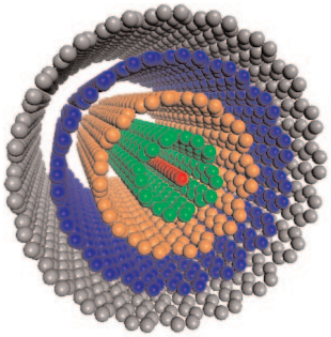
HSE

Health and Safety Executive

Review of the adequacy of current regulatory regimes to secure effective regulation of nanoparticles created by nanotechnology

The regulations covered by HSE



Contents

1 The reason for the review

1 Recommendations 8 and 11 of the Royal Society and Royal Academy of Engineering report 'Nanoscience and nanotechnologies: opportunities and uncertainties' (see Appendix I) make reference to the need for government to consider the adequacy of regulatory frameworks in relation to nanoparticles, especially nanoparticles that will arise from the application of nanotechnology. The government accepted these recommendations. Accordingly, each government department has undertaken to analyse and document how current regulations for which they have responsibility accommodate nanoparticles. This is HSE's analysis in relation to its responsibilities. The aim of this review is therefore to set out and discuss issues arising in relation to the following:

- whether or not nanoparticles are covered by the scope of the regulations for which HSE has responsibility; and
- whether or not the requirements of these regulations are appropriate and sufficient to protect human health in relation to occupational exposure to nanoparticles (this does not include the availability of advice relevant to nanoparticles).

2 Background information

2 With respect to nanomaterials, HSE has critically reviewed the available information on their physicochemical and toxicological hazards of relevance in the workplace and the occupational exposure situation (see summaries attached as Appendices II, III and IV). The reviews focused on poorly soluble or insoluble particles (including fibres) intentionally generated to have applications in nanotechnology, with one or more physical dimension(s) being less than 100 nm (0.1 micrometre). These reports indicate that there are very few good quality studies on novel nanomaterials of relevance to the assessment of human health hazards or exposure, although some limited but useful information is also available on more familiar materials reduced in size to the nanoscale.

3 Given the paucity of information available and the concerns raised by some of the data that does exist, a cautious approach to risk management has been recommended in an information note aimed at researchers and developers potentially exposed to nanomaterials (HSE, 2004).

Overview of current legal framework

4 Legislation to regulate the health and safety hazards of industrial chemicals and the risks they pose in the workplace has been developed and standardised across the European Union (EU); these regulations have been accommodated in the UK under the umbrella of the Health and Safety at Work Act 1974 (the HSW Act). There are also other agreements determined at a global level that may influence these EU regulations, for instance the Globally Harmonised Scheme for classification and labelling and the OECD guidelines for the testing of chemicals. In reviewing the current legislation the reader should be aware that the EU chemicals policy is on the verge of a major shift to a different regulatory framework based on the 'Registration, Evaluation and Authorisation of Chemicals' (REACH) which will have consequences for all the current legislation addressed in this review. Hence, at this time, there is little opportunity to modify the current legislation. It is also premature to specify precisely how future REACH-related legislation would accommodate the relevant issues identified in this review, as the negotiations shaping the new legislation are ongoing.

5 The current regulatory framework and the roles involved can be summarised as follows.

Legislation aimed at suppliers

6 EU Directives implemented in the UK by the Chemicals (Hazard Information and Packaging for Supply) Regulations (CHIP) require that suppliers of chemicals should seek out and convey information to the recipients on the physicochemical (eg flammability) and toxicological hazards of their chemicals. This is done through EU-standardised classification and labelling (C&L) and Safety Data Sheets (SDS). In recognition of the dearth of reliable hazard information on many industrial chemicals, the 7th Amendment to the EU Dangerous Substances Directive (DSD) implemented in the UK as the Notification of New Substances (NONS) Regulations, requires (among other things) standardised testing of hazardous properties of industrial chemicals new to the market. There is also a responsibility on suppliers to address the downstream risks and their management. Since the early 1990s there has also been an EU-wide attempt to capture and improve the hazard information available for older industrial chemicals, and to assess the risks to health and safety via the Existing Substances Regulation (ESR). However, activity under this regulation is now winding down, in anticipation of the future REACH regime, which will subsume these supply-side regulations and extend the principles of supplier responsibility further.

7 The supply of biocides is addressed by EU Directive 98/8/EC which establishes a regulated single European market in biocides based on risk evaluation and harmonised authorisation. In 2001 this Directive was implemented as the Biocidal Products Regulations (BPR) in Great Britain and its equivalent regulation in Northern Ireland. Over time, these Regulations will replace the current UK national approval scheme for non-agricultural pesticides under the Control of Pesticides Regulations (1986 as amended) that remain in force until substances have been assessed under the new regulations. Under BPR and its equivalent regulations elsewhere in the EU, industry will be required to submit data on the active substance and a representative formulation which addresses the hazardous properties, classification and labelling and necessary risk management procedures, which will be evaluated by Member States (MS) and a risk assessment conducted. Evaluations are then harmonised and made usable across the EU under the principle of mutual acceptance of data.

8 **Recipients/users of chemicals** (and manufacturers/suppliers in relation to their own sites) are responsible for understanding their local situation. Using the information from suppliers, they should assess and appropriately manage the extent of worker exposure to hazardous chemicals so as to eliminate, or at least minimise, the health and safety risks ‘so far as is reasonably practicable’. This is a requirement of the EU Chemical Agents Directive and the Carcinogens Directive transposed into the UK legislation in the Control of Substances Hazardous to Health Regulations (COSHH) and Dangerous Substances and Explosive Atmospheres Regulations (DSEAR).

9 **As a regulatory authority**, HSE, with others, is responsible for the negotiation, agreement and enforcement of these regulations. In addition to contributing to the development of the regulatory framework, HSE also plays a more detailed role for some individual substances, for example by agreeing and specifying their classification or by establishing the appropriate degree of control of airborne exposure in the workplace via Workplace Exposure Limits (WELs). HSE also plays a role in the enforcement of the regulations concerning the storage of some hazardous materials under the Control of Major Accident Hazards Regulations (COMAH, 2005 as amended). This deals with assessing the risks and consequences to the surrounding populace and environment of fire, explosion and substantial release of toxic chemicals in an industrial accident situation.

10 In addition to the regulations there are different types of documented advice: eg 'Approved Codes of Practice' (ACOPs) and 'Approved Guidance' help duty holders to understand their duties and to carry them out to a legal standard. If challenged, the duty holder must be able to justify any deviations from the guidance given in these documents. Additional guidance to the regulations is also available, which also allows specific advice to be changed more quickly than would be the case with a regulation or ACOP.

11 Fundamental to the effective operation of this regulatory framework is the availability of reliable information on the properties of the substance in question. Historically, many substances have been marketed and used without their hazardous properties having been fully explored. The advent of the NONS Regulations required suppliers to produce a standardised set of information on the properties of their 'new' substance before introducing it onto the market. Hence, a key question for any nanomaterial is whether or not it is considered a new substance that requires notification under NONS.

3 Is a nanomaterial 'new' and hence notifiable under NONS?

12 The concept of a 'new' substance was defined in the late 1970s. To assist in the EU-wide operation of what in the UK are the NONS Regulations, a list of substances that were already supplied in the EU was drawn up. These were entered into a database called the European INventory of Existing Commercial Chemical Substances (EINECS). Standardised naming conventions and specific criteria were used to draw up the list. The substances on the inventory were called 'existing'; after this, any substance intended for placing on the market for the first time is designated 'new' and subject to notification requirements (with the exception of 'special category' substances covered by other specific legislation eg foods and food additives, pesticides, pharmaceuticals etc).

13 It is the responsibility of the supplier to determine whether or not their substance is on EINECS and therefore 'exisiting'. In some cases, the identity of the substance to be supplied can be difficult to describe or an EINECS entry can be difficult to interpret. When this occurs, the opinion of the 'competent authority' (CA) in the relevant Member State can be sought. HSE in partnership with the Environment Agency (EA) is the relevant UK CA for NONS. Over the years that NONS has been in force, many such questions have been raised both in the UK and in other EU MS. The outcomes and decisions made have been recorded into a 'Manual of Decisions'. This document records precedents and procedures for the interpretation on the New Substances legislation; it is helpful guidance but not legally binding.

14 As yet there are no entries in the Manual of Decisions relating to the issue of nanoparticle notification. HSE's current thinking on whether or not individual nanomaterials can be being regarded as 'new' is explained in this review.

15 In relation to their production, nanomaterials roughly divide into two classes: 'top-down' and 'bottom-up'. 'Top-down' nanomaterials are those made by making familiar substances at the nanoscale (eg by grinding down). Broadly speaking, such materials are less likely to require notification under NONS. There is more potential for novel substances made as nanomaterials by 'bottom-up' construction to require notification. There are two examples already in the regulatory domain, illustrated in the following examples.

16 In relation to suppliers making an initial judgement as to whether or not their substance may be new, general information is freely available (publications, HSE Infoline, HSE website, European Chemicals Bureau website) to assist suppliers to judge whether or not the relevant criteria are met. However, in our view, more will need to be done to raise the awareness of those involved in the manufacture and supply of nanomaterials about the potential notifiability of novel nanomaterials and to develop appropriate guidance.

Example 1 – A 'top-down' material
Titanium dioxide in a nanoscale form demonstrates desirable properties for use in sunscreens. There is an entry for 'titanium dioxide' in EINECS and the particle size of a solid substance does not affect its EINECS status. Therefore, we would consider that the nanomaterial is not subject to notification under NONS.

Example 2 – a 'bottom-up' nanomaterial where NONS may apply
Various carbon structures in the form of fullerenes were some of the first bottom-up nanomaterials. Carbon has three entries in EINECS, two for the allotropes graphite and diamond and one for amorphous carbon. Carbon fullerenes are regarded by a an authoritative body of experts, the International Union of Physical and Applied Chemists (IUPAC), as distinct and separate allotropes of carbon. Hence, we consider that the entries for carbon on EINECS do not cover the fullerene allotropes (or their derivatives). Thus, carbon fullerenes and their derivatives, including carbon nanotubes, should be regarded as 'new' chemicals.

4 NONS Regulations: Issues for a notifiable material

17 If a nanomaterial is deemed to be notifiable under NONS, a structured notification procedure applies. A NONS package requires information in the following categories, under which the particular issues arising from nanomaterials are discussed.

NONS: Identity and properties

18 The critical issues here relate to particle size and shape. For engineered nanomaterials there is a need to know the physical characteristics and dimensions of the particles. The commonly used granulometric tests used to determine particle size ranges may not be appropriate for nanoparticles; in many cases electron microscopy will be needed to ascertain particle dimensions. While use of electron microscopy is an option in the current EC guidance on granulometry to assess the physical characteristics of particles, the necessity to use this method for notified nanomaterials will need to be stressed to notifiers.

NONS: Hazard identification

19 Data from standard test methods, or information equivalent to this standard, is required on the physicochemical, toxicological and eco-toxicological properties of notified substances. The studies should be performed to agreed quality standards (methods equivalent to those in Annex V of DSD, OECD Test Guidelines). In HSE's opinion, the available test guidelines for the assessment of physicochemical and human health hazards will be able to capture the necessary information on the hazardous properties of nanomaterials.

20 Regarding testing strategies, HSE's current thinking is that the timing and extent of testing required may need to be different from a standard NONS package. For example, it could be useful to have data at an early stage on the ability of the nanomaterials to be absorbed across the respiratory tract, skin and gastrointestinal tract. Early data on its likely distribution around the body once absorbed would also be useful, so as to obtain information on which are the most appropriate toxicological endpoints on which to focus attention. For all new substances, guidance indicates that toxicological testing should be conducted using the most relevant route of exposure. However, in general, many notified substances are tested for acute and repeated-exposure toxicity via the oral route. For nanomaterials in the form of nanoparticles, it appears to us that the inhalation route should be brought into play earlier and more often because of the identified concerns for toxicity towards the respiratory tract via this route of exposure.

21 Nowadays within NONS there is considerable use of 'read-across' (see section 5 for details). This approach has the potential to greatly reduce the burden of testing, particularly toxicological testing using experimental animals. There could be contentious or difficult issues in seeking to use read-across approaches for notifiable nanomaterials.

NONS: Exposure assessment

22 There is also a need to assess the potential for exposure. Given that the notification process will pre-empt full-scale production there is not usually any measured data available. Therefore, exposure assessment tends to be more qualitative, with a reliance on semi-quantitative modelling to predict potential exposure using the EASE (Estimation and Assessment of Substance Exposure) model. The ability of this model to accommodate nanomaterials will need to be examined and further developed as more information becomes available on the properties of nanomaterials. For example, at present the exposure predictions that the EASE model gives are based on mass of either inhalable or respirable particles; a different metric might be needed for nanoparticles.

NONS: Risk assessment and risk management

23 There is also a need for the notifier to conduct a risk assessment, with the help of the CA if necessary. To assist in the judgment about the completeness of a risk assessment, the CA has some flexibility under NONS to request further information if 'it is satisfied that the further information is reasonably required to evaluate the risks created by the substance to human health or the environment'. Hence, the information requirements of the current regulations appear to be sufficiently flexible to accommodate the pursuit of any issues of concern.

24 The information generated for a NONS notification should enable recipients of new substances who use them in their workplace to apply satisfactorily the requirements of COSHH. In terms of controlling the potential for exposure to nanomaterials, the main tools likely to be recommended for nanomaterials are containment and the use of personal protective equipment (PPE). These issues are discussed further in the section on COSHH.

25 Many of the same issues discussed above will translate across to other 'supply side' regulatory schemes based on health assessment, exposure assessment and risk management (eg BPR, ESR).

5 Chemicals (Hazard Information and Packaging for Supply) Regulations (CHIP)

26 CHIP enacts the EC Dangerous Substances Directive (DSD), the Dangerous Preparations Directive, and the Safety Data Sheet Directive. The CHIP Regulations make it the responsibility of suppliers to:

- identify, and where appropriate, categorise the hazards of the material as supplied using internationally agreed criteria - this is called classification;
- give information about the hazards and appropriate precautions to the user, normally through labelling on the product packaging and a suitable Safety Data Sheet; and
- package the material safely.

27 CHIP applies to the vast majority of supplied 'substances' and 'preparations' (mixtures of substances), if hazardous. Some chemicals such as cosmetics and medicines are outside the scope of CHIP and have their own legislation; the associated work is led by government departments other than HSE.

28 The issue of 'objects', sometimes called 'articles', also impinges on CHIP legislation. CHIP does not define articles, but in using this term refers to a definition previously used to determine if a substance was reportable under EINECS (an 'object' was excluded from reporting). Under CHIP, objects which by their use release hazardous substances, creating potential exposure for the user, may need to be packaged and labelled to indicate the presence of classified substances. The future of nanotechnology holds the potential for the creation of 'nanodevices', entities that are nanomaterials or contain nanomaterials within them. As regards the nanomaterials in such a 'device', the implications and requirements in relation to CHIP will need to be worked through.

29 Once a nanomaterial entity is considered within scope of CHIP then there are three issues, covered under the subheadings below.

Classification and labelling of an individual substance

30 Nanomaterials examined under NONS, ESR or BPR in the UK (or, in other EU Member States, the corresponding regulations) will have their classification and labelling agreed at EU level and entered into 'Annex I' of the Dangerous Substances Directive.

31 This 'Annex I' (transposed into the UK 'Approved Supply list', ASL) also lists the C&L for a considerable number of other existing substances that have been through the EU-wide procedure of agreeing C&L positions. Suppliers are obliged to use this classification if the substance is listed.

32 As yet, no 'existing' substances in nanosized form have been through this EU system. In such a situation, the supplier of such a material will need to gather and consider all of the relevant data on that substance and determine the classification themselves using the guidance available (principally, Annex VI to the DSD, or in the UK, the Approved Classification and Labelling guide). This process is called 'self-classification'; in undertaking it there could be two problems, as seen from the regulatory authority standpoint.

33 Absence of data on the nanomaterial in question. From the review summarised at Appendix (II) it is apparent that currently there is a distinct lack of data available

on the hazards of existing substances in their nanoform. In our experience, some suppliers of chemicals regard the absence of data as being synonymous with the absence of hazard. It is a concern that such a philosophy could lead to a supplier of a nanomaterial not assigning classification or labelling to their substance, without any attempt being made to think through its potential health hazards.

34 Inappropriate use of 'read-across'. Some suppliers of existing substances look for data on structurally related chemicals and read across such data as a prediction of the toxicity of the substance being supplied. Regulatory authorities also use this approach; for example in the EU, unless there is data to show otherwise, all isocyanates should be classified as sensitising and labelled 'May cause sensitisation by inhalation'. However, read-across must be used judiciously. We are concerned that suppliers of a nanosized material may consider reading across directly data available for the microsized form. However, it is evident that the properties of nanoscale entities are not necessarily the same as the microsized form of the same substance.

35 Concerns surrounding these issues illustrate the need for appropriate guidance.

Classification and labelling of a preparation

36 The classification and labelling of a preparation can be determined from data on the preparation itself and/or by calculation methods using the data and known classification of the components. There might be issues here in relation to nanomaterials but at this stage they are too speculative and detailed to be included in this document.

Safety Data Sheet requirements

37 The requirements of CHIP to make available Safety Data Sheets with specified format for the laying out of information will apply to hazardous nanomaterials. In completing a SDS, the heading structure will bring out a number of issues covered elsewhere in this review. The important role played by SDSs raises concerns for the quality of the information that will be included by suppliers and the interpretation of that information by users. We have already seen, in an SDS for carbon nanotubes, references made to hazard information on respirable graphite, without any further explanation to users about the relevance of such data.

6 Workplace risk management

Control of Substances Hazardous to Health (COSHH) Regulations

38 The COSHH Regulations require employers to either prevent, or where this is not possible, control the potential risks from exposure to hazardous chemicals for their particular work situation. The principles of COSHH follow a familiar pattern in that there is a need to assess the hazards, the potential for exposure and the risks posed to worker health; from there, employers then need to make risk management decisions and to specify the hierarchy of the measures that will be applied to deliver adequate control. COSHH has recently been amended (in 2004) to emphasise the principles of good practice for control of exposure by placing within the regulation itself the requirement to apply the 'eight principles of good practice'.

39 In COSHH a substance is deemed to be 'hazardous to health' if it meets one or more of the following criteria:

- is listed in the Approved Supply List with a classification of Harmful, Toxic, Very Toxic, Irritant or Corrosive;
- is present as a dust at a concentration greater than 4 mg/m3 (respirable fraction) or 10mg/m3 (inhalable fraction), as 8-hour time-weighted average values;
- has an approved occupational exposure limit; and/or
- represents a risk to human health from its presence or the way it is used in the workplace.

'Hazardous' materials in the scope of COSHH include both supplied substances and substances generated during work activity.

COSHH: Assessment of hazards and exposure

40 COSHH regulation 6 specifies that an employer has to assess the risks arising from work by using available information on the hazards and knowledge of the local conditions of exposure. Regulation 6 sets out the elements which are required in a COSHH risk assessment. The ones of most relevance to this review are:

- hazard;
- exposure;
- the circumstances of the work;
- the results of any exposure monitoring; and
- the results of any health surveillance.

41 Therefore, in order to do a suitable and sufficient assessment, a substantial amount of information is required. For nanomaterials, our current perspective is that there are deficiences in the available information available, ie we lack:

- sufficient toxicological hazard information for most nanoparticles;
- reliable, affordable and standardised exposure measurement and characterisation methods; and
- an agreed definition of the most appropriate dose metric(s) to use in hazard and exposure studies.

42 Without these basic strands of information, carrying out a reliable COSHH risk assessment will be very difficult. Also, without sufficient hazard information it is difficult to know when and in what form health surveillance becomes appropriate.

43 The purpose of the assessment is for employers to be able to demonstrate to themselves and others (including safety representatives and enforcing authorities) that they have made valid decisions about the measures necessary to prevent or adequately control the exposure of employees to hazardous substances arising from their work. They need to show that they have considered all of the factors pertinent to the work and reached an informed and valid judgement on the risks and the management of them. With the current level of information and knowledge on nanomaterials this will be very difficult.

44 Often employers rely on the information given in a supplier's Safety Data Sheet to carry out their assessment. However, the completion of an SDS for a nanomaterial is beset by the same problems.

45 Until such time as there is sufficient information and knowledge available on the toxicological hazards, the appropriate dose/exposure metric(s) and the levels of exposure to nanoparticles experienced, employers will not be able to carry out

adequate risk assessments. However, once the relevant information becomes available, there should be no reason why employers cannot fulfil their duties under COSHH.

46 One issue which may require attention in relation to the treatment of nanomaterials under COSHH is the definition of dust exposures deemed to be potentially hazardous to health. From current, limited understanding of the toxicology of nanomaterials it would be unwise to regard exposures to nanomaterials at or below 4 mg/m3 (8h TWA) respirable dust as representing adequate control associated, confidently, with health protection.

COSHH: Prevention or control of exposure

47 COSHH Regulation 7 requires employers to ensure that the exposure of employees to hazardous substances is either prevented, or where this is not reasonably practicable, adequately controlled. It gives a list of control measures appropriate to the activity, in order of priority, that can be used. There are extra provisions for control of carcinogens and mutagens in addition to the ones given for other substances.

48 Regulation 7, as amended in 2004, now also states that control of exposure shall only be treated as adequate if:

- the principles of good practice for the control of exposure are applied;
- any Workplace Exposure Limit (WEL) is not exceeded; and
- exposure to any carcinogen, mutagen and asthmagen is reduced to as low a level as is reasonably practicable.

Prevention of exposure

49 An employer's first duty is to prevent exposure, other than by means of PPE. The best way to comply with this requirement is to eliminate the substance entirely. Given the current high cost of nanomaterials, it is likely that they will only be used in applications for which they have a specific and integral purpose and therefore substitution is not likely to play a major role in prevention of exposure.

Control of exposure

50 Where prevention of exposure is not reasonably practicable, employers must comply with the duty to adequately control exposure by all routes. To achieve this they must consider and apply, where appropriate:

- the design and use of appropriate processes, systems and engineering controls;
- the provision and use of suitable work equipment and materials;
- the control of exposure at source;
- where adequate control of exposure cannot be achieved by other means, the provision of suitable PPE;
- the principles of good practice for the control of exposure of hazardous substances; and
- the requirement not to exceed any Workplace Exposure Limit (WEL).

There are additional requirements for carcinogens and mutagens.

51 An employer must apply the principles of good practice in all circumstances, but it will not always be necessary to use all of the available control options. The principles of good control elucidated in COSHH give general advice and as such will be adaptable to cater for the control of exposure to nanomaterials. However, there will be issues to examine surrounding the performance and effectiveness of conventional control approaches, including PPE, when applied to nanomaterials.

52 One of the recommendations in the Royal Society/Royal Academy of Engineering report (Appendix I) is to suggest the introduction of occupational exposure limits for manufactured nanoparticles that are lower than might be the case for somewhat similar materials in larger particle form. The current (newly introduced) single type of occupational exposure limit in the UK is the Workplace Exposure Limit (WEL). At present, WELs are based on the mass of inhaled particles and all have been derived from information on, and with the thinking that they would be relevant to, larger sized particles. If a current WEL for any individual substance were to be applied to the same material in a nanosized form we would not be confident of health protection when inhaling the vast numbers of nanoparticles inherent in such an exposure. However, at present we do not have sufficient data to know whether or not to adjust downwards any such WEL value to cater specifically for the substance in nanosized form and, if so, by what amount. Furthermore, the listing of two (or more) different WEL values alongside the same substance name, covering different size fractions, might be confusing.

53 The other option is to build up from first principles the derivation of a specific WEL for each nanomaterial of interest. As yet, we do not have sufficient knowledge on the toxicological hazards, appropriate dose/exposure metric(s) and prevailing/potential exposure conditions to do this. This is an issue which will need to be revisited when there is more of such data available on nanomaterials.

COSHH: Monitoring exposure

54 When a COSHH assessment indicates the need, monitoring of exposure should be carried out using a valid and suitable method. Although some methods to measure nanoparticles are available currently, they are not practical for routine monitoring of personal exposure in the workplace, requiring the use of large pieces of expensive equipment that are not easily portable. Research is underway to try to develop a portable personal sampler. A decision will also need to be made on the most appropriate exposure metric(s) to use in making exposure assessments.

55 Nanoparticles in the form of fibres, such as carbon nanotubes, may need specific exposure measurement methods to be developed. Current methods of fibre counting involving light microscopy would not be appropriate with nanoscale fibres.

COSHH: Health surveillance

56 COSHH regulation 11 requires health surveillance to be carried out where it is necessary for the protection of employees' health. The stated objectives of such health surveillance are: to protect the health of individual employees by detecting as early as possible adverse changes that may have been caused by exposure to hazardous substances; to help evaluate the effectiveness of measures taken to control exposure; and to collect and use data for determining and evaluating the hazardous properties of substances.

57 Currently there is insufficient knowledge of the risks to health posed by nanomaterials under specified circumstances to enable employers or regulators to make valid assessments of what health surveillance would be appropriate and when.

COSHH: Instruction and training

58 Employers must provide employees with suitable information, instruction and training to allow them to carry out their jobs in a safe manner. This includes information on the risks to health and what the employee needs to do to control their exposure. Despite the evident gaps in knowledge for nanomaterials,

employers should still inform their employees about what is known and what the employer considers to be the appropriate guidelines to be followed for safe conditions of work.

COSHH: Risks to others

59 COSHH requires employers to address the risks not only to workers but also to other people on the premises or others who might be directly affected by the work activity, 'so far as is reasonably practicable'. Employers and other stakeholders will need to equip themselves to assess the risks posed by a nanomaterial to such people.

Summary of issues under COSHH

60 Overall, the principles and basic elements of COSHH are appropriate to accommodate the challenges provided by nanomaterials in the workplace. However, for many actual or potential future nanomaterials there is a lack of the necessary relevant information in a number of important areas to allow employers to conduct the necessary assessments, and for employers and regulators to judge whether or not those assessments are adequate.

61 As more information becomes available, ACOPs and other guidance in support of COSHH may need to be revised to take account of both the uncertainties and what become the known differences between nanomaterials and other substances.

Dangerous Substances and Explosive Atmospheres Regulations (DSEAR)

62 Substances capable of forming explosive atmospheres fall under DSEAR and the requirements of these Regulations to assess and manage the risk of explosion. There is a need to identify those materials which may be explosive and, explosivity being an issue for dusts in general, this is a consideration for nanoparticles which may become airborne. A recent review of fire and explosion hazards reported that it is not possible to predict these properties for nanomaterials on the basis of the knowledge gained from testing larger sized particles (Pritchard (2004)). Given the uncertainties regarding the properties of nanomaterials in this respect, until better data is available there is a need for users to understand that there are uncertainties regarding flammability and explosivity surrounding the use of nanomaterials.

7 Other specific legislation (EU Existing Substances Regulation; Biocidal Products Regulations; Major Hazard (COMAH) legislation)

Existing Substances Regulation (ESR)

63 The EU Existing Substances Regulation (and, for the UK, the associated UK enforcement regulations) require suppliers of existing chemicals to submit hazard information to the European Commission. This is a prelude to the prioritisation, selection and undertaking of comprehensive risk assessments leading to conclusions about the need for risk management measures beyond those currently in place, to protect all sectors of the human population and the environment. The UK Competent Authorities for ESR are HSE and the Environment Agency (EA).

None of the substances reviewed to date have been identified as being available in the form of nanoparticles. In anticipation of the forthcoming REACH regulations (see section 8), very few if any further substances will be assessed under ESR. Hence there is nothing further to consider here in the context of nanomaterials.

Biocidal Products Regulations (BPR)

64 HSE is the UK Competent Authority for the regulation of biocidal products across the EU under Biocidal Products Directive 1998, enacted in the UK as the Biocidal Products Regulations (2002, and amendments). No nanoscale substances have yet been identified as coming under the requirements of these Regulations. However, there is the potential for this to change in the future. Were this to be the case, the issues that would arise are similar to those covered above in relation to other legislation.

Control of Major Accident Hazards Regulations (COMAH)

65 COMAH legislation requires notification (in the UK, to HSE) of sites where substances with hazardous properties that correspond to certain CHIP classification criteria are stored in quantities above specified tonnage triggers. Part of the notification procedure is to reach agreement between the site operator and the regulator on a risk assessment and the identification of the necessary measures to mitigate the risks of a release to as low as is reasonably practicable. The onus is on the site operator to identify the appropriate hazard classification of the material(s) stored, in order to determine whether or not COMAH applies. This raises issues discussed previously in this review concerning the identification of the hazards of nanomaterials. However, at this stage in the development of the nanotechnology industries, it seems unlikely that the quantities of materials being produced and stored will be relevant to this legislation.

8 REACH

66 It is anticipated that new legislation on chemicals, known by the acronym REACH (Registration, Evaluation and Authorisation of Chemicals) and currently under negotiation, will be introduced across the EU sometime in the next few years (possibly 2007). It is expected that some current major pieces of chemicals legislation, including NONS and ESR, will be replaced by the REACH system.

67 Given that the content and procedural aspects of REACH are currently under active negotiation, it is premature to assess in detail in this review how REACH will accommodate nanomaterials. However, one key feature of the draft REACH system is that the tonnage triggers for required information are higher than in NONS. Given that it seems likely that many nanomaterials will be speciality chemicals produced at relatively low tonnages, it might well be that the demand for the collection and submission into the regulatory system of information on nanomaterials may be more relaxed under REACH than it would be for a nanomaterial deemed subject to the requirements of the current NONS Regulations. Those negotiating the final form of the REACH legislation may need to give this point some consideration.

68 Beyond this, the issues raised above in relation to current legislation will need to be borne in mind and carried through appropriately into the REACH system, in relation to both novel nanomaterials created by a ‘bottom-up’ process and the ‘top-down’ conversion of familiar substances into nanosized forms.

9 Conclusions

69 This review has considered the relevant regulations for which HSE is (fully or in partnership with others) the responsible authority in the UK and has examined how such legislation accommodates nanomaterials. The regulations covered are concerned with the protection of health and safety in the workplace and, in some cases, with the assessment of hazards and risks to health of humans in all sectors of the population. The review has attempted to consider both the current position and also likely developments in the future, in terms of the nanotechnology industry, the advancement of scientific research and understanding of the properties of nanoparticles, and foreseeable changes in the regulatory framework.

70 The overall conclusion reached is that the principles of the existing regulations and the interconnections between them are appropriate and applicable to nanomaterials. We perceive no need to fundamentally change the regulations themselves, nor to introduce new regulations. However, there are important issues which require attention if, in reality, the current and foreseeable future general regulatory framework is to operate effectively in relation to nanomaterials.

71 In this context, **four themes** are drawn out here that need to be borne in mind and responded to appropriately.

72 **Firstly**, there are currently many gaps in our knowledge of nanoparticles such that there are important uncertainties surrounding the toxicological and physicochemical hazards, the appropiate dose/exposure metric(s), the means of measuring exposures, the risks to health and the effectiveness of control measures. This absence of data and knowledge means that all involved in the regulatory process (eg manufacturers and suppliers, recipients and users, regulatory authorities) will have great difficulty at present in confidently discharging their responsibilities within the various regulations covered here. However, we do expect that there will be rapid advances in understanding of the scientific and technological issues surrounding nanomaterials, such that one can have reasonable confidence that this position will be much improved in the next few years.

73 **Secondly**, there are currently several areas where, because of the newness of the nanoparticles field and the gaps in understanding, judgements need to be exercised to determine the appropriate position within various regulations and regulatory obligations. There is clearly the potential for different players within the regulatory systems to reach different judgements on such matters. Three examples are:

- the notifiability of, and associated information gathering and submission requirements for, a novel nanomaterial under the NONS Regulations (see section 3);
- 'reading across' toxicological hazard data from materials of larger particle size to nanomaterials judged to be somewhat related in chemical or physical terms (see section 5);
- in the absence of data, the appropriate conclusions to draw and actions to take in relation to workplace risk assessment and risk management of nanomaterials.

HSE has already issued an Information Note (HSE 2004a)[1] in relation to the last point, but we suggest that there is more to be done to bring all participants in the various regulatory processes to the same level of understanding and judgement.

74 **Thirdly**, it must be recognised that all of the legislation reviewed here is not specific to the UK but operates on an EU-wide basis. Furthermore, not only are the

regulations EU-wide, but also (and increasingly) the accompanying guidance, precedents (captured in manuals of decisions) and standards (eg specific classification decisions, occupational exposure limits) are also reflections of EU-wide agreements. There is almost no scope for changing regulations and supporting elements on a purely national, UK basis; almost all such envisaged changes would need to be negotiated and a position ultimately agreed across the EU. In some cases (eg test methods) the international dimension goes wider than the EU, for example to the OECD.

75 **Fourthly**, much of the current EU legislation discussed in this review will be altered, in some cases dramatically and even to the point of being subsumed, by the envisaged REACH system that is currently under negotiation. Alongside this, it is also now envisaged that the new Globally Harmonised Scheme (GHS) for classification and labelling of substances and preparations will be introduced into the EU in the next few years, replacing the current EU C&L system. Realistically, one can anticipate that across the EU there will be little appetite for negotiating in depth and/or bringing about significant changes to current legislation which might take a considerable time to resolve, only to be swept away within a short time period by the introduction of REACH (and GHS). Indeed, it might be more profitable to concentrate such regulatory negotiation efforts on issues surrounding the envisaged treatment of nanomaterials within REACH (and GHS), rather than, for example, within current NONS and C&L/CHIP legislation.

Appendix I

Abstracted from the Recommendations of 'Nanoscience and nanotechnologies: opportunities and uncertainties' July 2004.[2]

Regulatory issues

R8
We recommend that all relevant regulatory bodies consider whether existing regulations are appropriate to protect humans and the environment from the hazards outlined in this report and publish their review and details of how they will address any regulatory gaps.

R9
We recommend that regulatory bodies and their respective advisory committees include future applications of nanotechnologies in their horizon scanning programmes to ensure any regulatory gaps are identified at an appropriate stage.

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

R10
We recommend that chemicals in the form of nanoparticles or nanotubes be treated as new substances under the existing Notification of New Substances (NONS) Regulations and in the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) (which is currently under negotiation at EU level and will eventually supersede NONS). As more information regarding the toxicity of

nanoparticles and nanotubes becomes available, we recommend that the relevant regulatory bodies consider whether the annual production thresholds that trigger testing and the testing methodologies relating to substances in these forms should be revised under NONS and REACH.

R11
(i) We recommend that the Health and Safety Executive (HSE) review the adequacy of its regulation of exposure to nanoparticles, and in particular considers the relative advantages of measurement on the basis of mass and number. In the meantime, we recommend that it considers setting lower occupational exposure levels for manufactured nanoparticles.

(ii) We recommend that the HSE, Department for Environment Food and Rural Affairs and the Environment Agency review their current procedures relating to the management of accidental releases both within and outside the workplace.

(iii) We recommend that the HSE consider whether current methods are adequate to assess and control the exposures of individuals in laboratories and workplaces where nanotubes and other nanofibres may become airborne and whether regulation based on electron microscopy rather than phase-contrast optical microscopy is necessary.

R12
(i) We recommend that ingredients in the form of nanoparticles undergo a full safety assessment by the relevant scientific advisory body before they are permitted for use in products. Specifically: we recommend that industry submit the additional information on microfine zinc oxide that is required by the SCCNFP as soon as reasonably practicable so that it can deliver an opinion on its safety.

(ii) We recommend that manufacturers publish details of the methodologies they have used in assessing the safety of their products containing nanoparticles that demonstrate how they have taken account that properties of nanoparticles may be different from larger forms.

(iii) We recommend that the ingredients lists of consumer products should identify the fact that manufactured nanoparticulate material has been added.

(iv) We recommend that the EC's new Scientific Committee on Emerging and Newly Identified Health risks give a high priority to the consideration of the safety of nanoparticles in consumer products.

(v) In the light of the regulatory gaps that we identify we recommend that the EC (supported by the UK) review the adequacy of the current regulatory regime with respect to the introduction of nanoparticles into consumer products. In undertaking this review they should be informed by the relevant scientific safety advisory committees.

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

R14
We recommend that manufacturers of products that incorporate nanoparticles and nanotubes and which fall under extended producer responsibility regimes such as end-of-life regulations be required to publish procedures outlining how these materials will be managed to minimise human and environmental exposure.

R15
(i) We recommend that researchers and regulators looking to develop methods to measure and monitor airborne manufactured nanoparticulates liaise with those who are working on the measurement of pollutant nanoparticles from sources such as vehicle emissions.

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

Appendix II

HSE (2004b) *A review of the toxicity of particles that are intentionally produced for use in nanotechnology applications, seen from an occupational health perspective*.[3]

Summary and conclusions

1 There is a paucity of information and extensive gaps in our knowledge of the potential health effects of particles intentionally produced for nanotechnology applications. This lack of information and understanding applies particularly to novel nanoparticles, such as carbon nanotubes. The limited information that is available, certainly for carbon nanotubes, suggests that they do possess significant inherent toxicity, at least towards the respiratory tract.

2 There is an extensive body of information on the health effects of existing micrometre-sized particulate material, particularly towards the respiratory tract following inhalation exposure. Some studies have compared this toxicity with that produced when the material is rendered nanometre-sized. The general picture that emerges from experimental animal studies is that on a mass dose basis, pulmonary toxicity is enhanced when particle size is reduced from the micrometre to the nanometre range. The increase in toxicity appears to be related, at least in part, to the increase in particle surface area. However, what also becomes apparent from the data is that different existing materials in the nanometre size range exhibit different degrees of toxicity towards the respiratory tract. The reasons for these differences are currently poorly understood. Consequently, it is not possible to reach generic conclusions about toxicity based on consideration of size alone; the potential toxicity of each individual nanoparticulate material needs to be considered on a case by case basis.

3 Consideration of the potential toxicological properties of particulate materials intentionally produced for use in nanotechnology applications must address the consequences of exposure in terms of local and systemic effects, following single and repeated exposure by relevant routes. For the occupational setting, the exposure routes of relevance are inhalation and dermal.

4 One aspect that may be of particular importance to the novel carbon-based materials, the production of which involves the use of metal catalysts, is the issue of toxicity due to the residual metal contained within the final product. Such metals might contribute to the overall expression of toxicity by the material, either from their location within the material or by leaching out from it. For example, exposure to nickel could be an issue for some carbon nanotubes, which have a relatively high (by mass) residual nickel content. Further information on the residual metal content of carbon nanotubes and other nanoparticles and leaching rates in biological systems would be required to determine whether metal exposure is likely to be important in the expression of respiratory tract, and any other toxicity.

5 Overall, therefore, there is a clear lack of information on the potential health effects of nanoparticles produced for nanotechnology applications. From the limited information that is available, the indications are that they might possess significant toxicity potential.

Appendix III

Pritchard (2004) *Literature review – explosion hazards associated with nanopowders.*[4]

Executive summary

Objectives

1 Nanopowders are composed of particles in size range from about 1 to 100 nanometres (nm). One nanometre is equivalent to 10-9 metres. The growing demand for nanopowders arises from the change in physical, chemical and electrical properties exhibited by particles when their size falls below about 100 nm. The laws of quantum physics, rather than the laws of classical physics, come into play at these small particle sizes and the behaviour of the surfaces start to dominate the bulk behaviour of the material. For example, materials that would normally be conductors of electricity can become insulators at the nanoscale, or vice versa. Titanium dioxide and zinc oxide, which are widely used in sunscreens, become transparent at the nanoscale, a cosmetically desirable property for sunscreen products. Nanopowders are also referred to as nanomaterials, nanoparticles or ultra fine particles.

2 Along with the increasing production and use of nanoscale particles there has been a growing concern over the impact of this new technology on health and safety and the environment. This has almost exclusively concentrated on the potential health hazards of nanopowders. One potential hazard that appears to have received little attention to date is their explosibility. A literature review has been commissioned by the Corporate Science and Knowledge Unit (CSKU) of HSE to explore the use of nanopowders in industry and the potential explosion hazards. This report presents the findings of the review and assessment of the explosion risks associated with the processing and use of nanopowders.

Main findings

3 An increasing range of materials that are capable of producing explosive dust clouds are being produced as nanopowders. At the same time new uses of nanopowders are further adding to the demand for these powders. While some of these nanopowders are only being produced in very small quantities at present, and may continue to be for the foreseeable future, the production of others is likely to increase significantly over the next few years.

4 There is a growing concern over the impact the increased use of nanopowders and other nanomaterials will have on health and safety and the environment. These concerns are almost exclusively centred on the potential toxic effects of nanomaterials. The potential explosion hazards of nanopowders have not been addressed.

5 There is a considerable body of knowledge on the explosion characteristics of micronscale powders (particle sizes ranging from about 10 to 500 mm). A literature search has found no data for nanopowders (particle sizes of 1 to 100 nm). It is considered that the extrapolation of the data for larger particles to the nanosize range cannot be carried out with any degree of confidence, due to marked change in the chemical and physical properties of particles below sizes of about 100 nm.

Recommendations

6 It is recommended that the explosion characteristics of a representative range of nanopowders be determined using the standard apparatus and procedures already employed for assessing dust explosion hazards. Comparison with data for micronscale powders of the same materials will allow knowledge of particle size effects to be extended into the nanosize range.

7 Although it is recommended using standard apparatus and procedures for measuring the explosion characteristics of nanopowders, if agglomeration is thought to be occurring in the test vessel it may be necessary to modify the way the powder is dispersed. This is to ensure that the worst-case characteristics will be measured.

Appendix IV

Aitken et al (2004) *Nanoparticles: An occupational hygiene review.*[5]

Executive summary

1 Nanotechnology is a broad interdisciplinary area of research, development and industrial activity which has been growing rapidly worldwide for the past decade. It is a multidisciplinary grouping of physical, chemical, biological, engineering and electronic processes, materials, applications and concepts in which the defining characteristic is one of size. Nanoparticles are the end products of a wide variety of physical, chemical and biological processes some of which are novel and radically different, others of which are quite commonplace. In this review we have focused on processes for the deliberate development and manufacture of nanoparticle products. Nanoparticle products include nanotubes, nanowires, quantum dots and 'other' nanoparticles. We have reviewed and considered the following, for nanoparticle production processes:

- potential routes for human exposure;
- industrial sources of occupational exposure;
- level of exposure;
- means of, and effectiveness of control measures;
- potential numbers exposed;
- ease with which gaps in knowledge could be filled;
- trends in the (potential) use of nanotechnology;
- views as to the likely impact of the transition from research use to full-scale industrial use.

2 The review is comprised of four main elements:

- a conventional scientific review;
- a web-based review;
- discussion with key individuals prominent in relation to scientific or industrial development of nanoparticles, their health effects or risk assessment; and
- the experience and interpretation of the project team.

Conclusions

3 Based on our review of occupational hygiene aspects of nanoparticle production, we conclude that:

- There are four main groups of nanoparticle production processes (gas-phase, vapour deposition, colloidal and attrition) all of which may potentially result in exposure by inhalation, dermal or ingestion routes.
- From an occupational hygiene perspective, the processes are not dissimilar to existing chemical production processes.
- Only gas-phase processes have the potential to cause exposure to primary nanoparticles by inhalation during the synthesis stage. All processes may give rise to exposure (by inhalation, dermal and ingestion) to agglomerated nanoparticles during recovery, powder handling and product processing.
- For exposure by inhalation, control approaches and methods are available which should be effective in nanoparticle processes.
- For dermal or ingestion exposure, control methods based on personal protective equipment may not be as effective as they are in existing processes.
- The most appropriate metric in most cases for assessment of inhalation exposure to nanoparticles is particle surface area. There are no effective methods currently available that enable particle surface to be assessed in the workplace.
- Current knowledge is inadequate for risk assessment purposes.
- No information has been identified about workers' exposures to nanoparticles in the university/research sector or in the new nanoparticle particle companies in the UK.
- Only very limited information is available for existing chemical, pharmaceutical and refining companies. Information from other powder handling processes indicates that exposures may be significant.
- Approximately 2000 people currently employed in the university/research sectors and new nanoparticle companies are involved in activities in which they may potentially be exposed to nanoparticles in some form. A maximum of 500 workers are considered to be potentially exposed to nanoparticles through existing ultra fine manufacturing processes, mostly through the manufacture of carbon black. Around 100 000 individuals may potentially be exposed to fine powders through various powder handling processes, including the pharmaceutical industry. It is not possible to say what proportion of these may be exposed to nanoparticles. More that 1 000 000 workers in the UK may be exposed to nanoparticles via incidental production in processes such as welding and refining.
- The number of people in the university/research sector and in new nanoparticle companies may double over the next five years. The proportion of those involved in existing chemical and pharmaceutical companies and in other powder handling activities who are exposed to nanoparticles is likely to increase.

4 In summary, we conclude that there is little evidence to suggest that the exposure of workers arising from the production of nanoparticles has been adequately assessed.

Knowledge gaps

5 Arising from the review we also identified key knowledge gaps and made recommendations as to how they may be filled. These are:

The nanoparticle nomenclature is not sufficiently well described or agreed

Currently there are no agreed definitions for nanoparticles, nanoparticle aerosols, or for the various types of nanoparticles which are produced. Definitions proposed need to define a size interval to take account of the distribution in sizes likely to be present, to consider whether the definition should be based on physical dimensions (eg length, diameter, surface area) or on some behavioural property such as diffusivity and also take account of agglomerated aerosols. Progress on nomenclature issues is usually best achieved based on consensus.

There are no convenient methods by which exposures to nanoparticles in the workplace can be measured or assessed

For inhalation, the most appropriate metric for assessment of exposure to most nanoparticles is particle surface area. Currently there are no effective methods available by which particle surface area can be assessed in the workplace. There is a need for more research into the development of new and improved methods, combinations and strategies to provide reliable assessments of exposure to nanoparticles and nanoparticle aerosols. Development of appropriate methods to evaluate dermal and ingestion exposure is also necessary. HSE should consider how best to promote the development of appropriate metrics and exposure assessment approaches.

Insufficient knowledge concerning nanoparticle exposure is available

Much more information is needed regarding the exposure of workers involved in the production of all of the various types of nanoparticles via all of the production processes. In the absence of suitable measurement systems, coherent approaches as described above should be adopted. At this stage there is insufficient evidence to judge whether exposure to the various forms of nanoparticles is occurring at significant levels in nanoparticle production processes. HSE should consider how to encourage the collection of such data.

The effectiveness of control approaches has not been evaluated

Better understanding is required relating to the effectiveness of control of nanoparticles. This will be better informed given the development of appropriate methods for assessment of exposure to nanoparticles and a better understanding on the levels of exposure that may be acceptable. This is true for both inhalation, dermal and ingestion risks. HSE should consider how to promote the evaluation of control approaches.

Knowledge concerning nanoparticle risks is inadequate for risk assessments

Current knowledge is inadequate for risk assessment. Risk assessment approaches will have to consider how best to use information which is currently available, and plan to collect new information. An effective strategy for collecting, storing and disseminating this information is also necessary. Development of appropriate databases and other information resources to collect and disseminate information on studies investigating exposure or toxicological assessment of nanoparticles will be a key element in this. HSE should consider what it can do to collate, maintain and disseminate information relevant to nanoparticle risk issues.

References

1) HSE 2004(a) Horizons Scanning Information Note No HSIN1 Available online at: www.hse.gov.uk/pubns/hsin1.pdf

2) *Nanoscience and nanotechnologies: opportunities and uncertainties* The Royal Society and The Royal Academy of Engineering London 2004

3) HSE 2004(b) *Health effects of particles produced for nanotechnologies* HSE Hazard assessment document EH75/6 December 2004 Available online at: www.hse.gov.uk/horizons/nanotech/healtheffects.pdf

4) Pritchard D K 2004 *Literature review – explosion hazards associated with nanopowders* Health and Safety Laboratory Report HSL/2004/12 Available online at: www.hse.gov.uk/research/hsl_pdf/2004/hsl04-12.pdf

5) RJ Aitken, KS Creely, CL Tran (2004) *Nanoparticles: An occupational hygiene review* RR274 HSE Books 2004 ISBN 0 7176 2908 2 Available online at: www.hse.gov.uk/research/rrpdf/rr274.pdf

Further information

HSE produces a wide range of documents. Some are available as printed publications, both priced and free, and others are only accessible via the HSE website, www.hse.gov.uk.

HSE priced and free publications are available by mail order from HSE Books, PO Box 1999, Sudbury, Suffolk CO10 2WA Tel: 01787 881165 Fax: 01787 313995 Website: www.hsebooks.co.uk (HSE priced publications are also available from bookshops and free leaflets can be downloaded from HSE's website: www.hse.gov.uk.)

For information about health and safety ring HSE's Infoline Tel: 0845 345 0055 Fax: 0845 408 9566 Textphone: 0845 408 9577 e-mail: hse.infoline@natbrit.com or write to HSE Information Services, Caerphilly Business Park, Caerphilly CF83 3GG.

This document contains notes on good practice which are not compulsory but which you may find helpful in considering what you need to do.

This document is available web only at www.hse.gov.uk/horizons/nanotech/