Working Safely with Nanomaterials

IN RESEARCH & DEVELOPMENT

Third Edition

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Developed by :

The UK NanoSafety Group

CONTENTS

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Dedicated to James Wheeler, HM Specialist Inspector, ambassador, colleague, and friend.

ACKNOWLEDGMENTS

This guidance has been produced from the contributions of those listed below who constitute the UK NanoSafety Group (UKNSG). It provides help and support to research laboratories in industry, research and training organisations and academia on how to comply with their occupational health and safety legal obligations; it also includes additional information to help improve health and safety systems when working with nanomaterials. It should be noted that the guidance may go further than the minimum required to comply with the law. The Health and Safety Executive (HSE) welcomes this guidance and will continue to work with partners to ensure that the health and safety risks to employees in the nanotechnologies industry are appropriately controlled.

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RSC – Royal Society of Chemistry

ORIGINAL FOREWORD BY JUDITH HACKETT CBE

As an engineer myself, I take a good deal of interest in the exciting technological developments taking place today.

The many challenges which face our own and future generations on this planet require the very best of scientific and technological innovation to provide solutions in healthcare, medicine, energy, climate change, transport to name but a few. Whilst we may recognise that the way we live our lives today is unsustainable, the future is about innovation in new products and new materials. Nanomaterials have the potential to provide solutions in many fields.

As a regulator, HSE sees its role as enabling business to innovate, develop and grow whilst ensuring that health and safety issues are identified and addressed as part of that introduction process. We all recognise that there are huge potential benefits offered by nanomaterials but understanding and managing the risks they may pose is vital to enabling them to be developed to their full potential.

Partnership working brings together key players from all sides to ensure that health and safety issues are jointly owned and solutions identified. The UK NanoSafety Group brings together key experts in the field of nanotechnology and helps to establish links with others who have interests in this area to address those issues and enable the technology to move forward. I wish the UK NanoSafety Group continued success.

Judith Hackitt CBE
Former Chair of the Health and Safety Executive

This original foreword was drafted for the first edition (2012) and the second edition (2016).

PREFACE TO THE THIRD EDITION

The UK Nanomaterials Safety Group (UKNSG) successfully completed its mission in 2025. Since its formation in 2009, the group has played a key role in promoting safety practices related to nanomaterials. During the period, two versions of the guidance have already been released, reflecting ongoing developments and best practices in the field.

This third edition takes into account updates regarding changes in legislation, recent studies in the literature, and best practice since 2016. In particular, specific sections have been revised to account for the full implementation of the Globally Harmonised System (GHS), which came into force on 1 June 2015, through the Classification, Labelling and Packaging of Chemicals (CLP) regulations. It also now reflects UK Registration, Evaluation, Authorisation and Restriction of Chemicals (UK REACH), which regulates chemicals placed on the market in Great Britain (GB).

The document explains the approaches currently being used to select effective control measures for the management of nanomaterials, more specifically, control banding tools currently in use, as listed in Table 1. Significant changes can be found in the following sections: 'Legal Duty', 'Toxicology', and 'Health Surveillance'. The section on hazard banding has been replaced with one on 'Alternative Approaches to Enable Risk Mitigation'.

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SCOPE OF GUIDANCE

This Guidance Document draws attention to the possible health hazards that could result from exposure to nano-objects, including nanoparticles, nanotubes, nanofibres, nanoplates, etc. It provides advice on the precautions that may be needed to prevent or adequately control exposure as required by the Control of Substances Hazardous to Health Regulations (COSHH) 2002 (as amended) [1].

The aim of this document is to provide guidance on factors relating to establishing a safe workplace and good safety practices when working with nanomaterials. The document is applicable to a wide range of nanomaterials.

This guidance is aimed at employers, managers, health and safety advisors, and users of nanomaterials in research and development. It should be read in conjunction with the Approved Code of Practice on COSHH, the other literature referred to below, and the Appendices.

The document has been produced taking into account the safety information currently available. It is presented in the format of guidance and recommendations to support the implementation of suitable protocols and control measures by employers and employees, by advocating a precautionary strategy to minimise potential exposure.

This document applies to a broad set of nanomaterials, including powders, liquid suspensions, gels, and bound materials containing nano-objects, as well as nano-objects such as nanoparticles, nanofibres, nanotubes, nanowires, and nanoplates and their aggregates and agglomerates. The 'nano' terms used in this document are those defined by the International Organization for Standardization (ISO).

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1. INTRODUCTION

1 There are three major properties of nano-objects that make them unique and give them the properties leading to their increased use across a wide spectrum of fields for a large variety of uses. These are that in the "free state", nano-objects are highly mobile and reactive, secondly, they have an enormous specific surface area in relation to their physical size, and finally, they may exhibit what is termed quantum effects. It is the combination of these properties that provides exciting opportunities for nano-based technologies to provide additional functionality and improve efficiency, sustainability, and speed to already existing manufacturing and industrial processes. This has led to their use in sunscreen products, as additives in composites, as vehicles for tissue-specific drug delivery, and their use by the clothing industry to provide properties to fabrics such as microbe-killing silver, where odour from a variety of sources is reduced or prevented. Materials can also be made waterproof or stain-resistant, or used as anti-static agents. Recently, graphene nanoplates as an additive in rubber, cement or concrete have been explored. It is also these properties that have led to the widely accepted view that there is a crucial need for further information and knowledge concerning the implications of exposure to manufactured nanomaterials on both human health and their effect on the global environment as a whole. Risk assessment requires a detailed examination of the properties of the nano-objects or particles that are being used and may include some or all of the following:

- chemical composition
- particle size
- surface area
- stability
- surface properties
- solubility
- chemical reactivity

2 Some, or perhaps all, of these properties may not be known. However, comparisons with well-known existing hazards may help inform the risk assessment. Existing hazards used in this way could include those from airborne fine particles and also fibres.

3 There is a growing concern that the use of nanomaterials in products may increase the risk of environmental exposure [2, 3]. Environmental exposure to nanomaterials could be unintended due to an accident (e.g., due to an incident at a production or manufacturing site), through the use of products containing a nanomaterial (for instance, after the weathering of a nano-enabled coating), at the point of disposal (e.g., landfilling or incineration) or at recycling sites. To this end, there has been a growing number of studies examining the behaviour of nanomaterials in different environmental compartments, including air, water, and soil, as well as their uptake by organisms, including plants, fish, and higher animals [4-7]. There have been large-scale projects studying the potential impact that nanomaterials may have on the environment, which have introduced frameworks to allow stakeholders from

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research, industry and regulatory communities to better manage the risks of environmental exposure (e.g., NanoFASE and PATROLS).

4 Over the last 25 years, there has been a growing number of studies examining the potential environmental risk posed by nanomaterials [5]. Despite all of the recent work in this area, there remain some knowledge gaps about how specific nanomaterials may behave in different environmental compartments. Some nanomaterials may concentrate in particular "hot spots", either by agglomerating with minerals or by interacting with organic matter. They may move from the environment into organisms through the food chain or remain in the environment, where they may be a hazard due to long-term, low-level exposure. Some nanomaterials interacting with the environment may have decreased reactivity, bioavailability or toxicity and thus present a reduced risk to the environment [4].

5 There are concerns regarding potential risks to the environment, manipulation, use and disposal of these materials. The increasing volumes of nanomaterials that are being produced and introduced into commerce have resulted in a need to address exposure and risk assessment data gaps.

6 This document has been developed in collaboration between the UK NanoSafety Group and the Health and Safety Executive (HSE). It is recognised that the field of nanotechnology is rapidly expanding and transcends the traditional academic discipline boundaries, and incorporates a wide range of products, production processes, and uses. The document is primarily concerned with the use, storage and disposal of manufactured nanomaterials. It does not deal with natural or anthropogenic release of ultrafine particles such as those from diesel exhaust and welding fumes.

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2. LEGAL DUTY

2.1. CONTROL OF SUBSTANCES HAZARDOUS TO HEALTH (COSHH)

7 The synthesis/manufacture and use of nanomaterials is regulated under the Control of Substances Hazardous to Health (COSHH) Regulations 2002 (as amended) [8].

8 COSHH places a duty on employers to carry out a risk assessment for work which is liable to expose employees to hazardous substances. Embodying the principles of proportionality and risk assessment, COSHH enables employers to make a valid decision about the measures necessary to prevent or adequately control the exposure of their employees. Employers must understand the risks and make sure they are kept as low as is reasonably practicable.

2.2. DANGEROUS SUBSTANCES AND EXPLOSIVE ATMOSPHERES REGULATIONS (DSEAR)

9 The chemical and physical properties of some nano-objects mean that powders can give rise to a risk of fire and explosion, depending on how they are handled or used. If this is the case, the principal legislation applying to their control in the workplace is the Dangerous Substances and Explosive Atmospheres Regulations 2002 (DSEAR) [9].

10 DSEAR requires that the risks from dangerous substances are assessed and eliminated, or reduced so far as is reasonably practicable. The principle of risk assessment applies under these regulations.

2.3. REGISTRATION, EVALUATION, AUTHORISATION AND RESTRICTION OF CHEMICALS (REACH)

11 UK REACH is concerned with the Registration, Evaluation, Authorisation and Restriction of Chemicals. UK REACH operates alongside COSHH and aims to provide a high level of protection of human health and the environment from the use of chemicals, and makes those who place chemicals on the market (manufacturers and importers), responsible for understanding and managing the risks associated with their use.

12 The UK REACH and the EU REACH regulations operate independently from each other. Manufacturers and importers must ensure that they comply with both regulations, where necessary.

13 The Classification, Labelling and Packaging of Substances and Mixtures – the CLP Regulations, i.e. in both EU and GB, do not apply to substances and mixtures used

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for scientific research and development (provided that they are not placed on the market), and as long as they are used under controlled conditions in accordance with workplace and environmental legislation. Under CLP there is no legal duty on employers, managers, health and safety advisers, and users of nanomaterials in research and development. Although under certain circumstances, mixtures not intended for the general public may need to be labelled with EUH210 – 'Safety data sheet available on request'.

14 Further information about UK REACH and GB CLP can be found on the HSE website [10, 11]. Information about EU REACH and CLP can be found on the European Chemicals Agency website [12].

3. EXPOSURE RISK AND HAZARDOUS PROPERTIES OF NANOMATERIALS

15 Exposure to some nano-objects may occur by inhalation, ingestion, and/or skin penetration, with any resultant adverse effects depending upon the size, dose and reactivity of the particles. The exposure potential can be expected to be related to the structure and physical form of the nanomaterial; particles encapsulated in a matrix or strongly adhered to a substrate will have a lower exposure potential than that from 'free' aerosolised nano-objects, or those powders exhibiting high dustiness.

16 Some nano-objects may have inherent hazardous properties and may be classified as carcinogens, mutagens or asthmagens. Under COSHH, exposure to hazardous substances defined as carcinogens, mutagens or asthmagens must be kept as low as is reasonably practicable (ALARP). Some nano-objects may also have other hazardous properties as classified in the Classification, Labelling and Packaging of Substances and Mixtures – the CLP Regulations. It is generally agreed that the current knowledge regarding the toxicity of nano-objects is incomplete, and current safety data sheets may not adequately contain all the required safety information. Hence, at present, it is essential that a precautionary approach be used when uncertainties are encountered during exposure risk assessment.

17 Fire and explosions from dust clouds of organic, inorganic and metallic substances are well known. The potentially higher surface area and reactivity of nano-objects in powders mean that these safety hazards should be seriously considered and addressed in risk assessments. However, it should be noted that this guidance does not specifically address the potential risks associated with these safety hazards.

3.1. RISK MANAGEMENT PRINCIPLES

18 It is important to emphasise that existing legislation, such as the COSHH regulations applicable in the UK or their equivalent elsewhere, will always apply to workplace activities involving nanomaterials. The guidance and recommendations in this document closely mirror the eight generic principles set out in Schedule 2A: Regulation 7(7) Principles of good practice for the control of exposure to substances hazardous to health [8].

19 Nanomaterials are not necessarily intrinsically hazardous *per se,* but there is a need to take specific considerations into account during their risk assessment. Therefore, one purpose of the definitions provided in Appendix 1 is to provide clear and unambiguous criteria to identify materials for which any nanomaterial-specific considerations should apply. The process of risk assessment is the most suitable and systematic means to determine which hazard and exposure controls (i.e., risk management measures) are required.

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20 In general, the potential risks to health from nano-objects can be reduced by safe handling and control of exposure. Whilst no single piece of guidance can provide a definitive, step-by-step approach to safe handling of all nanomaterials in all circumstances, there are a number of general and specific good practice guidelines that can be used in most applications.

21 The general approach for safe handling of nanomaterials and control of nano-objects is similar to that for other types of chemical substances and seeks to:

- Identify the hazards and assess the risks;
- Identify who or what would be affected;
- Decide what precautions are needed;
- Prevent or adequately control exposure;
- Ensure that control measures are used and maintained;
- Monitor the exposure;
- Carry out appropriate health surveillance;
- Prepare plans and procedures to deal with accidents, incidents and emergencies;
- Ensure workers are properly informed, trained and supervised.

4. NANOMATERIALS' CHARACTERISATION

4.1. BACKGROUND AND CHALLENGES

22 Characterisation of nano-objects plays an essential role in a variety of overlapping contexts ranging from fundamental and applied research, through process and product quality control and commercialisation, to health and environmental protection. Fibre-like particles and platelets present distinct challenges for characterisation using many of today's routine measurement techniques, which are often based on principles suited to idealised spherical particles. However, high-resolution microscopy, such as scanning or transmission electron microscopy, permits the imaging and sizing of nanotubes or graphene platelets. Although time-consuming, these methods are still considered the gold standard for particle (including spherical particles) sizing, partially because they allow assessment of primary particle dimensions but also because they provide the regulatory-preferred metric of number-weighted analysis. The development of advanced multicomponent nanomaterials (MCNMs) adds increased complexity to characterisation, as composite chemical formulations and structural arrangements will also need to be defined. Moreover, not all particles with the same 'apparent' composition have the same potential to cause harm. As with other chemical substances, an understanding of the relationship between the wide range of physicochemical characteristics of nano-objects is crucial in comprehending their toxicology. Moreover, this understanding will enable a more pragmatic approach to assigning or predicting hazards, as discussed in Grouping and Read-across, Section 6.2. The implementation of reliable findings from experimental studies into regulatory frameworks with the objective of protecting human and environmental health is also subject to the limitations of inadequately characterised materials and the complexity of mixtures of particles in 'real world' exposures.

23 Nano-objects may exhibit properties and behaviours that are very different from the analogous non-nanomaterials of the same chemical identity. Knowledge of their size, shape and surface-related properties can be used to account for many of the observed differences. It is widely acknowledged that adequate characterisation of a nanomaterial is therefore necessary to interpret any toxicity study, particularly in cases where nano-objects (e.g., carbon nanotubes) can be produced by different processes yielding notionally the same material, but which exhibit quite different morphology and chemical properties (for instance, their surface properties, or their potential for dissolution).

24 It is important to recognise that no individual technique can provide an entirely holistic and meaningful characterisation of the sample. Multiple techniques are required to allow as complete an understanding of the nanomaterial's properties as necessary. Different techniques suit different sample forms (e.g., aerosol, suspension), and the optimal set of techniques should be selected based on the specific nanomaterial type, the form under investigation, and the purposes of the study.

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25 A further important challenge is how representative the sample is of the material, which may be influenced by the surrounding environment and may change or age as a function of time.

4.2. SELECTION OF PROPERTIES AND TECHNIQUES FOR CHARACTERISATION

26 It is important to recognise that complete characterisation of test materials is time-consuming, expensive, complex, and may never be fully achievable. The degree of characterisation required depends on the needs or objectives of the study, which can include informing a hazard exposure assessment and the overall risk posed by a material. Characterisation information required to comply with applicable regulatory or notification requirements must be identified and gathered. Recommended characterisation information is also evident in guidance on the preparation of safety datasheets. Beyond this, researchers in the field of nano-safety generally agree that information on a number of fundamental properties needs to be gathered, including but not necessarily limited to composition, size and shape, state of dispersion, surface area, surface chemistry and solubility.

27 A range of techniques have been adapted or developed for the characterisation of nano-objects, including microscopic, spectroscopic, spectrometric, and chromatographic methods. Whilst it is beyond the scope of this document to provide guidance on all properties and techniques, several reviews, publications, and standards are available that can provide appropriate details. Of note is that the NanoDefine project produced a manual for nanomaterial characterisation after a comprehensive evaluation of the available methods, which can guide a user in applying the most suitable approaches for their material of interest [13-15]. The selection of an appropriate technique depends on the type of material, the required characterisation and the resolution/quality of the data needed.

28 Taking the example of hazard assessment, there is consensus that thorough and accurate particle characterisation is an essential part of assessing the potential toxicity of nano-objects in biological systems. Using current hazard strategies such as grouping and read-across or Quantitative Structure Activity Relationship (QSAR) modelling, etc., attaining robust characterisation data can help in predicting hazard while keeping other testing to a minimum. Information is required on the response to the material against a range of potentially relevant dose metrics, including mass, surface area, and number concentration. Appropriate characterisation of test materials is important to ensure that the results are reproducible (within and between laboratories), and also to provide the basis for understanding the properties of nano-objects that determine their biological effects. Some of the key parameters influencing the biological activity of nano-objects remain to be fully understood at this point in time. Any study however conducted with material that has not been characterised with respect to a property later found to be critical for toxicity will ultimately be of little value. Evidence to support identification of a structure activity

relationship which links a physicochemical characteristic with a toxic response must include characterisation of the exposure-relevant form of the nanomaterial. This is required to take into account system-dependent changes such as agglomeration in an aerosol or dissolution in biological media.

29 A rationale and dataset should be developed and documented to meet the characterisation requirements. It is recommended that good practices advocated in published standards and guidance for nanomaterial characterisation should be adopted.

5. TOXICOLOGY

30 As a crucial and integral part of the risk assessment framework, an understanding of the hazard potential of a substance is important, and this is established on the basis of a toxicological assessment. The role of toxicology in chemical risk assessment is multi-factorial, but fundamentally, is there to provide information on the impact a substance may have on the body, and how, or if this may manifest with differing exposures. This assessment of impact can provide information on:

- The specific target organs, such as the lungs and likely health effects, for example, dyspnoea due to respiratory inflammation;
- Potency, for example, are profound effects associated with low exposures, or are relatively high exposures required to cause adverse health effects?
- The evidence base (preferably in conjunction with epidemiology data) for a robust health-based exposure limit, or in the absence of this, more prescriptive, process-based limits such as DNELs (Derived No Effect Levels) under REACH in the EU, or qualitative assessments such as hazard banding.

31 The quantity and quality of toxicological data available dictates the robustness and how informed a hazard assessment can be, and this can vary markedly from well-established substances for which a great deal of information exists (e.g., NaCl), to substances that are early in development, and for which there are little data.

32 The level of information available influences the type of assessment that can be performed, such as the development and adoption of a Workplace Exposure Limit (WEL), or the classification of a substance as carcinogenic, or not, by the International Agency for Research on Cancer (IARC). An IARC classification refers only to the potential hazard posed by a substance and does not take into account the extent of exposure required to result in carcinogenicity. However, a significant weight of evidence from human epidemiology or multiple long-term animal studies is required before a judgment on potential carcinogenicity classification can be made. An example of this is the outcome of the October 2014 IARC meeting to discuss carbon nanotubes (CNTs) as well as other fibrous materials (Monograph Volume 111) [16]. It is reported that the Working Group concluded that there was sufficient evidence for carcinogenicity in experimental animals with the multi-walled carbon nanotube 'MWCNT-7', considered to be one of the better studied; yet only *limited* evidence for other multi-walled carbon nanotube samples with dimensions similar to MWCNT-7, and *inadequate* evidence for single-walled carbon nanotubes (SWCNTs) [17]. This level of evidence was reflected in the Working Group's classification, and MWCNT-7 specifically was classified as possibly carcinogenic to humans (Group 2B), whilst other forms of MWCNTs (excluding MWCNT-7), and SWCNTs were determined not classifiable as to their carcinogenicity to humans (Group 3). This category of Group 3 is used for agents for which the evidence of carcinogenicity is inadequate in humans and inadequate or limited in experimental animals. Although, it should be noted that a

classification of Group 3 is not a determination of non-carcinogenicity or overall safety, rather that further research is needed [18]. Since the IARC classification, there has been evidence of other long MWCNTs as well as short SWCNTs inducing pulmonary malignancies in animal models [19]; however, although a considerable body of experimental data on CNTs and carbon nanofibres (CNFs) exists, significant data gaps remain. This precludes the adoption of a single classification across all forms of CNTs [20]. Evaluation of the factors that contribute to the differences in pulmonary responses to various types of CNTs and CNFs, including the role of dose and duration, physical-chemical properties, species/strain/gender, and other experimental factors in carcinogenic outcomes, has been highlighted as a critical research need. A view recently upheld [21], emphasising again the difficulties of demonstrating the causal relationship between this heterogeneous group of nanomaterials and deleterious effects upon the pulmonary system, with a similar call to not consider CNTs and CNFs under one unified approach to risk- and hazard-based decision making.

33 A similar high degree of evidence is needed for the derivation and adoption of a Workplace Exposure Limit (WEL) or recommended exposure limit (REL) (e.g., well-designed *in vivo* inhalation studies of a sufficient exposure period performed to internationally recognised guidelines, such as Organisation for Economic Co-operation and Development (OECD) Test Guidelines), which from a human safety point of view is the most robust form of exposure limit. Extrapolation from animal data can also lead to estimates of observed adverse effect levels (OAEL) to help establish safe exposure levels [21]. However, in many studies, e.g., in the assessment of CNTs, the assessment is of early-stage lung pathology and has not considered carcinogenic and cardiovascular effects [21]. The development of exposure limits is therefore currently based on lower-level toxicological assessments, which may be related to a high level of uncertainty and margin for error, dependent on the available data.

34 When considering the hazard potential of nano-objects, it is important to understand that the word "nano-objects" embraces an enormous variety of different particles in different compositions, shapes and sizes (with one or more aspects in the nanometre range). There is, therefore, no single measure of toxic potency that can be attributed to *all* nano-objects since there can be considerable variability in toxicity based upon physicochemical characteristics; specifically, not all nano-objects are toxic nor equally hazardous. Furthermore, it is important to note that the definition of the size cut-off for nano-objects has no basis in toxicology, meaning that there is no step-change in toxicity when a nano-object falls below 100 nm in any dimension. Mechanisms of toxicity by which nano-objects have been shown to operate largely reflect the driving factors of larger pathogenic particles [22, 23]. However, the differences in size and structure compared to larger particles may lead to divergent fate and toxicokinetics after exposure, resulting in toxic responses in unexpected tissues. Decreased size may also impact on the relative potency of the nanomaterial compared to analogous non-nanomaterials.

35 When searching for hazard information, it is necessary to define the nano-objects that are under consideration in as much detail as possible (see Nanomaterials'

Characterisation, Section 4). For example, "zinc oxide nanoparticles" or "carbon nanotubes" are very broad descriptions, and it would be better to give details such as "20 nm uncoated ZnO nanoparticles" or "multi-walled carbon nanotubes, in fibre form, with length range 620 nm – 52 µm, and 12% iron", in recognition of the impact a range of physicochemical characteristics beyond chemical composition have on the toxicology of a nano-object. The desire for optimum use of data related to nano-safety has resulted in a considered effort to ensure FAIR (findable, accessible, interoperable and reusable) data principles are used across the sector [24] and that data should be made available within easily shareable databases, such as eNanoMapper [25].

5.1. HAZARD INFORMATION

36 There is now an evidence base of toxicology showing considerable differences in hazard between different nano-objects. However, the literature is dominated by studies that employ non-validated *in vitro* tests, which form an unsuitable basis for risk assessment in part because the relationship between *in vitro* toxicological data and *in vivo* effects is unclear. In recent years, significant efforts have focused on the development of better *in vitro* models, so-called new approach methods (NAMs) [26], which are more physiologically relevant and predictive of *in vivo* outcomes. The wider testing and application of such models will support *in silico* hazard modelling and improved *in vitro-in vivo* extrapolation of nanomaterial hazard, of which there have been recent advances [27-31]. Efforts to accelerate the validation of NAMs are essential to mitigate the reluctance of regulators to accept non-animal evidence of hazard status instead of excessive *in vivo* testing.

37 For the majority of nano-objects in-depth quantitative toxicological data required for the determination of a WEL is unlikely to be available. Therefore, when such a limit is presented within a Safety Data Sheet, one should question if it is specifically for the nano-objects in question or if it relates to the analogous non-nanomaterial.

38 When looking rather generally at the current large toxicological evidence base across a wide breadth of nano-objects, it seems that:

- Many nano-objects are likely to pose a low acute hazard at plausible exposures to the lungs; however, the potential for the build-up and retention of biopersistent nano-objects in the lung tissue upon repeated or continuous exposure and translocation to the vascular system and other organs remains a cause for concern.
- Most nano-objects will pose little direct hazard to the skin as irritants or sensitisers, or cross into the human body through the skin barrier to any significant extent. For example, the European Commission's Scientific Committee on Consumer Safety (SCCS) has concluded that the use of zinc

oxide and titanium dioxide nanoparticles (at a concentration up to 25% as a UV-filter in sunscreens), can be considered not to pose any risk of adverse effects in humans after dermal application [32, 33]. It is important to note that the number of studies specifically examining the dermal route of exposure is limited, with the current evidence used to define dermal penetration by nano-objects reviewed by Gimeno-Benito *et al.* [34]. Hence, more work needs to be done to fully assess both the dermal toxicity of a broad panel of nano-objects and also the contribution of dermal exposure to systemic bioavailability, which may lead to toxic responses in secondary tissues.

39 It is important to remember that some nanomaterials may pose a hazard to human health due to their specific properties that may differ from, or potentiate the hazard posed by an analogous non-nanomaterial. Such hazards may not be readily predictable from knowledge of the chemical composition alone, thereby, highlighting the importance of robust, and comprehensive nanomaterial characterisation to fully understand this potential.

40 Below are listed several attributes in the form of questions that may indicate toxicity to nanomaterials, and as such, the presence of one or more of these physicochemical characteristics may suggest increased hazard potential. (Inclusion here is based upon generalisations and intended to help inform as to the potential risks, and hence, should not be seen as a replacement for robustly derived WELs, if available.)

- Is the particulate classified as a CMTR (carcinogen, mutagen, teratogen and reproductive toxicant), or a sensitiser?

  If a material is already classified as a CMTR or skin/respiratory sensitiser, there is a high likelihood that its nano-sized form will also demonstrate this toxic potential. Indeed, due to their characteristically large surface area, the nano-sized form may exhibit comparatively greater activity than that of the analogous non-nanomaterial and should therefore be considered as potentially hazardous.

- Is the nanomaterial composed of reactive metal(s)? Is the nanomaterial photoreactive? Does the nanomaterial have a highly charged surface?

  The presence of reactive metals is known to increase the toxicity of various complex particulate mixtures, such as welding fumes [35]. Therefore, a nanomaterial possessing a significant proportion of such metals (e.g., large amounts of catalyst remaining within unrefined carbon nanotubes) could be regarded as having a potentially hazardous component.

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When exposed to light, photocatalytic nanomaterials (e.g., certain forms of titanium dioxide) have been shown to release free radicals [36], which may generate toxicity by causing inflammation, oxidative damage, and genetic damage in experimental studies [37, 38]. However, the implications for human health remain inconclusive [32].

The surface properties of a nano-object will impact the interactions at the nano-bio interface, e.g., the charge of a nano-object is known to influence its propensity to agglomerate/aggregate, and can also play a prominent role during cellular uptake, or interactions with charged molecules such as proteins. The occurrence of reactive sites such as nearly-free silanol groups drives the toxicity of crystalline silica [39]. Modulation of surface chemistry through the addition of functional groups has also been demonstrated to impact the toxicity of a nano-object. Therefore, characterisation of a nanomaterial should also include information on the surface properties of the specific nanomaterial under investigation.

These attributes, singly or collectively, can contribute to the surface activity of a nano-object and are potential drivers of toxicity. The combination of high surface area and high reactivity may lead to the formation of a "double hazard" [40, 41].

- Is the (nano)material soluble?

The solubility of a (nano)object can have a positive, and/or negative influence on its propensity to cause harm. Specifically, if a particle is soluble in an aqueous environment but *does not* release toxic components, a progressive reduction/removal of dose will occur as the material dissolves. However, if the material releases reactive or cytotoxic components, such as toxic ions, as it dissolves, its toxicity could increase.

An attribute of nanoscale materials is the potential for changes in physicochemical characteristics, including solubility, compared to the analogous non-nanomaterial; for example, silver is insoluble in water, but nano-silver releases free silver ions in aqueous solutions by oxidative dissolution. Therefore, the contention that since the analogous non-nanomaterial is insoluble, the nanomaterial is also insoluble is not necessarily correct. The different media nanomaterials to which organisms may be exposed in different biological compartments should also be considered when assessing solubility. A material may be durable in the neutral pH of the lung lining fluid, but rapidly dissolve in the low pH of the phagolysosomal fluid when taken up by cells. The intracellular release of toxic ions may lead to cell death, propagation of an inflammatory response and oxidative stress *in vitro* and *in vivo*, via the so-called 'Trojan horse' mechanism [42, 43]. On the other hand, a poorly soluble

nano-object may bioaccumulate in tissues, causing harm if no clearance mechanism can operate, as aligned with poorly soluble low toxicity particle hazards in general [44]. As such, when considering the hazardous nature of a material, it is pertinent to consider both the insoluble (particle) and soluble components in the hazard assessment, as well as the potential location and biological environment where dissolution may occur.

- Is the nanomaterial fibrous?

  There is concern that fibrous nano-objects such as carbon nanotubes or nanowires may represent a similar danger to health as hazardous fibres such as asbestos, refractory ceramic fibres, or certain man-made vitreous fibres (MMVFs). The basis for this is the morphological similarity between these fibres and high aspect ratio nano-objects (HARN). However, if the fibre hazard paradigm is to be enacted, certainty is needed that it is a fibrous sample that is being dealt with, i.e. it should meet the criteria for the definition of a fibre, such as that of the World Health Organisation (WHO).

  The WHO defines a respirable fibre as an object with a length greater than 5 µm, a width less than 3 µm and a length-to-width ratio (aspect ratio) greater than 3:1 [45]. Those particles which do not meet these base criteria would not be considered as fibres, and are unlikely to represent a fibre-type hazard (although they may still represent a particulate-type hazard). Within fibre toxicology, a fibre presents difficulties to the normal clearance mechanisms in the lung when its length prevents its full enclosure by those cells tasked with clearing such particles (e.g., alveolar macrophages). This is considered to be between 10–15 µm in length [46]. A nano-object longer than 15 µm would therefore, potentially frustrate clearance mechanisms if deposited in the distal lung and lead to hazardous effects similar to those associated with other harmful fibres. Due to the uncertainty around the identification of a lower cut-off length for pleural inflammation [47], rather than for the lungs, the WHO length criteria of 5 µm could be seen as presenting a suitably conservative approach.

  Generalisations should not be based purely on the substance type when considering the potential hazard of a particle; not all HARNs will necessarily represent a fibre hazard as outlined above, and not all nanomaterials typically thought of as particulate always exist in particulate form. For example, not all carbon nanotubes are true fibres, as many form highly curled, dense bundles and, in such form, are better described as particulate in nature. Conversely, not all TiO_2 nanoparticles are particulates, since, like many materials, they can be formed into wires [48], which could represent a fibre hazard.

- Does the nanomaterial possess a low aerodynamic diameter yet one or more high aspects?

  The basis for respiratory toxicity arising from fibres requires a low aerodynamic diameter for penetration into the distal airways, yet a large physical aspect (e.g., fibre length, or particle diameter) causes frustration of normal cell-mediated clearance mechanisms. Therefore, it is worth bearing in mind that other shapes, not just fibres, can possess these properties. Plate-like structures such as graphene/graphite platelets can have a very large (>15 µm) diameter, yet be very thin (<100 nm), and as such possess a low aerodynamic diameter [49], allowing them to be respirable. In addition, low-density 'fluffy' bundles of fibres, often seen with carbon nanotubes, may also, due to their very low density, possess the potentially hazardous mix of low aerodynamic diameter with one or more high aspect ratios, making clearance from the distal lung difficult. However, much more research is needed into these particle types to understand if they are likely to represent a true hazard to humans.

41 Using hazard data or physicochemical properties, as per those listed above, it is possible to predict hazards or intervene during product development and/or innovation to ensure safe development of nanotechnology using approaches such as Safe by Design [50, 51], or by performing grouping or read-across [52], and can be assisted by development of Integrated Approach to Testing and Assessment (IATA); these concepts are discussed in the following section 'Alternative Approaches to Enable Risk Mitigation'.

Concluding from the above, it is imperative that the true physicochemical characteristics of the sample under consideration (and not just of the class of material), be established when considering the basis for hazard.

6. ALTERNATIVE APPROACHES TO ENABLE RISK MITIGATION

42 As discussed above, the currently available toxicology data for most nanomaterials would be considered to be minimal or suggestive, and this is incompatible with the rigorous data demands needed for the development of a WEL. Furthermore, the ever-increasing demand for hazard information for rapidly developing industries and the construction of advanced materials has resulted in new approaches being required to better inform and mitigate risk. A number of practical solutions to aid in the risk assessment of such materials are available, including hazard and control banding, grouping and read-across approaches, and safe-by-design strategies.

6.1. CONTROL BANDING AND RISK SCREENING TOOLS

43 Control banding as an approach has been adopted for occupational safety, health and hygiene assessment for several decades. Although originating within the pharmaceutical industry, it is applicable to most occupational settings, including within nanotechnology industries, where a release of process-related substances may pose a risk of serious health implications [53-55]. Developed as a means to deal with the problem that rapidly developed new compounds/substances often lack adequate toxicological data, and/or knowledge concerning the mechanisms by which they elicit their effects, control banding tools provide a practical approach to help mitigate the risks. Unknown compounds could be classed based on limited toxicological data into bands, which inform as to the relative hazard and maximum exposure levels, and are aligned with control schemes. This would mean in practice that a nanomaterial classed as "highly hazardous" could only be handled within full containment, with an associated low airborne mass concentration exposure limit. Whilst those classified as "low hazard" could be handled with good ventilation and use of appropriate Personal Protective Equipment (PPE).

44 Equally relevant to nanomaterials as to chemicals and pharmaceuticals is the problem of what to do with materials for which little information exists. An approach may be to use "physicochemical or structural alerts", such as size, coatings, dimensions/aspect ratio, solubility, and, where possible, toxicological endpoints such as genotoxicity or reactivity. Subject to these properties, control banding and risk screening tools may suggest a basis for hazard and promote a nano-object up the category scheme, necessitating tighter controls and exposure measures. Another approach is to adopt a default *preliminary* category associated with sufficient exposure control measures that would protect workers should a compound later be shown to be toxic. Movement out of such a category would be based upon toxicological evidence to allow its transfer to a lower or higher hazard category as appropriate. The latter approach is precautionary, whilst the former allows a case-by-case basis that reduces the number of non-toxic nano-objects being encumbered

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by what may subsequently be shown to be excessive control methods. Tools are available which can provide qualitative, semi-quantitative or quantitative results.

45 Control banding tools estimate the potential for hazard and exposure in a workplace setting and provide the level of precaution needed and the measures that should be applied to mitigate risk [56]. Risk screening tools are similar to control banding tools in that they are also simple to use, with low input requirements. However, risk screening tools can also be applied to consumer and environmental risk assessment, as their functionality is not limited to occupational settings, but also addresses further lifecycle stages. In 2021, the OECD published a report presenting the performance testing results of 15 control banding or assessment tools, consisting of ten nano-specific tools and five conventional chemical tools recommended by the European Chemicals Agency (ECHA), for use in occupational settings [56].

46 Quantitative tools such as SUNDS (The SUN Decision Support System) will require more input parameters and a greater level of expertise to operate and to predict hazard point-of-departure data [57]. An actual Derived No-Effect Level (DNEL) is required; the advantage, however, is that a full risk characterisation ratio is provided.

6.2. GROUPING AND READ-ACROSS

47 Grouping and read-across have long been applied in chemical safety and used to minimise testing of chemicals [58]. For nanomaterials, these approaches have largely been based on associating physicochemical properties with hazards, and more recently, by also making associations between life-cycle transformations and how these may influence hazards. In nanotechnology sectors, grouping enables the read-across between nanomaterials and non-nanomaterials, or between nanoforms, in accordance with shared physicochemical properties. A substance may have one or more different nanoforms, based on differences in, e.g., size distribution, shape and other morphological characterisation, surface treatment, functionalisation and specific surface area of the particles. Grouping is enabled by using information pertaining to data-rich substances to predict the hazard of a nanomaterial with less data available. Grouping can be made by the acceptance of a scientifically justified hypothesis describing a material's behaviour as based on its properties. These approaches can be utilised under a regulatory framework as a strategy for risk management, or in material innovation, with frameworks being developed recently under EU funding [52]. Justification of assigned groups can be done through the modelling of similarity.

48 An Integrated Approach to Testing and Assessment (IATA) is a tool used for the structured gathering of relevant information from existing sources or de novo experimentation to support efficient hazard assessment [59]. IATAs have been employed to provide insights into how data gaps can be filled to support grouping,

and aid in decision-making in the acceptance or rejection of grouping hypotheses [60-62].

6.3. SAFE BY DESIGN

49 Safe-by-design (SbD) is the process of balancing safety with product functionality, and economic and environmental impacts. It is a principle that has already been adopted by the EU in their Chemical Strategy for Sustainability as a strategy to meet EU Green Deal ambitions, and the OECD in their 'safe innovation approach' [63]. It is a further method to proactively address the uncertainties surrounding nanomaterial safety. Although useful at any stage of innovation, its use at an early stage is particularly beneficial in the context of this guidance. In principle, SbD asks the user to consider if human risks, functionality of the nanomaterial, or nano-enabled product, and costs associated with their use can be balanced during these early stages of innovation. Based on the outcome of this, a decision can be made as to the feasibility of the continued use of a nanomaterial, or whether to replace it, or redesign a process for better protection.

50 Structured around three pillars: to generate safer materials/products, use safer production techniques, or promote safer use of the product, SbD can be implemented via two stages. Firstly, to identify any hazards associated with a nanomaterial or nano-enabled product, and secondly, to address any concerns by using a system of interventions designed to circumvent any identified risks. Guidance is already available on how to implement SbD approaches when using nanomaterials [64], and EU-funded projects will provide e-infrastructure or computational infrastructure to make SbD more accessible and user-friendly (projects include SAbyNA [65], ASINA [66], SABYDOMA, SbD4Nano).

7. EXPOSURE CONTROL

51 UK and European law require workplace exposure to substances hazardous to health to be controlled adequately. This applies to nanomaterials, particularly where there is uncertainty about the risk. An employer's overriding duty and first priority is to consider how to prevent employees from being exposed to substances hazardous to health (including nanomaterials) by all routes. Employers who do not do this are failing to comply with a fundamental requirement of COSHH.

52 Achieving adequate control involves applying "good control practice", which is a consensus view of hardware, systems of work, and other measures that need to be put in place to control the risk.

53 The principles of the hierarchy of controls must be applied in order of priority. These are based upon inherent reliability and likely effectiveness. The duty to prevent exposure should be achieved by a combination of control methods other than just the use of personal protective equipment, which should be the last line of defence.

7.1. RISK ASSESSMENT

54 A risk assessment must be carried out (as set out under COSHH Regulation 6: The Control of Substances Hazardous to Health Regulations 2002 [67]) before an employee is allowed to work with nanomaterials. This risk assessment must be a suitable and sufficient assessment of the risk to health caused by the work. The HSE publication, "A step by step guide to COSHH assessment", describes in general terms the procedures to be followed in making an assessment [68]. The COSHH general Approved Code of Practice (ACOP), also provides guidance [1].

55 Assessment of the risk should include identifying all potential sources of exposure. Even if the exposure can be prevented, there remains a need to assess any potential for exposure. An action plan/check list for assessment would involve addressing the questions:

- What are the tasks or processes which could lead to the release of nanomaterials into the air or onto a surface?
- Is exposure likely?
- Who is likely to be exposed?
- Why can the exposure not be prevented?

56 Work activities involving nanomaterials which require special attention when assessing exposure include:

- Handling of powder containing nano-objects;

- Manufacturing of nano-objects (especially production of nano-objects in a gas phase), and the associated maintenance of equipment;
- Machining of materials containing nano-objects (e.g., sawing, polishing, grinding);
- Spraying of liquids containing nano-objects;
- Processing nano-objects in a liquid where a high energy output is involved;
- Recycling and waste disposal of nanomaterials;
- Cleaning and maintenance of equipment used in the manufacture/application of nanomaterials.

57 When making the assessment, careful attention should be paid to whether there is a possibility of inhalation of the nano-objects.

58 In all cases, the assessment should be written down and reviewed if circumstances change, new information becomes available on the hazard of the nanomaterials being used, or the composition of the nanomaterial is changed.

7.2. PREVENTION AND CONTROL OF EXPOSURE

59 Having made an assessment of the risk from exposure to nanomaterials, employers must ensure that such exposure is either prevented, or if that is not reasonably practicable, adequately controlled.

60 Employers need to consider the following precautionary measures in their prevention and control procedures, and adapt them to suit their circumstances. Employers should arrange to regularly review the adequacy of the precautions taken, particularly if the circumstances of use change, or in light of new technical developments, or information on the nanomaterials.

7.3. PREVENTION OF EXPOSURE: SUBSTITUTION

61 As with all substances potentially hazardous to health, the employer must give first priority to preventing workers from being exposed to nanomaterials. This can be achieved in a number of ways, for example by using a nanoform of lower hazard potential (see Section 6.3: 'Safe by Design' for more details on how this is achieved), or by changing the method of work. When considering substitution, it is important to take account of any hazards of the substitute materials or process and balance the risks these might present against the benefits.

7.4. WORKPLACE EXPOSURE LIMITS

62 At the time of publication, there are no UK legal Workplace Exposure Limits (WELs) specific for any nanomaterials. Therefore, in compliance with COSHH, the

principles of good occupational hygiene practice should be applied. This includes reducing exposure proportionate to the health risk until the cost becomes disproportionate, which is a very similar requirement to ALARP.

63 There have been many references made in the literature to proposed limits. A review published in 2017 by Mihalache *et al.* [69], identified 20 studies that proposed in total 56 Occupational Exposure Limit (OEL) values. Of these, two proposed a generic level for all manufactured nanomaterials , 14 proposed a generic OEL for a category of manufactured nanomaterials, and 40 proposed an OEL for a specific nanomaterial.

64 None of these limits are based on health effects; some ascertain they are achievable with good control practices; others are based on extrapolation from toxicological studies. In the United States, the National Institute for Occupational Safety and Health (NIOSH) has issued a recommended occupational exposure limit (REL) for silver nanoparticles [70], CNTs [71] and TiO_2 [72] nanoparticles, but currently there is no legal basis to use these limits in the UK. Hence, they should be used with extreme caution. Also, it should be noted that measuring nanomaterials in the workplace is a challenge, and there is considerable debate about which metric to measure. Notwithstanding this, in the UK under COSHH, the requirement remains to control exposure to ALARP.

65 It should be noted that the UK WEL for airborne 'Carbon Black' of 3.5 mg/m^3 (3500 $\mu g/m^3$) is not considered appropriate for carbon nanotubes. For example, NIOSH has established a recommended exposure limit (REL) of 1 $\mu g/m^3$ based on elemental carbon analysis [71]. This limit aims to reduce the risk for pulmonary inflammation and fibrosis. However, due to some residual risk at the REL and uncertainty regarding long-term health effects, exposures should be reduced as much as possible. It should be noted that proposed exposure limits for particulates should not be used for respirable fibres. For example, nanowires made of substances such as TiO_2, Al_3O_4, Ni, etc. should be considered as distinctly separate from the particulate form.

66 Measurement of airborne nano-objects is not a simple, quick or straightforward task. Therefore, the preferred/practical option in most research environments is to prevent potential exposure with rigorous containment via engineering controls within the context of reducing exposure proportionate to the health risk until the cost becomes disproportionate, rather than an extensive airborne nanomaterial monitoring regime.

7.5. APPROACHES TO SELECTING CONTROL MEASURES

67 Several approaches may be taken to identify the necessary control measures required to prevent exposure to particulate nanomaterials in the laboratory and workplace. Traditional approaches for risk assessment of substances cannot always be applied to all nanomaterials due to missing data or uncertainties with existing

information. An alternative approach is the utilisation of control banding, which is a simplified approach to evaluate the risks from activities and the substances they involve, and place them into bands according to the potential for exposure and the hazard. For each risk band, control measures are then suggested. A number of tools and models have been developed for assessing occupational and consumer exposure to manufactured nanomaterials (Table 1), albeit with assumptions and limitations, which may help *inform* the assessment and management of risks from working with all nanomaterials and indeed other chemical substances.

Table 1. List of tested models by OECD (OECD, 2021) [56] or caLIBRAte. Category 1 (nano-specific), Category 2 (conventional chemical ECHA recommended tools).

Nº.	Model	Model Type	Project
1	ISO/TS 12901-2:2014 CB nanotool v1.0 (Part 2)	Cat. 1	caLIBRAte
2	BIORIMA Risk assessment and risk control module Occupational exposure section)		OECD
3	Stoffenmanager nano v1.0		caLIBRAte
4	Engineered Nanoparticle Airborne Exposure (CPSC ENP Model) v1.0		OECD
5	LiCARA nanoSCAN v1.0		caLIBRAte
6	NanoSafer v1.1β		nanofibre + OECD
7	GUIDEnano		caLIBRAte
8	The SUN Decision Support System (SUNDS)[1]		caLIBRAte
9	Swiss Precautionary Matrix v3.0		caLIBRAte
10	ConsExpo nano 2.0		caLIBRAte
11	RISKOFDERM	Cat.2	caLIBRAte
12	MEASE2 2.0		OECD
13	EMKG Expo tool 2.0		OECD
14	Stoffenmanager 8.3		OECD
15	Advanced REACH Tool v1.5		OECD

7.6. CONTROL OF EXPOSURE TO NANOMATERIALS

68 COSHH requires control of exposure via all routes, including the skin. Use of good laboratory/good workplace practice is a prerequisite to controlling exposure to all substances hazardous to health. Where information on the toxicity of a specific

[1] Regarding SUNDS, the partners decided under the caLIBRAte project to not carry out the performance testing because it was covered sufficiently from the sensitivity analysis. In addition, SUNDS is based on other tools already assessed by caLIBRAte (e.g., a cloud solution with the basic exposure assessment model in NanoSafer).

nano-object is unknown or unclear, a precautionary approach should be adopted; i.e. it should be assumed, until proven otherwise, that the specific nano-object represents a hazard to health.

69 Wherever reasonably practicable, exposure to nanomaterials by all routes (inhalation, dermal and ingestion) should be eliminated or controlled by the use of engineering controls. If total prevention of exposure to nanomaterials is not reasonably practical, the duty under COSHH is to r*educe exposure to hazardous substances as low as reasonably practicable*. (Appendix 3 shows a nanomaterial control measures selection flowchart).

70 If engineering controls and good laboratory/good workplace practice are not adequate to control exposure, consideration must be given to using additional controls, such as Respiratory Protective Equipment (RPE) to prevent inhalation. Whatever system is chosen, there is a need to check that it is, and remains, effective.

71 In most cases, the principal potential exposure route to nanomaterials in the laboratory or workplace is via inhalation. Therefore, wherever possible, the release of airborne nano-objects should be prevented or minimised by the use of appropriate processes, practices, systems and engineering controls.

7.7. INHALATION RISK

72 Where there is a risk of nano-objects becoming airborne, the following measures should be used where possible to control and prevent exposure:

- Minimise the quantity of nanomaterials in use at any one time;
- Minimise the number of people potentially exposed;
- Minimise the potential exposure time;
- Ensure that all those potentially exposed to nanomaterials have had suitable and sufficient information, instruction and training;
- Use engineering controls such as Local Exhaust Ventilation (LEV) to control airborne exposure;
- Where other control measures are either not reasonably practicable or fail to achieve adequate control, the use of RPE is a valid control strategy. RPE should only be used, however, when all other reasonably practicable measures have been taken, but these have not, in themselves, achieved adequate control;
- Where dust exposure from contamination of work clothing could be significant, use clothing made from a low dust-retention and low dust-release fabric; how often clothing needs to be changed and laundered will be task dependent. As a minimum, it is suggested that laboratory coats should be changed at least once a month. Do not allow work wear to be taken home for laundering.
- Keep all bottles/vessels containing nanomaterials sealed when not in immediate use since it has been shown that the action of opening vessels

containing free nano-objects can cause them to be drawn from the vessel so that they become airborne;
- Where possible, keep particulate materials wet or damp, or use slurries, and avoid energetic processes that might generate airborne dusts to reduce the risk of nano-objects becoming airborne;
- Use a damp sheet of paper towel or tissue on the bench when weighing out nano-objects, and dispose of it in a sealed plastic bag whilst it is still damp;
- Use a damp paper towel or tissue to wipe up spilt nano-objects, and dispose of it in a sealed plastic bag whilst it is still damp.

7.8. DERMAL AND INGESTION RISK

73 Contact with the skin should be avoided. Where there is a risk of nano-objects contacting the skin, the following measures, in addition to those detailed above for preventing exposure by inhalation, should be used to control and prevent exposure:

- Suitable gloves must be worn;
- Change the disposable gloves after every task;
- Ensure gloves are removed in a safe manner and disposed of safely;
- If possible, use instruments/tools to prevent contact with the skin;
- Good housekeeping is important with easy to clean surfaces, containment of spills and keeping the workplace surface clean using wet wipes;
- Good personal hygiene/skin care is also important; suitable welfare facilities should be provided;
- Always wash hands before leaving the laboratory/work area.

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8. ENGINEERING CONTROL MEASURES

74 Engineering control measures will vary depending on the requirements of each workplace. It may be necessary for those working with nanomaterials to use a combination of methods to control exposure. These methods range from total enclosure of the process and automatic handling techniques to partial containment by LEV, such as extracted enclosures and fume cupboards. Total enclosures or partial enclosures, such as fume cupboards, should be reasonably practicable for many operations with nanomaterials, including manufacture/synthesis and weighing. For cutting, sawing, or polishing, bespoke extracted enclosures could be considered. Care should be taken when using movable capturing hoods, as these are not suited to large diffuse sources or when the release is energetic. They have a limited capture zone and rely on the operator to reposition the hood to ensure that any release of nano-objects is within the limited capture zone of the hood; therefore, staff training is essential. Depending upon the process, down-draught benches may be an alternative option.

75 All LEV equipment should be designed and installed to a standard such that the system can at all times contain, capture or receive the contaminant cloud within the LEV hood and conduct it away. It should also be commissioned to demonstrate control effectiveness (see HSG 258: Controlling airborne contaminants at work, A guide to local exhaust ventilation (LEV) [73].

8.1. LOCAL EXHAUST VENTILATION (LEV)

76 The most effective class of LEV are enclosures. In the laboratory setting, there are generally two types: full or partial. Full enclosures (e.g., a glove box with high efficiency particulate air (HEPA) filtration (BS 1822, 2019 [74]) are the most effective as they provide physical separation between the worker and the material being handled. However, their inherent features can make them impractical as a control option and therefore partial enclosures are frequently used. These may be designed specifically for the process or be commercially available units. Examples of partial enclosures suitable for handling particulate nanomaterials include: HEPA-filtered fume cupboards, HEPA-filtered containment cabinets or HEPA-filtered microbiological safety cabinets (MSCs). Using double HEPA-filtered cabinets increases the level of protection and can provide a safer means of carrying out filter changes. More Information can be found in Appendix 4.

77 The small size and "low inertia" of nano-objects means they move with the air generated by the process in a manner more akin to gases than conventional particles. Therefore, correctly designed LEV systems should be an effective control measure.

78 The effectiveness of any control measure cannot be automatically assumed when handling nanomaterials. Respirators, HEPA-filtered cabinets and most importantly fume cupboards were not specifically designed for this task, and so

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evidence should be sought as to their effectiveness before use. For newer installations, information may be sought in the LEV commissioning report (see HSG 258 [73] and BS EN 14175 [75]).

79 It is important to make sure that the LEV achieves and maintains adequate control of exposure at all times. The system requires regular maintenance/periodic monitoring to ensure controls are working, and thorough examination and testing at least "once a year" (COSHH allows a maximum of 14 months between tests) by a competent person. Although in higher risk scenarios this may be more often, i.e., can be 6-monthly if following good practice (see HSG258 [73]). In addition to velocity measurements, flow visualisation using smoke will show whether the LEV is truly effective. Furthermore, a smoke test performed with the process/operation running will show:

- The extent and behaviour of the airborne contaminant cloud;
- The capture zone and boundaries of capture hoods;
- Whether containment is maintained within a partial enclosure;
- Draughts, giving an indication of their direction and size;
- The general movement of air around an enclosure;
- Eddying and encroachment into the operator's breathing zone.

80 If there is any doubt about the capability of a fume cupboard, then it may be necessary to carry out an on-site containment test, as detailed in BS EN 14175-3:2019 [75] and BS EN 14175-4:2004 [76].

81 All users should be trained on how to use the LEV, and records should be kept of all LEV checks.

8.2. HEPA FILTRATION EFFICIENCY

82 Wherever reasonably practicable, the exhaust air from an LEV system should be filtered through a HEPA filter, preferably H14, to remove the airborne nano-objects before venting to a safe place outside the building. This is particularly important when handling HARNs such as carbon nanotubes or other fibrous/rod-like nano-objects. If it is not reasonably practicable to vent the exhaust air to a safe place outside, it must never be re-circulated directly back into the workplace unless it has been effectively filtered to remove nano-objects by at least one HEPA H14 filter (see Appendix 2). Nano-objects and their aggregates and agglomerates have also been shown to be captured by electrostatic collectors.

83 HEPA filters H14 are designed to remove at least 99.995% of airborne particles at the Most Penetrating Particle Size (MPPS) for which filtration is at a minimum. For micro-glass filter mediums, the MPPS is usually in the range of 120 nm to 250 nm. Larger and smaller particles should be filtered with even higher efficiency. Studies

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indicate that HEPA filters of this grade are efficient at capturing the relatively limited number of nano-objects and their aggregates and agglomerates (as small as 2 nm in diameter) tested. It should be noted that different grades of HEPA filters have differing efficiencies in the nanoparticle range. In addition, different nano-objects and their aggregates and agglomerates may have differing MPPSs and penetration rates depending on their shape, density, and charge.

84 Ultra Low Penetration Air (ULPA) filters are designed to remove 99.9995% to 99.999995% depending upon the classification (Class U15 to U17) of airborne particles at the MPPS. They are used in some commercial recirculatory enclosures designed for use with nanomaterials.

85 The high filtration efficiency of HEPA filters can be compromised during installation. For example, the filter or filter seal can be damaged, or the filter is not seated correctly. It is, therefore, worth considering undertaking an in situ dispersed oil penetration (DOP) test to check for leaks, or filter damage after fitting a HEPA filter.

8.3. DUCTED MICROBIOLOGICAL SAFETY CABINETS (MSCS)

86 Ducted MSCs can handle nanomaterials in a similar way to other HEPA-filtered containment cabinets. A Class I MSC operates like a fume cupboard and protects the worker by drawing air through the front opening. Class II and III MSCs provide protection for both the user and the material in the cabinet. All these cabinets exhaust air through a HEPA filter.

87 It should be noted that Class II MSCs recirculate up to 70% of the air inside the cabinet, albeit through a HEPA filter, and therefore, care should be taken. Class II MSCs should only be used for handling small quantities of nanomaterials and based on risk assessment.

8.4. DUCTLESS RE-CIRCULATING HEPA-FILTERED CONTAINMENT CABINETS AND RE-CIRCULATING MSCS

88 Ductless re-circulating HEPA-filtered containment cabinets and MSCs that "re-circulate" air back into the room from the cabinet's interior through a HEPA filter can be used for small quantities of nanomaterials in the absence of hazardous vapours or gases. However, the use of a ductless re-circulating cabinet or enclosure to control any hazardous substance must be subject to rigorous risk assessment and should only be considered where external venting to a safe place outside is not reasonably practicable. The containment cabinet should be set aside for use with nanomaterials or chemically similar materials since some other chemicals, particularly those with the potential to evolve corrosive vapours or fumes, may affect the effectiveness and integrity of the fitted filter.

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89 HEPA-filtered re-circulating cabinets do NOT absorb or capture gases or vapours, for which external venting to a safe place would be required in addition to the HEPA filter. If corrosive vapours or fumes could be generated, a glass fibre rather than cellulose HEPA filter should be used, and the exhaust vented to a safe place outside.

90 The International Organization for Standardization Technical Report (ISO/TR 12885, 2018 [77]), on nanotechnology proposes a series of qualifications on the use of MSCs based on their mode of operation, and the quantity of nanomaterial that could be safely handled in them (Appendix 1).

91 If using a re-circulating MSC, the following must be considered:

- The filter must be HEPA; charcoal filters alone must not be used;
- The cabinet should have a filter blockage warning/alarm;
- The cabinet should have a low airflow warning/alarm;
- How a filter is to be safely changed;
- How the contaminated filter is to be safely disposed of (incineration is recommended);
- Cabinets must be subject to regular maintenance, including a filter integrity test.

92 The cabinet must be subject to thorough examination and testing (including a filter integrity test) at intervals not exceeding 14 months, and more frequently if the assessment identifies a higher risk; i.e., it can be 6 months if following good practice (see HSG 258 [73]).

8.5. MAINTENANCE, EXAMINATION AND TESTING OF CONTROL MEASURES

93 Regulation 9 of COSHH requires that every employer who provides any control measure to meet the requirement of Regulation 7 shall ensure that it is maintained in an effective state, in an efficient working order and in good repair, and be in a clean condition.

94 In order to comply with Regulation 9 it should be ensured that:

- All measures used to control exposure to nanomaterials are maintained in good working order and in good repair. (The manufacturer/supplier of plant should be able to help with appropriate information);
- Competent persons undertake frequent visual checks and periodically carry out thorough examinations of equipment to ensure they are being maintained adequately;

- All LEV plant is examined and tested at least every 14 months (a record of such tests must be kept for at least 5 years after the date on which they were made).

95 Further general information about LEV is contained in HSG 258 – Chapter 10 – Thorough Examination and Test [73].

9. PERSONAL PROTECTIVE EQUIPMENT (PPE)

9.1. EYE PROTECTION

96 Suitable eye protection must be worn when handling any chemicals, including nanomaterials (minimum of close-fitting safety glasses).

9.2. RESPIRATORY PROTECTIVE EQUIPMENT (RPE)

97 There will be situations where other control measures are either not reasonably practicable or fail to achieve adequate control. In these circumstances, the use of RPE is a valid control strategy. RPE should only be used, however, when all other reasonably practicable measures have been taken but these have not, in themselves, achieved adequate control [78].

98 It must be emphasised that the use of RPE as a means of preventing exposure should be a last resort (COSHH), and must not be undertaken lightly or without full consideration of the practicality of using engineering controls.

99 Disposable respirators (often referred to as a mask; no less than FFP3 standard), are only suitable as a secondary precautionary measure against accidental "spillage"- not as a first line of protection. Full-face P3 APF40 (Assigned Protection Factor 40) particulate respirators that protect the eyes and lungs are required for any work in an atmosphere containing airborne-nano-objects.

100 All tight-fitting RPE, including disposable respirators, must be suitable for the task, manufactured to the appropriate standard, and face-fit tested for the individual by a competent face-fit tester [78]. The wearer must also be clean shaven.

101 Those using RPE should be trained in its use, and if the equipment is re-usable, it should be regularly cleaned as per the manufacturer's instructions, checked to ensure that it remains effective, and monthly maintenance records kept. For further information on the selection, use and maintenance of RPE, see COSHH basics

9.3. GLOVES

102 The gloves selected should be suitable and manufactured to an appropriate standard (e.g., EN ISO 374-1:2024 [79]). For many nanomaterials, good quality, single-use disposable gloves should be adequate. However, consideration must also be given to other chemicals used in the procedure/process. Organic liquids, including solvents, can not only permeate through gloves quickly in their own right, but may also facilitate the penetration of small nano-objects through gloves. Guidance on choosing the appropriate gloves to protect skin from a variety of substances can be found on HSE website (Choosing the right gloves to protect skin: a guide for employers [80]).

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103 Glove material thickness is a major factor in determining the diffusion rate of chemicals through gloves and consideration may need to be given to wearing two layers of disposable gloves for some materials.

104 Polychloroprene, butyl rubber, and latex gloves can be suitable, but their barrier effectiveness also depends on the glove thickness (ISO/TS 12901-1:2024 [79]). If the risk assessment indicates that latex gloves are the safest choice, then only low-protein, powder-free gloves should be used.

105 All those working with nanomaterials should be properly trained in how to put on and remove gloves without contaminating themselves. Guidance on removing single-use gloves can be found in the HSE training video, available on the HSE website (Removing single-use gloves without contaminating your hands [81]).

9.4. PROTECTIVE CLOTHING

106 When working with nanomaterials, suitable laboratory coats, coveralls or where appropriate, disposable overalls should be worn. Provision must be made to allow clean overalls/laboratory coats to be put on, and dirty ones removed in a manner that does not contaminate the individuals or the general workplace.

107 If dust exposure from contamination of work clothing could be significant, clothing made from a low dust-retention and low dust-release fabric such as polyethylene textiles is recommended [82]. ISO/TS 12901-1:2024 [83] advises using Type 5 nonwoven chemical protective clothing (CPC) for full-body protection against airborne particulates. However, some studies have found certain Type 5 CPC models perform poorly against airborne nanomaterials under simulated workplace conditions (ISO/TS 12901-1:2024) [83].

108 If re-usable laboratory coats or overalls are used, provision should be made for their regular laundering and the prevention of secondary exposure. (In the event of a "one-off" gross contamination, consideration should be given to treating even "re-usable" PPE as disposable.)

9.5. CLEANING SPILLAGES

109 The work area and all equipment should be thoroughly cleaned after use or following a spillage by wet-wipe cleaning.

- **Do not** brush.
- **Do not** use compressed air for cleaning.
- **Do not** use a standard vacuum cleaner.

110 If a vacuum cleaner is the only reasonable practical means of cleaning, it must be a **dedicated, commercial, Class-H** cleaner, noting that these Class-H vacuums

are usually sold with either a H13 or a H14 filter, H14 being the preferred option. The filter and bag that contain the nanomaterial dust are regularly changed under controlled conditions. The filter and bag must be disposed of appropriately and safely. The cleaner itself must only be used for this task and will need to be decontaminated at the end of its life before it is disposed of, taking a precautionary approach.

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10. SPECIFIC ADVICE FOR HIGH ASPECT RATIO NANOMATERIALS (HARNS)

111 Fibrous nano-objects, including certain CNTs and nanowires, are substances of high concern. Although not all HARNs will meet the criteria to present a fibre-like hazard (i.e. insufficient length, tangled/non-rigid morphology), unless sound mitigating evidence is available for a specific case, a strict precautionary approach should nonetheless be taken to risk management. This is to reflect the severity of the potential hazard outcome, namely, lung tumour or mesothelioma formation. Indeed, this approach is reflected in the number of recommended OELs for HARNs, for example, as low as 0.01 fibres/ml [69]. It should also be noted that, as described in the HSE guidance "*Using nanomaterials at work*", plate-like structures (sometimes called nanoplatelets), where only one dimension falls within the nano size range, could also be considered to be HARNs [84].

112 If the use of HARNs cannot be avoided, then the implementation of a risk management programme in the workplace may help to minimise the potential for exposure. Such a programme should include the following:

- Assess the worker's job and tasks to determine the potential for exposure;
- Use appropriate work processes, systems and engineering controls, and provide suitable equipment and materials to limit the likelihood of release i.e. minimise the amount of HARNs produced. Alternatively, produce them in a form that reduces the chance of them becoming airborne. Where possible, use equipment that fully encloses the process;
- Control exposure at source by carrying out all tasks, including packaging for disposal, in a ducted fume cupboard with a HEPA filter, or in other suitable LEV fitted with a HEPA filter. When using other types of LEV, try to enclose the process as much as possible. Ductless, HEPA filtered safety cabinets, and re-circulating HEPA filtered MSCs can be used with small quantities of CNTs and other HARNs as long as they are subject to rigorous maintenance, and checks are carried out to ensure they are effective at all times. See Appendix 2 for more information;
- Reduce the number of employees handling HARNs, and minimise the level and duration of exposure and the quantities used;
- If possible, keep the material wet or damp to reduce the risk of it becoming airborne;
- Provide RPE for emergencies, and only for use in addition to other control measures. All employees who use RPE must be trained and have had face-fit testing performed. HSE recommends RPE with an assigned protection factor (APF) of 40 or higher;
- Provide PPE (e.g., gloves, non-woven coveralls). Use single-use disposable gloves where possible. Glove material thickness is a major issue in determining the diffusion of nano-objects and therefore, at least two layers of gloves are

recommended when handling HARNs. If the risk assessment indicates that latex is the safest choice, then only use low-protein, powder-free gloves. Provide protective clothing such as polyethylene textiles (e.g., Tyvek) which perform better and do not retain dust or allow dust to penetrate – do not use wool, cotton or knitted material;

- Consider maintenance, filter replacement, storage and disposal in risk assessments for the control of exposure to HARNs;
- Use 'wet-wiping' wherever practicable for cleaning and avoid the use of vacuum cleaners. If vacuum cleaners are the only reasonably practical option, they must be Class-H with either a H13 or a H14 filter (H14 being the preferred option) and decontaminated before further use. Contaminated wet wipes should be double-bagged and treated as hazardous waste;
- Emergency procedures should be in place to deal with spills, accidents and emergencies;
- Educate and train workers in the proper handling of nanomaterials (e.g., good work practices) and keep records of all training carried out.

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11. INFORMATION, INSTRUCTION AND TRAINING

113 To comply with Regulation 12 of COSHH, employers should give all their employees who may be exposed to nanomaterials at work, sufficient information, instruction and training to understand the risks to their health caused by potential exposure to nanomaterials and the precautions that should be taken to avoid, or minimise exposure.

114 It is important that the person carrying out the research carries out a COSHH risk assessment and is trained in how to do this. A senior member of staff should check and sign off the assessment, but should not write it *per se*. A central record of all health and safety training in COSHH and risk management should be kept within the department and this can be used for future employment.

115 Employers should provide adequate supervision, particularly to new and inexperienced employees. The training should detail how control measures are to be used. Employees should be instructed to report any obvious defects in the control measures to their supervisor. The risk assessment should note all these requirements.

116 Where RPE is used, employees should be trained to check that it fits properly and given clear instructions about when it should be used, serviced or, if it is disposable, thrown away. Details on this can be found in the COSHH ACOP Reg 7 Prevention or control of exposure to substances hazardous to health – Suitable RPE (paras 160 – 162) [1].

117 Control of substances hazardous to health (Sixth edition) [1]. Information, instruction and training should, in particular, enable employees to:

- Understand the risks to health arising from exposure;
- Use the control measures provided effectively;
- Use suitable PPE in combination with other control measures, where adequate control of exposure cannot be achieved by other means.

118 A record of all the information, instruction and training should be kept for each employee as laid out in the COSHH ACOP Reg 12 (3)(a) and (b) [1]. The information, instruction and training shall be:

- Adapted to take account of significant changes in the type of work carried out, or methods of work used while carrying out the research;
- Provided in a manner appropriate to the level, type and duration of exposure identified by the risk assessment.

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12. MONITORING

119 One of the general principles of risk management includes taking measures to prevent or minimise the exposure of workers to nanomaterials and their release into the environment. Monitoring is important to assess whether potential exposure occurs and whether the engineering controls are adequate. Exposure to nano-objects can occur by ingestion, skin penetration or inhalation, with inhalation being the primary route of exposure for airborne nano-objects. There is currently no consensus on which is the most appropriate metric or method to measure airborne nano-objects and their aggregates and agglomerates in the workplace. Sampling strategies based on extensive real-time measurements and off-line characterisation of airborne nano-objects have been described in ISO/TR 12885:2018 [77], ISO ISO/TS 12901-1:2024 [83], and Brouwer *et al.* (2009) [85]. However, workplace exposure measurement surveys based on extensive monitoring using a large set of sophisticated equipment require training and expert knowledge.

120 Guidance documents, particularly those from ISO/BSI and NIOSH, provide recommended approaches to undertaking exposure monitoring. Approaches based on simple-to-use, hand-held instruments have been developed. NIOSH has proposed the Nanoparticle Emission Assessment Technique (NEAT) [86-88]. An OECD document (2015) presented a three-tiered approach for conducting field-based measurement of airborne nano-objects [89]. Tier 2 focuses on conducting a basic exposure or release assessment using a straightforward approach for determining whether an exposure to nano-objects may occur. The approach utilises easy-to-use, portable equipment.

12.1. INSTRUMENTS USED

121 The sampling method described in Appendix 6 proposes the evaluation of respirable and/or inhalable mass concentration(s) and particle number concentration using real-time hand-held instruments such as Condensation Particle Counters (CPCs) and Optical Particle Counters (OPCs). Hand-held CPCs and OPCs measure particle number concentrations in the size range from 10-20 nm to about 1 µm, and 0.5 µm to about 15 µm, or greater, respectively. They are portable, easy to use, cost-effective, fast-response instruments capable of detecting transient releases. The use of an OPC instrument in addition to a CPC instrument can be beneficial. In some circumstances, for example, when monitoring powder-handling activities, the nano-objects are likely to agglomerate to form larger particles and can be detected using the OPC rather than the CPC.

122 Airborne nanoobjects and their aggregates and agglomerates should be collected on filters or appropriate substrates for off-line analysis, e.g., X-ray fluorescence (XRF), Inductively Coupled Plasma Mass Spectrometry (ICP-MS), inductively coupled plasma atomic emission spectroscopy (ICP-AES), electron microscopy, or thermal optical analysis (TOA).

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12.2. SAMPLING STRATEGY

123 The protocol described in Appendix 6 is designed to be a pragmatic approach to rapidly assess particle release and whether the control measures or changes implemented are effective. It requires a respirable and/or an inhalable sampler, and at least a CPC and an OPC. An additional sampler for subsequent morphological or chemical analysis may be needed. For carbon nanotubes and graphene, a combination of off-line electron microscopy analysis and thermal gravimetric analysis can be used. Placement of personal samplers in the breathing zone of the workers, and static samplers at the source location, can be undertaken. Hand-held real-time instruments should be placed close to the task. Another CPC and OPC, positioned away from the task/process, can also be used. See Appendix 6 for more information.

124 Background is defined as airborne particles present in the workplace and differs from manufactured nano-objects released during manufacturing, use, or handling. It includes "ultrafines" originating from various sources, including urban pollution.

125 For real-time measurements, it is important that the background level of ultrafine particles is established before and after any production or processing of the nanomaterial is started. This is because there is a natural background level of ultrafine particles in the air, which can confound the interpretation of results. The amount of ultrafine particles will depend on the location.

12.3. LIMITATIONS

126 Measuring particle number concentrations using CPCs and OPCs is challenging due to the lack of portable and personal instruments that are selectively sensitive to manufactured nano-objects against a background of non-manufactured nano-objects (which can fluctuate). As the handheld CPC and OPC instruments in their basic form give no or limited size discrimination in the size range detected, the source must be "detected" by increases in particle counts relative to the background, over a wide size range. More sophisticated instruments are available, which offer much improved size discrimination and may help to better define the source, but still rely on a comparison to the background count. Offline analysis of the particles collected using samplers can confirm the presence or absence of the particles of concern. Although limited to the measurement of airborne nano-objects and their aggregates and agglomerates up to about 500–700 nm, personal real-time instruments that measure the alveolar lung-deposited surface area (LDSA) concentration can be useful.

127 There are challenges in quantifying airborne carbon-based nano-objects, nanotubes and nanofibres. This approach should be supported by external expert advice where necessary. Since these materials are mainly made of elemental carbon, techniques such as thermal-optical analysis (TOA) can be used to quantify their presence. In addition, CEN TS 18117:2025 [90] provides guidelines for the detection

and characterisation of airborne nano-objects including nanotubes using electron microscopy for including nanotubes.

128 The protocol describes "current best practice"; however, if in doubt, this approach should be supported by external expert advice where necessary.

13. HEALTH SURVEILLANCE

129 On-going research on the hazards of nano-objects is needed along with the continual reassessment of available data to determine whether specific health surveillance is warranted for workers who are producing or using nanomaterials.

130 Health surveillance *specific* for hazardous nanomaterials is not practical at the present time due to a lack of information about anticipated health effects and suitable biomarkers.

131 HSE proposes that good practice would involve keeping a record of all those staff who are working with nanomaterials via the equivalent of a COSHH work activity record form, in a similar way to other substances of concern. Alongside such records of work activity, the dates, the type of nanomaterials handled, the duration of work with the material, and the exposure scenarios should be documented. An example of a work activity record can be found in Appendix 5.

132 The health hazards related to the material, irrespective of the nanoscale form, should still be considered as part of the usual COSHH risk assessment. This should be informed by considering the likely routes of exposure for the material of concern.

133 If it is likely that an identifiable disease or adverse health effect associated with exposure to a particular substance will occur in the workplace, health surveillance should be considered. It is necessary that there are technically feasible, available, and medically accepted techniques for detecting the disease or adverse health effect. It is also important that any assessments performed as part of health surveillance are of low risk to the employee.

134 It might be expected that there could be a long latency in the development of disease associated with exposure to some nano-objects and their agglomerates and aggregates (NOAA). Therefore, medical screening tests such as those used to detect occupational respiratory diseases should be considered and might be appropriate for workers exposed to nano-objects [91]. The same screening recommendations would be applicable to NOAAs in workers when nano-objects are chemical substances for which validated screening approaches exist [92].

135 Nevertheless, it would be useful to collect information about the materials being used, including the duration of use. Such information could help to improve knowledge on potential exposures, which could be important for future epidemiological studies, should any health effects emerge in the exposed population at a later date. This information could also be used in the interim to support risk management decision-making to protect workers who are potentially exposed to hazardous materials.

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14. DISPOSAL OF LABORATORY WASTE NANOMATERIALS

136 There are currently no waste regulatory frameworks in the UK specific to nanomaterials. Nonetheless, the Waste (England and Wales) Regulations 2011 [93], The Waste Management Licensing (Scotland) Regulations 2011 [94], and The Waste Regulations (Northern Ireland) 2011 [95] apply.

137 The responsibility under UK law of any individual who is the holder of controlled waste is to ensure that it is managed properly, recovered or disposed of safely, does not cause harm to human, animal or plant health, or pollution of the environment, and is transferred only to someone who is authorised to receive it. In general, research laboratories produce relatively small quantities of hazardous waste (i.e., ≤kg), and often diluted in solvent or present as a minor component in a solid matrix compared to manufacturing, which typically produces waste on a larger scale (e.g., tonne scale).

138 Nano-objects (e.g., nanoparticles, nanotubes, nanofibres, etc) in powder form or dispersed in liquid may present a greater exposure risk than a solid matrix impregnated with nano-objects. It is important that nanomaterial waste is identified and characterised (e.g., dust filters contaminated with CNTs or HARNs, paper tissues impregnated with colloidal silver, metal oxide nanoparticles on carbon black), in order to determine which controls are needed to reduce the risk of exposure. In the absence of sufficient knowledge, the nano-object waste should be classified at least as hazardous as the non-nanoscale form of that substance. Consideration should be given to the possibility of increased hazard in the presence of one or more of the physicochemical characteristics listed in Section 5.1 (paragraph 40).

139 If a composition contains a nanomaterial that in itself is non-hazardous but is in association with other components in that composition which are hazardous, then that whole composition must be regarded as being hazardous and treated as such in terms of waste. For larger consignments of waste nanomaterials (e.g., from manufacturing), see CEN/TS 17275:2018 [96].

140 The environmental fate of nanomaterials is an obvious concern [97], as recognised in the first edition, and outside the scope of the guidance, but a summary was recommended reading [98]. The second edition included references such as Kumar *et al.* (2014) [2], Wagner *et al.* (2014) [99], and Kühnel *et al.* (2014) [100]. More recent studies have since provided updates, including works by Kumar *et al.* (2022) [101], Mortimer and Holden (2019) [102], Rawat *et al.* (2018) [103], Krug *et al.* (2018) [104], and Garner and Keller (2017) [105]. Additionally, the OECD reviewed nanomaterials in waste streams [106].

141 Determining the method of waste disposal for nanomaterials is dependent on the nature and character of the nanomaterial waste; for example, the solubility of the nano-object or whether the nanomaterial waste is a solid/powder, nano-objects are in a liquid dispersion, or nano-objects are embedded in a matrix. The waste disposal route will also depend on whether or not the waste is hazardous waste according to

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waste classification. In addition, consideration should be given to the possibility of enhanced hazard from the nano-objects due to the potential for enhanced (eco) toxicological, physical properties or increased mobility during disposal.

142 Drawing on previous guidance [107], nanomaterial waste can be broadly classified into the following waste streams:

- Pure nano-objects (e.g., CNTs);
- Items contaminated with nano-objects (e.g., wipes/paper towels);
- Liquid suspensions containing nano-objects (e.g., colloids);
- Solid matrices with nano-objects that are friable or attached to the surface;
- Nano-objects embedded in a solid matrix that are unlikely to be released on contact with air or water: i.e. the nanomaterial is immobilised.

143 The level of controls for the safe disposal of nanomaterial waste will depend on its nature. Unless there is evidence that the materials to be disposed of do not present any hazards, a precautionary approach should be taken for handling, packaging, and disposal. Waste should be disposed of in such a manner that the risk of exposure to the nanomaterials is minimised.

144 It is recommended that waste nanomaterials and waste containing nano-objects are double-bagged or doubly contained, labelled, and sealed in preparation for disposal. (OECD 2010) [108].

14.1. PREPARATION OF NANOMATERIAL LABORATORY WASTE PRIOR TO DISPOSAL

145 The risk of exposure to nanomaterial waste must be either prevented or controlled wherever possible. All nanomaterial waste should be contained. Generation of nanomaterial waste should be minimised. A comprehensive description of the principles of waste management in relation to nanomaterials is presented in CEN/TS 17275:2018 [96].

146 Containment can be achieved by employing suitable, sturdy, compatible containers (e.g., plastic clip-top containers), which prevent the escape of nano-objects. Containers must be clearly and indelibly labelled, provide a description of the waste and include the hazardous properties (either known or suspected).

147 In general, all nanomaterial waste, including contaminated laboratory consumables such as paper towels, wipes, disposable gloves and suits, blotters, and other moderately contaminated items, should be double-bagged for disposal (i.e., transfer to the waste contractor). It is recommended that:

- Prior to disposal, the contaminated waste is placed in a sealable, plastic bag inside a fume cupboard/ biosafety cabinet;
- The sealed bag should then be placed inside another sealable, plastic bag and clearly labelled, identifying the contaminated material.

148 It is suggested that, where possible, nano-objects dispersed in liquid or in a powder form are treated in an appropriate way to inactivate the nanomaterial [108]. For example, liquid waste, which tends mainly to be solvent-based, can be placed in a waste solvent stream (ultimately incinerated), fixed in a resin [109], or adsorbed onto a solid substrate (e.g., silica or carbon). Other examples of inactivation include: aggregating the nano-objects in solution (e.g., centrifuging gold nanoparticles) or dissolving the nano-objects in solution (e.g., treating silver nanoparticles with aqua regia (a mixture of hydrochloric acid and nitric acid)). Solid nanomaterial waste (e.g., powder), which presents a risk of exposure through inhalation, can be considered for disposal via existing solid hazardous waste streams, for example, in a similar manner to waste fine silica employed for column chromatography (hazardous by virtue of potential inhalation). Such waste is double-bagged, sealed, and transferred into a suitable sealable container (e.g., a metal or plastic clip-top drum) for collection by a licensed waste contractor.

149 It has been recommended [109] that, where surfaces or materials have been decontaminated (e.g., wiped or washed down), producing a contaminated residue, the resulting residue/waste is treated as chemical waste (hazardous waste).

150 Nanomaterials should not be disposed of via "non-hazardous waste" disposal routes (through landfill or drains), unless it can be demonstrated that such nanomaterials are proven to be non-hazardous and disposal via these waste streams is safe and does not contravene environmental legislation. A precautionary approach has been generally adopted: (in the absence of sufficient knowledge on the hazard); no free manufactured nano-objects should enter any non-hazardous waste stream or be disposed of via the drains [110].

14.2. DISPOSAL BY WASTE CONTRACTORS

151 There are currently no waste regulatory frameworks in the UK specific to nanomaterials. However, the Duty of Care Code of Conduct applies, which is available from the Statutory guidance Waste Duty of Care Code of Practice (Department for Environment, Food & Rural Affairs and Environment Agency, 2018. [111]).

152 The Environmental Agency technical guidance, 'WM3', [112], which has been amended to reflect the Global Harmonised System (GHS), provides a detailed protocol for classifying waste, whether it is hazardous or not. According to EA 'Hazardous Waste Assessment Methodology' [113], where knowledge on the composition of the waste is deficient and if the information, which demonstrates the waste is non-hazardous, is insufficient then the waste is classed as 'hazardous'. The

EA states in 'WM3', "This procedure is a general guide; it applies in most circumstances and must be used with the supporting appendices. If unsure, advice should be sought from a 'competent person'."

153 The EA guidance [112], states threshold limits of ≥0.1% for 'HP6' ('Acute toxicity' 'Oral Tox. 1' and 'Inhal. Tox. 1'); 'HP7' ('Carcinogenic' 'Carc. 1A & Carc. 1B'); 'HP11' 'Mutagens' 1A & 1B, and a range of limits from 1–25% for hazardous materials as described by the GHS (ascribed 'HP' codes) by mass. It remains to be determined whether this approach is applicable to nanomaterial waste. Most nanomaterial waste will fall into either "H5" or "H6" waste categories, i.e. 'harmful' or 'toxic' respectively if inhaled, or ingested, or absorbed through the skin. In some cases, ascribing waste to either "H7" (carcinogenic), or "H13" (sensitising) categories may be applicable as well.

154 Incineration of solid waste containing nanomaterials has been identified as the "conservative option" even though the nanomaterials are present at low levels (<1%) [114]. With respect to CNTs and biopersistent HARNs, high-temperature incineration is the preferred method of disposal [84]. Note, HSE guidance states that other technologies may be suitable if it can be demonstrated that they render the waste safe. The disposal of nanomaterials by incineration has been reviewed [115] and further information is available in Annex D of CEN/TS 17275 [96].

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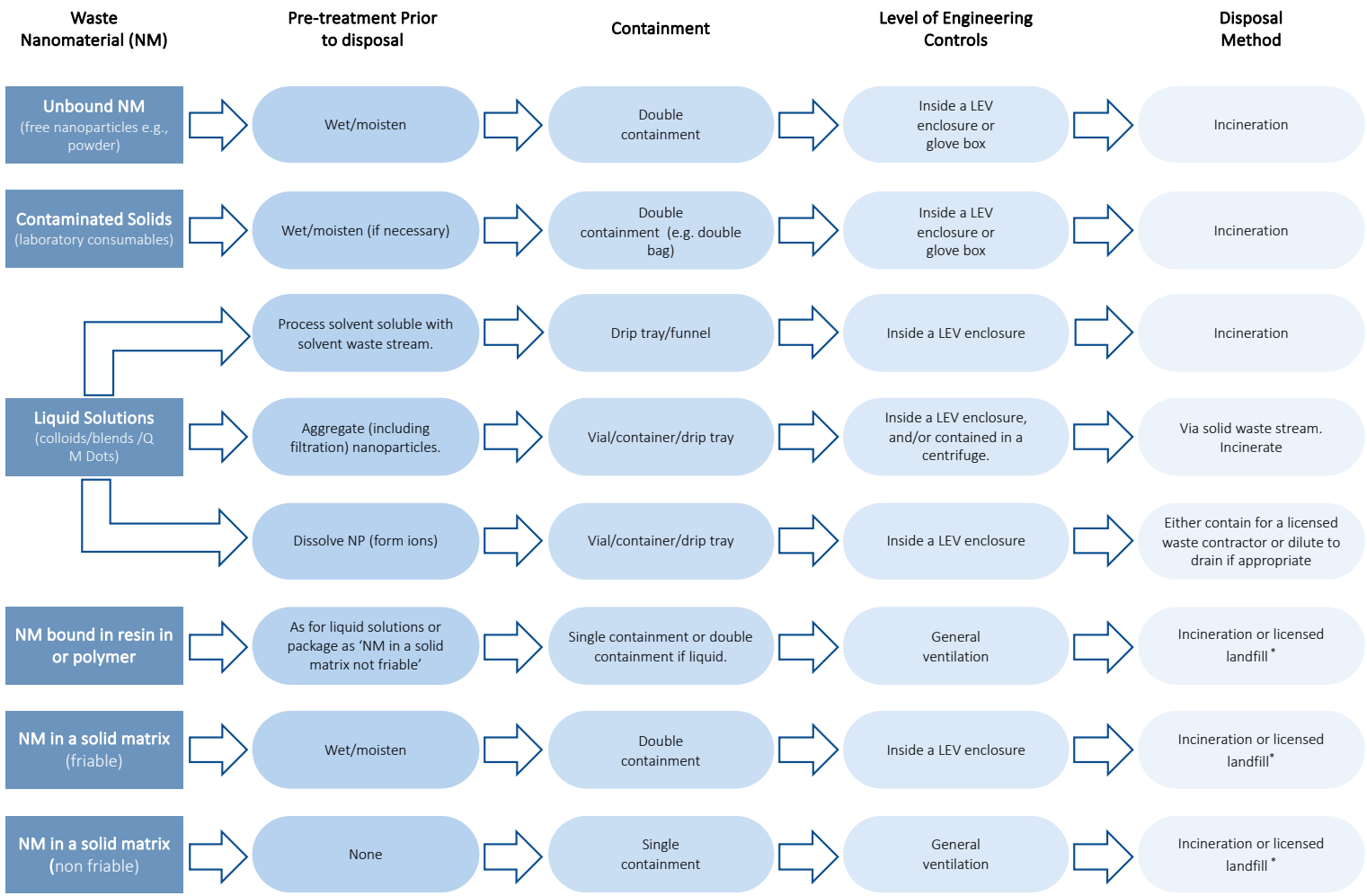
Figure 1. Summary of treatment and control conditions for laboratory waste nanomaterials.



Note: for larger consignments, refer to CEN/TS 17275 (§ 12.1) [96]. * The NM must be known (identified) as well as its properties (i.e. its toxicity)

15. LABELLING AND SIGNS

155 A requirement and/or standardised approach to labelling and safety signs for use with nanomaterials does not currently exist. It is recommended that a diligent approach is taken using, for example, Hazard and Precautionary statements and warning signs to provide adequate, relevant, and specific information on any actual or potential hazards and safety risks.

156 The European Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures (CLP) [116], was progressively implemented between 20 January 2009, and 31 May 2015 in all EU member states, including the UK. The EU CLP Regulation as amended was retained in GB law (referred to as GB CLP) following the UK's departure from the EU. It adopts the Globally Harmonised System (GHS) on the classification and labelling of chemicals.

157 Guidance from the European Chemicals Agency (ECHA) is available on how to label and package chemical substances and mixtures in accordance with the CLP Regulation [117]. Although not specific to nanomaterials, the guidance documents provide useful examples and aim to clarify:

- What aspects to consider when estimating the label size needed;
- What types of supplemental information are possible, and where to place this information on the label;
- The conditions for small packaging exemptions;
- The interaction between CLP and transport labelling rules;
- How to select the most appropriate set of Hazard and Precautionary statements for the label.

158 Hazard and Precautionary statements are used to convey information derived from the hazard, exposure and risk assessments, in Safety Data Sheets (SDS), and COSHH assessments

159 A Hazard statement is a phrase that describes the nature of the hazard in the substance or mixture. A hazard statement will be determined by the application of the classification criteria. Examples of hazard statements include "Causes serious eye damage", "Toxic if swallowed", "Toxic to the aquatic life with long-lasting effects", and "May cause allergy or asthma symptoms or breathing difficulties if inhaled".

160 A Precautionary statement is a phrase that describes recommended measure(s) to minimise or prevent adverse effects resulting from exposure to a hazardous substance or mixture due to its use or disposal. Examples of Precautionary statements include "Wear eye protection", "Do not eat, drink or smoke when using this product", "Avoid release to the environment", and "In case of inadequate ventilation, wear respiratory protection". Suppliers determine the appropriate Precautionary statements (usually no more than six) based on the required hazard statements.

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161 The GHS aims to bring together the various national and regional hazard communication systems that control the supply of hazardous chemicals. It also aims to ensure that information on physical hazards and chemical toxicity is available in order to enhance the protection of human health and the environment during the handling, transport and use of these chemicals. Activity associated with the GHS may, in the future, provide a consistent approach for labelling of nanomaterials, but the assignment of hazard and precautionary statements will always be contingent upon a consideration of the hazardous nature of the material where data are available, and in the absence of data, will require a precautionary approach.

162 The selection of appropriate hazard labels, signs or pictograms should be based on the available hazard information for the material. In the absence of information, a precautionary approach to labelling should be adopted.

163 *Ad hoc* signs or pictograms should be posted in areas to provide a visual indication of local instructions or rules in place, for example, on storage cabinets, fume cupboards, and instruments dedicated for use with nanomaterials. The content and format of the signs should be consistent with any in-house requirements.

164 Generic pictograms, adopting the format of the yellow/orange warning triangle, have emerged for "nanomaterial hazards", and whilst these have no official recognition by authorities, their use may be considered to provide a visual indication of the presence of nano-objects, as appropriate. It should be noted that these generic signs do not provide any information on the nature of the hazard, and any known or suspected hazards (e.g., oxidising, explosive) should be adequately indicated.

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APPENDIX 1: TERMS AND DEFINITIONS

The terms and definitions used in this document are based on internationally accepted definitions wherever possible, specifically those defined by ISO. The definitions from the European Commission are also provided.

EUROPEAN COMMISSION DEFINITIONS

NANOMATERIAL: as defined by the European Commission [118]: a natural, incidental or manufactured material consisting of solid particles that are present, either on their own or as identifiable constituent particles in aggregates or agglomerates, and where 50% or more of these particles in the number-based size distribution fulfil at least one of the following conditions:

a) One or more external dimensions of the particle are in the size range 1 nm to 100 nm;

b) The particle has an elongated shape, such as a rod, fibre, or tube, where two external dimensions are smaller than 1 nm, and the other dimension is larger than 100 nm;

c) The particle has a plate-like shape, where one external dimension is smaller than 1 nm, and the other dimensions are larger than 100 nm.

In the determination of the particle number-based size distribution, particles with at least two orthogonal external dimensions larger than 100 µm need not be considered. However, a material with a specific surface area by volume of < 6 m^2 /cm^3 shall not be considered a nanomaterial.

PARTICLE: a minute piece of matter with defined physical boundaries; single molecules are not considered 'particles'.

AGGLOMERATE: a collection of weakly bound particles or aggregates where the resulting external surface area is similar to the sum of the surface areas of the individual components.

AGGREGATE: a particle comprising strongly bound or fused particles.

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ISO DEFINITIONS

NANOMATERIAL: material with any external dimension in the nanoscale or having internal structure or surface structure in the nanoscale (ISO/TS 80004-1:2023 [119], def 2.4).

- Note 1 to entry: This generic term is inclusive of nano-object and nanostructured material.
- Note 2 to entry: See also engineered nanomaterial, manufactured nanomaterial and incidental nanomaterial.

NANOFIBRE: nano-object with two external dimensions in the nanoscale, and the third dimension significantly larger (ISO/TS 80004-1:2023 [119], def 3.3.5).

- Note 1 to entry: The largest external dimension is not necessarily in the nanoscale.

NANO-OBJECT: discrete piece of material with one, two or three external dimensions in the nanoscale (ISO/TS 80004-1:2023 [119], def 3.1.5).

NANOPARTICLE: nano-object with all external dimensions in the nanoscale (ISO/TS 80004-1:2023 [119], def 3.3.4).

- Note 1 to entry: If the dimensions differ significantly (typically by more than 3 times), terms such as nanofibre or nanoplate may be preferred to the term nanoparticle.

NANOPLATE: nano-object with one external dimension in the nanoscale, and the other two external dimensions significantly larger (ISO/TS 80004-1:2023 [119], def 3.3.6)

- Note 1 to entry: The larger external dimensions are not necessarily in the nanoscale.

NANOSCALE: length range approximately from 1 nm to 100 nm (ISO/TS 80004-1:2023 [119], def 3.1.1).

NANOTUBE: hollow nanofibre (ISO/TS 80004-1:2023 [119], def. 3.3.8).

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APPENDIX 2: US MICROBIOLOGICAL SAFETY CABINET CHARACTERISTICS AND APPLICABILITY FOR NANOMATERIALS

The International Organisation for Standardisation Technical Report (ISO/TR 12885) with respect to the use of HEPA filtered cabinets for nanomaterials [77].

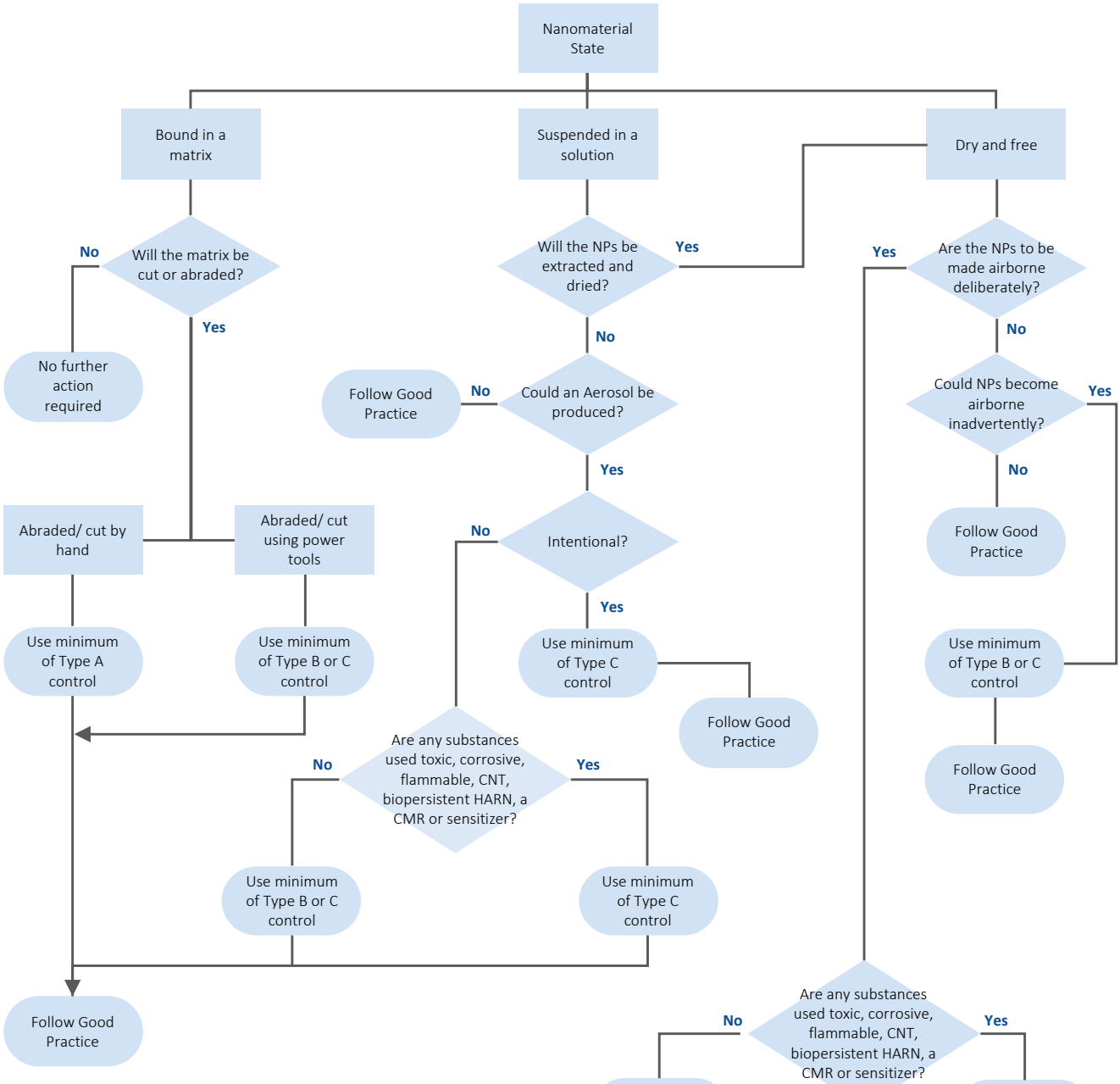
MSC Class	Face Velocity (m/s)	Airflow Pattern	Applications	
			Non-volatile Toxic Chemicals	Volatile Toxic Chemicals
I*	0.4	In at front then through HEPA to the outside or recirculate into the room through HEPA.	Yes	When exhausted outdoors [2,3]
II, A1	0.4	70% recirculated to the cabinet work area through HEPA; 30% balance can be exhausted through HEPA back into the room or to outside through a canopy unit.	Yes (minute amounts)	No
II, B1	0.5	30% recirculated, 70% exhausted. Exhaust cabinet air must pass through a dedicated duct to the outside through a HEPA filter.	Yes	Yes (minute amounts) [2,3]
II, B2	0.5	No recirculation; total exhaust to the outside through a HEPA filter.	Yes	Yes (small amounts) [2,3]
II, A2	0.5	Similar to II, A1, but has 0.5 m/s intake air velocity and plenums are under negative pressure to room; exhaust air can be ducted to outside through a canopy unit.	Yes	When exhausted outdoors (Formerly "B3") (minute amounts) [2,3]
III	N/A	Supply air is HEPA filtered. Exhaust air passes through two HEPA filters in series and is exhausted to the outside via a hard connection.	Yes	Yes (small amounts) [2, 3]

[2] Installation may require a special duct to the outside, an in-line charcoal filter, and a spark proof (explosion proof) motor and other electrical components in the cabinet. Discharge of a Class I or Class II, Type A2 cabinet into a room should not occur if volatile chemicals are used.

[3] In no instance should the chemical concentration approach the lower explosion limits of the compounds.

*A Class I microbiological safety cabinet is similar in operation to a HEPA filtered fume cupboard or HEPA filtered cabinet, drawing in air through the front opening before HEPA filtering the exhaust.

APPENDIX 3: NANOMATERIAL CONTROL MEASURES SELECTION FLOWCHART



Control Types:

A – Capturing hood, ideally discharged to a safe place outside. HEPA filtration to be used if recirculation back to the workplace

B – Partial enclosure with HEPA filtration with recirculation to the workplace

C – Partial enclosure with HEPA filtration and discharged to a safe place outside. E.g. , a fume cupboard or a well-designed bespoke partial enclosure

D – full enclosure with HEPA filtration and discharged to a safe place outside.

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APPENDIX 4: ENGINEERING CONTROLS

LOCAL EXHAUST VENTILATION (LEV):

Conventional ducted fume cupboards fitted with HEPA filtration and ducted microbiological safety cabinets may be used for HARNs, see below.

FUME CUPBOARDS

A fume cupboard is an enclosure designed to contain and exhaust vapours and gaseous contaminants generated inside it. A fume cupboard is a key engineering control device, therefore the selection of the appropriate fume cupboard design and the adherence to safe work practices are crucial to user safety.

For use with HARNs the fume cupboard exhaust air should be HEPA filtered, and wherever reasonably practicable vented to a safe place.

It is important that a fume cupboard complying with BS EN 14175 is used and that the fume cupboard does not lose containment during normal use. In most circumstances, velocity measurements and smoke test will show whether the fume cupboard is effective. Smoke tests, with appropriate detection, can be used to investigate a number of problems, such as:

- Irregular airflow and eddy characteristics resulting in air movement out of the cupboard;
- The possible negative effects of equipment on airflow;
- The possible negative effect of heat sources within the cupboard on airflow;
- Leakage from the cupboard or ducting.

However, if there is any doubt about the integrity of the fume cupboard then it may be necessary to carry out a containment test as described in BS EN 14175-3:2019 [75].

Installation of fume cupboards **must only** be undertaken by those with knowledge of British Standard CEN/TS 14175-5: 2006 'Fume cupboards, recommendations for installation and maintenance' [120]. In particular, fume cupboards must not be sited:

- On heavy pedestrian traffic routes;
- Adjacent to doors;

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- Adjacent to opening windows.

  As the above can cause air turbulence and wake effects that can affect the cupboards' containment.

- At the open end of a u-shaped laboratory bay, since a fire or explosion within the cupboard, may trap workers in the bay.

MICROBIOLOGICAL SAFETY CABINETS

Ducted microbiological safety cabinets can be used, although it should be noted that a Class II cabinet re-circulates up to 70% of its air and therefore care should be taken. The Class II and III microbiological safety cabinets, unlike the Class I type, provide protection for both the user and the material in the cabinet is working environment. All these cabinets exhaust air through a HEPA H14 filter.

DUCTLESS RECIRCULATING HEPA FILTERED SAFETY CABINETS AND RECIRCULATING MICROBIOLOGICAL SAFETY CABINETS

Safety cabinets and microbiological safety cabinets which recirculate air from the cabinet's interior, through a HEPA H14 filter, back into the laboratory can be used for small quantities of HARNs in the absence of hazardous vapours or gases.

If using a recirculating safety cabinet or recirculating microbiological safety cabinet, the following must be considered: Fume cupboards must conform to British Standard BS 7989:2001.3.

- The filter must be HEPA; charcoal filters alone must not be used†.
- The cupboard should have a filter saturated warning/alarm.
- The cupboard must have a low airflow warning/alarm.
- How is a saturated filter to be safely changed?
- How is the contaminated filter to be safely disposed of? (incineration)
- Ensure that the filter integrity test is performed.
- Subjected to thorough examination and testing at periods not greater than 14 months and more frequently if the assessment identifies higher risk; every 6 months would be good practice (see HSE guidance HSG258) [73].

Activated carbon filters are designed to absorb gases and vapours and fumes, for which they have a finite capacity. When the capacity is exceeded, contaminate is

returned to the workplace. Carbon filters alone are not designed for filtering solid materials and for these reasons the use of such systems should be avoided.

Users should take steps to ensure that the standard of supervision, training, system of work and record keeping is up to date. The safety cabinet should be set aside for use with HARNs or chemically similar materials because some other chemicals may affect the effectiveness and integrity of the fitted filter.

HEPA filter recirculating fume cupboards or cabinets can be used to control any potentially airborne 'dusty' hazardous substance as long as it is subjected to a rigorous risk assessment **BUT** should only be considered where external venting to a 'safe place' is not reasonably practicable.

NB: HEPA filtered recirculating cabinets do NOT absorb or capture, gases or vapours, for which external venting to a safe place would be required in addition to the HEPA filter.

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APPENDIX 5: EXAMPLE OF A RECORD OF WORK ACTIVITY FORM (TO BE ADAPTED AS APPROPRIATE)

Record of Work Activity Using Nanomaterials

COSHH Regulations require all individuals working with substances that can cause certain identifiable diseases or adverse health effects to be monitored. As a pre-cautionary measure, the employer could complete a Record of Work Activity for all individuals working with nanomaterials and nano-objects (particles of approximately 100 nm or less in at least one dimension) with unknown toxicological properties.

Personal Details	
Surname:	Forenames:
	Date of Birth:
N.I. Number:	
Date commenced present job:	
Permanent address:	
Postcode:	Dept Tel No:
Status: Staff/ Undergraduate student/ Postgraduate student/ Visitor/ Other (Delete as appropriate)	
Department:	
Supervisor's name and contact telephone number:	
Signed:	**Date:**

PLEASE COMPLETE SUBSTANCE DETAILS OVERLEAF

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SUBSTANCE DETAILS					
Date(s)	**Name(s) of nano-objects**	**Physical state[1]**	**Quantity, amount[2]**	**Frequency/duration of use[3]**	**Control measures in use[4]**

Key:
1 Powder, liquid, solid – this includes free nano-objects, nano-objects in liquid suspension, or nano-objects in a solid matrix
2 Include amount and units if known
3 Daily, weekly, monthly, rarely
4 Fume cupboard, laminar flow bench, Local Exhaust Ventilation (LEV), glove box or other form of containment, personal protective equipment (please specify)

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APPENDIX 6: SAMPLING PROTOCOL TO ASSESS RELEASE OF PARTICULATE NANOMATERIALS TO AIR

This protocol is designed to assess the release of nano-objects into workplace air. It allows the effectiveness of the controls to be checked and, if necessary, to confirm that exposure to the particles of concern was taking place. Positive results should trigger a review and improvement of the control approaches used. Other more comprehensive strategies (e.g., Brouwer *et al.* (2009) [85], OECD (2015) [89]) are described in the literature, which may give improved background discrimination. Given the developmental nature of this field of measurement, the detection limits for any of the strategies are not yet well-defined.

COLLECTION OF SAMPLES FOR MASS CONCENTRATIONS AND OFF-LINE ANALYSIS

Airborne nano-objects and their aggregates and agglomerates should be collected on filters using respirable, and/or inhalable samplers. The filters are gravimetrically and chemically analysed, e.g., for metal-based nanoparticles by X-ray fluorescence (XRF) or inductively coupled plasma atomic emission spectroscopy (ICP-AES) or Inductively coupled plasma mass spectrometry (ICP-MS).

Open-faced samplers are used for sampling carbon nanotubes and graphene on filters. Since these materials are primarily elemental carbon, techniques such as thermal-optical analysis (TOA) can be used to quantify their presence. However, background samples are needed, as elemental carbon may also be present from other sources in the environment.

A number of sampling techniques for the collection of airborne particles and subsequent transmission or scanning electron microscopy (TEM or SEM) analysis are available and include:

- Filtration onto filters or carbon films supported on transmission electron microscopy (TEM) grids using a conventional sampling pump. TEM grids with a holey carbon film can be attached to filters. Filters can be pre-coated with gold for subsequent scanning electron microscopy (SEM) analysis.
- Precipitation using thermal or electrostatic precipitators.

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A sampler should be personal, and/or positioned close to the activity/process, and at a distance of at least 2 to 3m from the process/task (optional) alongside the CPCs and OPCs. Samples collected inside containments/fume-cupboards are also very useful for comparison with samples collected outside containments/fume-cupboards. Blank field samples should also be deployed.

Additional information is provided in MDHS 14/4 [121], ISO 20581:2016 [122], ISO 15202-1:2020 [123], ISO 30011:2010 [124], Harper and Demange (2007) [125], and Asbach *et al.,* (2016; NanoIndEx guidance) [126].

REAL-TIME MEASUREMENTS OF PARTICLE NUMBER CONCENTRATIONS

Particle number concentrations of airborne particulate nanoparticles including the aggregates and agglomerates are monitored using a CPC and an OPC. An initial assessment without the process / task running should be carried out. A CPC and an OPC are moved around to investigate any other potential sources of non-manufactured nano-objects and the range in the background concentration. If possible these sources should be isolated or stopped during the monitoring period.
Measurements using a CPC and an OPC should be carried out before, during and after the activity under study takes place. The CPC and the OPC are stationary and positioned close to the worker's task (within an approximate 1 m radius of the worker's head) taking care that they do not hinder or interfere with the worker's normal duties. Non-activity periods (before and after the activity period) should be monitored for at least 15 minutes if possible.

Measurements using a second CPC and a second OPC could be carried out before, during and after the activity under study takes place. The instruments are stationary and should be located at a distance from the activity, such that it measures airborne particle concentrations that are representative of the background concentration near the activity. A distance of at least 2 to 3 m is suggested. The non-activity periods (before and after the activity period) should be monitored for at least 15 minutes if possible.

A CPC could also be used with the telescopic probe attachment to monitor particle number concentration inside containment/fume cupboards during activity periods.

Be aware that any other extraneous sources of non- manufactured nano-objects or ultrafine particles such as: passing lorries/forklift trucks, electric motors, smoke-generating systems, welding/soldering activities, open doors and windows can influence particle concentration readings greatly.

Smoke tubes, for testing the efficacy of local exhaust ventilation, should not be used during the monitoring of the activities. It has been shown during previous studies that these can be a source of very high concentrations of airborne non- manufactured nano-objects or ultrafine particles.

All instruments should be calibrated in accordance with manufacturer's guidance and at least every year and regularly checked to ensure consistent operation, especially their performance relative to each other if several of the same instruments are used

RECORD AND CONTEXTUAL INFORMATION

The times at which the real-time monitors and samplers were started and stopped together with the sampler flow rates should be recorded. It is also critical that detailed contextual information of all activities before, during, and after the task/process takes place are recorded as an increase in particle number concentrations from the real-time instruments may be unrelated to the task/process.

INTERPRETATION OF RESULTS

Particle number concentration should be plotted and arithmetic means, minimum and maximum concentrations before, during, and after the task/process should be calculated. A difficult question to answer is if an increase in particle number concentration means there has been a corresponding emission of nano-objects from the task/process. For that, the "task/process" particle number concentration must be higher than the "background" particle number concentration and this increase has to be statistically significant. However, some critical judgement should also be applied. The background may greatly fluctuate, or it can gradually increase or decrease with time. The contextual information is important in this decision-making as well as knowing whether other sources of non-manufactured nano-objects or ultrafine particles are present. The off-line analysis of the sample will confirm the presence or absence of the manufactured nano-objects, and if necessary, may be used to quantify the number concentrations related to the task/process.

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For risk management purposes, the monitoring data and analysis results can be used alongside an occupational hygiene assessment of the effectiveness of the control measures (using techniques such as air velocity measurements, smoke tubes and expert knowledge to determine the level of control achieved).

ADDITIONAL INFORMATION AND REFERENCES

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