineers and Scientists  
Association of the British Pharmaceutical Industry

David Rickerby (W)  
Malcolm Grant (O)  
William Janzen (O)  
Michael Festing (M)  
David Vaughan-Lee (W)  
Richard Balmer, Hon Secretary (W)  
Mike Murray (M)

### B

BASF group - Ruediger Iden (M)  
Begbroke Science Park

Better Regulation Taskforce  
Biotechnology and Biological Sciences Research Council  
Boots  
British Nuclear Fuels  
British Telecom  
Brunel University  
BT Exact (W)

University of Oxford - Peter Dobson (W & M), Jason Wiggins (W)  
Rex Symons (M)  
Amanda Collis (W)  
Mike Brown (M)  
Sue Ion (W)  
Chris Tuppen (M)  
Alan Irwin (O)

### C

Center for Biological and Environmental Nanotechnology, USA  
Center for Responsible Nanotechnology, USA  
Chemical Industries Association  
Cientifica Ltd  
Computing Research Committee (W)  
Cosmetics, Toiletry and Perfumery Association

Kristen M Kulinowski (O)  
Mike Treder, Executive Director (W)  
Amit Khandelwal (M)  
Tim Harper (W & O), Paul Holister (M)  
Vic Hyde (M)

### D

DAART Centre for Disability and Human Rights  
Department for the Environment, Food and Rural Affairs  
Martin  
Williams (M)  
Department for Trade and Industry  
Demos  
DSM, The Netherlands  
DuPont

Richard Light  
Colin Church (M), Benjamin Dent (M),

David Southerland (M)  
James Wilsdon (M)  
Germ Visser (W)  
David Warheit (W)

### E

Eastman Kodak Company, USA  
EC Health and Consumer Protection  
Economic and Social Research Council  
Engineering and Physical Sciences Research Council  
Environment Agency  
Environmental Protection Agency, USA  
Eric Potter Clarkson IP Services  
ETC (Action Group on Erosion, Technology and Concentration)  
Eversheds LLP Solicitors

Vicki Barbur (W)  
Phillippe Martin (M)  
Adrian Alsop (W)  
Dave Holtum (W)  
Michael Depledge (M), Emma Hayes (M)  
Nora Savage (W)  
Nick Fox-Male (W)  
Jim Thomas, Programme Manager and  
Pat Mooney (W, O & M)  
Julian Hitchcock (W)

### F

Filtronic  
Food Standards Agency  
Foreign and Commonwealth Office (W)

Wolfgang Bosch (M)  
Glynis Griffiths (M)

Foresight Institute  
Forum for the Future

Friends of the Earth

## G

GeneWatch UK (W)  
George Mason University, Fairfax, USA  
GlaxoSmithKline  
Greenpeace

Eric Drexler (W & O)  
Vidhya Alakeson, Principal Policy Advisor (W), Tim Aldrich (M)  
Tony Juniper (W)

Robin Hanson (W)  
Beatrice Leigh (M), David Merrifield (M)  
Doug Parr (W & O)

## H

Harvard University  
Health and Safety Executive

George Whitesides (O)  
Julian Delic (M), Brian Fullam (M),  
Stuart Hawksworth (M), Maureen Meldrum (M), Christine Northage (M),  
Bob Rajan (M), Christine Northage (M),  
Alexander Tsavalos (W & M)

## I

IBM  
ICI

Ilford  
Imerys  
Imperial College London

Don Eigler (O)  
Steve Downing (M), David Bott (M),  
David Sutton (M)  
Ian Pilkington (M)  
David Gittins (M)  
Brian Briscoe (M), Tony Cass (M), David Gann (W), Julia Polak (M), Matthew Schneemilch (M), Richard Syms (M), Alistair McLeod (M)  
David Gann, Director Innovation Studies Centre (W)  
Alex Arnall (W)  
Peter Dowding (M)  
Vic Morris (M)

Imperial College, Business School and Department of Civil and Environmental Engineering  
Imperial College London Centre for Energy Policy and Technology  
Infinaeum  
Institute of Food Research  
Institute of Food Science and Technology (W)  
Institute of Occupational Medicine, Edinburgh  
Institute of particle science and engineering (W)  
Institute of Physics (W)  
Intermediate Technology Development Group  
  
International Nanobiological Testbed Ltd  
ION IT Ltd

Fintan Hurley (M), Lang Tran (M)

David Grimshaw (M), Andrew Scott, Policy and Programmes Director (W)  
Salvatore Santoli (W)  
Dinesh Kumar (W)

J  
Johnson Matthey

Dr Stan Golunski (W), Barry Murrer (M)

K  
Kodak

Andrew Clarke (M)

L  
L'oreal  
London Centre for Nanotechnology

London School of Pharmacy

Francis Quinn (M)  
Gabriel Aepli, Director (W), Patrick Mesquida (M)  
Sandy Florence (M)

M  
Massachusetts Institute of Technology  
Media Services Sussex Ltd  
Medical Research Council (W)  
Medicines and Healthcare products Regulatory Agency

Charles Vest (O)  
John Dimmock - Technical Director (W)

Andrea Molyneaux (M), Rob Higgins (M),

David Hook (M)  
Ministry of Defence  
MRC, Centre for Inflammation Research, University of Edinburgh

Doug Burgess (O)  
Ken Donaldson (W & M)

**N**  
Nanotechnology Victoria  
National Consumer Council  
National Institute for Occupational Safety and Health (W)  
National Physical Laboratory (W)  
National Physical Laboratory  
  
National Science Foundation US

Peter Binks (W)  
Sue Dibb, Senior Policy Officer (W)

Natural Environment Research Council  
Novartis Foundation  
Ntera UK Ltd (W)

Peter Cumpson (M), John Gallop (M),  
Kamal Hossain (W)  
Mike Roco, Senior Adviser NSF and  
Chair of US Nanoscale Science,  
Engineering and Technology (W & O),  
Julia Moore (M)  
Deborah Cosgrove (W)  
Derek Chadwick (W)

**O**  
Office of Science and Technology  
Oxonica

Rita Wadey (M)  
Kevin Matthews (M)

**P**  
Patients Association  
PEALS  
Policy, Ethics And Life Sciences Research Institute  
Policy Research in Engineering, Science and Technology

Simon Williams (M)  
Tom Wakeford (M)  
Tom Wakeford (M)  
Denis Loveridge, Honorary Visiting  
Professor (W)

**Q**  
Qinetiq Nanomaterials

Paul Reip (O)

**R**  
Rice University  
Rolls Royce  
Rouse Patents  
Royal Institute of Technology, Stockholm, Sweden  
Royal Society of Chemistry

Richard Smalley (O)  
Mike Howse (W)  
Robert Harrison (O)  
Anders Flodstrom (O)  
Rachel Brazil, Manager, Materials  
Chemistry (W & M)

**S**  
Saïd Business School, Oxford University  
Science Technology and Governance in Europe  
Scientific committee on cosmetic and non-food product packaging (O)  
Scientists for Global Responsibility  
St Johns Institute of Dermatology, Kings College London  
Sun Chemical Co  
Sustech

Steve Rayner (O)  
Peter Healey, Coordinator (W)  
  
Stuart Parkinson, Director (W)  
Anthony R Young (M)  
Derek Illsley (M)  
Tilo Weiss (M)

**T**  
Technopreneur limited  
Thomas Swan & Co Ltd

David Tolfree (W)  
Harry Swan (M)

**U**  
UK Computing Research Committee  
Unilever  
Uniqema  
Universitat Dortmund, Experimentelle Physik III  
Université Louis Pasteur

Robin Milner and Susan Stepney (W)  
Michael Adams (M)  
Graham Dransfield (M)  
Juergen Altmann (W)  
Dorothy Sutherland Olsen (W)

|   |  |
|---|--|
| University College Dublin                             | Donald Fitzmaurice (M)   |
| University College London                             | Jacquie Burgess (O), Andrew Fisher (M)   |
| University of Aarhus, Denmark                         | Flemming Besenbacher   |
| University of Aberdeen                                | Anne Glover (M), Sean Semple (M)   |
| University of Aston                                   | Peter Brett & Xianghong Ma, Peter J Conley (W)   |
| University of Birmingham                              | Richard E Palmer (W & M), Graham J Davies (M), Lynn Macaskie (M & W)                               |
| University of Bristol                                 | Professor PNT Wells FRS FREng (W), Mervyn Miles (M)  |
| University of California, Los Angeles, Chemistry Dept | James Gimzewski FREng (W)  |
| University of Cambridge                               | Chris Calladine FRS FREng (W), John Carroll (W), Cyril Hilsum (W), Mike Kelly (M), Alan Windle (M) |
| University of Cardiff                                 | Duc Pham FREng (W)   |
| University of East Anglia                             | Geoffrey Allen (M)   |
| University of Edinburgh                               | Ken Donaldson  |
| University of Essex                                   | Ian Colbeck (M)  |
| University of Glasgow                                 | Chris Wilkinson (M)  |
| University of Leeds                                   | Simon Biggs FREng (W), Professor I M Ward (W)  |
| University of Liverpool                               | Vyvyan Howard (M)  |
| University of Maryland, Dept of Physics               | Mark Gubrud (W)  |
| University of Napier                                  | Vicki Stone (M)  |
| University of Newcastle                               | Ken Snowdon (M)  |
| University of Nottingham                              | Martin Garnett (W)   |
| University of Oxford                                  | Peter Dobson (M), John Knowland (M), Jeremy Sloan (M), George Smith (M)                            |
| University of Saskatchewan                            | Michael D Mehta (W)  |
| University of Sheffield (W)                           | Ray Allen (M), Richard Jones and Stephen Wood (W & O)  |
| University of Sheffield                               | Thomas Krauss (M)  |
| University of St Andrews                              | RA Pethrick (W)  |
| University of Strathclyde                             | Barry Evans (W)  |
| University of Surrey                                  | Raymond Whitby (W)   |
| University of Sussex                                  | Arie Rip (O)   |
| University of Twente                                  | Derek Chetwynd (M), Mr Neil Wilson (M)   |
| University of Warwick                                 | Barbara Karn (W)   |
| US Environmental Protection Agency                    | Edward R Greisch (W)   |
| US Military   |  |
| <b>W</b>  |  |
| Warwick Nanosystems Group, UK                         | SB Palmer (W)  |
| Welsh School of Pharmacy                              | Ruth Duncan (W)  |
| <b>X</b>  |  |
| X-FAB UK Ltd  | John Ellis (M)   |



## Annex D Mechanical self-replicating nano-robots and 'Grey Goo'

Media coverage of nanotechnologies has invariably raised the spectre of the 'grey goo': a doomsday scenario in which nanoscale robots self-replicate out of control, producing unlimited copies of themselves, consuming all available material and ultimately laying waste to the planet. Whereas most of the scientific community considers this to be science fiction, others have argued that it is a possible outcome of unregulated nanotechnology. The level of public and media interest in nanotechnology therefore justifies the following question: Is 'grey goo' a real concern, or is it a distraction from the important issues?

The original concept of molecular manufacturing described by Dr Eric Drexler, Chairman of the Foresight Institute, imagined the synthesis of materials and objects by a mechanical 'assembler'; that is, a machine with the ability make any object by selecting atoms from the environment and positioning them, one at a time, to assemble the object. This assembler can be programmed and is independently powered. As it can make any object, it can reproduce itself. If the process malfunctions or is corrupted, intentionally or not, the self-replication process could continue indefinitely. Over the past 20 years or so, Drexler and his colleagues have continued theoretical studies of the feasibility of such machines, but as far as we are aware there is no research in this field that has been supported by funding agencies, and there has been no practical experimental progress over this period. The reason is simple: there are many serious fundamental scientific difficulties and objections, to the extent that most of the scientific community believes the mechanical self-replicating nano-robot proposal to be impossible.

The scientific issues have been debated in open correspondence between Dr Drexler and Professor Rick Smalley, co-recipient of the Nobel Prize for Chemistry in 1996 for the discovery of carbon 60—so called buckyballs. In summary, there are two major difficulties: first, to lift and position atoms one needs very fine manipulators, of a similar size to the atoms being worked with; second, the atoms being manipulated must first attach – i.e. chemically bind – to the manipulator, and then unbind from the manipulator and bind to the object. Although scientists have used atomic force microscopes to manipulate a restricted group of individual atoms and molecules into simple structures on surfaces, the properties of matter on this lengthscale appear to be incompatible with the requirements for a mechanical self-replicating technology. These objections have been termed by Smalley as 'thick fingers' and 'sticky fingers'. Professor George Whitesides has questioned the feasibility of the energy management system that would be needed to handle the large energy input and release that occurs at the different stages of the construction process. Because the assembler is a nanomachine, its positioning accuracy is severely limited by the intense bombardment it receives from atoms in the environment – whether gaseous or liquid – which causes Brownian motion. It is quite clear: making a mechanical self-assembler is well beyond the current state of knowledge.

Our experience with chemistry and physics teaches us that we do not have any idea how to make an autonomous self-replicating mechanical machine at any scale, let alone nanoscale. Where we can find self-replicating machines is in the world of biology. The cell, thousands of nm in size, is the smallest unit we know that contains all the machinery essential for the process of reproduction, given a suitable environment. In fact, the planet we know today is quite different from its earliest form: biology evolved and turned a desert into the ecosystem of which we are now a part. At present however, the complete details of operation of even a simple cell are far beyond our understanding.

Given the above, we have heard no evidence to suggest that mechanical self-replicating nanomachines will be developed in the foreseeable future, and so would direct regulators at more pressing concerns outlined in chapter 8.

Quotations about mechanical self-replicating nano-robots and 'grey goo':

'I think there is no such thing as the assembler.' (Professor George Whitesides in evidence to the Working Group, with reference to the mechanical molecular assembler proposed by Dr Eric Drexler).

'My argument is that I believe that it is so implausible that I wouldn't worry about it...proving an impossibility is a very difficult thing to do and I've only done it in small parts.' (Professor Richard Smalley in evidence to the Working Group).

'... when people say "this isn't what we should be worrying about" I think they are right. I believe it's very much the wrong issue to focus on for a variety of practical and sensible reasons.' (Dr Eric Drexler in evidence to the Working Group).



## Acronyms and abbreviations

|        |  |
|--------|--|
| AFM    | atomic force microscope                              |
| AHRB   | Arts and Humanities Research Board                   |
| BRTF   | Better Regulation Task Force (UK)                    |
| BSE    | bovine spongiform encephalopathy                     |
| CD     | compact disk   |
| CNT    | carbon nanotube                                      |
| CVD    | chemical vapour deposition                           |
| DAMs   | directed assembly of monolayers                      |
| DEFRA  | Department for Environment Food and Rural Affairs    |
| DfT    | Department for Transport                             |
| DNA    | deoxyribonucleic acid                                |
| DH     | Department of Health                                 |
| DTI    | Department of Trade and Industry                     |
| DVD    | digital versatile disk                               |
| EA     | Environment Agency                                   |
| EBL    | electron beam lithography                            |
| EC     | European Commission                                  |
| EINECS | European Inventory of Existing Commercial Substances |
| ELID   | electrolytic in-process dressing                     |
| ELV    | End-of-Life Vehicles Directive                       |
| EPSRC  | Engineering and Physical Sciences Research Council   |
| EU     | European Union                                       |
| FDA    | Food and Drug Administration (USA)                   |
| FIB    | focused ion beam                                     |
| GDP    | gross domestic product                               |
| GM     | genetically modified                                 |
| HRTEM  | high-resolution transmission electron microscopy     |
| HSE    | Health and Safety Executive (UK)                     |
| ICT    | information and communication technology             |

|        |  |
|--------|--|
| IT     | information technology   |
| ITRS   | International Technology Roadmap for Semiconductors                                    |
| LCA    | life cycle assessment  |
| µm     | micrometre   |
| MBE    | molecular beam epitaxy   |
| MEMS   | micro-electromechanical systems  |
| mm     | millimetre   |
| MOD    | Ministry of Defence  |
| MOCVD  | metal oxide chemical vapour deposition   |
| MRI    | magnetic resonance imaging   |
| MWNT   | multi-walled carbon nanotube   |
| NEMS   | nano-electromechanical systems   |
| NGO    | non-governmental organization  |
| NIST   | National Institute for Standards and Technology (USA)                                  |
| NPL    | National Physical Laboratory (UK)  |
| nm     | nanometre  |
| NONS   | Notification of New Substances   |
| NSF    | National Science Foundation (USA)  |
| OEL    | occupational exposure limit  |
| OLED   | organic light-emitting diode   |
| OST    | Office of Science and Technology   |
| POST   | Parliamentary Office of Science and Technology   |
| PV     | photovoltaic   |
| R&D    | research and development   |
| RCUK   | Research Councils UK   |
| REACH  | Registration, Evaluation, Authorisation of Chemicals                                   |
| RFID   | radio frequency identification   |
| RIE    | reactive ion etching   |
| SAM    | self-assembled monolayer   |
| SCCNFP | Scientific Committee on Cosmetic Products and Non-food Products intended for Consumers |

|         |  |
|---------|--|
| SCENIHR | Scientific Committee on Emerging and Newly Identified Health Risks |
| SEM     | scanning electron microscopy                                       |
| SPM     | scanning probe microscopy  |
| STM     | scanning tunnelling microscope                                     |
| SWNT    | single-walled carbon nanotube                                      |
| TBT     | tributyl tin   |
| TEM     | Transmission electron microscopy                                   |
| UV      | ultraviolet  |
| WEEE    | Waste Electrical and Electronic Equipment Directive                |





