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SERIES ON THE SAFETY OF MANUFACTURED NANOMATERIALS
Number 10

IDENTIFICATION, COMPILATION AND ANALYSIS OF GUIDANCE INFORMATION FOR
EXPOSURE MEASUREMENT AND EXPOSURE MITIGATION: MANUFACTURED
NANOMATERIALS

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**OECD Environment, Health and Safety Publications
Series on the Safety of Manufactured Nanomaterials**

No. 10

**IDENTIFICATION, COMPILATION AND ANALYSIS OF GUIDANCE INFORMATION FOR
EXPOSURE MEASUREMENT AND EXPOSURE MITIGATION: MANUFACTURED
NANOMATERIALS**

IOMC

INTER-ORGANIZATION PROGRAMME FOR THE SOUND MANAGEMENT OF CHEMICALS

A cooperative agreement among UNEP, ILO, FAO, WHO, UNIDO, UNITAR and OECD

**Environment Directorate
ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT
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- No. 1, *Report of the OECD Workshop on the Safety of Manufactured Nanomaterials: Building Co-operation, Co-ordination and Communication (2006)*
- No. 2, *Current Developments/ Activities on the Safety of Manufactured Nanomaterials: Tour de table at the 1st Meeting of the Working Party on Manufactured Nanomaterials (2006)*
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- No. 8, *Preliminary Analysis of Exposure Measurement and Exposure Mitigation in Occupational Settings: Manufactured Nanomaterials (2009)*
- No.9, *EHS Research Strategies On Manufactured Nanomaterials: Compilation Of Outputs (2009)*
- No.10, *Identification, Compilation and Analysis of Guidance Information for Exposure Measurement and Exposure Mitigation: Manufactured Nanomaterials (2009)*

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FOREWORD

The OECD Joint Meeting of the Chemicals Committee and Working Party on Chemicals, Pesticides and Biotechnology (the Joint Meeting) held a Special Session on the Potential Implications of Manufactured Nanomaterials for Human Health and Environmental Safety (June 2005). This was the first opportunity for OECD member countries, together with observers and invited experts, to begin to identify human health and environmental safety related aspects of manufactured nanomaterials. The scope of this session was intended to address the chemicals sector.

As a follow-up, the Joint Meeting decided to hold a Workshop on the Safety of Manufactured Nanomaterials in December 2005, in Washington, D.C. The main objective was to determine the “state of the art” for the safety assessment of manufactured nanomaterials with a particular focus on identifying future needs for risk assessment within a regulatory context.

Based on the conclusions and recommendations of the Workshop [ENV/JM/MONO(2006)19] it was recognised as essential to ensure the efficient assessment of manufactured nanomaterials so as to avoid adverse effects from the use of these materials in the short, medium and longer term. With this in mind, the OECD Council established the OECD Working Party on Manufactured Nanomaterials (WPMN) as a subsidiary body of the OECD Chemicals Committee. This programme concentrates on human health and environmental safety implications of manufactured nanomaterials (limited mainly to the chemicals sector), and aims to ensure that the approach to hazard, exposure and risk assessment is of a high, science-based, and internationally harmonised standard. This programme promotes international co-operation on the human health and environmental safety of manufactured nanomaterials, and involves the safety testing and risk assessment of manufactured nanomaterials.

This document is intended to provide information on the outcomes and developments of the WPMN related to the safety of manufactured nanomaterials. It compiles guidance information for exposure measurement and exposure mitigation for manufactured nanomaterials in occupational settings; and addresses their adequacy for manufactured nanomaterials.

The Working Party endorsed this report at its 5th Meeting on March 2009. This document is published on the responsibility of the Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology of the OECD.

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THE WORKING PARTY ON MANUFACTURED NANOMATERIALS (WPMN)

The Working Party on Manufactured Nanomaterials¹ was established in 2006 to help member countries efficiently and effectively address the safety challenges of nanomaterials. OECD has a wealth of experience in developing methods for the safety testing and assessment of chemical products.

The Working Party brings together more than 100 experts from governments and other stakeholders from: a) OECD Countries; b) non-member economies such as Brazil, China, the Russian Federation, Singapore and Thailand; and c) observers and invited experts from UNEP, WHO, ISO, BIAC², TUAC³, and environmental NGOs.

Although OECD member countries appreciate the many potential benefits from the use of nanomaterials, they wished to engage, at an early stage, in addressing the possible safety implications at the same time as research on new applications is being undertaken.

The Working Party is implementing its work through eight main areas of work to further develop appropriate methods and strategies to help ensure human health and environmental safety:

- Development of a Database on Human Health and Environmental Safety (EHS) Research;
- EHS Research Strategies on Manufactured Nanomaterials;
- Safety Testing of a Representative Set of Manufactured Nanomaterials;
- Manufactured Nanomaterials and Test Guidelines;
- Co-operation on Voluntary Schemes and Regulatory Programmes;
- Co-operation on Risk Assessment;
- The role of Alternative Methods in Nanotoxicology; and
- Co-operation on Exposure Measurement and Exposure Mitigation.

Each area of work is being managed by a steering group, which comprises members of the WPMN, with support from the Secretariat. Each steering group implements its respective “operational plans”, each with their specific objectives and timelines. The results of each project are then evaluated and endorsed by the entire WPMN.

This document was prepared by the WPMN steering group 8 leading the work on *Co-operation on Exposure Measurement and Exposure Mitigation*. The Working Party endorsed this report at its 5th Meeting on March 2009.

¹ Updated information on the OECD’s Programme on the Safety of Manufactured Nanomaterials is available at: www.oecd.org/env/nanosafety

² The Business and Industry Advisory Committee to the OECD

³ Trade Union Advisory Committee to OECD.

CO-OPERATION ON EXPOSURE MEASUREMENT AND EXPOSURE MITIGATION

In November 2007, the OECD Working Party on Manufactured Nanomaterials decided to start work on **Co-operation on Exposure Measurement and Exposure Mitigation**. A steering group lead by the US, and comprising delegates from the WPMN, was tasked with developing this work.

The operational plan outlines three phases of work: 1) exposure in occupational settings; 2) exposure to humans resulting from contact with consumer products and environmental releases of manufactured nanomaterials; and 3) exposure to environmental species resulting from environmental releases of manufactured nanomaterials including releases from consumer products containing manufactured nanomaterials.

The objectives of phase 1 are described as:

- To identify and compile guidance information for exposure measurement and exposure mitigation for manufactured nanomaterials in occupational settings, including manufacture and use of products in industrial, institutional and commercial settings; and
- To analyze existing guidance information for their adequacy in addressing manufactured nanomaterials, identify issues that are unique to manufactured nanomaterials, and prepare recommendations for next steps to be undertaken by the WPMN.

This report compiles guidance information for exposure measurement and exposure mitigation for manufactured nanomaterials in occupational settings; and addresses their adequacy for manufactured nanomaterials.

More information about the work of the WPMN, as well as publications and updates on efforts of governments and other stakeholders to address safety issues of nanomaterials is available at <http://www.oecd.org/env/nanosafety>.

INTRODUCTION

The Ministry of Housing, Spatial Planning and the Environment from the Netherlands (VROM) allocated specific resources to support the work of the WPMN project Co-operation on Exposure Measurement and Exposure Mitigation. The resources funded the contractor *TNO Quality of Life* (TNO) to further the analysis on guidance information for exposure measurement and exposure mitigation.

This project aimed at:

- a) Compiling guidance information for exposure measurements and exposure mitigation for manufactured nanomaterials in occupational settings as identified by the WPMN;
- b) Collecting information on existing data and ongoing activities with respect to actual exposure measurements in occupational settings;
- c) Analysing and evaluating existing guidance information on exposure measurements and exposure mitigation for adequacy in addressing manufactured nanomaterials; and
- d) Prepare an overall report and recommendations for next steps to be undertaken by the WPMN.

Accordingly, the TNO group prepared several drafts of the document *Identification and compilation and analysis of guidance information for exposure measurements and exposure mitigation*, to which the WPMN steering group leading this project, provided inputs.

The final document was presented at the 5th WPMN (March 2009). The 5th WPMN agreed to send it to the Chemicals Committee with a request for its declassification.

MATERIALS AND METHODS

The WPMN provided a bibliography of identified guidance documents. In addition, two other documents were identified with potentially relevant information for the purpose of the project.

A template was developed to characterize the documents for an overall evaluation and to address the following questions:

- Does the existing information reflect ‘state-of-the-art’ on exposure measurements and mitigation?
- Does the evaluation reveal ‘information/knowledge gaps’ on exposure measurements and mitigation?

The template consists of the following key parameters:

- General characterization
 - Purpose or scope;
 - Document type;
 - Origin authors (background);
 - Focus of contents.
- Contents and level of detail
 - Exposure (Risk assessment)
 - Measurement Methods Inhalation;
 - Measurement Methods Dermal;
 - Measurement/ Sampling strategy;
 - Recommendations;
 - Evaluation of gaps or needs.
 - Exposure mitigation (risk management)
 - Risk management strategies;
 - Control Hierarchy;
 - Specific measures;
 - Data on effectiveness;
 - Recommendations;
 - Evaluation of gaps or needs.
- Evaluation
 - Specificity (Engineered) nano particles;
 - Robustness of data.

In addition to the identified documents, it was tried to include information, e.g. web site information, presentations etc, generated by ongoing, completed and/or started (EU-supported) projects on

related topics e.g. NANOTRANSPORT⁴, NANOSAFE and its follow-up project NANOSAFE2⁵, and NANOSH⁶, NANODEVICE⁷ and NANOIMPACTNET⁸ as far as considered relevant and accessible to non-participants. Moreover, the recently available overview of European and National projects overview document available on the web⁹ and different relevant documents of various European Technology Platforms (ETPs) including, e.g. the Industrial Safety¹⁰ were consulted to obtain further relevant information.

⁴ <http://research.dnv.com/nanotransport/>

⁵ <http://www.nanosafe.org/>

⁶ <http://www.ttl.fi/Internet/partner/Nanosh/>

⁷ see presentation at the EC Workshop held 17+18 April 2008 on <http://cordis.europa.eu/nanotechnology/src/events.htm>

⁸ <http://www.nanoimpactnet.eu/> and presentation at the EC Workshop held 17+18 April 2008 on <http://cordis.europa.eu/nanotechnology/src/events.htm>

⁹ <ftp://ftp.cordis.europa.eu/pub/nanotechnology/docs/final-version.pdf>.

¹⁰ www.industrialsafety-tp.org: <http://euvri.risk-technologies.com/events/>.

INFORMATION

Documents

The documents that were identified, summarized if available and/or included in the evaluation are listed in Annex I (Table A1.1). In total twenty documents were identified, from which sixteen were available. Of fourteen documents a summary was available (see Annex II). Document #10 (ICON) consists of two parts, which were assessed separately.

The summaries of key documents as drafted by the WPMN as such are included in Annex II. In total ten documents, with information on exposure assessment, were summarized and eight documents in the field of exposure mitigation. Extended summaries/abstracts of documents #11, 15 and 16 were copied and are also represented in Annex II.

The complete template is listed in Annex III. A general description with emphasis on purpose/scope, type of document, and scope of contents is given for all 16 available documents (Table A3.1). Since document #14 (Weis et al.) was not specifically dedicated to nanomaterials, it was considered obsolete for the purpose of the present review and it was not further assessed.

Table A3.2 specifies whether the documents address the listed topics in the area of exposure assessment (instrumentation, methodologies etc) and exposure mitigation, and if so to what extent. In addition, it is indicated whether the document provides recommendations or identifies knowledge gaps for the specific area.

Two main categories of documents were distinguished:

- a) Documents intended to provide guidance for exposure, hazard, risk assessment and/ or safe use of (manufactured) nanomaterials;
- b) Documents intended to identify research needs for nanomaterials from environmental, health and safety perspectives.

Amongst the documents of the first category four documents were drafted by Standardization bodies (ASTM, BSI and ISO) and four documents by Governmental bodies/ agencies. The documents of the second category were published by NIOSH (US), EPA (US), EU Commission, and by (inter)national nanotechnology bodies.

In a preliminary evaluation (Table A3.3), it is indicated whether the documents are specific for or dedicated to engineered/manufactured nanomaterials or address nanomaterials more in general. In addition, transparency of the underlying sources, diversity of references and cross references are considered as indicators for robustness of documents contents.

Information from on-going European research projects and part of activities within European Technology Platforms (ETPs)

Additional information was requested from a number of ongoing FP6 and new FP7 EU-projects on related topics including, e.g. NANOSAFE, NANOSAFE2, NANOSH, NANOTRANSPORT, NANODEVICE and NANOIMPACTNET.

Within the NANOSH project field studies are in preparation and some interesting developments can be observed with respect to measurement/sampling strategy¹¹. Information about the NANOSAFE2 project could be obtained from several websites (see footnotes); where as some preliminary results of the NANOTRANSPORT project were obtained through personal communication. The major results so far are listed in table 1.

Table 1. Overview of interesting studies (in preparation/ ongoing) with respect to exposure assessment (measurement, sampling) and exposure mitigation

¹¹ <http://www.ttl.fi/Internet/partner/Nanosh/>

Item	Project	Description	Status
Identification of sources of engineered/ manufactured nano particles	NANOSH	Chain / combination of measurements to distinguish Manufactured Nanoparticles (MNPs) from other Nanoparticles (NPs).	Included in revised sampling strategy for main study
Characterization of particles; sampling	NANOSH, NANODEVICE, NANOIMPACTNET	Use of precipitators for direct deposition of nano particles on TEM grid and for NANODEVICE identification of relevant physical and chemical properties for specific measurement of airborne manufactured nanoparticles including the investigation of relationships between physical and chemical properties of airborne manufactured nanoparticles including their potential toxicity or bioactivity and for NANOIMPACTNET define joint strategies and protocols for nanomaterials exposure assessment	Pilot studies showed feasibility of its application: Included in revised sampling strategy for main study and for NANODEVICE project currently under negotiation and for NANOIMPACTNET work started in April 2008
Characterization of particles; sampling and on-line detection including assessment of various methodologies	NANOSAFE2, NANODEVICE , NANOIMPACTNET	Development of new devices sampling (and on-line detection) including assessment of various methodologies and for NANODEVICE identification of relevant physical and chemical properties for specific measurement of airborne manufactured nanoparticles including the investigation of relationships between physical and chemical properties of airborne manufactured nanoparticles including their potential toxicity or bioactivity and for NANOIMPACTNET define joint strategies and protocols for nanomaterials exposure assessment	In progress and NANODEVICE project currently under negotiation and for NANOIMPACTNET work started in April 2008
Characterization of particles; personal exposure	NANOSH, NANODEVICE	Direct deposition of nano particles on TEM grid in breathing zone and for NANODEVICE development of technologies that enable the utilisation of new concepts in miniaturised and field-worthy specific monitors for airborne manufactured nanoparticles including the development of methods for calibration and testing of newly developed concepts, methods and devices in simulated and real exposure settings	Included in revised sampling strategy and NANODEVICE project currently under negotiation
Qualitative assessment of dermal exposure	NANOSH, NANOIMPACTNET	Introduction of a slightly modified version of a structured questionnaire (DREAM) & for NANOIMPACTNET define joint strategies and protocols for nanomaterials exposure assessment	Pilot studies showed feasibility of its application and evidence of dermal exposure potential & for NANOIMPACTNET work started in April 2008
Decrease of particle release during production of Manufactured Nanoparticles (MNPs)	NANOSAFE2, NANOIMPACTNET	Development of reactor for synthesis of powders & for NANOIMPACTNET define joint strategies and protocols for handling of nanomaterials	In progress & for NANOIMPACTNET work started in April 2008
Air purification/ respirators	NANOSH/ NANOSAFE2	Filter efficacy testing	Scheduled/ in progress
Aerosol dynamics of NPs	NANOTRANSPORT	Adherence and coagulation of NPs after release	Preliminary results

ANALYSIS

General

The majority of the guidance information was identified and compiled by the WPMN (see also Annex I and Annex III). Several documents, especially country specific guidance documents, were in a preliminary stage of drafting and therefore not available.

We categorized the documents according to its primary objective or scope, i.e. intended to provide guidance for exposure, hazard, and/or risk assessment, and intended to identify knowledge gaps

In the category of documents intended to provide guidance for exposure, hazard, and/or risk assessment all documents except for one address inhalation exposure assessment and sampling strategy. A relatively high level of detail was provided in most documents. Most documents provide some recommendations on sampling strategy. Only two documents address dermal exposure assessment issues.

The two research papers (#12 and 15) are not focused on exposure mitigation. Most of the other documents address risk management strategies and the hierarchy of control and summarize specific control measures, however in most documents data on effectiveness are lacking.

The documents intended to identify research needs for nanomaterials from environmental, health and safety perspectives (second category), address exposure assessment and mitigation approaches and methodologies from a perspective of adequacy to provide information for decision/policy making. Therefore, the level of details is less compared to the documents of the first category mentioned above.

Document #1 (ISO TC 229 WG3 report) is the most recent and considered as most comprehensive document in view of providing state-of-the-art-information on exposure assessment and mitigation. The documents cross refers extensively to the other documents. Therefore, this document will form the basis of the preliminary analysis.

Exposure measurement and sampling

Objectives of exposure sampling would be:

1. evaluation of exposure processes and pathways is an important tool for selecting an adequate sampling strategy and for effective risk management;
2. evaluation of control measures is relevant in view of effectiveness of exposure reduction and post-intervention surveillance;
3. results for risk assessment purposes should be linked to results of hazard assessment;
4. to investigate possible associations between exposure and health effects by epidemiological investigations estimates of relevant parameters of exposure are needed; and
5. compliance sampling is relevant in case exposure limits have been set.

It is recognized that, for the time being, there is no agreement on key exposure metrics that is appropriate for an adequate risk assessment.

Inhalation exposure

On-line detection

Several measurements techniques/ instruments are identified that are capable for on-line detection and quantification of mass-concentration of aerosols in (aerodynamic diameter) nano-range (e.g. ELPI, or TEOM), number-concentration of aerosols in (mobility diameter) nano-range (e.g. SMPS), and (Fuchs) surface area concentration of (nano) aerosols (e.g. Diffusion Charger). Apart from on-line results as provided by SMPS and ELPI, the results can also be used for calculations of mass (SMPS and ELPI), number (ELPI) and surface area (SMPS and parallel use of ELPI and SMPS).

Sampling and off-line detection

With respect to (size fractionated) sampling and off-line detection size selective sampling as provided by (low pressure cascade) impactors e.g. Berner type and ELPI, can be used for off-line analysis by weighing, by electron microscopy (SEM and TEM) or a variety of detection techniques (XRD;XRF, ICPMS, XPS etc.). Identification of the particles, by determination of specific characteristics such as geometry, agglomeration state, projected diameter and crystallinity or chemical composition, is also important to distinguish between Manufactured Nanoparticles (MNPs) and non-MNPs in workplace air.

Recently, within the NANOSH project (electrostatic) precipitators are used for nano size selective sampling of NPs directly onto a TEM grid, to facilitate appropriate TEM analysis without sample preparation. The concept of direct sampling onto a TEM grid has also been explored for personal sampling.¹²

A comprehensive characterization of aerosols, i.e. size distribution, concentration and chemical for both on-line chemical monitoring and workplace surveillance, is envisaged in the NANOSAFE2 project. New devices for collection of samples based on diffusion and negative thermophoresis as well as portable sampling devices are currently developed within this project.

Sampling strategy

Possible overestimation of indoor MNP-levels by penetration of outdoors sources and/or other incidental released airborne materials resulting in relatively high background levels emphasize the need for source identification (emission) and/ or material characterization.

Sampling strategy issues have been elaborated within the NANOSH project, with emphasis on source identification (multi-location sampling, ventilation patterns etc), and work tasks observations for interpretation of static sampler results.

Dermal Exposure

General sampling principles for dermal exposure, e.g. removal and interception procedures, are considered to have potential for appropriate sampling of NPs to estimate dermal exposure, however, their applicability has not been demonstrated so far.

Within the NANOSH project, a subjective method based on structured observations to assess dermal exposure qualitatively (DREAM) has been explored successfully (Brower, 2007).

¹² Deliverable 2.1 www.ttl.fi/internet/partner/NANOSH

Observations/ considerations

With respect for interpretation of the results for (personal) exposure it should be noted that

- These static instruments will only monitor aerosols at a given location over a device-driven response time, possibly underestimating temporal variations.
- These static instruments will not take into account both spational and temporal variations of aerosol concentration and size-distributions in the breathing zone of a worker (i.e. position will differ in time from position of static instruments)
- These instruments do not distinguish between MNPs and non-MNPs or source-emission from background/ ambient contamination.

Several future (FP7) projects e.g. NANODEVICE, will address these issues and are aimed at the development of portable, relatively inexpensive and easy-to use devices that could be used for breathing zone measurements of potential relevant exposure parameters.

Exposure mitigation***Control Hierarchy***

General principles of control, e.g. the hierarchy of control, are recommended for complementary approaches by most documents. Recommendations are discussed along this format with variable level of detail.

Eliminating exposures- through effective design

General considerations are given in most of the documents.

Recently, within the NANOSAFE2 project, a reactor has been developed allowing powder synthesis under supercritical conditions in a confined area which avoids potential nanoparticle release/ emission to the workplace air and exposure in the work place atmosphere. Moreover, a liquid recovery method was developed for MNPs produced by laser pyrolysis.

Substitution

General considerations and principles are given including changes of the physical form of the materials to prevent or decrease emissions, eg. dispersion instead of powder, or nanomaterials-specific embedding and encapsulation or coating of nano particles.

Engineering techniques

General engineering techniques, e.g. enclosure, isolation, extraction) used to prevent or reduce emissions of particles, fumes and vapors are discussed. Most of these techniques are used in nanotechnology industries; however, for most techniques no data on performance for nanomaterials are reported.

It will be feasible to implement many of the engineering controls for small-scale use scenarios. For industrial use scenarios and operations, more specifically bagging, and cleaning and maintenance operations, extraction (fume hoods/ LEV) is the most commonly used technique. However, some specific designs for safe collection of nanomaterials have been described.

Key issue in filtration for air recirculation is the performance of HEPA filters. Although current methods for certification of HEPA do not routinely require testing at particles size below 100nm, filtration

theories predict a decrease of particle penetration with the decrease of size. However, for particles below 2 nm this might be different.

Filter efficiency testing is a topic that is addressed by many ongoing projects e.g. NANOSAFE2, NANOSH and NIOSH research programs [see also *Personal Protective Equipment (PPE)*].

Administrative means

General approaches, e.g. modification of work practices, limiting number of exposure worker, instruction and training etc, and (non-nanomaterial) routine procedures are described.

Personal Protective Equipment (PPE)

Both protection from inhalation and dermal exposure are addressed. For respirator performance, filter and mask performance, is referred to US (OSHA and NIOSH) approaches, e.g. APF and Decision Logic. The concern about the performance of filters in the subnano-range (< 2 nm) is similar as for the HEPA filter air purification performance.

For dermal exposure protection it recognized that material testing for certification e.g. CE, based on permeation testing, will probably only hold for liquids. Nanotechnology industries report that material selection is based on the solvents being used. Standard penetration tests performed with macro sized particles will probably overestimate the protection performance of permeable materials.

Effectiveness testing of PPE (respiratory and skin protective devices and materials) for nanoparticles is part of many research programs (NIOSH) and projects (NANOSH and NANOSAFE2). Currently, the first NANOSAFE2 dissemination report¹³ published the first results, indicating that HEPA filters and respirator cartridges made with fibrous filters are even more efficient for nanoparticles. Non woven fabrics (air-tight materials) seem to be effective against nanoparticle penetration, whereas cotton fabrics are less effective. In addition, some commercially available glove materials show substantial penetration, especially for 80 nm nanoparticles.

Observations/ considerations

Most of the exposure control/ mitigation measures are based on performance and proven adequacy for (multi-sized) aerosols rather than specifically for nanosized aerosols. Since there is lack of information on size-distribution of MNPs in most exposure scenarios this might not be improper, assuming rapid agglomeration of primarily particles or attachment to larger background particles (preliminary results from the NANOTRANSPORT project).

Since no safe levels/ thresholds for exposure have been established and there is no guidance what level the remaining exposure can be considered as safe, the ability of control measures to reduce exposure can only be evaluated with respect to relative effectiveness, as percentage of penetration, percentage reduction etc.

Emphasis is given on prevention/ decrease of inhalation exposure e.g. by changing physical form of powders (embedding, or liquid suspensions).

¹³ Nanosafe Dissemination report DR-325/326-200801-1, January 2008; www.nanosafe.org

For small-scale use of nanomaterials (start-up/ lab scale) more general control measures as is common practice for known hazardous substances are sufficient and feasible to use.

Discussion

The documents as identified seem to reflect state-of-the-art information as far as publicly accessible. The most recent information and results of ongoing research projects provide a very valuable update. It should be noted that most of this type of information is only made accessible during the life time of the project by dissemination of results in scientific meetings or through the project website; however, detailed information seems to be generated only after the end of the project.

Only dedicated projects or task forces will be able to cover most recent information of all types.

There are two important underlying knowledge gaps, which affects the needs on exposure assessment and mitigation strongly. Since exposure assessment and mitigation should be directed on reduction of risks, both hazard and dose (resulting from exposure) should be known. With respect to hazard (toxicity), only a few types of nanomaterials have been studied so far, mostly in in-vitro studies. Currently, no insight exists in the basis characteristics of nanomaterials that will determine toxicity. This can even be more complicated by observations that modifications or impurities can change toxicity. With respect to dose, it is largely unknown in which way (e.g. state of aggregation or agglomeration) nanomaterials are presented to humans. This may largely influence internal dose related to both inhalation and dermal exposure, and hence the potential to elicit adverse health effects.

Knowledge gaps on exposure assessment are discussed in some of the documents. There is consensus on the following issues;

Currently, there is lack of agreement on metric of exposure for an appropriate risk analysis. Consequently, no specific exposure limits have been established. Multifaceted approaches are used and recommended to characterize workplace exposure.

Since no commercially available personal devices are capable to measure relevant exposure parameters in the breathing zone, the focus for inhalation exposure assessment is on area sampling and/or on-line detection. Current running and proposed projects will address the issue of the development of personal devices.

Spatial and temporal variations of aerosol concentration, size distributions etc resulting from aerosol dynamics limit the accuracy of interpretation of the results from static devices to personal exposure. Sampling strategies are developed and adjusted to enable more reliable estimates.

Since on-line measurement devices do not discriminate between manufactured NPs and unintended NPs originating from other sources, sampling and off-line characterization is considered a key factor for evaluation of data generated by other devices. Currently running research projects address the issue of appropriate sampling of aerosols, both in workplace air and the breathing zone.

Since there are many gaps on knowledge of the hazard nanomaterials, precautionary risk management of occupational production and use of nanomaterials is focused on exposure control. For guidance on safe production and use of MNPs, it is recognized that the conventional approaches exposure control as given in the hierarchy of control will provide sufficient guidance for exposure mitigation. This is based on the current knowledge, data on effectiveness of control for (general and not necessarily specific for nanosized) aerosols, and dedicated testing studies

Based on aerosol dynamics, however, it can be argued in which exposure scenarios both in production and down-stream use of MNPs single nanosized aerosols will be present at substantial levels. Current and proposed research should be able to give directions in due time.

Efficiency testing of PPE (devices and materials) for real workplace conditions and with commercially available nanomaterials is considered to be relevant since real workplace conditions and properties of commercial nanomaterial products may affect permeation and penetration through materials differently compared to laboratory test conditions or specially prepared test materials.

For small-scale production and use exposure scenarios, e.g. research/ development) conventional safety guidelines and practices based on general hazardous materials will be feasible to use. For up scaled production and use existing approaches for exposure mitigation might be effective, however, their effectiveness for the nanomaterials has not completely been proven yet.

CONCLUSIONS AND RECOMMENDATIONS

Provide recommendations on measurement techniques and sampling protocols for inhalational and dermal exposures in the workplace

There is a strong need for guidance on the development of appropriate sampling protocols for inhalation and dermal exposures in the workplaces. These sampling protocols should include a) *selection of appropriate exposure metrics and exposure measure(s)*, b) *selection of an appropriate sampling- or measurement strategy*; and c) *guidance to evaluate the measurements results*.

a) Selection of appropriate exposure metrics and exposure measure(s)

Most of the currently performed measurements with respect to nano particles are explorative by nature and focused on range finding. Data collected during the measurements can be used for benchmarking of exposure scenarios or tasks.

In case exposure assessment is meant to be linked to hazard assessment or health effects, i.e. objectives 3 and, or 4 (see page 17), the exposure metrics should be driven by the hazard/ risk assessment. Focused on nano particles, ideally it should be known what dose (and thus exposure) metric(s) is/ are relevant, i.e. mass of particles, numbers of particles, or surface area of particles, and thus the relevant exposure metrics (mass concentration ($\mu\text{g}/\text{m}^3$), number concentration (p/cm³), total particles surface area concentration ($\mu\text{m}^2/\text{cm}^3$). In addition, it should be known what exposure measure(s) is/ are relevant (for the health effects (exposure –response relationship), i.e. average concentration, peak concentration, and or cumulative concentration.

The state-of-the-art knowledge of hazard and risk related to nano particles, however, does not provide guidance for exposure assessment, rather than that all exposure parameters should be determined. As exposure-relationship for effects (if any) are unknown yet neither indications can be given of the most appropriate exposure metric(s). Again, the most feasible approach would be to determine all types of exposure measures.

b) Selection of an appropriate sampling- or measurement strategy

In general, the data output from (static) devices do not enable a straight forward interpretation to personal exposure to MNPs for three major reasons. Firstly, (near) real-time monitoring instruments do not provide a positive identification of type/identity of aerosols or distinguish between ‘background’ aerosols and MNPs; secondly, the time-response characteristics or time resolution of the devices may not be sufficient to detect rapid temporal variances of air contaminant parameters due to process or tasks characteristics, or air movements, etc. Thirdly, spatial variances of air contaminant parameters, e.g. concentration and size distributions, limit simple extrapolation of the data for one location to ambulant positions of a person/worker.

To distinguish MNPs from non-MNP currently several approaches, either stand-alone or combined, are used as part of a sampling strategy.

- I. Evidence-based. In case (potential) exposure is assumed to result from distinct activities or tasks, e.g. bag emptying of a MNP product, task-related ‘exposure’ measurements can be compared

with ‘background’, i.e. without activities. In situations where (semi) continuous emission is likely, and thus far field exposure, this approach might not be feasible.

- II. Sampling for characterization/ identification. Simultaneously with the real-time monitoring, samples are taken either by a static device or by personal sampling (breathing zone). Appropriate devices (e.g. electrostatic precipitators) afford direct deposition of (nano-sized) onto TEM-grids for electron microscopic analysis, possibly followed by chemical analysis.

Recent research on aerosol formation during mechanical agitation or dumping of NMP products (Schneider et al. 2007) show a fast variation of aerosol size distributions and number concentration. A commonly used instrument for size-selective detection of particle concentration such as the Scanning Mobility Particle Sizer in its basic configuration uses approximately 30-120 s for a complete run over the various size fractions, whereas the recently introduced Fast Mobility Particle Sizer (TSI) reduces run time until approximately 1 s.

Spatial variances of size distributions and number concentration, e.g. due to dilution, agglomeration, impaction and deposition, has been demonstrated. Since currently personal devices are not available, no direct measurements relevant for personal exposure can be made. Estimates, however, can be based on results from static devices in well-designed studies/ measurement strategies.

c) *Guidance to evaluate the measurements results*

In addition to considerations related to interpretation of data generated by static devices for personal ‘exposure’, processing and reporting of the data is an important issue. Currently, very few data sets of air contaminant parameters for (M)NP exposure scenarios are (publicly) available. These few data do not show, however, a clear relationship between the various exposure metric, e.g. between number concentration and surface area (Ramachandran et al., 2005), and between mass concentration and number concentration (Demou et al., 2008). Preliminary conclusion drawn from the observations could be that classification or ranking of tasks etc according to level of ‘exposure’ may differ with respect to the exposure metric, and thus a multiple exposure metric approach is warranted for both exposure assessment and exposure evaluation.

Currently, no guidance is available on the evaluation of data with respect to exposure. The way data can be analysed will depend on the time-basis of the measurement device, e.g. x-s averages, and the duration of the measurements, e.g. task or shift-based.

Data processing should enable an evaluation of the data with respect to different exposure measures, i.e. that mean values, peak values and cumulative (intensity times duration) exposure can be calculated, where guidance should be available how to define peaks. In addition to absolute levels it seems appropriate to calculate and report ‘relative’ levels, e.g. ratios of ‘exposure’ levels (activity/task/shift) and ‘background’ levels [increment of exposure (Nasterlack et al., 2008)], or ratios of results from various locations.

To compile such recommendations and guidance, it is recommended to compare and evaluate available protocols. Point of reference might be the ISO TC 229 WG3 draft report, however the results of recently concluded (NANOTRANSPORT¹⁴), started (NANOIMPACTNET¹⁵) and proposed (NANODEVICE¹⁶) EU projects should be considered as well.

¹⁴ <http://research.dnv.com/nanotransport/>

Compare guidance on control measures e.g. engineering and work practice controls, worker training and education, and personal protective equipment (clothing, gloves and respirators) for selected exposure scenarios in research, production and down-stream use of MNPs.

To ensure an evaluating loop, control measures to reduce exposure should be embedded in either risk management frameworks dedicated to nano materials, e.g. Nano Risk Framework¹⁷, or generic frameworks, e.g. COSHH¹⁸. Basically, the main steps in such a framework are: identification of hazards and assessment of risks; decision on what precautions are needed; prevention or adequate control of exposure; ensure implementation, use and maintenance of control measures; monitoring of (resulting) exposure; conduct of appropriate health surveillance; preparation of plans and procedures to deal with accidents, incidents and emergencies; and ensure employees are properly informed, trained and supervised.

In view of the knowledge gap for risk related to exposure to MNPs, exposure should be as low as reasonable practical, limited by technical and economical feasibility.

Next step might be the definition of good practices for ‘standard’ exposure scenarios or tasks, by using exposure data in combination with extensive contextual information, as a starting point for benchmarking. As performance specific ‘nano exposure’ criteria for control measures are lacking, the efficiency of control measures on location can be evaluated by benchmarking

To compile such recommendations and guidance, it is recommended to compare and evaluate available guidance documents and make use of the started activities within the EU, NANOIMPACTNET-Project. Points of reference might be the ISO TC 229 WG3 draft report, BSI report Guide to safe handling and disposal of MNP and ASTM (2006) Standard Guide for handling Unbound Engineered Nanoscale Particles in Occupational Setting (draft)

General conclusion and recommendations

With respect to the objectives of the project as given in the Introduction section, it can be concluded the existing guidance information is only partly adequate to address exposure measurement and exposure mitigation issues related to manufactured nanomaterials.

Comprehensive state-of-the-art documents with recommendations on safe handling use of MNP and exposure control measures exist (e.g. ISO, BSI, ASTM), as well as guidance documents for measurement of exposure (parameters) or monitoring. For the time being, these documents afford the implementation of a precautionary approach for manufacturing and use of MNPs, without being too restrictive.

However, for many exposure control measures specific data underlying the assumed effectiveness are lacking. As a result of many ongoing projects such data are and will be generated in the (near) future. It is essential that these data are collected and reported in a harmonized manner in order to optimize use of exposure data. It should be realized, however, that currently and in near future the resulting or remaining (reduced) exposure cannot be evaluated with respect to exposure limit values.

¹⁵ <http://www.nanoimpactnet.eu/> and presentation at the EC Workshop held 17+18 April 2008 on <ftp://ftp.cordis.europa.eu/pub/nanotechnology/docs/final-version.pdf>

¹⁶See presentation at the EC Workshop held 17+18 April 2008 on <ftp://ftp.cordis.europa.eu/pub/nanotechnology/docs/final-version.pdf>

¹⁷ <http://www.nanoriskframework.com>

¹⁸ Control of Substances Hazardous to Health Regulations 2002

To prioritize future work items or research, it is strongly recommended to initiate a harmonized stepwise pragmatic approach toward production and use of MNP as a possible starting point for more science-based guidance by building upon and making use of the different activities outlined in the section “*Information*”¹⁹ of this report:

- Firstly, for various generic tasks or operation units, e.g. transferring, mixing, filling, bag dumping, spraying etc, so called ‘good practices’ should be set. This might be either existing practice(s) as acknowledged by experts or a more theoretically defined exposure scenario using a mixture of (type of) control measures that are considered to be practically achievable. The identified guidance documents would be very helpful for this process.
- Secondly, a comprehensive description of the exposure scenario including control measures etc should be documented. More specifically contextual information should be made available, for example by summarizing it in ‘fact sheets’.
- To characterize these (good practice) scenarios, the next step would be to collect data with respect to exposure. The data should be collected using harmonized and appropriate sampling strategies and equipment, enabling an interpretation for various exposure metrics and exposure measures (see recommendation in page 23 and 24). Data storage (e.g. in a data base) should enable future analysis for example with respect to effectiveness of control measures. To ensure harmonized storage of exposure and contextual data, a framework should be developed and made available to organizations collecting this type of information
- The final step would be quantitatively benchmarking the good practice scenarios to other scenarios for similar operation units.

¹⁹ See “Information from on-going European research projects and part of activities within European Technology Platforms (ETPs)” in page 14 and table 1.

ANNEX I BIBLIOGRAPHY OF IDENTIFIED, SUMMARIZED AND EVALUATED KEY DOCUMENTS

Table A1.1 The reviewed documents and their availability

Reference	Title	Available yes/no	Summary yes/no
1	ISO TC 229: Technical Report entitled “Health and safety practices in occupational settings relevant to nanotechnologies”.	Yes	Yes
2	French good practice guide for the workplace	No	-
3	German Nanocommission: Code of Good Practice	No	-
4	Japan Ministry of Economy, Trade and Industry: preliminary survey on safe handling of nanomaterials at manufacturing sites and research laboratories.	No	-
5	UK British Standards Institute: Guide to Safe Handling and Disposal of Manufactured Nanomaterials.	Yes	No
6	US National Institute for Occupational Safety and Health: “Approaches to Safe Nanotechnology” (August, 2006) ²⁰	Yes	Yes
7	Thailand National Nanotechnology Center: nanosafety guidelines.	No	-
8	German Chemical Industry Association (VCI) and German Federal Institute for Occupational Safety and Health (BAuA): best practice guideline for handling and use of nanomaterials in the workplace.	Yes	Yes
9	US ORC Task Force on Nanotechnology: workplace guidelines including exposure measurements and exposure mitigation as a web-based resource ²¹	Yes	Yes
10a	International Council on Nanotechnology (ICON): Phase One Report: Current Knowledge and Practices Regarding Environmental Health and Safety in the Nanotechnology Workplace ²²	Yes	Yes
10b	International Council on Nanotechnology (ICON): Phase Two Report: Survey of Current Practices in the Nanotechnology Workplace, available on-line at http://cohesion.rice.edu/CentersAndInst/ICON/emplibrary/ICONNanotechSurveyFullReduced.pdf .	Yes	Yes

²⁰ Available on-line at <http://www.cdc.gov/niosh/topics/nanotech/safenano/>

²¹ Available on-line at <http://www.orc-dc.com/Nano.Guidelines.Matrix.htm>

²² Available on-line at

http://cohesion.rice.edu/CentersAndInst/ICON/emplibrary/Phase%20I%20Report_UCSB_ICON%20Final.pdf

Reference	Title	Available yes/no	Summary yes/no
11	The National Nanotechnology Initiative "Environmental, Health, and Safety Research Needs for Engineered Nanoscale Materials." 2006	Yes	No
12	Health and Safety Executive, RR513, "The Assessment of Different Metrics of the Concentration of Nano (Ultrafine) Particles in Existing and New Industries".	Yes	Yes
13	USEPA Nanotechnology White Paper, 2007 ²³	Yes	Yes
14	Weis, et al. (2005). Personalized Exposure Assessment: Promising Approaches to Human Environmental Health Research. Environmental Health Perspective, 113(7): 840-848.	Yes	Yes
15	Borm PJA, Robbins D, Haubold S. et al. (2006) The potential risks of nanomaterials: a review carried out for ECETOC. Particle and Fibre Toxicology 3:11 ²⁴	Yes	Yes*
16	SCENIHR (2006). The appropriateness of existing methodologies to assess the potential risks associated with engineered and adventitious products of technologies ²⁵ .	Yes	Yes*
17	ISO TC 146 SC2WG1 TR 27628 (2007). Workplace Atmospheres – Ultrafine, nanoparticle and nano-structured aerosols – Exposure characterization and assessment.	Yes	Yes
18	Department of Energy Nanoscale Science Research centers (2007). Approach to nanomaterial ES&H ²⁶	Yes	Yes
19	ASTM (2006) Standard Guide for handling Unbound Engineered Nanoscale Particles in Occupational Setting (draft)	Yes	Yes*
20	Japan Ministry of Health, Labour and Welfare's notification on present preventive measures for the prevention of exposure at workplaces manufacturing and/or handling nanomaterials.	No	-

* abstract/executive summary from the original document

²³ www.epa.gov/OSA/nanotech.htm

²⁴ <http://www.particleandfibretoxicology.com/content/3/1/11>

²⁵ http://ec.europa.eu/health/ph_risk/documents/synth_report.pdf

²⁶ http://www.sc.doe.gov/News_Information/News_Room/2006/nano/NSRC%20ESH%20Approach%20Doc%20Rev2%202007-06-15.pdf

ANNEX II. SUMMARIES OF DOCUMENTS

A. Summary documents as prepared by the WPMN project on Exposure Measurement and Exposure Mitigation

Brief summaries made in the phase 1 report of the OECD Working Party on Manufactured Nanomaterials' project Co-operation on Exposure Measurement and Exposure Mitigation²⁷. The summaries do not necessarily reflect the views of the WPMN. These summaries do not necessarily reflect the official views of the Organisation or of the governments of its member countries.

1. ISO TC 229 draft Technical Report "Health and safety practices in occupational settings relevant to nanotechnologies".

Exposure measurement section of ISO TC 229 WG3 PG1 draft technical report contains information from the ISO Technical Report 27628:2007 on Workplace atmospheres – Ultrafine, nanoparticles and nano-structured aerosols – Inhalation exposure characterization and assessment.

Ideally the equipment for taking the occupational hygiene measurements should be:

- portable;
- capable of measuring multiple nanoparticle characteristics (particle count, mass, surface area, charge, size distribution, differentiate engineered from background particles, temporal variation etc.);
- capable of obtaining breathing zone samples;
- capable of being used in industrial settings;
- battery-powered;
- real-time;
- relatively inexpensive.

At this time there is not a single instrument for nanomaterials that meets all of these criteria.

While a strong case may be made for using aerosol surface-area as an exposure metric, it is also necessary to consider characterizing exposures against aerosol mass and number concentration until further information is available. For each of these exposure metrics, but particularly in the case of mass concentration, particle size selective inlets will need to be employed to ensure only particles within the relevant size range are sampled.

The actual cut size that particle selection should be made for assessing potential human health impact is still open to debate and depends upon particle behaviour and subsequent biological interactions. The currently proposed cut size for nanoparticles is 100 nm, although this is not derived from particle behaviour in the respiratory tract following deposition and it excludes larger particles of nanomaterials.

²⁷ In September 2007

Mass concentration can be determined by a number of direct reading instruments utilizing collection of particles on filters (aerosol samplers, cascade impactors and oscillating microbalance) and resonator crystals (piezobalance). It is also possible to derive estimates of mass by calculation using a tandem of instruments such as Electrical Low Pressure Impactor and Scanning Mobility Particle Sizer.

The most widely used instrument for determining the number concentration of nanoparticles is the Condensation Particle Counter (CPC). This device exploits vapor condensation on nanometer size (and larger) particles in order to grow the particles to a size range that can be detected optically. A second instrument type that is sensitive to nanoparticles is an electrometer.

The diffusion charger measures the Fuchs or active surface area of the aerosols from the attachment rate of positive unipolar ions to particles, from which the aerosol active surface-area can be inferred.

Nanoparticle size distributions can be measured using particle mobility analysis and inertial impaction. The most common instrument used for measuring size distributions of aerosols of nanoparticles is the Scanning Mobility Particle Sizer (SMPS). Cascade impactors are widely available in a number of configurations, allowing either personal or static sampling with a range of particle size cut points.

Determination of the physical and chemical properties of airborne nanomaterials relevant to their potential effect on human health is often required. Parameters such as particle size, shape, surface area, composition, agglomeration state, crystallinity, solubility and bio-persistence provide the basic information for the exposure and toxicological evaluation of new nanomaterials. The surface coating on the particles and their electrical charge will also have a significant impact on their state of agglomeration, which will in turn influence their physical behaviour and subsequent biological responses. Because particle structure affects transport and locations of deposition within the respiratory system and may affect toxicology, it is important to characterize structures of airborne materials used for toxicology studies. The main analytical techniques routinely available for determining the particle size, shape and composition are high resolution electron microscopy combined with x-ray microanalysis and electron diffraction.

Sampling. Until it has been agreed which is(are) the most appropriate metric(s) for assessing exposure to nanoparticles in relation to potential adverse effects, it has been recommended that a range of instrumentation be used to provide full characterization of the aerosols in workplaces where nanoparticles are being produced, handled or used to make new materials.

New instruments are being continuously developed and there are small portable instruments for particle number concentrations, particle surface area concentrations and health-related surface area concentrations. While most of instruments are not yet truly personal, they are compact enough to be carried from location to location in the workplace and to be sited close to the worker at each location. Currently however, these instruments do not provide enough information for full characterization of the workplace, so static instruments such as the SMPS, ELPI and thermal/electrostatic precipitators for collecting particles for characterization should be included. Care should be taken in setting these static samplers as aerosol characteristics can change with distance from source, leading to spatial and temporal variation of nanoaerosol mass and number concentration.

To improve the comparability of exposure data, the accepted practice of giving personal exposure as an eight-hour-shift value should also be observed in the case of nanoaerosols. In consequence, wherever possible exposure measurement results concerning shorter measurement intervals should be converted into shift data by time weighted recalculation. In all cases, where short-term exposure itself is the target of

investigations, the time base of measurements needs to be documented. A time base of 15 minutes for short-term exposure measurements is recommended as it is generally used in occupational hygiene.

Unless the workplace is operating under clean room conditions or has high efficiency filters on the inlet air through well defined inlets, outdoor sources of nanoaerosols (e.g. vehicle exhausts, other industrial activities, power stations, etc.) will penetrate indoors and result in overestimation of the levels of nanoparticles emitted from the process under investigation. This will inevitably lead to an overestimation of the worker exposure to nanoparticles derived from that process. One way to overcome this problem is to determine ambient or background particle counts prior to the commencement of manufacturing or processing of the nanoparticles.

Dermal exposures

Sampling of nanoparticles deposited on skin in the workplace can be accomplished by adapting well established sampling methods developed for chemicals. The direct assessment of dermal exposure to nanoparticles can be accomplished by measuring the amount of the nanoparticles in contact with the skin over a period of time. The methods developed for such purposes entail either the removal of accumulated contaminants from the skin or interception of the material as contact occurs.

Electron microscopy can be used to characterize size distribution, number concentration and shape of nanoparticles collected on samplers. In wipe methods, use of mixed-cellulose ester filters as wipes could facilitate such analysis. Light scattering, laser diffraction, size exclusion chromatography, acoustic techniques and field flow fractionation could be used to characterize size distribution and number concentration, while spectroscopic techniques can be useful in obtaining information about chemical composition and structure of nanoparticles. These techniques can work with rinse sampling methods.

Biomarkers

Internal exposure is more directly linked to adverse health effects. Dose can be determined by measuring amount of nanoparticles of interest and/or their metabolites. Biomarkers can provide direct evidence for the exposure to a particular toxicant if there is a unique correlation between a particular biomarker and a toxicant. Biomarkers of exposure to nanoparticles are in the early development stage complicated by great variety of nanoparticles chemical and physical properties resulting in wide range of biological responses. Inhalation exposure to poorly soluble low toxicity nanoparticles was shown to cause inflammatory response. For example, nitric oxide in the exhaled air was proposed as a biomarker of inflammation.

Health surveillance

Health surveillance should be considered for all workers where there is risk of exposure to nanoparticles, and where it has been demonstrated that there is a relationship between exposure to the substance and a measurable biological indicator. It is strongly recommended that a health surveillance program is established for workers if nanoparticles contain chemicals or components for which current guidelines recommend health surveillance.

Given that exposure to very low concentrations of nanoparticles may be significant, measurable changes in biological indicators from baseline levels, rather than comparison of body burden with the Biological Exposure Index (BEI), may be the most appropriate parameter to examine. The use of health surveillance in this context is as an indicator of whether exposure is occurring, rather than in determining that levels of exposure are safe. Due to the currently limited capability for measuring airborne concentrations of nanoparticles, the use of biological indicators may be a very useful approach in evaluating the effectiveness of control measures introduced.

At this stage, where the impact of nanoparticles on human health is unclear, continuous health checks for workers are particularly important to detect any adverse effects from nanoparticles. Health check records are important evidence in identifying adverse health effects.

Future developments

The exposure measurement area is moving fast and instrument manufacturers are currently developing new devices that they hope will become the mainstay of future nanoparticle exposure assessments. Besides recently-introduced health-related surface area monitors, there are a number of developments in the pipeline, including: personal CPCs; small portable diffusion charger surface area monitors; small, portable instruments that provide particle number size distributions (similar to the information provided by the SMPS) and small, portable particle mass monitors. In addition, there are many other long-term developments including a possible portable device that should be able to discriminate between engineered and combustion nanoaerosols. So, assuming that international agreement can be obtained about which metric or metrics is the most appropriate to use as the basis of exposure assessment for inhalation of airborne nanomaterials, then the future looks promising that a suitable sampling methodology will be available. The choice of sampler or monitor depends upon the role for which it is to be used and a device for exposure assessment may be different from that used to determine sources and to assess the efficiency of control systems.

6. US National Institute for Occupational Safety and Health, "Approaches to Safe Nanotechnology: Information Exchange with NIOSH," 2006.²⁸

This document provides an overview of techniques available to characterize exposures in the workplace and provides specific recommendations.

Until more information becomes available on the mechanisms underlying nanoparticle toxicity, it is uncertain as to what measurement technique should be used to monitor exposures in the workplace. Current research indicates that mass and bulk chemistry may be less important than particle size and shape, surface area, and surface chemistry (or activity) for nanostructured materials.

Many of the sampling techniques that are available for measuring airborne nanoaerosols vary in complexity but can provide useful information for evaluating occupational exposures with respect to particle size, mass, surface area, number concentration, composition, and surface. Unfortunately, relatively few of these techniques are readily applicable to routine exposure monitoring. Currently, no commercially available personal samplers are designed to measure the particle number, surface area, or mass concentration of nanometer aerosols. However, several methods are available that can be used to estimate surface area, number, or mass concentration for particles smaller than 100 nm. In the absence of specific exposure limits or guidelines for engineered nanoparticles, exposure data gathered from the use of respirable samplers can be used to determine the need for engineering controls or work practices and for routine exposure monitoring of processes and job tasks. When chemical components of the sample need to be identified, chemical analysis of the filter samples can permit smaller quantities of material to be quantified, with the limits of quantification depending on the technique selected. The use of conventional impactor samplers to assess nanoparticle exposure is limited to a lower efficiency of 200 to 300 nm. Low-pressure cascade impactors that can measure particles to ³ 50 nm may be used for static sampling, since their size and complexity preclude their use as personal samplers. A personal cascade impactor is available with a lower aerosol cut point of 250 nm, allowing an approximation of nanometer particle mass concentration in the worker's breathing zone. For each method, the detection limits are of the order of a few micrograms of material on a filter or collection substrate. Cascade impactor exposure data gathered

²⁸ Available on-line at <http://www.cdc.gov/niosh/topics/nanotech/safenano>

from worksites where nanomaterials are being processed or handled can be used to make assessments as to the efficacy of exposure control measures.

The real-time (direct-reading) measurement of nanometer aerosol concentrations is limited by the sensitivity of the instrument to detect small particles. Many real-time aerosol mass monitors used in the workplace rely on light scattering from groups of particles (photometers). This methodology is generally insensitive to particles smaller than 300 nm. Optical instruments that size individual particles and convert the measured distribution to a mass concentration are similarly limited to particles larger than 100 to 300 nm. The Scanning Mobility Particle Sizer (SMPS) is widely used as a research tool for characterizing nanometer aerosols, although its applicability for use in the workplace may be limited because of its size, cost, and the inclusion of a radioactive source. The Electrical Low Pressure Impactor (ELPI) is an alternative instrument that combines a cascade impactor with real-time aerosol charge measurements to measure size distributions.

Relatively few techniques exist to monitor exposures with respect to aerosol surface area. Isothermal adsorption is a standard off-line technique used to measure the specific surface area of powders that can be adapted to measure the specific surface area of collected aerosol samples. Portable aerosol diffusion chargers provide a good estimate of aerosol surface area when airborne particles are smaller than 100 nm in diameter.

Aerosol particle number concentration can be measured relatively easily using Condensation Particle Counters (CPCs). These are available as hand-held static instruments, and they are generally sensitive to particles greater than 10 to 20 nm in diameter. CPCs designed for the workplace do not have discrete size-selective inputs, and so they are typically sensitive to particles up to micrometers in diameter. Commercial size-selective inlets are not available to restrict CPCs to the nanoparticle size range; however, the technology exists to construct size-selective inlets based on particle mobility, or possibly inertial pre-separation. An alternative approach to estimating nanoparticle concentrations using a CPC is to use the instrument in parallel with an optical particle counter. The difference in particle count between the instruments will provide an indication of particle number concentration between the lower CPC detectable particle diameter and the lower optical particle diameter (typically 300 to 500 nm). Although using nanoparticle number concentration as an exposure measurement may not be consistent with exposure metrics being used in animal toxicity studies, such measurements may be a useful indicator for identifying nanoparticle emissions and determining the efficacy of control measures. Portable CPCs are capable of measuring localized aerosol concentrations, allowing the assessment of particle releases occurring at various processes and job tasks.

Currently, there is not one sampling method that can be used to characterize exposure to nanosized aerosols. Therefore, any attempt to characterize workplace exposure to nanoparticles must involve a multifaceted approach incorporating many of the sampling techniques mentioned above. The first step would involve identifying the source of nanoparticle emissions. A CPC provides acceptable capability for this purpose. It is critical to determine ambient or background particle counts before measuring particle counts during the manufacture or processing of the nanoparticles involved. If a specific nanoparticle is of interest (e.g. TiO₂), then area sampling with a filter suitable for analysis by electron microscopy should also be employed. Transmission electron microscopy (TEM) can identify specific particles and can estimate the size distribution of the particles. Once the source of emissions is identified, aerosol surface area measurements should be conducted with a portable diffusion charger and aerosol size distributions should be determined with an SMPS or ELPI using static (area) monitoring. A small portable surface area instrument could be adapted to be worn by a worker, although depending on the nature of the work, this may be cumbersome. Further, losses of aerosol with the addition of a sampling tube would need to be calculated. The location of these instruments should be considered carefully. Ideally they should be placed close to the work areas of the workers, but other factors such as size of the instrumentation, power source, etc. will need to be considered. Lastly, personal sampling using filters or grids suitable for analysis by

electron microscopy or chemical identification should be employed, particularly if measuring exposures to specific nanoparticles is of interest. Electron microscopy can be used to identify the particles, and can provide an estimate of the size distribution of the particle of interest. The use of a personal cascade impactor or a respirable cyclone sampler with a filter, though limited, will help to remove larger particles that may be of limited interest and allow a more definitive determination of particle size. Analysis of these filters for air contaminants of interest can help identify the source of the respirable particles. Standard analytical chemical methodologies should be employed.

By using a combination of these techniques, an assessment of worker exposure to nanoparticles can be conducted. This approach will allow a determination of the presence and identification of nanoparticles and the characterization of the important aerosol metrics. However, since this approach relies primarily on static or area sampling some uncertainty will exist in estimating worker exposures. When feasible, personal sampling is preferred to ensure an accurate representation of the worker's exposure, whereas area sampling (e.g., size-fractionated aerosol samples) and real-time (direct reading) exposure measurements may be more useful for evaluating the need for improvement of engineering controls and work practices.

Health surveillance

The unique physical and chemical properties of nanomaterials, the increasing growth of nanotechnology in the workplace, and information suggesting that engineered nanoscale materials may pose a health and safety hazard to workers all underscore the need for medical and hazard surveillance for nanotechnology. Every workplace dealing with nanoparticles, engineered nanomaterials or other aspects of nanotechnology should consider the need for an occupational health surveillance program.

8. German Chemical Industry Association (VCI) and German Federal Institute for Occupational Safety and Health (BAuA). Guidance for handling and use of nanomaterials in the workplace (Status 28.03.2007).

This document provides guidance regarding OSH measures in the production and use of intentionally produced nanomaterials in the workplace reflecting the current state of science and technology. Nano- and micro-scale particles can be measured in the workplace with only relatively coarse resolution of the particle size distribution. It is critical to measure background incidental particle concentrations. Commonly used methods are:

- Condensation Particle Counter is the most wide-spread method for particle counts in the nanometer range. It is commonly combined with an upstream connected fractionating unit. Scanning or Stepped Mobility Particle Sizer is the most frequently used instrument to measure particle size distribution in the size range from 3 to 800 nm.
- Aerosol mass spectrometry is a wide-spread method for the chemical on-line analysis of particles and aggregates in the size range of over 100 nm. Electron microscopy (TEM and SEM) is used as an off-line method to characterize size, morphology and particle structure. Energy Dispersive X-Ray Fluorescence Analysis in combination with electron microscopy enables resolution of spatial elemental distribution.
- Nano-Aerosol Sampler can be used to characterize and semi-quantitatively measure particle morphology and elemental composition for particles in the size range from 1 to 100 nm.

Exposure measuring methods for nanoparticles are not fully standardized as yet. Existing standardized particle exposure methods measure mass of dust respirable fraction. There is a need to develop complementary measuring methods for particle counts and sizes using for example SMPS.

Assessment of health hazards based exclusively on particle mass is not sufficient in every case. At present, factors assumed to influence health hazards – such as particle surface area, surface structure and surface composition – still require highly sophisticated measuring methods in the nanometer range. So far, there is no uniform approach in the characterization of nanoparticles. In Germany the suitability of measuring and protection methods is assessed by the umbrella organization of employer's liability insurance associations (HVBG).

9. ORC Worldwide. Nanotechnology Consensus Workplace Safety Guidelines²⁹

The web site contains a selection of peer-reviewed Health, Safety & Environment tools and reference materials that may be useful to practitioners involved in deployment of nanotechnology. Specifically, for the area of exposure measurements there are a number of detailed and practical documents on Assessment Strategy for Nanoparticle Aerosols, Qualitative Exposure Assessments, and State-of-the-art Monitoring Techniques.

Assessment Strategy for Nanoparticle Aerosols³⁰ is a basic assessment strategy for evaluating nanoparticles aerosol concentrations in occupational settings, which follows common exposure assessment principles not unique to nanomaterials.

Qualitative Exposure Assessment Tool³¹ describes how to detect exposure sources, conduct systematic analysis and rank sources in terms of risk and provides a sample survey matrix. The tool was developed for detection of micron sized dusts derived from a potential respiratory allergen and has not been tested for nano sized dusts.

State-of-the-art Monitoring Techniques³² provides description (including limitations, size and costs) of instrumentation available to assess nanoaerosol concentrations in the workplace in the form of mass, number and surface area. The recommendations largely apply to area rather than personal sampling. It recommends to use cascade impactor for measuring mass concentration due to the relatively low cost, ease of use and direct mass measurement; scanning mobility particle sizer for monitoring number concentration due to it providing a full size distribution in a short period of time; diffusion charger for measuring surface area since it provides a real time measurement over a wide detection range and less expensive than other methods. In addition, the document describes particle collection techniques (thermal precipitator, nanometer aerosol sampler, cascade impactor) and particle characterization using electron microscopy.

10a and 10b. International Council on Nanotechnology (ICON), Review of Current Practices in Nanotechnology.

Phase One Report: Current Knowledge and Practices Regarding Environmental Health and Safety in the Nanotechnology Workplace³³, and Phase Two Report: Survey of Current Practices in the Nanotechnology Workplace, are available on-line³³.

²⁹ Available at <http://www.orc-dc.com/Nano.Guidelines.Matrix.htm>

³⁰ http://www.orc-dc.com/oshmem/nanotech/Assess_Strategy_Nanoparticle_Aerosols.pdf

³¹ http://www.orc-dc.com/oshmem/nanotech/QUAL_EXP_Assess_Tool.pdf

³² <http://www.orc-dc.com/oshmem/nanotech/QEAI1.pdf>

³³ Available at: Phase I:

http://cohesion.rice.edu/CentersAndInst/ICON/emplibary/Phase%20I%20Report_UCSB_ICON%20Final.pdf, and Phase Two Report:

<http://cohesion.rice.edu/CentersAndInst/ICON/emplibary/ICONNanotechSurveyFullReduced.pdf>

The first report compiles and summarizes global efforts to document current practices and to establish risk assessment frameworks. The reviewed efforts are critically evaluated for their approaches, completeness and foci.

The second report presents the findings of an international survey of current environmental health and safety and product stewardship practices in the global nanotechnology industry. Specifically, the questionnaire inquired about the following areas: environmental health and safety training, use of engineered controls, personal protective equipment and clothing recommendations, exposure monitoring, waste disposal, product stewardship practices, and risk characterization.

12. Health and Safety Laboratory, RR513, "The Assessment of Different Metrics of the Concentration of Nano (Ultrafine) Particles in Existing and New Industries", 2006.

This report describes results of a study investigating relationships between mass (using Tapered Element Oscillating Microbalance), number (using Scanning Mobility Particle Sizer) and active surface area (using Diffusion Charging) of nanoscale particles of different chemical composition and particle shape. Specifically, measurement were conducted on sodium fluorescein (amorphous shape with 120-257 nm mean diameter), sodium chloride (cubic with 35-175 nm mean diameter), latex (spheres with 88 – 773 nm mean diameter), caffeine (rods with aspect ratio of 6:1 and mean diameter of 34-247 nm), zinc oxide (rods with aspect ratio of 3:1 and mean diameter of 91-167 nm).

For each of the five aerosol types investigated the response of the TEOM and the DC at a particular size is consistent with increasing particle number concentration measured by SMPS but overall the response of the TEOM and the DC shows no consistent ranking with size. No simple relationship was found for predicting the active surface area as measured by DC, from SMPS measurements. But for aerosols smaller than 100 nm the DC results for most of the materials investigated were broadly similar to those calculated from the SMPS data. The degree of agglomeration was more likely to be responsible for the inconsistency of instrument response to size. The filter in the TEOM is mechanical in action and so is not totally efficient in capturing nanoscale particles.

The following recommendations were made:

- Because of the lack of consistent relationships between measurements of mass, number and surface area, measurements of all three parameters should be conducted in the workplace. None of these parameters taken in isolation can give sufficient information to predict toxicity.
- The performance of any device, currently available, that can discriminate between ultrafine/nano particle species should be investigated.
- For reasonable accuracy the SMPS must not be used to calculate surface area and mass without prior knowledge of aerosol composition and state of agglomeration.
- Improve efficiency of the TEOM filter.

13. U.S. EPA Nanotech White Paper³⁴.

The document describes challenges of environmental detection and analysis of nanomaterials and available techniques.

³⁴ EPA 100/B-07/001, 2007, available at <http://www.epa.gov/OSA/pdfs/nanotech/epa-nanotechnology-whitepaper-0207.pdf>

Challenges:

- unique and varying physical structure and physico-chemical characteristics
- interactions of nanomaterials with and in the environment, including agglomeration, and chemical surface treatments complicate the detection and analysis
- need to distinguish between the nanoparticles of interest and other ultra-fine particles.

The level of effort needed and costs to perform analysis for nanomaterials will depend on which environmental compartment samples are being taken from, as well as the type of desired analytical information. The analysis of nanomaterials from an air matrix requires significantly less “sample” preparation than samples taken from a soil matrix. Analyzing samples for number concentration requires significantly less effort than broadening such analyses to include characterization of particle types and elemental composition.

In the case of inseparable mixtures of engineered and other nanomaterials, the use of single particle analysis methodologies may be necessary to provide definitive analysis for the engineered nanomaterials.

Methods and technologies are available commercially that have demonstrated success. For aerosols, multi-stage impactor samplers based upon the aerodynamic mobility properties are available commercially that can separate and collect nanoparticles size fractions for subsequent analysis, for example, micro-orifice uniform deposit impactors and electrical low-pressure impactors. There are also aerosol fractionation and collection technologies based upon the electrodynamic mobility of particles such as differential mobility analyzers and scanning mobility particle sizers. Available technologies for the size fractionation and collection of nanoparticles fractions in liquid mediums include size-exclusion chromatography, ultrafiltration and field flow fractionation. On-line particle size analysis in liquid mediums can be done using various techniques including dynamic light scattering to obtain a particle size distribution. Inductively-coupled plasma mass spectrometry can provide chemical characterization information. Single-particle laser microprobe mass spectrometry can provide chemical composition data on single particles from a collected fraction. Electron microscopy techniques can provide particle size, morphological and chemical composition information on collected single nanoparticles in a vacuum environment. Atomic Force Microscopy can provide particle size and morphological information on single nanoparticles in liquid, gas, and vacuum environments.

Biological monitoring

Biomonitoring data, when permitted and applied correctly, provides the best information on the dose and levels of a chemical in the human body. Biomonitoring can be the best tool for understanding the degree and spread of exposure information that cannot be captured through monitoring concentrations in ambient media. Biomonitoring, however, is potentially limited in its application to nanotechnology because it is a science that is much dependent on knowledge of biomarkers, and its benefits are highest when there is background knowledge on what nanomaterials should be monitored.

14. Weis, B. K., et al. (2005). *Personalized Exposure Assessment: Promising Approaches to Human Environmental Health Research. Environmental Health Perspective, 2005, July; 113(7): 840-848.*

The report describes a “toolbox” of methods for measuring external (environmental) and internal (biologic) exposure and assessing human behaviors that influence the likelihood of exposure to a broad range of environmental agents.

The methods are discussed in relation to current use in human health research; specific gaps in the development, validation, and application. Recent efforts have focused on automated “lab-on-a-chip” sensing devices for detecting environmental agents.

17. ISO, Workplace atmospheres – Ultrafine, nanoparticles and nano-structured aerosols – Inhalation exposure characterization and assessment. PD ISO/TR 27628:2007.

In addition to the techniques described in the ISO TC 229 draft Technical Report “Health and safety practices in occupational settings relevant to nanotechnologies,” aerosol mass spectrometry is highlighted as the predominant commercial method for on-line size-resolved chemical analysis of nanoscale aerosols, while scanning probe microscopy such as Atomic Force Microscopy are described as methods to map topographic features of individual nanoparticles at sub-nanometer resolution.

18. U.S. DOE Nanoscale Science Research Centers, Approach to Nanomaterials ES&H, 2007³⁵

The document offers “reasonable guidance for managing the uncertainty associated with nanomaterials whose hazards have not been determined and reducing to an acceptable level the risk of worker injury, worker ill-health and negative environmental impacts” in laboratories of Nanoscale Science Research Centers.

The document recommends basic worker health and environmental monitoring consisting of:

- identifying staff (nanoparticles workers) exposed to engineered nanoparticles of unknown health effects;
- conducting workplace characterization and worker exposure assessments;
- providing nanoparticles workers with “baseline” medical evaluations and; including them in a nonspecific routine health monitoring program;
- checking wastes for evidence of uncontrolled release of engineered nanomaterials;
- effluent monitoring.

Any worker meeting one or more of the following criteria is considered an “engineered nanoparticles worker”:

- Handles engineered nanoscale particulates that have the potential to become dispersed in the air
- Routinely spends significant amounts of time in an area in which engineered nanoparticles have the potential to become dispersed in the air
- Work on equipment that might be contaminated with materials that could potentially release engineered nanoparticles during servicing or maintenance.

It is recommended that each laboratory:

- record the identity of engineered nanoparticles workers
- use available methods to characterize workplace conditions and exposures of engineered nanoparticles workers

³⁵ Available at http://www.sc.doe.gov/bes/DOE_NSRC_Approach_to_Nanomaterial_ESH.pdf

- ensure that engineered nanoparticle workers are offered periodic medical evaluations that may include routine test such as pulmonary, renal, liver, and hematopoietic function and pulmonary function testing
- revisit and refine the definition of engineered nanoparticle workers and make recommendations to the Site Occupational Medical Director for changes to any applicable medical examination program.

Workplace characterization and nanomaterial exposure assessment challenges include:

- substantially different “parameters” may prove hygienically significant for different nanomaterials
- materials of the same chemical composition can have markedly different forms at the nanoscale and the different forms can have markedly different properties
- no professional consensus on monitoring instrumentation and protocols exists and it may be decades before one emerges.

For monitoring and characterization the document recommends to:

- Conduct “baseline” monitoring by measuring conditions prior to start up. Measure again at the conclusion of system commissioning and periodically thereafter. These efforts should be considered a vital part of an overall strategy of ensuring that controls are well conceived, well constructed, and remain effective.
- Use direct-reading particle-measuring devices to screen for suspect emissions and atypical conditions.
- Use more sophisticated techniques, to collect and analyze samples to characterize emissions and potential exposure and to determine if a control is needed or must be upgraded or serviced.
- Use Laboratory’s data management system to link environmental data indicative of exposure to engineered nanoparticle workers exposed to engineered nanoparticles of unknown health effects.

Appendix to the document contains description of an example Industrial Hygiene Sampling Protocol for Nanomaterials.

B. (Executive) summary or abstract from the original document.

15. Borm PJA, Robbins D, Haubold S. et al. (2006) *The potential risks of nanomaterials: a review carried out for ECETOC. Particle and Fibre Toxicology 3:11*³⁶.

Abstract

During the last few years, research on toxicologically relevant properties of engineered nanoparticles has increased tremendously. A number of international research projects and additional activities are ongoing in the EU and the US, nourishing the expectation that more relevant technical and toxicological data will be published. Their widespread use allows for potential exposure to engineered nanoparticles during the whole lifecycle of a variety of products. When looking at possible exposure routes for manufactured Nanoparticles, inhalation, dermal and oral exposure are the most obvious, depending on the type of product in which Nanoparticles are used.

This review shows that:

Nanoparticles can deposit in the respiratory tract after inhalation.

For a number of nanoparticles, oxidative stress-related inflammatory reactions have been observed. Tumour-related effects have only been observed in rats, and might be related to overload conditions. There are also a few reports that indicate uptake of nanoparticles in the brain via the olfactory epithelium. Nanoparticle translocation into the systemic circulation may occur after inhalation but conflicting evidence is present on the extent of translocation. These findings urge the need for additional studies to further elucidate these findings and to characterize the physiological impact.

There is currently little evidence from skin penetration studies that dermal applications of metal oxide nanoparticles used in sunscreens lead to systemic exposure. However, the question has been raised whether the usual testing with healthy, intact skin will be sufficient.

Uptake of nanoparticles in the gastrointestinal tract after oral uptake is a known phenomenon, of which use is intentionally made in the design of food and pharmacological components.

Finally, this review indicates that only few specific nanoparticles have been investigated in a limited number of test systems and extrapolation of this data to other materials is not possible. Air pollution studies have generated indirect evidence for the role of combustion derived nanoparticles (CDNP) in driving adverse health effects in susceptible groups. Experimental studies with some bulk nanoparticles (carbon black, titanium dioxide, iron oxides) that have been used for decades suggest various adverse effects. However, engineered nanomaterials with new chemical and physical properties are being produced constantly and the toxicity of these is unknown. Therefore, despite the existing database on nanoparticles, no blanket statements about human toxicity can be given at this time. In addition, limited ecotoxicological data for nanomaterials precludes a systematic assessment of the impact of Nanoparticles on ecosystems.

³⁶ <http://www.particleandfibretoxicology.com/content/3/1/11>

16 SCENIHR (2006). *The appropriateness of existing methodologies to assess the potential risks associated with engineered and adventitious products of technologies*³⁷.

Executive summary

In view of the growing importance of nanotechnologies, and following from the conclusions of the Council of the European Union on the European strategy for nanotechnologies¹ highlighting the importance of the “assessment of potential risks throughout the life cycle of nanotechnology based products” and the nanotechnologies action plan², the European Commission asked the independent experts of the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR)³ for a scientific opinion on the appropriateness of existing methodologies to assess the potential risks of nanotechnologies. This report provides this Opinion and the relevant scientific background.

SCENIHR concludes that current risk assessment methodologies require some modification in order to deal with the hazards associated with nanotechnology and in particular that existing toxicological and ecotoxicological methods may not be sufficient to address all of the issues arising with nanoparticles. For exposure evaluation, dose requires information on the number of nanoparticles and/or their surface area in addition to traditional mass concentration characterization. Equipment for routine measurements in various media for representative exposure to free nanoparticles is inadequate. In addition, existing exposure assessment methods may not be appropriate to determine the environmental fate of nanoparticles.

Very little is known about the physiological responses to nanoparticles. Although some conventional toxicity and ecotoxicity tests have been shown to be useful in evaluating the hazards of nanoparticles, existing methodologies may require modification regarding hazard evaluation, including the assessment of whether nanoparticles can exacerbate pre-existing medical conditions, and the detection of nanoparticle distribution in the human body and in environmental compartments. The Committee points to major gaps in the knowledge necessary for risk assessment. These include nanoparticle characterisation, the detection and measurement of nanoparticles, the dose-response, fate, and persistence of nanoparticles in humans and in the environment, and all aspects of toxicology and environmental toxicology related to nanoparticles. Of special importance are the questions concerned with the transport of nanoparticles in the human body and the mechanisms of interaction at the sub-cellular and molecular levels. The monitoring of occupational exposure and the epidemiological data on the potential impact of nanoparticles on human health constitute priorities for further research.

This Report describes nanomaterials properties, identifies sources of free nanoparticles, discusses their detection and measurement and then examines interactions between nanoparticles and living systems. The report addresses the toxicology of nanoparticles and the potential exposure scenarios, and then addresses risk assessment methodologies, the core of the Scientific Opinion, through exposure assessment, hazard identification and characterization, risk characterization and an integrated assessment. The Report complements this scientific background and Opinion by an assessment of the gaps in knowledge required to address the risks of nanotechnologies and an examination of regulatory aspects related to risk assessment.

³⁷ http://ec.europa.eu/health/ph_risk/documents/synth_report.pdf

Summary of Guide

This Guide presents the elements of an UNP handling and exposure minimization program including considerations and guidance, based on a consensus of viewpoints, for establishing such a program.

The six principal elements are:

- a) establishing management commitment to the control principle
- b) identifying and communicating potential hazards;
- c) assessing potential UNP exposures within the worksite;
- d) identifying and implementing engineering, and administrative controls consistent with the control principle for all relevant operations and activities;
- e) documentation and (f) periodically reviewing its adequacy.

The Control Principle

Exposure control guidance in this Guide is premised on the principle (established in this guide) that, as a cautionary measure, occupational exposures to UNP should be minimized to levels that are as low as is reasonably practicable. This principle does not refer to a specific numerical guideline, but to a management objective, adopted on a cautionary basis, to guide the user when (a) assessing the site-specific potential for such exposures; (b) establishing and implementing procedures to minimize such exposures; (c) designing facilities and manufacturing processes; and (d) providing resources to achieve the objective. Additional discussion of the application of the control principle is set forth in Annex A1.

ANNEX III SUMMARY TABLES OF EVALUATION PARAMETERS

Table A3.1 General description of the documents

Nr	Year	Purpose or scope	Document type	Authors	Background authors	Focus of content
1	2007	Technical report with the scope: a description of health and safety practices	Review and guidance	ISO: International Standards Developing Organization	Industry/research	Exposure, hazard, risk management
5	2007	The published document gives guidance on assessing risks and recognizing uncertainties in the development, manufacture and use of nanomaterials, and on the developing and implementing an effective strategy to address and control the risks	Guidance and recommendations	BSI; British Standards Institute. BSI committee NTI/1 with contribution of SAFENANO	Industry/ research	Exposure. Risk, Risk Management
6	2006	Provides an overview of what is known about nanomaterial hazards and measures that can be taken to minimize workplace exposure	Review	NIOSH (USA)	Research	Exposure, hazard, risk management
8	2007	Provides some guidance with respect to regarding control measures in the production and use of nanomaterials at the workplace.	Consensus	BAUA and VCI (Germany)	Government/ industry	Risk management and measurement
9	2006*	Gives an overview of peer-reviewed web-based health and safety & environment tools and reference materials	Other: web based tool	ORC worldwide (private company)	Consultancy	Hazard, exposure, process safety, HS&E risk assessment and risk control

Nr	Year	Purpose or scope	Document type	Authors	Background authors	Focus of content
10a	2006	Purpose is to document current practices and ongoing research, and to establish risk assessment frameworks	Inventory	ICON (International Council on Nanotechnology) prepared by university of California, Santa Barbara (Gina Gerritzen)	Research	Health and safety practices for nanomaterials and best practices guidelines for risk management
10b	2006	Presents the results of an international survey of 64 organizations in the nanotechnology industry on current EHS and product stewardship practices	Inventory; summary of current practices	ICON (International Council on Nanotechnology) prepared by university of California, Santa Barbara (Gina Gerritzen)	Research	Exposure, risk management
11	2006	Identify health, and safety research and information needs related to understanding and managing the potential risks of engineered nanoscale materials that may be used in commercial or consumer products, medical treatment, environmental applications, and research	Review/ policy	National Science and Technology Council (USA)	Government	Risk management
12	2006	To determine what relationships exist between the mass, number and active surface area for current instrumentation measuring in terms of these parameters, and to determine how these relationships are affected by particle characteristics such as composition and morphology	Research paper; report on experimental results	HSL/HSE (UK)	Research	Measurements
13	2007	To identify and discuss scientific information needed to address decision making	Review	US- EPA	Government	Exposure and hazard
14	2005	The paper is focused on identification of new technologies and methods for deriving personalized exposure measurements. It is not specifically dedicated to nanomaterials, and therefore obsolete for the purpose of the present review	Review	Weis et al.	Research	Exposure
15	2006	Review of potential risks of nanomaterials	Review	Borm et al.	Research	Hazard and exposure

Nr	Year	Purpose or scope	Document type	Authors	Background authors	Focus of content
16	2006	Opinion on appropriateness of current risk assessment methodology for assessing the potential risks associated with the manufacture and use of products incorporating engineered nanomaterials	Review / policy	SCENIHR (EU) Working group and external experts	Expert group	Exposure, hazard, risk management
17	2005	Technical report which provides generally accepted definitions and terms well as guidelines on measuring occupational nanoaerosol exposure against a range of metrics.	Review/ guidance	ISO	Industry/research	Exposure
18	2007	Develop site specific controls that will protect workers and the environment; and offer guidance for managing the uncertainty associated with nanomaterials	Consensus/ guidance	Office of Science: US Department of Energy (DOE) Nanoscale Science Research Centre	Government	Risk management
19	2006	The purpose is to offer general guidance on exposure minimization approaches for UNP based upon a consensus of viewpoints	Guidance / consensus document	ASTM; The US National Standards Developing Organization.	Industry/research	Exposure, hazard, risk management

*document will be regularly updated

Table A3.2 Content information of the documents

Scope/purpose	Provide guidance for risk ass and safe use										Identify knowledge gaps/ research needs				
	1	5	6	8	9	12	15	17	18	19	10a	10b	11	13	16
Exposure assessment															
Measurement Methods inhalation	+	+	+	+	+	+	+	+	-	+	-	-	-	-	+
- Online detection	+	+	+	+	+	+	-	+	n/a	+	n/a	-	n/a	n/a	+
- Offline detection	+	±	+	+	+	+	+	+	n/a	+	n/a	-	n/a	n/a	-
- Sampling	+	-	+	+	+	+	+	+	n/a	+	n/a	+	+	-	+
* <i>Level of detail</i>	B	A	A	A	A	B	A	B	n/a	B	n/a	A	A	A	A
- Recommendations	-	-	+	-	-	+	-	-	n/a	-	n/a	-	-	-	-
Measurement methods dermal	+	-	-	-	-	-	+	-	-	-	-	-	-	-	+
- Sampling	+	-	n/a	n/a	n/a	n/a	+	n/a	n/a	n/a	n/a	n/a	n/a	n/a	+
* <i>Level of detail</i>	B	n/a	n/a	n/a	n/a	n/a	A	n/a	n/a	n/a	n/a	n/a	n/a	n/a	A
- Recommendations	-	n/a	n/a	n/a	n/a	n/a	-	n/a	n/a	n/a	n/a	n/a	n/a	n/a	-
Measurement / sampling strategy	+	+	+	-	+	+	+	+	+	+	-	-	-	-	+
* <i>Level of detail</i>	B	B	A	n/a	A	B	A	B	B	B	n/a	n/a	n/a	n/a	A
- Recommendations	-	-	+	n/a	+	+	+	+	+	+	-	-	n/a	n/a	-
Evaluation, gaps or needs	n/a	-	+	n/a	-	+	+	-	-	+	-	-	+	-	+
Exposure mitigation															
Risk management strategies	+	+	+	-	-	-	-	-	+	+	-	-	-	-	-
* <i>Level of detail</i>	B	B	A	n/a	n/a	n/a	n/a	n/a	A	A	n/a	n/a	n/a	n/a	n/a
Control hierarchy	+	+	-	+	+	-	-	-	+	+	-	-	+	-	-
* <i>Level of detail</i>	B	B	n/a	A	A	n/a	n/a	n/a	A	A	n/a	n/a	A	n/a	n/a
Specific measures	+	+	+	+	+	-	-	-	+	+	-	+	+	+	-
* <i>Level of detail</i>	B	A	B	A	B	n/a	n/a	n/a	A	B	n/a	B	A	A	n/a
Data on effectiveness	+	-	+	-	-	-	-	-	-	-	-	-	-	-	-
- Recommendations	-	+	-	+	+	-	-	-	-	-	-	-	-	+	-
Evaluation, gaps or needs	+	±	+	-	+	-	-	-	-	-	-	-	+	-	-

+ topic addressed - topic not addressed; A low level; B high level ; n/a not applicable

Table A3.3 Preliminary evaluation

Nr	Specificity	Robustness			
	Engineered nano particles	Transparency data/ source information	Diversity of references	Cross references ^A	Time window
1	Yes	Transparent; references listed per section	extensive	6, 10b, 12, 13, 16, 17	1990-2007
5	Yes	Transparent; Sources are well described	extensive	1,6, 17	1985-2007
6	Yes	Many clear references	extensive	17	1977-2006
8	No	Sources of information are not given.	-	n/a	-
9	No	Of some tools the sources are described.	moderate	6, 11, 13, 17	
10a	Yes	Sources are well described	extensive	n/a	2005-2006
10b	Yes	Sources are well described	extensive	n/a	2005-2006
11	Yes	Sources are well described	moderate (focus on documents 6 and 13)	6, 13, 16	1993-2006
12	Yes	Not many references	moderate	17	1975-2003
13	Yes	References are well described, except for the methods of exposure assessment	extensive	11, 16	1988-2006
15	Yes	Sources are well described	extensive	-	1974-2005
16	Yes	Transparent and many references	extensive	-	1985-2005
17	No	Sources are well described	extensive	6, 13, 16	1964-2004
18	No	Sources are described	limited	6	1995-2006
19	Yes	Many references, from different sources	extensive	6, 13, 17	1980-2007

^A Refers to (actual or previous versions of) other documents listed

n/a not applicable

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