NMP4-CT-2005-013968

Guidance Booklet on Safe Handling of Nanoparticles

D. McCormack, N. Malanowski, P. Sermon, J. Hoeck

Contributed by the **IMPART** Project

"Improving the understanding of the impact of nanoparticles on human health and the environment"

(Coordination Action funded by the European Community under the "Structuring the European Research Area" Specific Programme Research Infrastructures action)

Authors:

- Dr. Declan McCormack, Dublin Institute of Technology, Ireland
- Dr. Norbert Malanowski, VDI Technologiezentrum GmbH, Germany
- Prof. Paul Sermon, University of Surrey, United Kingdom
- Dr. Juergen Hoeck, TEMAS AG, Switzerland

Project name:	Improving the understanding of the impact of nanoparticles on human health and the environment
Project acronym:	IMPART
Project type:	FP6 Coordination Action funded by the European Community
Contract number:	NMP4-CT-2005-013968
Project Co-ordinator:	TEMAS AG
Task:	WP4.4 report: Guidance Booklet on Safe Handling of Nanoparticles

Table of contents

1 Introduction

1.1 Aim of this booklet

Nanotechnologies are a fast evolving scientific and technological field with a high potential impact on science, economy, and society. Like with all new and quickly developing technologies it is important to weigh benefits versus risks at the earliest possible convenience.

Building on the results of the IMPART project, this booklet is intended to give a review of the actual knowledge in the field of nanospecific risks, deriving recommendations for the safe handling of nanoparticles for executives in industry, public organisations, and NGOs. The booklet is also intended to give an outlook on possible developments in the near future and "life after IMPART".

1.2 Nanotechnologies: Scope, applications and risks

Nanotechnology refers to a field of applied science whose theme is the control of matter on an atomic and molecular scale, creating new functions due to the small size of the structures, generally 100 nanometers or smaller, and involves developing materials or devices within that size[1]. Nanotechnology is thus not a homogeneous area, but a multi-disciplinary range of diverse technological fields, each of which involves the utilisation of nanoscale structures or materials.

It is recommendable not to use the term nanotechnology too generally, but rather to refer to different "nanotechnologies".

In many cases, nanotechnological applications have already reached the market, some of the more commonplace ones being:

- finishes and plastics reinforced by nano additives and pigments
- flat irons, where ceramic nanoparticles improve smoothness and heat resistance
- sunglasses with protective and antireflective nanocoatings
- clothes with nanofibres for water and stain repellence as well as wrinkle-free behaviour
- socks and underwear with silver nanoparticles for antibacterial properties
- bicycle frames integrating carbon nanotubes for excellent stiffness and strength with concomitant weight reduction
- sunscreens based on mineral nanoparticles

According to current state of knowledge it cannot be ruled out that exposure to nanomaterials might have specific effects, different to the effects of larger structures in the micrometer range, giving rise to potential nanospecific risks for health and environment of those nanomaterials.

[1] Definition taken from Wikipedia, the free encyclopedia

When talking about risks of nanotechnologies one has to be very careful to refer to the respective nanotechnological field under discussion, because there is no overall nano risk, but specific risks for specific nanotechnological areas. In fact, the main risks associated with nanotechnologies result from the presence and availability of "nano-objects", as defined by ISO[2].

According to the ISO draft – which was adopted as the working definition by OECD – nanomaterials are understood to be either so-called nano-objects or nanostructured materials. 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.

The reasons for nano-objects bearing potential nanospecific risks are twofold:

- physico-chemical properties compared to bulk materials may change considerably in nanoparticles, leading to new types and mechanisms of toxicology
- as a pure size effect, new exposure routes and mechanisms as well as specific dislocation pathways have to be envisaged

Remark: In this Guidance Booklet the older and still widely used term "nanoparticles" as a summary of all relevant objects will be used instead of the new term "nano-objects" for reasons of coherence with older IMPART reports.

A distinction has to be made between

a. man-made, engineered nanoparticles (ENPs)
b. accidentally released nanoparticles from combustion or wear processes (fine dust)
c. ubiquitous nanoparticles which have occurred naturally over many ages

This guidance booklet is concerned exclusively with category a., and the implications of targeted synthesis and application of engineered nanoparticles.

1.3 The IMPART project, goals and implementation

The EC funded FP6 Coordination Action IMPART (www.impart-nanotox.org) is concerned with improving the understanding of the impact of nanoparticles on human health and the environment. The objective was to prevent knowledge of the health and environmental implications of nanoparticles from lagging behind the technological advances. The specific project challenge was to foster communication between different initiatives, streamlining resources and facilitating cooperation.

The project focus was thus put on the inventory and assessment of existing knowledge, elaboration of recommendations, and the dissemination to the different stakeholder groups.

In order to achieve this, the following project structure has been implemented:

1. Inventory of ongoing projects and state-of-the-art

[2] C.f. Technical Specification ISO/TS 27687, Nanotechnologies - Terminology and definitions for nanoparticles, Proof, © ISO 2007.

2. Assessment of existing data and identification of missing data (gaps) in the fields: toxicology, risks, best practices, legislation
3. Recommendations and guidelines for legislation policy makers, research policy makers, and industry, the public and other stakeholders
4. Dissemination and knowledge transfer via Home Page, a dedicated database, conferences, workshops

The "recommendations for legislation policy makers" as well as the "recommendations for research policy makers" are available upon request, or can be downloaded from the IMPART web site starting from November 2008.

As a particular deliverable of the IMPART project, the dedicated database has been set up, giving access to a full text research tool to find publications, projects and other sources of information about nanosafety issues.

1.4 Current state of knowledge

International research and other activities: Research and other activities in the field of nanosafety are currently conducted widely all over the world. Accordingly, the accessible knowledge base is constantly growing.

IMPART builds on data from a variety of sources like own results of the IMPART experts, or of external research projects, conferences, workshops, publications in peer reviewed journals or by bodies like the EC, ISO and OECD. All those sources are listed in the IMPART database at www.temas.ch/Impart/ImpartProj.nsf.

Data have been included in the IMPART reporting up to end of September 2008, in only very few cases up to October 2008.

Prominent examples of the used sources include, but are not restricted to:

- European and national projects in Europe: Nanoderm, CANAPE, Particle-Risk, CellNanoTox, NanoSafe 2, NANOSH, NanoImpactNet, NanoCare, INOS, Tracer
- Workshop on research projects on the safety of nanomaterials: reviewing the knowledge gaps", proceedings available at ftp://ftp.cordis.europa.eu/pub/nanotechnology/docs/final_report.pdf.
- Communication from the Commission to the European Parliament, the Council and the European Economic and Social Committee: Regulatory Aspects of Nanomaterials [SEC(2008)2036]
- ISO/TR 12885:2008(E): Nanotechnologies - Health and safety practices in occupational settings relevant to nanotechnologies
- OECD, Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology, Series on the Safety of Manufactured Nanomaterials, Number 6, "List of Manufactured Nanomaterials and List of Endpoints for Phase one of the OECD Testing Programme" (ENV/JM/MONO(2008)13/REV)
- EU Scientific Committee on Emerging and Newly-Identified Health Risks (SCENIHR): Modified Opinion on the Appropriateness of Existing Methodologies to Assess the Potential Risks Associated with Engineered and Adventitious Products of Nanotechnologies (2006)

- German Chemical Industry Association (VCI): Responsible Production and Use of Nanomaterials (2008)
- "Progress Toward Safe Nanotechnology in the Workplace", a Report from the NIOSH Nanotechnology Research Center, 2007
- International Council On Nanotechnology (ICON): EHS database (available at http://icon.rice.edu/research.cfm)

Nanoparticle families looked at within IMPART: The current library of nanomaterials reported is so extensive that it would be impossible to examine every single category (were it possible to categorize such materials). Therefore, within the frame of the IMPART project materials which are well documented, widely used and are persistent within an organism or the environment for a sufficient length of time to accumulate to an appreciable concentration, were investigated:

- ceramics
- metals and metal oxides with a particular emphasis on TiO_2
- fullerenes with a particular emphasis on organic C_{60} & inorganic WS_2 & MoS_2
- carbon both single & multi-walled and inorganic nanotubes
- quantum dots with a particular emphasis on CdS, CdSe and their derivatives

Health, exposure and environment: With regard to the nanoparticle families looked at, our work summarises existing knowledge about the impact of nanomaterials on human health, exposure and the environment, but it specifically excludes issues relating to medical applications.

In the field of **health**, the state of knowledge investigated includes

- hazards and toxicity of nanoparticles
- the role of impurities in toxicological properties
- differences between local and systemic toxic effects
- parameters relevant for the expression of dosing
- current test protocols
- organ specific effects in the biological system, cellular uptake and accumulation
- administration of nanoparticles for in-vivo and in-vitro studies
- long term studies at realistic / meaningful concentrations

In relation to **exposure**, the following items have been considered:

- relevance of occupational exposure
- applicability of measuring devices and possibility of indirect measurements
- influence of other particles present
- detection limits in biological samples
- possible biomarkers

For the impact of nanoparticles on the **environment** the points which have been considered include

- natural nanoparticles in geological systems
- binding of toxic elements and compounds to nanoparticles
- mobility of nanoparticles within the environment

Legislation: Regulatory reviews on national as well as European legislation have shown that current legislation covers, in principle, potential risks with regard to nanomaterials, and is thus valid and applicable to nanospecific issues. What needs to be improved is the implementation of the existing legislation as well as the conducting of voluntary actions. For the implementation of legislation a number of elements like test methods, thresholds, risk assessment methods and others must be available. Due to a current lack of knowledge these elements cannot yet be fully elaborated. Therefore, the first step in improving the implementation of legislation must be the improving of the scientific knowledge base.

It has to be kept in mind that we need to understand what happens to nanomaterials during all the stages on their way from the production line to waste disposal when legislative aspects are discussed. In addition, the results of work done in IMPART show that it is not possible to address hazards and risks of nanoparticles in a general way, as each type of nanoparticle needs to be evaluated individually with regard to its toxicity and exposure. This means that for responsible legislative and regulatory measures, nanomaterial specific data are needed for each stage of the life cycle for the assessment of risks for workers, consumers and the environment, respectively.

In this context the willingness of nanotechnology industries to take responsibility and participate in projects accumulating risk data to address relevant problems as early as possible is considered a major advantage.

1.5 Conclusions

From the thorough analysis of the state of knowledge as described above, the experts of the IMPART Consortium have identified existing gaps in current knowledge, ways to use existing knowledge, and defined necessary steps to be taken in the respective fields.

Toxicology, hazards, risks and environmental issues: IMPART describes the chemistry, uses and in-vitro and in-vivo **toxicology** and **hazards** of SiO_2, TiO_2 and carbon nanotubes (CNTs). These have been ascribed to induced oxidative stress and induced DNA damage. It describes the effect of nanomaterial chemistry, structure, particle size, particle morphology, impurities and crystallinity on their toxicity and the use of coatings in minimising this impact. Additional points to consider include the following:

- interference of nanomaterials with the tests
- verification of oxidative stress as a marker for potential toxicity
- genotoxic effects

- translocation of nanoparticles in the blood stream
- dosimetrics modification by particle aggregation
- models to predict the potential impacts of nanoparticles over their entire life time

Dedicated work on **risk** issues, including **environmental issues** connected to nanoparticles reveals that nanoparticles have different levels of interactions with biological systems and have different mobilities based on their size, shape, composition and additional parameters; each type of nanoparticle must be tested individually when health or environmental risks are expected. More research into hazards and exposure pathways of nanoparticles regarding health and environment is necessary, current research regarding environment generally has to be enhanced. Fundamentals of nanochemistry in the environment, such as the process of contaminant transformation at the nanoparticle-water interface should be explored.

As an overall résumé, the following needs for actions have been established:

- publication of physicochemical properties together with toxicological data
- new test strategies to determine the mechanisms of potential injury
- integration of theory, modelling, and simulation into experimental design
- deeper understanding of the differences between nano and bulk
- consequences of agglomeration and deagglomeration of the particles
- evaluation of current test methods for "normal" toxicity with respect to their applicability for nanotoxicological testing
- techniques for the in vivo detection of nanomaterials
- international consensus on measurement techniques or standards for monitoring nanoparticles in the workplace (aerosol measurements)
- measurement device that can differentiate between engineered nanoparticles and the background level of natural nanoparticles
- information about production volume and occupational exposure potential
- realistic methods for exposure assessment
- behaviour of nanomaterials during their journey from manufacture to waste disposal

Generally, a closer collaboration between scientists and industry is needed in the sense that industry defines the most pressing needs and priorities for research. This will help to focus available resources on topics with high relevance.

Best practices: In order to propose, agree and establish best practices regarding the preparation, handling, manipulation, integration and deployment of engineered nanomaterials it is first necessary to identify and characterise the hazard and hence determine and manage the potential risk associated with such materials. The initial stages of bulk production and packaging have been recognised as having the greatest potential hazard and, for this reason, our initial studies have focussed on surveying (by questionnaire and personal contact) nanoparticle producers.

In brief the questionnaire found that

- there was a good degree of awareness of the potential hazards associated with such materials
- potential exposure routes were inhalation (50%) and dermal (33%)
- the majority of producers take measures to control/prevent exposure
- measurement of such exposure was less prevalent, particularly amongst SMEs
- there was a good degree of risk awareness at all levels

The survey shows that there is serious interest, both on the side of management and labour, in understanding whether there are risks upon exposure to nanoparticles but the lack of structured information lessens, in many cases, the seriousness of concerns.

According to the survey, best practices currently mainly suffer from the following gaps / weaknesses:

- low information exchange regarding best practices due to a reluctance of the industries to make publicly available their internal procedures
- limited application of medical monitoring programmes for workers exposed to nanoparticles in SMEs
- accidental exposure is not examined in similar detail as normal work
- exposure is underestimated due to estimated low levels of exposure and lack of hard data on effects
- low seriousness of concerns due to a lack of structured information
- best practices are often diffuse, because they have to cope with largely unknown or unexplored effects.

In summary best practice at present, although quite diverse, tends to rely on conventional methods and practices. These include exposure control (conventional fumehoods, high efficiency particulate filters), conventional personal protective equipment and conventional waste disposal as hazardous material. Workplace monitoring for the presence of nanoparticles is less commonplace.

Existing guidelines: Determining what constitutes reasonable steps has been the remit of a number of private, commercial and public bodies in Europe and the U.S.A, most of which have recently published guidelines for the safe handling and use of nanomaterials in the workplace. These include:

- ISO, TC229 – Nanotechnologies
- NIOSH: Progress Towards safe Nanotechnology in the workplace (2007)
- BAuA: Guidance for Handling and Use of Nanomaterials at the Workplace (2007)
- British Standard Institute, Guide to safe handling and disposal of manufactured nanomaterials (2007)
- Department of Energy, Nanoscale Science Research Center: Approach to Nanomaterial ES&H (2007)
- Occupational Safety and Health: Nanotechnology Consensus Workplace Safety Guidelines

- Center for High-Rate Nanomanufacturing, Toxics Use Reduction Institute (TURI): Interim Best Practices for Working with Nanoparticles (2007)
- International Council on Nanotechnology: A Review of Current Practices in the Nanotechnology Industry, Phase two report, Survey of current practices in the Nanotechnology Workplace (2006)
- Bayer and BASF

Links to all mentioned documents are available via the IMPART database. For a more thorough list of documents from governments, industries and universities on this topic the reader is referred to the web site of the Nanoscale Science and Engineering Research Center at the University of Wisconsin at Madison, which presents a continuous update of all documents with links to their respective sources (www.nsec.wisc.edu/NanoRisks/NS--HS_Protocols_BestPractices.php).

Legislation: It is especially necessary to develop and validate methods for evaluating the health, safety and environmental impact of engineered nanomaterials. Without this validation it will be difficult to develop a solid basis for modifications in current legislation and regulation. The scientific uncertainty involved in evaluating potentially harmful properties of engineered nanomaterials complicates the implementation of suitable regulatory measures by legislators. But good occupational hygiene practices and existing knowledge on how to work with hazardous substances provide a useful basis for working in a safe way with nanomaterials.

It can be concluded that a standardised and trust-based framework for the risk assessment of health, safety and environment for nanomaterials (including for instance standard reference samples and toxicology protocols) will help to modify current legislation, regulation, and its implementation where necessary.

2 Guiding notes for coping with nanotechnological uncertainties

2.1 General remarks

The guidance booklet's aim is to provide orientation regarding measures in the production and for the use of nanomaterials, reflecting current state of science and technology in this field. The focus is on minimising risks for workers, consumers as well as the environment.

The booklet addresses:

- industries (production, processing, trade), to give them guidelines for safe handling and implementation of functionalities of nanomaterials for all processes involved during the life cycle of the nanomaterials as well as to recommend measures to be taken in order to minimise risks for workers, consumers, and the environment
- NGOs and the broad public, to give them a source of information about the state-of-the-art in nanomaterials safety, and thus to increase transparency as well as objectivity for the communication and discussion of nanosafety issues

Overall recommendations:

- nanotechnologies are a quickly developing scientific and technological area with increasing importance for science, economy, and society. In order to secure a responsible development in the area of synthetic nanomaterials both benefits and risks need to be analysed and communicated in an appropriate manner
- to the extent that nanotechnology is a highly interdisciplinary area, one can recommend that collaboration between industry, economists, ethicists, researchers, lawmakers and other related stakeholders is established to account for the complexity of nanotechnologies and their related risks
- a maximum use of resources by sharing existing knowledge and data is achievable through intensification of collaboration between industry and research: many data are already known by industry, but not being published because of constraints like confidentiality or lack of confidence in partners. An open and honest dialogue with the industries should thus be fostered so that research community as well as policymakers can use these data
- it is highly recommended to base all debates at any time on scientific findings and consolidated data. However, fears and uncertainties cannot always be addressed by pure facts - an appropriate communication in an understandable way is a must as well.

2.2 Safe handling of nanoparticles in different environments

General guidelines for handling nanomaterials with a focus on the safety of workers, consumers and the environment simultaneously can be summarised as follows:

- look at the whole life cycle of the materials, including R&D, production, processing steps, system integration, packaging, transport, usage, recycling, disposal

- get interlinked with all stakeholders involved along the whole life cycle in order to set up an efficient dissemination of data about the nanomaterials in question
- regard distinct steps separately (production, pro-cessing, packaging, transport, use, disposal, recycling)
- consider effects on workers, consumers and environment separately for every distinct step of the life cycle
- on a voluntary basis include nanoparticles with dimensions up to 500 nm, because within this range macrophages are not able to cope with particles; this means that as a pure nano-size effect those particles could do harm which would not be regarded when sticking to the border of 100 nm

A **first rough risk ranking** can be done by generally considering risk higher when

- particles are poorly soluble / persistent
- at least one diameter is below 100 nm (better: 500 nm)
- aerosols are involved
- production volume is high (> 1t / year)
- aspect ratio is higher than 100:1; in order to err on the side of caution in relation to needle-like shaped nanoparticles, aspect ratios of 10:1 might be significant enough to regard them as more risky
- toxicological / ecotoxicological data are not available

Some points to be additionally mentioned:

- accidental risks during production, maintenance, packaging, transport and use need to receive more focus. With increasing production this type of risk will play a more prominent role
- ecotoxicology must be stressed more than has been done so far. In this area much less data are available, in addition the field is more complex with respect to different environmental conditions in different compartments. Exposure routes back from environment to humans
- prevention of specific nano risks, also for consumers and environment, can be possible by careful evaluation of alternatives

2.2.1 Workers

An inspiring example for a recent voluntary action by industry is the “Guidance for Handling and Use of Nanomaterials at the Workplace”[3]. It shows the current need for

[3] Also the “Guide to safe manufacture and for activities involving nanoparticles at workplaces” by BASF and the “Code of Good Practice on the Production and On-Site-Use of Nanomaterials” by Bayer are coping with the aspects treated in the publication by Baua / VCI and can be seen as additional voluntary action by industry.

more voluntary integrative actions towards the handling of nanoparticles. Main points of this guidance are included in this chapter.

In Germany a joint survey on occupational health and safety in the handling and use of nanomaterials was conducted in spring 2006 among VCI member companies by BAuA and VCI. 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, a "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[4], which are also included in this chapter.

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. In order to ensure safe handling, the following points should be regarded:

- gaseous phase synthesis of nanomaterials should take place predominantly in closed systems. As an extra measure, these systems should be run at reduced 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.
- for activities in liquid media (e.g. precipitation reactions, dispersion in the liquid phase), intake by inhalation should be excluded by avoiding aerosol formation.
- 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. Accordingly, they should also be treated with due caution.

Specifically in the field of workers' safety the following course of action to protect workers from hazards, as laid down in the Dangerous Substances Ordinance, is recommended:

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

[4] Baua / VCI: Guidance for Handling and Use of Nanomaterials at the Workplace, Frankfurt 2007

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

This course of action shows that 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[5]. Until specific threshold values are laid down for nanoparticles or certain nanomaterials, one should strive to minimise exposure[6].

Assessment of existing data: In view of the fact that data on exposure assessment are lacking, a full risk assessment of nanoparticulate materials in most cases is not feasible at present. However a ranking of potential risks can be achieved by applying hazard trigger algorithms. Relevant factors which can give a first estimation of potential risks of nanoparticles are:

- production volume
- potential exposure to customers, workers, environment
- potential aerosol release during production, handling, processing
- solubility
- aspect ratio (to distinguish between fibers and particles)
- particle diameter (taking into account a potential deagglomeration in body liquids e.g. in the lungs)
- toxicological and ecotoxicological parameters

A scheme for assessing the risks of nanomaterials is depicted in the following figure (Fig. 1). This scheme is to be regarded separately from registration processes of new chemical substances in the frame of existing chemical regulations, because particle size does not play a role in current chemical legislation.

[5] Pursuant to TRGS 900 (TRGS = Technische Regeln für Gefahrstoffe/technical rules for hazardous substances) 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).

[6] Recommendations of TRGS 401 should be observed regarding dermal exposure.

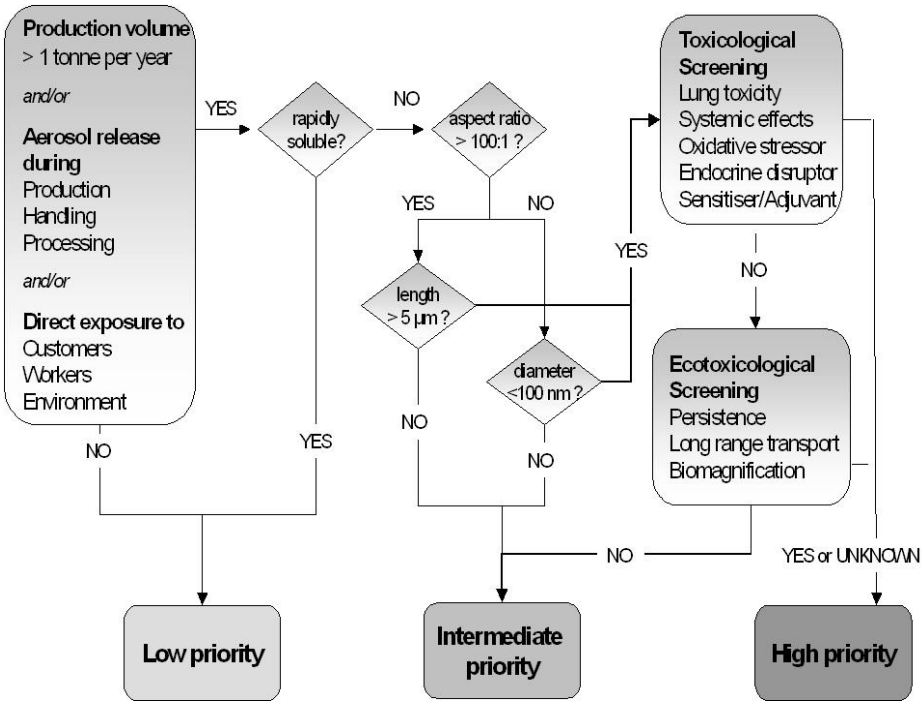

Fig. 1: Hazard trigger algorithm (source: VDI-TZ, modified from Howard and de Jong, 2004)

The following **protection measures** are recommended:

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.

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 re-circulated without exhaust air purification (Caution: actions like maintenance or cleaning are generally sources for higher exposure for workers!). Extracted materials must be handled with due care and should be disposed like hazardous substances

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.
- 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.

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.
- 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).
- in addition 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.
- in addition 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 oxidisable 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 the occupational exposure levels at the workplace for further working substances - e.g. for solvents – are observed inter alia.
- the effectiveness of applied protection measures (e.g. personal protective equipment) must be reviewed.

In as much as nanoparticles have, potentially, mutagenic and carcinogenic properties as well as other health hazards, and are comparable to some of the substances defined in the 2004 directive[7], this directive provides an excellent framework for monitoring and protecting workers who handle nanoparticulate material.

2.2.2 Consumers

In order to assure the safe use of nanomaterial containing products, it is essential to know in which products the produced nanomaterials will end up. A strong interconnection between producers, processors (including recyclers) and sellers of nanomaterials or their products is thus highly recommended along the whole life cycle of the materials. This is to make sure what type of nanoparticles in what type of environment (air, liquid, solid matrices…) might be present in any given consumer product. With this knowledge available appropriate guidelines for the safe use can be given.

The following overall recommendations always apply:

- make sure that the data you have available for the nanomaterial in question are sufficient at all to judge potential risks for users. If this is questionable, arrange for detailed studies to be conducted or seek advise from research experts
- when recommending safety measures for the use of products containing nanoparticles, put a special focus on applications where exposure is likely via the lungs (gaseous compounds, aerosols), skin or gastro-intestinal tract (liquids, cremes)
- for professional users of certain products, who necessarily have a higher exposure to the materials, recommend safety measures according to workers' safety measures already applied in the work places
- consider alternative materials in case the used ENPs have a high potential risk, or an appropriate risk assessment is entirely impossible for a given application

2.2.3 Environment

The environment is an even more complex system for the analysis of the impact of nanoparticles. Available data are currently not sufficient to understand or predict nanoparticle behaviour in the different environmental compartments. An important point to notice is that with a future increasing amount of ENPs introduced into the environment, the feedback loop back to human beings will be enhanced.

Consequently, the main recommendation to be made at the moment is to reduce the input of ENPs into the environment wherever feasible.

[7] Council Directive 2004/37/EC (2004) on the protection of workers from risks related to exposure to carcinogens or mutagens at work

2.3 Fostering research: a future understanding of the toxicity of nanomaterials

Although there is no reason to expect fundamentally new kinds of toxicity for nanoparticles (NPs), we still do not basically understand how such nanomaterials interact with or are taken up by cells or tissue. Hence in future there needs to be a detailed analysis and rationalisation of the health impacts of nanoparticles and a comparison with those of diesel-emitted particles.

Direct rationalisation of the toxicological risks of engineered nanoparticles appears better than simply extrapolating from particle toxicology seen with coal mining or asbestos or vehicle particulates. It will require their in-situ characterisation in biological media in terms of surface composition, particle size, particle morphology, surface structure, solubility, reducibility, portals of entry into the body, translocation to organs and hot-spots, and interaction with surrounding bio-fluids. Such studies will need new methods for analysing NPs, i.e. more discriminating microscopes, and calibration with bench-marking standards by interdisciplinary and transnational groups.

The quantified risks of engineered NPs need to be compared with and bench-marked against those for airborne particulates that we all frequently encounter, and compared to naturally-occurring nanomaterials. Thus, the toxicity of NPs could be compared with molecular chemical toxins, such as aflatoxins. Their investigation is at the same level of detail that NPs now need to be characterised in-situ.

IMPART recommends that we assess the impact of nanoparticles by monitoring their physical properties (i.e. size, morphology, crystallinity, fractal dimension, and solubility), chemical properties (i.e. surface versus bulk composition, wettability and reactivity) and toxicity (i.e. bio-properties). There is an increasing need for this multidisciplinary assessment since, while there is an increase in the number of man-made NP types and their applications (i.e. NP production in 2020 may be 25 times that today), there is a paucity of studies characterising their effects and toxicity.

In summary then, we need a generic framework with which a future producer could predict the health and environmental impact of the nanomaterial that they are designing some time from now. At present that generic framework does not exist. For future success it will be a prerequisite that all stakeholders and industries work together in order to create impulses for research from all sides.

For the moment it appears that the size, surface chemistry and morphology of these nanoparticles are pivotal in defining their toxicity and often this is not known in-vivo. We expect rapid advances in a topic at present still in its infancy and hope that sufficient support will be available for research, which is indispensible for a future understanding of the toxicity of nanomaterials.

2.4 Communication strategies

The possible audience for information risk issues in nanotechnologies is broad and consists of:

- civil society – consumers, workers, potential users, environmentalists, activists, etc.
- science - scientific advocates, academic institutions, researchers

- industry – manufacturers, suppliers, waste removal services, professional associations, etc.
- public bodies – regulatory, safety, environmental health & monitoring, public education and awareness, funding bodies
- media – press, web, radio & TV, scientific publications

It is important that each audience be provided with the correct breadth and depth of information. For example in communicating with mainstream press it is useful to identify a well-defined “news” story with which journalists can engage. In other situations short, clear commonplace examples of nanotechnology may be more appropriate. Whilst the term “nano” has become more prevalent through products such as the iPod “Nano”, the Tata “Nano” and Via’s new “Nano” processor, it is evident that the majority of the public has little in-depth understanding of what exactly nanotechnology is. In this regard it is important to highlight the real beneficial aspects of nanotechnology when attempting to balance the potential risks associated with a developing technology.

IMPART engenders debate on the issues surrounding nanomaterials through a variety of mechanisms. These include:

- national & international conferences
- digital media such as www.impart-nanotox.org
- publications such as targeted instructional literature, scientific papers, briefing documents
- archive material such as scientific reports which have been delivered to the Commission through this project, along with other reports produced by members of this consortium

Successful communication is built on the following principles:

- deliver well-researched, high quality information
- identify and develop networks which can extend the delivery of knowledge in the field
- assist those stakeholders wishing to develop an understanding of the area
- provide suitable stimuli for public debate
- gain some insight into the effectiveness of such communication strategies through feedback and evaluation

It is also important that a detailed risk management protocol be developed along with clear strategies for emergencies or crises (related to nanomaterials) which may occur in the future. The speed and clarity of response to such a situation may be crucial to the future developments in the different areas of nanotechnology.

3 Conclusion

Risk assessment and management for the production and use of nanomaterials containing nanoparticles is a highly complex issue, even more so when regarding both health and environmental issues along the whole lifecycle for any given type of nanoparticle.

There is a consensus among legislators that current legislation covers, in principle, potential risks with regard to nanomaterials, and is thus valid and applicable to nanospecific issues. This puts responsibility on all involved stakeholders in the area of nanotechnologies for the safety of human health as well as the environment with regard to risks that are specific to nanomaterials.

Effective risk reduction for workers can be achieved by applying conventional measures known from the long experience in the chemicals sector. This is still on a generic level without considering nanospecific material properties, certain recommendations will have to be adapted when more data on nanoparticle specific behaviour are available.

In order to secure the safe use of nanomaterials by consumers, it is necessary to make sure what type of nanoparticles might be present in what type of environment in any given consumer product, and clarify potential risks under those conditions as already known from other fields like workers' hygiene. Recommended measures according to this knowledge should then be communicated to sellers and/or customers.

With regard to the environment the input of ENPs should be reduced wherever feasible.

In any case, a rough estimation of potential risks of nanoparticles can be made on the basis of production volume, potential exposure to customers / workers/ environment, potential aerosol release during production / handling / processing, solubility, aspect ratio, and particle diameter.

In view of the precautionary principle, two rules should always be obeyed:

- seek alternative materials where necessary and feasible
- in cases of doubt, start investigations or refrain from the use / application of the material in question

New results in the field of nanoparticles and their impact on human health and environment will become constantly available. The crucial point will be their interpretation, implementation and communication. As a prerequisite for future safe application of nanomaterials, the strong interconnection along the whole life cycle and across all stakeholder areas, including NGOs and the broad public, is indispensible.

4 Outlook

Based on current knowledge, the IMPART project has generated a number of tools to further the development of safe nanotechnologies:

- a nanosafety database
- a state of the art report of relevant knowledge
- an inventory of ongoing projects
- an assessment of existing, and identification of missing, data
- recommendations for legislation policy makers
- recommendations for research policy makers
- this guidance booklet

They are meant for immediate use - nanotechnologies are rapidly evolving -, and for serving as a discussion basis for further advancement in the field, be that the implementation of adequate funding, the development of regulations, or communication to the broad public.

Despite the fact that the IMPART project is finished, the established networks and tools are still existing. All stakeholders in nanotechnologies are invited to use them, in order to further "prevent knowledge of the health and environmental implications of nanoparticles from lagging behind the technological advances", and to "foster communication between different initiatives, streamlining resources and facilitating cooperation".