HM Government

Characterising the potential risks posed by engineered nanoparticles

A first UK Government research report

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Foreword

The Royal Society and Royal Academy of Engineering report '*Nanoscience and nanotechnologies: opportunities and uncertainties',* highlighted that many nanotechnologies pose no new health and safety risks and that concerns at this time relate to the potential impacts of engineered nanoparticles and nanotubes in a free rather than embedded form. The Royal Society and Royal Academy of Engineering identified these materials as a priority area for research, and we agreed in our response to develop a programme of research aimed at reducing the uncertainties relating to toxicity and exposure pathways for nanoparticles, as well as developing instrumentation to monitor these in the workplace and the environment. Developing a proper understanding of their properties is an essential step to proportionate regulation of any risk from these and other engineered nanomaterials.

This first report describes our research objectives to characterise the potential risks posed by engineered free nanoparticles and funding mechanisms to address these. The programme builds on the work of the Royal Society and Royal Academy of Engineering, and draws on detailed reviews that we have since commissioned to give us a detailed picture of our current state of knowledge in this area. Our programme has also been shaped by a series of meetings that we have held with stakeholders, including industry, academia, and civil society groups. This research programme is set within the wider context of our overall agenda to secure the responsible development of nanotechnologies published in February 2005, and our wider programme for public engagement on nanotechnologies published in August 2005. Understanding and responding to public aspirations and concern is critical to the responsible development of nanotechnologies and for that reason forms an integral part of our agenda.

A major aim of this report is to raise awareness of research priorities and funding opportunities both here and in Europe, as a first step towards developing a research community in the UK that can make its contribution to what will be a global endeavour in addressing the scientific uncertainties related to the safety of nanoparticles. We look to the scientific community in the UK to respond to this challenge and grasp the funding opportunities available.

Lord Bach of Lutterworth
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Lord Sainsbury of Turville
Minister for Science and Innovation
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Lord Hunt of Kings Heath
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Department for Work & Pensions

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Executive Summary

Background and introduction

1. The Government, in responding to the Royal Society and Royal Academy of Engineering (RS/RAEng) report '*Nanoscience and nanotechnologies: opportunities and uncertainties',*[1] recognised the gaps in our knowledge associated with the risks posed by nanoparticles to human health and the environment and committed to produce a first report on on-going and projected research in this area[2]. This report therefore meets the commitment set out in the Government response to recommendation three of the RS/RAEng report.

2. This first report sets out a programme of research objectives to characterise the potential risks posed by nanoparticles, and to describe ongoing activities and funding mechanisms to address these priorities. It will lead to the development of an appropriate framework and measures for controlling any unacceptable risks.

3. The report focuses on a range of free engineered nanoparticles which the RS/RAEng report, the Government response and the European Commission's Scientific Committee on Emerging and Newly Identified Health Risks[3] have identified as areas of concern. The term "nanoparticle" has been used in this report to represent all forms of engineered free nanomaterial.

4. Following on from the Government response to the RS/RAEng report we commissioned two scoping studies on hazard[4] and exposure[5], as well as a study into current and foreseeable manufacture and uses of engineered nanoparticles in the UK. This report has been developed primarily from evidence collected from those studies, although further evidence was collected from other sources during the preparation of this report. The research objectives have been identified and developed as a co-ordinated effort across Government Departments, Agencies and the Research Councils, and in discussion with stakeholders.

5. Three key areas have been identified where further research is needed to develop a risk management framework for nanoparticles:

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[1] The Royal Society and Royal Academy of Engineering (2004) *Nanoscience and Nanotechnologies: opportunities and uncertainties.* London: The Royal Society. See: http://www.nanotec.org.uk/finalReport.htm

[2] HM Government (2004) *Response to the Royal Society and Royal Academy of Engineering Report: 'Nanoscience and nanotechnologies: opportunities and uncertainties'.* London: DTI. See: http://www.ost.gov.uk/policy/issues/index.htm

[3] SCENIHR (2005) *Opinion on the appropriateness of existing methodologies to assess the potential risks associated with engineered and adventitious products of nanotechnologies.* Brussels: European Commission. See: http://europa.eu.int/comm/health/ph_risk/committees/04_scenihr/scenihr_cons_01_en.htm

[4] Tran, L., *et al.* (2005) *A scoping study to identify hazard data needs for addressing the risks presented by nanoparticles and nanotubes.* Edinburgh: Institute of Occupational Medicine.

[5] Mark, D., *et al.* (2005) *A scoping study to identify exposure data needs for addressing the risks presented by nanoparticles and nanotubes*. Buxton: Health and Safety Laboratory.

- properties, characterisation and metrology, including standardisation;
- human and environmental exposure; and
- hazard to human health and the environment.

6. A fourth area is understanding the societal and ethical dimensions of nanotechnologies as they arise.

7. Overarching this is a need for the development of and international agreement on nomenclature and definitions.

Public engagement and social research

8. The Government committed to addressing the societal and ethical dimensions associated with nanotechnologies, as these arise, in its response to the RS/RAEng report. Considerable progress has been made in putting in place the structures and processes for delivering open, constructive and informed social dialogue on nanotechnologies. These include a number of projects funded through the Department of Trade and Industry's (DTI's) Sciencewise scheme and by the Economic and Social Research Council (ESRC). In August 2005, government published its outline programme on public engagement on nanotechnologies.

9. A programme of stakeholder involvement will continue throughout the development and implementation of the research programme to ensure that research priorities and findings are formulated and discussed in a fully transparent and inclusive forum. Concerns expressed to date centre on the need for adequate management and controls around the development and use of nanotechnologies, and the equitable distribution of the benefits from their exploitation.

10. With regard to future research, within its commitment to the research challenges raised by succeeding in the global economy, the ESRC has a joint investment of up to £2.5M, initially with other public sector funding partners, to address the social and economic dimensions of nanotechnologies.

11. The Nanotechnology Issues Dialogue Group (NIDG) and the Nanotechnology Research Coordination Group (NRCG), the Government's policy and research groups for progressing work in this area, will additionally examine the outputs from current public engagement activities, and will identify and where necessary commission further public engagement activities and social research projects around nanotechnologies. This will be an on-going process, subject to periodic review.

Characterisation, properties and metrology

12. Robust measurement and characterisation methods for nanoparticles and their physico–chemical properties, underpin the assessment of their risks. This had previously been identified in the Government Response as a priority area for research. Building on this, three research objectives have been identified in this area.

13. Firstly, there needs to be clear identification, in the context of exposure and hazard assessment, of what measures (size, shape, surface characteristics) will be undertaken and how these measurements will be made. Associated with this is the need to establish standardised, well-characterised nano-scale reference materials for use in metrology, characterisation, exposure and hazard assessment (notably for comparative 'benchmarking' purposes in toxicology). Finally, one focussed area requiring further research is the need to understand the properties of nanoparticles in the context of their ignition and explosion potential. This includes the assessment and, where necessary, development of methods for evaluating such potential.

14. Government has recognised that this area is a high priority and is already funding, with industry and academia, the Measurements for Emerging Technology Programme at approximately £2.6M.

Exposure

15. Factors determining human and environmental exposure are the source of the nanoparticle, the pathway that it takes from the source to humans and the environment, and its fate and behaviour during transport. Given our current understanding of nanoparticle manufacture and use, a number of potential sources of exposure for nanoparticles have been identified. These include the workplace, both deliberate and unintentional environmental releases, and direct application from consumer and medical products.

16. It is clear however that our understanding of sources of nanoparticles is incomplete and that finding out more about sources of exposure is an important research objective. Government has started this work by mapping the manufacture and use of nanotechnologies across the UK, which will help in identifying sources of nanoparticles, their nature and magnitude.

17. An understanding of human and environmental exposure to nanoparticles is underpinned by technologies that enable their measurement and characterisation in important exposure pathways (air, soil, surface and groundwaters and direct application). This is fundamentally linked with research objectives within the field of metrology and characterisation and takes into account potential behaviour of nanoparticles in the natural environment, such as agglomeration. The development of such exposure assessment techniques in air, water, soil and organisms (including humans) was identified as a priority area

in the Government response and is reiterated in the current report. The optimisation and development of such techniques will allow us to understand more fully the fate and behaviour of nanoparticles in the indoor and natural environment. This, and an understanding of sources will enable us to identify which, if any, organisms are at risk of exposure and what form that exposure may take.

Hazards to human health

18. The Government response to the RS/RAEng report clearly identifies as a research priority the need to understand the hazards which nanoparticles may pose to human health as a result of consumer, medical, occupational and environmental exposure.

19. Six key research objectives in the area of human health hazard have been identified by Government. These aim to understand how nanoparticles can enter the human body, where they go within it and their toxicological and disease–causing effects, notably associated with important portals-of-entry such as the respiratory system, skin and gut. Some evidence from research involving non–engineered nanoparticles points to specific mechanisms of toxicity and effects such as inflammation. Research is needed to understand whether these effects are also associated with nanoparticle exposure.

20. An overarching priority is the development of testing strategies for human health hazard assessment and an evaluation of how suitable existing standard methods are when applied to nanoparticles. This is seen as a key priority and will require international development and harmonisation. There is considerable work being undertaken on the international stage in this area and organisations such as the OECD are best placed to take this forward. The Government will support work conducted through such international initiatives.

Hazards to the environment

21. Nanoparticles in the wider environment could pose a hazard to a large number of species including plants, micro-organisms, invertebrates, fish and mammals, potentially acting at the individual or population level and impacting on the structure and function of the ecosystem as a whole. The risk posed by nanoparticles to organisms will depend on the magnitude and nature of sources of exposure, their properties and behaviour in the environment, their associated environmental fate, their toxicity and persistence in organisms and their bioaccumulation and bio-magnification potential through the food chain.

22. A better understanding of sources of nanoparticles, their physical properties and their fate and behaviour in the environment will help us to identify which organisms are at risk of being exposed to nanoparticles.

23. One specific area of environmental exposure maybe from remediation of polluted groundwaters and contaminated land. As such, research to establish the uptake, toxicity and effects of nanoparticles on microorganisms, fauna and flora in soils and groundwaters has been identified as a research objective. More generally, there is also a need to understand the uptake, mechanisms of toxicity and effects of nanoparticles to key ecological groups including invertebrates, vertebrates and plants. A key aspect of such work should be the facilitating of knowledge transfer from human toxicological studies to inform ecotoxicology. Finally, the development of testing strategies and associated methods has, as with human hazard assessment, been identified as a priority objective, which should be met as part of an international effort.

Research funding and capacity building

24. A major aim of this first report is to raise awareness of the research priorities and funding opportunities here and in Europe, as a first step towards developing a research community in the UK that can make its contribution to what will be a global endeavour in addressing the scientific uncertainties related to the safety of nanoparticles.

25. In broad terms, the Government and its agencies are already supporting research in a number of important areas. Department of Trade and Industry (DTI), the Engineering and Physical Sciences Research Council (EPSRC) and the Health and Safety Executive (HSE) together with academia and industry are funding research in the area of measurement and characterisation to the sum of £6.5M. Another £4M will be available in the near future. This is strategically a very important area underpinning health and environmental safety research.

26. On the environment, the Department for Environment, Food and Rural Affairs (Defra), the Environment Agency and the Natural Environment Research Council (NERC) have aligned with several of the research objectives. Defra will be spending £1M over the next two years to address some of our knowledge gaps. The HSE is currently funding research and are partners in the international Nanoparticle Benchmarking Occupational Health and Safety research project which covers issues such as aerosol permeation, personal protective equipment and the effectiveness of filters.

27. On human health, the Medical Research Council (MRC) supports research on areas of toxicology, respiratory medicine and environmental health as part of their portfolio on the Physical Systems and Clinical Sciences Research Board. The MRC also supports basic research involving nanoparticles through their Molecular and Cellular Medicine Board. It is also prepared to commit up to £200K on the Environment and Health capacity building programme. The Biotechnology and Biological Research Council (BBSRC) funds research that will provide knowledge to underpin several of the objectives in this report.

28. Much of the Research Council funding is provided through the “responsive mode” which encompasses a range of research funding mechanisms. This

includes directed programmes, such as the new cross-Research Council programme on Environment and Health. It offers a very flexible route for funding under which proposals can be submitted at any time, in any area, for any amount and duration. Collaborative proposals with other funders, including other Government departments, are particularly welcome. Each of the Research Councils has indicated that they would welcome high quality bids addressing the relevant research objectives identified in this report.

29. The report highlights work being undertaken internationally to meet these objectives, for example the Nanoderm project funded under the 6th Framework Programme aims to develop new methodologies to study the quality of the skin as a barrier against formulations containing nanoparticles. In the near future there will be further funding opportunities under the 7th Framework Programme. We also anticipate that other stakeholders, notably industry, will play a major role in helping to meet many of the research objectives in this report.

30. Recognising the inherently cross-disciplinary nature of much of the research in this area, Research Councils will ensure a coherent, co-ordinated approach to addressing relevant research objectives and have established a co-ordinating group under the auspices of Research Councils UK. In order to encourage the research community, the Research Councils are supporting key networks to bring together researchers, policy makers and other stakeholders, to help identify and work up exciting, novel research proposals.

Reporting and next steps

31. Research funded by Government and Research Councils under this programme will be peer reviewed and made available to independent scientific advisory committees to consider. This, and subsequent reports, will be made publicly available.

32. The Government will continually review progress towards meeting the research objectives within this report. This will ensure that all relevant areas are being covered. A second report summarising this progress and updating our knowledge and research objectives will be published by the end of 2007.

1 Introduction

1.1 Background

1. In June 2003, Lord Sainsbury, the UK Government's Minister for Science and Innovation, asked the Royal Society and Royal Academy of Engineering (RS/RAEng) to consider the potential opportunities and uncertainties associated with nanoscience and nanotechnologies.

2. The RS/RAEng, in their response entitled *'Nanoscience and Nanotechnologies: opportunities and uncertainties'*[6], made a number of recommendations aimed at ensuring the responsible development and management of nanotechnologies. Particular emphasis was placed on the potential risks posed by free engineered nanoparticles to human health and the environment, a view recently supported by the European Commission's Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR)[7] .

3. The Government's response[8], published in February 2005, made a formal commitment, among many others, to address this area through an iterative and ongoing process of research, which would be outlined in a first report to be published in the autumn of 2005.

4. Since this time, the Nanotechnology Research Co-ordination Group (NRCG)[9], the Government's dedicated vehicle for co-ordinating work in this area, has made significant progress in developing a fit for purpose programme of research to enable Government to understand and manage the potential risks posed by nanoparticles. In this first report, an initial set of research objectives and funding opportunities are outlined.

1.2 Aims and objectives

5. The report's primary aim is to set out a programme of research objectives to characterise the potential risks posed by nanoparticles, and to describe ongoing activities and funding mechanisms to address these objectives. Following the Government's response to the RS/RAEng report, the following priorities were developed:

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[6] The Royal Society and Royal Academy of Engineering (2004) *Nanoscience and Nanotechnologies: opportunities and* uncertainties. London: The Royal Society. See: http://www.nanotec.org.uk/finalReport.htm

[7] SCENIHR (2005) *Opinion on the appropriateness of existing methodologies to assess the potential risks associated with engineered and adventitious products of nanotechnologies.* Brussels: European Commission. See: http://europa.eu.int/comm/health/ph_risk/committees/04_scenihr/docs/scenihr_o_003.pdf

[8] HM Government (2004) *Response to the Royal Society and Royal Academy of Engineering Report: 'Nanoscience and nanotechnologies: opportunities and uncertainties'.* London: DTI. See: http://www.ost.gov.uk/policy/issues/index.htm

[9] See: http://www.defra.gov.uk/environment/nanotech/nrcg/meetings/index.htm

- consideration of the societal issues surrounding the development and use of nanotechnologies;

- determination of the extent and nature of nanoparticle production and use in the UK. Regulators require an overview of potential sources of specific nanoparticles, and thus, the potential areas where action to control risks may be required;

- the development of robust and reliable measurement, detection and monitoring technologies for nanoparticles. This work is of fundamental importance in determining and monitoring potential exposure routes, both in indoor and outdoor environments and for meaningful assessment of hazard;

- work on the environmental behaviour, fate and potential bioaccumulation of nanoparticles; and

- work to underpin the robust assessment of potential hazards associated with nanoparticles. In particular, investigation of their toxicology, both to humans and ecological receptors. An important component of this will be the optimisation of current and/or the development of new, standard toxicological methods appropriate for nanoparticles.

6. In each case, the report has a number of more specific objectives, to:

- summarise gaps in our current understanding;

- set out research objectives in support of policy development for managing and controlling potential risks. As data becomes available, these priorities will need to be reviewed and may change;

- identify ongoing UK research and other international activities to meet the identified research objectives; and

- raise awareness of and describe the mechanisms for funding the research objectives both in the UK and overseas.

1.3 Definitions and scope

7. An internationally agreed set of terms and definitions (i.e. nomenclature) for nanotechnologies is needed and this has been identified as a priority. All stakeholders need to be certain that they are talking about the same activities, issues and parameters, when using ‘nano’ related vocabulary. Agreeing definitions of, for example, ‘engineered nanoparticles’ will define what substances fall within the scope of risk assessment and management.

8. The Department for Trade and Industry (DTI) and the British Standards Institute (BSI) have made considerable progress in this area through the National

Standardisation Strategic Framework, and in May 2005, the BSI published a Publicly Available Specification (PAS 71)[10] for a set of terms and definitions for nanotechnologies. The following are most relevant to the focus of this report:

- *Nanoscience*: study of phenomena and manipulation of materials at atomic, molecular and macromolecular scales, where properties differ significantly from those at the larger scale.

- *Nanotechnology*: design, characterisation, production and application of structures, devices and systems by controlling shape and size at the nanoscale.

- *Nanoparticle*s: particles with one or more dimensions at the nanoscale.

- *Nanoscale*: having one or more dimensions of the order of 100nm or less.

- *Engineered nanoparticles*: nanoparticles manufactured to have specific properties or a specific composition.

9. This is not, however, a standardised, internationally agreed framework, which will be essential given the global nature of nanotechnologies' developments and markets. Work in this area is being taken forward by the International Standards Organisation (ISO). The UK provides the chairman and secretariat for the newly established ISO Technical Committee (TC 229) for nanotechnology standards, which will include terminology and nomenclature as part of its remit.

10. In accordance with the advice of the RS/RAEng and the European Commission's SCENIHR, the focus of the more technical sections of the report is the risks posed by engineered, free nano-scale materials, including nanoparticles, quantum dots and nanotubes. Unless there is information on specific forms, these materials are referred to throughout the report as nanoparticles.

11. The report will not, therefore, set out research gaps relating to releases of unintentionally produced, free nanoparticles, such as combustion products or naturally formed free nanoparticles, including soil particles and dust. It is acknowledged, however, that data on the health effects of these non-engineered nanoparticles will inevitably play a significant role in helping us to understand the properties and effects of nanoparticles. In fact, much of the current knowledge presented in the report is derived from studies of combustion products and other nanoparticles that are unintentionally produced. This cross learning will continue to be important as we take forward research on nanoparticles. It will additionally enable us to assess risks to health from nanoparticles in the context of ambient nanoparticle exposure.

[10] BSI (2005) *PAS 71:2005 Vocabulary – Nanoparticles.* London: BSI. See: http://www.bsiglobal.com/Manufacturing/Nano

1.4 Process

12. In its response to the RS/RAEng report, the Government agreed to establish a group whose responsibility was to ensure the development of a comprehensive risk research programme in the area of nanoparticles. The NRCG was subsequently set up and this report has been developed by that group. It is chaired by the Department for Environment, Food and Rural Affairs (Defra), and comprises representatives of the Research Councils (BBSRC, EPSRC, ESRC, MRC, NERC)[11], the National Physical Laboratory, the Devolved Administrations, and the relevant government departments (Defra, DH, DTI, FSA) and regulatory agencies (HSE, the MHRA, and the EA) with responsibilities for the environment and human health and safety related policy and research agendas.

13. The Group's specific role is to develop and oversee the implementation of a research programme into the potential human health and environmental risks posed by free nanoparticles. This aims to ensure the responsible development of nanotechnologies, inform regulation, and underpin regulatory standards. This includes the outputs of dialogue between stakeholders, researchers and the public, with a view to enhancing and informing research decisions. The Group is further charged with establishing links with Europe and internationally, to promote dialogue and to draw on and facilitate exchange of information relevant to the Group's research objectives.

14. In developing the research programme, and to build on the work of the RS/RAEng, the Group commissioned two scoping studies on hazard[12] and exposure[13] data gaps. Both were peer reviewed by the Government's Advisory Committee on Hazard Substances (ACHS)[14], and also, at the Committee's request, research teams working on nanoparticles at the Universities of Oxford and Cambridge.

15. The development of the research report has also been supported by a series of meetings with key stakeholders, including industry, academia and civil society groups[15]. At an initial meeting, stakeholders were invited to put forward issues that should be considered in developing controls, in particular data/information gaps and research needs. At subsequent meetings, comments were invited on specific research priorities and an appropriate risk management framework. The programme of stakeholder involvement will continue throughout the development and implementation of the research programme to ensure that research priorities and findings are formulated and discussed in a fully transparent and inclusive forum.

[11] See annex 1 for a glossary of acronyms.
[12] Tran, L., *et al.* (2005) *A scoping study to identify hazard data needs for addressing the risks presented by nanoparticles and nanotubes.* Edinburgh: Institute of Occupational Medicine.
[13] Mark, D., *et al.* (2005) *A scoping study to identify exposure data needs for addressing the risks presented by nanoparticles and nanotubes.* Buxton: Health and Safety Laboratory.
[14] See: http://www.defra.gov.uk/environment/chemicals/achs/index.htm
[15] See: http://www.defra.gov.uk/environment/nanotech/nrcg/meetings/index.htm

16. In seeking to address these research objectives the Government recognises its commitment to replacing, reducing and refining animal testing.

17. Ongoing and future research commitments by Government for the research objectives identified in the report are discussed in chapter 6 and annex 3. In addition, Government will, in 2007, undertake a comprehensive spending review. During this review, research funding in this area will be re-examined. This report will act as a background document for consideration of further spending on nanoparticle risk–related research.

18. In addition to UK initiatives, there will be funding opportunities under the EU 7th Research Framework Programme where there is a theme planned on the development of nanotechnologies and nano-scale materials. This will also cover issues of environmental and human health and safety. There have been a number of relevant research projects under previous Framework Programmes (see Annex 2). We also anticipate that other stakeholders, notably industry, will play a major role in helping to meet many of the research objectives within this report.

1.5 Structure of the report

19. Structurally, the report is organised into eight sections. Following the introduction, the second section considers the wider social context in which the development and management of nanotechnologies is situated. Specifically, it highlights the ongoing need for research into the wider social and ethical dimensions of the risks posed by nanotechnologies as they arise. This section also describes the progress that the Government and the ESRC have made in addressing this agenda. The third section examines the measurement and characterisation of nanoparticles, including research objectives to ensure that we have the information necessary to underpin the development of an appropriate risk management framework. The fourth section addresses the research objectives for assessing exposure to nanoparticles, including their fate and transport in the environment. The fifth section covers research objectives for assessing the hazards posed by nanoparticles to human health and the environment. The sixth section briefly explains funding sources that can address the research objectives set out in the report, with mechanisms described in Annex 3. Examples of other programmes undertaken in the EU are also listed in Annex 2 for each of the objectives. The penultimate section explains our plans for reporting and reviewing the research programme and how this fits with other activities, and finally, we draw conclusions on the report.

2 Public engagement and social research

2.1 Introduction

20. Developments in some areas of science and technology, such as nuclear power, genetic modification, and stem cell research, have demonstrated that it is rarely possible to separate environmental and human health risks from their wider social and economic context. Against this backdrop, the RS/RAEng report indicates that it seems highly likely that some nanotechnologies will raise significant social and ethical concerns and that these seem to be most likely for developments envisaged for the medium (5-15 years) and much longer (more than 20 years) time horizons.

21. As the RS/RAEng points out, social and ethical issues are typically associated with specific applications. The wider use of nanotechnologies in sensing and surveillance devices, for example, could both deliver increased security, but also impact on people's sense of privacy. Other concerns centre on the need for adequate management and controls around the development and use of nanotechnologies, and the equitable distribution of the benefits from their exploitation.

Research Objective 1 (social and ethical dimensions): To understand the social and ethical implications of nanotechnologies, through a programme of public dialogue and social research.

22. The Government committed to addressing this wide-ranging and complex agenda in its response to the RS/RAEng report on nanotechnologies. Since its publication, considerable progress has been made in putting in place the structures and processes for delivering open, constructive and informed social dialogue on nanotechnologies.

23. This dialogue has been designed to inform both the policies for addressing the implications of nanotechnologies, and the development of nanotechnologies themselves. The Government is committed to enabling public and corporate R&D organisations to access information about societal aspirations and concerns, and hence take account of these in their policy and decision-making early in the nanotechnologies development process.

24. This section of the report outlines the infrastructure and activities that have been put in place to provide information on the many social and ethical dimensions of nanotechnologies. The Government feels that it is important to learn from these activities, in discussion with other stakeholders, to maximise the impacts of any further initiatives.

2.2 Understanding the uses and applications of nanotechnologies

25. The Government acknowledges its need to understand the uses of nanotechnologies to inform its consideration of their potential social and ethical implications. This includes the focus of future public engagement activities and social research projects. There are two initiatives underway to meet this objective:

- Defra, the EA and the HSE commissioned the Central Science Laboratory (CSL) to undertake a scoping study of the products and applications of nanotechnologies in the UK. The analysis will take the form of a searchable database that will be updated on a regular basis. There will also be an accompanying report, setting out wider trends in the development of nanotechnologies.

- The Office of Science and Technology's (OST's) new Horizon Scanning Centre[16] is undertaking research that will identify, at the earliest possible stage, areas where potential health, safety, environmental, social and ethical issues arise from a range of new and emerging technologies, including nanotechnologies. This work will also draw on the horizon scanning activities of other NRCG members.

2.3 Public engagement activities

26. In August 2005, the Government published its outline programme for public engagement on nanotechnologies[17]. The programme has been designed to enable the science community and the public to explore their aspirations and concerns about the development of nanotechnologies. The outcomes will help policy makers to shape research priorities and directions, and the nature of appropriate controls for nanotechnologies. We expect a wide range of stakeholders to take due account of the findings in defining their own research and innovation agendas.

27. The programme is currently centred on three Government funded projects: Nanodialogues, the Nanotechnology Engagement Group (NEG), and Small Talk. It has been designed to complement other projects funded through alternative sources.

28. Nanodialogues[18] is supported by a grant of £120,000 from the DTI's Sciencewise[19] programme, with matched funding from other partners. It is led by Demos, Lancaster University, the EA, the BBSRC, and the EPSRC. Practical Action, an international development group, is also involved.

[16] See: http://www.foresight.gov.uk/HORIZON_SCANNING_CENTRE/index.html
[17] See: http://www.ost.gov.uk/policy/issues/programme12.pdf
[18] See: http://www.demos.co.uk/projects/currentprojects/nanodialogues/
[19] See: http://www.sciencewise.org.uk/

29. The project examines the practicalities of the concept of ‘upstream’ public engagement through a series of case studies looking at: the control of nanoparticles to remediate land contamination; the shaping of strategic research directions; and the global diffusion of nanotechnologies. The organisers intend to attract a corporate partner to provide a fourth case study on how public values can inform corporate R&D on technologies.

30. The NEG[20] is also funded through the DTI’s Sciencewise scheme (with a grant of approximately £115,000) and aims to bring greater coherence to the increasing number of projects and activities that address the interface between technical and social understandings of the potential risks posed by nanotechnologies. It consists of a core research team comprising Involve, the Cambridge Nanoscience Centre, the University of Sheffield, and the Policy Studies Institute, plus a forum of approximately twenty people, including members from both the NRCG and the NIDG to ensure a connection with policy discussions. There is also a wider network of those interested in and affected by its work. Professor Richard Jones from the University of Sheffield chairs the NEG.

31. The NEG will map out and analyse the current practices of public engagement on nanotechnologies. This exercise is intended to inform the Government and others about the conditions under which early public engagement can influence policy and decision-making. It also provides a forum for deliberation on the implications of ongoing public engagement activities around nanotechnologies for future research and public engagement priorities. The Government sees this as a significant initiative for informing future plans for public engagement and social research needs on nanotechnologies, ensuring that they have maximum impact.

32. The Government is also funding Small Talk, a project that pulls together the findings of a wide range of activities around the UK that are focussed on discussing nanotechnologies with the public and scientists. It is a £50,000 Copus project delivered by a collaboration of the British Association for the Advancement of Science, Ecsite-UK, the Royal Institution, the Cheltenham Science Festival, and is managed by Think Lab. The interim and final outputs will feed into the NEG, with the project reporting formally in summer 2006.

2.4 The Economic and Social Research Council (ESRC) and nanotechnologies

33. In response to the increasing controversy over the possible effects of nanotechnologies, in 2003, the ESRC funded the University of Sheffield to report on the social and economic aspects of nanotechnologies[21]. In particular, the study identified two dimensions to the debate on the social implications of nanotechnologies. The first focused on radical, long-term technological possibilities, including a future in which fabrication from a molecular level of

[20] See: http://www.involving.org/index.cfm?fuseaction=main.viewSection&intSectionID=213&intParentID=2
[21] See: http://www.shef.ac.uk/physics/people/rjones/PDFs/SECNanotechnology.pdf

virtually any material or structure is possible. The second concerned much more incremental, short-term outcomes, such as the enabling of sensing devices.

34. Building on this work, the ESRC awarded the University of Lancaster £226,450 for a project entitled *'Nanotechnology Risk and Sustainability: Moving Engagement Upstream.*[22] The project, which runs from 2003 to the end of 2005, considers how dialogue between the public, scientists and regulators could shape the innovation and regulation of nanotechnologies, and more specifically, how public debate about new technologies could be moved closer to the heart of the R&D processes around nanotechnologies. The findings will be reported early in 2006.

35. The University of Plymouth holds an award of £48,070 for *'Nanotechnology and News Production: Scientists', and Journalists' and Editors' Views.'* This project, which concludes at the end of 2005, aims to further our understanding of the complex factors that influence the communication of news and information about biomedical nanotechnology, specifically taking account the views of scientists and journalists.

36. In a related area, the University of Surrey was awarded £45,405 for *'Spinning Science: the Nanotech Industry and Financial News'* , which is due to end in October 2006. The project examines the relationship between nanotechnology companies and the messages they provide to financial institutions.

[22] See: http://www.demos.co.uk/projects/currentprojects/ESRCnanotech/

3 Particle properties, characterisation and metrology

3.1 Introduction

37. There is a lack of reliable, affordable and standardised measurement methods for:

- measuring nanoparticle size and shape; and
- characterising nanoparticles, e.g. their composition and surface behaviour.

38. Addressing these gaps will be essential for conducting meaningful and valid research that produces results that are comparable, repeatable and accepted by the scientific community, and on which a reliable system of risk identification, assessment and management can be based.

39. Associated with this is the need to define the most appropriate particle metric or metrics for use in exposure and hazard studies. It is important to be clear about what is going to be measured, why a particular metric has been chosen and how to carry out measurements. It is possible that the most suitable metrics will differ for different types of nanoparticles; for example, surface area for nanoparticles and fibre number for nanotubes.

Research Objective 2 (characterisation and metrology): To identify the most suitable metrics and associated methods for the measurement and characterisation of nanoparticles.

40. There is at the same time a need to establish standardised, well-characterised nanoparticles that vary in size, shape, durability, composition and surface reactivity *for use in metrology, characterisation, exposure and hazard assessment* (notably for comparative benchmarking purposes in toxicology). The setting up of accreditation programmes for laboratories involved in characterisation and metrology will also need to be considered.

Research Objective 3 (characterisation and metrology): To develop standardised, well-characterised reference nanoparticles.

41. Research objectives for methodologies relating to exposure and hazard assessment are addressed in their respective chapters.

3.2 Ignition and explosion potential

42. One specific, potential hazard posed by nanoparticles for which a detailed understanding of their properties is urgently needed, is the potential to cause fire or explosion. A similar effect is observed in larger particles when they are released to the atmosphere and subject to an ignition source. A study undertaken by the HSE[23] indicated that nanoparticles are almost certain to give rise to a dust explosion hazard and that due to their large specific surface area they may well be spontaneously flammable on exposure to air. This is particularly the case with metal nanoparticles as they oxidise easily.

43. Since the energy required to ignite particles is a function of particle diameter, and nanoparticles are likely to have enhanced electrostatic charging (which may result in their being sufficiently charged as to act as their own source of ignition if dispersed in air), it is important to measure and understand the properties of nanoparticles in the context of their ignition potential. The tendency of nanoparticles to form agglomerates makes testing difficult, since current methods may not adequately disperse agglomerated particles, and the surface area exposed for reaction will be less than if the nanoparticle was fully dispersed. These tests will need to be reviewed for suitability with respect to nanoparticles.

Research Objective 4 (characterisation and metrology): Understand the properties of nanoparticles in the context of their ignition and explosion potential, and assess/develop methods for evaluating this.

3.3 Ongoing activities

44. Work has begun at the National Physical Laboratory (NPL) on the development of methods, calibration techniques, and chemical characterisation of nanoparticles, liaising closely with existing airborne vehicle emission work and relevant materials research.

45. Measurement requirements for nanotechnology are also being defined in various DTI funded National Measurement System (NMS) programmes that are currently under development. In addition, the new NMS Measurements for Emerging Technologies programme includes a significant project on Micro and Nanoparticle Characterisation. The project includes research on nanoparticle detection by micro-fabricated devices, chemical analysis of nanoparticle surfaces and rapid measurement of total surface area. It will address, step-by-step, key measurement issues for regulators and for quality control in industry.

46. HSE, in conjunction with the Health and Safety Laboratory (HSL), is identifying specific research needs in this area, including the feasibility of

[23] *HSE (2005) Explosion hazards associated with nanopowders (*EC/04/03). London: HSE.

methods for measuring ignition and explosion properties of nanoparticles. They are also looking to develop scaled methods that use less material than current methods, so that results may be obtained before large quantities of material are available.

4 Exposure

4.1 Introduction

47. Following the Government's response to the RS/RAEng report, the HSL were commissioned to undertake a scoping study to examine our current knowledge on exposure to nanoparticles and identify gaps[24].

48. In taking a risk based approach to assessing and managing the impact of nanoparticles, it is important to understand the nature and extent of human and environmental exposure. Exposure will depend on the source of the nanoparticles and the pathways they take to reach the human and environmental receptors. This provides information on where any potential risk is most likely to occur.

4.2 Sources of exposure

49. Both the RS/RAEng report and exposure scoping study identify likely current sources of human and environmental exposure to nanoparticles. These are:

- occupational exposure in the workplace (human);
- exposure from deliberate environmental releases, e.g. remediation of contaminated groundwaters and land (environment and possibly human);
- exposure from 'unintentional' environmental releases, e.g. from fuel additives and in industrial and domestic waste streams (environment and human);
- exposure from consumer products, such as cosmetics (human); and
- exposure from medical products, including drugs, treatments and devices (human).

50. However, there is at the same time still uncertainty over the sources of nanoparticles, in particular unintentional releases into the environment. Gaining a thorough understanding of these sources has been identified as a research objective.

Research Objective 5 (exposure): Further identification of sources of nanoparticles.

[24] Mark, D., *et al*. (2005) *A scoping study to identify exposure data needs for addressing the risks presented by nanoparticles and nanotubes.* Buxton: Health and Safety Laboratory.

4.3 Pathways of exposure

51. The HSL scoping study identified several pathways that nanoparticles can take from the source to the human or environmental receptor where an effect may be elicited, including through the air, soil and water. It is apparent from the scoping study on exposure that there are gaps in our knowledge about the fate and behaviour of nanoparticles passing through these pathways.

52. It may be possible to gain some understanding of the behaviour of nanoparticles in the environment from existing knowledge of chemical and biological degradation processes, for example, pesticide and other chemical degradation models and the behaviour of diesel exhaust fumes.

53. Significant factors affecting exposure include the extent and effect of agglomeration on the properties of the nanoparticles, including the effect on transport and persistence, how they interact with naturally occurring substances, such as organic material in water and soil, and how they interact with and influence the behaviour of pollutants (e.g. metals). These factors may also have implications for the toxicity and therefore hazards that nanoparticles pose.

4.4 Exposure via air

54. The atmosphere is a major route of human and environmental exposure to particulates, in particular through inhalation. While there are data on the overall atmospheric exposure to non-engineered nanoparticles, none of this is specific to nanoparticles. Most exposure data is from non-engineered nanoparticles (often referred to as ultrafine particles) largely from combustion processes. Data from the UK Air Quality Expert Group report, 'Particulate Matter in the UK'[25], issued in 2001, suggests that 17% of the particulate pollution emitted in the UK from human sources was in the nanoparticulate fraction.

55. The exposure scoping study suggests that the greatest exposure for humans to nanoparticles via air at the moment is likely to be to those who manufacture, process or use nanoparticles in the workplace or research laboratory. Exposure of the general population to nanoparticles is likely to be very small. However, to place this in context, the main form of human exposure to nanoparticles via air is from non-engineered nanoparticle combustion products, in particular from diesel engines, which accounted for half the total of nanoparticle emissions in 2001.

56. Our current understanding of the behaviour of combustion products may allow us to draw some inferences for nanoparticles in the areas of particle transport and deposition and exposure of humans and the environment.

[25] Air Quality Expert Group (2001) *Particulate Matter in the UK*. London: Defra. See: http://www.defra.gov.uk/environment/airquality/aqeg/particulate-matter/index.htm

57. A number of metrics for measuring non-engineered nanoparticles in the atmosphere could be used for nanoparticles, including mass, particle size, particle numbers and surface area. As outlined in section 3, there is a need to assess how appropriate these are for nanoparticles, notably in the context of their hazard to human health. Associated with this, a range of methods is available for measurement of non-engineered nanoparticles in air that are of variable reliability, sensitivity, timeliness and cost. Instrumentation used in the outside environment may also be applicable in the occupational environment and vice versa. However, these methods have not been fully evaluated for nanoparticles and standard protocols do not exist, in particular for surface area measurement, which may be one of the preferred metrics. Since personal monitors are not available, direct exposure to individuals cannot be measured.

58. Exposure assessment techniques must be able to distinguish between engineered and non-engineered nanoparticles in air.

59. The development of such technologies and protocols will allow us to develop a more comprehensive understanding of the fate and behaviour of nanoparticles in air.

Research Objective 6 (exposure): Optimisation and development of technologies that enable the measurement of occupational and environmental exposure to nanoparticles via air

Research Objective 7 (exposure): Understanding of fate and behaviour of nanoparticles in air.

4.5 Minimising exposure in the workplace

60. Given the potential for occupational human exposure via air (and also via skin), and that we are still unclear about any potential health effects associated with exposure to nanoparticles it may be sensible to develop and implement exposure reduction devices for both aerial and dermal exposure. These should be developed in the context of the development of best practice guidelines for handling and working with nanoparticles.

Research Objective 8 (exposure): Development of exposure control devices

4.6 Exposure via soil and water

61. There is no direct information about water as a potential source of exposure to nanoparticles and very little is known about their behaviour in aquatic environments. It is, however, reasonable to assume that the primary route of human exposure would be through drinking water, i.e. abstraction.

62. Remediation of contaminated groundwater using nanoparticles presents an immediate opportunity to remediate polluted aquifers but also presents a potential pathway of exposure to the environment (and humans if there is abstraction). An understanding of the fate and behaviour of nanoparticles used for remediation purposes (for example, zero valent iron proposed for use in groundwater remediation of chlorinated solvents) is considered to be a priority research need.

63. There has recently been a dramatic improvement in the techniques used to assess the concentrations and the chemical and physical properties of nanoparticles in water, primarily exploited for naturally occurring nanoparticles. The applicability of these methods for engineered nanoparticles is as yet not known.

64. Within this, a number of measurement methods are available which can potentially routinely measure nanoparticles, (e.g. cross flow ultra-filtration). However, there are no direct data on their application for nanoparticles in complex natural water systems.

65. Exposure to nanoparticles in soils will result from a number of activities, including deliberate releases via soil and water remediation technologies (see section on water above), potential agricultural uses (e.g. fertilisers) and potential unintentional releases via air, water and from sewage sludge applied to land. There may be risks of contamination of groundwater as a result of transport of nanoparticles through the soil profile.

66. There are no suitable methodologies for exposure assessment of nanoparticles in soils. Exposure will depend on the chemical and physical properties of the soil. Instrumentation is currently available to measure many of these properties but has not been assessed in the context of nanoparticle exposure.

67. Very little is known about the behaviour, transfer and fate of nanoparticles in soils. For example, nanoparticles may be taken up and degraded by soil organisms, but little data exists on this. The data that is available is for nanoparticles used in the remediation of contaminated land. Much of this has focused on nanoparticle transport in the soil, since effective remediation requires movement of particles through the soil.

Research Objective 9 (exposure): Optimisation, development and application of technologies that enable the measurement of exposure to nanoparticles in soil and water.

Research Objective 10 (exposure): Research to understand the environmental fate, behaviour and interaction of nanoparticles in soil and water.

4.7 Deliberate and direct exposure

68. There are a number of deliberate exposures to humans from nanoparticles, most notably from:

- medical applications including drugs and medical devices; and
- consumer products including cosmetics.

69. Government takes the risks to human health and safety posed by deliberate exposure to nanoparticles very seriously and it is anticipated that these will be controlled under sector specific regulation. However, it is ultimately the responsibility of the manufacturers of products containing nanoparticles to make sure that they are safe for use. Characterisation of these deliberate exposures will be part of the safety assessment that needs to be completed before marketing.

70. The nature and extent of these deliberate exposures may be more easily understood than environmental exposures since they relate directly to the function and use of products containing nanoparticles. Exposure is likely to be via all possible routes including products applied to the skin, such as cosmetics, and swallowed in medicines and injected, inhaled and implanted via medical products.

71. To a limited extent, information from research on deliberate exposure to nanoparticles will inform our knowledge of unintentional exposures and hazards. However, most of this research will be performed by industry and the results will not necessarily be in the public domain. Additionally, the physico-chemical properties of these nanoparticles may be different from those that will result in unintentional exposure, because the fate and behaviour in the human body will be part of the intended design characteristics of the product.

4.8 Ongoing activities

72. Defra, the EA and the HSE have funded the development of a database that outlines the current manufacture and use of nanotechnologies in the UK. This will provide important information on sources of nanoparticles. The database will be updated so that manufacture and use of emerging products and applications can be monitored. It draws on the directory of the DTI sponsored

Micro and Nanotechnology (MNT) network[26], which additionally provides a valuable source of information on current manufacturing and application trends in the UK. The Food Standards Agency (FSA) has sought bids for research to assess new and potential applications of nanotechnology for food contact materials in the UK, considering the consumer safety and regulatory implications of their possible use.

73. Defra is also funding research into understanding source attribution for atmospheric pollution by particulates. While this does not focus on engineered nanoparticles *per se* it may provide some information about unintentional and engineered nanoparticle sources, which will provide important contextual information.

74. Defra is funding further research on ambient air quality including characterisation of particulate pollutants in urban areas, modelling of pollutants, and the distribution and environmental effects of heavy metals. This includes a research network of automatic instruments measuring particle number concentrations. Defra are also considering increasing the air quality monitoring of fine particles (particles less than 2,500nm in diameter) and some of their main components (such as nitrates, sulphates and certain metals). Whilst not focused on engineered nanoparticles, as with the evidence presented above, the data and knowledge from this research may be applicable to them.

75. The HSE is considering funding work on workplace monitoring exposure capabilities and strategies, including the design of portable monitoring instrumentation. They are also pursuing the development of exposure control devices with the US National Institute of Occupational Safety and Hygiene (NIOSH), and will have a clearer view as to specific activities to meet this research priority in mid-December 2005.

[26] See: http://www.mnt-directory.org/

5 Hazards to humans and the environment

5.1 Human health and safety hazards

5.1.1 Introduction

76. The Government's response to the RS/RAEng report clearly identifies as a research priority the need to understand the hazards nanoparticles may pose to human health as a result of consumer, medical, occupational and environmental exposure. The Institute of Occupational Medicine (IOM) were commissioned to undertake a scoping study to examine our current knowledge of hazards to human health to identify the current evidence, the weight of evidence, and to comment on where the information gaps lie[27].

5.1.2 Toxicokinetics – entry into and distribution around the human body

77. A primary recommendation of the IOM hazard scoping study was further research into the so called 'toxicokinetics' of nanoparticles associated with exposure via the lung, skin and gut (see Figure 1). In essence, toxicokinetics look at how a particle may get into the body, how it is circulated and distributed within it, and how it may be metabolised and excreted. Understanding this is important as it allows consideration of the important target organs that may or may not be affected, to predict realistic exposure doses and to understand how the body responds to nanoparticle exposure in terms of metabolism and excretion. To date, few, if any, adsorption, distribution, metabolism and excretion (ADME) studies have been conducted for nanoparticles.

Research Objective 11 (human health hazard): Research to establish a clear understanding of the adsorption of nanoparticles via the lung, skin and gut and their distribution in the body (i.e. toxicokinetics), identifying potential target organs/tissues for toxicity assessment.

[27] Tran, L., *et al.* (2005) *A scoping study to identify hazard data needs for addressing the risks presented by nanoparticles and nanotubes.* Edinburgh: Institute of Occupational Medicine.

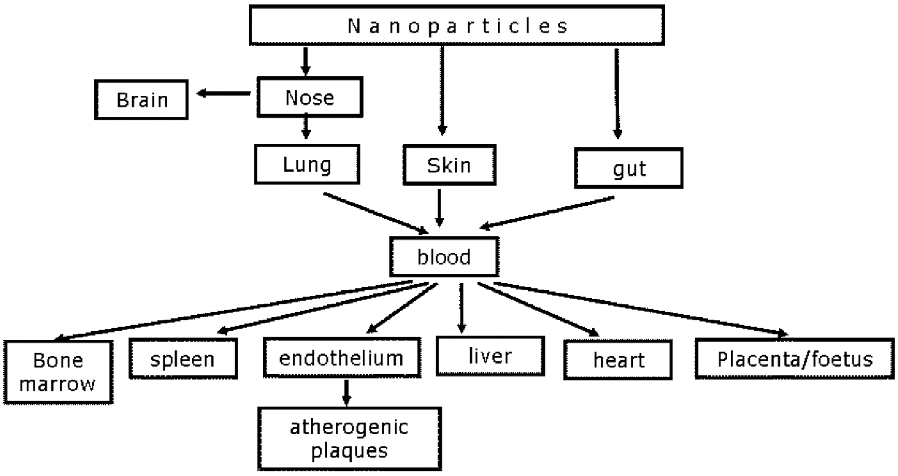

Figure 1 - Summary of the hypothetical toxicokinetic pathways for nanoparticles

5.1.3 Movement within and between cells and their cellular toxicity

78. The scoping study emphasised the need to understand the localisation of nanoparticles within cells and their cellular toxicity. In particular, transport of nanoparticles across membranes both between and within cells (e.g. into mitochondria) and an understanding of their toxic effects (e.g. oxidative stress, genotoxicity, inflammatory cytokine production, apoptosis) are important. Such *in vitro* cell studies provide an understanding of the mechanisms of toxicity, how cellular defence mechanisms respond and possible pathogenic effects. This will lead to the selection of relevant endpoints for standard methods to assess hazard (see below). Within this, the role of particle size, composition, aggregation and disaggregation should be considered and the nature and magnitude of biochemical responses that influence cellular fate, biopersistence and degradation studied.

Research Objective 12 (human health hazard): Research to establish a clear understanding of inter and intracellular transport and localisation of nanoparticles and their cellular toxicity.

5.1.4 Oxidative stress, inflammatory effects and genotoxicity

79. Both the RS/RAEng and scoping study reports suggest good quality evidence from ‘traditional’ combustion-derived nanoparticles (e.g. carbon black, diesel and welding fume) that indicate that particle properties of size, shape and composition are important factors influencing the toxicity of nanoparticles. For example, the harmful effects of fibres are driven by three important factors: length, diameter and persistence. Such studies also show that some

nanoparticles have an enhanced ability to cause inflammation in organs when compared to larger particles of the same material. The generally accepted paradigm for initiating pathogenic effects is oxidative stress leading to inflammation, frequently associated with genotoxicity (i.e. damage to genetic material such as DNA). High surface area, metals and organic chemicals can all contribute to these responses. The scoping study noted that it is not known whether this model is applicable to all new nanoparticles.

80. Some human studies also suggest that ‘dirty nanoparticles’ (i.e. with attached metals and organic chemicals such as diesel combustion products) may be more liable to cause inflammation than ‘clean’ nanoparticles, that is to say surface chemistry modification is important. This challenges any assumptions that knowledge of the properties and toxicity of one nanoparticle may be transferable to others.

Research Objective 13 (human health hazard): To establish a clear understanding of whether oxidative stress, inflammatory effects and genotoxicity apply to nanoparticles.

5.1.5 Respiratory system, cardiovascular system and brain

81. Given our understanding of the relative importance of potential exposure in the workplace and in the environment via the air, a particular focus of research should be in the airways and lung. Here there is good evidence of pathogenic effects from non-engineered nanoparticles. Most of the available information concerns the effect of ultrafine combustion products on inhalation toxicology. Some data, partly inferred from particulate pollution studies and supported by work on combustion derived carbon nanoparticles, indicate that these can have inflammatory effects in the lung. This inflammatory response has been observed to be greater for nanoparticles than for the same mass of larger particles of that substance, but has not been observed for all particle types. This supports the suggestion that particle chemistry and surface characteristics as well as size and dose determine toxicity.

82. It is not clear how transferable these findings are to nanoparticles. There are few reliable published data on the deposition, distribution, durability (biopersistence), toxicity and pathogenic effects of nanoparticles in the lung, and those studies that have been conducted have not involved inhalation experiments (the most relevant route of exposure).

83. In particular, there is a paucity of reliable data on the distribution, toxicity and pathogenic effects of single and multi walled carbon nanotubes in the airways and lung. Given their shape, size and solubility, this is a specific area where more research is needed.

84. The scoping study reports a small amount of evidence that shows that nanoparticles can transport into, between and through tissue layers in the lung.

Several studies using radioactive nanoparticles have also shown translocation of nanoparticles from the lungs into the blood and that there may be impacts on the cardiovascular system. There is a suggestion that nanoparticles may be associated with inflammatory and pro-clotting effects in the blood. Therefore, the effect of nanoparticles on the cardiovascular system, with special reference to atheromatous plaque development, endothelial function, platelets, the clotting system and vascular function is an area where research is needed.

85. Other work has also shown that some nanoparticles can pass to the brain via the central nervous system following inhalation; while the exact pathway for this is uncertain, the olfactory nerve is considered as one mechanism.

86. In general the role of particle shape, size, composition and aggregation/ disaggregation should be assessed within such studies.

87. The scoping study also recognised the importance of using plausible doses of nanoparticles in studies (taking care not to overload organs) to get an idea of the realistic hazards and therefore risks posed to human health that need to be controlled.

Research Objective 14 (human health hazard): Research to establish a clear understanding of the deposition, distribution, toxicity, pathogenicity and translocation potential and pathways for nanoparticles in the airways and lung and their potential impacts on the cardiovascular system and brain (linked to RO 12).

5.1.6 Skin, gut and other organs

88. As discussed above, current uses of nanoparticles in consumer products and concerns regarding occupational exposure point to the skin as being an important portal of entry for the human body. However, the extent to which nanoparticles are able to penetrate the skin and cause adverse effects is not fully understood.

Research Objective 15 (human health hazard): Given the current use of nanoparticles in consumer products there is a need to further our understanding of dermal uptake, penetration and toxicity in the skin.

89. For the gut, there is good evidence that larger microparticles cross the gut barrier under normal conditions, but no evidence exists as to whether this is increased in the case of nanoparticles. There is insufficient evidence to determine whether nanoparticles adversely affect the gut. Research under Research Objective 11 will contribute to our understanding of the toxicokinetics of nanoparticles in the gut.

90. Likewise, no data exists on the dose of nanoparticles likely to reach other organs such as bone marrow, spleen, liver, heart and the placenta/foetus after exposure. Studies undertaken as part of research into the toxicokinetics under Research Objective 11 will provide important information in this regard.

91. Ultimately, the data provided through the human health research objectives above should be integrated into structure/activity model(s) aiming to assess whether biological activity and effects can be predicted from physiochemical properties and chemical structure.

5.1.7 Testing strategies and methods for human hazard assessment

92. Cutting across all the research priorities identified above is the need to develop tiered testing strategies for routine hazard assessment of nanoparticles and within this a clear set of toxicological and particle physico-chemical property endpoints to be measured. A key element of this will be to assess how fit for purpose current standard tests for chemicals (i.e OECD or equivalent test guidelines) are for nanoparticles, and, where gaps are seen, to develop appropriate tests. This should include specific tests for the respiratory system, gut and skin as appropriate. As part of this there is a need for developing standardised, well characterised reference materials for such studies and against which comparative *toxicological* data can be benchmarked (see above). In some cases, the use of existing materials such as quartz may be advocated. The development of standard methods has previously been identified in this report as a major international research priority.

93. Toxicity and pathogenicity of nanoparticles will relate not only to chemical composition but also to particle size, shape and surface area and properties. An important feature of toxicological tests is the need to undertake physical and chemical metrology and characterisation of the nanoparticles *within the testing process*. This will allow the correct interpretation of toxicological tests and an understanding of what key aspects of physico-chemical characteristics and behaviour relate to any toxic effects.

94. Underpinning this is the need to establish a freely-accessible electronic archive of scientific and technical publications and the establishment of a dedicated database of toxicological and ecotoxicological data. One such database has recently been developed by the International Council on Nanotechnology (ICON), which contains some 1,300 research papers covering the field and is freely accessible[28].

Research Objective 16 (human health hazard): To develop testing strategies for human health hazard assessment and assess how fit for purpose current test methods are as applied to nanoparticles.

[28] See: http://icon.rice.edu/

5.1.8 Epidemiology

95. There is a large body of knowledge from epidemiological research concerning the links between human health and exposure to particles – in the workplace and in outdoor and indoor air. There are, for example, extensive data confirming excess cancer mortality (lung cancer, mesothelioma) and respiratory morbidity following occupational exposure to asbestos, and other fibres. However, few if any studies have involved nanoparticles, although it is appreciated that the time period required for development of key pathologies is of the order of a decade. Exposure metrics, measurement technologies and basic toxicology will need to be understood before it is clear whether any epidemiological studies are required.

96. Also, the numbers of individuals potentially exposed on a regular basis to free nanoparticles are currently low and the hazards uncertain. Should the numbers of people exposed increase and a better understanding of the hazards justify it then action can be taken to develop *systems* for facilitating epidemiology studies in new industries.

5.1.9 Ongoing activities

97. The Medical Research Council (MRC) are currently funding approximately £1M worth of research in the areas of toxicology, respiratory medicine and environment and health. Projects range from the investigation of nanoscale technology for studying DNA repair and chromatin dynamics to particulate air pollution mechanisms. The MRC also funds work on particulate air pollution at the MRC Centre for Inflammation Research in Edinburgh, where research is being undertaken into particles in the air that might cause inflammatory lung disease.

98. MRC is prepared to commit up to £200K to a capacity building programme in Environment and Human Health led by Natural Environment Research Council (NERC). The programme aims to bring communities together and to encourage interdisciplinary research. Priority issues identified through a consultation preceding this programme include the assessment of exposure to particles (including nanoparticles).

99. The MRC also contributes to two Interdisciplinary Research Collaborations in Nanotechnology and Bionanotechnology (in partnership with EPSRC and BBSRC) at a cost of £3M over 6 years.

100. There is a considerable level of international progress being made in the area of testing strategies and methods development for example the SCENIHR published its Opinion regarding the appropriateness of existing methodologies

for risk assessment in October 2005 [29]. It concluded that risk assessment methodologies would require some modification and that current methods may not be sufficient to address all the issues arising with nanoparticles. The Opinion also contained useful decision trees for risk assessment. Similarly, elements of a screening strategy for hazard identification of nanomaterials has been developed from an expert working group convened in the US by the International Life Sciences Institute Research Foundation/Risk Science Institute, which has recently been published[30]. One conclusion of this group was that there was a strong likelihood that biological activity of nanoparticles would depend on physicochemical parameters not routinely considered in toxicity screening studies.

101. In Europe, ECETOC (the European Centre for Ecotoxicology and Toxicology of Chemicals) are also looking at testing strategies to establish the safety of nanomaterials.

5.2 Environmental hazards

5.2.1 Introduction

102. The natural environment is composed of many complex ecosystems comprising atmospheric, terrestrial, fresh water and marine compartments. Unlike human exposure, the number of species potentially at risk from nanoparticles is extremely large. Hazards associated with nanoparticle exposure can potentially act at individual or population level and might also impact on the structure and function of the ecosystem as a whole.

103. As with human health, the assessment of the environmental impacts of nanoparticles will depend upon the physico-chemical properties and behaviour of the material, the residence time of particles in the environment and their environmental fate, toxicity (both acute and long-term), persistence in organisms and bioaccumulation and biomagnification potential. The RS/RAEng report and IOM hazard scoping study both highlight the fact that there are very limited data in all these areas. The European Commission has particularly flagged ecotoxicology of nanoparticles as an area where there is very little data and requiring substantial further research.

104. Until a comprehensive understanding of sources of nanoparticles to the environment and a fuller understanding of their basic environmental fate and behaviour and environmental fate is understood, it is hard to identify which, if any, components of these ecosystems (soils, surface waters, air) are at risk of

[29] SCENIHR (2005) *Opinion on the appropriateness of existing methodologies to assess the potential risks associated with engineered and adventitious products of nanotechnologies.* Brussels: European Commission. See: http://europa.eu.int/comm/health/ph_risk/committees/04_scenihr/scenihr_cons_01_en.htm

[30] Oberdorster, G., *et al.* (2005) *Principles for characterizing the potential human health effects from exposure to nanomaterials: elements of a screening strategy,* Particle and Fibre Toxicology, 2(8).

contamination from nanoparticles. The understanding of manufacture and uses of nanotechnologies will allow us to understand more about potential sources of release to the environment: identifying these sources and understanding environmental behaviour (e.g. agglomeration, partitioning between water and sediments, mobility within soils) will help us identify which environmental compartments and biota (or ‘receptors’) are most likely to be at risk and should be investigated more fully.

5.2.2 Effects in groundwaters and soils

105. One area where we are certain that there will be environmental exposure is in the use of nanoparticles for groundwater and contaminated land remediation. A research priority previously identified was to understand the environmental fate and behaviour of such nanoparticles in soils and groundwaters.

106. The IOM study reported that some preliminary studies have shown that a number of nanoparticles have demonstrated toxicity to bacteria. Given the presence of microorganisms in soils and groundwaters and their importance, we can identify such microorganisms as important receptors where remediation technologies use nanoparticles. As such, the uptake, toxicity and effects on growth and survival and community composition and function of soil and groundwater microorganisms can be considered a research priority. It is acknowledged that in some contaminated environments (e.g. groundwaters) microbial diversity may be poor and there is the potential for improving this through remediation, although such potential benefits have not as yet been measured.

107. The uptake and toxicity of nanoparticles to soil flora and fauna should also be considered.

108. The environmental fate and toxicity of nanoparticles to microbes within sewage treatment works may also need to be considered, particularly once sources of these to sewer have been confirmed.

Research Objective 17 (environmental hazard): Research to establish the uptake, toxicity and effects of nanoparticles on groundwater and soil microorganisms, animals and plants, especially in the context of remediation.

5.2.3 Wider effects associated with unintentional release

109. In addition to microorganisms, both the RS/RAEng report and the IOM hazard scoping study identified that current knowledge of hazard to other key ecological groups, including plants, invertebrates and vertebrates was very limited. It noted one published study on the toxicity to fish of fullerenes and more recent, but as yet unpublished, work on toxicity tests with some fresh water invertebrates (e.g. *Daphnia sp*). There is poor understanding of the uptake and toxicokinetics of nanoparticles in microorganisms, invertebrates, vertebrates and plants. At the cellular level there is also poor understanding of cellular uptake, localisation and toxicity. The effects at low doses and over longer timescales should be considered. Exploring the combined effects of nanomaterials and other contaminants, such as metals and organics, should also be considered.

110. There is the potential to use mammalian toxicology data to inform ecotoxicology. Toxicological information from the effects of particle chemistry and physical characteristics, cellular effects and toxicological mechanisms may impact at cellular and molecular levels with common cellular responses. While in some cases there may be limited read across (e.g. impacts on photosynthesis) in other areas read across may be more applicable.

Research Objective 18 (environmental hazard): Research to establish the mechanisms of toxicity, toxicokinetics and in vivo effects of nanoparticles to key ecological groups (including invertebrates, vertebrates (e.g. fish) and plants). A key aspect of such work should be the facilitating of knowledge transfer from human toxicological studies to inform ecotoxicology.

5.2.4 Testing strategies and methods for ecotoxicological hazard assessment

111. An understanding of particle physico–chemical properties and basic mechanisms of toxicity can lead to the definition of appropriate endpoints for standard tests used in hazard assessment. In particular, evaluating how appropriate current tests for evaluating persistence, bioaccumulation and toxicity (PBT) of chemicals are for addressing nanoparticles. This should lead to a defined set of agreed, standard protocols for routine use in hazard assessment. As part of this the development of a suite of standard reference materials for use on ecotoxicological research will be important (see above).

Research Objective 19 (environmental hazard): Define endpoints to be measured in ecotoxicological studies and assess how fit for purpose current standard tests for persistence, bioaccumulation and toxicity are when considering nanoparticles. This should lead to the defining of a suite of standard PBT protocols for use in environmental hazard assessment.

5.2.5 Ongoing activities

112. For the other research objectives, there is as yet limited activity in this area in the UK. NERC and the EA have recently awarded a Co-operative Awards in Sciences of the Environment (CASE) studentship (£50,000) investigating the toxicity of engineered nanoparticles to freshwater fish.

113. CSL has funded a PhD studentship (£48,000) with Napier University to generate basic knowledge for use in the assessment of environmental risks posed by synthetic nanomaterials. The student will investigate the relative susceptibility of selected terrestrial and aquatic species to the toxicity of a range of synthetic nanoparticulates.

6. Research funding and capacity building

114. A major aim of this report is to provide the conditions that will lead to the development of a research community in the UK that can make its contribution to what will be a global endeavour in addressing the potential risks posed by nanoparticles. To build research capacity in this area, a number of Government departments, agencies and Research Councils are identified as responsible for funding research under each of the research objectives identified in this report (see Table 1). These organisations have different mechanisms for funding research, details of which are set out in Annex 3.

115. Nanotechnologies, including the research in support of the objectives identified in this report, are an emerging science and present a significant challenge for established research communities and disciplines. There will need to be work across a range of disciplines to build capacity, and encourage and facilitate the development of a new research community to address this rapidly emerging area. Therefore, where it is needed, the Research Councils will target funding through use of "health of disciplines" and capacity building mechanisms to support studentships, fellowships and professorships to help to build the necessary research community.

116. Much of the Research Council funding is provided through "responsive mode" which encompasses a range of mechanisms for funding research, including both what is understood as traditional "responsive" research, as well as key elements from within directed programmes , such as the new programme on "Environment and Health". It offers a very flexible route for funding under which proposals can be submitted at any time, in any area, for any amount and duration. Collaborative proposals with other funders, including other Government departments, are particularly welcome. Each of the Councils has indicated that they would welcome high quality bids addressing the relevant research objectives identified in this report, both in "responsive" mode and other, directed programmes.

117. Recognising the inherently cross-disciplinary nature of much of the research in this area, Research Councils will ensure a coherent, co-ordinated approach to addressing relevant research objectives and have established a co-ordinating group under the auspices of Research Councils UK. In order to encourage the research community, the Councils are supporting key networks to bring together researchers and policy makers and other stakeholders, to help to identify and work up exciting, novel research proposals:

- NANOMIST[31] (Nanoparticles at the medicine interface with science and technology network) aims to bring together those involved in the production, characterisation and applications of nanoparticles with the health effects community in order to develop a greater knowledge within the health effects community of types of nanoparticles being used or developed for industrial applications, as well as the possibility of harnessing the skills of the physical

[31] See: http://www.gees.bham.ac.uk/research/NANOMIST

science and engineering community to manufacture custom-built particles which could be used in health effects studies to elucidate mechanisms of adverse effect. NANOMIST also aims to encourage multi-disciplinary research and development in the area of nanoparticles to improve the information, instrumentation and methods available to those interested in bio-responses to ambient particles;

- NANOsafeNET aims to bring together a multi-disciplinary network of respected active researchers from academia, industry and those involved in policy making and regulations. It will enable the sharing and dissemination of information pertaining to nanotechnology safety, its usage, health and safety aspects and potential societal and ethic implications.

118. As discussed in section 7 on reporting and review, the NRCG and NIDG will monitor how effective this approach is and provide evidence to the Council for Science and Technology (CST) in their 2007 review.

Table 1 - NRCG Research Programme: Ongoing and Committed Funding

Research Objectives (in summary)	Responsibility	Ongoing Funding	Future Funding
RO1 Social and ethical implications of nanotechnologies	ESRC EPSRC BBSRC OST/DTI EA Defra	£320K £92K £17K £285K £30K	**** Responsive mode Under review Under review ***
RO2 Measurement and characterisation	EPSRC HSE DTI	£3M £97K £2.6M*	Responsive mode Under review £4M
RO3 Development of standard reference materials	International**		
RO4 Fire and explosion properties of nanoparticles	HSE		Under review
RO5 Sources of nanoparticles	Defra EA HSE	£15K £15K £15K	*** Under review Under review
RO6 Technologies for measurement of nanoparticles via air	EPSRC HSE Defra	£200K	Responsive mode Under review ***
RO7 Fate and behaviour of nanoparticles in air	Defra NERC EA		*** Responsive mode Under review
RO8 Exposure control devices	HSE	£35K	Under review
RO9 Technologies for measurement of nanoparticle exposure in water and soils	Defra EPSRC		*** Responsive mode
RO10 Environmental fate and behaviour of nanoparticles in soils and water	Defra NERC EA		*** Responsive mode Under review
RO11 Toxicokinetics of nanoparticles in the human body	MRC		Responsive mode
RO12 Intra and intercellular transport, localisation and toxicity of nanoparticles	MRC BBSRC		Responsive mode Responsive mode
RO13 Oxidative stress, inflammatory effects and genotoxicity of nanoparticles	MRC	£684K	Responsive mode
RO14 Impacts of nanoparticles on the cardiovascular system and brain via the lung	MRC	£20K	Responsive mode
RO15 Dermal uptake, penetration and toxicity of nanoparticles	MRC HSE		Responsive mode
RO16 Development of testing strategies and methods for human health hazard assessment of nanoparticles	International**		
RO17 Uptake, toxicity and effects of nanoparticles on groundwater micro-organisms, and soil micro-organisms, flora and fauna	Defra EA NERC		*** Under review Responsive mode
RO18 Effects of nanoparticles in invertebrates, vertebrates (non human) and plants	Defra NERC/EA BBSRC	 £50K	*** Responsive mode Responsive mode
RO19 Development of testing strategies and methods for environmental health hazard assessment of nanoparticles	International**		

- * Includes £1.86M funded by DTI and £695K from industry and academia.
- ** Development of testing strategies and methods should occur within an international forum, supported by activities of NRCG members.
- *** Defra has allocated £1M over 2 years between these areas, specifics of which are currently being reviewed. Approximately £100K of this has already been committed to specific projects.
- **** Additional ESRC joint investment of up to £2.5M.

7. Reporting and review

119. This is the first report of an ongoing programme of research that will be reviewed and updated to reflect developments in our knowledge. Defra will be responsible for this and will produce a second report that will summarise and update our knowledge and the research objectives, which will be produced by the end of 2007. This and subsequent reports will be made publicly available. Table 2 below sets out the planned actions for reporting and reviewing the research objectives in this report.

Table 2 – Reporting and reviewing of the research objectives

Action	Responsible Organisations	Timing
Review progress against the research objectives	Defra lead with other government departments, agencies and Research Councils	Ongoing
Produce second report	Defra lead with other government departments, agencies and Research Councils	2007
Publication of research reports/findings	Government departments, agencies and Research Councils	Ongoing, on completion of research projects
Peer review of new data by independent scientific advisory committees	- Advisory Committee on Hazardous Substances (ACHS)[32] - Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, the Consumer Products and the Environment (COT[33], COM[34] and COC[35]) - Committee on Medical Effects of Air Pollutants (COMEAP[36]) for consideration	Ongoing, as data becomes available
Review progress on the research objectives as part of the implementation of the Government's response to the RS/RAEng report	Council of Science and Technology (CST)	2007 and 2010
Introduce and report back on progress on research objectives to department chief scientific advisors	Government's Chief Scientific Advisor's Committee (CSAC)	Early 2006 and annually
Ensure that guiding principles for public dialogue on science and technology are followed	OST	Ongoing

[32] See: http://www.defra.gov.uk/environment/chemicals/achs/index.htm
[33] See: http://www.food.gov.uk/science/ouradvisors/toxicity
[34] See: http://www.advisorybodies.doh.gov.uk/com/index.htm
[35] See: http://www.advisorybodies.doh.gov.uk/coc/
[36] See: http://www.advisorybodies.doh.gov.uk/comeap/index.htm

8. Conclusions

120. This report has summarised our current state of knowledge on the potential risks posed by nanoparticles. The information will make an important contribution to the evidence base on which we can develop policy to ensure the responsible management and control of the potential risks posed by nanoparticles.

121. A key part of this evidence base will be information on the social and ethical implications of nanotechnologies. The Government has already made considerable progress in addressing this agenda, and as the map of the future landscapes of nanotechnologies becomes clearer and more accurate, so will the need for further public engagement and social research. The regulatory review, the horizon-scanning and landscaping studies, will all be of tremendous help here.

122. Our understanding is perhaps most advanced in the area of human toxicology, and in particular, the effects resulting from the inhalation of non-engineered nanoparticles. Here, as with the other areas covered in the report, much of our knowledge is derived from studies of combustion product particles in urban environments.

123. There are a substantial number of evidence gaps to be filled. A priority, in the first instance, is to identify suitable metrics and develop the methods with which to measure, characterise and assess the behaviour and properties of nanoparticles. Establishing freely available, standard reference materials for research purposes will be an important component of this. Further research priorities cover the issues of hazard and exposure.

124. The members of the NRCG have committed to fund research. However, the large scale of the job to be done demands collaboration both with industry, other stakeholders, and partners in the EU and internationally. This will enable us to make maximum use of the resources we have available, to share knowledge and data, and to standardise techniques so that results are comparable and widely accepted.

125. This report is considered to be part of an ongoing process of furthering our knowledge, accessing data and identifying our research priorities. There will be an on-going review of progress and a second Government research report in 2007. The NRCG will be responsible for the review and will continue to involve stakeholders in the process.

Annex 1

Acronyms

ACHS	Advisory Committee on Hazardous Substances
ADME	Adsorption, distribution, metabolism and excretion
BBSRC	Biotechnology and Biological Research Council
BSI	British Standards Institute
CEN	European Committee for Standardisation
COC	Committee on Carcinogenity in Food, Consumer Products and the Environment
COM	Committee on Mutagenicity in Food, Consumer Products and the Environment
COMEAP	Committee on Medical Effects of Air Pollutants
COT	Committee on Toxicity in Food, Consumer Products and the Environment
CASE	Co-operative awards in sciences of the environment
CSAC	Chief Scientific Advisors' Committee
CSL	Central Science Laboratory
CST	Council for Science and Technology
Defra	Department for Environment, Food and Rural Affairs
DfID	Department for International Development
DH	Department for Health
DTI	Department of Trade and Industry
EA	Environment Agency
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemicals
EPSRC	Engineering and Physical Sciences Research Council
ESRC	Economic and Social Research Council
EU	European Union
FP7	EU 7th Research Framework Programme
FSA	Food Standards Agency
HSE	Health and Safety Executive
HSL	Health and Safety Laboratory
IOM	Institute of Occupational Medicince
IRC	Interdisciplinary Research Collaboration

ICON	International Council on Nanotechnology
ISO	International Standards Organistion
MHRA	Medicine and Healthcare Products Regulatory Agency
MNT	Micro and nanotechnology network
MRC	Medical Research Council
NEG	Nanotechnology Engagement Group
NERC	Natural Environment Research Council
NIDG	Nanotechnology Issue Dialogue Group
NIOSH	National Institute for Occupational Safety and Health
NMS	National Measurement System
NPL	National Physical Laboratory
NRCG	Nanotechnology Research Co-ordination Group
OECD	Organisation for Economic Co-operation and Development
OST	Office of Science and Technology
PAS	Publicly Available Specification
PBT	Persistence, Bioaccumulation potential and Toxicity
RAEng	Royal Academy of Engineering
RS	Royal Society
SCENIHR	Scientific Committee on Emerging and Newly Identified Health Risks

Annex 2

Framework Programme Projects

The European Union (EU) Framework Programmes support a large number of research projects and networks involving nanosciences and nanotechnologies. The primary portal is Nanoforum[37] which is a pan-European nanotechnology network to provide information on European nanotechnology efforts and support to the European nanotechnology community. Nanoforum publishes its own specially commissioned reports on nanotechnology and key market sectors, the economical and societal impacts of nanotechnology, as well as organising events throughout the EU to inform, network and support European expertise. Some examples of Framework Programme projects and networks include:

Nanoderm

The Nanoderm[38] project aims to develop new methodologies to study the quality of skin as a barrier against formulations containing nanoparticles.

NANOSAFE2

The overall aim of NANOSAFE2[39] is to develop risk assessment and management for secure industrial production of nanoparticles. A number of reference nanoparticles will be applied as representative of main particle characteristics, main production processes and related risks. NANOSAFE2 starts from the paradigm of risk assessment and risk management, which is used in risk analysis worldwide. In NANOSAFE2 the two different types of risks will be assessed: explosion during manufacturing processes and human health due to nanomaterial exposure.

Nanologue

Nanologue[40] is a Europe-wide dialogue on benefits, risks and social, ethical and legal implications of nanotechnologies. Nanologue's overarching objective is to facilitate a dialogue among researchers, business and civil society about the benefits and potential impacts of nanoscience and nanotechnology applications.

[37] See: http://www.nanoforum.org/
[38] See: http://www.uni-leipzig.de/~nanoderm/
[39] See: http://www.nanosafe.org/
[40] See: http://www.nanologue.net/

Nanopathology[41]

The aim of this European-wide Nanopathology[42] project is to investigate the possible pathogenic role of nanoparticles in human cryptogenic diseases, with the use of experimental models *in vitro* and *in vivo*.

IMPART

The primary aim of the IMPART[43] project is to prevent knowledge of the health and environmental implications of nanoparticles from lagging behind the technological advances by fostering communication links between a number of regional, national and international initiatives. This should help to reduce duplication of effort, pool expertise and facilitate co-operation between networks.

NANOTOX

The global aim of the NANOTOX[44] project is to provide support for the elucidation of the toxicological impact of nanoparticles on human health and the environment. Public organisations and nanotechnology companies will work together to document potential methods of dispersal and contamination by nanoparticles and agglomerated nanocrystals.

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[41] See: http://www.nanopathology.it/paginei/menu.htm
[42] See: http://www.nanopathology.it/paginei/menu.htm
[43] See: http://www.impart-nanotox.org/impartnanotox/index.html
[44] See: http://www.impart-nanotox.org/impartnanotox/index.html

Annex 3

Funding mechanisms

DTI

The Department for Trade and Industry (DTI) National Measurement System (NMS) funds 21 science and technology programmes. The programmes cover fundamental research into measurement, development of new measurement techniques, maintenance of the primary national measurement standards and dissemination of measurement technologies and good measurement practice to industry and other measurement users.

The NMS is a portfolio of programmes that are either focused on a particular technical area, e.g. optical, time, flow or measurement techniques relevant to a particular sector (e.g. biotechnology), or in the case of Measurements for Emerging Technologies, its remit is to develop measurement techniques for technical areas that have been identified as crucial to the UK's future.

Nanotechnology projects are currently spread across the programme portfolio covering areas such as nanostructured multilayer characterisation, nanoparticle characterisation and surface and nano analysis.

The programmes are currently formulated as three-year packages of work, which are awarded through single tender to the National Measurement Institutes or by competitive tender. There are opportunities for collaboration. For further details please contact: Enquiry.NMS@dti.gsi.gov.uk

Defra

Research carried out under the Department for the Environment Food and Rural Affairs (Defra) nanotechnologies research programme of £1M over two years supports the development of policy in this area including the social and ethical dimensions. Related research may be funded under water quality, soil and air quality research programmes. Research is commissioned either through open competition or limited invitations to tender. Open competitions are advertised on the Defra science web pages[45]. Invitations to tender are issued to suitable candidates who register an interest for nanotechnologies topics listed in Defra's Environmental Research Newsletter[46]. For further details please contact the Defra nanotechnologies policy team at nano.technology@defra.gsi.gov.uk.

[45] See: http://www.defra.gov.uk/science/funding/competitions.htm
[46] See: http://www.defra.gov.uk/environment/research/

Environment Agency

The Environment Agency accesses science through a combination of in-house research, competitively tendered research contracts and by working in collaboration with others. Research funding is allocated to eight thematic programmes as outlined in their science strategy 'Solving Environmental Problems Using Science.'[47]

Nanotechnologies risk assessment and communication work would primarily fall within the Environment and Human Health Theme and Integrated Catchment Science Theme (Remediation). The Environment Agency is currently funding work on public engagement through the Nanodialogues project, and has recently co-funded work to assess the extent of nanotechnologies manufacture and use in the UK. Future funding in this area is being considered within the Science Group's 5 year thematic planning process, which is currently in review.

The Environment Agency welcomes proposals for collaborative research in areas aligned to the Science Strategy. The Environment Agency is not eligible as an industrial partner for NERC Industrial CASE awards but can be involved in non-industrial CASE studentships. An example of this is a CASE studentship recently awarded to the University of Exeter and funded by NERC and the Environment Agency, which will investigate the toxicity of engineered nanoparticles to aquatic organisms.

For further details contact Richard Owen (richard.owen@environment-agency.gov.uk)

HSE

The Health and Safety Commission (HSC) Science Strategy sets out how the Health and Safety Executive (HSE) will apply science and engineering to provide a sound evidence base to help deliver the HSC's vision and mission to protect people's health and safety by ensuring that risks in the changing workplace are properly controlled. HSE will continue to commission scientific research in accordance with our arrangements and apply research:

- Where independent advice is required by HSE on the extent and nature of the hazards and risks involved.
- Where there is a need for informed HSE participation in national and international standards making.
- Where information is needed in the light of incident experience or to support specific enforcement activities or policy initiatives.
- Where projects, though with clear health and safety benefits are too risky for firms to go ahead with themselves; for example, when timescales are long and/or the technical risks are high.

[47] See: http://www.environment-agency.gov.uk/science

- When the particular part of industry lacks the relevant scientific and technological expertise.
- When entry costs are high for manufacturers of safety-related equipment and the industry is small and fragmented.
- Where industry is complacent or not innovative and requires the stimulus and competition of new ideas to encourage improvement.
- When the potential beneficiaries are too diffuse for any one company to undertake the research on its own or the availability of results will be restricted.
- Provide support for HSE's regulatory activities through the commissioning of scientific support, with HSL as primary supplier.

The Chief Scientist, a member of the HSE Board, is responsible for the deployment of research funding, advised on strategic direction, quality issues and use of resources by the Science Strategy Committee. Bids for funding into the area of nanotechnology must compete with bids for research to support the delivery of HSE's strategic priorities and PSA targets. Ongoing research in the area of nanotechnology includes:

- Current investigation of the relationship between mass, number and surface area concentrations of airborne nanoparticles (£97K).
- Membership of a EU Framework 6 project on the safe production and use of nanomaterials (NANOSAFE2). HSE's main role is to investigate how any measurement and control technology and guidelines produced link with current EU standards and legislation (£60K).
- Studies into a range of properties of nano aluminium and nickel particles undertaken by QinetiQ (£10K).
- Partners in an international industry led project "Nanoparticle Benchmarking Occupational HS&E Project". It includes studies into the behaviour and measurement of solid-in-air aerosols, permeation of personal protective equipment and the effectiveness of filters (the nominal cost to HSE is £34K but provides access to the results of a multimillion dollar project).

For further details contact Dr Brian Fullam (0151 951 4115; brian.fullam@hse.gsi.gov.uk)

MRC

The Medical Research Council (MRC) supports research in the areas of toxicology, respiratory medicine and environment & health as part of the portfolio of the Physiological Systems and Clinical Sciences Research Board. It also supports basic research involving nanoparticles through the Molecular and Cellular Medicine Board. Applications for research grants in these areas are considered through the MRC's response mode funding schemes.

MRC is prepared to commit up to £200k to a capacity building programme in Environment and Human Health led by NERC. The programme aims to bring communities together and to encourage interdisciplinary research. Priority issues identified through a consultation preceding this programme included the assessment of exposure to particles including nanoparticles.

Contacts for further information are Jo Dekkers (jo.dekkers@headoffice.mrc.ac.ul) for nanotechnology, Heike Weber (heike.weber@headoffice.mrc.ac.uk) for toxicology or Gavin Malloch (gavin.malloch@headoffice.mrc.ac.uk) for cardiovascular and respiratory medicine.

EPSRC

The Engineering and Physical Sciences Research Council (EPSRC) is structured in a series of programmes (e.g. chemistry, materials, mathematics, ICT, life sciences interface); given the nature of the subject, nanoscience and nanotechnology research spans the majority of these Programmes and is not separated out for particular consideration. Some 60-70% of EPSRC's grant funds are spent on responsive mode research, that is research proposals that are submitted at any time in any area of EPSRC's remit. The balance of funding is provided in managed mode to support particular scientific or strategic priorities identified by EPSRC. Currently there is no specific managed activity in nanoscience or nanotechnology.

In responsive mode EPSRC supports over 260 current research grants with a total value of £107M in the area of nanotechnologies and nanoscience. This includes EPSRC support for the two nanotechnology IRCs jointly with MRC and BBSRC. These grants cover a very broad area across much of EPSRC's remit, some of it beyond the definitions used in this report, and much of it beyond the thrust of this report, including such diverse areas as quantum information processing, electronic devices, nano electromechanical systems and catalysts. However, much of this work will involve fundamental characterisation and measurement that could underpin work relevant to this report. EPSRC is always open for bids in responsive mode and would welcome high quality applications in the area of nanoscience and nanotechnology. EPSRC is also keen to support collaborative proposals between industry and academia. The general contact point for nanotechnology is David Holtum (01793 444052; david.holtum@epsrc.ac.uk).

ESRC

The Economic and Social Research Council (ESRC) has announced a strategic objective to create new research opportunities relevant to succeeding in the global economy. The ESRC will take forward, initially with other public sector funding partners, a joint investment of up to £2.5M in research to address:

- securing competitive advantage in specific nanotechnologies through upstreaming issues of public confidence and societal shaping;

- investigating the emergent multi-level regulation of nanotechnologies in a global economy; and
- innovation in science communication and developments in nanotechnologies.

In each case the emphasis will be on social scientists working in partnership with stakeholders including leading edge scientists, public, regulators and non-governmental organisations. Participation from business and voluntary sector funding partners will be welcome. Contact: Dr Fiona Armstrong Fiona.Armstrong@esrc.ac.uk; Tel 01793 413048.

The Council also welcomes proposals in these areas through the recently expanded range of responsive mode funding. Proposals can be submitted at any time, through the Je-S system, to ESRC. Enquiries about the funding process should be directed to rtdenquiries@esrc.ac.uk; Tel 01793 413085.

ESRC also has a joint funding programme with the Department for International Development (DfID), to the extent of £13M, on poverty alleviation. Proposals that examine how nanotechnologies can be developed and managed to meet this objective are welcome. Enquiries about the ESRC and DfID initiative should be directed to Oliver Moss on oliver.moss@esrc.ac.uk; Tel 01793 442858.

NERC

The main funding routes available at the Natural Environment Research Council (NERC) are the responsive mode blue skies schemes including Standard, Small, New Investigators and Consortium grants, and Knowledge Transfer partnership awards[48] Any application to these schemes must be related to environmental science and NERC's remit. Other opportunities include studentships and fellowships, in particular CASE studentships have recently been widened to include public sector partners as well as partners from industry [49], and this may be a useful avenue for research in this area.

NERC is also very interested in the wider issue of Environment and Human Health, and has committed £2.4M to setting up a programme in this area. The Programme has still to define its remit, but could potentially include nanotechnology. This multi-disciplinary programme will initially focus on capacity building activities e.g. networks, workshops, discipline hopping and small proof of concept studies[50]. Contact Lucy Parnall on lcpa@nerc.ac.uk; 01793 411981.

BBSRC

The Biotechnology and Biological Research Council (BBSRC) supports research in bionanotechnology through the responsive mode and the area has priority

[48] See: http://www.nerc.ac.uk/funding/policy/fundingguide.shtml
[49] See: http://www.nerc.ac.uk/aboutus/consult/envhh/.
[50] See: http://www.nerc.ac.uk/aboutus/consult/envhh/.

status within the Engineering and Biological Systems Committee. The Council also supports the Interdisciplinary Research Collaborations (IRC) in Nanotechnology and Bionanotechnology jointly with EPSRC and MRC. The combined funding for bionanotechnology in 2004-05 (through responsive mode, studentships, BBSRC-sponsored Institutes and the IRC's) was approximately £20M. BBSRC supports basic research in bionanotechnology which aims to understand, amongst other areas, the fundamental science of how nanostructures and biological systems interact. The Council also supports fundamental biological science, including molecular, cellular and physiological studies, which may provide knowledge that underpins several of the objectives identified within the report. Research to establish how nanoparticles are transported and localised within cells and tissues is of relevance to BBSRC.

For details of BBSRC's portfolio of research in bionanotechnology and related areas, please refer to the BBSRC website (http://www.bbsrc.ac.uk/science/areas/ebs/priorities/bionano.html).

The BBSRC contact point for bionanotechnology and related queries is Dr David McAllister (david.mcallister@bbsrc.ac.uk).

Other UK funding

It is anticipated that other stakeholders in the UK will fund research including different industries producing and using nanoparticles, medical research charities, research institutes (using their own funds) and possibly some environmental and civil society groups.

EU and International initiatives

There are a range opportunities to access research funding and for the UK research community and other stakeholders including Government to collaborate on research issues at EU and international levels.

There will be funding opportunities under the EU 7^{th} Research Framework Programme (FP7) where there is a theme planned on the development of nanotechnologies and nano-scale materials, which will also cover issues of associated environmental and human health and safety. There have been a number of relevant research projects under previous Framework Programmes (see Annex 2).

The European Commission's Action Plan on Nanotechnologies commits the Commission to action and calls for action by Member States in a range of areas including research and risk issues. This offers a framework for the Government to cooperate with our partners in the EU and access to results of other EU Member State projects and programmes.

International collaboration on the risks posed by nanoparticles is currently being considered through the OECD, with ongoing efforts to agree standards for hazard, and exposure assessment methods, coordinate research activities and access data and knowledge carried out in other member country. The UK is involved in organisation of an OECD workshop to be held in December 2005, that aims to contribute to this effort. There is also the ongoing work to reach agreement of standards for metrics and characterisation of nanoparticles at the European level through CEN and at the international level through ISO.

In addition to the funding mechanisms and Government initiatives set out above it is anticipated that the UK research community will make the most of existing and new contacts and networks with research communities in Europe and internationally.

PB 11485