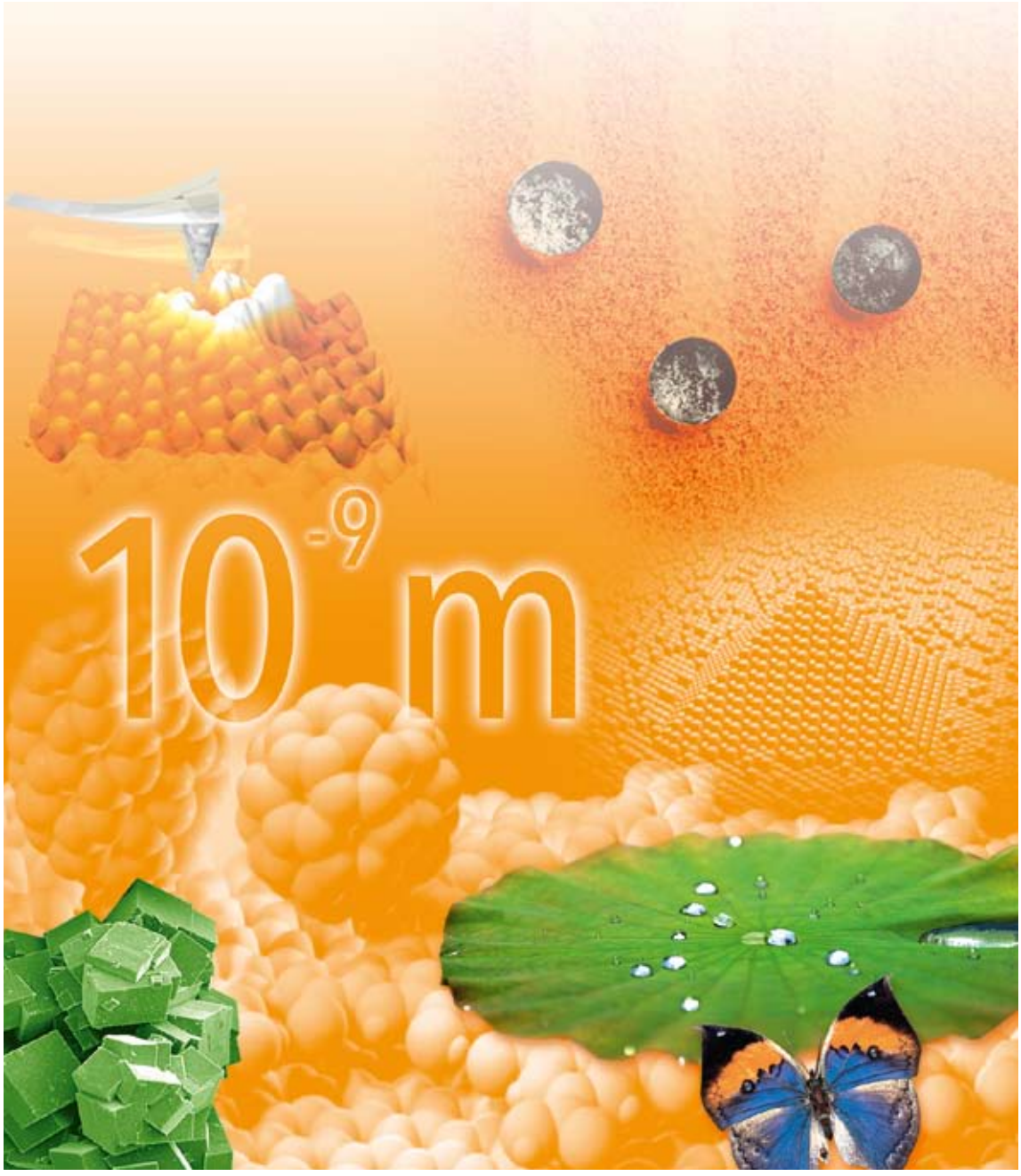
VERBAND DER CHEMISCHEN INDUSTRIE e.V.
German Chemical Industry Association

VCI



Responsible Production and Use of Nanomaterials

11 March 2008

VERBAND DER CHEMISCHEN INDUSTRIE e.V.
German Chemical Industry Association

VCI

The German Chemical Industry is committed to a responsible production and use of nanomaterials.

To support member companies, and customer companies in the value chain, to manage the health, safety and environmental aspects of nano-materials throughout the life cycle, the German Chemical Industry Association (VCI) has issued this comprehensive document. It provides guidance on all aspects of a good product stewardship on nanomaterials.

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11 March 2008

CONTENTS

PRINCIPLES DOCUMENT

REGULATORY DOCUMENTS

DOCUMENTS ON SAFETY RESEARCH

Implementing Responsible Care® for a Responsible Production and Use of Nanomaterials

26 February 2008

The protection of human life and the environment is a fundamental principle for our industry.

The German chemical industry is highly committed to contribute to a sustainable and responsible development of nanomaterial applications under the core principles and commitments of the Responsible Care Global Charter of the International Council of Chemical Associations (ICCA).

Responsible Care is the global chemical industry's health, safety and environmental initiative to drive continuous improvement in performance. It achieves this objective by meeting and going beyond legislative and regulatory compliance, and by adopting cooperative and voluntary initiatives with government and other stakeholders. Responsible Care is both an ethic and a commitment that seeks to build confidence and trust in an industry that is essential to improving living standards and the quality of life. The Responsible Care Global Charter arose from an examination of chemical industry practices and performance that has evolved since the mid-1980s, and was shaped by considering the recommendations of independent stakeholders from around the world. The Responsible Care Global Charter can be found at www.icca-chem.org.

The following **"Global Core Principles"** of the Responsible Care Global Charter commit companies and national associations to work together to:

- Continuously improve the environmental, health and safety knowledge and performance of our technologies, processes and products over their life cycles so as to avoid harm to people and the environment.
- Use resources efficiently and minimise waste.
- Report openly on performance, achievements and shortcomings.
- Listen, engage and work with people to understand and address their concerns and expectations.
- Cooperate with governments and organisations in the development and implementation of effective regulations and standards, and to meet or go beyond them.
- Provide help and advice to foster the responsible management of chemicals by all those who manage and use them along the product chain.

Good Product Stewardship: A key pillar of Responsible Care

Product stewardship is an important pillar of Responsible Care and is the chemical industry's key mechanism for managing the health, safety and environmental aspects of a chemical throughout its life cycle. Product stewardship is a shared responsibility between chemical producers, their suppliers and their customers. It requires the development of close, sustained dialogue and working relationships with suppliers, customers, and others in relevant value chains. These parties should share information up and down the value chain to ensure that chemicals are used and managed safely throughout their life-cycle. In doing so, they will meet the increasing demand for safe and environmentally-sustainable uses of chemicals.

Product stewardship provides the platform for companies to identify risks at an early stage and manage those risks along the value chain, thereby enabling adequate protection of human health and the environment. Evaluation and avoidance of risk reduces the potential for harm and potential liabilities, making product stewardship a "value added" business proposition.

In December 2007, the International Council of Chemical Associations (ICCA) has published **"Product Stewardship Guidelines"** to advance the use of product stewardship throughout the global industry and the chemical value chain. These Guidelines shall assist companies in designing and implementing product stewardship programs built on a management systems approach. The ICCA Product Stewardship Guidelines, containing a Plan-Do-Check-Act model, can be found at www.icca-chem.org.

What is nanotechnology?

For over 100 years, scientists in the disciplines of chemistry, physics and biology have studied and worked with objects that have nanoscale dimensions.

Nanotechnology is the characterization, design, production and use of structures and systems that require exact control of size and form on the nanometre scale. Materials having such minute structures are found to often exhibit different properties compared to "traditional bulk materials" made from the same chemical composition. For example, nanomaterials may offer different mechanical, optical, chemical, magnetic or electronic properties not found in the bulk materials. The ability to selectively manage the size of nanoscale materials now allows the chemical industry to develop materials with new properties that offer significant advantages in our macroscopic world.

Nanotechnologies will facilitate the development of novel applications for very different aspects of our daily lives from biomedical advances to applications in information technology. Nanotechnology has the potential to open up new perspectives to economic, environmental and social benefits and is an innovation driver offering significant opportunities for sustainable development, growth and employment in Europe.

Implementing the Global Responsible Care Core Principles for nanomaterials

The German chemical industry is committed to establish and disseminate best practices for a responsible production and use of nanomaterials. VCI has, therefore, issued guidance documents and recommendation papers to help companies in the sustainable and responsible development of nanotechnology-based applications. These guidance documents and recommendation papers are addressed in the following chapters. The published documents can be found at www.vci.de. Additionally, the German chemical industry has expanded its dialogue with society to address societal expectations and concerns relating to nanomaterials.

Product Safety and Regulatory Compliance

First, and above all, the chemical industry must ensure a high level of protection of human health and the environment and must comply with all regulations.

To support companies in regulatory compliance and maintaining a high level of product safety, VCI has issued the documents

- **"Requirements of the REACH Regulation on Substances which are Manufactured or Imported also as Nanomaterials"** and
- **"Guidance for a Tiered Gathering of Hazard Information for the Risk Assessment of Nanomaterials".**

Worker protection

Ensuring the workplace safety of our employees is at the heart of our industry's culture. Workplace safety is also ensured when nanomaterials are used.

The German chemical industry has decades of experience assessing materials to help ensure that all precautions are taken to assure the safety of workers whilst using chemical materials. We identify sources of risk for our employees in our laboratories, production plants, packing facilities and storage facilities and eliminate these using the appropriate measures. In the event of any health and environmental hazards arising as a result of our operations, we take immediate action. We are pursuing the further development of measuring techniques for nanoparticles and take the necessary actions to protect our employees.

For worker protection, VCI, together with the German Federal Institute for Occupational Safety and Health (BAuA), has issued a

- "**Guidance for Handling and Use of Nanomaterials at the Workplace"** (including a check list).

Information in the value chain: Employees, customers and logistics partners

The German chemical industry only markets products, if health and environmental safety can be assured on the basis of all available scientific and technological information. The German chemical industry provides information about the safe transportation, storage, use, processing and disposal of their nanoscale products to their employees and their customers and logistics partners.

To establish a best practice for submitting information on nanomaterials in the value chain, VCI has issued a

- **"Guidance for the Passing on of Information along the Supply Chain in the Handling of Nanomaterials via Safety Data Sheets"** (including a check list)

Closing gaps in knowledge on health, safety and environmental aspects

The German chemical industry has decades of experience in managing the risks of new technologies: We evaluate carefully and comprehensively any potential risks and take the appropriate measures to safeguard humans and the environment. We are actively involved in the ongoing development in improving and refining testing and assessment methods for nanomaterials.

To close the gap on uncertainty on possibly hazardous effects of nanomaterials, safety research has been intensified and a lively exchange of experiences is taking place in numerous expert groups in order to put new findings into practice. For example, there is a whole series of joint safety research activities of industry and science, such as the EU projects NanoDerm, NanoSafe 1 and NanoSafe 2 as well as the German project NanoCare, supported by the German Research Ministry (BMBF). Studies include, inter alia, suitable particle measuring methods, intake routes, toxicokinetic and toxico-dynamic properties and, by way of testing exemplary substances, a possible organo-toxicity of nanoparticles. In particular inhalation and dermal intake routes are studied. A further major aspect is the assessment of exposure.

For closing gaps in knowledge on health, safety and environmental aspects of nanomaterials, VCI and the German Society for Chemical Engineering and Biotechnology (DECHEMA) have issued the documents

- **"Roadmap for Safety Research on Nanomaterials"** (with a priority list for the European 7th R&D Framework Programme and National Research Programmes) and
- **"Environmental Aspects of Nanoparticles"** (with a priority list for the European 7th R&D Framework Programme and National Research Programmes).

VCI is also actively participating in standard setting activities for nanomaterials of ISO and others and has issued the document:

- **Strategy paper of the German Chemical Industry on the Standardisation of Nanomaterials**

Open dialogue with society to address societal expectations and concerns

The German Chemical industry strives for a dialogue with all stakeholders, based on openness and trust. Transparent reporting about both opportunities and potential risks of nanotechnologies, addressing societal and ethical concerns, disclosure of new findings to the authorities and the public, as well as a proactive engagement with stakeholders are part of the German chemical industry's commitment and contribution to the current debate on nanotechnologies.

Prominent examples of VCI's activities are the

- **Stakeholder Workshops on Nanomaterials**, moderated by the Stiftung Risiko-Dialog, St. Gallen. Two workshops were held on occupational safety aspects on 26 September 2005 and 19 April 2007, and a third one on the information flow in the supply chain on 5 March 2008.
- **Public Fora on Nanomaterials** (as part of VCI's "Forum Zukunft" series), held on 13 October 2006 in Berlin and on 11 October 2007 in Munich.

VCI is, inter alia, an active partner in the

- **"Nano-Dialog" of the German Environment Ministry** and the
- **OECD Working Party on Manufactured Nanomaterials**

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Some terminology

Nanomaterials *are understood to be either so-called* ***nano-objects*** *or* ***nanostructured materials*** *according to the draft definition of the ISO Technical Committee 229 "Nanotechnologies" which was taken over as working definition by the OECD.* ***Nano-objects*** *are materials which are confined in one, two, or three dimensions at the nanoscale (approximately 1 – 100 nm); typical examples are nanoplates, nanorods and nanoparticles.* ***Nanoparticles*** *are nano-objects with three dimensions at the nanoscale.* ***Nanostructured materials*** *have an internal structure at the nanoscale. Typical examples are aggregates and agglomerates of nano-objects. Chemically, nanomaterials can be, for example, pure or mixed oxides, salts, metals, and organic substances.*

Requirements of the REACH Regulation on Substances which are Manufactured or Imported also as Nanomaterials

26 February 2008

1. Introduction

Nanomaterials are understood to be either so-called *nano-objects* or *nanostructured materials* according to the draft definition of the ISO Technical Committee 229 "Nanotechnologies" which was taken over as working definition by the OECD. *Nano-objects* are materials which are confined in one, two, or three dimensions at the nanoscale (approximately 1 – 100 nm); typical examples are nanoplates, nanorods and nanoparticles. *Nanoparticles* are nano-objects with three dimensions at the nanoscale. *Nanostructured materials* have an internal structure at the nanoscale. Typical examples are aggregates and agglomerates of nano-objects. Chemically, nanomaterials can be, for example, pure or mixed oxides, salts, metals, and organic substances.

With a few exceptions, listed in Article 2 of the REACH Regulation, all substances, regardless of their physical state (e.g. their particle size), fall under REACH.

The purpose of the REACH Regulation is to ensure a high level of protection of human health and the environment. As explicitly stated in Article 1 of the REACH Regulation, the provisions of the Regulation are underpinned by the precautionary principle. The precautionary principle is, therefore, already the base for all information requirements for the registration of substances according to Article 12 which are specified in detail in the Annexes VII – X.

REACH requires that all substances, independent of the manufactured or imported quantity, do not adversely affect human health or the environment. For substances manufactured or imported, by a single manufacturer or importer, in quantities of more than one tonne per year a substance registration must be submitted to the European Chemicals Agency.

It should be noted that there are also legal requirements below the threshold of 1 tonne per year for a REACH registration: Obligations for, e.g., risk assessment, classification and labelling, occupational health and safety, as well as the Chemical Agents Directive 98/24/EEC, continue to apply; and there are no volume thresholds for these obligations. This means that manufacturers or importers must classify substances, or even specific products, according to the hazardous properties of the substances or products, label them if necessary, and provide specific safety information. It is possible that some nanomaterials have a different wording in specific chapters of the safety data sheet and a different classification and a different labelling than corresponding bulk products of the same chemical composition. Different classification and different labelling of products with the same chemical identity is not uncommon and occurring e. g. in the case of pyrophorous metal powders and different allotropes of phosphorous.

2. Substance definition

In Article 3 of the REACH Regulation, "substance" is defined as a chemical element and its compounds in the natural state or obtained by any manufacturing process. This definition of a substance includes all physical states, crystal structures, and dimensions of particles of the substance in powder form or in suspension – even if the particle size would go beyond the nanoscale to individual atoms or molecules.

The European Chemicals Agency has stated on 3 December 2007 at the European NanOSH Conference in Helsinki that REACH treats both, the bulk material and the nanosized material, as the same substance. The Agency added that this, however, does not prevent the registrant from identifying dangerous properties of this substance depending on its size and classify the different types accordingly.

Requirements for substance identification are specified in Annex VI, section 2 of the REACH Regulation.

3. Registration

For substances which are manufactured or imported, by a single manufacturer or importer, in quantities of more than one tonne per year, a registration dossier must be submitted to the European Chemicals Agency. If now a solid matter substance is, at the same time, manufactured as an ingot, as coarse crystals, as fine, ultrafine or nanoscale powder, and as a suspension of fine, ultrafine or nanoscale particles in a liquid, all these products, regardless with which process they are manufactured, fall under the definition of the same substance und must, diligently, be included in the registration dossier of this substance. The European Chemicals Agency has stated on 3 December 2007 at the European NanOSH Conference in Helsinki that the whole weight of the substance, nanoscale or not, counts for the threshold above which a registration dossier has to be submitted.

According to Annex VI, section 3 of the REACH Regulation, the registration dossier must include information on the manufacturing process(es) and all identified uses, i.e. also the identified uses of the substance in its nanomaterial state.

For the risk assessment of substances, the REACH registration requires a set of physicochemical, toxicological and ecotoxicological information in the technical dossier, duely reflecting the spectrum of all identified uses of the substance, i.e. also the identified uses of the substance in its nanomaterial state. The minimum information requirements for different tonnage levels of the substance according to Article 12 of the REACH Regulation are specified in detail in the Annexes VII – X. It should be noted that apart from what is required according to the tonnage level, Article 12 also states that the technical dossier must include any other physicochemical, toxicological and ecotoxicological information that is relevant and available to the registrant. To support manufacturers and importers in the process of completing the technical dossier, VCI has issued the document “Guidance for a Tiered Gathering of Hazard Information for the Risk Assessment of Nanomaterials”.

It should be noted that the requirement to include all identified uses of a substance in the registration dossier of this substance also applies to identified uses with volumes of less than one tonne per year if those uses are no longer scientific research and development (R&D) according to Article 3, No. 23 of the REACH Regulation.

Uses of a substance for product and process oriented R&D are exempt for five years from the obligation to be included in the registration dossier of this substance according to Article 9, No. 1 of the REACH Regulation; this exemption can be extended according to Article 9, No. 7. Other obligations, e.g. for risk assessment, classification and labelling, and occupational health and safety, nevertheless, apply.

After a REACH registration, the registrant is responsible, according to Article 22 of the REACH Regulation, to update, without undue delay, the registration dossier if relevant new information is available which includes e. g. new identified uses for which the substance is manufactured, or new knowledge on the risk of the substance to human health and/or the environment which leads to changes in the safety data sheet or the chemical safety report.

4. Chemical safety report

A chemical safety report is mandatory for substances in quantities of more than ten tonnes per year per registrant. All uses of a substance identified in the registration dossier, i.e. also the identified uses of the substance in its nanomaterial state, must, diligently, be included in the chemical safety report of this substance. This applies also to identified uses with volumes of less than ten tonnes per year.

For substances classified as dangerous in accordance with Directive 67/548/EEC, or are assessed to be a PBT or vPvB, exposure scenarios have to be developed for the identified uses, i.e. also the identified uses of the substance in its nanomaterial state, and information be provided on how risks can be avoided or controlled by providing adequate risk management measures, duely reflecting all identified uses of the substance.

5. Information in the supply chain according to Title IV of the REACH Regulation

VCI is has issued a specific guidance document on how to appropriately fill in the safety data form sheet for nanomaterials.

It is common practice in the German chemical industry to use safety data sheets for the communication with downstream users for all products, even if the product is not classified as dangerous in accordance with Directive 67/548/EEC. This includes, of course, also the generation of safety data sheets for nanomaterials which are not classified as dangerous.

Guidance for a Tiered Gathering of Hazard Information for the Risk Assessment of Nanomaterials

28 February 2008

1. Introductory remarks

Nanomaterials are understood to be either so-called *nano-objects* or *nanostructured materials* according to the draft definition of the ISO Technical Committee 229 "Nanotechnologies" which was taken over as working definition by the OECD. *Nano-objects* are materials which are confined in one, two, or three dimensions at the nanoscale (approximately 1 – 100 nm); typical examples are nanoplates, nanorods and nanoparticles. *Nanoparticles* are nano-objects with three dimensions at the nanoscale. *Nanostructured materials* have an internal structure at the nanoscale. Typical examples are aggregates and agglomerates of nano-objects. Chemically, nanomaterials can be, for example, pure or mixed oxides, salts, metals, and organic substances.

For the risk assessment of substances, REACH requires a set of physicochemical, toxicological and ecotoxicological information, duely reflecting the spectrum of all identified uses of the substance, i.e. also the identified uses of the substance in its nanomaterial state. The minimum information requirements for different tonnage levels of the substance according to Article 12 of the REACH Regulation are specified in detail in the Annexes VII – X.

VCI proposes gathering the physicochemical, toxicological and ecotoxicological information on nanomaterials in a tiered approach: The case-by-case evaluation should start with a gathering of basic information, followed, if necessary, by a gathering of extended information on nanomaterials with specific toxicity and/or widespread use and repeated exposure (esp. in consumer products). This is outlined in chapters 2 and 3.

Depending on the physicochemical properties of the nanomaterial, a science based decision has to be taken whether data for the nanomaterial must be generated or can be extrapolated from the bulk material of the same chemical composition, and whether a reasonable read-across or waiving approach is appropriate. Existing data could be used as laid down in Annex XI of the REACH Regulation. The decision on the tests specifically needed should be based on a scientific case-by-case evaluation of the respective nanomaterial.

If solids are provided in liquid media as requirement for the stability of the nanomaterial, the tests should be performed in this state if this is possible and if the hazardous properties are not being determined by the hazardous properties of the liquid.

Polymer nanocomposites contain nanomaterials which are firmly bound within the polymer matrix. Therefore, an easy release of nanoparticles by mechanical forces is not expected. Polymer nanocomposites are, consequently, not addressed in this guidance document.

2. Recommended basic information

The test methods to be used for gathering toxicological and ecotoxicological data may require adaptation according to the physicochemical properties. The physicochemical properties should, therefore, be determined first.

Step 1: Physicochemical information[1]

- Chemical composition[2]
- Information related to molecular and structural formula[2]
- Impurity profile[2]
- Surface chemistry/coating (only to the extent as appropriate and needed for the risk assessment and filling in the SDS)
- Relative density[3]
- Water solubility[3]
- Partition coefficient n-octanol/water (where relevant, e.g. for coated nanomaterials)[3]
- Flash-point[3]
- Flammability[3]
- Explosive properties[3]
- Self-ignition temperature[3]
- Morphology, crystalline phase, shape, surface structure (qualitative description)
- Particle size and size distribution
- Agglomeration and aggregation in native material and in preparation (qualitative description)
- Specific surface area
- Known catalytic activity

Step 2: Toxicological and ecotoxicological information

Toxicological information

- Skin irritation or skin corrosion[3]
- Skin sensitisation[3]
- Eye irritation[3]
- Mutagenicity: In vitro gene mutation study in bacteria[3,4]
- Acute toxicity, by oral/dermal/inhalative route (as appropriate)[3,4]

Ecotoxicological information

- Aquatic toxicity: Short-term toxicity testing on invertebrates (preferred species: daphnia) and/or growth inhibition study on aquatic plants (preferred species: algae)[3,4]
- Degradation: Biotic: Ready biodegradability (where appropriate)[3,4]

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[1] Validated test methods may not exist for all endpoints

[2] Required by REACH, Annex VI

[3] Required by REACH, Annex VII

[4] Part of VCI's voluntary commitment of 23.11.1997

3. Recommended extended information

Depending on the specific case and taking into account the collected basic hazard information and the suggested risk reduction measures, some of the following data might be of relevance.

Physicochemical information[5]

- Dustiness (for powders)
- Porosity
- Dispersion stability in water (or in other media)
- Zeta potential (surface charge)
- Radical formation potential
- Photocatalytic activity

Toxicological information

- Mutagenicity (appropriate in vitro tests)[6]
- Short-term repeated dose toxicity study (28 days), by oral/dermal/inhalative route (as appropriate)[6]
- Sub-chronic toxicity study (90 days), by oral/dermal/inhalative route (as appropriate)[7]
- Reproductive toxicity (appropriate tests)[6]
- Toxicokinetics: Assessment of the toxicokinetic behaviour of the substance to the extent that can be derived from relevant available information[6]
- Carcinogenicity study (in very special cases)[8]

Ecotoxicological information

- Fate and behaviour in the environment: Adsorption/desorption screening[6]
- Appropriate long term aquatic toxicity[9]
- Bioaccumulation in aquatic species (preferably fish)[7]

4. Research activities in the risk assessment of nanomaterials

VCI recommends continuing the efforts in research activities aiming at a further development of risk assessment approaches for nanomaterials. This should include the evaluation of a proposed short term inhalation toxicity test (5 days) under the “Long-range Research Initiative” (LRI) of the European chemical industry.

[5] Validated test methods may not exist for all endpoints

[6] Required by REACH, Annex VIII

[7] Required by REACH, Annex IX

[8] Required by REACH, Annex X

[9] Required by REACH, Annex VIII and IX

Guidance for Handling and Use of Nanomaterials at the Workplace

27 August 2007

Foreword

In spring 2006 the German Federal Institute for Occupational Safety and Health (Bundesanstalt für Arbeitsschutz und Arbeitsmedizin, BAuA) and the German Chemical Industry Association (Verband der Chemischen Industrie, VCI) conducted, among VCI member companies, a joint survey on occupational health and safety in the handling and use of nanomaterials. The purpose of the survey was to obtain an overview of occupational health and safety methods currently applied in the chemical industry in activities involving nanomaterials. A further aim was to develop, on the basis of the survey results, this "Guidance for Handling and Use of Nanomaterials at the Workplace" – with recommendations and operating instructions for the handling and use of nanomaterials in the chemical industry.

The starting point for both joint initiatives of BAuA and VCI was the stakeholder dialogue event on "Synthetic Nanoparticles" on 11./12. October 2005 in Bonn.

The questionnaire survey was evaluated by BAuA; this "Guidance for Handling and Use of Nanomaterials at the Workplace" was elaborated predominantly by VCI. In both activities several expert talks were held between BAuA and VCI in the development phases.

This Guidance wants to provide some orientation regarding measures in the production and use of nanomaterials at the workplace. The recommendations given here reflect the current state of science and technology.

It is planned to adapt this Guidance to the advancing state of knowledge and to bring it in a more specific form, by mid-2008 at the latest.

Berlin/Dortmund/Frankfurt, August 2007

Contents

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1. Introduction

1.1 Background

In spring 2006 the German Federal Institute for Occupational Safety and Health (Bundesanstalt für Arbeitsschutz und Arbeitsmedizin/BAuA) and the German Chemical Industry Association (Verband der Chemischen Industrie/VCI) conducted, among VCI member companies, a joint survey on occupational health and safety in the handling and use of nanomaterials. The purpose of the survey was to obtain an overview of occupational health and safety methods currently applied in the chemical industry in activities involving nanomaterials. A further aim was to develop, on the basis of the survey results, this "Guidance for Handling and Use of Nanomaterials at the Workplace" – with recommendations and operating instructions for the handling and use of nanomaterials in the chemical industry.

The survey was initially addressed to industrial manufacturers and users of nano-materials, covering primarily products that had been manufactured and used for many years. Products still in the research phase were also included in the survey; they are taken into account in this Guidance.[10]

This Guidance wants to provide some orientation regarding measures in the production and use of nanomaterials at the workplace. The recommendations given here reflect the current state of science and technology.

[10] Also start-up companies (list of the federal ministry of education and research/BMBF) took part in the survey. In this way, also companies were included that handle nanomaterials within research activities (in volumes > 10 kg/year).

Nanomaterials are understood to be either so-called *nano-objects* or *nanostructured materials* according to the draft definition of the ISO Technical Committee 229 "Nanotechnologies" which was taken over as working definition by the OECD. *Nano-objects* are materials which are confined in one, two, or three dimensions at the nanoscale (approximately 1 – 100 nm); typical examples are nanoplates, nanorods and nanoparticles. *Nanoparticles* are nano-objects with three dimensions at the nanoscale. *Nanostructured materials* have an internal structure at the nanoscale. Typical examples are aggregates and agglomerates of nano-objects. Chemically, nanomaterials can be, for example, pure or mixed oxides, salts, metals, and organic substances.

Usually highly sophisticated chemical and physical processes are needed to manufacture nanomaterials as nanoparticles in isolated form. However, in most products currently manufactured commercially in larger volumes, nanoparticles do not come as individual particles but as aggregates and agglomerates of various particles.

Aggregates and agglomerates are not nanoparticles in the meaning of this definition (see above); they are nanostructured materials whose nanoparticles are linked with each other. Without major energy input a release of nanoparticles from these aggregates and agglomerates is often not possible.

In some instances, nanoparticles are processed into granules, formulations, dispersions or composites already by their manufacturers. In many cases a release of isolated nanoparticles in subsequent uses is largely no longer to be expected.

1.2 Production processes

The chemical industry produces nanomaterials mainly in two processes: By synthesis in the gaseous phase, i.e. through reaction in a flame, or by reaction in solution. In the gaseous phase reaction, individually produced primary particles very rapidly link to form larger units. Isolated nanoparticles can be produced through reaction in solution, by adding stabilizing agents and depending on the solution medium. Such isolated nanoparticles are either further processed as dispersions, or they are obtained by evaporating the solvent and then further processed.

If only for technical reasons, gaseous phase synthesis of nanomaterials takes place predominantly in closed systems. As an extra measure, these systems are often run at under pressure. Workers' exposure in production is possible mainly at interfaces – such as filling, sampling, cleaning and maintenance work – or in disruptions of normal operations, which call for a particularly high degree of attention where safety technology is concerned.

In activities in liquid media (e.g. precipitation reactions, dispersion in the liquid phase), intake by inhalation is usually excluded by avoiding aerosol formation.

2. General occupational health and safety rules

Like for all other chemical substances, activities involving nanomaterials are subject to occupational health and safety rules and to the provisions of the German Dangerous Substances Ordinance (Gefahrstoffverordnung), with the legal basis being formed by relevant EC Directives. By assessing possible hazards to workers that might be connected with their activities, employers must identify occupational health and safety measures to be taken. These include design and structure of the workplace in its entirety and of individual workstations, as well as measures to reduce exposure to physical, chemical and biological impacts. Furthermore, technical rules for hazardous substances laid down at a subordinate legal level (e.g. TRGS 500, TRGS 401) must be observed (TRGS = Technische Regeln für Gefahrstoffe/technical rules for hazardous substances).

For many insoluble nanomaterials it cannot be excluded at present that an intake by inhalation of these very small particles might pose hazards at the workplace – irrespective of the classification of these substances based on their chemical composition.

The following course of action to protect workers from hazards is laid down in the Dangerous Substances Ordinance:

1. Information gathering
2. Hazard assessment
3. Determination of protection measures
4. Review of effectiveness of measures
5. Documentation

To be taken into account are all work processes and operating states, including maintenance, repairs, disruptions/breakdowns and control activities.

2.1 Information gathering

- Information on the product used (properties, volume, type and form of use).
- Information on the activity (in particular work steps that can lead to intake by inhalation or to dermal or oral intake). For oxidizable materials, also fire and explosion risks must be included.
- Information on substitution options for hazardous substances (including any use of processes or preparations of the substance that result in lower hazard).

- Also to be gathered is information on the effectiveness of protection measures already in place and, if applicable, information on implemented activities in preventive occupational medicine.

- In case of data gaps, this lack of information must be adequately taken into account when determining protection measures.

Sources of information gathering on substance properties are, inter alia, material safety data sheets, labelling information, communications from manufacturers, technical rules and rules by employers' liability insurance associations (Berufsgenossenschaften), publications by competent authorities and organisations, as well as literature data.

2.2 Hazard assessment

Hazard assessments are implemented based on information gathered. Under the German Industrial Health and Safety Act (Arbeitsschutzgesetz), a hazard assessment must take into consideration substance-related hazards and all further hazards (e.g. mechanical or electrical hazards).

2.3 Determination of protection measures

In order to determine technical, organisational and personal protection measures, the following points must be examined based on the hazard assessment:

- Substitution options:
  Examination whether health-endangering substances or technical processes can be replaced by less dangerous substances or processes (e.g. substance variations with reduced emissions).

- Technical protection measures:
  Use contained installations and capture, limit and remove dangerous gases, vapours and dusts, at source if possible.

- Organisational protection measures:
  Adequate washing facilities, protected storage of clothing not worn for work purposes, further hygiene measures, time arrangement of operational sequences, training and instruction, access and storage rules etc.

- Personal protection measures:
  Use of personal protective equipment additionally to technical and organisational measures.

2.4 Review of effectiveness of measures in place

Like for all other working materials, the effectiveness of measures in place must be reviewed regularly for nanomaterials, too. Also in cases where no health-based limit values have been laid down so far, the exposure of workers should be determined after relevant measures were introduced according to good working practice. The following statements in this Guidance are intended to provide assistance in this respect, also pointing to possibly suitable measuring methods.

2.5 Documentation

The documentation of hazard assessments is a binding requirement pursuant to the Dangerous Substances Ordinance. Especially in connection with nanomaterials, for which no health-based limit values can be established as yet, it is particularly important to document protection measures taken, substances used, working conditions and possibly available measurement data on strains – for assessment at a later stage.

3. Recommendations for workers' protection in the handling and use of nanomaterials

Protection measures necessary at the workplace are determined based on hazard assessments. Existing threshold values – e.g. general dust limit values for the alveolar and respirable dust fraction or substance-specific limit values – must be observed.

According to the current state of knowledge it cannot be ruled out that exposure to nanomaterials might have specific effects, different to the effects of larger particles in the micrometre range.

Pursuant to TRGS 900 general dust limit values do not apply in the assessment of ultra-fine dusts (this is understood to mean a dust fraction with a particle size of under 0.1 µm diffusion equivalent diameter, including its agglomerates and aggregates).

Up until specific limit values are laid down for nanoparticles or certain nanomaterials it should, therefore, be striven to minimise exposure. Recommendations of TRGS 401 must be observed regarding dermal exposure.

The following course of action is recommended to determine protection measures:

1. Substitution options:

- Bind powder nanomaterials in liquid or solid media. Use dispersions, pastes or compounds instead of powder substances, wherever this is technically feasible and economically acceptable.

2. Technical protection measures:

- Perform activities in contained installations, wherever this is possible.
- If this cannot be done, avoid the formation of dusts or aerosols. To this end, extract possibly forming dusts or aerosols directly at their source (e.g. in filling and emptying processes), depending on the materials produced and production conditions. Ensure regular maintenance and function testing of extraction facilities.
- Extracted air must not be recirculated without exhaust air purification.

3. Organisational protection measures:

- Instruct the workers involved, in a targeted manner, about the specific physical properties of free nanoparticles, the need for special measures, and potential long-term effects of dusts. Include relevant information in the operating instructions.
- Keep the number of potentially exposed workers as small as possible. Furthermore, deny unauthorised persons access to the relevant work areas.
- Ensure clean work wear. Work wear must be cleaned by the employer. Work wear and private clothing must be stored separately. Ensure the regular cleaning of workplaces. The only way to remove deposits or spilled substances is with a suction device or to wipe them up with a moist cloth; do not remove them by blowing.

4. Personal protection measures:

- Where technical protection measures are not sufficient or cannot be put into place, personal protection measures – such a respiratory protection (e.g. filters of protection levels P2, FFP2, P3 or FFP3, to be selected in the hazard assessment) – are a suitable step. Depending on substance properties, it might be necessary to wear protective gloves, protection goggles with side protection and protective clothing. Where respiratory protection equipment is used, limited wearing times and preventive occupational medical checks must be observed.
- With particles in the size range between 2-200 nm the efficacy of filters increases with decreasing particle size. This is because below 200 nm the diffusion of particles gets much stronger; when flowing through the filter medium, the particles are thus more likely to collide with the fibres of the filter

medium where they are bound. Measuring data from the Berufsgenossenschaftliches Institut für Arbeitsschutz (BGIA)[11] substantiate a "total number penetration efficiency" for three P3 filters – used for sodium chloride particles from 14 and 100 nm – of between 0.011 and 0.026%, referred to the particle count. Data for P2 filters show a penetration of 0.2%, referred to the particle count.

- In the selection of protective gloves, it must be ensured that the glove material is suitable. The glove material must fulfil requirements for maximum wearing time under practical conditions. An important relevant criterion is the permeation time (break-through time depending on glove material and material strength). Additionally to hand protection, it can be necessary to protect further parts of the skin with protective equipment. This includes in particular protective suits, aprons and boots.

- Additionally to the dust protection measures mentioned here, it is also necessary to observe further measures ensuing from special substance properties – e.g. extra anti-explosion measures in the handling of oxidizable nanomaterials, or specific protection measures in the handling of reactive or catalytic nanomaterials. Besides measures designed specifically for nanomaterials, all measures resulting from the hazard assessment must be complied with, too, so that inter alia the occupational exposure levels at the workplace for further working substances – e.g. for solvents – are observed.

- The effectiveness of applied protection measures (e.g. personal protective equipment) must be reviewed.

5. Flowchart "Hazard Assessment for Nanoparticles at the Workplace (respiratory route)"

- The scope of this flowchart covers targeted activities involving nanoparticles (see attached flowchart).

4. Current situation and development of measuring methods for nanoparticles

At present, it is not yet possible to definitely state how nanoparticles should best be characterized for their HSE effects. Studies point to specific surface and particle number concentrations as well as structure and composition of nanoparticles for dose measurement. In this context, particle mass seems to be of less importance. Thus standard gravimetric measuring methods can be used only as accompanying steps when determining exposure to nanoparticles.

[11] The BGIA is an institute for research and testing of the German Berufsgenossenschaften (BG), the institutions for statutory accident insurance and prevention in Germany.

In measurement of nanoparticles, stationary equipment is used to determine particle number concentration and surface concentration of nanoparticle emissions in air at the workplace. This is an expensive and work-intensive measuring method which meets the state-of-the-art, but it is not yet standardized or validated.[12]

In measuring activities, particles manufactured industrially and intentionally cannot be differentiated from nanoparticles from other sources (background exposure at the place of production). Such influences must be taken into account in evaluations of measurements of nanoparticles (e.g. ca. 1 million particles/cm^3 in a smoker room or 100,000 particles/cm^3 at roads with heavy traffic).

4.1 Measuring methods

The following measuring methods are currently available:[13]

- The Condensation Particle Counter (CPC) is the most wide-spread method for measurements of particle number concentration in the nanometre range. CPC enables particle counts in the nanometre range and above, with detection by light dispersion, but CPC does not obtain data on particle size and chemical composition of particles.[14] Quite often, CPC is used in combination with a size classifying instruments such as a Scanning Mobility Particle Sizer (SMPS). The SMPS is the most frequently used instrument for measuring particle size distribution in the size range from 3 to 800 nm. The SMPS method determines the mobility or diffusion equivalent diameter, respectively. Modifications of this method enable a wider range of measurable sizes. However, possibilities to use this method are limited due to its complex nature.

- Aerosol mass spectroscopy 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/SEM) is the available off-line method to find out about size, morphology and particle structure. But here, too, wider use in routine measuring is hampered by complex technical aspects. Energy Dispersive X-Ray Fluorescence Analysis in combination with electron microscopy enables a substance determination of particles with resolution of spatial element distribution. So far, this method allows only semi-quantitative analysis.

[12] The suitability of measuring methods and protection methods is assessed by the federation of institutions for statutory accident insurance and prevention (Hauptverband der gewerblichen Berufsgenossenschaften – HVBG). Further information on suitable measuring methods is given e.g. in the BGIA work folder "Measuring of dangerous substances" (Arbeitsmappe: Messung von Gefahrstoffen). The websites of HVBG and employers' liability insurance associations contain more details on the suitability of respiratory protection filters.

[13] This description of measuring methods includes commonly used methods, with no claim to completeness.

[14] In measuring technology the term particle is used not only for single particles but also for agglomerates and aggregates.

- Besides SMPS, the Nano-Aerosol Sampler (NAS) is a further option for separating particles in the size range from 1 to 1000 nm, e.g. on a TEM grid, for subsequent characterisation with TEM/EDX regarding morphology and element composition. However, up until now only a semi-quantitative evaluation is possible.

4.2 Use of measuring methods in operational practice

Up until now, particle strains are assessed based on mass concentration. However, the measuring of nanoparticles based on mass is only of limited informative value: The total mass of nanoparticles remains comparative low at high particle concentrations. In particular, it must be emphasised that individual measuring results for nanoparticles in air cannot really be compared with each other, because at present the exposure measuring methods are not fully standardized yet.

A standardized – and thus generally accepted – method is the monitoring of work areas by measurement of dustiness (respirable fraction).[15] In the scientific discussion this method is deemed insufficient. There is a need to develop standardized and, most importantly, personal measuring methods for particle counts and sizes. In future, measuring with the "Scanning Mobility Particle Sizer" technique for particle count and particle size distribution could provide further information on exposure in work areas.

4.3 Standardization of measuring methods

The standardization of general conditions for measuring methods relevant in occupational health and safety (i.a. sampling, sample treatment, monitoring methods in occupational health and safety, reference materials) is currently driven forward by the International Standardization Organization (ISO) and the German standardization institute (Deutsches Institut für Normung, DIN).

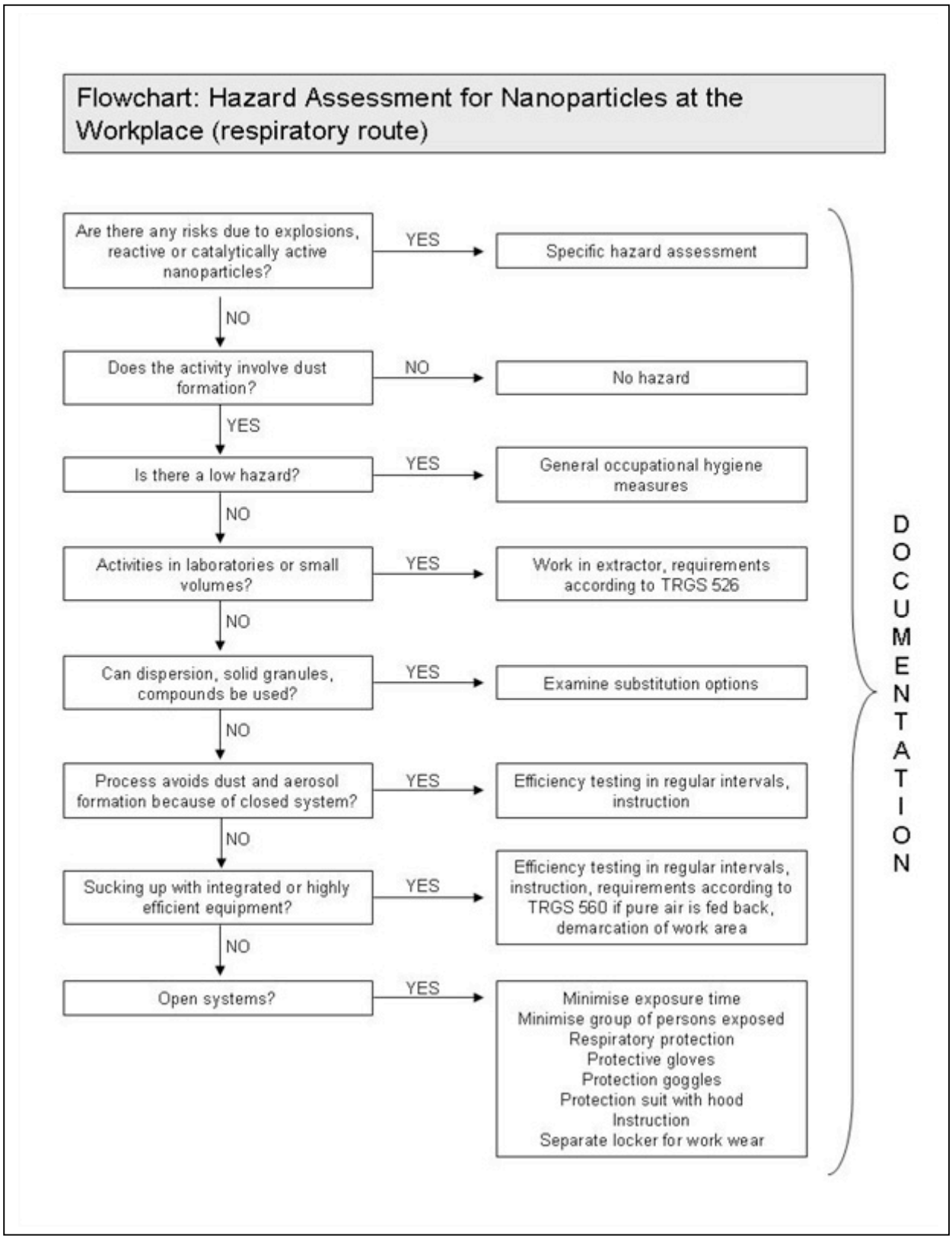
4.4 Safety research regarding measuring methods

"NanoCare" is a cooperation project of chemical industry companies and university research institutes, promoted by the German federal ministry of education and research (BMBF). The project examines, inter alia, agglomeration and aggregation behaviour as well as the stability of agglomerates and aggregates of primary particles at the nanoscale. Furthermore, NanoCare compares existing measuring methods for the determination of airborne particles and aerosols, using materials that are modified and adjusted in a targeted manner to be taken as reference materials in this project. Another NanoCare activity is the further development of measuring methods for parameters of dustiness (Staubungskennzahlen).[16]

[15] According to BGIA work folder, method 7284, and fine dust measuring (alveolar dust fraction) according to BGIA – method 606.
[16] Measuring of the tendency of certain substances to release dusts.

The chemical industry has a decisive role in further projects, such as e.g. "Nanosafe II", "Nanoderm", "Tracer" and also implements own research projects. All ongoing research projects were already specified in the "Roadmap for Safety Research on Nanomaterials" of the DECHEMA/VCI working group "Responsible Production and Use of Nanomaterials".

In November 2006 BAuA (federal institute for occupational safety and health), UBA (federal environment agency) and BfR (federal institute for risk assessment) and the ministries BMAS (labour and social affairs), BMU (environment, nature conservation and nuclear safety) and BMELV (food, agriculture and consumer protection) discussed their draft for a research strategy regarding potential risks of nanotechnology with delegates from science, research and industry, taking first steps toward its implementation.


Flowchart: Hazard Assessment for Nanoparticles at the Workplace (respiratory route)
Are there any risks due to explosions, reactive or catalytically active nanoparticles?
YES
Specific hazard assessment
NO
Does the activity involve dust formation?
NO
No hazard
YES
Is there a low hazard?
YES
General occupational hygiene measures
NO
Activities in laboratories or small volumes?
YES
Work in extractor, requirements according to TRGS 526
NO
Can dispersion, solid granules, compounds be used?
YES
Examine substitution options
NO
Process avoids dust and aerosol formation because of closed system?
YES
Efficiency testing in regular intervals, instruction
NO
Sucking up with integrated or highly efficient equipment?
YES
Efficiency testing in regular intervals, instruction, requirements according to TRGS 560 if pure air is fed back, demarcation of work area
NO
Open systems?
YES
Minimise exposure time
Minimise group of persons exposed
Respiratory protection
Protective gloves
Protection goggles
Protection suit with hood
Instruction
Separate locker for work wear
DOCUMENTATION

List of abbreviations

AGW: **Arbeitsplatzgrenzwert nach Gefahrstoffverordnung**
(Workplace limit value under the German Dangerous Substances Ordinance)

BAuA: **Bundesanstalt für Arbeitsschutz und Arbeitsmedizin**
(Federal institute for occupational safety and health)

BfR: **Bundesinstitut für Risikobewertung**
(Federal Institute for risk assessment)

BGIA: **Berufsgenossenschaftliches Institut für Arbeitsschutz**
(Institute for research and testing of the German Berufsgenossenschaften/BG)

BMAS: **Bundesministerium für Arbeit und Soziales**
(Federal ministry of labour and social affairs)

BMBF: **Bundesministerium für Bildung und Forschung**
(German federal ministry of education and research)

BMELV: **Bundesministerium für Ernährung, Landwirtschaft und Verbraucherschutz**
(German federal ministry of food, agriculture and consumer protection)

BMU: **Bundesministerium für Umwelt, Naturschutz und Reaktorsicherheit**
(Federal ministry for the environment, nature conservation and nuclear safety)

CPC: **Condensation Particle Counter**

DECHEMA: **Gesellschaft für Chemische Technik und Biotechnologie e. V.**
(Society for Chemical Engineering and Biotechnology)

DIN: **Deutsches Institut für Normung e. V.**
(German standardization institute)

EDX: **Energy Dispersive X-Ray Analysis**

HVBG: **Hauptverband der gewerblichen Berufsgenossenschaften**
(Federation of institutions for statutory accident insurance and prevention)

ISO: **International Organization for Standardization**

NAS: **Nano-Aerosol Sampler**

SEM: **Scanning Electron Microscopy**

SMPS: **Scanning Mobility Particle Sizer**

TEM: **Transmission Electron Microscope**

TRGS: **Technische Regeln für Gefahrstoffe**
(Technical rules for hazardous substances)

UBA: **Umweltbundesamt**
(Federal environment agency)

VCI: **Verband der Chemischen Industrie e. V.**
(Chemical industry association)

VERBAND DER CHEMISCHEN INDUSTRIE e.V.
(German Chemical Industry Association)

Guidance for the Passing on of Information along the Supply Chain in the Handling of Nanomaterials via Safety Data Sheets

Status: 6 March 2008

Contents

I. General explanations

1. Introduction

This Guidance document wants to provide assistance for the compilation and use of Safety Data Sheets (SDSs) in the handling of nanomaterials. The present Guidance is to be understood as a supplement to VCI's general "Guidance Safety Data Sheet" ("Leitfaden Sicherheitsdatenblatt") of 28 June 2007 and VCI's general "Questionnaire for the Review of Safety Data Sheets" ("Fragebogen zur Überprüfung von Sicherheitsdatenblättern") of 26 May 2004 (these German-language documents are available for download at www.vci.de).

Safety Data Sheets are of central importance in occupational safety and health, in transport and plant safety and in the assessment of environmental protection issues. For purchasers of chemical products (i.e. substances/preparations), Safety Data Sheets are essential sources of information from which they derive adequate safety measures. Without correct and complete information about chemical products, it is generally not possible to make correct assessments and to take the resulting necessary protection measures at the workplace. In such cases, wrong assessments and wrong conduct cannot be excluded.

The submission of Safety Data Sheets is obligatory for substances/preparations classified as dangerous. However, on a voluntary basis, many companies submit SDSs also for substances/preparations not classified as dangerous. In consequence, SDSs have become a standard information system for chemicals.

Where chemical substances manufactured as nanomaterials are concerned, their properties can change in the transition to nanometer dimensions – this holds true both for physicochemical properties and for biological effects. The explanation lies in the fact that the surface/volume ratio increases compared with coarser materials, together with a higher surface energy and smaller particle sizes.

Depending on their properties, nanomaterials – like all other chemical products – need to be classified by their manufacturers/importers. Where applicable, they need to be labelled and relevant safety information needs to be attached. Manufacturers/importers are under the obligation to compile details for the safe handling of nanomaterials in Safety Data Sheets, in a product-related approach. All these obligations apply without any volume thresholds.

2. Legal situation

The legal basis for the compilation of Safety Data Sheets is the REACH Regulation (EC) No 1907/2006, Title IV in conjunction with Annex II to this Regulation, as in force at the relevant time. Obligations for information in the supply chain pursuant to Title IV of the REACH Regulation entered into force on 1 June 2007.

According to Article 31 and Annex II of the REACH Regulation, Safety Data Sheets must be structured in 16 headings in the given sequence. SDSs must be formulated clearly and comprehensibly, in a manner suitable for users. For example, SDSs should take into account any existing knowledge among the usual users.

Suppliers (every actor in the supply chain, e.g. manufacturer, importer, distributor) of

- substances or preparations classified as dangerous,

- substances or preparations classified as persistent, bioaccumulative and toxic or classified as very persistent and very bioaccumulative according to the criteria of Annex XIII of the REACH Regulation,

- substances that were included, for reasons other than those mentioned above, in the list established in accordance with Article 59, No. 1 of the REACH Regulation

must provide free-of-charge a Safety Data Sheet, at the latest with the first delivery. For reasons of liability law, the supply of a Safety Data Sheet to the customer must be verifiable.

In particular for preparations, a systematic approach in the compilation and regular revision of SDSs according to Article 31, No. 9 of the REACH Regulation prevent potential infringements of the updating requirement for Safety Data Sheets when new findings on individual components become available.

Pursuant to Article 32 of the REACH Regulation, any supplier of a substance on its own or in a preparation who does not have to supply a Safety Data Sheet in accordance with Article 31 must provide the recipient with the following information:

- Registration number(s), if available,

- if the substance is subject to authorisation and details of any authorisation granted or denied in this supply chain,

- details of any restrictions,

- any other available and relevant information about the substance that is necessary to enable appropriate risk management measures to be identified and applied including specific conditions resulting from the application of section 3 of Annex XI (General rules for adaptation of the standard testing regime set out in Annexes VII to X).

No SDS is necessary for substances and preparations distributed to private end consumers. However, in terms of product responsibility it makes sense to have SDSs available for all chemical products (substances/preparations), including products for which there is no legal obligation to compile a Safety Data Sheet.

3. Scope of this Guidance

The Safety Data Sheet contains all important items of information about substances/preparations which are needed for an adequate implementation of activities involving these chemical products. Furthermore, information given in SDSs shall contribute to safe transport and to the protection of the environment.

SDS information about substances/preparations is intended primarily for professional users and must enable professional users to take the measures necessary for health protection, safety and environmental protection at the workplace. For example, resorting to SDS information, users must

- assess hazards/risks that might arise in the use of the substance/preparation,

- elaborate operating instructions for their workforce,

- be able to find out about substitution options.

This Guidance covers exclusively intentionally manufactured nanomaterials, based on the working definition of the "OECD Working Party on Manufactured Nanomaterials". Thus intentionally manufactured nanomaterials have specific properties or a specific composition.

Nanomaterials are understood to be either so-called *nano-objects* or *nanostructured materials* according to the draft definition of the ISO Technical Committee 229 "Nanotechnologies" which was taken over as working definition by the OECD. *Nano-objects* are materials which are confined in one, two, or three dimensions at the nanoscale (approximately 1 – 100 nm); typical examples are nanoplates, nanorods and nanoparticles. *Nanoparticles* are nano-objects with three dimensions at the nanoscale. *Nanostructured materials* have an internal structure at the nanoscale. Typical examples are aggregates and agglomerates of nano-objects. Chemically, nanomaterials can be, for example, pure or mixed oxides, salts, metals, and organic substances.

Usually highly sophisticated chemical and physical processes are needed to manufacture nanomaterials as nanoparticles in isolated form. However, in most products currently manufactured commercially in larger volumes, nanoparticles do not come as individual particles but as aggregates and agglomerates of various particles.

Aggregates and agglomerates are usually not nanoparticles in the meaning of the OECD definition (see above); they are nanostructured materials whose nanoparticles are linked with each other. Without major energy input a release of nanoparticles from these aggregates and agglomerates is often not possible.

In some instances, nanomaterials are processed into granules, formulations, dispersions or composites already by their manufacturers. In many cases a release of isolated nanoparticles in subsequent uses is no longer to be expected.[17]

4. Recommendations by the German Chemical Industry Association VCI

VCI's recommendations for information in Safety Data Sheets are summed up in the "Checklist for the compilation and use of Safety Data Sheets (SDSs) in the handling of nanomaterials" (part II of this Guidance) – for implementation in operational practice. All headings of Safety Data Sheets are covered. In each individual case it must be examined whether the items of information recommended in the checklist are applicable for the substance/preparation concerned.

Some SDS headings are of special relevance to the safe handling of nanomaterials, such as e.g. heading 3 "Composition/information on ingredients", heading 7 "Handling and storage", heading 8 "Exposure controls/personal protection", heading 9 "Physical and chemical properties", heading 11 "Toxicological information" and heading 12 "Ecological information". Sections 9, 11 and 12 of the "Checklist for the compilation and use of Safety Data Sheets (SDSs) in the handling of nanomaterials" (part II of this Guidance) are based on the VCI document "Guidance for a Tiered Gathering of Hazard Information for the Risk Assessment of Nanomaterials" of 28 February 2008 (available for download at www.vci.de). That VCI document gives, first, recommendations for

[17] "Nanoparticle aerosols arising from mechanical processes (e.g. the breaking fracture of solid or liquid material) are unlikely to be formed. Grinding and surfaces finishing typically releases micrometre and submicrometre particles, possibly down to 100 nm but rarely below this" (Report of the Scientific Committee on Emerging and Newly Identified Health Risks [SCENIHR] of the EU Commission, March 2006).

gathering basic information about nanomaterials, intended to serve as a foundation for information in SDSs for nanomaterials.

Furthermore, the VCI document "Guidance for a Tiered Gathering of Hazard Information for the Risk Assessment of Nanomaterials" contains a listing of additional items of information about nanomaterials which might be of relevance – depending on the specific individual case and taking into consideration existing information as well as recommended risk reduction measures. Those additional items of information are also included in the checklist in part II of this Guidance regarding Safety Data Sheets in the handling of nanomaterials.

In the German chemical industry it is common practice to use SDSs for the passing on of information along the supply chain. This is done for all substances and preparations, also where the substance or the preparation are not classified as dangerous according to Directive 67/548/EEC. This includes, of course, the compilation of SDSs for nanomaterials not classified as dangerous.

No Safety Data Sheets are legally required for substances and preparations intended for private consumers. However, SDSs should be made available on request. Moreover, in some cases the submission of SDSs is necessary in decision-making by public authorities, e.g. for certain licensing procedures under immission protection law.

On 27 August 2007 the German Federal Institute for Occupational Safety and Health (BAuA) and VCI published jointly the "Guidance for Handling and Use of Nanomaterials at the Workplace". This publication is recommended to all manufacturers and users of nanomaterials (available for download at www.vci.de).

II. Checklist for the compilation and use of Safety Data Sheets (SDSs) in the handling of nanomaterials

This checklist serves for the compilation and use of Safety Data Sheets by manufacturers, processors and users of nanomaterials within the scope of this Guidance (see I. 3.).

Consistency

Was a comparison made with the manufacturer's technical data sheet ("Technisches Merkblatt")?
Yes □ No □ Comments:_____

1. Identification of the substance/preparation and of the company/undertaking

Is the identification of the substance/preparation stated? Product trade names should be stated, too.
Yes □ No □ Comments:_____

Are the most important or the most frequent uses of the substance/preparation stated?
Yes □ No □ Comments:_____

Is the identification of the company/undertaking stated?
Yes □ No □ Comments:_____

2. Hazards identification

Are the hazards stated here derived from the information on physicochemical properties, toxicology and ecology/eco-toxicology of the substance/preparation?
Yes □ No □ Comments:_____

Are the R-phrases in the labelling consistent with the stated hazards? A purely formal description of potential hazards – pursuant to the criteria of the [German] Chemicals Act (Chemikaliengesetz) or of the [German] Hazardous Substances Ordinance (Gefahrstoffverordnung) – is not sufficient.
Yes □ No □ Comments:_____

Is dust formation mentioned among the potential hazards?
Yes □ No □ Comments:_____

Are further hazards with no relevance to classification stated (e.g. suffocation, skidding, specific hazards to the environment)?
Yes □ No □ Comments:_____

3. Composition/information on ingredients

Does the information on the chemical composition of the preparation include all ingredients with dangerous properties and, where applicable, the impurities (to the extent that this is necessary for classification and for the deriving of occupational health and safety measures)? Are shares or concentration ranges, respectively, of ingredients with dangerous properties stated? Is reference made to heading 8 ("Exposure controls/personal protection")?
Yes □ No □ Comments:_____

Where applicable, is general information given on surface modification of the nanomaterial – to the extent that this is necessary for classification, risk assessment and for the deriving of occupational health and safety measures (e.g. hydrophobicity/hydrophilicity, surface charge, general chemical functionality)?
Yes □ No □ Comments:_____

Within the European Union – are the EINECS nos. and, where applicable, the chemical structural formulas stated for all ingredients with dangerous properties? Where there is no EINECS no., the CAS no. must be stated. For worldwide use, preferably the CAS no. should be stated. Generic names can be used, too.
Yes □ No □ Comments:_____

Are all substances with a common occupational exposure limit stated for workplace exposure? Reference to heading 8 ("Exposure controls/personal protection) is admissible.
Yes □ No □ Comments:_____

4. First-aid measures

Case-by-case decision necessary.

5. Fire-fighting measures

Case-by-case decision necessary.

6. Accidental release measures

Are the measures stated here congruent with the statements under heading 2 ("Hazards identification"), under heading 11 ("Toxicological information") and under heading 12 ("Ecological information")?
Yes □ No □ Comments:_____

7. Handling and storage

Do certain forms of uses (e.g. uses in which aerosols can form) need to be excluded or is it necessary to propose risk management measures for these uses, respectively?
Yes □ No □ Comments:_____

Does the information include both safety-relevant technical measures as well as safety-relevant advice for handling?
Yes □ No □ Comments:_____

Where applicable, should a note be inserted, stating that the provided safety information does not apply for all uses?
Yes □ No □ Comments:_____

Is the risk of an explosive mixture pointed out, if information is provided on the lower and/or upper explosion limit under heading 9 ("Physical and chemical properties")?
Yes □ No □ Comments:_____

8. Exposure controls/personal protection

Are existing workplace limit values for all ingredients listed under heading 3 ("Composition/information on ingredients") stated here, to the extent that they are available for the substance (see list in TRGS 900; TRGS = Technical Rules for Dangerous Substances of the [German] Hazardous Substances Ordinance)?
Yes □ No □ Comments:_____

Are there exposure limits to be observed?
Yes □ No □ Comments:_____

Are workplace limit values stated for specific decomposition products mentioned under heading 10 ("Stability and reactivity"), which form in intended use?
Yes □ No □ Comments:_____

Is the measuring method stated for exposure determination of the substance/ preparation (e.g. measuring method according to German DIN standard or BGIA Work Folder; BGIA = Institute for Research and Testing of the German Institutions for Statutory Accident Insurance and Prevention)?
Yes □ No □ Comments:_____

Is the information on physicochemical properties of the nanomaterial under heading 9 reflected in the information about exposure controls and personal protection?
Yes □ No □ Comments:_____

Are preventive occupational health and safety measures recommended? If measures are necessary, technical measures for exposure controls should be recommended.
Yes □ No □ Comments:_____

If necessary, is information provided on personal protection (respiratory protection and hand protection), stating mask/filter type, wearing time, penetration time and glove material?
Yes □ No □ Comments:_____

If necessary, is detailed information given on eye protection?
Yes □ No □ Comments:_____

Is the information about the suitability of personal protection (mask/filter, gloves) sufficiently substantiated (e.g. testing with substances other than common salt, information from KCL database; KCL = protective glove manufacturer)?
Yes □ No □ Comments:_____

Where protection measures are concerned, can differentiations be made according to uses?
Yes □ No □ Comments:_____

Are use-relevant protection measures known from workplace monitoring?
Yes □ No □ Comments:_____

Is a note inserted, stating that the [German] "general dust limit value" ("Allgemeiner Staubgrenzwert") does not apply for the assessment of ultra-fine dusts? Therefore, exposure minimization should be a goal for nanoparticles or for certain nanomaterials. Regarding dermal exposure, the recommendations of TRGS 401 (TRGS = Technical Rules for Dangerous Substances of the [German] Hazardous Substances Ordinance) must be observed.
Yes □ No □ Comments:_____

9. Physical and chemical properties

Is the substance/preparation a powder, and is this stated? The term "powder" needs to be defined more closely.
Yes □ No □ Comments:_____

Are the following items of information about the nanomaterial provided, to the extent that they are necessary for classification and for the deriving of occupational health and safety measures?

- Relative density

Yes □ No □ Comments:_____

- Flash point

Yes □ No □ Comments:_____

- Flammability

Yes □ No □ Comments:_____

- Explosive properties

Yes □ No □ Comments:_____

- Self-ignition temperature

Yes □ No □ Comments:_____

Are the following items of information provided, regarding the physicochemical properties of the nanomaterial?

- Water solubility

Yes □ No □ Comments:_____

- Partition coefficient: n-octanol/water

Yes □ No □ Comments:_____

- Morphology, crystalline phase, shape, surface structure (qualitative description)

Yes □ No □ Comments:_____

- Particle size, particle size distribution

Yes □ No □ Comments:_____

- Agglomeration and aggregation in native material and in preparations (qualitative description)

Yes □ No □ Comments:_____

- Specific surface area

Yes □ No □ Comments:_____

- Known catalytic activity

Yes □ No □ Comments:_____

Should the following items of information about the nanomaterial be included in the Safety Data Sheet – depending on the specific case and taking into consideration existing information as well as recommended risk reduction measures?

- Dustiness (for powders)

Yes □ No □ Comments:_____

- Radical formation potential

Yes □ No □ Comments:_____

- Photocatalytic activity

Yes □ No □ Comments:_____

- Are test/measuring methods listed for the stated physicochemical properties?

Yes □ No □ Comments:_____

10. Stability and reactivity

Can external conditions influence the stability of the substance/preparation?
Yes □ No □ Comments:_____

Are stabilizers necessary or recommended, in order to avoid decomposition?
Yes □ No □ Comments:_____

Is the effect of the stabilizers limited in terms of time?
Yes □ No □ Comments:_____

Is an exothermal reaction possible in certain conditions?
Yes □ No □ Comments:_____

Can hazardous decomposition products be formed?
Yes □ No □ Comments:_____

Are decomposition reactions possible in contact with other substances?
Yes □ No □ Comments:_____

11. Toxicological information

Are general statements made regarding the toxicological effects of the substance/ preparation, to the extent that this is possible?
Yes □ No □ Comments:_____

For preparations that consist of several individual components – are the provided items of toxicological information clearly related to the respective components? Where necessary, notes must be inserted regarding the applicability of performed toxicological tests to nanomaterials.
Yes □ No □ Comments:_____

Are the following items of information provided, regarding the toxicological properties of the nanomaterial?

- Skin irritation or skin corrosion

Yes □ No □ Comments:_____

- Skin sensitisation

Yes □ No □ Comments:_____

- Eye irritation

Yes □ No □ Comments:_____

- Mutagenicity (*in vitro* gene mutation study in bacteria)

Yes □ No □ Comments:_____

- Acute toxicity: oral, dermal, inhalation – depending on use

Yes □ No □ Comments:_____

Should the following items of information about the nanomaterial be included in the Safety Data Sheet – depending on the specific case and taking into consideration existing information as well as recommended risk reduction measures?

- Mutagenicity (appropriate *in vitro* tests)

Yes □ No □ Comments:_____

- Short-term repeated dose toxicity (28 days): oral, dermal, inhalation – depending on use

Yes □ No □ Comments:_____

- Sub-chronic toxicity (90 days): oral, dermal, inhalation – depending on use

Yes □ No □ Comments:_____

- Reproductive toxicity

Yes □ No □ Comments:_____

- Toxicokinetics

Yes □ No □ Comments:_____

- Carcinogenicity (in very specific cases)

Yes □ No □ Comments:_____

Are data gaps addressed? Where necessary, it must be additionally pointed to scientific studies and ongoing research projects.
Yes □ No □ Comments:_____

Are the stated properties consistent with the protection measures recommended in this Safety Data Sheet?
Yes □ No □ Comments:_____

Was a comparison made between experiences in humans and the stated potential hazards? Where applicable, it must be pointed to the current scientific discussion.
Yes □ No □ Comments:_____

12. Ecological information

For preparations that consist of several individual components – are the provided items of ecological and eco-toxicological information clearly related to the respective components? Where necessary, notes must be inserted regarding the applicability of performed ecological and eco-toxicological tests to nanomaterials.
Yes □ No □ Comments:_____

Are the following items of information provided, regarding the ecological and eco-toxicological properties of the nanomaterial?

- Aquatic toxicity: Short-term toxicity to invertebrates (preferably: daphnia) and/or growth inhibition study on aquatic plants (preferably: algae)

Yes □ No □ Comments:_____

- Biodegradability (where appropriate)

Yes □ No □ Comments:_____

Should the following items of information about the nanomaterial be included in the Safety Data Sheet – depending on the specific case and taking into consideration existing information as well as recommended risk reduction measures?

- Fate and behaviour in the environment: Adsorption/desorption screening

Yes □ No □ Comments:_____

- Appropriate long-term aquatic toxicity

Yes □ No □ Comments:_____

- Bioaccumulation in aquatic species (preferably: fish)

Yes □ No □ Comments:_____

Are data gaps addressed? Where necessary, it must be additionally pointed to scientific studies and ongoing research projects.
Yes □ No □ Comments:_____

Are the stated properties consistent with the recommended items of information regarding accidental release and disposal?
Yes □ No □ Comments:_____

13. Disposal considerations

The measures listed here should be congruent with the statements under heading 6 ("Accidental release measures").

Are suitable disposal measures stated for the substance/preparation and for contaminated packaging?
Yes □ No □ Comments:_____

Are residues stated, which might pose a hazard in disposal?
Yes □ No □ Comments:_____

14. Transport information

Case-by-case decision necessary.

15. Regulatory information

Case-by-case decision necessary.

16. Other information

Depending on the properties of the substance/preparation – is it made quite clear on a case-by-case basis that the items of information about the specific substance/preparation, as provided under headings 3 to 15, cannot be transferred to other substances/preparations?
Yes □ No □ Comments:_____

Are other relevant documents specified (e.g. technical data sheets, safety studies etc.)?
Yes □ No □ Comments:_____

Strategy Paper of the German Chemical Industry on the Standardisation of Nanomaterials

October 2007

1. Introduction

In June 2007, the 4th Technical Committee meeting of the ISO/TC 229 "Nanotechnologies" was held. The Technical Committee consists of

- Working Group 1 "Nomenclature and definitions"
- Working Group 2 "Measurement and characterisation"
- Working Group 3 "Health, Safety and Environment (HSE)"

Chairman of the ISO/TC 229 is Dr. Peter Hatto (UK), the secretariat is at the British Standards Institute (BSI). The Technical Committee will set no requirements for specific products, but develop horizontal standards that will be applicable to a variety of products. In this context, the work of the Working Group 3 is of special interest as it will define framework conditions for health, safety and environment (HSE) aspects of nanomaterials. Because of the growing public awareness regarding HSE aspects of nanomaterials and accompanying calls for regulatory measures by some stakeholders, it is expected that the work of the Working Group 3 will be of highest priority within the ISO/TC 229.

In Germany, the German Institute for Standardization (Deutsches Institut für Normung - DIN) has established the Working Committee NA 062-08-17 AA "Nanotechnologies" which deals with the subject of ISO/TC 229 at national level and designates the German delegates for the international bodies.

2. Analysis of the current situation

It has to be realized that the work of ISO/TC 229 is increasingly gaining momentum. The number of proposals for standardization is currently rising significantly, and another sharp increase is to be expected as soon as the Working Group roadmaps have been finalized. The proposals for standardization are predominantly of Asian, US and UK origin. The German industry is already severely impacted by some proposals in the field of measuring standards for carbon nanotubes and toxicological test methods. ISO has clearly expressed interest in elaborating toxicological and ecotoxicological test protocols. In addition, the US delegation speaks for exposure limits at the work place by way of ISO standards. China has submitted at ISO the first two national product standards (e.g. for titanium dioxide) as New Work Item Proposals (NWIP). UK is preparing seven Public Available Specifications (PAS) and two Public Documents (PD) with a high impact for the German chemical industry as NWIP for ISO (incl. "PD 6699-1 Good practice guide to specifying nanomaterials", "PD 6699-2 Good practice guide to safe handling and disposal of engineered nanoparticles", "PAS 130 Guidance on the

labelling of manufactured nanoparticles and manufactured products containing nano-particles").

3. Proposal for priority themes for the standardization of nanomaterials

The following projects will have a strong impact on the development of nanotechnology in Germany and can be substantially influenced by German expertise:

- Nomenclature

- Product exposure at the workplace (aerosol measurement)
  - Methods (mass, concentration, particle size distribution)
  - Measurement strategy (background level)

- Characterisation strategy (sampling methods, characterisation protocols)
  - for products
  - for toxicological testing
  - Sample preparation for toxicology testing: Proposals from existing projects (e.g. NanoCare, project of Wacker-Chemie)

- Methods for the evaluation of risk management measures for occupational workplace safety
  - Technical measures
  - Personal Protective Equipment (PPE)

- Emission of nanoparticles throughout the life cycle
  - Conditions/forces to emit nanoparticles from nanomaterials
  - Emission of nanoparticles from products for specified uses (e.g. lacquers)

These issues should be preferably worked out as New Work Item Proposals (NWIP) and fed in at ISO. On these issues, project management should also be striven for; where this is not possible, an intensive participation of Germany's chemical industry should be ensured.

DECHEMA e.V.

Society for Chemical Engineering and Biotechnology

VCI

German Chemical Industry Association

Roadmap for Safety Research on Nanomaterials

– with a priority list for the European 7th R&D Framework Programme and national research programmes –

5 July 2007

1. Introduction

Nanotechnology is the technology that characterises, designs, produces and uses structures and systems that require exact control of the size and form of matter on the nanometre scale. A nanometre is a billionth of a meter.

Nanotechnology will enable new developments and novel applications from biomedicine to information technology. Chemistry is the science that delivers basic materials for those technologies by producing “nanomaterials”.

Nanomaterials are understood to be either so-called *nano-objects* or *nanostructured materials* according to the draft definition of the ISO Technical Committee 229 "Nanotechnologies" which was taken over as working definition by the OECD. *Nano-objects* are materials which are confined in one, two, or three dimensions at the nanoscale (approximately 1 – 100 nm); typical examples are nanoplates, nanorods and nanoparticles. Nanoparticles are nano-objects with three dimensions at the nanoscale. *Nanostructured materials* have an internal structure at the nanoscale. Typical examples are aggregates and agglomerates of nano-objects. Chemically, nanomaterials can be, for example, pure or mixed oxides, salts, metals, and organic substances.

Nanomaterials may exhibit new substance properties, especially due to an increased surface/volume ratio, a higher surface energy and a smaller particle size, which may lead, in some cases, to other toxicological and ecotoxicological properties than the properties of the corresponding bulk materials. These possible changes in substance properties currently give rise to the question whether existing exposure measurement techniques and toxicological testing strategies are appropriate to assess potential hazards and analyse potential risks of nanomaterials. This is currently intensively studied worldwide by industry and academia.

Nanomaterials must be safe for man and the environment. As with any other emerging technology, safety research is necessary to ensure a responsible use of nanomaterials.

In Germany, DECHEMA and VCI have established as early as 2003 the joint working group "Responsible Production and Use of Nanomaterials" which consists of high-level European academic and industrial experts and is regularly joined by representatives from German authorities. The group shares scientific findings and best practices on safety aspects of the production and use of nanomaterials.

The DECHEMA/VCI working group has already addressed safety aspects of nanomaterials at a very early stage in a roadmap for safety research. This roadmap, shown in the Annex of this document, is continuously reviewed and updated. The roadmap contributed, i.a., to the “NanoCare” project, co-funded by the German Federal Ministry of Research (BMBF).

This document also provides recommendations which research issues should be addressed in the European 7th R&D Framework Programme, especially in the European Technology Platforms for Sustainable Chemistry (SusChem) and for Industrial Safety (ETPIS), and in national research programmes.

2. Overview of the most urgent issues and ongoing research projects concerning the safety and potential risks of nanomaterials

In close cooperation with academia, the chemical industry works already on almost all of the most urgent research issues:

- The BMBF project "NanoCare" project will
  - investigate decisive parameters which trigger toxic effects (size, chemical composition, effects of surface, morphology) by the end of 2007.
  - develop and assess toxicity testing methods with respect to their suitability to detect different specific effects in bodies under practical circumstances, e. g. at the working place, by mid 2008.
  - study the toxicology of other materials than titania and carbon black by the end of 2007.
  - develop methods to reproducibly provide inhalable atmospheres of nanomaterials suitable for toxicological studies by the end of 2007.
  - investigate the stability of agglomerated nanoparticles in body fluids by mid 2008.

- The project "Nanosafe II" funded by the European Commission
  - develops and assesses toxicological testing methods with respect to their suitability to detect different specific effects in the body under practical circumstances, e. g. at the working place, by the end of 2008.
  - studies the toxicity of other materials than Titania and carbon black by the end of 2008.
  - develops methods to reproducibly provide nanoscaled aerosols for toxicological studies by mid 2008.
  - investigates mechanisms to take particles into the lung by the end of 2008.
  - investigates the real morphology (isolated, agglomerated) of nanoparticles and develops methods to detect the kind and concentration at the working place by the end of 2008.

- The Centre for Functional Nanostructures of the Deutsche Forschungsgemeinschaft (DFG; German Research Foundation) has launched a project that
  - has investigated the transport of nanoparticles into and through cells and the crossing of organ barriers (blood-brain barrier, placenta barrier, etc.)

- The research project "Nanoparticle Exposure on Workplaces (NEW)" at the Institute for Environmental Technology and Analytics (IUTA) and the “NanoCare” project will
  - investigate the real morphology (isolated, agglomerated) of nanoparticles and develop methods to detect the kind and concentration at the work place by mid 2008.

- The DFG Priority Programme SPP 1313 "Biological Responses to Nanoscale Particles" investigates the manufacturing and characterisation of nanoparticles, the transition of nanoparticles into and interaction with the biological environment, and the impact of nanoparticles on fundamental biological functions.

- "TRACER" is a project of several German companies within one value chain, co-funded by the German BMBF, which evaluates cytotoxity and biocompatibility of carbon nanotubes (CNT) and will derive recommendations for a safe processing, handling and use of these products.

- "INOS" (UFZ Dresden) will evaluate possible adverse health effects at production, characterization and processing of nanoscale powders.

- The FP 6 EU project "IMPART" reviews the latest scientific and technological developments related to the risks of nanoparticle exposure on human health and the environment and will in the end formulate guidelines and recommendations for future nanoparticle standards and exposure limits.

- FP 6's "Nanotox" project analyses information on the toxicological impact of nanoparticles by reviewing information on
  - physical and chemical properties of different types of nanoparticles and agglomerated nanocrystals, manufacturing and use, human health effects including side effects, animal toxicology; environmental impacts, mutagenicity/ genotoxicity, metabolism/pharmacokinetics, standards for safe use, safe laboratory methods, etc.
  - the potential methods of dispersal of, and contamination by, nanoparticles and agglomerated nanocrystals (e.g. adsorption, desorption, transport, aggregation, deposition, biological-uptake).

- The EU Project "NEST Particle Risk" is devoted to study the health hazards posed by new types of particles like nanotubes or fullerenes. The partners will also develop methods to detect and quantify the presence of the particles in living tissues. Mice will be used to assess the uptake and transport of the particles in living systems. In-vivo toxicity testing will use a mouse model, in vitro-tests will use cultured cells.

- The EU project "Nanoderm" investigated the uptake of titania and zinc oxide nanoparticles via the skin. The project has been finalized; the final report is still pending. The interim results confirm the effectiveness of the healthy skin as protective barrier.

- A German company investigated the skin penetration of zinc oxide and titania nanoparticles according to OECD guidelines: No skin penetration was found.

- The EU project "NANOTRANSPORT" addresses the behaviour of aerosols released to ambient air from nanoparticle manufacturing. The proposed pre-normative study has the objective of bringing into light and to document the need for standardised test aerosols adapted to the scope of nano-toxicology and occupational health studies.

Further issues not mentioned here but identified by the DECHEMA-VCI working group (see roadmap in the Annex) are addressed in company projects and in projects of the Institute for Environmental Medicine at the Heinrich-Heine-University, Duesseldorf.

As demonstrated in the Annex, almost all of the important issues concerning the safety and potential risks of nanomaterials are already under evaluation. Issues to be addressed within the European 7th R&D Framework Programme and within national research programmes and to promote European co-operation are described in the following chapter.

3. Recommendations for the European 7th R&D Framework Programme and national research programmes

Nanoparticles are mostly produced in closed systems, thus avoiding the release of particles and side products in the workplace and the environment. Most applications do use free isolated nanoparticles. Characteristically, nanoparticles firmly stick together in the course of the formulation processes or are firmly embedded in products. Great efforts have to be made to generate stable isolated nanoparticles for special applications. Therefore, to assess potential risks of nanomaterials, DECHEMA and VCI jointly recommend focusing in the first step on the exposure assessment.

DECHEMA and VCI recommend:

- the development of a robust and effective standard analytical method to measure surface and number concentration, morphology and chemical composition of individual particles and agglomerates under real workplace and environmental conditions and to determine the size distribution for high number concentrations. Especially, methods for environmental analysis for particles between 0.5 nm and 20 nm and processes to analyze non-spherical forms of nanoparticles (tubes, plates, etc.) are called for.

- The development of new methods to determine the particle number, size, composition, and the real morphology (isolated nanoparticles, aggregates, agglomerates, particle/protein or particle/DNA complexes, etc.) of nanoscale products in liquid media.

- The international harmonization of analytical standards (methods for reproducible particle generation, detection and characterisation of atmospheric nanoparticles and of nanoparticles in biological tissue, reference materials).

- The development of basic toxicology test protocols or guidelines for short term testing (genetic toxicity, extra-pulmonary distribution, bioavailability) and long term testing (long-term pulmonary inflammation, chronic effects).

- The investigation of life cycle aspects of selected articles containing nanomaterials (esp. accumulation potential and fate at the end of the life cycle).

Annex

Roadmap of the DECHEMA/VCI working group for safety research on nanomaterials

The roadmap summarizes the most urgent issues for safety research on nanomaterials and for a deepened understanding of biological effects and mechanisms. The issues already undertaken in ongoing projects are marked and scheduled.

Expected results of high prioritized (DECHEMA/VCI) topics

Priority and description		2005		2006		2007		2008	
		1st	2nd	1st	2nd	1st	2nd	1st	2nd
1	Decisive parameters for toxicity of nanoparticles			INOS NC FZK GSF Nanotox Tracer	**INOS NC FZK GSF** Nanotox Tracer	**INOS NC FZK GSF** Nanotox Tracer	INOS GSF Nanotox Tracer	INOS	INOS
2	Development of the validated toxicological methods			NS GSF	NC FZK NS GSF	INOS NC FZK NS GSF	**INOS NC FZK NS GSF**	**INOS NC FZK NS GSF**	INOS NS
3	Studies on materials other than TiO_2 and Carbon Black		NC FZK NS Tracer INOS	**INOS NC FZK NS GSF PR** INOS	**NC FZK NS GSF PR** INOS	**NC FZK NS GSF PR** INOS	**NC FZK NS GSF PR** INOS	NC NS FZK GSF PR INOS	INOS NS
4	Development of methods to reproducibly produce nano-aerosols		NC FZK ASO	NC FZK ASO NS GSF	**NC FZK ASO NS GSF**	**NC FZK ASO NS GSF**	**NC FZK ASO NS GSF**	NS	
5	Transport mechanisms of particles in/through cells		CFN	**CFN PR NS**	**CFN PR NS**	PR NS INOS	PR DFG NS INOS	DFG INOS	DFG INOS
6	Mechanism to take in particles through skin	**BA**	ND	**ND**					
7	Mechanism to take in particles by lung	**GSF LS**	**GSF LS**	**PDL GSF NS LS**	**PDL GSF NS LS**	**PDL GSF NS LS**	**PDL GSF NS LS**	NC LS	NC LS
8	Exposure Assessment (Methods to measure/identify conc., morphology and type of nanoparticles in environment and at the working place)		NEW NS	NEW GSF	NEW GSF	NEW GSF	NEW GSF	DFG NEW	DFG NEW
9	Stability of agglomerates under practical conditions			NC GSF	NC GSF	NC GSF	NC GSF	NC	NC
10	State of particle aggregation/agglomeration in human body			GSF NEW NS	GSF NEW NS	GSF NEW NS	NS NC GSF NEW	NS NC GSF NEW	NS NC GSF NEW
11	Disintegration of agglomerates in body fluids		DE	**DE INOS**	INOS	INOS	NC INOS	**NC INOS**	INOS

Environmental Aspects of Nanoparticles

– with a priority list for the European 7th R&D Framework Programme and national research programmes –

21 September 2007

Opportunities and risks of manufactured nanomaterials – environmental aspects

The application of nanotechnologies and the use of manufactured nanomaterials have the potential to significantly reduce the environmental impact of technical processes and products. New and innovative materials which, at the same time, have a lower weight and are more stable can help to reduce the consumption of energy and resources. Dirt repellent surfaces reduce cleaning efforts and hence the consumption of water and cleaners. Nanomaterial based sensors and membranes will have a positive impact on the detection of contaminants and on the cleaning of water and the environment from pollutants. Enhanced fuel cells, solar panels and high-capacity batteries will save primary energy consumption, allow a more effective use of regenerative energy sources and will help constructing cars with lower carbon dioxide emissions.

Besides these positive effects, also potential negative effects of nanomaterials must be considered. Especially, potential negative effects of free nanoparticles on the environment must be explored early on. Typical questions are:

- Can special nanoparticles harm certain compartments of the environment?
- Is there a release of nanoparticles from sun creams, coatings and paints to the environment?
- What is the fate of released nanoparticles? What is their impact on water and soil? Are there any unforeseen effects?

In Germany, DECHEMA and VCI have established as early as 2003 the joint working group "Responsible Production and Use of Nanomaterials" which consists of high-level European academic and industrial experts and is regularly joined by representatives from German authorities. The group shares scientific findings and best practices on safety aspects of the production and use of nanomaterials.

In this document, the DECHEMA/VCI working group has addressed environmental aspects. The document describes in a first part (“A”) some anticipated positive environmental effects using manufactured nanomaterials. The list in the second part (“B”) addresses open research topics to evaluate the potential risks associated with the release and fate of nanoparticles from end products during manufacturing, handling, use and disposal. The list describing future priorities for R&D is divided in two categories, describing high priority, and medium and low priority projects, respectively.

A. Positive environmental effects of manufactured nanomaterials

The application of nanotechnologies and the use of manufactured nanomaterials have the potential to significantly reduce the environmental impact of technical processes and products. In addition, the use of nanomaterials may lead to innovation in other sectors, such as the health, medical, automotive, aeronautics and energy sectors. Some examples of positive environmental effects using nanomaterials are given below. There are many other promising areas and applications for manufactured nanoparticles.[18, 19, 20]

- Catalytic steps are widely used in the chemical industry. Nanoscale catalysts significantly reduce the use of raw materials and minimize side streams and energy consumption. One striking example are the automotive catalysts, reducing hydrocarbon, nitrogen oxide and carbon monoxide emissions by 90%. In mobile as in stationary applications, nanomaterial based catalysts and filters will lead to cleaner combustion processes and hence a reduction of emissions. Also, by using nanomaterials, the efficiency of regenerative energy sources like solar cells can be improved. Manufactured nanomaterials significantly improve efficient and low cost methods for energy transformation and storage (i.e. fuel cells and lithium ion batteries), enabling low emission and low fuel consumption cars.

- Water purification can be made more effective by using nanosized/nanostructured materials. Membranes and highly sensitive nanostructured sensors enhance the early recognition of pollutants before damage can occur. In addition, nanomaterials can substitute (eco-)toxicological hazardous substances (i.e. flame retardants and toxic corrosion inhibitors).

- Useful for the health sector is the coating of implantation materials with biocompatible surfaces or easy-to-clean surfaces due to nanocoatings with biocidic or anti-adhesion properties. New drug delivery systems based on manufactured nanomaterials to cure, e.g., neurodegenerative diseases are of strong interest for the pharmaceutical sector.

[18] publifocus “Nanotechnologien und ihre Bedeutung für Gesundheit und Umwelt”
Nanotechnologien in der Schweiz: Herausforderungen erkannt
Bericht eines Dialogverfahrens
Zentrum für Technikfolgenabschätzung
TA-P 8/2006 d, Bern, 2006, ISBN-Nr. 3-908174-25-2
[19] NanoRoad SME: http://www.nanoroad.net
[20] Nachhaltigkeitseffekte durch Herstellung und Anwendung nanotechnologischer Produkte, Schriftenreihe des IÖW 177/04, Berlin

B. Release of nanoparticles from end products during manufacturing, handling, use and disposal – research priorities for analysis and assessment of effects

High priority topics

Development of methodologies for effect assessment
1. Development of globally harmonised methods for measuring environmental impact and ecotoxicity (standardisation is recommended) ➢ Investigation to find out whether existing methods can be applied for measuring environmental impacts of nanoparticles. If necessary, the test procedures will have to be adapted with respect to standard sample preparation (stirring, ultrasound mixing, filtration, etc.). The test methods should include all kinds of solvents and should consider possible side effects, such as the interaction of nanoparticles with the analytical samples. ➢ Development of a standard procedure for the determination of the particle size during individual tests
2. Identification and preparation of reference nanoparticles ➢ Identification and definition of long-term producers and suppliers of the identified reference materials ➢ Identification of the main parameters for the characterisation of the nano-state of the reference materials
Substance properties
3. Determination of agglomeration/segregation of specific nanoparticles (stability of the nanoparticle state); generalisation of the results to develop a standard model for agglomeration/segregation ➢ Determination of the conditions and the rate of agglomeration/segregation of specific nanoparticles ➢ Investigation of the thermodynamic principles regulating “phase transitions” and of relevant physical properties of the particles ➢ Investigation to discover whether the behaviour of nanoparticles depends on the structural properties and whether the effect can be generalized ➢ Comparison of the kinetics of standardised material ➢ Development of a standard procedure for the determination of particle size during individual tests
4. Life-cycle aspects (disposal of dusts, recycling) ➢ Investigation of the emission of nanoparticles from products during their life cycle ➢ Performance of life-cycle assessments for different nanoparticles or for one example of a relevant nanoparticle used in different applications ➢ Investigation of direct environmental effects (e.g. release of nanoparticles into the environment, stability of nanostructures) and indirect effects (e.g. disposal of dusts, recycling, energy demand and carbon dioxide emissions) ➢ Assessment of the natural background of specific materials (iron oxides, titania, silica)

High priority topics (continued)

Behaviour and fate in the environment
5. Determination of the mobility of persistent manufactured nanoparticles in surface waters, groundwaters and soils (depositions, mobilisation, adsorption, desorption, kinetics, distribution, morphology) and the master parameters governing their mobility ➢ Modelling of the diffusion and dispersion of nanoparticles in water, soil and air ➢ Development of models describing the interaction between the nanoparticles and other substances in the compartments ➢ Investigation to find out whether other substances, e.g. dissolved organic matter, may influence the stability of the nanostructure and/or possible ways of transportation
6. Development of methodologies which are able to identify and quantitatively determine nanoparticles in the environment (air, water, soil) at relevant (i.e. low) concentrations. ➢ Methods must be able to distinguish between naturally occurring nanoparticles and manufactured types of nanoparticles.
7. Determination of the background burden of nanoparticles in the environment to estimate the contribution of anthropogenic sources ➢ Background burden includes natural colloidal nanoparticles and unintentionally released nanoparticles (e.g. from combustion processes) and needs to comprise all environmental compartments (soil, water, air). ➢ An intensive exchange with other projects is recommended in which determination/quantification of nanoparticles at the workplace or in living cells is already a topic. ➢ Development of methods for on-site analysis might be interesting (instrumentation which is easy to handle and to transport and results can be achieved in a short time on-site).
Effects on organisms
8. Investigation of the uptake of persistent nanoparticles by living organisms/ microorganisms (in-vivo and in-vitro). Compilation of information on toxicokinetics, deposition and accumulation of persistent nanoparticles. ➢ The living organisms/microorganisms used should be the relevant species from standard toxicity testing. ➢ Investigations should consider different routes of uptake and kinetics.

Medium and low priority topics

Development of methodologies for effect assessment
1. Development of methods (in-vivo/in-vitro correlation) to transfer the results of ecotoxicological investigations with idealised nanoparticles to real formulations in order to minimize animal tests ➢ Deriviation of suitable uncertainty factors, QSAR modelling, consideration of matrix effects
2. Development of methods to extrapolate the results of ecotoxicological tests to chemically similar nanoparticles with different forms, surface modifications and size ➢ A combination with topic no. 3 of the high priority topics should be considered
Substance properties
3. Investigation of binding and mobilisation (particle-based transport mechanisms) of toxic manufactured nanoparticles (e.g. heavy metals and toxic hydrocarbons) ➢ Discrimination between contaminations that enter the environment together with the manufactured particles or that are mobilised in the environment by binding to the manufactured particles ➢ Follow-up of topic no. 5 of the high priority topics: interaction between particles and other substances in the compartments
Behaviour and fate in the environment
4. Investigation of the persistence (accumulation, degradation) of nanoparticles in the environment ➢ A combination with topic no. 5 of the high priority topics should be considered
5. Investigation of the fate of remediation products ➢ Investigations of the fate of the nanoparticles after use
Effects on organisms
6. Investigation of the biokinetic fate of persistent nanoparticles in the food chain ➢ Investigation to determine whether nanoparticles remain in the food chain in nanostructured form ➢ Investigation of effects on organisms; comparison of nanoparticles and the corresponding bulk material ➢ Detection of nanoparticles and nanomaterials in the food chain that do not exist in the natural environment (e.g. fullerenes or carbon nanotubes)