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# Guide for the Safe Handling of Nanotechnology-based Products

2009 Version

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# Guide for the Safe Handling of Nanotechnology-based Products

2009 Version

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Science and Technology Branch  
Environment Canada

## **Management Perspective**

The purpose of this document is to provide information on the potential risks associated with the handling of engineered nanomaterials in research laboratories. The document also contains recommendations and guidance, such as good laboratory practices, for ensuring a safe work environment for laboratory personnel.

Given the paucity of data on the potential short- and long-term health effects of nanomaterials, this document will be revised and updated if necessary on a yearly basis.

## ABSTRACT

Nanotechnology is a rapidly expanding area of our economy. A nanomaterial is defined as a material with at least one dimension in the 1 to 100 nm size range. It is estimated that the annual production of products derived from nanotechnology will increase from the current level of 1 to 2 tonnes per year to about 60,000 tonnes per year in 2020. This economic boom has prompted universities and government agencies to initiate various research programs on the release and the fate and toxicity of nanomaterials in aquatic and terrestrial environments.

This report is intended to provide guidelines and practical recommendations for the safe handling of nanomaterials in the workplace (environmental chemistry and toxicology laboratories). The proposed recommendations are based on published guidelines and on our own workplace experience. It is clear that the manipulation of solid nanomaterials (dust) should be avoided if possible and that liquid formulations of nanomaterials are much safer to handle. A number of measures are suggested to safely handle these products in liquid forms. In the event that it is not possible to work with liquid suspensions, a series of measures are proposed to ensure special conditions are maintained for the safe handling of nanopowders. It is also recommended that hand-held monitors be used to take direct, real-time measurements of fine particles and that real-time air filters (which capture aerosols) be used to detect workplace contamination.

## RÉSUMÉ

La nanotechnologie représente un secteur en croissance rapide de notre économie. Un nanomatériau se définit comme un matériau dont au moins l'une de ses dimensions est comprise entre 1 et 100 nanomètres. On estime que la production annuelle de ce type de substance qui s'élève de 1 à 2 tonnes aujourd'hui atteindra environ 60 000 tonnes en 2020. Cet essor économique a amené les universités et les organismes gouvernementaux à entreprendre divers programmes de recherche sur le devenir et la toxicité des nanomatériaux rejetés dans les milieux aquatique et terrestre.

Le présent rapport vise à formuler des lignes directrices et des recommandations pratiques afin de permettre la manipulation sécuritaire des nanomatériaux en milieu de travail (laboratoires de recherche en chimie et en toxicologie de l'environnement). Les recommandations proposées reposent sur des lignes directrices déjà publiées par d'autres instances et sur l'expérience acquise par nos scientifiques au travail. Il faudrait évidemment éviter si possible de manipuler les formulations solides de nanomatériaux (poussière) et favoriser plutôt la manipulation des formulations liquides. On suggère une série de mesures pour manipuler les préparations liquides de la façon la plus sécuritaire possible. S'il est impossible d'éviter la manipulation des nanopoudres, on recommande des précautions particulières à prendre pour les manipuler de façon sécuritaire. On recommande aussi de mesurer directement, en temps réel, la présence de particules fines à l'aide de détecteurs portatifs et de déceler, également en temps réel, la contamination du milieu par des trappes à air (aérosols) afin de détecter leur présence dans le milieu de travail.

# Table of Contents

ABSTRACT .....	iii
RÉSUMÉ.....	iv
DEFINITIONS.....	vii
LIST OF ABBREVIATIONS .....	viii
<b>1 INTRODUCTION .....</b>	<b>1</b>
<b>2 NANOTECHNOLOGY RESEARCH AT ENVIRONMENT CANADA .....</b>	<b>3</b>
<b>3 ROUTES OF EXPOSURE TO NANOPARTICLES .....</b>	<b>4</b>
3.1 Inhalation .....	4
3.2 Skin Absorption.....	4
3.3 Ingestion .....	4
<b>4 PROTECTION FROM NANOPARTICLES AND RISK REDUCTION.....</b>	<b>5</b>
4.1 Using Containment Methods for Research Activities.....	5
4.2 Minimizing the Dispersion of Nanopowders in the Air .....	5
4.3 Minimizing the Dispersion of Aerosols from Nanosolutions or Suspensions.....	6
4.4 Personal Protection .....	6
4.4.1 Skin protection .....	6
4.4.2 Respiratory protection .....	7
4.4.3 Eye protection.....	7
4.5 Technical Characteristics of Laboratories.....	7
4.6 Evaluation of Exposure and Validation of Work Methods .....	8
<b>5 STORAGE, TRANSPORT, CLEANING AND SPILLS.....</b>	<b>9</b>
5.1 Storage .....	9
5.2 Transport.....	9
5.3 Cleaning.....	9
5.4 Spills .....	9
<b>6 MANAGEMENT OF NANOWASTE .....</b>	<b>10</b>
<b>7 CONCLUSION .....</b>	<b>11</b>
<b>SUGGESTED READING .....</b>	<b>12</b>
<b>INTERNET LINKS (2009).....</b>	<b>13</b>
<b>REFERENCES .....</b>	<b>14</b>

## List of Figures

Figure 1. Nanotechnology: overview of the nanometric scale .....	2
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## List of Tables

Table 1. Occupational exposure routes: handling of nanoparticles in the laboratory.....	4
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## DEFINITIONS

**Aerosol** – A collection of fine liquid droplets or solid particles that remain suspended in air for a prolonged period.

**Colloid** – A substance with properties between those of a solution and a fine suspension, which is often considered a nanoparticle or a natural material.

**Nanomaterial** – A material composed of nano-objects which have novel properties. There is no official consensus on the definition of a nanoparticle, and work is under way at Environment Canada to develop a precise definition.

**Nanoscale** – Relates to a polymer or a particle with one or more dimensions in the size range from 1 to 100 nm.

**Nanoparticle** – Small object with at least one dimension between 1 and 100 nm.

**Nanotechnology** – The manufacture of any substance with at least one dimension in the size range from 1 to 100 nm.

**Nanotoxicity** – Toxic properties associated with a nanoparticle or a nanotechnology.

**Polymer** – Term derived from the Greek word *polu* (many) and *meros* (part), which denotes an organic or inorganic macromolecule consisting of repeated linked units, or monomers (from the Greek *monos* [one or single] and *meros* [part]), which are connected by covalent bonds. More specifically, a polymer is a substance composed of molecules characterized by chains of one or more monomers.

## LIST OF ABBREVIATIONS

MSDS	Material Safety Data Sheet
nm	nanometre ( $10^{-9}$ m)
OECD	Organisation for Economic Co-operation and Development
PAMAM	polyamidoamine dendrimers
RPD	respiratory protective device
$\mu\text{m}$	micrometre ( $10^{-6}$ m)

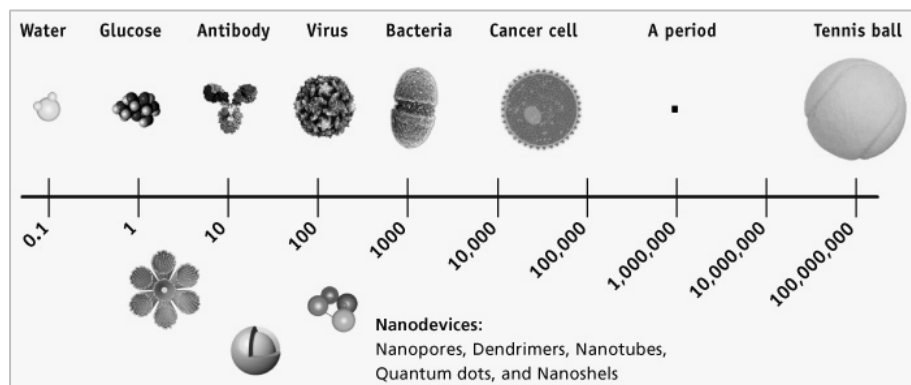
# 1 INTRODUCTION

Nanoparticles occur in nature as a by-product of phenomena such as volcanic eruptions and forest fires, and they are also produced incidentally by high-temperature industrial processes such as combustion, welding and motor vehicle exhaust. However, with the advent of nanotechnology and the mass use of nanotechnology-based products in various manufacturing sectors, the presence of nanoparticles in the natural environment is likely to increase.

Nanotechnology, a multidisciplinary field, consists in exploiting the unique properties of nanoscale particles to develop revolutionary procedures and technologies that hold benefits for a number of economic sectors, including health, energy, the environment, information technologies and communications. Contamination of the environment by nanomaterials could have significant consequences in the near future. Concerns about the potential for environmental contamination led to the establishment of university and government research programs designed to support regulatory and environmental protection requirements. These programs will permit the development of more effective means of detecting and determining the persistence of nanotechnology by-products and their toxic effects on aquatic and terrestrial wildlife.

Within the scientific community, nanoparticles (sometimes termed ultrafine particles) are defined as particles with one or more dimensions in the 1 to 100 nm size range. Carbon nanotubes provide a good example of nanoparticles since their diameter is smaller than 100 nm and their maximum length is a few micrometres.

**Figure 1. Nanotechnology: overview of the nanometric scale**



**Source: National Cancer Institute**

At the nanoscale, significant changes can be observed in physical (optical, mechanical, electrical and magnetic) properties as well as chemical properties (reactivity and stability). These new characteristics suggest that nanoparticles could present a higher level of risk or new toxicity mechanisms. Research into the toxic properties of nanoparticles has given rise to a new branch of toxicology, called nanotechnology, in which effects are not only studied as a function of dose and exposure duration but also as a function of nanoparticle size, shape and surface area and the presence of dielectric and semi-conductor properties (Gagné et al., 2007). Based on current knowledge, the risks associated with nanoparticles relate primarily to the particles' ability to cross biological barriers (due to their small size) and to their persistence in air owing to aerosolization (fine dusts), as well as to the increased reactivity resulting from their large surface area.

Little information is available on the toxicity of nanoparticles at present. However, dozens of research laboratories are striving to define and understand the effects of nanoparticle interactions on living organisms and ecosystems. A number of countries have joined together in international initiatives carried out under the aegis of organizations like the OECD (Organisation for Economic Co-operation and Development) to establish standards that will permit more effective supervision of nanotechnology-related activities.

Classic information tools used in health and safety, such as material safety data sheets (MSDS), usually provide a good starting point for the adoption of safe laboratory practices. In the case of nanoparticles, however, vigilance is in order, since in most cases material safety data sheets contain very little information in this regard. MSDSs sometimes contain toxicological data on the constituents of nanoparticles without giving an indication of their nanometric size or their surface properties. Studies have also shown that nanoparticles of similar chemical composition have a higher potential toxicity than a micron-sized particle (Barlow et al., 2005; Duffin et al., 2007; Midander et al., 2009). Consequently, nanoparticles should always be considered as toxic substances when only limited or ambiguous information is available concerning their toxicity.

## **2 NANOTECHNOLOGY RESEARCH AT ENVIRONMENT CANADA**

The nanotechnology research activities carried out in Environment Canada's River Ecosystems Research Section are aimed primarily at gaining a better understanding of the impact of nanotechnology-based products on river ecosystems. They deal specifically with the persistence and distribution of such products in the aquatic environment, including sediments and food chain organisms, that is, bacteria, algae (cyanobacteria), invertebrates (microcrustaceans, hydra and bivalves) and fish.

The research activities encompass several components:

- Development of bioassays and biomarkers that can be used to assess the nanotoxicity of nanoparticles (size, shape, surface properties, vectorization, etc.)
- Physico-chemical characterization of nanoparticles in various water and soil matrices
- Evaluation of degradation products of nanoparticles
- Study of transformations of nanoparticles in the environment
- Toxicological analyses of various organisms representative of aquatic ecosystems (organisms representative of a food chain)
- Development of approaches related to the toxicogenomics of nanoparticles and to their vectorization: nanovectors or drug transporters

The nanoparticles under study consist mainly of quantum dots (CdTe) used in imaging and renewable energy production (solar panels), silver nanoparticles known for their antibacterial properties and polyamidoamine dendrimers (PAMAM), that is, nanopolymers developed for the formulation of pharmaceutical products, among others. Other nanoparticles have also been studied, including metallic oxides, carbon nanotubes and nanocellulose.

### 3 ROUTES OF EXPOSURE TO NANOPARTICLES

For nanoparticles, like conventional chemical compounds, there are three main routes of exposure: inhalation, skin absorption and ingestion. It should be noted that nanoparticles have certain intrinsic properties (such as pinocytosis) that make it easy for them to enter cells. At the cellular level, nanoparticles can be found in various compartments, and even in the cell nucleus, which contains all the genetic information (Lovric et al., 2005; AshaRani et al., 2009).

#### 3.1 Inhalation

In the workplace, the inhalation of nanoparticles in the form of liquid or solid aerosols is the primary exposure route (Table 1). Pulmonary retention of inhaled particles smaller than 20 nm can be as high as 80% to 100% (Ostiguy et al., 2008; University of California, 2008). Nanoparticles that are inhaled into the lungs can reach the alveoli, or air sacs. Close contact between the alveoli and the circulatory system can facilitate the translocation of nanoparticles to other organs, such as the liver and the brain (Oberdörster et al., 2002; *id.*, 2004). Other studies have shown that nanoparticles can travel to the central nervous system along the olfactory nerve (Elder et al., 2006; Wang et al., 2008).

#### 3.2 Skin Absorption

Absorption through the skin can be a route of exposure to nanoparticles. There is no consensus in the literature at present concerning the risk of dermal absorption of engineered nanoparticles. Some studies have shown that small quantities of such particles can cross the skin barrier after just 24 h of exposure (Mortensen et al., 2008; Larese et al., 2009), whereas other studies have reported that nanoparticles do not penetrate beyond the *stratum corneum*, that is, the outermost layer of the epidermis (Cross et al., 2007; Zhang et al., 2008; Zvyagin et al., 2008). It is difficult to draw general conclusions about all nanoparticles given the diversity of findings.

#### 3.3 Ingestion

Workers can be accidentally exposed to nanoparticles by hand-to-mouth transfer of materials. Ingestion can also occur when nanoparticles in the respiratory system are transferred toward the oropharyngeal cavity and are swallowed. The particles can then move through the digestive tract and even cross the intestinal wall, after which they can be transported in the bloodstream.

**Table 1. Occupational exposure routes: handling of nanoparticles in the laboratory**

Potential routes of exposure	
Manipulation of nanopowders (weighing and preparation of samples)	Inhalation (solid aerosols) > skin absorption
Preparation of a suspension of nanoparticles in an aqueous medium. Methods used for placing into suspension, sonication and/or vigorous shaking (e.g., vortexing) in non-stoppered tubes	Inhalation (liquid aerosols) or skin absorption
Manipulation of nanoparticles in solution (pipetting, filtration and pouring/transferring)	Skin absorption or inhalation (liquid aerosols)
In vivo exposure to an aqueous media requiring aeration	Inhalation (liquid aerosols) or skin absorption

## **4 PROTECTION FROM NANOPARTICLES AND RISK REDUCTION**

### **4.1 Using Containment Methods for Research Activities**

- Set aside specific locations within the laboratory for nanotechnology-related activities. Appropriate containment helps to prevent contamination of work areas.
- Identify work areas in which nanoparticle research activities are to be carried out.
- Use dedicated labware for nanotechnology-based products and ensure appropriate maintenance of this equipment.

### **4.2 Minimizing the Dispersion of Nanopowders in the Air**

- Encourage the use of products in solution and purchase commercial preparations of nanoparticles in suspension.
- Work with nanopowders must be done in a fume hood, a glove box, a class II biological safety cabinet (type B1 or B2) or a portable fume hood that can vent the exhaust air directly into a chemical fume hood. A balance can be used in this type of fume hood.
- Use an antistatic device (Mettler Toledo) to remove the static electricity from nanopowders before weighing them. This step helps to further reduce the risk of aerosolization of nanopowders.
- Always use fume hoods or biological safety cabinets that discharge the exhaust air outside the building.
- Never handle nanopowders in a fume hood or a biological safety cabinet that recirculates air within the laboratory.
- Always use containment equipment: do not manipulate nanopowders directly on laboratory benches.
- Cover work surfaces with absorbent paper (Versi-Dry type) to protect against spills and facilitate cleaning.

To obtain more information on biological safety cabinets, consult the third edition of *Laboratory Biosafety Guidelines* (2004), published by the Public Health Agency of Canada, in particular Chapter 9 entitled “Biological Safety Cabinets” ([www.phac-aspc.gc.ca/publicat/lbg-ldmbl-04/ch9-eng.php?option=print](http://www.phac-aspc.gc.ca/publicat/lbg-ldmbl-04/ch9-eng.php?option=print)).

### 4.3 Minimizing the Dispersion of Aerosols from Nanosolutions or Suspensions

- Activities that generate aerosols (sonication, filtration, vigorous shaking and aeration) must be carried out in a fume hood or, if none is available, hermetically sealed containers must be used.
- Pipetting and pouring procedures can also generate aerosols. It is important to carry out these manipulations in a fume hood or in a well-ventilated area where the air is vented in such a way that aerosols are directed away from the experimenter as quickly as possible (i.e., with the person's back to the direction of ventilation).
- For procedures requiring sterile conditions, Class II biological safety cabinets (type B1 or B2) should be used, if available. Class II cabinets protect the operator, the product and the environment, and they are used mainly in level 2, 3 and 4 laboratories.
- Cover work surfaces with absorbent paper (Versi-Dry type) to provide protection in the event of spills and facilitate cleaning.

### 4.4 Personal Protection

#### 4.4.1 *Skin protection*

- **Laboratory coats** must be worn as in all laboratory work. It is also recommended that lab coats be kept in the laboratory.
- A laboratory coat or disposable sleeve covers should be worn when high levels of exposure or splashes are anticipated (e.g., exposures to considerable volumes when working with living organisms).
- Lab coats and clothing contaminated with nanoparticles must be removed immediately, such as when an incident occurs, and they must be treated as hazardous waste.
- **Nitrile gloves** should be used for all manipulations. Nitrile gloves can better withstand perforations, chemicals (solvents) and microbial agents than latex gloves.
- Change gloves on a regular basis or when contamination occurs.
- Double gloving is recommended in situations involving significant contact with the substance (i.e., work with concentrated solutions).
- Keep wrists covered by gloves or by the sleeves of the laboratory coat.
- Wash hands immediately after removing gloves.

#### **4.4.2 Respiratory protection**

- Promote work methods that eliminate the risk of inhalation. The use of biological safety cabinets or fume hoods is recommended. Working with nanoparticles in solution helps to significantly reduce respiratory tract exposure.
- Respiratory protection devices (RPDs) should not be worn when working with nanopowders. A respiratory protection program should be implemented when these powders are used. Effective training and proper equipment selection and maintenance are key measures for minimizing the risks associated with the use of RPDs.
- As is the case for large particles, the protection that masks provide against nanoparticles depends on the face-seal. When properly selected and used, RPDs appear to provide effective protection from nanoparticles.
- When working with nanopowders in a fume hood, always limit the manipulations to small quantities and work as far as possible from the sash window (at least 15 cm). Avoid sudden movements within the hood and near the face of the hood that could create turbulence and result in dispersion of the contaminants (nanopowders) outside the fume hood. Keep the fume hood opening in a safe area, 20 to 40 cm from the work surface (preferably at a level below the experimenter's chin). The fume hood must be kept free of unnecessary equipment and clutter.
- The use of an RPD does not appear to be necessary when manipulating nanoparticles in solution, unless the procedures are likely to generate liquid aerosols. A mask (HEPA P100 type) may be useful for protecting against aerosols especially when manipulations are done outside a biological safety cabinet.

#### **4.4.3 Eye protection**

- Safety glasses are mandatory when manipulating nanoparticles, whether in powdered form or in solution.
- For increased protection, safety goggles with a full seal around eyes should be worn for certain applications (e.g., those involving significant exposure to aerosols). Some universities recommend that a face shield be worn.

For more information about eye protection, consult the section on safety glasses on the Web site of the Canadian Centre for Occupational Health and Safety ([www.ccohs.ca/oshanswers/prevention/ppe/glasses.html](http://www.ccohs.ca/oshanswers/prevention/ppe/glasses.html)).

### **4.5 Technical Characteristics of Laboratories**

- Laboratories that conduct research on nanoparticles should have a ventilation system in which the air is not recirculated, but is exhausted outside the building and changed at least 6 to 12 times per hour.
- The air in the laboratory should be at negative pressure with respect to adjacent areas.

- In some laboratories, adhesive floor mats are installed near access points to minimize the dispersion of particles outside the room.

## **4.6 Evaluation of Exposure and Validation of Work Methods**

- Obtain a fine particle sampler (compact model) and install an aerosol capture system to assess the real-time distribution of aerosols and nanodusts in the laboratory. Use small aerosol collectors (0.2  $\mu\text{m}$  paper filters 3 cm in diameter) at various locations in the work area (and even on the lab coat) and measure the nanoparticle products to determine the dispersion of aerosols or dusts (e.g., monthly measurement of total cadmium on the filter if working with cadmium-based quantum dots). This permits validation of the methods adopted to ensure safe handling for a given work space.
- Care must nevertheless be exercised in selecting methods and instruments for assessing exposure to nanoparticles. Data interpretation must take into account the sensitivity (quantity) and selectivity (size) of the fine particle detectors used.
- By placing filters on lab coats, it is possible to measure all dusts in the ambient air that also contain metals. Modern detection techniques can be used to identify the presence of numerous metals. Distinguishing the nanoparticle contribution of the laboratory air will be a difficult task. Using containment methods therefore appears to be a more suitable approach.

## **5 STORAGE, TRANSPORT, CLEANING AND SPILLS**

### **5.1 Storage**

- To store nanoparticles, follow the recommendations on the MSDS for the product. Since some nanoparticles are highly reactive, specific operating conditions must be ensured to minimize the risk of fires and explosions.
- In the case of nanopowders, make sure that the containers are properly closed after use. As a preventive measure, every container must be sealed with Parafilm and placed in a hermetically sealed, shock-resistant container.

### **5.2 Transport**

- Nanopowders must be transported in hermetically sealed, shock-resistant containers.

### **5.3 Cleaning**

Always wear the requisite personal protective equipment.

- Clean work spaces and equipment, including laboratory fume hoods and the exposure area following use.
- Carry out wet cleaning (with damp absorbent paper) for nanopowders to prevent aerosolization and the dispersion of nanoparticles in the air.

### **5.4 Spills**

Every laboratory that works with nanoparticles should have a kit with the requisite material to safely neutralize and clean up a spill.

The kit should contain the following elements:

- Tight-fitting filtering half masks (HEPA P100 type) (fit test done) or disposable filtering half masks (HEPA P100 type)
- Safety goggles with a good seal
- Sealable plastic bags
- Absorbent material
- Adhesive floor mat (e.g., Tacky Mat®)

Double Nitrile gloves should be worn in case of spills. When major spills of nanopowders occur outside a biological safety cabinet, disposable filtering masks and goggles with a good seal should be used for effective respiratory and ocular protection. Use wet absorbent paper to minimize the dispersion of nanoparticles in the air. Place all waste in sealable plastic bags. A vacuum cleaner with a HEPA filter can also be used (Nilfisk GM80CR). However, certain precautions must be taken (Massachusetts Institute of Technology, 2008).

## 6 MANAGEMENT OF NANOWASTE

Since current knowledge about the toxicity of engineered nanoparticles is limited, all nanoparticles should be considered hazardous substances until proven otherwise.

Collect all nanowaste and contaminated material:

- Nanoparticles and pure nanosolutions
- Samples and material contaminated with nanoparticles (absorbent paper, filters, gloves, etc.)
- Liquids containing nanoparticles in suspension
- Solid materials (easily damaged) that can release nanoparticles into the air or water

**Liquid wastes** must be stored in leak-proof containers. Glass or rubber stoppers should not be used.

**Solid and contaminated wastes** must be placed in heavy duty plastic bags or leak-proof containers. When plastic bags are used to hold waste, be sure to use double bags by placing the first sealed bag inside a second one to make it more leak-proof and minimize the risk of perforation.

All containers and bags of waste must be properly identified and labelled as “nanoproducts.” Wastes, including nanoparticles containing metals or toxic chemicals, must also be identified the same way.

## **7 CONCLUSION**

This document has been written by drawing on various information sources (reports, university laboratory guides, articles and Web sites) that deal with the handling of nanotechnology-based products and it provides a basis for developing an approach to ensure safe laboratory practices. However, all participants need to assess the risks associated with their own research activities and take the necessary measures to maximize their own protection and that of their colleagues.

## **SUGGESTED READING**

Agence française de sécurité sanitaire de l'environnement et du travail (2008). Les nanomatériaux : Sécurité au travail. Rapport scientifique de l'Agence, 247 p.

National Institute for Occupational Safety and Health (2009). Approaches to Safe Nanotechnology: Managing the Health and Safety Concerns Associated with Engineered Nanomaterials. NIOSH scientific report, 125 p.

Ostiguy, C., B. Roberge, L. Ménard and C.A. Endo. (2008) Guide de bonnes pratiques favorisant la gestion des risques reliés aux nanoparticules de synthèse. Études et recherches, guide technique R-586, 73 p. (English version available, R-599)

## INTERNET LINKS (2009)

**Key words: handling nanomaterials, nanosafety, nanotechnology awareness, working with nanomaterials.**

International Council on Nanotechnology. Database of literature on the environmental, health and safety implications of nanotechnologies.

<http://icon.rice.edu/research.cfm>

Public Health Agency of Canada. Laboratory *Biosafety Guidelines: 3rd Edition 2004.*

[www.phac-aspc.gc.ca/publicat/lbg-ldmbl-04/ch9-eng.php](http://www.phac-aspc.gc.ca/publicat/lbg-ldmbl-04/ch9-eng.php)

Harvard University, University Operations Services, Environmental Health & Safety.

*Working safely with nanomaterials.*

[www.uos.harvard.edu/ehs/ih/nanotech\\_control.shtml](http://www.uos.harvard.edu/ehs/ih/nanotech_control.shtml)

Massachusetts Institute of Technology, Environmental Programs/EHS. *Potential Risks of Nanomaterials and How to Safely Handle Materials of Uncertain Toxicity.*

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