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Best practices guidance for nanomaterial risk management in the workplace

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Chemical and Biological Hazard Prevention

Studies and Research Projects

REPORT **R-899**

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ABSTRACT

Today's nanotechnologies can substantially improve the properties of a wide range of products in all sectors of activity, from the manufacture of materials with ground-breaking performance to medical diagnostics and treatment—yet they raise major technological, economic, ethical, social and environmental questions. Some of the spinoffs we can expect include the emergence of new markets, job creation, improvements in quality of life and contributions to protection of the environment. The impact of nanotechnologies is already being felt in sectors as diverse as agro-processing, cosmetics, construction, healthcare and the aerospace industry. Most universities in Québec and many research centres are working to design new applications. Many companies have projects in the start-up phase, while others are already producing nanomaterials or have incorporated them in their processes to improve product performance, a trend expected to accelerate over the coming years. These new developments, which could mean exposure of a growing number of workers to these infinitesimally small particles, are of particular concern to workers in industry and staff in research laboratories. It is estimated that in 2015 about 10% of manufacturing jobs worldwide will be associated with nanotechnologies, and more than 2,000 commercial products will contain nanomaterials.

Given our fragmentary knowledge of the health and safety risks for workers and the environment, the handling of these new materials with their unique properties raises many questions and concerns. ***In fact, many studies have already demonstrated that the toxicity of certain nanomaterials differs from that of their bulk counterparts of the same chemical composition.*** Nanomaterials enter the body mainly through inhalation but also through the skin and the GI tract. Animal studies have demonstrated that certain nanomaterials can enter the blood stream through translocation and accumulate in different organs. Animal studies also show that certain nanomaterials cause more inflammation and more lung tumours on a mass-for-mass basis than the same substances in bulk form, among many other specific effects documented. In addition, research has shown that the physicochemical characteristics of nanomaterials (size, shape, specific surface area, charge, solubility and surface properties) play a major role in their impact on biological systems, including their ability to generate oxidative stress. ***It is thus crucial that risks be assessed and controlled to ensure the safe handling of nanomaterials.*** As with many other chemicals, a risk assessment and management approach must be developed on a case-by-case basis.

There is still no consensus, however, on a measurement method for characterizing occupational exposure to nanomaterials, making quantitative risk assessment difficult if not impossible in many situations. As a result, a precautionary approach is recommended to minimize worker exposure. In Québec, the employer is responsible for providing a safe work environment, and preventive measures must be applied by employees. Accordingly, preventive programs that take into account the specific characteristics of nanomaterials must be developed in all work environments where nanomaterials are handled, so that good work practices can be established and preventive procedures tailored to the risks of the particular work situation can be introduced.

Fortunately, current scientific knowledge, though partial, makes it possible to identify, assess and effectively manage these risks. This best practices guide is meant to support the safe development of nanotechnologies in Québec by bringing together current scientific knowledge on hazard identification, strategies for determining nanomaterial levels in different work

environments, risk assessment and the application of various risk management approaches. Some knowledge of occupational hygiene is required to use this guide effectively. Designed for all work environments that manufacture or use nanomaterials, this guide provides practical information and prevention tools for the safe handling of nanomaterials in laboratories and pilot plants as well as industrial facilities that produce or incorporate them.

To be effective, risk management must be an integral part of an organization's culture, and health and safety issues must be considered when designing the workplace or as far upstream as possible. This is crucial for good organizational governance. In practice, risk management is an iterative process implemented as part of a structured approach that fosters continuous improvement in decision-making and can even promote better performance. The purpose of this guide is to contribute to the implementation of such an approach to the prevention of nanomaterial-related risks only. Depending on the process, other risks (associated with exposure to solvents, gas, heat stress, ergonomic stress, etc.) may be present, but they are not addressed in this guide.

The authors recommend a preventive approach designed to minimize occupational exposure to nanomaterials. Given the different exposure pathways, the many factors that can affect nanomaterial toxicity and the health risks, our approach is essentially based on hazard identification, different risk assessment strategies and a hierarchy of control measures, incorporating knowledge specific to nanomaterials when available. Risk assessment makes it possible to select processes, equipment and work methods that reduce occupational exposure, in particular by controlling nanomaterial emissions at the source. It also makes it possible to select collective and individual preventive measures and to determine administrative management measures and training needed to protect all workers—operators as well as those who maintain equipment and workspaces.

This second edition incorporates new information in the scientific literature. In addition, appendices have been included describing initiatives in Québec workplaces; examples of at-risk situations described in the literature; preventive measures and data on their relative efficacy; and the implementation of measures to control exposure. ***Finally, we note that solutions for any particular workplace must be developed on a case-by-case basis taking into account the risk assessment of each workstation.***

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ANSI: American National Standards Institute (United States)
APF: Assigned protection factor (under ideal laboratory conditions)
BSI: British Standards Institution
CB: control banding
CNC: condensation nuclei counter
CNF: carbon nanofibre
CNT: carbon nanotube
CSST: Commission de la santé et de la sécurité du travail
CVD: chemical vapour deposition
DNA: deoxyribonucleic acid
DRI: direct reading instrument
EEPS: exhaust emission particle sizer
ELPI: electrical low pressure impactor
EM: electron microscopy
EU-OSHA: European Occupational Safety and Health Administration
f/mL: fibres per millilitre
FMPS: fast mobility particle sizer
g/m^3: grams per cubic metre
GHS: Globally Harmonized System
h: hour
HEPA filter: high efficiency particulate arrestor filter (99.9+ efficient)
ICP-MS: inductively coupled plasma – mass spectrometry
INEL: indicative no-effect level
INRS: Institut national de recherche et de sécurité (France)
IRSST: Institut de recherche Robert-Sauvé en santé et en sécurité du travail
ISO: International Organization for Standardization
LOAEL: lowest observed adverse effects level
m/s: metres per second
mg/m^3: milligrams per cubic metre
min: minute
MOUDI: micro-orifice uniform deposit impactor
ms: millisecond
MSDS: material safety data sheet
MWCNT: multiwalled carbon nanotube
N/A: information not available

ND : not detected

ng/m^3: nanograms per cubic metre

NIOSH: National Institute for Occupational Safety and Health (United States)

NOAEL: no observed adverse effects level

OEL: occupational exposure limit (see WEL, a synonym)

OHS: occupational health and safety

OPC: optical particle counter

OSHA: Occupational Safety and Health Administration (United States)

PAPR: powered air-purifying respirator

PPE: personal protective equipment

PPR: positive pressure respirator

RPE: respiratory protective equipment

SAR: supplied-air respirator

SCBA: self-contained breathing apparatus

SMPS: scanning mobility particle sizer

SWCNT: single-walled carbon nanotube

TEOM: tapered element oscillating microbalance

TLV: threshold limit value

TWAEV: time-weighted average exposure value

µg/m3: micrograms per cubic metre

µm: micrometre

µs: microsecond

UL: Underwriters Laboratories, a certification company

ULPA filter: ultra-low penetration air filter (99.999%+ efficient)

UV: ultraviolet

WEL: workplace exposure limit (see OEL, a synonym)

WHMIS: Workplace Hazardous Materials Information System, Canada's national hazard communication standard

WPF: workplace protection factor

XRD: x-ray diffraction

1. BACKGROUND, OBJECTIVES AND INTENDED READERSHIP

The field of nanotechnologies is developing at a breathtaking pace. Since nanomaterials radically transform the properties of finished products (making them stronger or better electrical conductors, giving them unique optical properties, etc.), anticipated applications will affect all sectors of industrial activity. The exceptional properties of nanomaterials are not found in substances of larger size with the same chemical composition. Thanks to these unique properties, an estimated 10% of manufacturing jobs will soon involve nanotechnologies [1]. In fact, about 250 new products containing nanomaterials have been introduced to the market annually since 2006 [2], and it is estimated that in 2015 the worldwide nanotechnology-related market will reach US$1 trillion [3], with related industries employing about two million workers [4].

Given the economic impact, all industrialized countries want their share of the market and have come up with nanotechnology development plans [5, 6], many investing colossal sums in research. Québec is no exception. Researchers in most Québec universities are working on the design of new nanomaterials, new nanotechnology products or nanotechnology applications, and at least four general and vocational colleges (CEGEPs) have a nanotechnologist training program. It is estimated that more than 100 companies are already using or in the process of introducing nanotechnologies [7]—including producers of nanomaterials, companies that purchase nanomaterials and incorporate them in processes to improve product performance, nanotechnology importers/exporters and special consultants.

Recent studies clearly demonstrate that perception of the risks specific to nanomaterials varies widely not only from one country to the next, but also within one and the same country depending on the workplace [8, 9]. Given the uncertainty regarding possible risks that are still poorly understood, nanomaterials are handled in many workplaces without any specific preventive measures. The purpose of this guide is to collect, summarize and share recent evidence-based information that can assist research organizations and companies in the safe, ethical and responsible development of nanotechnologies in Québec.

This second edition of this best practices guide was a joint effort, with two researchers from the Institut de recherche Robert-Sauvé en santé et en sécurité du travail (IRSST) and two from the Université de Montréal supported by an advisory committee composed of workers and employers from universities, manufacturers, colleges (CEGEPs), industry associations and even NanoQuébec. A public health physician also contributed to the work of the advisory committee.

This guide describes, supports and suggests an approach, prevention advice and practical solutions exclusively for the safe handling of nanomaterials produced and used in a variety of work environments. The suggested approach, detailed in Chapter 9, is designed to reduce nanomaterial emissions, taking into account the specific nature of each work environment: research laboratories, demonstration plants, plants that synthesize nanomaterials and plants that incorporate nanomaterials in their products to improve their properties as well as workplaces where mechanical operations (drilling, sanding, etc.) are performed on composites that include nanomaterials and generate dust containing nanomaterials. This guide does not address other risks associated with the synthesis and use of nanomaterials—ergonomic, optical (lasers), biological (microorganisms), electrical (high voltage), chemical (solvents and gases), etc.—

though these must be considered in developing and implementing a comprehensive prevention program for any establishment.

In sum, this guide introduces nanotechnologies with a reminder of the huge diversity of nanomaterials (Chapter 2) and goes on to describe the main processes used to synthesize them and their fields of use (Chapter 3). Given their very small size, nanomaterials may present particular behaviours and hazards (Chapter 4), and a different approach may be required to assess their presence in the air or on work surfaces (Chapter 5). As our knowledge of nanomaterials is still incomplete and there are no standards specific to them (Chapter7), conservative assumptions about missing information in addition to current evidence must be considered in assessing risks and determining preventive measures (Chapter 6). As caution is often the best strategy under the circumstances, a preventive approach is suggested (Chapter 8) as well as a practical approach to risk management that is applicable to all situations (Chapter 9). Last, Appendix A summarizes initiatives taken in different Québec workplaces, and Appendix B offers a practical plan for controlling exposure in a research laboratory based on estimated risk level. Appendix C provides real exposure control data from a variety of workplaces.

This guide should be helpful not only to employers, workers and members of occupational health and safety committees in laboratories and industry in developing and monitoring prevention programs but also to members of the occupational health and safety prevention network (inspectors, hygienists, doctors, nurses and technicians), consultants, legislators and any person or organization involved in the field of nanotechnologies. Some knowledge of occupational hygiene is required to use this guide.

2. A WIDE VARIETY OF NANOMATERIALS

International consensus defines nanomaterial as material with at least one external dimension in the nanoscale, that is, between 1 and 100 nanometres (nm or 10^{-9} m), or material having an internal or surface structure in the nanoscale [10, 11]. To visualize how little a nanometre is, imagine the diameter of the Earth as representing 1 m: then 1 nm would be the diameter of a dime. There are three different sources of nanomaterials: some nanomaterials are deliberately synthesized to exploit unique properties exhibited only at nanoscale dimensions (engineered nanomaterials); some nanomaterials are of human origin; and some nanomaterials are of natural original. Nanomaterials of natural or human origin are composed mainly of undesirable products, known as ultrafine particles, that come from mechanical operations (metal machining, for example), thermal operations (diesel engine emissions, for example), or natural phenomenon (volcanic smoke, sea air or forest fires, for example).

Engineered nanomaterials fall into two categories: nano-objects and nanostructured materials [10, 11]. A nano-object is a material with one, two or three external dimensions in the nanoscale: a graphene sheet, for example has one external dimension in the nanoscale; nanotubes, nanofilaments and nanowires have two; and titanium dioxide and fullerene have three. Nanostructured materials are larger in size and have an internal or surface structure in the nanoscale.

Given the intended readership for this guidance, a decision was made to use the term nanomaterial, a term more meaningful for the reader than nano-object. Nonetheless, only nano-objects are addressed in this guidance based on the definitions in international standards [10, 11].

Many nanomaterials exist only in nanoscale dimensions. A number of forms of carbon, for example, are cases in point: carbon nanotubes, fullerenes, graphene nanosheets, carbon nanofibres, etc. However, many inorganic products (metals, metal oxides, etc.) as well as organic products (polyvinyl chloride, latex, etc.) can be synthesized in nanoscale dimensions. All solids can be reduced to nanoscale size, but not all are then considered nanomaterials as they don't all demonstrate properties that are new, improved or of commercial interest at the nanoscale [11, 12].

2.1 Carbon nanotubes

Carbon nanotubes (CNTs) are a new crystalline (allotrope) form of carbon that exists only in the nanoscale [12] (Figure 1). CNTs are composed of graphite sheets wound around themselves in one or more layers. A metal catalyst is normally required to synthesize CNTs and is found in the final product. CNT diameter ranges from one to several dozen nanometres and they can be several millimetres long. With excellent chemical and thermal stability, CNTs are good heat conductors

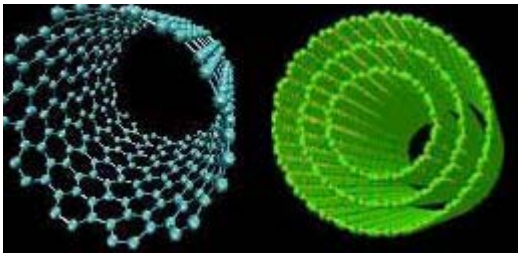


Figure 1: Schematic illustration of a single-walled carbon nanotube (SWCNT) and a multiwalled carbon nanotube (MWCNT)

and have a strong molecular absorption capacity as well as metallic and semi-conductive properties depending on the method of synthesis. More than 50,000 varieties of CNT have been reported to date [13].

2.2 Fullerenes

Pure fullerenes are another new carbon allotrope [12]. Fullerenes are hollow spheres composed of anywhere from 28 to over 100 carbon atoms, the most common fullerene (C_{60}) being composed of 60 carbon atoms. Like CNTs, fullerenes can be modified by bonding with organic or inorganic groups or by incorporation in a variety of products. These modifications have a major impact on fullerene properties and toxicity.

2.3 Quantum dots

Quantum dots are typically composed of combinations of chemical elements from groups II and IV or groups III and V of the periodic table. They were developed in the form of semiconductors, insulation, magnetic materials or metal oxides. Only a few nanometres in size, quantum dots have unique optical and electronic properties [12]. For example, quantum dots can absorb white or ultraviolet light and re-emit it at a specific wavelength depending on the composition and size of the quantum dot. The fluorescence spectrum of the light emitted can range from blue to infrared.

2.4 Organic polymers

Many common organic polymers can be produced at nanoscale dimensions. Polyvinyl chloride or latex can, for example, be solubilized or chemically modified under certain conditions. Many of these polymers can be prepared in the form of nanowires, and then used in developing liquid- or gas-phase ultrafiltration systems, or as sensors.

2.5 Dendrimers

Dendrimers are synthetic, three-dimensional, repetitively branched macromolecules built up from a monomer by adding new branches in steps until a tree-like structure is created. Dendrimers are considered a key element for large-scale synthesis of nanostructures displaying unique properties as they allow precise atom-by-atom control of nanostructure synthesis to desired dimensions, shape and surface chemistry.

2.6 Biologically inspired nanomaterials

Biologically inspired nanomaterials are very diversified but generally consist of structures in which a biological substance is encapsulated, imprisoned or absorbed at the surface. Lipids, peptides and polysaccharides serve as chemical agents in medical imaging as well as drug delivery vectors, receptors and nucleic acids.

3. NANOMATERIAL SYNTHESIS

Nanomaterials can be synthesized using a bottom-up or top-down approach. The bottom-up approach involves building up nanomaterials an atom or a molecule at a time using processes such as chemical synthesis, self-assembly and positional assembly. The top-down approach consists in taking a bulk material and modifying it down to nanoscale dimensions. Hot-acid etching, precision engineering, lithography and milling are common top-down approaches. A number of these techniques are used in white rooms in the electronics industry. The size of the particles produced tends to be the same no matter which approach (top-down or bottom-up) is used. The bottom-up approach produces a wider variety of architectures and generally allows better control of the nanometric state (molecule positioning, product homogeneity, size and monodisperse particle size distribution). The top-down approach, on the other hand, is generally capable of higher volume production, but control of the nanometric state is more delicate.

The Agence française de sécurité sanitaire de l'environnement et du travail (AFSSET, French environmental and occupational health and safety agency)* divides nanomaterial synthesis processes into three categories [14]: chemical methods, physical methods and mechanical methods (Table 1).

Table 1: Principal methods of synthesizing nanomaterials

Chemical methods
Vapour-phase reactions (carbides, nitrides, oxides, metal alloys, etc.)
Reactions in liquid or solid media (most metals and oxides)
Sol-gel techniques (most oxides)
Supercritical fluids with chemical reaction (most metals, oxides and some nitrides)
Chemical co-precipitation or hydrolysis
Physical methods
Inert- or reactive-gas condensation/evaporation under partial pressure (Fe, Ni, Co, Cu, Al, Pd, Pt, oxides)
Laser pyrolysis (Si, SiC, SiCN, SiCO, Si_3N_4, TiC, TiO_2, fullerenes, carbon black, etc.)
Microwave (Ni, Ag)
Ion/electron irradiation (production of nanopores in material of macroscopic dimensions or nanostructures immobilized in a matrix)
Low-temperature annealing (complex metallic and intermetallic alloys with three to five Al, Zr, Fe base elements)
Thermal plasma synthesis (ceramic nanopowders such as carbides [TiC, TaC, SiC], silicides [$MoSi_2$], doped oxides [TiO_2] or complex oxides [perovskites])
Physical vapour deposition (especially deposition of TiN, CrN, (Ti, Al)N)
Mechanical methods
Mechanosynthesis and mechanically activated powder metallurgy processing – high-energy milling (all types of materials: ceramics, metals, polymers, semi-conductors)
Consolidation and densification
Severe plastic deformation by torsion, rolling or friction

*AFSSET became ANSES (Agence nationale de la sécurité sanitaire de l'alimentation, de l'environnement et du travail, French food, environmental and occupational health and safety agency) in 2010, by ministerial order authorizing the merger of AFSSET and AFSSA (Agence française de sécurité sanitaire des aliments, French health safety agency).

3.1 Nanomaterial applications

Table 2 lists properties and applications of particular nanomaterials [14-16].

Table 2: Some nanomaterial applications

Nanomaterial	New properties	Applications
Fullerenes (C_{60})	High electron affinity	Improved magnetic properties, catalysts, pyrolysis, lubricants, solar cells, electrolyte membranes, ion-exchange membranes, oxygen and methane storage, drug delivery
TiO_2	Anti-UV and UV-visible optical properties, photocatalytic effect	Solar cells, UV sunblock creams, anti-UV paint, environmental treatments, transparent wood coatings, self-cleaning materials, antimicrobial agent, cancer treatment
Quantum dots	Colorimetric and electronic properties that can be precision-controlled	Dyes, nanoelectronics and quantum computers, medical imaging, medical therapies, solar cells, catalysts
CNTs and inorganic nanotubes (e.g., molybdenum disulfide)	High electrical conductivity, exceptional mechanical strength	Nanoelectronics and quantum computers, ultra-strong materials, electrostatic dissipators, hydrogen storage, biosensors, chemical sensors, electromagnetic armour, super condensers, reinforced polymer composites, super-strong cable, ultra-light parts for land, air and space vehicles, additives
Polymers/glass/ nanochannels	Miniaturization of chemical reactions	Lab on a chip
Liposomes	Biodegradable components	Drug delivery, veterinary use
Silver	Antimicrobial agent	Medical equipment, consumer products, food packaging, anti-odour textiles, electronic and household appliances, cosmetics, disinfectants
Photonic materials	Tunable light transmission	Telecommunications, optical computers
Graphenes	Electrical conductivity	Substitutes for silicon chips, high-frequency transistors
Metal oxides (e.g., Zn, Fe, Ce, Zr)	Large surface area, optical properties	Ceramics, anti-scratch coatings for lenses, cosmetics, sun screens
Nanoclays	Improved catalytic properties, stronger, harder, more heat and fire resistant	Oil refining, modification of composite and material properties, fire retardant, mechanical reinforcement, rubber additive
Carbon black	Large surface area	Rubber, paint and ink industries
Silica fume	Rheological properties	Superior-quality and special concretes used in the construction of bridges, roads, marine structures and water purification and distribution systems as well in the ceramics industry, mortars and plastic and rubber additives
Dendrimers	Hydrophilic/hydrophobic	Medical and biomedical applications

4. NANOMATERIAL BEHAVOUR AND HAZARD IDENTIFICATION

To get a real grasp of the hazards nanomaterials can present, their behaviour as solid aerosols (airborne particles), particularly in the workplace, must be understood, as inhalation is the most common route of occupational exposure.

4.1 Nanomaterial behaviour

Particle size is the critical factor in the behaviour of any aerosol [3, 12, 16]. Airborne particle behaviour is determined by three main forces: diffusion, gravitational pull and inertia. With particles of micrometric dimensions, inertial and gravitational forces dominate. However, as aerosol particle size diminishes, diffusion increasingly dominates and the behaviour of the solid particles starts to resemble that of a gas or vapour. Diffusion is thus the main mode of transport of nanomaterials, and the smaller the particle, the faster the diffusion regardless of particle concentration. This is why a nanomaterial leak can cause rapid contamination of large areas, and exposure of a large portion of the workers present, even those far from the leak.

4.1.1 Diffusion and agglomeration

Nanomaterials diffuse readily through the workplace, like a vapour or a gas. When nanomaterials hit other diffusing particles, they have a natural tendency to agglomerate, that is, to join together and form fewer particles of larger size. The speed at which nanomaterials agglomerate depends on the number of particles present and their mobility. Table 3 shows the time required for half the particles present to agglomerate depending on particle size and concentration. This is called the half-life or coagulation time. As the table clearly shows, small particles agglomerate rapidly, even at low concentrations. On the other hand, the agglomerates thus formed are still small and may continue to agglomerate with other particles while diffusing farther and farther from the leak or source of emission [16].

Table 3: Nanomaterial coagulation time as a function of particle size and concentration [16]

Particle diameter (nm)	Half-life			
	1 g/m^3	1 mg/m^3	1 µg/m^3	1 ng/m^3
0.5	0.39 µs	0.39 ms	0.39 s	6.5 min
1	2.2 µs	2.20 ms	2.2 s	36.67 min
2	12 µs	12 ms	12 s	3.34 hours
5	0.12 ms	0.12 s	2 min	33.34 hours
10	0.7 ms	0.7 s	11.67 min	8.1 days
20	3.8 ms	3.8 s	63.34 min	43.98 days

4.1.2 Sedimentation

The phenomena just described lead to the conclusion that the smaller the particles, the greater their ability to travel long distances, their size growing slowly and their composition possibly

changing over time as they meet up with other particles. The bigger the particle grows, the heavier it gets relative to the air, and the more its movement is affected by gravity. Some airborne particles may thus settle—on the floor, on workers, on equipment, on tools, on walls, on beams and on work surfaces. Air turbulence being equal, the heavier a particle the faster the sedimentation. Sedimentation, however, is useless as a method of controlling airborne nanomaterial concentrations [16], given the time it takes for the nanoparticle to grow large and the considerable distance it can travel before sedimentation. Thus airborne nanomaterials can travel throughout the workplace because they diffuse so readily, leading to longer occupational exposure and possibly exposure of more workers.

In other words, when a leak occurs, nanomaterials can diffuse over large areas, reach many workers and settle throughout the workplace if they are not captured directly at the source—unlike particles of larger size, whose deposition tends to be localized close to the leak.

4.1.3 Dustiness and resuspension

Dustiness may be defined as the tendency of a powder to generate airborne dust during handling [17, 18]. Though it has been demonstrated that some CNTs do not easily become resuspended, [19] silica or titanium dioxide of nanometric size, on the other hand, can be extremely difficult to weigh because these nanoparticles will resuspend with even the smallest draft [17]. There are instruments that can measure the resuspension facility of nanomaterial powders by measuring dustiness under standardized experimental conditions. The nanomaterials studied include some SWCNTs, carbon black, silica fume, titanium dioxide and aluminum [17, 18, 20, 21].

A number of processes require use of nanomaterials in the form of powder. Nanomaterials may be released to the air in the laboratory or the plant during different stages of these processes (synthesis, transfer, drying, bagging and debagging) due to leaks, maintenance operations, equipment malfunctions or broken containers. Settled dust can be resuspended by drafts or by human or mechanical activity (passage of a lift truck, vibration of a ventilation system, etc.) as well as by housekeeping activities, repairs or accidental spills.

The resuspension of nanomaterials is a complex phenomenon, because a number of factors can play a role—including particle size, shape, electrostatic charge, surface characteristics and ambient humidity. Resuspended nanomaterials are generally found in the form of agglomerates.

4.2 Hazards

Hazardousness is a property specific to a substance that stems from its toxicity or its inflammability. With respect to toxicity, the hazard lies in a substance’s potential or capacity for causing harmful health effects. Hazard must not be confused with risk (Chapter 6), which is the probability that harmful effects will occur under given circumstances. It is thus important to understand that the risk to human health posed by a nanomaterial depends on the probability of exposure and the concentration and duration of exposure on the one hand, and, on the other hand, on the fact that these materials, once inside the body, demonstrate specific behavior associated with their nanostructure [22]. In terms of prevention, this means that even if a nanomaterial is toxic, the risk of developing an occupational disease is minimal if worker exposure is reduced to a minimum.

4.2.1 Health hazards

The development of nanomaterials is very recent. To our knowledge, there is not a single publication that demonstrates toxic effects developed in humans following exposure to nanomaterials. Figure 2 shows different factors that could contribute to the development of health effects as a result of exposure to nanomaterials.

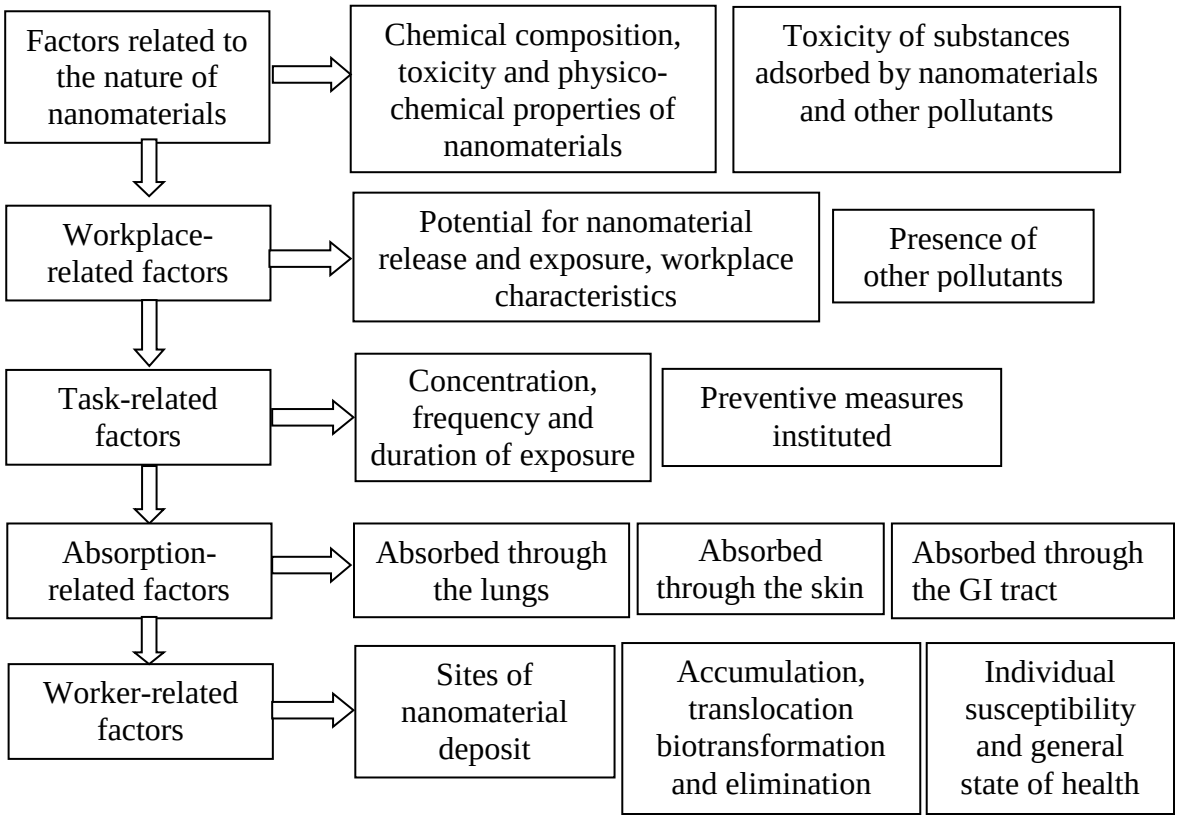


Figure 2: Factors contributing to possible impact of nanomaterials on worker health

4.2.1.1 Factors related to the nature of nanomaterials

A specific nanomaterial may be hazardous because of its nature and its particular characteristics—its toxicity, flammability, explosibility or catalytic reactivity, for example. However, only toxicity is addressed in this guide.

Many studies [23-33] and literature reviews [11, 14, 16, 22, 34-48] address the toxicity of different nanomaterials: SWCNTs, MWCNTs, metals, metal oxides, fullerenes, quantum dots, etc. Some are animal studies, others investigate effects on different types of cells, but most examine acute effects and extrapolation of the results to humans is generally difficult. In addition, the information available for specific nanomaterials, if any, is generally fragmentary, only a fraction of what is required to come to any definitive conclusions about the nanomaterials' toxicity or safety. However, though our knowledge is still fragmentary, more severe effects have

been noted with certain nanomaterials than with products of similar chemical composition but larger size. This is true for different metals and metal oxides as well as products that exist only in nanometric dimensions, such as carbon nanotubes, fullerenes and quantum dots. Among the effects noted in rats with a number of nanomaterials are inflammation, oxidative stress, fibrosis and the formation of granulomas and lung tumours.

Results to date clearly show that nanomaterials are often more toxic and, on a mass-for-mass basis, have greater inflammation potential than micrometric products of the same chemical composition.

Toxicity has been reported with certain metals and metal oxides, including oxidative stress, increase in reactive oxygen species, oxidative DNA damage, lipid peroxidation, production of nitric oxide, reduced cell growth and micronuclei formation (an indication of genotoxicity). Increased expression of genes related to inflammation, lipid peroxidation, cell permeability alteration, apoptosis induction, cell viability decline and cell death were noted as well.

The results of experimental animal studies clearly demonstrate that certain nanomaterials, including CNTs, can have serious cardiac and lung effects (inflammation, fibrosis and granulomas). Other organs may also be affected (reproductive system, kidneys, skin, cellular systems, etc.) Thus a fraction of CNTs deposited in the lungs transit through the pleura and lead to mesothelioma [26, 29, 31, 36, 38, 40, 48]. In a recent study, NIOSH systematically reviewed 54 laboratory animal studies of lung exposure to CNTs and CNFs [48]. More than half of these studies report inflammation, granulomas and pulmonary fibrosis as a result of inhalation but not cancer. Moreover, the effects developed rapidly, within weeks of exposure, and proved persistent. Also, compared to other fibrogenic materials (silica, ultrafine carbon black and asbestos, for example), CNTs proved to be of similar or greater potency [48]. Some cell studies showed CNTs or CNFs to have genotoxic or carcinogenic effects. Intraperitoneal injection of MWCNT resulted in malignant mesothelioma when the MWCNT injected was longer than 5 µm. Pulmonary exposure to CNTs also produced systemic responses, including an increase in inflammatory mediators, oxidative stress in aortic tissue and increased plaque formation in an atherosclerotic mouse model. Pulmonary exposure to MWCNT also depresses the ability of coronary arterioles to respond to dilators [48]. The results of studies to date lead to the conclusion that, as a precautionary default, all biopersistent CNTs or CNT aggregates of pathogenic fibre dimensions should be considered as presenting a potential fibrogenic and mesothelioma hazard [34].

Though results to date are preliminary, there is already sufficient information to conclude that nanomaterials must be handled with care and that occupational exposure must be reduced to a minimum, as a number of toxic effects have been documented, and these vary widely from one product to the next.

The translocation capability of nanomaterials, that is, their ability to penetrate protective membranes, allows a fraction of absorbed nanomaterials to reach distant sites in the lungs and to interact with cells, nucleic acids, proteins and other organs in the body. Animal studies have demonstrated significant accumulations of nanomaterials in the lungs, brain, liver, spleen and

bones [11, 16, 38]. As yet we have only a partial understanding of the factors essential for prediction of health risks. Some factors have a direct impact on bioavailability and biopersistence, and hence on a nanomaterial's potential for accumulation in the body and on its biological activity.

Thus the toxicity of a nanomaterial is specific to that material and can vary, even for the same product, depending on synthesis method, age, functional groups and critical surface coverage likely to affect, among other things, the nanomaterial's hydrophilic/hydrophobic properties. The presence of other pollutants—products of nanomaterial synthesis (metals used to produce CNTs, for example, that can themselves be toxic) or absorbed substances (toxic components of diesel engine emissions, for example, in a work environment where there is simultaneous exposure to nanomaterials and diesel emissions)—can also contribute to the health risks.

A number of factors seem to play a role in nanomaterial toxicity: chemical composition, particle-size distribution, number of particles, particle size and morphology (physical shape and porosity), degree of aggregation and agglomeration, surface properties (specific surface area, load, reactivity, surface chemistry and surface defects), solubility and crystal shape.

4.2.1.2 Workplace-related factors

Workplace-related and task-related factors are not hazards but they do affect nanomaterial exposure potential. They are included here because they play a major role in the possible health impacts of occupational exposure to nanomaterials.

The nature of the process in which nanomaterials are used or produced has a major impact on potential air emissions of nanomaterials and hence occupational exposure. Liquid-phase and closed-system operations, for example, limit possible exposure, whereas handling of powders in open or unsealed spaces promotes suspension of nanomaterials and their dispersal throughout the workplace. Airborne nanomaterials can aggregate or agglomerate with one another or other pollutants present, and their diffusion depends, in part, on the characteristics of the workplace: area, volume, ventilation, crowding, etc. Some liquid-phase operations (use of a spray gun or strong agitation) can also result in aerosolization of nanomaterials.

In industry as well as in research, nanomaterials can come in the form of powders, gels or pellets, in suspension or in solution. When work methods or processes are inadequate, the risk of occupational exposure and absorption through the lungs, skin or GI tract can be substantial.

4.2.1.3 Task-related factors

Depending on the tasks to be performed, the preventive measures introduced and the work methods used, the worker may be exposed to very different concentrations of nanomaterials. It matters, for example, whether the worker is in a control room at a distance from the process or if

The effectiveness of the measures introduced to control exposure (see Chapter 8) has a major impact on possible occupational exposure when carrying out a specific task.

he or she must open a reactor to perform maintenance. Not only the airborne concentrations of nanomaterials, but also the frequency and duration of exposure to them must be considered, and these are directly related to the tasks performed, the time required to carry them out, the nanomaterial contamination level, the collective and personal protective equipment and the work methods used.

4.2.1.4 Absorption-related factors

The respiratory tract is generally the primary route of entry of nanomaterials into the body. Once inhaled, nanomaterials, agglomerated or not, are either deposited in different parts of the respiratory tract or exhaled and returned to the air.

A key feature of nanomaterials is their pattern of deposition within the respiratory tract (Figure 3). Deposit site, it appears, is very much dependent on particle size

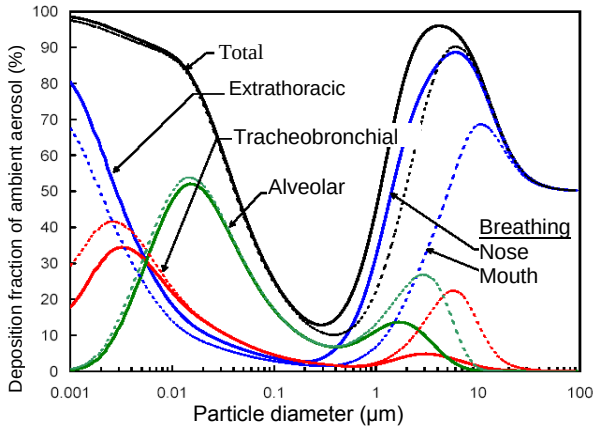


Figure 3: Model of inhaled particle deposition in airways [49]

Whereas nanomaterials of one or several nanometres are intercepted mainly by the nose, mouth and larynx, nanomaterials more than 7 nm in diameter are deposited mainly in the alveoli. In fact, more than 50% of inhaled nanomaterials measuring 15-20 nm are deposited in the pulmonary alveoli. The model for spherical particles is based on parameters of a health reference population with a work load consisting of work in a sitting position for one-third of the work shift and light work during the other two-thirds of the shift [49].

Percutaneous absorption can be a major exposure route for workers handling nanomaterials prepared and used in colloidal form. Results suggest that the smaller the size of certain non-agglomerated nanomaterials, the greater their skin penetration potential [50-54]. The surface properties of nanomaterials (their lipid solubility, for example), perspiration, local lesions, repeated flexions and pressure exerted by handling tools are some of the factors that promote nanomaterial penetration of the skin. With some nanomaterials that are poorly absorbed by the skin, an allergic reaction and/or contact dermatitis may be observed.

In most workplaces, the potential for absorption through the lungs is much greater than the potential for absorption through the skin or the GI tract.

Good personal hygiene practices in the workplace can have a major impact on minimizing ingestion of nanomaterials. However, nanomaterials can nonetheless be found in the GI tract, swallowed after transport by the mucociliary escalator from where they were deposited in the respiratory system. In fact, certain nanomaterials are now used as additives in the food industry, in medications and in associated products to enhance absorption. A certain quantity of nanomaterials widely used in industrial, agricultural or other products is found in the

environment. Nanomaterials can thus eventually enter the food chain. To date, few studies have been conducted to find out if the eyes or ears can be routes of nanomaterial penetration [55, 56].

4.2.1.5 Worker-related factors

The theoretical airway deposition pattern shown in Figure 3 does not necessarily apply to all cases. A number of factors can affect the structure and functioning of the respiratory tract, such as work load, sex, age, smoking and respiratory disease, and this in turn affects lung deposition as well as particle clearance. The particle deposition fraction is higher during exercise [57, 58] and in people with asthma or chronic obstructive pulmonary disease [59, 60].

Given their very small size and their tendency to bind with proteins, many nanomaterials can, once absorbed into the body, overcome the body's protective barriers and circulate as solid particles. This is called translocation. Thus insoluble nanomaterials are found in the bloodstream, having passed through the body's respiratory, cutaneous or gastrointestinal barriers, and they migrate to the different organs of the body, including the brain [11, 16, 38, 40, 61]. Moreover, some nanomaterials demonstrate a propensity to cross cell barriers, enter cells and interact with subcellular structures, inducing oxidative stress, the main mechanism of action of nanomaterials. In a healthy worker, only a very small percentage of nanomaterials are able to overcome natural defense mechanism. In a worker with lung disease, translocation can be much more substantial.

Accumulation of insoluble or poorly soluble nanomaterials, particularly in the lungs, can promote development of occupational disease over the medium or long term.

Though general trends are emerging suggesting a variety of toxic effects, it is clear that toxicity is product-specific. Given the resulting uncertainty, and the virtual impossibility of obtaining all the information necessary for adequate assessment of a product's toxicity, a precautionary approach based on strict preventive measures to achieve minimum exposure remains the best method of protecting workers and preventing the development of occupational disease.

4.2.2 Safety hazards

4.2.2.1 Explosion and fire

It is well known that a cloud of combustible or readily oxidizable dust formed from pyrophoric materials, certain carbon compounds, organic substances that react to air or certain hydrolysable or oxidizable metals can constitute an explosive atmosphere. Aluminium, magnesium and lithium are a few examples of substances that can be very explosive. Generally, explosion violence and severity as well ignitability tends to increase as particle size decreases [62], whereas minimal explosive concentration varies little as particle size decreases [63, 64]. Thus, it is well known that normally the finer the dust the faster the rate of pressure rise and the lower the ignition energy, provided particle size diameter exceeds 1 μm [1, 16, 65-72].

However, given the often unique physicochemical properties of nm-particles, these trends cannot be extrapolated with any certainty to nanomaterials. Though there is relatively little data on fire and explosion risks specific to nanomaterials, some interesting findings have emerged from the few studies conducted [68-72]. For the same material, ***explosion probability is much higher*** when the powder is composed of nm-particles than of particles of larger size. This stems from two characteristics of nanomaterials: ignition energy as well as ignition temperature is much lower. On the other hand, ***explosion severity is not necessarily greater,*** due to the strong interactions between nanomaterials and their natural tendency to agglomerate. Nanomaterials do not disperse easily, and when dispersion is incomplete, coagulation rate is very high, such that effective particle size is much greater than the particles' primary nanometre size.

The risk of explosion can be greater with combustible airborne nanomaterials than with their larger counterparts as nanomaterials require much less ignition energy, have a lower ignition temperature and burn much more quickly.

A number of conditions must be met simultaneously for an explosion to occur. All of the following must be present: a sufficient quantity of combustible particles at an explosible concentration; a sufficient concentration of fuel (oxygen); and an ignition source with enough energy to cause the particles to explode. Figure 4 shows the main factors likely to promote an explosion or a fire.

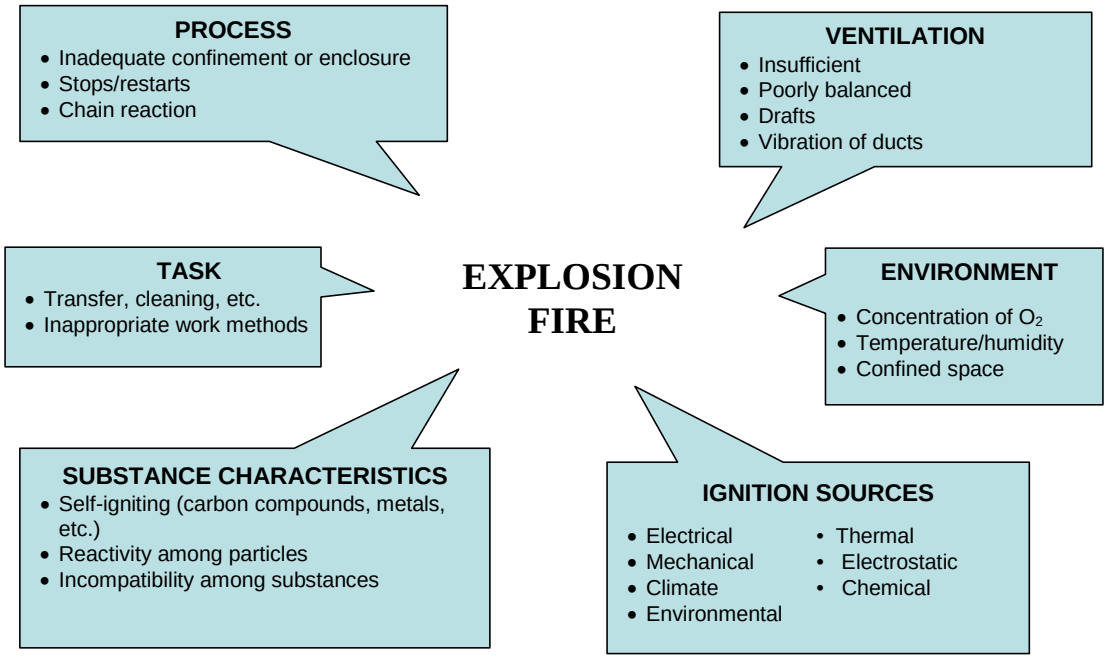


Figure 4: Main factors contributing to the likelihood of explosion or fire [12]

4.2.2.2 Particle release and suspension

A number of factors promote suspension of nanomaterials and create conditions that could lead to their ignition and explosion if in a confined space or a closed room: type of process, equipment leaks, deficient ventilation, inappropriate maintenance and dust accumulation, transfer of nanomaterials, inadequate handling, transport or storage methods, etc. Closed systems that produce, transfer or store these particles must be equipped with safety devices that meet the standards of the National Fire Protection Association, (NFPA), as stipulated in the Regulation respecting occupational health and safety [73].

Unless adequate preventive measures are taken, the risk of explosion can be high when mixing or transferring nanomaterials, when cleaning up accidental spills, when nanomaterials accumulate in ventilation ducts, etc.

4.2.2.3 Storage

Given the reactivity of certain particles, care must be taken to ensure the integrity of containers holding reactive nanomaterials so as to prevent leakage and site contamination. Depending on the storage conditions, two substances could come in contact in case of leaks from containers that have been poorly maintained or are not leak-proof. To minimize this risk, incompatible substances should never be stored near one another.

To prevent oxidation and hence explosion of certain metal dusts, suitable protective measures must be taken with respect to nanomaterials stored in sealed containers.

4.2.2.4 Catalytic reactions

Nanomaterials and porous materials of nanometric dimensions have been used for decades as catalysts to increase reaction speeds or lower the temperature at which certain chemical reactions will take place. In fact, given their reactivity, certain nanomaterials can initiate an unanticipated catalytic reaction, increasing the risk of explosion or fire.

4.2.3 Environmental hazards

Engineered nanomaterials from a variety of sources are liable to be returned to the environment, with possible impacts that are still poorly understood. Life cycle assessments of particular nanomaterials make it possible to predict all possible sources of environmental contamination [74-76], but this is not discussed here as it is well beyond the scope of this guide.

To protect human populations, flora and fauna, air, water and soil, all effluents and all industrial and laboratory waste must be incinerated or treated before release to the environment.

5. EXPOSURE CHARACTERIZATION

In the workplace, exposure to nanomaterials is mainly through inhalation, but cutaneous exposure may constitute a significant part of overall exposure under certain circumstances. Workers are liable to be exposed to nanomaterials in a variety of situations:

- Production of solid nanomaterials in open or poorly sealed enclosures
- Collection, transfer, weighing, sampling, handling or processing of nanometric powders
- Loading or emptying a reactor
- Packaging, storing or transport
- Transfer, resuspension, vigorous mixing or drying of a liquid suspension
- Use of nanomaterials and their incorporation in organic or mineral matrices; aerosol application
- Mechanical work on products containing nanomaterials: polishing, cutting, milling or sanding
- Cleaning of equipment, work areas and ventilation systems
- Repair and maintenance of equipment: dismantling a reactor, changing a filter (hood, ventilation system, vacuum cleaner)
- Leaks, accidental spills, equipment malfunction
- Waste management (collection, transport or storage)

A variety of factors affect the degree of occupational exposure, including the nature of the nanomaterial (powder, gel, liquid suspension or pellets), extent of agglomeration, quantities handled, methods of use or manufacture, frequency of exposure and preventive measures taken.

Though there is still no international consensus on the best approach for characterizing nanomaterial exposure, recent publications demonstrate some convergence on strategies used [3, 11, 16, 48, 77-92]. In fact, there are many reasons why preventionists want to characterize possible occupational exposure to nanomaterials [12, 16]:

- Identification of main emission sources to establish or improve emission control strategies
- Assessment of the efficacy of control measures
- Assessment of dustiness in situations that could mean a risk of accident
- Assessment of personal exposure for correlation of exposure and health effects
- Assessment of personal exposure to check compliance with standards, recommended maximum levels or specific thresholds for implementation of control measures

As demonstrated in Section 4.2.1 on health hazards, weight and chemical composition alone are not enough to characterize nanomaterial exposure. The specific surface area, number, size, shape, agglomeration or aggregation status, crystal structure, surface properties, solubility and various other parameters of the particles must also be taken into consideration. In addition, deposition in the lungs varies tremendously depending on the size of the nanomaterial or its aggregates and agglomerates. The assessment strategies as well as the sampling and analysis techniques selected must thus be appropriate for the specific goals of the characterization and allow for correlation of nanomaterial exposure and toxicity. However, given the many parameters that must be measured, there is no one instrument that can generate a specific analysis of all relevant characteristics of exposure to engineered nanomaterials.

It is important to measure as many parameters as possible, including aerosol mass per particle-size fraction, in order to have maximum information for complete characterization of the work environment.

Ideally, occupational exposure to nanomaterials would be measured in the breathing zone and include determination of parameters associated with inhalation health risks.

As there is currently no one instrument or method that can adequately characterize nanomaterials in the breathing zone, the best strategy is to use a variety of instruments so that as many parameters as possible can be characterized.

Despite the challenges of assessing nanomaterials in the workplace, a traditional occupational hygiene approach offers a structured method—from risk forecasting through to risk management. Chapter 4 looked at the toxic and physical (fire and explosion) hazards of many nanomaterials. Exposure assessment is then required to gather the information needed for risk assessment. Once the risks have been identified, the level of exposure control can be determined and suitable preventive measures introduced. The next step is thus to develop a strategy for assessing nanomaterial exposure or dustiness that is tailored to the particular situation [3, 11, 16, 48, 77-92] (Figure 5).

The optimal exposure assessment strategy is determined after rigorously documenting the situation to be assessed (Figure 5) with the goal of determining the maximum number of representative parameters.

Ultrafine particles of nanometric size are already present in all workplaces and they interfere with nanometric measurements. These particles come from contaminated outdoor air (dust, fumes, pollen, etc.), workplace operations that generate them (diesel engine emissions, welding fumes, etc.), resuspension of ultrafine particles and nanomaterials that have settled in the workplace as a result of movements of workers or equipment or drafts. This background concentration, variable from one workplace to the next as well as from one day to the next in any given workplace, must be taken into account when characterizing air contamination by nanomaterials and interpreting results.

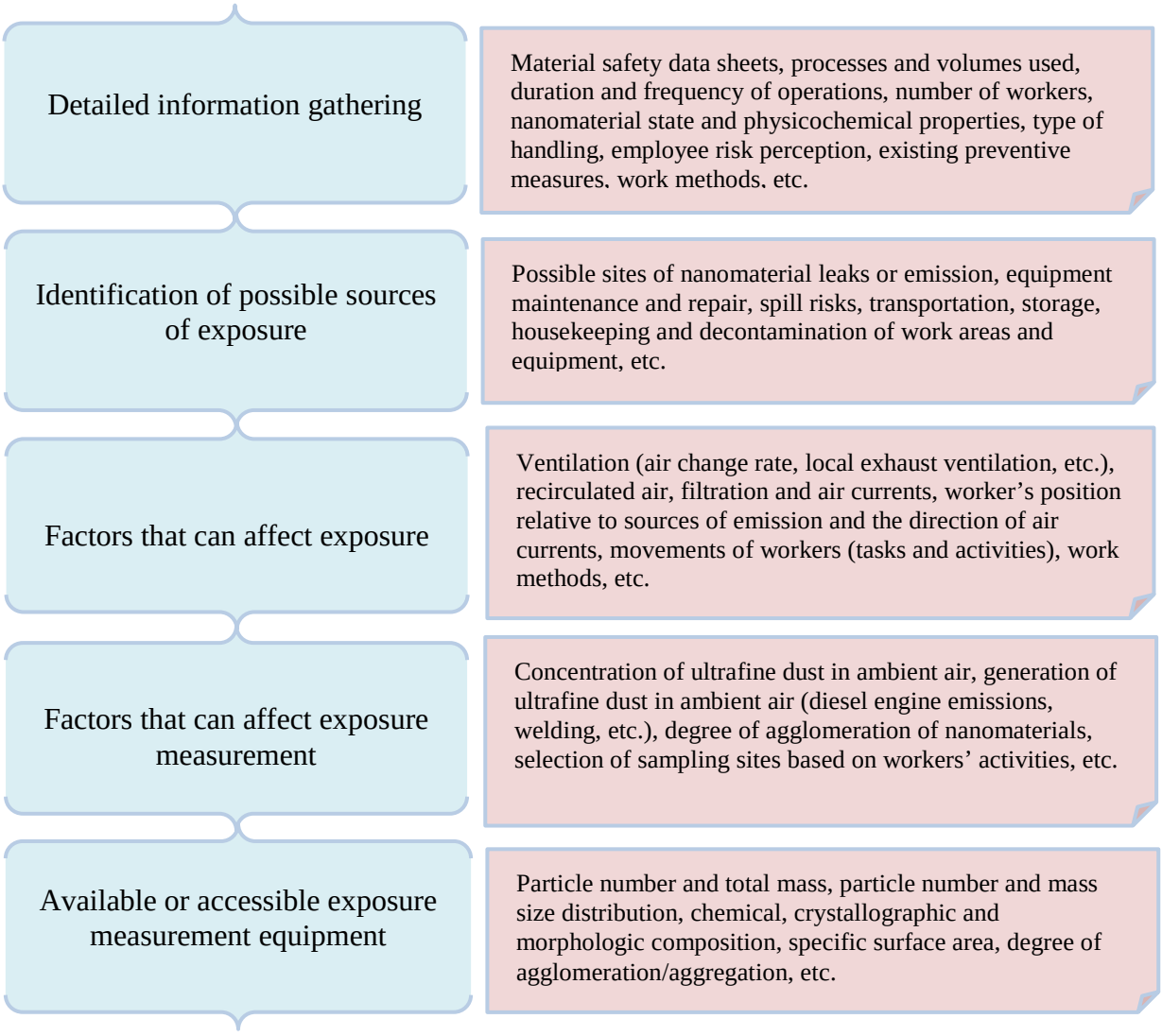


Figure 5: Documenting the workplace [12]

There are many situations which can lead to occupational exposure to nanomaterials. Here are some examples directly related to production: fugitive emissions from a reactor, weighing, transferring and pouring operations, loading or emptying reactors or hoppers, powder processing, suspension or incorporation in matrices, sampling for quality control, mixing, packaging and storage operations, and dismantling, maintenance or cleaning of equipment or work areas. In addition, the collection, processing, storage and transport of waste (from production, maintenance or housekeeping operations) or contaminated individual protective equipment can also lead to exposure of workers when waste that contains nanomaterials must be managed, as can the dispersal of intermediates (solids or liquids) or ready-to-use products containing nanomaterials (vaporization, pouring) and the machining of nanocomposites (grinding, sawing or cutting of finished products), which may [93] or may not [94] release free nanomaterials. The collection of detailed information also requires checking the quality of the available data (Figure 5). For example, do the material safety data sheets [95-98] take risks specific to nanometric size into account? The physicochemical properties should document chemical composition in particular, as well as any alteration (anti-agglomeration coating) or chemical

functionalization, the proportion of nanomaterials in the product, the risk of ignition, explosion or catalytic reaction, and the product's solubility, powderiness, particle-size distribution, morphology (spherical particle, fibre, etc.), agglomeration/aggregation state and crystallinity as recommended in the International Organization for Standardization (ISO) standard [99] on preparing nanomaterial safety data sheets.

Once the specific conditions of the workplace have been thoroughly documented, the sampling strategy is developed by answering the following questions [16, 100]:

- What are the sampling objectives?
  - Search for sources of fugitive emissions (often of very short duration)
  - Exposure exploration
  - Characterization of breathing-zone and cutaneous exposure, or tracking of the contaminant cloud in the workplace
  - Verification of effectiveness of preventive measures
  - Risk assessment
  - Development of a job-exposure matrix for future epidemiological research
  - Compliance with a standard or benchmark
- What substances must be measured?
- At which workstations? When and for how long?
- How many samples are to be collected or measurements taken per workstation and per worker?
- What sampling methods are to be used?
  - Exactly which parameters are to be measured? What are the background concentrations?

An additional question arises for those in the OHS prevention network and researchers wanting to perform workplace assessments:

- Are multiple visits to the workplace possible?
  - If so, preliminary sampling is performed with a small number of portable instruments (condensation nuclei counters, optical particle counters and sample collector for electron microscopy) while information is gathered to document the workplace and the working conditions. This will confirm the presence of nanomaterials, identify sources of their air emission and help in planning the sampling strategy. An in-depth investigation of the workplace using a variety of instruments can be performed on one or more subsequent visits, for full nanomaterial characterization depending on objectives. Variants of this strategy are used or recommended by standardization authorities including the Organisation for Economic Co-operation and Development (OECD) and experts in different countries.
  - If access is restricted, sampling using all instruments available may be the best option. This is much more time-consuming, the targeting may not be ideal, and optimal use may not be made of the available resources, but it may be the only option in certain situations.

Many instruments on the market today can directly determine or estimate in real time a number of key parameters for nanomaterial characterization (Table 4). Samples can also be collected for

subsequent laboratory analysis to determine morphology (electron microscopy), elemental chemical composition (scanning electron microscopy, carbon-specific analysis, metal determination by ICP-MS), degree of agglomeration/aggregation, nanomaterial fraction of the samples and crystal structure. ***Careful documentation of the performance and limits of the instruments, especially their sensitivity and specificity and the particle-size distribution range to which they respond, is crucial*** [101-105]. It has recently been demonstrated that direct-reading instruments are of limited use in assessing and quantifying personal exposure but are very helpful in identifying emission sources, evaluating control measures and mapping the workplace [82].

Table 4: Devices used to characterize nanomaterials

Parameter measured	Device	Remarks
Mass (direct measurement)	Cascade impactor (Berner cascade impactor, MOUDI or nano-MOUDI)	Samples particles <100 nm for gravimetric analysis in individual assessments
	TEOM (tapered element oscillating microbalance)	Sensitive real-time measurement of nanoaerosol mass concentration
	Filters	With appropriate preselectors as needed, samples nanomaterials for mass determination or subsequent laboratory analysis
Mass (estimate)	ELPI (electrical low pressure impactor)	Real-time size-selective detection of active-surface area concentration, giving aerosol particle-size distribution. Data may be interpreted in terms of mass concentration if particle charge and density are known or can be assumed. Samples at each stage can then be analyzed in the laboratory. Lower limit: 7 nm
	SMPS/FMPS/EEPS (scanning mobility particle sizer spectrometer/fast mobility particle sizer spectrometer/engine exhaust particle sizer spectrometer)	Electric mobility classification for real-time size-selective detection of number concentrations, giving aerosol particle-size distribution. Mass concentration can be determined if particle shape and density are known or can be estimated
	MOUDI/nanoMOUDI (micro-orifice or nano-micro-orifice uniform-deposit impactor)	Determines aerodynamic diameter by cascade impaction
Number of particles (direct measurement)	CNC (condensation nuclei counter)	Real-time number concentration measurements within particle-diameter detection limits. Without a particle-size selector, this instrument is not specific for nanoscale materials. The P-Trak offers preselection and its particle size detection range is 1,000 to 20 nm. Lower detection limit of the TSI 3007 is 10 nm
	OPC (optical particle counter)	Real-time particle number concentration measurements (particles 300 to 10,000 nm in diameter). Though OPCs do not count individual nanoparticles, they are nonetheless excellent for determining number concentrations of nanomaterial agglomerates and measuring background concentrations

Parameter measured	Device	Remarks
	SMPS/FMPS/EEPS (scanning mobility particle sizer spectrometer/fast mobility particle sizer spectrometer/engine exhaust particle sizer spectrometer)	Real-time detection based on electrical mobility diameter (size-related) and number concentration
	Electron microscopy	Offline analysis providing information on shape, particle-size distribution and number concentration of aerosol particles
Particle number per calculation (estimate)	ELPI and MOUDI/nanoMOUDI (electrical low pressure impactor and micro-orifice or nano-micro-orifice uniform-deposit impactor)	Real-time size-selective detection, giving aerosol size distribution. Data may be interpreted in terms of particle number if the particle charge and density are known or considered. Size-selected samples can then be analyzed in the laboratory.
Specific surface area (direct measurement)	Diffusion charger	Real-time measurement of aerosol active surface area with commercially available instruments giving readouts for particles < 100 nm. Nanoscale-specific if used with an appropriate pre-separator. TSI's AeroTrak 9000 is an example of an instrument that gives real-time measurements of surface area concentrations
	ELPI and MOUDI/nanoMOUDI (electrical low pressure impactor and micro-orifice or nano-micro-orifice uniform-deposit impactor)	Real-time size-selective detection of aerodynamic diameter and active surface concentration. Samples from each stage can then be analyzed in the laboratory
	Electron microscopy	Offline analysis providing information about particle surface area relative to size. Transmission electron microscopy provides information about the projected surface area of the particles analyzed, which can be linked to the geometric surface for certain forms of particles
Specific surface area per calculation (estimate)	SMPS/FMPS/EEPS (scanning mobility particle sizer spectrometer/fast mobility particle sizer spectrometer/engine exhaust particle sizer spectrometer)	Real-time detection of number concentration based on electrical mobility diameter. Data may be interpreted in terms of specific surface area under certain conditions
	Parallel use of SMPS and ELPI (scanning mobility particle sizer spectrometer and surface electrical low pressure impactor)	Differences in aerodynamic diameter and mobility measurements are used to infer particle fractal dimension, which can be further used to estimate particle surface area

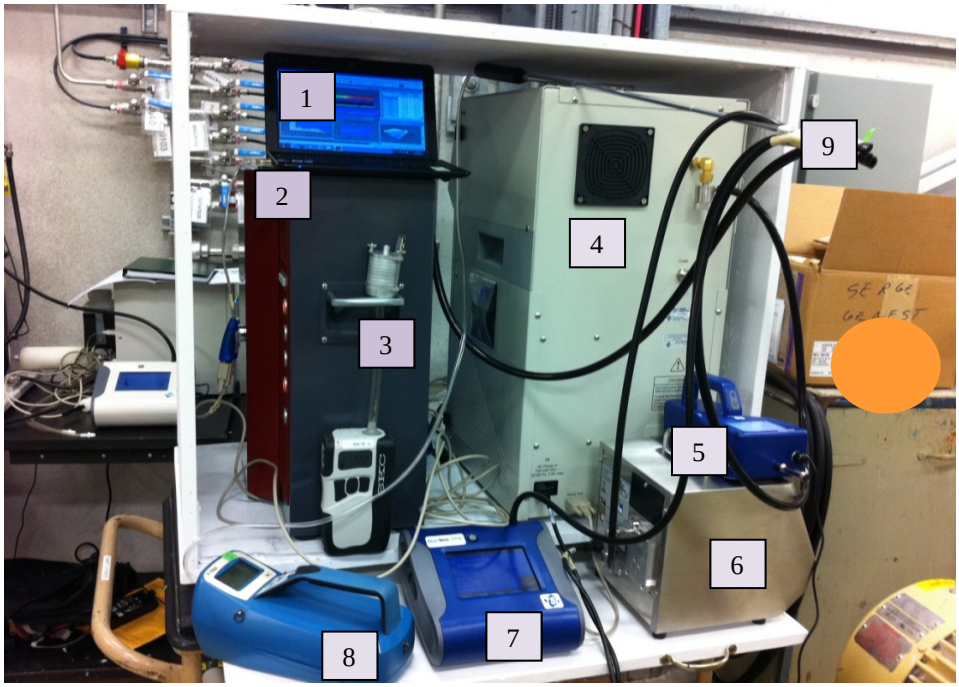
New sampling instruments have been designed [106, 107] and new strategies developed to analyze representative workplace samples [108, 109]. However, given the many parameters that must be measured, no one instrument can, at present, generate data on all relevant parameters needed for nanomaterial-specific analysis.

Ideally, all parameters that can contribute to nanomaterial toxicity should be measured. In practice, however, this is generally difficult if not impossible.

We must not forget that the first step in nanomaterial assessment is to document baseline airborne pollutants already present in the workplace (interference) or generated by other activities, processes or workers before beginning the operations specifically involving nanomaterials, to be able to compare results to this background.

Airborne nanomaterial emissions are often fugitive and unstable, and there is still no consensus within the scientific community on a strategy for assessing occupational exposure in the breathing zone or on the surface of the skin.

Figure 6 shows equipment used by our team to measure nanomaterials in the workplace. A system of sensor rods samples the air as close to the worker's breathing zone as possible ("quasi-personal" sampling). Measurements are taken right before the operations involving nanomaterials, to determine background concentration, and then during the operation, to evaluate any changes associated with the use of nanomaterials.



1. Data acquisition system
2. Electrical low pressure impactor (ELPI)
3. Sioutas cascade impactor
4. Exhaust emission particle sizer (EEPS)
5. Ultrafine particle counter (AeroTrak 9306, TSI))
6. Surface analyzer (AeroTrak 9000, TSI)
7. Optical particle counter (DustTrak DRX, TSI)
8. Ultrafine particle counter (P-Trak, TSI)
9. Sensor rods

Figure 6: Principal equipment used by our team for workplace assessments [79, 110].

Laboratory procedures such as electron microscopy, inductively coupled plasma-mass spectrometry (ICP-MS) and inorganic carbon analysis, are used to complete the characterization of the workplace samples.

In recent years, a growing number of publications have reported measurement data on nanomaterial concentrations in different workplaces. Several summaries of the data available in the scientific literature have also been published recently [111-113].

Current studies demonstrate pulmonary exposure in research laboratories, pilot plants and production plants under different circumstances, including handling of nanomaterials, equipment maintenance, housekeeping, storage, transport, accidental spills, recycling and waste disposal. Skin contact was also suspected in some cases, but there is almost no numerical data for lack of a specific assessment methodology.

6. RISK ASSESSMENT

Workstation risk assessment provides essential information for selecting the control level and the measures needed to reduce the risks to an acceptable level [1, 3, 11, 12, 16, 114-117]. The level of risk indicated by the risk assessment determines the control measures that must be included in a prevention program for each workstation.

Many people can contribute to the risk assessment, especially those involved in developing and implementing processes as well as supervisors, managers and occupational hygienists. Nonetheless, the limited knowledge we now have about nanomaterials suggests that it can be difficult for anyone without expertise specific to nanomaterials to assess the risks of a particular workstation [115]. Thorough documenting of all aspects of the workplace that relate to nanomaterials is thus suggested before undertaking a risk assessment (see Figure 5, Chapter 5).

The toxic risk to which a worker handling nanomaterials is exposed can be expressed as follows:

$$Risk_t = f\{toxicity \times exposure\}$$

Toxic risk assessment can then be considered as an estimate of the probability that harmful health effects will result from exposure to certain toxic chemicals.

For there to be a risk, the nanomaterial has to be toxic AND the worker must be exposed to it. Since toxicity is often unknown or poorly documented, exposure control remains the best option for minimizing risk.

Identification of hazards is crucial for quantitative assessment of nanomaterial-related risks, as is a thorough understanding of product toxicity (dose-response relationship) and of exposure levels at each workstation [1, 3, 11, 12, 16, 114-117]. However, as the preceding chapters of this guide show, our toxicological knowledge of nanomaterials is still largely incomplete, though developing rapidly, and risk assessments must to be carried out on a case-by-case basis [114-116]. Some researchers nonetheless suggest reference values (Table 5) for different nanomaterials based on their own risk assessment models and taking into account published data and their research findings.

To our knowledge, however, there are as yet no regulations with respect to any of these values. Note that these values are derived from studies of particular nanomaterials, and some of the properties of these nanomaterials that affect their toxicity may have differed from one study to the next depending on how they were prepared, their size and surface characteristics, other pollutants present, the degree of agglomeration, etc. Taking these limitations into account, the researchers determined no observed adverse effect concentrations (NOAEC), lowest observable adverse effect concentrations (LOAEC) and indicative no-effect levels in human beings (INEL), and some suggest reference values (Table 5). As we will see later (Table 7, Chapter 7), some non-regulatory bodies have already suggested reference values or standards for some insoluble nanomaterials. For some substances, however, including nanoclay and nanocellulose, it was not possible to make any recommendations.

Table 5: Reference values suggested by different stakeholders

NM[1]	NOAEC[2] (µg/m^3)	LOAEC[3] (µg/m^3)	INEL[4] (µg/m^3)	Suggested reference value (µg/m^3)	Remarks	Reference
Fullerene	2200				3 h/day, 10 days	[118, 119]
	830		7.4		3 h/day, 10 days	[118, 119]
	3100			390	Literature review	[120]
Nano TiO_2	500				90 days + 52 weeks	[119, 121]
	250		17		90 days + 52 weeks	[119, 121]
				610[6]	90 days	[122,123]
MWCNT[5]	100			1-2	90 days + 90 days post-exposure	[119, 124]
		400			90 days + 90 days post-exposure	[124]
		100			90 days	[119, 125]
	370		80	30	Inhalation 90 days	[126]
MWCNT (Baytubes)	50		2	50	90 days + 90 days post-exposure	[119, 124]
MWCNT (Nanocyl)		50	1	2.5	90 days	[119, 125]
CNT	130		30	30		[126]
Nano-Ag		49			90 days, reduced lung function	[119, 127]
		25	0.33		90 days, reduced lung function	[119, 127]
		133			90 days	[119, 127]
		67	0.67		90 days	[119, 128]

1. NM: nanomaterial; 2. NOAEC: no observed adverse effect concentration; 3: LOAEC: lowest observable adverse effect concentration; 4. INEL: human indicative no effect level; 5.MWCNT: multiwalled carbon nanotubes; 6. Expressed as respirable dust

In addition, there are few workplaces where occupational exposure potential is adequately documented. Clearly, then, given the current ***uncertainty stemming from major gaps in our current knowledge,*** quantitative assessment of risks associated with nanomaterials is impossible in most situations found in the workplace because it requires knowledge not only of product toxicity but also of occupational exposure level. An approach for assessing nanomaterial toxicity (Figure 7) based on available toxicological data has been suggested [129].

Given that it is often difficult to suggest reference values or estimate NOAEC or LOAEC, **a precautionary approach is wise, minimizing occupational exposure to avoid overexposure that could lead to the development of occupational disease.**

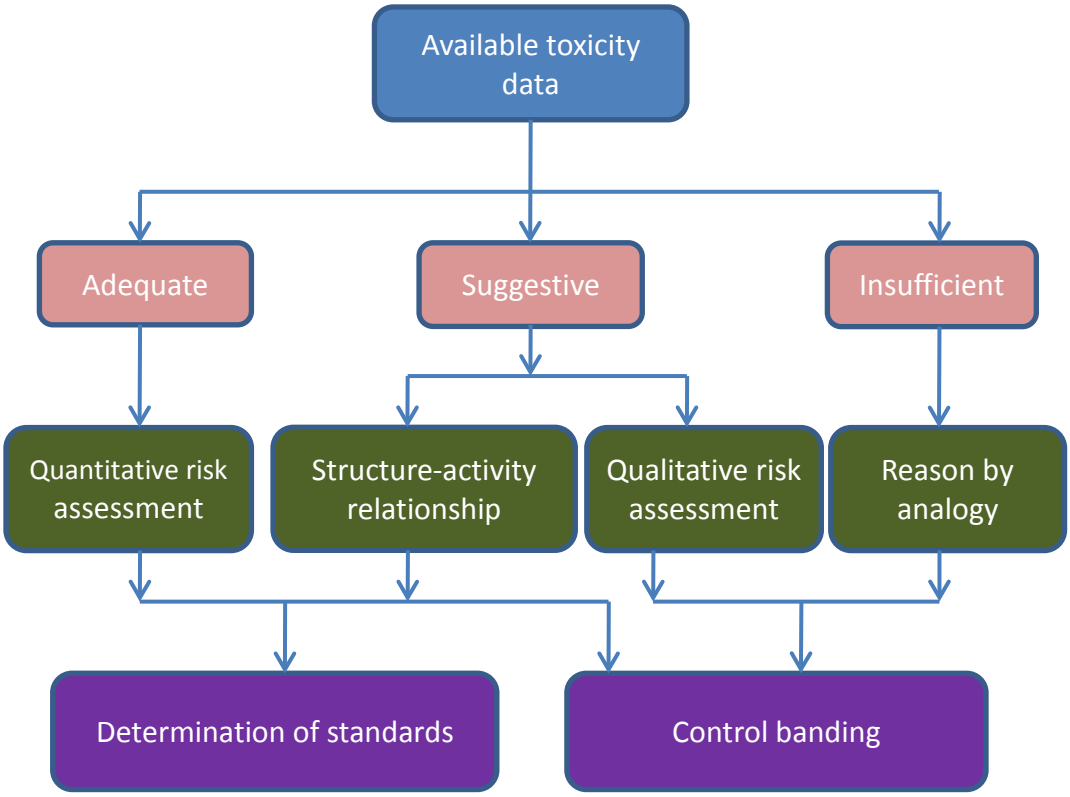


Figure 7: Proposed approach for toxicity assessment (Adapted from Schulte et al. [129])

The precautionary principle is based on two general criteria [130]: appropriate action should be taken in response to limited but plausible and credible evidence of likely and substantial harm; the burden of proof is shifted from demonstrating the presence of risk to demonstrating the absence of risk.

This leads us to introduce control measures to minimize exposure.

6.1 Control Banding

As mentioned above, when there are sufficient data, risks can be quantitatively assessed. When the data are less conclusive or incomplete, a qualitative or semi-quantitative risk assessment is preferable and a preventive (precautionary) approach is recommended. Control banding is the approach most commonly recommended for assessing nanomaterial-related risks [1, 11, 12, 16, 114, 115, 131-145]. A recently published ISO standard [146] should provide an international consensus approach.

It is important to remember that control banding is only one element in any establishment's prevention program.

In control banding, hazards are identified and allocated to bands (hazard bands) based on current knowledge of the nanomaterials involved and conservative assumptions about missing information. These hazard bands are combined with estimations of occupational exposure potential (exposure bands) to infer a risk level. For each risk level, there is a corresponding appropriate minimum control technology. The application of this approach requires expertise in chemical risk assessment and management, but it can be used to rank risks at each workstation and hence to set priorities for implementation of minimum preventive measures [1, 11, 12, 16, 114, 115, 131-146]. Parameters generally considered are size, morphology, chemical composition, solubility, toxicity and quantity of nanomaterials used as well as dustiness or aerosolization potential of powder nanomaterials, number of workers concerned and the duration of the operations. As our knowledge of hazards and exposure levels is constantly evolving, the data used for control banding must be regularly updated, risk levels must be re-evaluated and the prevention program and approach must be continuously improved based on the new data. As the level of uncertainty declines with the acquisition of new information, risk assessment tends to become more and more quantitative (Figure 8).

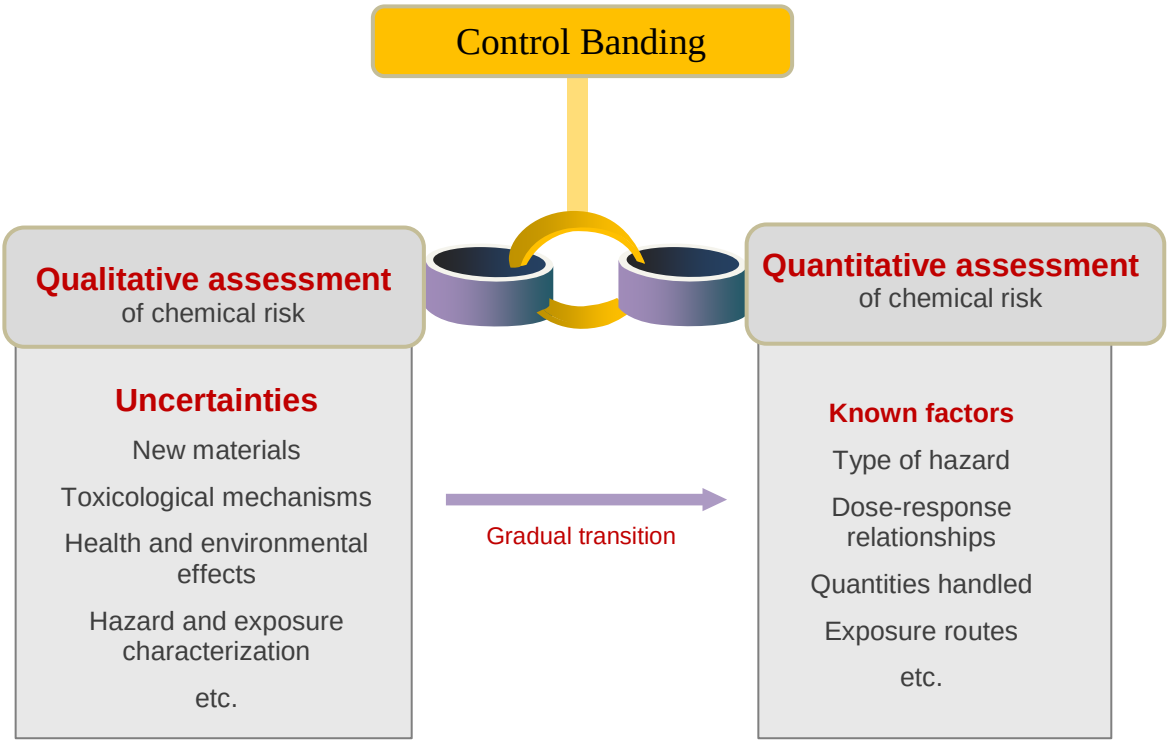


Figure 8: Shift in method of risk assessment as new knowledge is acquired [141]

6.1.1 Hazard identification and characterization

As in any risk assessment, the first step is to gather information that is as detailed and complete as possible on all nanomaterials present at each workstation, on potential sources of emission and on work methods (see first two information groups in Figure 5, Chapter 5). Special attention should be paid to the content of the material safety data sheet, as many do not yet consider particle size-which means the toxicity information is often inadequate [95-98]. This prompted the ISO to develop a standard for preparation of material data safety sheets [99], something Switzerland had already done [147].

Remember that nanometric particles are at least as toxic as and often more dangerous than particles of the same chemical composition but of larger size (Chapter 4).

A review of literature dealing specifically with the toxicity of the nanomaterials concerned (absorption, distribution, metabolism, clearance, acute and chronic toxicity, effect of repeated doses, reproduction, development and genetic toxicity, data on human health effects, etc.) is required and detailed information must be obtained about their physicochemical characteristics (Figure 9). Potential physical hazards (reactivity, inflammability, explosivity) must also be documented.

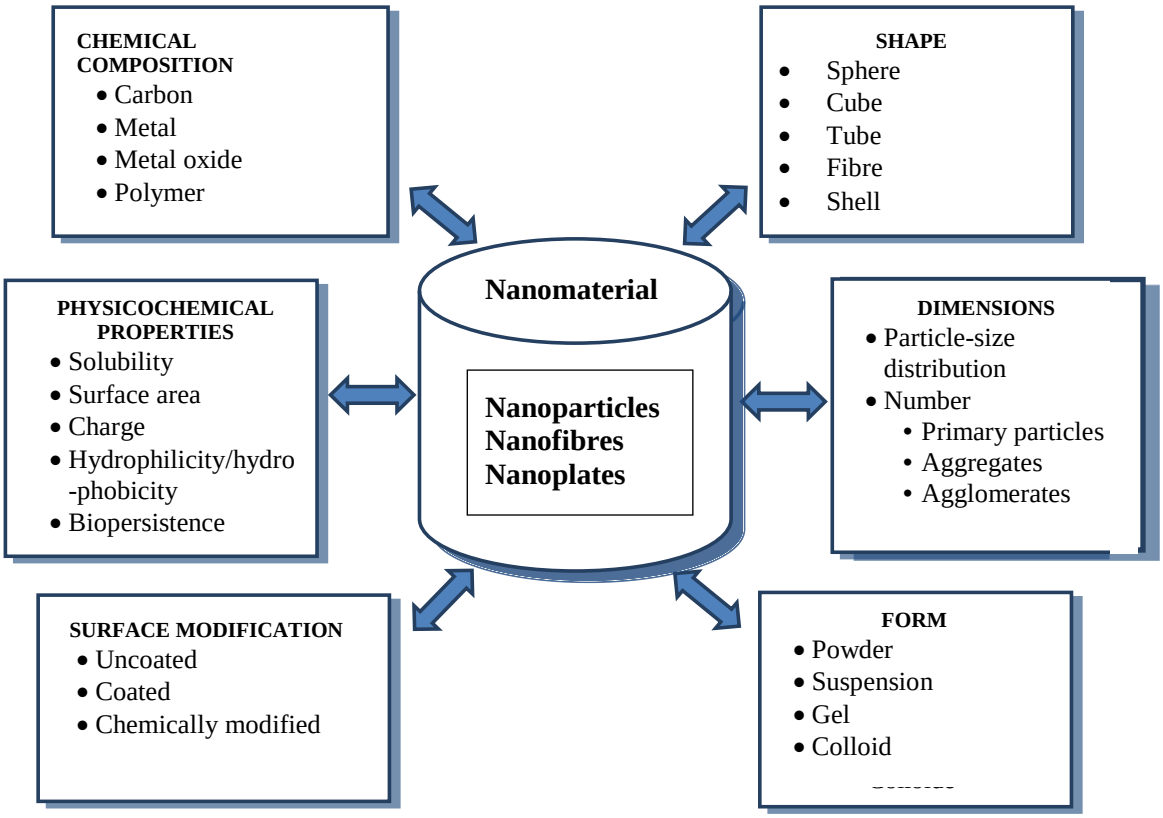


Figure 9: Physicochemical characteristics of nanomaterials [12]

6.1.2 Estimating exposure potential

Each workstation must be rigourously analyzed to identify operations that might expose workers to nanomaterials.

Exposure potential is estimated based on the physicochemical characteristics of the products handled and the operations likely to lead to occupational exposure: processes and procedures used, state of the nanomaterials (solid, gel, liquid suspension, pellets, incorporated in a solid, deposited on the surface of a solid matrix, etc.), the quantities involved, propensity to aerosolize (dustiness) or to settle on work surfaces, number of workers, duration and frequency of operations, possible exposure routes and preventive measures introduced.

There are many situations likely to lead to occupational exposure, in the laboratory as well as in industry. These may be related to ***processes*** (e.g., aerosolization of nanomaterials, polishing, milling, sanding or cutting of nanocomposites), ***equipment used*** (e.g., open or poorly sealed reactor, ineffective fume hood), ***production or research operations*** (e.g., opening of bags and containers, pouring and transferring, weighing, loading or removing nanomaterials from a reactor, processing, packaging and handling powders), ***peripheral operations*** (e.g., sampling, dismantling, cleaning and maintaining equipment, housekeeping, changing filters, maintaining vacuuming and ventilation systems, waste management, and storage and transportation of products and waste containing nanomaterials) or ***exceptional events*** such as a reactor leak, a conduit break or an accidental spill.

Chapter 5 suggests a strategy for assessing nanomaterial exposure based on existing knowledge.

Once each workstation is thoroughly documented, it is best, if possible, to quantify occupational exposure, or at least to determine airborne nanomaterial concentrations at the workstation. In many situations, only a qualitative assessment of potential occupational exposure is possible. Control banding is used for such assessments.

6.1.3 Risk assessment

Control banding makes it possible to rank risks, prioritize preventive actions and establish minimum preventive measures for each workstation.

Once the hazards and the exposure potential are well documented, control banding that takes into account existing information can be used to assess risks by making some conservative assumptions and exercising professional judgment. It then becomes possible to assign a hazard band (toxicity or severity, depending on the model) and an exposure band in the control banding model selected [1, 11, 12, 16, 114, 115, 131-146]. The resulting matrix establishes a risk level with which risk control measures are associated (Table 6).

The ISO standard [146] begins with a summary characterization of the product: Is it really a nanomaterial? Is it soluble in water? Has its toxicity been established? Is there a standard or reference value? Does it fit the fibre paradigm? If the nanomaterial can still not be classified once these questions are answered, the approach is to compensate for the lack of toxicity

information by considering some more easily accessible parameters, such as the solubility or reactivity properties of similar chemicals (bulk counterpart of the same chemical composition or an analogous product of the same chemical family). Relying on the Globally Harmonized System of classification (SGH) and standard European risk terminology, the ISO standard uses five bands to classify toxicity, ranging from no significant risk to health (Category A) to severe hazard (Category E). Exposure is divided into four bands, based on processes and quantities used, form of the nanomaterial (powder in the form of elementary particles, aggregates or agglomerates, suspended in a liquid, integrated in a matrix, deposited on a solid surface, etc.).

The result is the matrix shown in Table 6, where each box of the matrix represents a minimum exposure control solution to be introduced. There are two different approaches: a proactive approach that does not take into consideration preventive measures already introduced; a retroactive approach, which considers preventive measures already introduced and may assess the residual risk [115, 136, 139, 140, 141, 146]. Other models suggest different approaches for assessing hazard and exposure bands, but all yield exposure control bands.

Table 6: Control band matrix from airborne nanomaterials hazard and emission potential bands

		Emission potential band			
		EP1	**EP2**	**EP3**	**EP4**
Hazard band	**A**	CB1	CB1	CB1	CB2
	B	CB1	CB1	CB2	CB3
	C	CB2	CB3	CB3	CB4
	D	CB3	CB4	CB4	CB5
	E	CB4	CB5	CB5	CB5

The five exposure control bands are as follows:

- CB1: *Natural or mechanical general ventilation*
- CB2: *Local exhaust ventilation*: extractor hood, slot hood, arm hood, table hood, etc.
- CB3: *Enclosed ventilation*: ventilated booth, fume hood, closed reactor with regular openings
- CB4: *Full containment*: glove box, glove bag, continuously closed system
- CB5: *Full containment and review by a specialist required*: seek expert advice

It is important to remember that in applying the control banding method to nanomaterials, assumptions must to be formulated about information that is desired but unavailable. It is thus an approach recommended only for those with recognized expertise not only in chemical risk prevention but also in the risks of nanomaterials in particular [115, 136, 146]. Successful implementation of control banding requires solid expertise together with a critical analysis of occupational exposure potential to ensure that appropriate control measures are introduced and the approach taken is conservative [115, 136, 141, 146]. In addition, there are tools, including the

Stoffenmanager Nano [139, 140], designed specifically for small or medium-sized businesses. In fact, the Stoffenmanager[1] website is designed to allow implementation of the approach without the help of a specialist, processing all worker activities (time, frequency and duration of exposure) as well as collective and personal preventive measures already introduced.

A number of approaches are currently being evaluated in different workplaces to determine the level of expertise required to correctly classify hazard and exposure bands and hence identify an appropriate control level [142]. It has been demonstrated that health committee members trained in control banding can, under certain circumstances, obtain risk classifications very similar to those obtained by certified industrial hygienists. [143]. A number of websites[2] offer control banding toolkits.

The control banding method is an iterative four-step process based on the plan-do-check-act (PDCA) continuous improvement model: plan, implement, assess, take corrective action … repeat.

The control banding process is an integral part of the overall system of health and safety management in the workplace [114, 115, 132, 136]. It is based on the plan-do-check-act (PDCA) continuous improvement model, with the cycle repeated at regular interval to take into account advances in our knowledge [114, 115, 132, 136, 141].

[1] http://nano.stoffenmanager.nl/

[2] CB Nanotool [download]: http://www.controlbanding.net/Services.html
COSHH Essentials [web-based]: http://www.coshh-essentials.org.uk/
COSHH Essential sector guidance sheets [web-based]: http://www.hse.gov.uk/pubns/guidance/
EMKG-Expo tool [download]: http://www.baua.de/de/Themen-von-A-Z/Gefahrstoffe/EMKG/EMKG.html
ECETOC TRA [download]: http://www.ecetoc.org/tra
Korean Occupational Safety and Health Agency Control Banding chemical classification and engineering controls: http://www.kosha.or.kr/bridge?menuId=1475
InterICCT [web-based]: http://www.ilo.org/legacy/english/protection/safework/ctrl_banding/toolkit/icct/index.htm
Stoffenmanager [web-based]: https://www.stoffenmanager.nl/default.aspx
Stoffenmanager Nano [web-based]: http://nano.stoffenmanager.nl
Danish NanoSafer: http://nanosafer.i-bar.dk

7. LAWS, REGULATIONS AND OBLIGATIONS OF THE PARTIES

At present, there is ***no legislation that specifically*** governs the handling of nanomaterials in Québec. This does not mean, however, that there is a regulatory vacuum or a legislative gap, as establishments are nonetheless required to ensure safe management of chemicals by applying all pertinent laws and regulations [73, 148]. One of the key features of nanotechnologies is their wide range of applications, everything from cosmetics to paint, from environmental measures to aeronautics. However, existing legislation in the different fields of application is not attuned to the specific properties, and in some cases greater toxicity, of nanoscale materials. In addition, the properties of a nanomaterial, and possibly its health impacts, can be deliberately or involuntarily altered by changing its physical structure or surface properties. Accordingly, "nano-specific" regulatory oversight is a real challenge [149].

Many countries recognize the many uncertainties with respect to nanomaterial-related risks. Some have issued codes of conduct and recommend the development of voluntary limits coupled with application and adaptation of regulations already in effect [150]. In 2007, for example, the European Union issued a call for good work practices based on the precautionary principle, anticipating potential environmental, health and safety impacts of nanoscience and taking necessary preventive measures. [151]. A detailed review of regulations was made in 2010 [16].

Though a growing number of researchers and organizations are recommending reference values for certain products, our insufficient knowledge of the toxicity of nanoscale materials makes it impossible for regulatory bodies to issue numeric standards.

7.1 In Québec and Canada

Laws and regulations governing the protection of human health, safety and physical integrity apply to all workers. In Québec, the Act respecting occupational health and safety [148] and the Regulation respecting occupational health and safety [73] cover general aspects of obligations with respect to development of in-house prevention programs and control of risk factors to reduce occupational exposure. Schedule 1 of the Regulation (respecting occupational health and safety), which lists permissible exposure values, gives standards for a number of chemical substances of the same chemical composition as certain nanomaterials. However, the regulation does not consider particle size or the possibility that it might affect the toxicity of a substance, though particle shape and size are among the parameters that can determine not only the absorption of a substance but its distribution and interactions within the body and hence its toxicity. To our knowledge, no country has yet adopted nano-specific exposure limits though certain recommendations have been made (Table 5). This guide provides detailed information specific to nanoscale materials. The primary goal of this guide is to support establishments in developing prevention programs and in assessing and managing risks using a conventional or precautionary approach depending on the degree of uncertainty about occupational risk.

Use of this guidance does not release an employer or that employer's workers from any of their legal or regulatory obligations.

The Canadian Workplace Hazardous Materials Information System (SIMDUT), soon to be replaced by the Globally Harmonized System (SGH), requires that suppliers label chemicals and draft Material Safety Data Sheets (MSDSs) describing them—including their health and safety risks, their main characteristics and necessary preventive measures. Employers are required to ensure that MSDSs are available and to train their workers. However, existing MSDSs generally do not consider powder size, which means that toxicity assessments are often inadequate in the case of nanomaterials [95-98] and prevention recommendations may thus not be adequate either.

Most existing Material Safety Data Sheets (MSDS) do not consider possible hazards stemming specifically from the nanometric size of powders. As a result, vigilance is required to ensure that necessary preventive measures are taken to protect the health of workers.

Health Canada and Environment Canada are currently studying the advisability of specific regulations governing the manufacture, import, export, use and environmental management of nanomaterials. To our knowledge, the only Canadian regulatory obligation for companies producing or importing certain nanomaterials is an obligation to provide information to Environment Canada or Health Canada [152]. Environment Canada and Health Canada are currently studying the question of CNTs and may make recommendations so that Canadian legislation can be adopted. A number of other provincial or federal laws (governing the transport of hazardous materials or protection of the environment, for example) could apply to nanomaterials as they do to other chemicals. Last, in 2011 Canada and the United States announced the creation of the Canada-United States Regulatory Cooperation Council to facilitate the movement of goods both ways across the border. As the use of nanotechnologies is expanding rapidly, this should encourage better alignment of regulatory approaches to nanotechnology applications in the two countries.

7.2 Elsewhere in the world

Many countries are currently studying the possibility of enacting legislation with respect to nanotechnologies, and some have decided their regulations are adequate, while recommending a precautionary approach. Other countries, however, have already begun passing legislation to take into account the hazards specific to the nanostructure of nanomaterials, which they consider as new chemical substances. This is the case in the United States and the European Union [74, 153-165]. The European Union adopted the following definition of a nanomaterial in October 2011 [153]:

- Nanomaterial means a natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50% or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm-100 nm.
- In specific cases and where warranted by concerns for the environment, health, safety or competitiveness the number size distribution threshold of 50% may be replaced by a threshold between 1 and 50%.

- By derogation from the preceding definitions, fullerenes, graphene flakes and single-walled carbon nanotubes with one or more external dimensions below 1 nm should be considered as nanomaterials.

In 2011, the European Food Safety Authority published a guide on risk assessment that includes determination of an exposure scenario and a toxicity testing strategy [161]. In 2012, the European Union's Scientific Committee on Consumer Safety issued a guidance for safety assessment of nanomaterials in cosmetics [163]. In France, since January 2013, all manufacturers, distributors and importers must declare any use of substances in the nanoparticle state.

The U.S. Food and Drug Administration has also published similar guidances and considers nanomaterials as new products when their synthesis alters the size, properties or effects of a product that has already been approved [164]. Some U.S. authorities have started legislating on nanotechnologies. To ensure consistency, the Office of Science and Technology Policy announced in 2011 that the Emerging Technologies Interagency Policy Coordination Committee, which reports to the White House, had developed a set of principles for the regulation and monitoring of nanotechnology applications. An exhaustive review of European and U.S. regulations demonstrates regulatory convergence and concludes that existing regulations governing chemicals cover nanomaterials and nanotechnologies relatively well [160], with some limitations [165].

7.3 Threshold limit values suggested by different organizations

Table 7 below summarizes threshold limit values suggested by research organizations and standardization bodies.

For the moment, the suggested threshold limit values can provide guidance for workplace control measures.

Nonetheless, as long as the health effects of nanomaterials remain poorly understood, as long as specific sampling of a worker's breathing zone is impossible and regulated exposure limits are unavailable, it is strongly recommended that occupational exposure be minimized by taking a preventive, that is, precautionary, approach.

Table 7: Exposure limit values suggested by different organizations

Substance	Suggested exposure limit value	Organization/Remarks	Reference
Carbon nanotubes and nanowires (length > 5µm, diameter < 3 µm, length/diameter ratio > 3:1) for which effects similar to asbestos are not excluded	0.01 f/mL	Suvapro, Dutch Social Partners, British Standards Institution (BSI), Institute for Occupational Safety and Health of the German Social Accident Insurance (IFA)/Fear of mesothelioma formation; no measurement methodology suggested	[166-169]
MWCNT	2.5 µg/m^3	Nanocyl	[119, 125]
Carbon nanotubes (SWCNT and MWCNT)	1 µg/m^3	NIOSH/Recommendation based on the analytical limit of quantification and a risk assessment	[48]
CNT	30 µg/m^3	National Institute of Advanced Industrial Science and Technology (AIST)	[126]
Fibrous nanomaterials	0.1 f/mL	Safe Work Australia/Assessed by transmission electron microscopy Social and Economic Council (SEC, Holland)	[170, 171]
Nanomaterials classified as carcinogenic, mutagenic, asthmagenic or reproductive toxins	0.1 x WEL	BSI/Precautionary approach. Safe Work Australia	[167, 170]
Insoluble nanomaterials	0.066 x WEL	BSI/Based on the first NIOSH study of TiO_2 toxicity	[167]
Insoluble nanomaterials	20,000 particles < 100 nm/mL and 0.066 x WEL	Safe Work Australia/Precautionary approach, simultaneous application of two exposure limits	[170]
Insoluble nanomaterials	20,000 particles < 100 nm/mL if density > 6,000 kg/m^3	IFA/Precautionary approach SEC	[169, 171, 172]
	40,000 particles < 100 nm/mL if density < 6,000 kg/m^3		
Insoluble nanomaterials	20,000 particles < 100 nm/mL	Dutch Social Partners	[168, 169]
Soluble nanomaterials	OEL	Dutch Social Partners/Risks related to chemical composition only	[168, 169]
Soluble nanomaterials	0.5 x WEL	BSI/Precautionary approach Safe Work Australia	[167, 170]
Nanometric titanium dioxide (10-100 nm)	0.3 mg/m^3	NIOSH/Based on literature review and epidemiologic studies	[173]
Nanometric titanium dioxide (21 nm)	1.2 mg/m^3	National Institute of Advanced Industrial Science and Technology (AIST), NEDO-1 project	[35]
Fullerene	0.8 mg/m^3	AIST, NEDO-2 project	[37]

8. PREVENTION

The end objective of any prevention program is to reduce all risks to an acceptable level. In the previous chapter, we made the following observations:

1) It is known that many nanomaterials are more toxic and more chemically reactive (i.e., constitute a greater explosion and fire hazard) than the same chemicals at a larger scale, yet current studies on cells or animals are generally limited in scope, which makes them difficult to extrapolate to humans. Consequently, there is still much uncertainty regarding the toxicity of nanomaterials (Chapter 4).
2) Portable instruments can detect the presence of airborne nanomaterials, and there are sophisticated instruments that can characterize them reliably. Some of these are direct-reading instruments, while others take samples to be sent to a laboratory. As yet, only a small number of workstations have been characterized; in most situations, specific assessment of a worker's breathing zone exposure remains impossible at this time (Chapter 5).
3) Quantitative risk assessment is rarely possible; however, control banding (qualitative or semi-quantitative) can be incorporated in a comprehensive in-house prevention program (Chapter 6).
4) To our knowledge, regulatory bodies have not adopted any standards prescribing specific exposure limits for nanomaterials. Nevertheless, the increasing number of reference values proposed by researchers (Chapter 6) and by highly reputable organizations (Chapter 7) can serve as initial guidelines for the level of exposure control needed.

In light of these observations and despite the many uncertainties that remain, adequate preventive measures must be developed and implemented to keep risks at an acceptable level. A precautionary approach is recommended for nanomaterials that present significant or unknown health and safety hazards and are insoluble or poorly soluble in the body. To reduce exposure as much as possible, risk management must be a major component of the prevention program, and the level of protection must be adapted to the specific risk presented by the nanomaterials, including in research laboratories [1, 3, 90, 174-179].

In our view, it is critical for the senior management of any establishment involved in nanotechnologies to develop an occupational health and safety policy, to implement it with the participation of all personnel, to devote the necessary resources to it and to follow up on it regularly. Moreover, to ensure optimal risk-control decisions, a prevention program specific to the establishment must be developed, implemented, reviewed regularly and improved as needed.

In practical terms, it means developing and implementing a prevention program based on safe practices that evolve with the advancement of scientific knowledge. The safe practices are very similar to those used in case of occupational exposure to hazardous chemicals. There are best practice guides on working in laboratories [1, 90, 175-177 180], on handling and use of carbon nanotubes [39, 48, 179, 181] and on exposure situations in general [3, 11, 12, 16, 178, 182-185, 187, 188]. There is also one on medical screening [186].

The aim of this chapter is to support the implementation of measures for controlling potentially toxic occupational exposure through a hierarchical risk reduction approach, similar to the approach used in fire and explosion prevention (Figure 10).

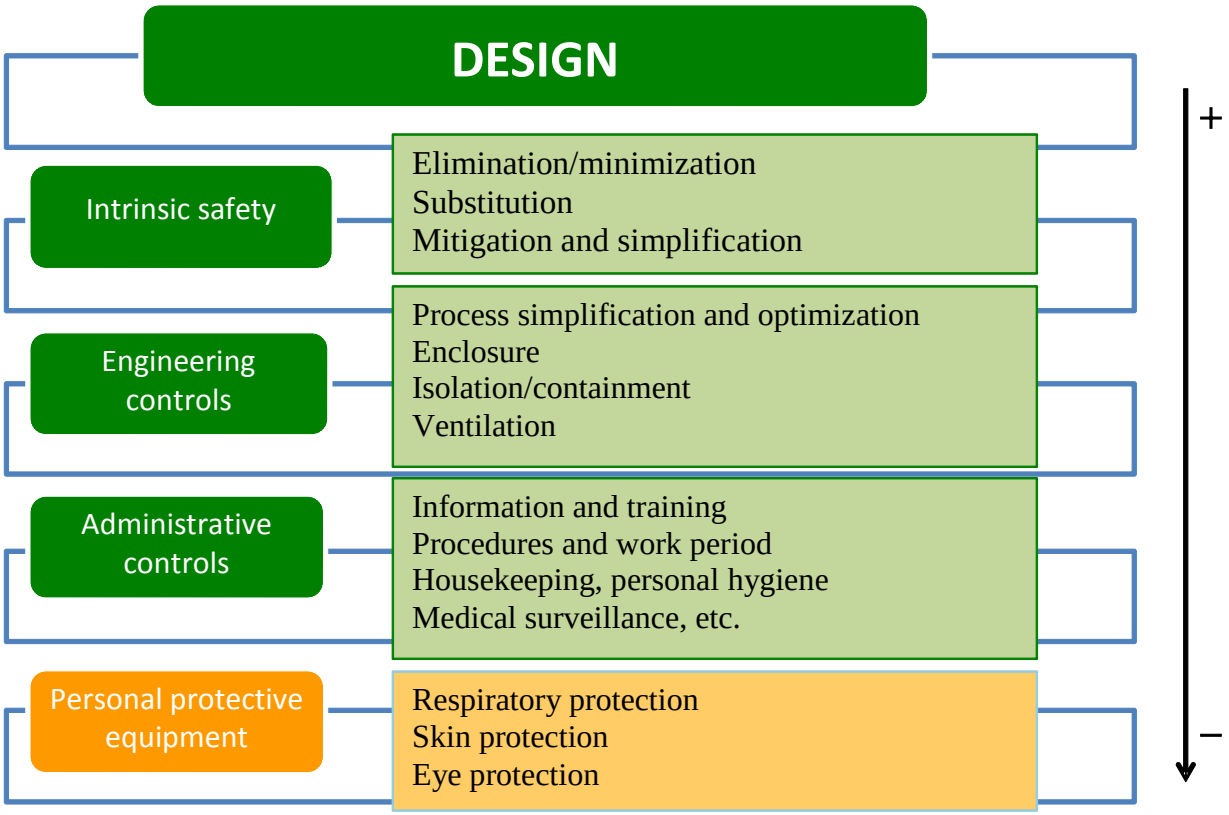


Figure 10: Hierarchy of nanomaterial exposure controls

8.1 Health risk control

Risks associated with nanomaterials can be controlled, ideally right from the site design stage; in fact, several Québec companies and research laboratories have already implemented effective programs in this respect.

8.1.1 Design

The design stage is the time to select a building plan, to choose reagents (whenever possible, choose suspensions, pastes, gels, premixed concentrates or pellets rather than powders; or consider nanomaterial encapsulation or functionalization) and production equipment (sealed and automated, as much as possible), to plan the systems for ventilation, supply, storage and shipping and to plan the work organization.

The design must be safe and based on elimination of contaminants at the source [189-191]. It is a decisive factor in prevention and is **the most determining and most economical** of the production organization stages for ensuring occupational safety. The design must take into account the four types of prevention measures (Figure 10) [1, 12, 16, 178, 192-196].

If the design is deficient, it is often difficult and very costly to modify the process, the equipment or the workstations to eliminate or reduce risks associated with toxic or hazardous materials.

In addition to taking health and safety hazards, regulatory requirements and production imperatives into account, workstations must be designed in a way that eliminates risky situations, both for the workers and for the process and equipment. If there is a leak in the production system, diffusion can cause nanomaterials to disperse into the environment, especially if the nanomaterials are non-agglomerated powders. The design team must therefore consider the properties of the chemicals used and plan ways to eliminate or at least limit nanomaterial emissions in the workplace—during maintenance or cleaning, for example, when enclosures must be opened. If explosible dusts are to be used or synthesized, the building structure, safety systems and process equipment must be appropriate and designed for that purpose. Appendix A lists a number of risky situations found in Québec workplaces along with the appropriate safety measures; Appendix B summarizes the control measures to implement according to the estimated risk level in a laboratory. Appendix C gives examples of the measured performance of exposure control measures. For example, placing a mixer inside ventilated containment reduced the CNT aerosol concentration from 172 to 0.018 f/mL; ventilation at source during cleaning of a manganese oxide reactor reduced the nanomaterial concentration from 3.6 to 0.15 mg/m^3, thus bringing the level below the 0.2 mg/m^3 threshold limit value for this particular situation. SWCNT synthesis by vapour-phase deposition in a constant flow fume hood with a face velocity of 0.7 m/s generated a concentration of 10^7 p/cc inside the hood, while the concentration in the worker's breathing zone was less than 2,000 p/cc.

8.1.2 Intrinsic safety

Intrinsic safety means eliminating or reducing risks before they are even introduced into the workplace [189-191]. Based on this concept, the goal is to eliminate toxic or hazardous nanomaterials or at least reduce the quantity used. However, nanomaterials cannot be eliminated from processes that involve synthesizing them or incorporating them into a finished product. In that case, safety can be improved through substitution [194-196], such as replacing the most toxic substances with less hazardous ones, replacing old equipment (to reduce leakage, ignition sources or malfunctions) or modifying work methods. Risks can also be reduced by switching from batch runs to continuous production. In addition, products can be used in less hazardous forms; for example, a process using powders can be replaced by one using suspensions, pastes, gels, premixed concentrates or pellets; or the process stages can be modified to automate or

eliminate certain risky operations such as pouring and transferring. Inflammable products such as hydrogen can be produced on-site as needed, rather than being stored in cylinders. Last, the simplification of processes and procedures so as to reduce the chances of error or accident can be considered an intrinsic safety approach as much as an engineering approach [189-191].

Intrinsic safety is part of the design stage and is **the most effective way to control occupational risks**.

8.1.3 Engineering controls

Engineering controls are strategies for limiting exposure, preferably at the source. The main approaches include process optimization and simplification, mentioned above. Carbon black, silica fume, nanometric TiO_2 and nanoscale metals and metallic oxides are examples of nanomaterials that require complete isolation and are normally synthesized in a closed system (containment). Process containment, combined with mechanization or automation where possible, is most likely to ensure effective emissions control, in particular by limiting operator involvement [1, 3, 12, 16, 100, 196]. With mechanization and automation, machines or pneumatic systems can transfer products, take samples, bag powders and even clean reactors without opening the enclosures.

Because some processes cannot be fully contained, there are operations that risk emitting nanomaterials into the air. In such cases, the equipment can be enclosed or isolated in another room and ventilated through separate ventilation systems, thus avoiding any possibility of contaminating workstations and exposing workers. Workers can also be isolated in controlled-atmosphere booths or rooms, from which they can observe and control the process.

Enclosures, isolation and containment should normally be effective enough to prevent worker contact with nanomaterials. However, the maintenance of such facilities requires special procedures, since some workers will have to access or enter the enclosures. Enclosing and ventilating an MWCNT production furnace, for example, reduced concentrations from 193 to 0.018 fibres per cubic centimetre of air [197].

8.1.3.1 Ventilation

Nanomaterials can be sporadically emitted into the air during certain processes or operations, since the latter do not always take place in sealed, failproof enclosures. How well the sources of nanomaterial emission can be predicted thus plays a role in designing the ventilation system. Documented sources of nanomaterial emission include opening bags, pouring, transferring, mixing, collecting and suspending powders, bagging, de-packaging, sampling, grinding, filtering, drying, weighing and changing vacuum bags or filters. If such sources are present, modification of the equipment should be considered (automating or enclosing it, for example) to prevent emissions. If this is impossible, carrying out the operations in a ventilated enclosure (enclosed

ventilation, control band 3) and capturing contaminants at the source by means of a suspended fume hood, suction table, extractor nozzle or suction ring (local exhaust ventilation, control band 2) are good ways to control workstation contamination. Any local exhaust ventilation (LEV) system proven effective with vapours or gases should be able to protect workers by preventing dispersion in the workplace, with minimal fresh air input needed. The nine principles set out by the Institut national de recherche et de sécurité (INRS France) and applicable to local exhaust ventilation systems (which should have a capture speed of 0.4 to 0.6 m/s at the emission point) are as follows [1]:

- Surround the nanomaterial production zone as much as possible
- Capture emissions as close to the source as possible
- Place the hood so that the operator is not between it and the pollution source
- Utilize the pollutants' natural movements
- Induce sufficient air speed
- Distribute air speeds uniformly within the capture zone
- Compensate air exhaust by equivalent air input
- Avoid drafts and thermal discomfort
- After filtering, exhaust polluted air outdoors, away from fresh air intake areas

The local exhaust ventilation system must be cleaned and maintained routinely. Its performance should be checked regularly, as malfunctions and leaks are unpredictable. When possible, suction systems should be set up; if not possible, the general ventilation system will dilute the ambient air by exhausting the contaminated air. General ventilation is still required, because it brings fresh air to workers and compensates for the air removed by local exhaust ventilation systems, laboratory fume hoods, etc. INRS recommends 10 to 20 air changes per hour for laboratories [1]. To save energy, some general ventilation systems filter the air and then recirculate it to the building; this may be prohibited by regulation in the case of certain substances. Unless it is well documented that the nanomaterials do not present a toxic hazard, filtered air should not be recirculated. General ventilation should not be regarded as a way to eliminate toxic nanomaterials from a workplace, unless the risks have been assessed and it has been proven that the use of general ventilation, combined with fresh air intake, is enough to keep ambient concentrations well below the significant risk threshold. If the air in the work areas contains nanomaterials, it must be treated before being discharged into the environment. For this, various approaches are possible, such as filtering through High-Efficiency Particulate Arrester (HEPA) filters (minimum 99.97% filtering of 300-nm particles) or Ultra-Low Penetration Air (ULPA) filters (minimum 99.999% filtering of 120-nm particles).

Several studies and knowledge reviews [198-202] have looked at whether ventilation is effective in controlling nanomaterial exposure. Tsai et al. [199, 200] showed that fume hood design has a significant impact on the quantity of nanoparticles released. Constant-flow hoods have highly variable performances and may allow nanoparticles to be carried into the worker's breathing zone, depending on sash position. Emissions from air-curtain hoods and

Ventilation system performance is closely tied to quality of design, efficiency, maintenance and, often, work methods. System efficiency must be checked regularly to ensure optimal performance. System specifications and quality should be similar to those of gas and vapour exhaust systems.

constant-velocity hoods (0.5 m/s) are normally low, except when the sash is completely raised and face velocity drops to 0.3 m/s. INRS recommends a face velocity of 0.4 to 0.6 m/s [1] while NIOSH [175] gives a detailed description of good practices for optimal use of a laboratory fume hood. The quantity of nanoparticles escaping from a fume hood is influenced by several factors, including design, operations, operating conditions (face velocity and sash position), work methods, the type and quantity of nanomaterials handled, ambient conditions and general ventilation. In addition, hood performance is greatly affected by the presence and movements of human subjects, the distance between the source and the breathing zone, and sash height [201, 202].

The literature documents cases of significant occupational exposure to nanoparticles due to deficient source capture systems. However, it has also been shown that such systems, when well designed and maintained, can be highly effective (see Appendix C). High-quality design, regular maintenance, the use of good work methods (for example, proper positioning of the extraction arm in relation to the emission source) and, especially, checking of the extraction rate are critical for ensuring adequate worker protection. Ventilation system cleaning must always be done in a vacuum with a high-efficiency filtration system using HEPA filters and, if explosible dusts are being handled, explosion-proof equipment.

Table 8 summarizes the performance that can be expected from engineering controls [3, 203].

Table 8: Expected performance of controls (adapted from [3, 203])

Control technology	Historical performance (µg/m^3)
General ventilation	>1000
Open handling with engineered LEV	100 – 1000
LEV with directional laminar flow and vacuum conveying	10 – 1000
Ventilated enclosures	10-100
Closed systems	1 – 10
High containment and robotics	< 1

8.1.4 Administrative controls

Certain administrative controls must be implemented without fail to complement the engineering controls.

In addition, other administrative measures must be used when engineering controls are not feasible or cannot fully control the risk factors, or while waiting for engineering controls to be implemented. Administrative controls, like personal protective equipment, can never substitute for engineering controls developed according to industry best practice.

The purpose of administrative controls is to reduce accident risk and occupational exposure while promoting optimal work methods. Essentially, the following must be developed and implemented:

- Training and information programs for workers and their supervisors (with clear training objectives) covering at least the following:
  - The identities of OHS resources
  - Key definitions: nanomaterial, risk vs. hazard, exposure, MSDS, etc.
  - The names, characteristics and potential risks of nanomaterials used in the workplace and what they represent in terms of health, fire or explosion hazards
  - Relevant laws and regulations
  - Reading and understanding MSDSs and labels
  - Organizational measures (preventive building design, etc.)
  - Collective protection measures and their use and maintenance
  - Good work practices, based on knowledge of the risks involved and required preventive measures:
    - During the manufacture, handling, transfer, conditioning, storage or shipping of nanomaterials, or the use or maintenance of equipment
    - During the manufacture of products containing nanomaterials
    - During mechanical treatment (sanding, drilling, etc.) of products containing nanomaterials
  - Personal protective equipment and how to maintain it, along with respiratory and skin protection programs
  - Cleanup and emergency procedures in the event of a leak or spill
  - Personal hygiene: wash hands frequently, and no smoking, eating, drinking or applying makeup on the premises
  - Waste management and treatment
  - What to do in the event of an incident or accident
- Regular updating of training and information programs; regular communication with workers to help them take charge of occupational health and safety
- Optimal work procedures designed to minimize the generation and airborne resuspension of nanoparticles; the procedures, preferably written, must be explained and managers must ensure that they are understood and applied
- Reduced work periods at a workstation
- Minimization of the number of workers exposed
- Permanent restriction of access to nanomaterial synthesis and handling sites to authorized and trained personnel, with all doors marked “Authorized personnel only”
- Standardization of all work surfaces, which should be non-porous and easy to clean
- Transportation of dry nanomaterials in closed containers at all times

- Housekeeping and preventive maintenance scheduled to promote continuous smooth operation of equipment and its maintenance according to good practice and in accordance with the specificities of the products that may accumulate in the workplace. Equipment must be locked out and thoroughly cleaned before being serviced. Work areas must be cleaned using HEPA filter vacuums at least once per work shift for any operation involving nanopowders. The vacuums must be used only for nanomaterials and must be clearly labelled as such. After each use, the vacuum must be kept running in order to suction in all the nanomaterials from the hose, and its exterior surfaces must be carefully cleaned. The vacuum filter should be changed under a fume hood if possible. If not, the operator must wear a full complement of personal protective equipment: coverall, gloves, glasses or face shield and respirator. In the case of explosible nanomaterials, the vacuums must be explosion-proof. Solvent-soaked cloths are used for final decontamination, once it has been determined that the solvent is compatible with the nanomaterials. The cloths must then be placed in sealed bags and disposed of along with other nanomaterial-contaminated waste.

  All methods that could cause particles to be resuspended (such as using a broom or compressed air) must be prohibited, both for regular housekeeping and for cleanup of spills or leaks.

- Measures promoting good personal hygiene inside and outside the workplace. Sinks and showers should be installed to allow workers to decontaminate, especially before eating, drinking, smoking or going home. In some situations, it would be advantageous to install double locker rooms to prevent work clothes from contaminating street clothes. Work clothes must be cleaned in a way that takes into account their possible contamination by nanomaterials, and must never be taken home.

The administrative controls are well known, and the reader may consult references [100] to find out more. In addition, the establishment must design and implement procedures for storage, accidental leaks and spills, emergency situations, waste management and environmental risk control. The development and implementation of a medical surveillance program could also be considered.

8.1.4.1 Medical surveillance

The body of scientific knowledge is currently insufficient to recommend ***specific medical screening*** for most nanomaterials and hence to determine the medical tests needed for exposed asymptomatic workers [16, 186, 204-207]. NIOSH recently became the first to recommend specific medical tests [48]: lung function tests for workers exposed to CNTs and carbon nanofibres [48]. For CNTs, NIOSH recommends documenting at least the worker's medical and occupational history followed by a physical examination, particularly of the lungs, and a lung X-ray; these tests must be repeated regularly [48].

For all other nanomaterials, a full checkup with a medical and occupational history at the beginning of employment, including a chest X-ray and a spirometry test, is suggested [186]. Medical surveillance could prove to be a highly useful research tool, especially in epidemiological studies. In Québec, the authors recommend studying the pertinence of medical surveillance, based on the availability of new scientific knowledge thanks to the approach

developed by the Expert Committee on Screening and Medical Surveillance in Occupational Health [208] (in French). Medical screening can nonetheless be considered in particular situations. For example, if there is a specific test for a normal-scale substance, the test might also apply to its nanoscale counterpart. ***It is extremely important to limit occupational exposure, given the uncertainties about the effects on health***. Investing in exposure control and measurement is an important prevention strategy, along with keeping an exposure registry [186, 209]. In addition, medical surveillance can, if planned and conducted with its limitations taken into account, be beneficial for the worker, the employer and society as a whole, as well as for epidemiological studies [209, 210].

8.1.4.2 Storage

Because certain particles are reactive and easily resuspended in air, the imperatives of preserving product properties and controlling risks are particular aspects of nanomaterial storage. Nanomaterials must be stored in completely sealed containers or double bagged, first of all, to prevent them from leaking and contaminating the premises (dispersion, slow sedimentation) and, second, to preserve their reactive and size-related properties. All containers must be clearly labelled and must indicate the presence of nanomaterials and their potential hazards. Storage facilities must be similar to those used for gases: cool, well-ventilated, protected from sunlight and away from all flammable materials and sources of heat or ignition.

Special measures must also be taken to preserve the product. Because the particles are so small, they often try to agglomerate, and they offer a large surface for contact with ambient air, which promotes chemical reactivity. Certain precautions can prevent the loss of nanoscale-specific properties, product deterioration (e.g., oxidation of metals) and the risk of fire or explosion. One possible solution is storage in the presence of an inert gas or in anhydrous conditions. In some cases, the nanomaterials can be coated with a protective layer composed of salts or various polymers, which can be disposed of before the product is used. For laboratories, there is an excellent guide to storage of chemical substances [211] (in French).

The storage facility should ideally be outside the main building; only a minimal quantity of nanomaterials should be kept in the actual work areas (laboratory or production unit). This will facilitate access in the event of an emergency and limit propagation in the event of a fire or explosion. The storage facility, or at least a part of it, must be reserved exclusively for nanomaterials, identified as such and off-limits to everyone except authorized and trained personnel. It must be well ventilated, and the walls and floors, as well as shelves and ventilated cabinets, must be smooth, impermeable, easy to clean and resistant to nanomaterials and other stored products. In many cases, epoxy-based paint may be suitable for the walls and floors. All material needed to clean up a leak or spill (HEPA filter vacuum, rags, absorbents, personal protective equipment) must be easily accessible in the storage facility. Last, conductive cabinets and shelves must be grounded to prevent static charge buildup.

8.1.4.3 Housekeeping

Regular housecleaning is necessary to remove dust from floors, work surfaces, instruments, equipment, furniture, walls, windows and doors, and to prevent nanomaterials from being resuspended in the air. At the end of each shift, a vacuum with a HEPA or ULPA filter (correctly installed and regularly replaced) must be used to remove dust, then all surfaces must be

thoroughly cleaned with damp rags depending on the specific process conditions, the products used and their hazards: explosibility, inflammability, incompatibility with water. The efficacy of the cleaning methods must be evaluated. In some cases, the nanomaterial electrostatic charge is a factor in choosing the right system. **As with any dry process, the use of compressed air, brushes, brooms or domestic vacuum cleaners, which could cause dust resuspension, is prohibited.** Cleaning procedures must be designed to prevent any contact between the worker (who must wear personal protective equipment) and waste, which must be disposed of in accordance with laws and regulations. Rags and other materials used for cleaning must be treated as hazardous waste and must not be re-used, so as to avoid particle resuspension.

8.1.4.4 Spills and emergency response measures

Each establishment must develop an emergency response plan, taking into account the particularities of the workplace, and must train its personnel to intervene in any spill or other emergency situation. All workers must know whom to contact in an emergency. The plan must cover the following: spill identification, classification and containment; hazard containment; risk reduction; cleanup; decontamination; and waste management. Some workers must be trained specifically to intervene in such situations and must have all the necessary materials and equipment, including a HEPA respirator and skin protection (see Section 8.1.5). Any accidental spill must be handled immediately by trained personnel, taking into account the specific hazards of the spilled product. Depending on the nature of the nanomaterials, cleanup methods may include vacuums with HEPA filters (properly installed and replaced according to the manufacturer's instructions), humidification of dry powders, application of absorbents, and the use of damp rags [3, 16, 175]. Liquid spills containing nanomaterials must be contained by means of absorbents or liquid traps, and the contaminated surface must be thoroughly cleaned. **As in housekeeping, the use of procedures liable to resuspend nanoparticles, such as sweeping or compressed-air cleaning, is prohibited.** Finally, waste must be handled and disposed of according to laws and regulations.

8.1.4.5 Waste management

All waste containing nanomaterials, including production waste, personal protective equipment (contaminated respirators, clothing, gloves and shoe covers), vacuum or ventilation system filters, cleaning rags, absorbents, cleaning liquids, etc. must be treated as hazardous waste and kept in clearly marked, sealed bags or containers until they can be disposed of. Product in liquid suspension or gel form must be collected, along with all cleaning liquids, in clearly marked, well-sealed containers (tanks or drums). Secondary containment is highly recommended, a plastic bag for solids or a container for liquids or solids, making sure they are well-sealed and clearly marked. Once full, bags and containers are put in a safe location in a suitable storage facility large enough to contain a storage area reserved specifically for waste and meeting the same criteria as the pure nanomaterials storage area.

All waste from processes using nanomaterials must be disposed of in accordance with municipal, provincial and federal regulations and standards. Specialized waste management companies are usually able to help the establishment, university or research centre dispose of nanomaterials in an environmentally safe manner, although some waste generators prefer to deal with their own waste. Possible solutions include *in situ* chemical treatment of nanomaterials through recycling, return to suppliers or incineration of organic nanomaterials.

8.1.4.6 Environmental risk control

Environmental risk control consists primarily in limiting the emission of nanomaterials into terrestrial and aquatic ecosystems. Good waste disposal practices are critical. There are various methods for stabilizing or incinerating waste. The best approach must be determined case by case. It is also important to limit emissions by filtering or treating production waste in accordance with industry practice and by following the procedures prescribed by municipal, provincial and federal regulations on the storage, treatment and disposal of hazardous waste.

8.1.5 Personal protective equipment (PPE)

Skin protection (coveralls, gloves, etc.) must be worn at all times; each item must offer the best possible compromise between safety and the ability to perform tasks comfortably. However, ***respirators must be used only as a last resort,*** when engineering and administrative controls do not offer sufficient protection. The purpose of PPE is not to substitute for proper engineering and administrative controls. However, PPE can be very important when handling powders, during equipment maintenance or when engineering controls have not yet been fully implemented.

Particular attention must be paid to the specific needs of maintenance and emergency personnel, who often have access to areas with a high exposure level.

The PPE required for risky tasks must be selected according to the estimated risk level and the desired protection level. The main tasks requiring PPE are emergency response (leaks, spills, aerosol spray), maintenance of premises and equipment, control sampling and in fact any situation where particles can be released or resuspended in the form of solid or liquid aerosols.

8.1.5.1 Respiratory protection

The main components of a respiratory protection program are as follows [212] (in French):

- Personnel training on respiratory risks and respirator maintenance, inspection, cleaning and evaluation
- Fit testing
- Environmental control
  - Using respirators according to manufacturer's recommendations
  - Assessment of respirator protection factor under real conditions (if possible) to confirm expected protection factor of respirator used
- Description of health risks
- Employer's and workers' responsibilities
- Program administration, including written procedures for respirator selection, use, training and testing

According to the Regulation respecting occupational health and safety [73], when respirators are needed, the establishment must have a respiratory protection program providing for worker training and for the selection of equipment according to specific hazards.

Once approved by senior management, the program should be administered by a person appointed for that purpose. Program results should be assessed at least once a year in order to ensure that the program is being applied properly by all respirator users.

According to OSHA [213], NIOSH [214], ANSI [216] and INRS [193] (in French), the respirators available on the market can have assigned protection factors (APFs) (i.e., as assessed under optimal laboratory conditions) of 5 to 10,000, meaning that the concentration inside the mask is 5 to 10,000 times less than outside. A detailed table of APFs is available [16].

In practice, there is a difference—sometimes substantial—between the protection factor under real conditions and the APF obtained under ideal laboratory conditions [216]. It has been shown that a poor seal between respirator and skin allows particles of 30 to 1,000 nm to enter the respiratory system. With the N95 respirator, for example, 7 to 20 times more particles penetrated through faceseal leakage than through the filter [217].

The efficacy of respiratory protection is influenced not nearly as much by filter performance as by other factors: hazard awareness, risk perception, perceived effectiveness of protection, attitudes of senior management and supervisors, safety culture in the organization and among workers, acceptability by the worker, adequacy of the faceseal (mask fit, matching of respirator to facial characteristics), duration and type of task, work methods, filter loading, physical comfort or discomfort, and respirator maintenance [238].

A number of studies involve laboratory assessments of respirator performance with nanomaterials [217-237]. At nanometric dimensions, theoretical models of Brownian diffusion apply to filtration through non-charged filters, that is, the most penetrating particle size (MPPS) is about 300 nm. This should mean that filtration efficiency will increase as particle size decreases. It has been reported [218] that the filtration efficiency of charged (pre-treated) fibres increases when the electrostatic charge is high and inhalation flow rate is low. However, the electrostatic charge present in commercial electret filters has a considerable impact on the MPPS, which shifts from 300 nm to 40 to 80 nm. In fact, the MPPS can vary depending on the filter material, the nature of the nanomaterial, air flow, filter/particle adhesion, temperature, pressure, and loading on the filter layer. Some of these parameters can also affect filter efficiency.

In some studies, N95 filters have shown a filtration efficiency of 95% or more for nanoparticles. However, in other studies, they have shown less than 95% efficiency at a constant flow rate of 85 L/min, which is the standard NIOSH test condition. Filtration efficiency decreases as the flow rate increases and according to the nature of the nanoparticle [217]. ***Last, the wearing of surgical masks must be prohibited, as laboratory tests have demonstrated penetration rates of 20.5 to 84.5% for a particle size of 80 nm at a flow rate of***

Some situations may increase sensitivity to risks or make jobs more difficult while wearing personal protective equipment. For example, the worker may experience respiratory resistance, thermal discomfort and difficulty communicating or performing the task while wearing the equipment. This can impede the efficient use of some kinds of PPE.

85 L/min. Given the many factors that can reduce respirator efficiency in a work situation, the significant increase in breathing resistance [228, 239] and constraints linked to discomfort [240], ***use of a powered air-purifying respirator (PAPR), rather than an N-Series, P-Series or R-Series disposable respirator, will usually increase acceptability by the worker along with comfort and protection. Moreover, use of a higher-efficiency N100 rather than N95 filter, combined with positive pressure inside the mask, will compensate for an imperfect seal between the skin and the mask.***

In most situations where quantitative risk analysis is impossible, the IRSST recommends treating nanomaterials as toxic and wearing a PAPR with a P100 cartridge in any potential exposure situation. This should provide adequate protection in most cases. If it does not, or if there is an immediate risk to the worker's health or life, a supplied-air or self-contained respirator should be worn for maximum protection.

For more information about selecting and maintaining a respirator, see the CSST guide to respiratory protection (www.prot.resp.csst.qc.ca) (in French).

8.1.5.2 Skin protection

Skin protection equipment must be used in all situations where there is potential exposure.

Advances in toxicology have raised awareness about the importance of including cutaneous absorption when assessing exposure risk. The nature of industrial processes may imply a high probability that cutaneous exposure occurs during the production, handling or use of nanomaterials or during equipment maintenance or repair because of surface contamination. Product collection and packaging, housekeeping, equipment maintenance and nanomaterial spraying are examples of opportunities for skin contact. Some nanomaterials can penetrate the skin by dissolution. In addition, some studies suggest that a small fraction of nanomaterials can penetrate the epidermis, make their way into the bloodstream and travel through the body without dissolving. Although there are no skin protection standards at present, it is preferable to take precautionary steps to reduce cutaneous exposure to a minimum.

Because nanomaterials can pass through very small spaces, protective garments must be designed to allow as little penetration as possible. Some protective garments let particles in through the seams, zippers and openings. The European Nanosafe2 program [241, 242] concluded that nonwoven, airtight fabrics are much better at stopping nanomaterials than woven fabrics such as cotton, or paper. ***The traditional cotton lab coat therefore does not offer adequate protection and should not be worn in the presence of nanomaterials*** [241-243]. Instead, workers should wear Tyvek® type hooded coveralls with elastic at the neck, cuffs and ankles, as well as aprons and shoe covers. Since there is no information on how to take care of nanomaterial protective clothing, disposable items should be used whenever possible [1, 12].

Gloves are available in various sizes and various degrees of resistance to chemicals, cuts and perforations. Permeability to the solvent used is an important factor in glove selection. Studies conducted under simulated workplace conditions suggest that a fraction of nanomaterials will pass through gloves [244-247]. For this reason, workers should wear two layers of gloves when handling nanomaterials for an extended period [241, 242] and should wear long gloves when

handling suspensions. Glove selection must be based on an analysis of the risks and conditions. Other factors include ergonomic requirements and the worker's individual health condition. Care must be taken to ensure that the gloves fit well, since their purpose is to prevent exposure without increasing overall risk. As in the case of respirators, the establishment must implement a glove management program that takes worker tasks and exposure into account and that covers glove selection, ergonomics, training, maintenance and safe disposal.

8.1.5.3 Eye protection

Workers should wear closed protective glasses, splash safety goggles with side shields or a face shield. A respirator with a full face shield provides both respiratory and ocular protection while allowing the worker to wear prescription eyeglasses.

8.1.5.4 Ingestion prevention

Ingestion usually occurs when there is contact between the hands and the mouth. In the case of nanomaterial dusts, a fraction of the material accumulated in the upper respiratory system will be pushed up by the mucociliary escalator and swallowed, thus entering the digestive system.

Exposure risk zones must be clearly identified and kept separate from "clean" areas, such as locker rooms and dining areas. Workers must remove their protective garments in a sequence that will reduce the risk of contaminating street clothing and clean areas. Protective clothing must be removed from work areas in hermetically sealed, clearly labelled bags and must be treated as hazardous waste in accordance with regulations.

8.2 Safety risk control

Given their very large specific surface area, some reactive nanomaterials (certain oxidizable metals in particular) can ignite easily or even explode if they are not handled safely (see Section 4.2). Fortunately, the establishments that use such products are generally very knowledgeable about the specific hazards of their use and manufacture and about the safety measures that can prevent accidents or reduce their consequences when these nanomaterials are produced or used. Only a brief summary will be offered here. More detailed descriptions of preventive measures can be found in some of the references [12, 16, 189-191, 248-251].

In order to reduce the risk of explosion, fire or uncontrolled catalytic reaction, it is necessary to control the main factors that can lead to ignition (see Figure 4, Section 4.2.2.1) and to take these into account in the equipment design. The main approaches include the following:

- Reducing the number of particles released
- Reducing oxidant concentration
- Controlling potential ignition sources
- Equipment design and UL certification

Other safety measures are worth mentioning here:

- Preventing particle buildup on equipment
- Whenever possible, using sealed mechanical and electrical equipment
- Preventing particle emissions from open hoppers and chutes
- Maintaining the highest possible housekeeping standards
- Isolating risky operations, either by distance or by a structure
- Installing explosion vents on equipment and buildings
- Ensuring adequate fire protection
- Storing nanomaterials in sealed containers or tanks
- Handling nanomaterials in closed, sealed tanks or lines
- Using exhaust systems to prevent the formation of particle clouds and particle buildup on surfaces
- Training workers on risks and safety measures associated with combustible, inflammable or explosible dusts
- Grounding all equipment

9. RISK MANAGEMENT

Risk management should be an integral part of any organizational culture, in both its philosophy and its business practices, since it is an essential component of good corporate governance. The previous chapters have shown that the industrial production of nanomaterials, or their use in a production line, can definitely pose specific risks to worker health and safety, and that these risks can be controlled. Therefore, before nanomaterials are handled, the organization must make sure that potential risks are understood, so that necessary controls can be selected and implemented. In particular, stringent measures must be implemented to reduce exposure risk to a minimum and prevent accidents. In practice, risk management is a process to be carried out in stages according to a certain logical sequence. Regular updates ensure continuous improvement in decision-making while promoting steady gains in performance.

To facilitate the development and implementation of a specific prevention program for nanomaterials, this chapter is partially based on observations made in establishments in Québec. It incorporates the joint labour/management approach typical of occupational health and safety in Québec, enriched by practices proven both here and elsewhere [1, 3, 11, 12, 16, 39, 48, 67, 90, 100, 114, 122, 131, 132, 134, 167, 172, 174-182, 185, 187-194, 196, 201, 202, 205, 212, 214, 248, 249, 252-261]. The proposed approach should be useful as a working reference for research laboratories, pilot plants and plants in the start-up phase, as well as established companies introducing lines producing or using nanomaterials. Plants that use products containing nanomaterials could find this approach useful, even if their mechanical operations (sanding, sawing, etc.) usually do not generate free nanoparticles because the nanomaterials remain within a matrix.

To have an impact, the prevention program must be part of the organization's basic values, culture and development plan, meaning that

1) occupational health and safety is a priority
2) management and all workers are fully committed to it
3) the necessary efforts are made to reach the prevention targets

Figure 11 illustrates the proposed risk management approach. Because each work situation is unique, we propose a comprehensive but flexible approach. It should be remembered that several aspects have been discussed in detail in the previous chapters; readers should therefore review those chapters as needed.

The proposed approach emphasizes the need to constantly improve risk management by continually incorporating new information into the risk assessment and then into the risk management program. It is an approach that is applicable to any establishment of any size and is not be limited to nanomaterials. It should be incorporated into the organization's occupational health and safety program.

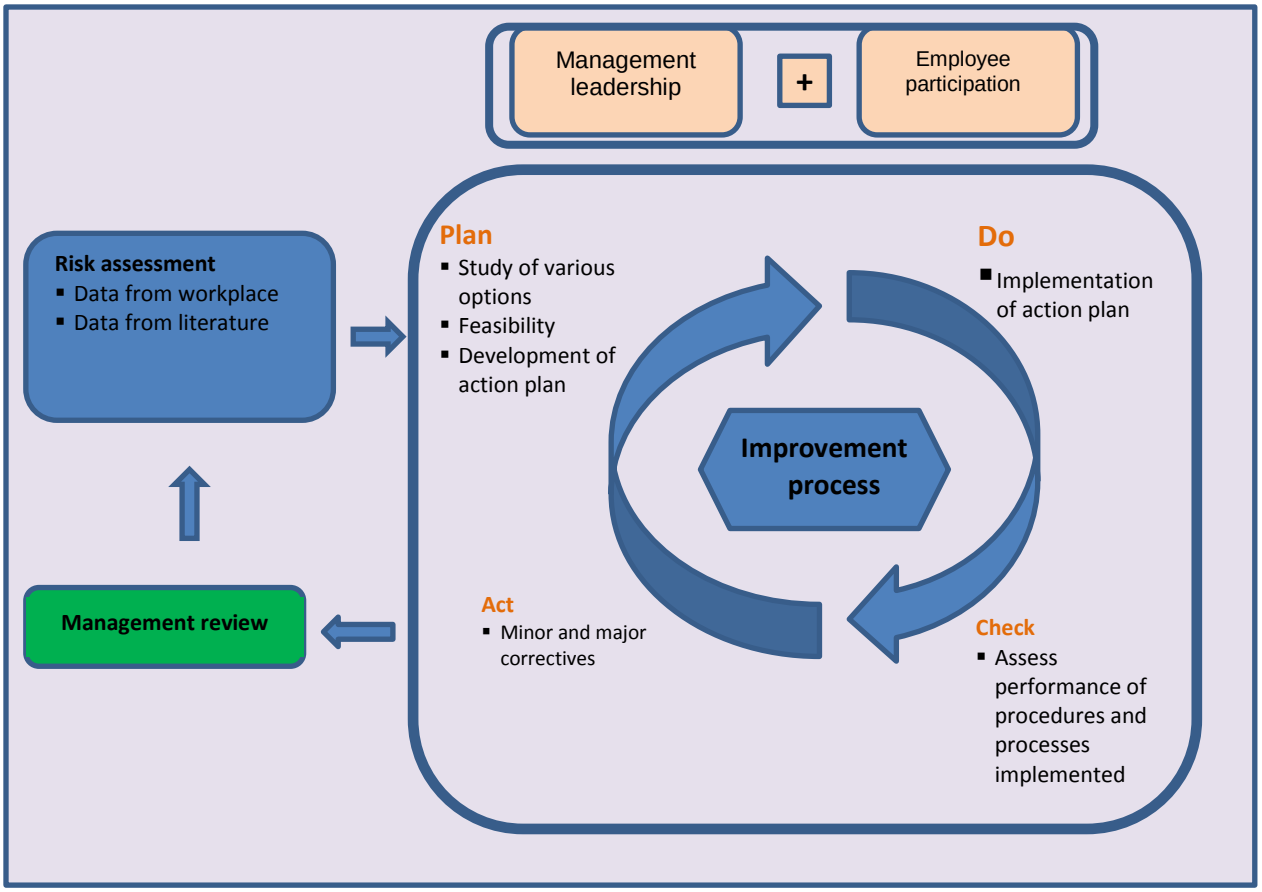


Figure 11: Iterative risk management

9.1 Management and worker involvement

9.1.1 Senior and middle management

The philosophy of the Act Respecting Occupational Health and Safety [148] and the Regulation Respecting Occupational Health and Safety [73] is clearly based on a joint approach where both employees and employer must work to ensure that prevention efforts are as effective as possible.

Two conditions are absolutely critical to the success of any OHS effort:

- **Leadership by senior management and accountability of middle management**
- **Worker participation**

Consequently, an OHS committee composed of employer representatives (including the OHS officer) and worker representatives must be established.

Senior management must assume leadership and general responsibility for the prevention program.

By leadership and involvement, we mean that senior management is actively engaged in improving OHS performance [12, 114]. Leadership must take the form of clear and known policies, promotion of OHS performance targets and recognition that managers are responsible for providing workers with a healthy and safe work environment. All of this must be supported by the human and financial resources needed to develop a culture aimed at continuous improvement in OHS. Performance must be measured and evaluated through regular management reviews followed by corrective action if the targets are not achieved. Through continuous involvement, senior management reminds workers that OHS is a priority for the organization. In this regard, it must clearly establish the separate responsibilities of the individuals mandated to implement and follow up on its decisions and encourage workers to participate. The OHS officer should report to senior management and should have the necessary authority to carry out his or her mission. Among other things, this person must clearly assign various responsibilities and procure the continuous commitment and support of senior management, middle management and the other OHS committee members.

The employer manages and supervises workers, equipment and work methods. Consequently, the employer has an obligation to comply with all laws and regulations and to take all reasonable measures to ensure worker safety.

Beyond regulatory obligations, prevention must be part of the fundamental values of any organization; for this reason, a prevention program should be developed, implemented, evaluated and continuously improved through an iterative documentation process. In addition, a prevention program that reduces absenteeism due to illness or accidents could rapidly turn into a competitive advantage by reducing production costs while fostering healthy labour relations.

9.1.2 Workers

Workers have a duty to participate and to be involved and accountable as part of the prevention and exposure control program.

Employees are usually the ones exposed to risks in the workplace. To foster a prevention culture and promote the implementation of the best preventive measures and safe work practices, employees must communicate and collaborate with the OHS committee or any other prevention structure present in their workplace. They must also take any training offered and apply the safe work methods developed by them or for them. They must not only carefully follow the instructions given, but they are also in the best position to report risky situations and, if possible, propose solutions [12]. They should be consulted and should participate in the development, planning, implementation and assessment of corrective measures.

9.2 Risk assessment

Risk assessment (see chapters 4, 5 and 6) is a major component of the prevention program. All preventive measures to be implemented will stem directly from the risk assessment.

Every operation, at every workstation, should be subjected to an annual risk assessment—whether quantitative or using control banding (Section 6.1)—based on detailed documentation (Figure 5). The preventive measures needed will be directly linked to the risk assessment results (Chapter 6). The more precise the risk assessment, the easier it will be to determine exactly what preventive measures must be implemented and to do so at the lowest cost while providing adequate worker protection. For the greatest possible accuracy, the actual working conditions encountered in the establishment must be documented extensively and continuously. Whenever possible, worker exposure should be regularly documented (Chapter 5) to ensure that control measures (Chapter 8) are working and that worker exposure is kept at a very low level. Here are some examples of questions to ask during the risk assessment.

Products	▪ What is the chemical composition of the nanomaterials? (major and minor ingredients, e.g., CNTs containing metal catalysts) ▪ In what form are the nanomaterials: powder, liquid suspension, gel, pellets, incorporated into a matrix, deposited on matrix surfaces? ▪ What are the physical and chemical properties: size, specific surface area, particle-size distribution, surface charge (zeta potential), morphology, crystallinity, dustiness, porosity? ▪ Is there an MSDS? Does it take into account particle size and the specific risks associated with nanoparticles? ▪ If not, is there specific information on the toxicity of the nanomaterials? Are there standards, reference values, thresholds? ▪ Is there specific information on the inflammability or explosibility of each nanomaterial? ▪ Is cutaneous exposure possible while handling these nanomaterials? ▪ Is there data on worker exposure levels?
Process	▪ Could the operations lead to the generation of dust or airborne droplets? ▪ Is local exhaust ventilation used at the potential sources of nanomaterial emission? (Please specify.) Is it effective? ▪ Do workers have to wear PPE during production operations involving nanomaterials? Please specify PPE items. ▪ Who is responsible for housekeeping and for cleaning and maintaining the equipment? Are these workers informed and trained, and are they exposed to particular risks?

The risk assessment provides all the information needed to determine the equipment required and the procedures to be implemented for protection of workers, equipment and property.

In some situations, medical surveillance of workers may be wise and should be considered.

Based on the information available and carefully recorded, a decision must be made as to the measures to implement for worker safety.

9.3 Plan

Planning is a critical stage, because it determines the steps to carry out and leads to choices that l give concrete form to the decisions made to ensure the safe handling of nanomaterials.

Planning must take into account all production stages, from the laboratory to the shipping dock, including procurement, synthesis, use, storage, maintenance, transport and disposal. The aim of planning is to establish responsibilities as well as strategies and ways to achieve the objectives set. Planning is used to determine exactly 1) what work needs to be done; 2) by whom and how; 3) equipment specifications; 4) criteria to be met; and 5) a timeframe for implementation.

Planning is also an opportunity to determine specific programs to be implemented (respiratory protection, emergency response, etc.), the content of basic training and refresher training programs, information dissemination strategies, work schedules, good work practices, restricted-access areas, PPE to be used and the best strategy for contaminated clothing management and decontamination. In planning emergency response measures and procedures in the event of asphyxiation, electrocution, accident, spill, etc., processes and the specific properties of the products used, synthesized or handled are taken into account. By way of example, here are some factors to consider in planning.

9.3.1 Workplace design (Sections 8.1.1 to 8.1.3)

Intrinsic safety	**Task**	▪ Eliminate hazardous product from task. ▪ Eliminate task from process. ▪ Modify task (handle in an enclosure rather than an open area). ▪ Modify task order, e.g., add powder to solvent rather than vice-versa. ▪ Minimize, incorporate into production or automate operations liable to generate airborne nanoparticles (handling, transfer, cleaning, maintenance, collection, conditioning, storage and transport), in particular by using nanomaterials directly at their synthesis site.
	Product	▪ Modify product form. ▪ Replace a product with a less hazardous one.
	Process	▪ Automate the process. ▪ Use a continuous process rather than batch runs. ▪ Completely isolate the process (closed system, isolated room, enclosure, automation) and restrict access to trained workers to minimize risk of exposure.
Engineering controls	**Task**	▪ Use local exhaust ventilation as needed if it is impossible to have ventilated or sealed enclosures, and make sure it prevents worker exposure and pollutant migration to other areas of the workplace.
	Product	▪ Manufacture, use and handle nanomaterials in the form of suspensions, gels, aggregates, agglomerates, resins, pellets or organic or mineral matrices, rather than in powder form.
	Process	▪ Optimize the process to make it a single integrated process (from nanomaterial synthesis to final product), thus keeping handling to a minimum, maintaining confinement and minimizing possible exposure.
	Ventilation	▪ Equip the local and general ventilation systems with HEPA filters to avoid emitting nanomaterials into the outside environment, and set up a regular preventive maintenance and performance assessment program for these systems.
Administrative controls	**Work procedures**	▪ In laboratories, use fume hoods and biosafety cabinets, glove boxes or fully closed systems, and local exhaust ventilation as needed. ▪ During weighing or transfer, place a damp towel or cloth on the work surface so that any loose nanomaterials will collect there. ▪ Keep containers holding dry nanomaterials closed as much as possible, to prevent air currents from resuspending the nanomaterials in the air.
	Housekeeping	▪ Make sure all work surfaces are smooth, non-porous and easy to clean.

9.3.2 Good work practices and maintaining premises, equipment and PPE (Section 8.1.4)

Workers and exposure	▪ Minimize the number of workers potentially exposed and the duration of exposure. ▪ Remove work clothes and thoroughly wash your hands and face before eating, drinking or smoking. ▪ Never take a contaminated object home, since it could expose family members. ▪ Do not store food, gum, cigarettes or other personal objects in the work area. ▪ Change into work clothes (including shoes) before starting your shift. ▪ At the end of your shift, take a shower and put your street clothing and shoes back on, leaving your work clothes at work.
Hygiene and housekeeping	▪ Promote good personal hygiene. ▪ Make the necessary facilities available (showers, sinks, closed recipients for used work clothes, etc.). ▪ If dry nanomaterials are present, use a commercial vacuum equipped with a rated HEPA filter, then clean with a damp cloth compatible with the nanomaterial in question. ***Never use a broom or compressed air.*** ▪ Clean and decontaminate work surfaces daily after each shift and immediately after an incident such as a spill. ▪ Clearly indicate on each piece of equipment whether it has been cleaned and decontaminated. ▪ Provide workers with a clean locker room and laundry facilities near the work area. ▪ Have used work clothes laundered by employees inside the establishment or by an external firm, making sure those involved are well informed and trained in the potential effects of toxic substances, exposure routes and control methods.
Work procedures	▪ Transfer and store nanomaterials in sealed and labelled containers. ▪ Make sure nanomaterials are delivered in sealed containers with double packaging (two sealed bags one inside the other, or a sealed bag inside a sealed container). ▪ Provide access to the work area through an airlock, and make sure the work area is under negative pressure in relation to other areas to prevent any possibility of contamination. ▪ Formally prohibit eating, drinking, smoking, chewing gum and biting in the work area. ▪ Ensure that breaks and meals are taken in a clean area separate from the work area. ▪ Keep street clothing separate from work clothes.
Equipment and material	▪ Consider using disposable, nonwoven lab coats and work surface coverings. ▪ Place a tacky mat at the exit from the work area. ▪ On a regular basis (at least annually), evaluate the performance of all prevention equipment, including ventilation systems and vacuums, and make sure it is in line with the manufacturer's specifications. ▪ Regularly clean ventilation ducts to prevent dust accumulation and risk of explosion. ▪ Clearly identify all areas where nanomaterials are handled or stored, and restrict access to authorized and trained personnel. ▪ Limit electrostatic charges by grounding conductive components, isolating power sources and using suitable electrical outlets and equipment.

9.3.3 Training and risk communication (Section 8.1.4)

- Train and inform all persons liable to be exposed about the specific potential risks and hazards of nanomaterials and how to protect themselves, as well as the location of emergency equipment (eye wash, shower, extinguishers, fire alarms and absorbents) and the contact information of the person in charge of emergency response.

9.3.4 Personal protective equipment (Section 8.1.5)

- Use PPE (closed shoes, long pants without cuffs, long-sleeved shirt, lab coat of nonwoven fabric, lab gloves, eye protection and respiratory protection) at all times when there is a risk of exposure.
- Remove gloves and other PPE before leaving the work area so as to avoid contaminating other areas and shared equipment such as multi-user computers, telephones and door handles.

9.3.5 Emergency response (Sections 8.1.4 and 8.1.4.4)

- Have an emergency response plan. Such a plan must be part of any prevention program, and there must be personnel with adequate training in emergency response.
- In an emergency situation (accident, spill or equipment malfunction), use protective suits made of laminate (such as Tyvek®), with double gloves, shoe covers and respiratory protection—PAPR or greater level of protection.

9.3.6 Waste storage and management (Section 8.1.4.2)

- Draw up a waste storage procedure and a waste management plan (collection, storage and disposal) taking into account the nature of the risks associated with nanomaterials and the quantities involved.

9.3.7 Medical surveillance (Section 8.1.4.1)

- In Québec, the authors recommend analyzing the need for medical surveillance, based on scientific advances and using the approach developed by the Expert Committee on Screening and Medical Surveillance in Occupational Health [208] (in French).
- Depending on the product used, regular medical checkups geared to the potential risks to workers' health may be scheduled, especially if the product's large-scale counterpart has already demonstrated specific toxic effects.
- Checkup results must be kept confidential by the establishment's health department or external health services provider.

9.3.8 Other program components

- The prevention program must also incorporate other programs related to occupational health and safety:
  - Training and information
  - Respiratory protection (Section 8.1.5)

- Emergency response plan
- Written instructions describing how to perform various operations, efficiently and safely, etc.

9.3.9 Documentation

- All information, data, assumptions, certainties and limitations, conclusions, decisions, actions and methodologies used to assess and manage risk, evaluate performance, conduct audits or develop and follow up on the prevention program must be meticulously compiled and conserved in accordance with regulations. This information must be clear, comprehensible and easily accessible.

9.4 Implementation ("Do")

The action plan is implemented in stages as set out during the planning. Implementation is the practical application of all the previous efforts to identify risks and select the measures needed to control them.

9.5 Evaluation ("Check")

This often-neglected step consists in checking the performance of all processes and procedures used. It must be carried out after implementation of the action plan and repeated regularly. It is critical to the achievement of the objectives set during planning.

Once the action plan has been implemented, it is important to check the performance of the new procedures and processes, and of any improvements made to the workplace. Each new element or modification—whether it involves equipment, responsibilities, work methods or anything else—must be evaluated to make sure it meets the initial objectives.

Moreover, compliance must be monitored through a planned program of regular audits. The efficacy of the prevention plan components and the achievement of the initial objectives must be constantly demonstrated. In various research projects, the authors have observed that among the main factors that undermine the efficacy of preventive measures over time are process changes without adjustments to work methods or assessment of the impact on potential emission of airborne pollutants; installation of new equipment without assessment and without dissemination of necessary information about associated risks; arrival of new employees without proper training; inadequate maintenance of ventilation systems; and foremen and workers forgetting instructions.

9.6 Correction ("Act")

Corrective action must be taken rapidly after any check or audit showing performance that fails to meet the initial program objectives. The corrective measures taken must be evaluated in turn, and the process repeated until the objectives are reached. Do not forget to document everything.

9.7 Management review

A prevention program is a dynamic entity that must be regularly presented and discussed with senior management. It must be continually updated in order to improve it and incorporate new knowledge. Updating is done through an iterative process and on a regular basis.

From the current scientific data, it may be concluded that there is only partial knowledge about the specific risks of nanomaterials and the exposure levels in most workplaces. Research is on-going, and the literature is being continually enriched by new and useful knowledge. Laboratories and production plants also evolve over time, with new production lines and new workers. Medical surveillance, if deemed useful and introduced, may even identify new risks that were not suspected before. In short, the prevention program must be updated to incorporate new knowledge.

The management review is an opportunity for management to take stock of the work done, to find out about new knowledge acquired (e.g., worker exposure levels, efficacy of control measures, new scientific data), to set new prevention targets along with the necessary resource allocations and to reassert the importance of prevention. In this way, the improvement process can continue.

Access to specialized resources

Given the complexity of many aspects of nanotechnologies, optimum use of this guidance requires a certain knowledge of occupational health and safety.

In situations where the establishment does not have the required expertise, external resources may be needed. In Québec, the CSST, joint sector-based associations, regional health and social services agencies, CSSSs involved in occupational health and safety, prevention mutuals and some consultants are able to develop a conventional occupational hygiene approach and direct the establishment toward more specialized resources if needed.

The occupational hygiene laboratory of the Occupational and Environmental Health Department, School of Public Health, Université de Montréal, has the expertise to assess workplaces that use nanomaterials (see Appendix A).

10. CONCLUSION

This best practices guide for handling nanomaterials was produced by a joint research team from the IRSST and the Université de Montréal with the support of an advisory committee made up of industry stakeholders, all joining forces to achieve a common goal: *to promote the safe development of nanotechnologies in Québec* by developing and disseminating a tool for occupational health and safety management in research laboratories and establishments producing or using nanomaterials.

The nanotechnology industry is expanding rapidly, and the number of workers potentially exposed to nanomaterials and their hazards—fire, explosion, toxicity—is rising steadily. Although research on health risks has increased significantly in recent years, many questions remain unanswered. The knowledge developed in the past five years has nevertheless shown the effectiveness of preventive measures when used correctly.

This makes it possible to support the safe development of nanotechnologies in Québec. In this guide for researchers and industry, we have tried to summarize the state of knowledge and to provide information and recommendations for managing and controlling risks in order to prevent accidents and occupational diseases.

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APPENDIX A: AIRBORNE ENGINEERED NANOMATERIALS AND PREVENTIVE MEASURES IN QUÉBEC WORKPLACES

The IRSST and the occupational hygiene laboratory of the environmental and occupational health department at the Université de Montréal went to eight workplaces in Québec (research laboratories and production or integration facilities) to characterize the air quality and assess potential occupational exposure to engineered nanomaterials during various tasks. Another objective was to assess the preventive measures implemented in these workplaces.

Two measurement strategies were used: 1) real-time measurement of mass concentration, number concentration, specific surface area concentration and particle size distribution using direct-reading instruments (DRIs) (Table A1), and 2) particle sampling for electron microscopy analysis (Table A2).

Table A1: Direct-Reading Instruments

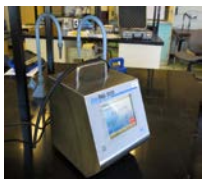
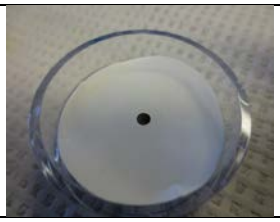
Instrument	TSI P-Trak 8525	TSI DustTrak DRX 8533	TSI AeroTrak 9000	TSI AeroTrak 9306	Dekati Electrical Low Pressure Impactor (ELPI)	TSI Engine Exhaust Particle Sizer 3090 (EEPS)
						
Detection mode	Condensation particle counter	Laser photometer	Diffusion charger	Optical particle counter	Electrical detection combined with low-pressure cascade impactor	Spectrometer
Parameter measured	Number concentration 20 to 1,000 nm	Mass concentration Size fractions PM1, PM2.5, PM10 and respirable	Specific surface area concentration Alveolar fraction 10 to 1,000 nm	Number concentration Size fractions 0.3 µm, 0.5 µm, 1 µm, 3 µm, 5 µm and 10 µm	Particle size distribution Aerodynamic diameter 12 size fractions between 24 nm and 6.7 µm	Particle size distribution Electrical mobility diameter 32 size fractions between 5.6 and 560 nm
Range	0–5 x10^5 particles /cm³	0.001–150 mg/m³	1–10,000 µm²/cm³	0–2x10^6 particles /cm³	-	-

Table A2: Electron microscopy analyses

	Information	Sampling equipment
FEG-SEM[1]	Morphology	 37-mm cassette with 2-µm polytetrafluoroethylene (PTFE) filter with attached electron microscope grid (copper, 200 mesh) SKC AirLite® 2L/min pump
TEM-EDX[2]	Morphology and elemental chemical composition	

1 FEG-SEM: Field emission gun coupled with scanning electron microscopy
2 TEM-EDX: Transmission electron microscopy coupled with energy dispersive x-ray spectrometry

Both fixed-station and "quasi personal" measurements were taken. "Quasi personal" refers to measurements taken as close as possible to a worker's respiratory tract by a technician or hygienist. Figure A1 shows all the direct-reading instruments used. The measurements covered

various types of engineered nanomaterials (nanometals [copper, zinc], boron nanotubes, single-walled and multiwalled carbon nanotubes, carbon nanofibres, nanocellulose and crystalline nanocellulose), various tasks (weighing, pouring, transfer, production, collection, cleaning, heating, homogenization, and maintenance) and various control methods (isolation, containment, restricted-access areas, local and general ventilation, PPE).

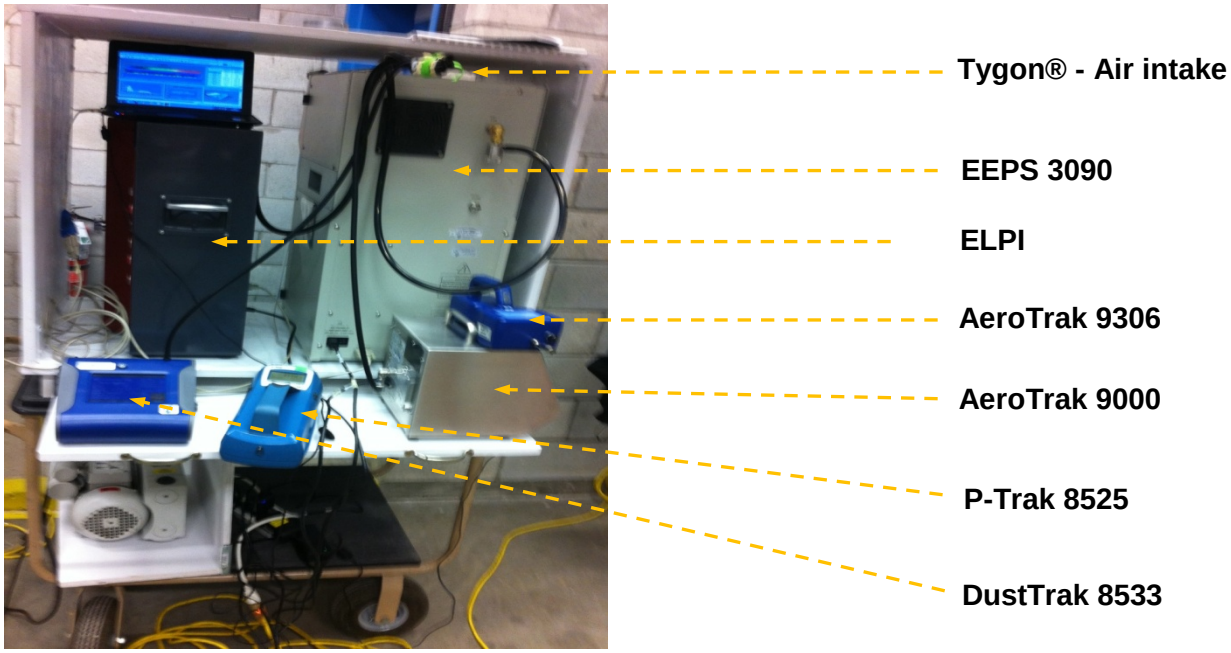


Figure A1: Direct-reading instruments used

Table A3 summarizes the measurement operations in the eight workplaces visited and the results obtained. First of all, the results confirmed that the strategy used to assess possible occupational exposure is effective for a wide range of products and workplaces. However, several limitations regarding the use of DRIs were also identified, in particular with regard to background particles. A high variability in background concentrations was observed in certain workplaces depending on the time of day or even the particular location within the plant or laboratory. In other workplaces, welding, the use of propane-powered lift trucks, waterblast cleaning operations or the heating of solvents and polymers could significantly influence instrument readings. In such situations, the use of DRIs must be combined with microscopy analyses.

- DRIs can be used not only to identify the tasks that generate airborne particles and to estimate the aerodynamic diameter or electric mobility of those particles, but also to determine whether nanoparticles are being emitted in the worker's breathing zone despite control measures such as a fume hood, a source capture system or containment of a process or work area.
- Microscopy can be used not only to characterize and confirm the nature of aerosols, their state of agglomeration, and their size and shape, but also to study the possibility of cross-contamination (engineered nanomaterials and background particles).

With regard to controls, source capture is recommended for controlling worker exposure (Section 8.1). Engineering controls (Figures A2 and A3) include glove boxes, fume hoods and

source capture ventilation systems. Glove boxes are extremely effective at containing nanomaterials at source; however, one of the glove boxes was defective, and tore the gloves. Most of the fume hoods proved highly effective or relatively effective. Nevertheless, it was demonstrated that particles could escape from them during some tasks. It is important to follow the INRS [1] and NIOSH [176] guidelines for optimum use of fume hoods (Section 8.1.3). Source capture ventilation systems do not ensure very good control of particles in the workplace (Table 8). Even when used according to industry best practice, they must never be the sole exposure control in place. Another effective at-source control method is to collect nanopowders in an airtight bag directly at the reactor output.

Figure A2: Source capture system and fume hood

Table A3. Summary of measurement operations and recommendations

NM type	Type of enterprise	Potential exposure	Airborne particle size (nm)	Particle form	Controls	Specific recommendations based on emission readings at workstations
Crystalline nanocellulose	Producer	Bagging Maintenance	[100–1,000] [1,000–10,000]	Amorphous agglomerate	Contained area Respiratory protection (APF=10)	Capture NMs at source during bagging Maintain respiratory protection program
Nanocellulose	Research/ Production	Grinding Production Sieving Cleaning	[5–40]	Fibrous	Fume hood	Capture NMs at source Repair and maintain general ventilation Follow recommendations for fume hood use Modify work practices Set up a respiratory protection program
Copper nanoparticles	Producer	Cleaning	[100–1,000]	Spherical	Source capture Fume hood Respiratory protection (APF=25-1,000)	Modify certain work practices Maintain respiratory protection program
Single-walled carbon nanotubes	Producer	Collection Cleaning	[200–10,000]	Fibrous agglomerate	Fume hood Contained production room Locker room adjoining work area Respiratory protection (APF=100)	Follow recommendations for fume hood use Revise respiratory protection program and conduct airtightness tests
Boron nanotubes	Research/ Production	Collection	[0–100]	Fibrous	Containment Respiratory protection (APF=10)	Maintain good work practices Check ventilation system in contained room Maintain respiratory protection program
Multiwalled carbon nanotubes	Research/ Integration	Homogenization Thermal analysis Milling	[24–500]	Fibrous	Glove box Respiratory protection (APF=10)	Change gloves in glove box Do the homogenization under a fume hood Modify polishing and sawing practices Maintain respiratory protection program
Zinc nanoparticles	Research/ Integration	Process Cleaning	[24–200]	Spherical	Restricted access to laboratory Respiratory protection (APF=10)	Capture NMs at source Revise respiratory protection program
Carbon nanofibres Nanometric inorganic salts	Research/ Integration	Collection Cleaning	[100–400]	Fibrous and spherical	Contained area Double locker room adjoining work area Fume hood General ventilation (20 air changes/h) Respiratory protection (APF=25-1,000)	Follow recommendations for fume hood use Modify locker room exit sequence Maintain respiratory protection program

NM: Nanomaterial; APF: assigned protection factor

Figure A3. At-source containment systems

Several other strategies for confining or limiting the generation of nanomaterials were evaluated and proven effective. Figure A4 shows other controls, such as confinement of stages likely to generate nanomaterials to specific areas or containment of the entire process in a dedicated room with its own ventilation system. Some of these dedicated areas have adjoining locker rooms (single or double) to prevent cross-contamination.

Figure A4. Work area containment

Finally, in most workplaces, respiratory and cutaneous protection equipment was used (Figure A5). For respiratory protection, workers used half masks, full masks, head covers with filter systems, powered air-purifying respirators (PAPRs) or supplied-air respirators (SARs). Because there are no exposure threshold limit values, the choice of respiratory protection cannot be based on a quantitative risk assessment, but it must take into account the type of nanomaterial, toxicological knowledge and estimated exposure potential. In some workplaces, shortcomings in the respiratory protection program were noted: no fit test, no training or follow-up, and sometimes even failure to enforce mandatory wearing of respiratory protection. Some had respiratory protection but no structured program for it, and in some cases the masks were not even certified. The recommendations in Section 8.1.5.1 should be implemented to ensure adequate respiratory protection for workers.

In many workplaces, Tyvex® coveralls or lab coats were worn. Note that lab coats must always be made of nonwoven fabric. Many workers also wore gloves and forearm guards for skin protection and to avoid contaminating clean areas.

Figure A5. Personal protective equipment

APPENDIX B: RESEARCH LABORATORY EXPOSURE CONTROL PLAN BASED ON EXPOSURE POTENTIAL

This research laboratory exposure control plan based on exposure potential is reproduced here with the permission of Janette de la Rosa Ducut, editor of the Nano Toolkit developed by the California Nanosafety Consortium of Higher Education, 2012, entitled *Working Safely with Engineered Nanomaterials in Academic Research Settings* [178].

Risk Level		Controls
Category 1 Low exposure potential	**Engineering**	• **Fume hood or biosafety cabinet.** Perform work with open containers of nanomaterials in liquid suspension or gels in a laboratory-type fume hood or biosafety cabinet, as practical.
	Work practices	• **Storage and labeling.** Store in sealed container near other compatible chemicals. Label chemical container with identity of content (include the term "nano" in descriptor). • **Preparation.** Line workspace with absorbent materials. • **Transfer in secondary containment.** Transfer between laboratories or buildings in sealed containers with secondary containment. • **Housekeeping.** Clean all surfaces potentially contaminated with nanoparticles (i.e., benches, glassware, apparatus) at the end of each operation using a HEPA vacuum and/or wet wiping methods. DO NOT dry sweep or use compressed air. • **Hygiene.** Wash hands frequently. Upon leaving the work area, remove any PPE and wash hands, forearms, face, and neck. • **Notification.** Follow institution's hazard communication processes for advanced notification of animal facility and cage labeling/management requirements if dosing animals with the nanomaterial.
	PPE	• **Eye protection.** Wear proper safety glasses with side shields (for powders or liquids with low probability for dispersion into the air). • **Face protection.** Use face shield where splash potential exists. • **Gloves.** Wear disposable gloves to match the hazard, including consideration of other chemicals used in conjunction with nanomaterials. • **Body protection.** Wear laboratory coat and long pants (no cuffs). • **Closed toe shoes.**
Category 2 Moderate exposure potential	**Engineering**	• **Fume Hood, Biosafety Cabinet, or Enclosed System.** Perform work in a laboratory-type fume hood, biosafety cabinet* (must be ducted if used in conjunction with volatile compounds), powder handling enclosure, or enclosed system (i.e., glove box, glove bag, or sealed chamber).
	Work Practices	• **Category 1 Work Practices.** Follow all work practices listed for Category 1. • **Access.** Restrict access. • **Signage.** Post signs in area. • **Materials.** Use antistatic paper and/or sticky mats with powders.
	ÉPI	• **Category 1 PPE.** Wear all PPE listed for Category 1. • **Eye protection.** Wear proper chemical splash goggles (for liquids with powders with moderate to high probability for dispersion into the air). • **Gloves.** Wear two layers of disposable, chemical-protective gloves. • **Body protection.** Wear laboratory coat made of non-woven fabrics with elastic at the wrists (disposable Tyvek®-type coveralls preferred). • **Closed toe shoes.** Wear disposable over-the-shoe booties to prevent tracking nanomaterials from the laboratory when working with powders and pellets. • **Respiratory Protection.** If working with engineering controls is not feasible, respiratory protection may be required. Consult an EH&S professional for more information (i.e., N95 respirator, or one fitted with a P-100 cartridge).
Category 3 Higher exposure potential	**Engineering**	• **Enclosed System.** Perform work in an enclosed system (i.e., glove box, glove bag, or sealed chamber).
	Work Practices	• **Category 2 Work Practices.** Follow all work practices listed for Category 2.
	PPE	• **Category 2 PPE.** Wear all PPE listed for Category 2. • **Body protection.** Wear disposable Tyvek®-type coveralls with head coverage. • **Respiratory Protection.** If working with engineering controls is not feasible, respiratory protection may be required. Consult an EH&S professional for more information (i.e., N95 respirator, or one fitted with a P-100 cartridge).

APPENDIX C: EXPOSURE CONTROL DATA FROM A VARIETY OF WORKPLACES

Table C1: Exposure levels and effectiveness of workplace controls

Material	Process	Operation	Control	Concentration without control	Concentration with control	Particle size	Comment Reference value	Reference
Carbon nanotube (research)	N/A	Mix for composites	Ventilated containment of mixer	172.9-193.6 f/mL in ambient and breathing zones	0.018–0.05 f/mL	Diameter: 52–56 nm Length: 1,473–1,760 nm		[197]
Carbon nanotube (research)	N/A	Mix for composites	Ventilated containment of mixer	37 µg/m^3 (weighing) 430 µg/m^3 (mixer)	Not detected	Diameter: 52–56 nm Length: 1,473–1,760 nm		[197]
Zinc oxide (insoluble)	Sol-gel spraying		Ventilation at source	225,000 particles/ cm^3	7,200–12,000 particles/cm^3			[255]
Manganese oxide (insoluble)		Reactor cleaning	Ventilation at source	3.6 mg/m^3	0.15 mg/m^3		0.2 mg/m^3	[255]
Cobalt oxide (insoluble)		Reactor cleaning	Ventilation at source	0.71 mg/m^3	0.041 mg/m^3		0.05 mg/ m^3	[255]
Silver oxide (insoluble)		Reactor cleaning	Ventilation at source	6.7 mg/m^3	1.7 mg/m^3		0.1 mg/m^3	[255]
Nanomaterial (type not specified – assumed insoluble)	Gas-phase synthesis	Synthesis	Complete enclosure		0.188 mg/m^3		3 mg/m^3	[256]
Nanomaterial (type not specified – assumed insoluble)	Gas-phase synthesis	Synthesis	Complete enclosure		59,100 particles/cm^3			[256]
Nanomaterials (several types, insoluble and soluble)	Flame spray pyrolysis	Synthesis	Extractor hood		0.037 mg/m^3 PM1 (max) Differentiated from background		3 mg/m^3	[256]
Nanomaterials (several types, insoluble and soluble)	Flame spray pyrolysis	Synthesis	Extractor hood		10,000–20,000 particles/cm^3			[256]
Nanoaluminum		Transfer/ pouring	Various extractor hoods		1,575–13,260 particles/cm^3			[192]

Material	Process	Operation	Control	Concentration without control	Concentration with control	Particle size	Comment Reference value	Reference
SWCNT and MWCNT (research environment)	Synthesis by vapour-phase deposition	Synthesis	Constant-flow hood with face velocity = 0.7 m/s	10^7 p/cc in hood for SWCNTs and $4x10^6$ p/cc for MWCNTs	< 2,000 p/cc in breathing zone for SWCNTs and traces for MWCNTs			[192]
Nano copper		Reactor cleaning	Ventilation at source with flange	714 µg/m^3	47 µg/m^3		In breathing zone	[257]
Nano copper				631 µg/m^3	3 µg/m^3		At source	
Nano nickel				1,467 µg/m^3	239 µg/m^3		In breathing zone	
Nano nickel				170 µg/m^3	6.4 µg/m^3		At source	
Nano iron				335 µg/m^3	32 µg/m^3		In breathing zone	
Nano iron				278 µg/m^3	ND µg/m^3		At source	
Nano manganese				952 µg/m^3	229 µg/m^3		In breathing zone	
Nano manganese				754 µg/m^3	35 µg/m^3		At source	
Welding fumes	Welding	Welding	Overhead exhaust		7.78 x 10^5 particles/cm^3		Quasi-personal	[258]
			Ventilated table + Overhead exhaust		1.48 x 10^4 particles/cm^3		Quasi-personal	
Aligned MWCNT film Research	Chemical vapour deposition	Growth and handling	Quartz tube on lab table; output connected to ventilation system. Purge before opening		No MWCNTs detected by DRI or by electron microscopy during recovery			[259]
MWCNT	Vapour-phase deposition	Synthesis	Closed system and double butterfly transfer valve + LEV at transfer site		1.4 µg/m^3 at packaging 1.0 µg/m^3 at extruder		2.5 µg/m^3 internal OEL	[112]

Material	Process	Operation	Control	Concen-tration without control	Concentra-tion with control	Particle size	Comment Reference value	Reference
Nano manganese	Vapour-phase production	Reactor cleaning	Ventilation at source	3,600 µg/m^3	150 µg/m^3		Near source	[260]
Nano cobalt				710 µg/m^3	41 µg/m^3		Near source	
Nano silver				6,700 µg/m^3	1,700 µg/m^3		Near source	
SWCNT Research and small production units	SWCNT production by laser ablation and high-pressure CO	Collection, transfer and reactor cleaning		0.7-53 µg/m^3				[19]
MWCNT laboratories and small production units 7 locations in all	Synthesis by CVD, ultrasonic dispersion and vaporizatio n	Synthesis by CVD, ultrasonic dispersion and vaporizatio n	Most handling takes place inside fume hood		0.008–0.32 mg/m^3 in breathing zone and 0.013–0.187 mg/m^3 in general Only metal aggregates found by EM, no MWCNTs			[261]
MWCNT, fullerenes, carbon black used in research	Weighing, transfer and ultrasonic dispersion		Fume hood with enclosed ventilation	Higher concentra-tion during sonication than during weighing and transfer				[261]

Other examples can be found in a document published by NIOSH [188] and another published by Safe Work Australia [198] (page 68 and following, download at http://www.safeworkaustralia.gov.au/sites/SWA/about/Publications/Documents/312/EngineeredNanomaterials_Evidence_Effectiveness_WorkplaceControlsToPreventExposure_2009_PDF.pdf)