Chemical Substances and Biological Agents

Studies and Research Projects

REPORT **R-599**

Best Practices Guide to Synthetic Nanoparticle Risk Management

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Brigitte Roberge
Luc Ménard
Charles-Anica Endo

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EXECUTIVE SUMMARY

A new industrial revolution is under way, based on nanotechnologies. The applications should substantially improve the performance of many products and favour economic development, a better quality of life and environmental protection. The very small size of engineered nanoparticles (NPs < 100 nanometres) confers them unique properties not found in larger products of the same chemical composition. Major impacts are anticipated in every field of economic and social activity. Most Québec universities and several researchers are already working on the design of new applications. Many companies are in the startup phase or in operation, or they already incorporate NPs into their processes to improve their products' performance. The trend should be accentuated in the years ahead. In 2007, at the international level, more than 500 nanotechnological products were commercially available, for a world market of $88 billion, which should almost double in 2008.

The synthesis and production of these new materials currently raise many questions and generate concerns, due to the fragmentary scientific knowledge of their health and safety risks. Nonetheless, research has shown real risks related to certain NPs. In general, NPs are more toxic than equivalent larger-scale chemical substances. Their distribution in the organism is differentiated and it is not currently possible to anticipate all the effects of their presence. Moreover, given the large specific surface area of particles of these products, some also present risks of fire or explosion.

These risks nevertheless can be managed effectively with the current state of knowledge, even in this uncertain context. To support safe development of nanotechnologies in Québec, both in industry and in the research community, this best practices guide assembles the current scientific knowledge on identification of the dangers, risk assessment and risk management, regardless of whether this knowledge is NP-specific. From this information, good work practices will be identified. We consider it essential to mention that risk management requires a balance between the searching for opportunities for gains and mitigating losses. To become more effective, risk management should be an integral part of an organization's culture. It is a key factor in good organizational governance. In practice, risk management is an iterative process to be carried out in a logical sequence, allowing continuous improvement in decision-making while facilitating constantly improved performance.

The authors favour a preventive approach aimed at minimizing occupational exposure to NPs when their risk assessment cannot be established precisely. They propose a step-by-step approach, followed by some examples of applications in industry or research. Considering the different exposure routes, the factors that can influence NPs toxicity and the safety risks, the guide essentially is based on identification of the dangers, assessment of the risks and a conventional hierarchy of means of control, integrating NP-specific knowledge when this is available. Its goal is to support Québec laboratories and companies in establishing good practices to work safely with nanoparticles.

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1. PURPOSE OF THIS GUIDE AND ITS INTENDED AUDIENCE

This good practices guide was prepared jointly by the Institut de recherche Robert-Sauvé en santé et en sécurité du travail (IRSST), the Commission de la santé et de la sécurité du travail du Québec (CSST) and NanoQuébec, which share the same objective: to support research organizations and companies in fostering the safe, ethical and responsible development of nanotechnologies in Québec.

The nanotechnology (NT) field is developing extremely rapidly. Over 650 products incorporating NT are already commercially available[1]. This compares to 500 products a year ago. The applications currently envisioned should allow spinoffs in every industrial sector, since nanoparticles (NPs) radically transform the properties of different finished products[2]: increased strength, better electrical conductor, unique optical properties, better resistance, etc. These unique NPs properties are not found in larger-scale substances with the same chemical composition.

NT thus has considerable potential. With the marketing that began barely a few years ago, the World market for products containing NPs reached $88 billion in 2007 and should pass the $150 billion market in 2008. By 2012, it is forecast that annual worldwide sales of “nano” products will exceed $1000 billion[3].

With such potential spinoffs, all industrialized countries have ambitions of capturing market share and have produced an NT development plan in this sense. Québec is no exception to the rule. Most Québec universities have research teams working on the development of new NPs, new products or new nanotechnological applications. At least four general and vocational colleges (CEGEPs) have a nanotechnology training program. More than sixty companies are established or in the startup phase in Québec, in addition to companies that purchase NPs to incorporate them into their processes or improve their products’ performance.

In this context, the guide could be useful not only to employers, employees and members of the health and safety committees for the development of the prevention program in their facilities, but to the stakeholders of the prevention network in occupational health and safety (inspectors, hygienists, physicians, nurses, technicians). It could also be useful to consultants, the Quebec legislator, and any individual or organization involved in the nanotechnology field.

1 Woodrow Wilson Center for Scholars; http://www.wilsoncenter.org/.

2 Claude Ostiguy, Gilles Lapointe, Luc Ménard, Yves Cloutier, Mylène Trottier, Michel Boutin, Monty Antoun, Christian Normand. “Nanoparticles: Current Knowledge about Occupational Health and Safety Risks and Prevention Measures”, Studies and Research, IRSST, Report R-470, September 2006, 100 pages.

3 Claude Ostiguy, Brigitte Roberge, Catherine Woods, Brigitte Soucy, Gilles Lapointe, Luc Ménard. “Nanoparticles: Current Knowledge about Occupational Health and Safety Risks and Prevention Measures”, Second Edition, Studies and Research, IRSST, *In preparation*.

2. A WIDE VARIETY OF NANOPARTICLES[4]

An international consensus establishes that NPs are engineered particles ranging from 1 to 100 nanometres (nm or 10^{-9} m). They are synthesized deliberately to exploit the unique properties revealed at these dimensions. To visualize this tiny size, the same ratio of 10^{-9} is obtained by comparing the diameter of a dime to the diameter of the earth.

The definition of NPs chosen in this guide excludes products of comparable dimensions originating from natural, human or industrial sources, such as part of the smoke or fumes generated by forest fires, cigarettes, internal combustion engines or welding operations. Every environment contains a certain quantity of non-NP nanometric particles: these particles are called ultrafine dusts (UFD).

NPs can be classified in various ways, but we should first remember that some will have only one nanometric dimension (e.g., graphene sheets), two dimensions (e.g., nanofibres) or three dimensions (e.g., cubes, spheres…), while some processes are capable of directly applying surface coatings with only one nanometric dimension (thickness). Another way to classify NPs is to divide them into two categories: particles that only exist in nanometric dimensions and particles that also exist in larger scales but are produced as NPs to take advantage of their unique properties on this scale.

Carbon nanotubes, fullerenes, quantum dots and dendrimers are the main particles that exist only in nanometric dimensions. On the other hand, many inorganic products (metals [cobalt, copper, gold, iron…], metal oxides [titanium dioxide, zinc oxide…], ceramics…) and organic products (polyvinyl chloride, latex…) can be synthesized in these sizes. In fact, nearly every solid product can be reduced to nanometric dimensions, but not all would necessarily exhibit commercially interesting properties.

Carbon nanotubes

Carbon nanotubes (CNT) (Figure 1) represent a new crystalline form of pure carbon, which only exists in these sizes. CNT are composed of cylinders of graphite sheets wound around themselves in one or more layers. Their synthesis normally requires the use of a metal catalyst, which will contaminate the end product. The diameter can be as small as 0.7 nm and the tubes can be as long as several millimeters. Since they are very stable chemically and thermally, CNT are good heat conductors, showing a strong molecular absorption capacity and metallic or semiconductive properties, depending on their mode of synthesis. CNT can be more than 60 times stronger than steel, while being six times lighter.

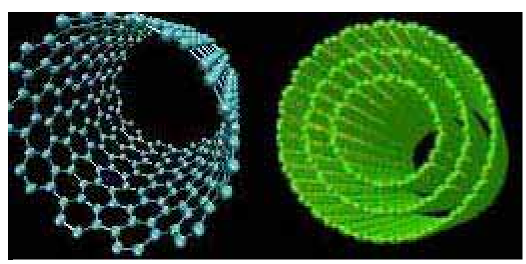


Figure 1: Schematic illustration of single-walled and multi-walled carbon nanotubes

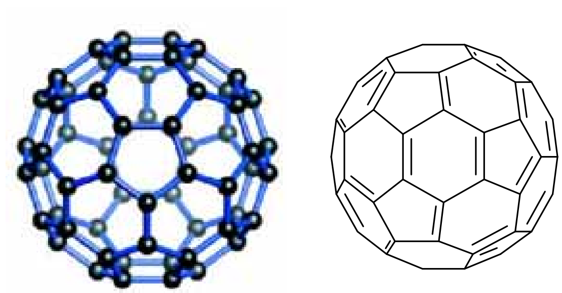
[4] To streamline the best practices guide, only a few references are included. A detailed list of relevant references is available in the two summary documents published by Ostiguy *et coll*. In 2008, which are available on the website at www.irsst.qc.ca

Among the many applications under study, we note the use of CNT in electromagnetic shielding, as polymer composites, for hydrogen storage and in batteries.

Fullerenes

Pure fullerenes are another new crystalline form of carbon (Figure 2). They have a variable number of carbon atoms, which can range from 28 to more than 100 atoms, forming a hollow sphere. The best-known form, containing 60 carbon atoms, is C_{60}. Fullerenes, like CNT, can be modified in many ways by bonding organic or inorganic groups to them or incorporating various products. These modifications will have a major impact on their properties and toxicity. In current studies of the potential applications of fullerenes, the most attention seems to focus on solar and lithium batteries, electronics, storage of gases, such as methane and oxygen, additives to rubber and plastics, and treatment of various diseases, including AIDS and cancer.

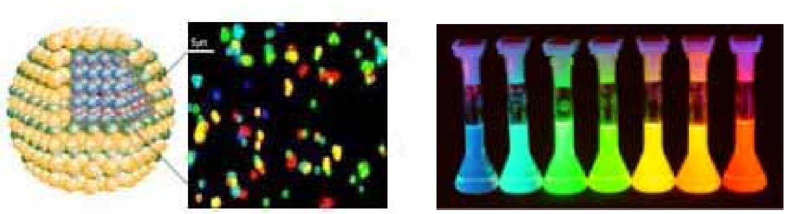
Figure 2: Schematic illustration of the C_{60} fullerene, showing alternating cycles of 5 and 6 carbon atoms, allowing strong electronic delocalization



Quantum dots

Quantum dots typically are composed of combinations of chemical elements from Groups II and IV or Groups III and V of the periodic table. They have been developed in the form of semiconductors, insulators, metals, magnetic materials or metal oxides. In sizes of about 1 to 10 nm in diameter, they display unique optical and electronic properties (Figure 3). For example, quantum dots can absorb white or ultraviolet light and reemit it as a specific wavelength.

Figure 3: Example of a quantum dot and its optical effects, depending on NPs size



Depending on the quantum dot’s composition and size, the light emitted can range from blue to infrared. The flexibility of quantum dots and their associated optical properties allow applications to be envisioned in different fields, such as multicolour optical coding in the study of gene expression, high-resolution and high-speed screens, and medical imaging. Some quantum dots are modified chemically to produce drug vectors, diagnostic tools and solar batteries.

Dendrimers

New structures have also been synthesized in these sizes. This is particularly true of dendrimers, which represent a new class of nanoscaled polymers with controlled structure. These are synthetic three-dimensional macromolecules developed from a monomer, with new branches added, step by step, in successive tiers, until a symmetrical structure is synthesized. Dendrimers are considered to be basic building blocks for large-scale synthesis of organic and inorganic nanostructures ranging in size from 1 to 100 nm and displaying unique properties. They allow precise, atom-by-atom control of nanostructure synthesis, depending on the dimensions, shape and chemistry of the desired surface. In particular, it is anticipated that they will be used extensively in the medical and biomedical field.

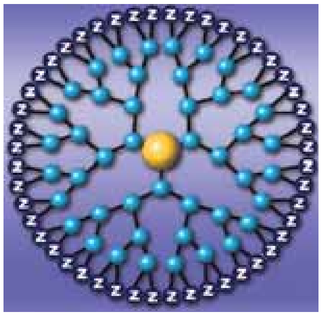


Figure 4: Dendrimer diagram

Other nanoparticles

There is a wide variety of NPs with organic or inorganic composition. Thus, most metals can be produced in nanometric dimensions. For example, gold NPs reveal an optical resonance spectrum in the visible range, which is sensitive to environmental conditions and to NPs size and shape. Their unique properties offer the prospect of a series of applications, particularly as optical markers or cancer treatment agents. Silver is currently used mainly for its antimicrobial properties. Metal nanowires of gold, copper, silicon and cobalt have also been produced, which can serve as conductors or semiconductors and could be used in nanoelectronics.

Several nanoscaled metal oxides have been fabricated, but the most common, because of their larger-scale production, are undoubtedly silica (SiO_2), titanium dioxide (TiO_2) and zinc oxide (ZnO). They are used in many fields, including rheology (SiO_2), as active agents and additives in the plastics and rubber industries (SiO_2), in sunscreens (TiO_2, ZnO) and in paint (TiO_2). Some structures display interesting properties, allowing potential applications to be envisioned in various fields: sensors, optoelectronics, transducers, medicine…

There are very many potential uses of NPs: energy saving for vehicles, development of renewable energies, pollution reduction, water filtration, construction materials, medical applications, cosmetics, pharmaceuticals, textiles, electronics, paints, inks, etc.

3. SYNTHESIS OF NANOPARTICLES

NPs can be synthesized according to a bottom-up or top-down approach. The bottom-up approach fabricates NPs one atom or one molecule at a time, using processes such as chemical synthesis, autoassembly and assembly by individual positioning. The top-down approach takes a large-scaled substance and modifies it to nanometric dimensions. Etching, precision engineering, lithography and crushing are common approaches. Some of these techniques are commonly used in a clean room in the electronics industry. The two approaches bottom-up and top-down tend to converge in terms of the size of the synthesized particles. The bottom-up approach appears to be richer, in the sense that it allows production of a wider variety of architectures and often better control of the nanometric state (positioning of molecules, homogeneity of products and sizes, and relatively monodispersed granulometric distribution). The top-down approach, while often capable of higher-volume production, makes control of the nanometric state a more delicate operation.

AFSSET (2006) divides the synthesis processes into three categories, depending on the approach used: chemical methods, physical methods and mechanical methods (Table 1).

Table 1: Main approaches to synthesis of nanoparticles (Afsset, 2006)

Chemical methods
Vapour phase reactions (carbides, nitrides, oxides, metal alloys, etc.). Reactions in liquid medium (most metals and oxides) Reactions in solid medium (most metals and oxides) Sol-gel techniques (most oxides) Supercritical fluids with chemical reaction (most metals and oxides and some nitrides) Reactions by chemical coprecipitation or hydrolysis
Physical methods
Evaporation / condensation under partial pressure of an inert or reactive gas (Fe, Ni, Co, Cu, Al, Pd, Pt, oxides) Laser pyrolysis (Si, SiC, SiCN, SiCO, Si_3N_4, TiC, TiO_2, fullerenes, carbonized soots, etc.) Combustion flames Supercritical fluid without chemical reaction (materials for vectorization of active principles) Microwaves (Ni, Ag) Ionic or electronic irradiation (production of nanopores in a material of macroscopic dimensions or nanostructures immobilized in a matrix) Low-temperature annealing (complex metal and intermetallic alloys with three to five basic elements - Al, Zr, Fe.) Thermal plasma (ceramic nanopowders, such as carbides (TiC, TaC, SiC), silicides ($MoSi_2$), doped oxides (TiO_2) or complex oxides (perovskites)) Physical deposit by vapour phase (deposits of TiN, CrN, (Ti,Al)N, in particular)
Mechanical methods
The mechanosynthetic and mechanical activation processes of powder metallurgy – high-energy crushing (all types of materials (ceramic, metallic, polymers, semiconductors)) Consolidation and densification Strong deformation by torsion, lamination or friction

4. IDENTIFICATION OF DANGERS

Danger is a property inherent in a substance or situation with the potential to cause effects when an organism, a system or a population is exposed to this agent, whereas risk is the probability that effects will occur on an organism, a system or a population in specific circumstances.

4.1 Health Effects of Nanoparticles

Several studies have been performed on different animal species to determine whether NPs can have toxic health effects. NPs soluble in biological fluids dissolve and their toxic effects are related to their different chemical components, independent of the particle's initial size. These effects are well known, depending on chemical composition, and are not specific to nanometric dimensions. The situation is completely different for NPs that are insoluble or very weakly soluble in the organism. The data currently available on toxicity of insoluble NPs are extremely limited and normally do not allow a quantitative risk assessment or an extrapolation to humans, except possibly for TiO_2. Nonetheless, they reveal some information, which, although fragmentary, gives reason to conclude that NPs must be handled with care. This is because a product mass of the same chemical composition is normally more toxic if it is nanoscaled than if it is larger in size. The worker's exposure thus must be minimized, because several toxic effects have been documented, even though they are extremely variable from one product to another.

Absorption of synthesized nanoparticles

The greatest absorption of dusts in the work environment normally occurs through the pulmonary route. The leading particularity of NPs is based on their pulmonary deposition mode. In fact, the deposit site is highly dependent on their size. Whereas NPs of one or a few nm will be deposited mainly in the nose and throat, more than 50% of NPs of 15-20 nm will be deposited at the alveolar level (Figure 5) (Ostiguy *et al*., 2006).

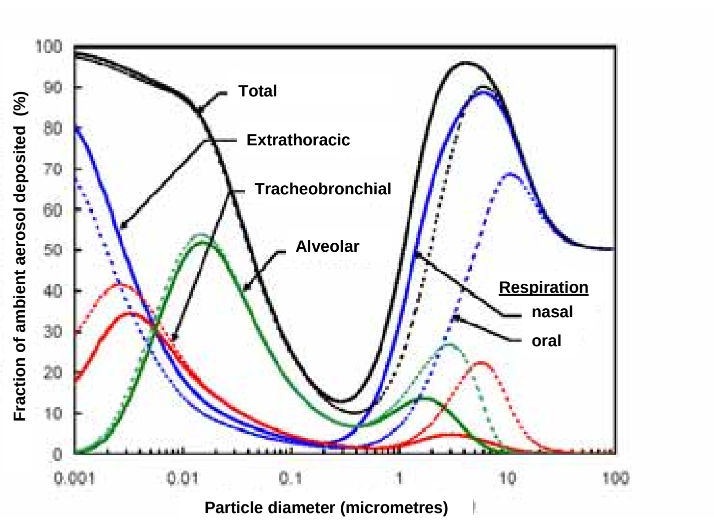


Figure 5: Deposition of inhaled dusts in the airways

Because of their extremely small size, NPs can pass through the extrapulmonary organs while remaining solid. This involves migration of certain solid particles, translocation through the pulmonary epithelial layers to the blood and lymph systems and through the olfactory nerve endings, along the neuronal axons to the brain. The NPs reaching the blood system circulate throughout the body and there is clear evidence that they can be retained by different organs, depending on the nature of the NPs. Several toxic effects have been documented for different organs and depend on the nature of the NPs.

Cutaneous absorption could be another major exposure route for workers handling NPs prepared and used in solution, since these NPs can end up in the circulatory system after passing through all the skin layers. Moreover, absorption can be facilitated when the skin is damaged or when exposure conditions in the work environment (e.g., the humidity rate) are conducive to it. In the case of NPs weakly absorbed by the skin, an allergy and/or contact dermatitis could be observed.

In most situations encountered in the work environment, potential pulmonary absorption would be at least one order of magnitude greater than cutaneous absorption.

Best practices in workplace personal hygiene should greatly limit NPs ingestion. However, NPs can end up in the digestive system after deglutition from the respiratory system via the mucociliary elevator. They are also now used as additives in the food industry, medications and certain related products, thus favouring their absorption. When they will be widely used in different industrial, agricultural or other products, a certain quantity will end up in the environment. NPs can then be chemically modified, absorbed by different bioorganisms and eventually enter the food chain. The translocation of some NPs from the intestine to the blood and the lymph has been shown.

Thus, insoluble NPs can end up in the blood after passing through the respiratory, cutaneous or gastrointestinal protection mechanisms and then be distributed to the different organs, throughout the body, including the brain. Moreover, NPs show a propensity to pass through cell barriers. Once they have penetrated the cells, they interact with the subcellular structures. This leads to induction of oxidative stress as the main NPs action mechanism. These properties of translocation are currently widely studied in pharmacology, because they could allow use of NPs as vectors in routing medications to targeted sites of the body.

On the other hand, in some companies, workers will be exposed by inhalation or by cutaneous contact, and NP could end up distributed throughout the body after absorption.

Nanoparticle toxicity

Toxicity of microscopic particles is normally well correlated to the mass of the toxic substance. However, the situation is totally different in the case of NPs. The different studies showed clearly that toxicity, for a specific substance, varied substantially according to size for the same NPs mass. In fact, toxicity is correlated to multiple parameters (Table 2). The most significant of these parameters seem to be chemical composition, specific surface area and the number and size of particles.

Table 2: Main parameters capable of influencing nanoparticle toxicity

The parameters most often reported	Other reported parameters
Specific surface area	Solubility
Number of particles	Shape, porosity
Size and granulometric distribution	Degree of agglomeration/aggregation
Concentration	Biopersistence
Chemical composition (purities and impurities)	Crystalline structure
Surface properties	Hydrophilicity/hydrophobicity
Zeta charge/potential, reactivity	Pulmonary deposition site
Functional groupings	Age of particles
Presence of metals/Redox potential	Producer, process and source of the material used
Potential to generate free radicals	
Surface coverage	

The literature review of NP-related health risks conducted by our team revealed the scope of the current research in this field and showed that the current knowledge of the toxic effects of NPs is still relatively limited (Ostiguy *et al.*, 2008). Different toxic effects have already been documented at the pulmonary, cardiac, reproductive, renal, cutaneous and cellular levels. Significant accumulations have been shown in the lungs, brain, liver, spleen and bones. Moreover, beyond all the parameters capable of influencing NPs toxicity, some authors consider that, most of the time, a comparison of published results between *in vivo* and *in vitro* tests indicates little correlation.

The context of uncertainty related to the physicochemical characteristics and toxic effects of NP justifies that all the necessary measures be taken immediately to limit exposure and protect the health of potentially exposed individuals, based on a preventive approach and the precaution principle.

Although major trends are emerging that warn of various toxic effects, it emerges that each synthesized NPs product, and even each batch, could have its own toxicity. In such an uncertain context, in which it is almost impossible to have all of the information allowing assessment of the risk, the introduction of strict prevention procedures remains the only way to prevent the development of occupational diseases.

4.2 Safety Risks Related to Nanoparticles

It is well known that an explosive or flammable dust cloud can be formed from organic or metallic materials or certain other inorganic compounds. One of the main factors influencing the ignition energy and violence of an explosion is particle size or area. Many NPs meet these criteria because of their chemical composition and their very small size. They could then exhibit explosive potential and flammability. Given their large surface, they could also have catalytic potential that can translate into an uncontrolled reaction. Other risks are also likely to be linked to their instability or their chemical reactivity.

4.2.1 Explosions

Conditions required to produce an explosion

There is very little documentation on NP-specific explosion risks. Nonetheless, it is possible to anticipate their behaviour by extrapolation based on knowledge related to fine and ultrafine powders. However, this approach cannot be practiced with certainty, given the chemical and physical properties that are often unique to nanometric dimensions. In general, the violence and severity of an explosion and the ease of ignition tend to increase as particle size decreases: the finer the dust, the greater the pressure and the lower the ignition energy. Thus, the NPs should tend to be more reactive, even explosive, than larger-scaled particles of the same chemical composition.

Several conditions must be fulfilled simultaneously for an explosion to occur: a sufficient quantity of combustible particles with an accumulation within the explosible range, these particles normally are found in a confined enclosure containing a sufficient concentration of comburant (oxygen) and subjected to an ignition source.

The special characteristics of the particles (type, chemical and surface composition, size, combustibility, etc.) and the environmental conditions (temperature, humidity, pressure) influence the explosible range. Several organic substances, metals, including aluminium, magnesium, zirconium and lithium, and some inorganic substances are particularly at high-risk.

Risks of explosion can be characterized using tests carried out on different substances of nanometric dimensions under controlled conditions. Some factors must be taken into consideration, including the size of the particles, their concentration in water, and air humidity. One of these tests determines a substance's minimum ignition energy and therefore the minimum energy necessary to make the substance explode (Method ASTM E2019-99 – *Standard Test Method for Minimum Ignition Energy of a Dust Cloud in Air*). Another test consists of estimating the severity of the explosion in order to obtain a virtual overview of the extent of the damage (*Method ASTM E1226-00 – Standard Test Method for Pressure and Rate of Pressure Rise for Combustible Dusts*). However, these tests cannot always be carried out for NPs because the quantity necessary (approximately 500 g) is not always available.

Release and suspension of particles

Solid NPs normally should always be produced and handled in closed, leakproof enclosure, in controlled atmospheres and under conditions designed to safeguard the NPs properties and eliminate any risk of fire or explosion. The equipment and workplaces should be free of any accumulation of deposited dusts that could be resuspended in the air.

Several conditions nonetheless can favour suspension of NPs in the ambient air and create favourable conditions for the occurrence of deflagration which, when produced in closed enclosures or closed rooms, can cause an explosion:

- Types of processes used: poorly insulated or uninsulated process, without enclosure, without local exhaust ventilation when reactors are opened, and generating dispersion of particles into the air, etc.;
- Equipment leaks: poor maintenance, unrepaired cracks…;
- Deficient ventilation: insufficient aspiration flowrate, no local exhaust ventilation, excessively strong ventilation and presence of air currents causing atmospheric resuspension of particles, etc.;
- Inappropriate work methods: inadequate technique for cleaning of premises and equipment, cleaning too infrequent, cleaning with pressured air guns;
- Transfer of particles from one container to another without local exhaust ventilation;
- Processes with frequent machine starts/stops;
- Inadequate handling, transportation and storage methods;
- Accidental spills.

Accumulation of particles in the lines and machines can also cause an explosion. Often it will depend on ventilation that fails to eliminate the particles released by the process during handling, accidental spills, cleaning or maintenance, etc. Closed systems that produce, transfer or store these nanoscaled particles must be equipped with safety devices prescribed by the NFPA (National Fire Protection Association) standards, among others.

Ignition source and environmental factors

The energy (or ignition) source that can cause particles to explode may be electrical (spark, heat release), thermal (heat, flames, etc.), electrostatic (sparks), mechanical (friction, heat, etc.), climatic (lightning, sunlight) or chemical (reactions with other chemical substances, heat release). This activation energy must be high enough (beyond the minimum activation energy) to stimulate a reaction. Within a cloud of particles, there can be a chain reaction, in which one particle’s reaction can trigger that of another particle, which triggers another… Thus, the reaction initiated by a single particle can cause a deflagration.

Other environmental factors could have an effect on the formation or the force of the deflagration. A deflagration into a closed vessel or a closed room could possibly yield an explosion of the vessel or of the room. Among others, temperature, particle turbulence, oxygen concentration (the lower the concentration, the less possibility of explosion), water concentration (the higher the concentration, the less risk for non water reactive NPs) and the simultaneous presence of solvent (if the solvent is flammable, the risks are higher) are factors that can influence the severity of an explosion.

The occurrence of an explosion in one part of the building can trigger suspension of particles, which in turn can cause the formation of a second explosion. A fire can also trigger an explosion.

4.2.2 Fires

Little specific information was found in the literature on the fire potential of NPs, but it is possible to rely on general knowledge concerning larger-sized particles or substances. In general, a fire needs a combustible (wood, metal, dust…), a comburant substance or gas (oxygen, peroxide …) and an ignition source (heat, flame, and spark). These three factors are indispensable to start the fire and the absence of one factor can prevent it. The risks of encountering favourable conditions are higher in the presence of an ignition source. A fire raging in a room containing a sufficient quantity of NPs can trigger a deflagration. Moreover, the fire can provoke various effects on the workers' health, such as asphyxia, cutaneous burns or injuries, in addition to equipment damage.

Ignition source

The ignition source can be electrical, thermal, electrostatic, mechanical, climatic or chemical, as described in the section on explosions. The combined reaction of substances with each other can cause a fire, just as some substances can ignite immediately in contact with air or depending on the ambient conditions.

Environmental conditions

The conditions of the NPs storage and handling environment can influence the outbreak of a fire. Thus, a high temperature may favour it, while a more humid environment may prevent or favour it, as the case may be. The reaction of water with certain oxidizable metals generates hydrogen, which can deflagrate in the presence of an ignition source.

Storage

Storage of nanomaterials is of particular interest due to the different granulometric characteristics, the reactivity of certain particles, possible resuspension and long sedimentation times. Containers must be very tight to avoid leaks and site contamination. Indeed, the small size of the particles, which often seek to agglomerate, offers a very large contact surface with the ambient air, thus sustaining chemical reactivity. To avoid oxidation, and even the explosion of certain metals, nanomaterials must be protected adequately. In particular, it is recommended that dry CNT be stored in double plastic packaging deposited in closed stainless steel drums, which can be stored under inert conditions, for example under vacuum or in a nitrogen atmosphere. Finally, depending on the storage conditions, there can be contact between two substances due to leaks, ventilation, poor maintenance or lack of tightness of the containers. The risk is higher if two incompatible substances are stored near each other.

Figure 6 summarizes the conditions of NPs release or suspension favouring the occurrence of a fire or an explosion.

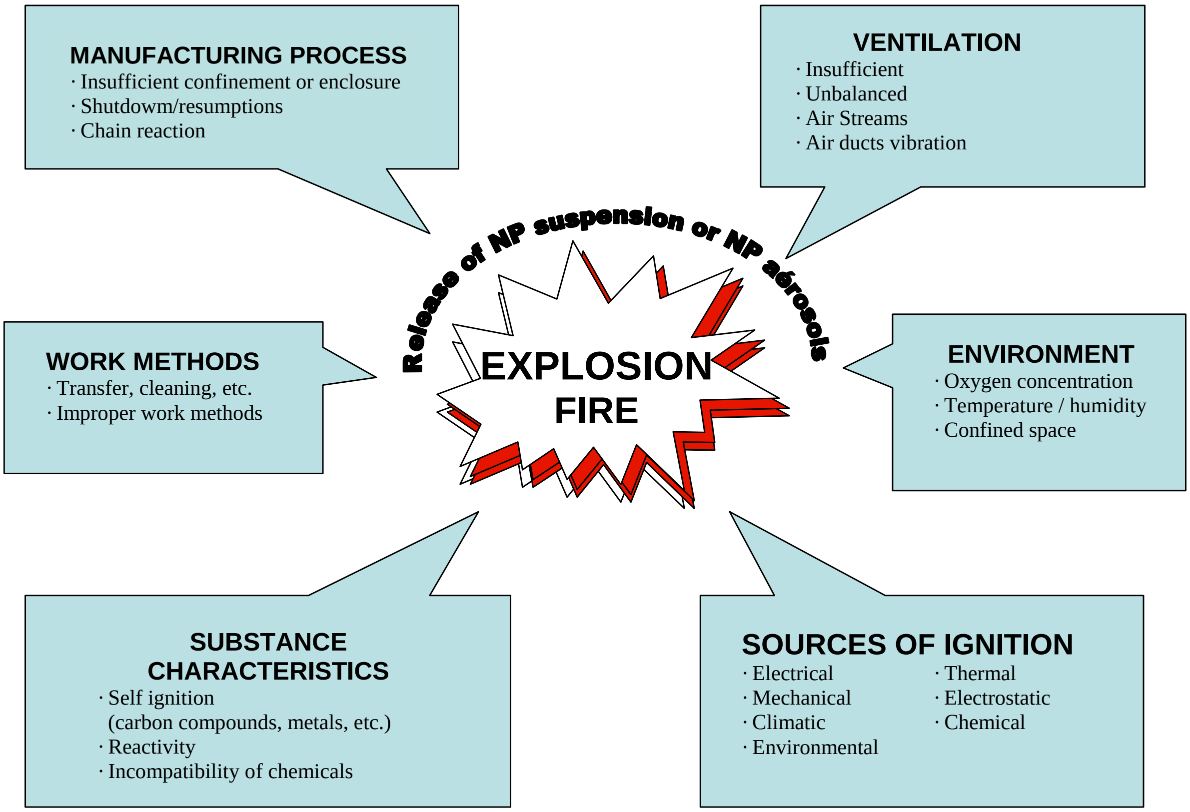


Figure 6: Main factors favouring an explosion or a fire

4.2.3 Catalytic Reactions

Another risk concerns the catalytic reactions that depend on NPs composition and structure. NPs and nanoscaled porous materials have been used for decades as catalysts to increase the speed of reactions or reduce the temperature necessary for reactions in liquids or gases. Consequently, because of their small sizes, they could initiate an unanticipated catalytic reaction and increase the deflagration and fire potential.

NPs leaks and spills thus can contribute to the formation of deflagrations followed by an explosion of a component of the system or of the building or fires, depending on the type and quantity of particles released and the ambient conditions, and expose workers by inhalation or cutaneous contact. These occupational exposures can also occur when there is little or no ventilation or during cleaning with an inappropriate method conducive to resuspension of the deposited particles (ex. compressed air).

4.2.4 Other Safety Risks

In addition to the risks related to the potential of explosibility, fire or catalytic reaction, some NPs could be incompatible and create a dangerous reaction when they come into direct contact with other products. Due to this fact, they would trigger a reaction with energy release, or be corrosive and cause damage to the contact site. Moreover, some NPs could be unstable, decompose, polymerize or display photoactivity, meaning that they have the capacity to produce radicals, which can then oxidize or reduce materials in contact with the NPs. The different processes involved in the synthesis of NPs could also represent specific risks that must be taken into account, for example, the use of high voltage.

4.3 Environmental Risks

Synthetic NPs are likely to be present in the environment due to factory releases (releases of air, wastewater, solid wastes), through leaks or spills during transportation, and via materials containing NPs (during their use, destruction or degradation). This presence is closely linked to the NPs life cycle, from production to use to treatment of releases or wastes.

Once in the environment, the NPs can interact with other particles present, be transformed and differ in size and composition from their point of origin. They then will be dispersed in the different media (water, air, soil) and can affect them and living organisms. In general, the environmental effects of synthetic nanoparticles are little known, while those of ultrafine particles, of dimensions similar to NPs, have been studied for a very long time. However, the studies performed on NPs give a general idea of the potential effects, which will depend on different factors, such as the availability of particles (whether or not they are bonded to other molecules or particles), their quantity, their charge, their toxicity and their sedimentation speed in the environment. The assessment of the consequences for the environment should account for the nature and significance of the emission sources, the transfer mechanisms and routes (air, rainwater and runoff, releases, wastes), the ecosystems (terrestrial and aquatic), living organisms and their interrelations (food, prey-predator).

Because of their very small size, NPs are extremely mobile in the environment. In air, water and soil, they can contaminate flora and fauna and thus end up in the human food chain. These very fine particles have a strong tendency to aggregate and agglomerate. However, if the environmental conditions do not favour their agglomeration and under very low pollution conditions, they could travel long distances by air. The largest particles will be deposited on the soil by gravity or will be drawn into the soil and watercourses by other particles, rain or snow. The characteristics of the substrate on which the NPs will be deposited will also have an effect. It is difficult to document the route and quantity of NPs in the environment, because to date no effective methods exist for monitoring and measuring them specifically[5].

> To protect human populations, air, water, soil, fauna and flora, all effluents, as well as releases from factories and laboratories, should be treated before they are returned to the environment or incinerated.

[5] A scheme of the interactions between the different environmental components is presented in Nanotechnology and Life Cycle Assessment A Systems Approach to Nanotechnology and the Environment, Woodrow Wilson International Center for Scholars.

5. RISK ASSESSMENT

Risk assessment, the process by which risk is estimated or calculated, assumes a good knowledge of the identity of the danger (safety and toxicity of products, dose-response relationships) and the exposure levels and characterization of the dangers at the various workstations.

Risk assessment is therefore a way of determining whether the conditions prevailing in the work environment can:

- Allow the emission of toxic NPs into the ambient air at concentrations high enough to impair workers' health;
- Allow the accumulation of solid aerosols of flammable or explosive NPs at concentrations and under conditions that favour the occurrence of an accident.

The risks related to fires, explosions, catalytic effects and chemical reactions were already discussed in section 4.2. Work with NPs can lead to the formation of inhalable airborne aerosols, mainly if the work is performed with dry solid products without using solvent. Work in a wet medium substantially reduces the potential of generating aerosols in the air without totally eliminating it. It should be used every time it is possible. When working conditions result in the formation of airborne aerosols, there is a risk of occupational exposure, whether in research, production, use, handling, maintenance of equipment and premises, storage, transportation, accidental spills, recycling or waste disposal. Cutaneous contact is also possible in various situations, especially in the presence of liquid suspensions.

The quantitative risk assessment will provide the basic data for the selection of measures and the level of control to be put in place to limit these risks. The control measures thus must be proportional to the different risks estimated during this approach.

5.1 Risk Analysis

The analysis of NP-related risks presupposes a detailed knowledge of the type of NPs handled and their toxicity, the potential exposure levels and the safety risks at the different workstations and for all tasks. It includes different complementary steps and is part of a comprehensive approach intended to control the risk factors. It must be repeated and refined regularly to account for new scientific knowledge and practical modifications related to the specific conditions of the work environment. A structured approach is proposed.

A ***case by case*** approach is to be preferred. In the absence of NP-specific data, it is initially possible to estimate the risks based on those known for the same larger-scaled substance. The overall approach is summarized in Figure 7 and will be detailed in the following sections. It is also applicable to the environment.

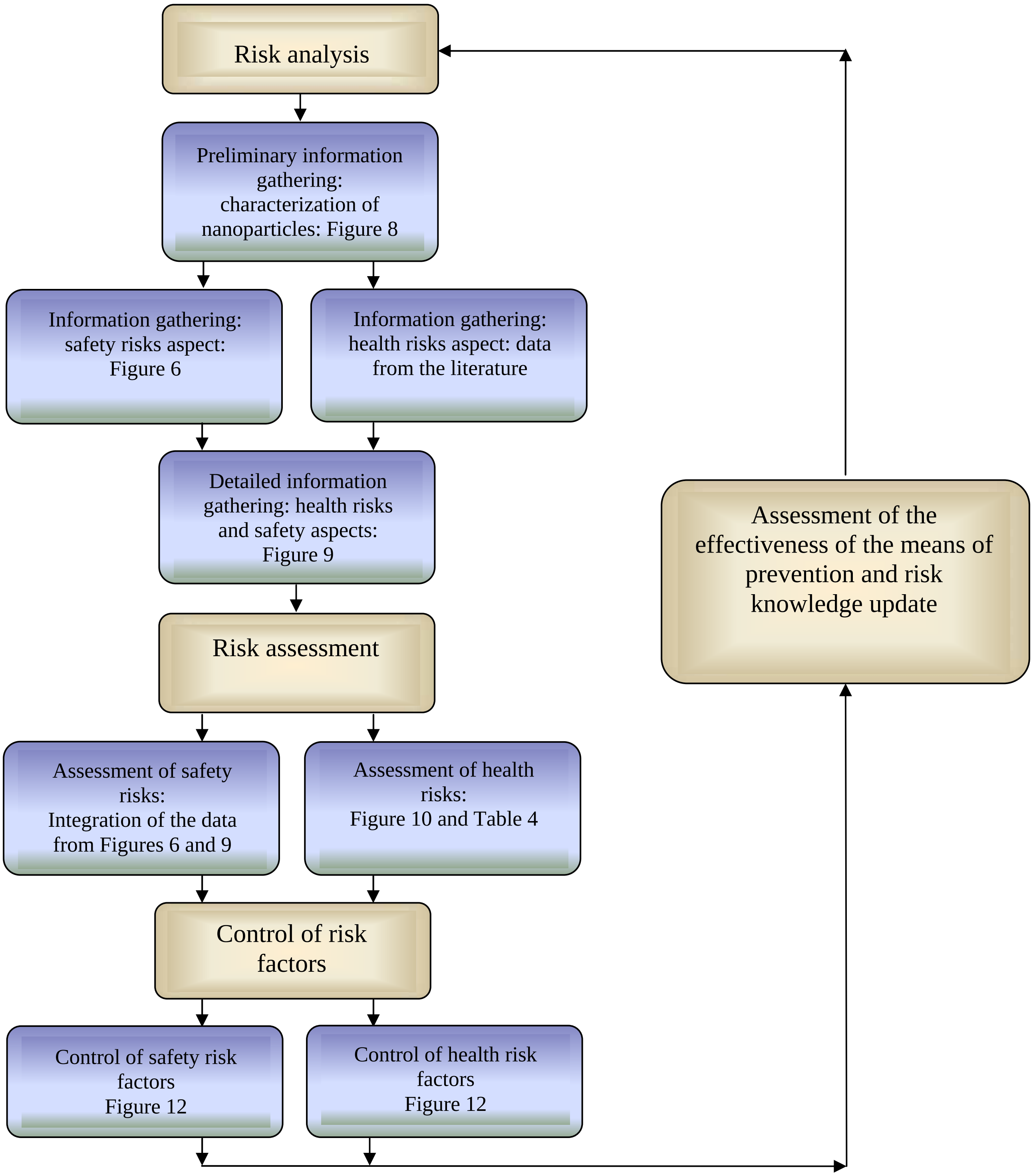


Figure 7: Overall risk analysis and risk management approach in the work environment

5.1.1 Preliminary Information Gathering

The first step of the risk assessment approach is to gather all the available written information allowing identification of the health and safety risk factors in the workplace. For example, Figure 8 summarizes different parameters that can be documented regarding the nature of NPs. They are grouped in major categories.

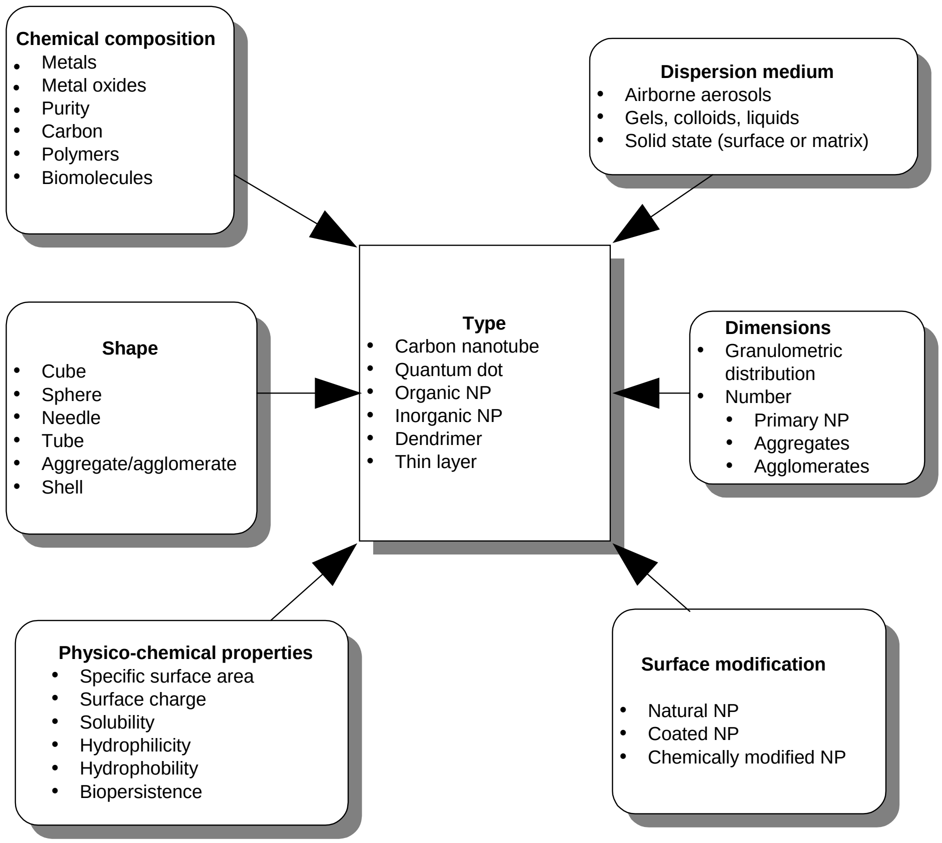


Figure 8: Physicochemical characteristics of nanoparticles

The available information can come from multiple sources: Material Safety Data Sheets produced by the supplier, articles and synthesis documents available in the written and electronic scientific literature, scientific popularization guides, previous documentation already collected on the workplaces, etc.

5.1.2 Detailed Information Gathering

When preliminary information gathering gives reason to suspect a potential risk related to the NPs implemented, it is appropriate to gather more detailed information. After a preliminary meeting with the personnel or management concerned, it is appropriate to visit all of the sites and qualitatively estimate the occupational exposure potential, which can lead to poisoning or generate high concentrations of combustible or explosive NPs likely to trigger an accident. To this effect, Figure 9 lists some major factors that must be documented and that could be required to quantify occupational exposure.

In particular, it is appropriate to document in detail, for each section and department of the work environment and for all operations:

- the concerns of the workers and managers related to the perceived or proven risk factors in the work environment;
- the physical form in which the NPs are handled or produced (raw materials, intermediate products, finished goods) and the ease of dispersion or projection in the air: in solid phase, NPs are more likely to become aerosolized than in liquid phase, in suspension or in colloidal form;
- the processes and equipment: degree of containment (closed or open circuit), potential leaks, etc.;
- the quantities of NPs implemented: the NPs flow in a continuous process;
- the different steps of the process, the departments concerned, the operations accomplished and the ways the NPs are handled, the different tasks and their duration;
- the potential exposure routes;
- the collective and individual means of control put in place: the data available on the actual performance of these systems;
- the number of workers exposed to each risk factor and the exposure time;
- etc.

The preliminary and detailed information gathering should make the required information available for a quantitative assessment of the existing risk in a work environment, whether this risk is toxicological (and thus can lead to poisoning or the development of an occupational disease) or physical (and thus can lead to a fire, an explosion or an undesirable chemical reaction).

5.1.3 Quantitative Assessment of the Accident Risk

In section 4.2, we drew up the guidelines of the risk factors that can lead to accidents, fires or explosions. Although this quantitative assessment must be performed case by case, the main obstacle currently is the lack of specific data available for NPs, particularly in terms of the dust potential of NPs and the explosibility limits. In many situations, the existing data for larger-scaled particles of the same chemical composition are the only data available and must be used as a starting point.

5.1.4 Characterization of the Dust Level and the Occupational Exposure Level

Several situations can favour exposure to nanoaerosols during their production. Among others, we should mention generation of solid NPs in open or non-airtight enclosures, collection, handling or packaging of nanometric powders, maintenance of equipment and the workplaces, and cleaning of ventilation systems. Exposure to NPs liquid aerosols is also possible, particularly during transfer or violent agitation operations. Accidental spills or equipment breakdowns and implementation of NPs for incorporation into products are also likely to expose workers. Finally, mechanical work on these products incorporating NPs, including polishing, cutting, grinding or sanding, could release NPs into the air.

Section 4.1 regarding the potential health effects of NPs has shown that the health effects of NPs exposure are not closely correlated to the mass of the particles, but rather to their specific surface, number, size, state of agglomeration or aggregation, shape, crystalline structure, chemical composition, surface properties, solubility and different other parameters. There is currently no international consensus on the best approaches to use for characterization and assessment of occupational exposure. Despite this situation, preventionists have multiple reasons to characterize NPs in the work environment:

- identification of the main emission sources to be able to establish or improve the emission control strategy;
- assessment of the effectiveness of the control measures put in place;
- assessment of the dust level in situations that could lead to accident risks;
- assessment of personal exposure, eventually allowing exposure to be linked to health effects;
- assessment of personal exposure regarding compliance with the standards in force, when they exist, or a specific action threshold aimed at implementation of control measures.

The assessment strategies and the selection of sample collection and analysis techniques must then be adapted to the specific objectives of the intervention. It has been clearly shown, however, that measuring the mass concentration alone was clearly insufficient for characterization of NPs, in view of this parameter's inability to predict health impairment risks.

It becomes more important to characterize NPs emissions and, as a minimum, estimate the concentration in number of particles, size distribution, specific surface area and chemical composition. Currently it would also be prudent to establish the aerosol mass exposure by granulometric fraction, so as to have maximum information to allow assessment of exposure.

In theory, the assessment of occupational exposure to NPs in the respiratory zone (RZ) should include determination of the different NPs parameters associated with health risks by inhalation and consequently favour characterization of the dispersed airborne particles. This assumes the use of portable instruments positioned at the worker's RZ level whenever possible. **Given the multiple parameters to be measured, no instrument currently can produce a specific NPs analysis to determine all of the relevant characteristics of exposure to synthesized NPs.** Several instruments, sometimes heavy and incompatible with measurement in the work environment, are poorly suited to this type of measurement and do not allow accumulation of data over the entire shift. Finally, no instrument is adapted to NPs sampling in the workers' RZ. NPs exposure can be estimated from samples collected at fixed stations (identification of emission sources, contamination at the workstation, etc.). However, this requires great prudence, because major variations in concentration have been reported in the literature (variations over time and depending on the distance from the source). Studies conclude that the concentrations measured at a personal station (RZ) are normally higher than concentrations at a fixed station.

Selection of a fixed station sampling site (or sites) is a major factor in assessment of exposure. Among other factors, it must account for emission sources, occupational activities, air currents and other particles already present or generated in the workplaces, which can influence the measurements. Ultrafine dusts (UFD) have dimensions similar to NPs and the assessment of the airborne dust level must consider these interfering products. Figure 9 allows development of a strategy to assess NPs exposure or the NPs dust level.

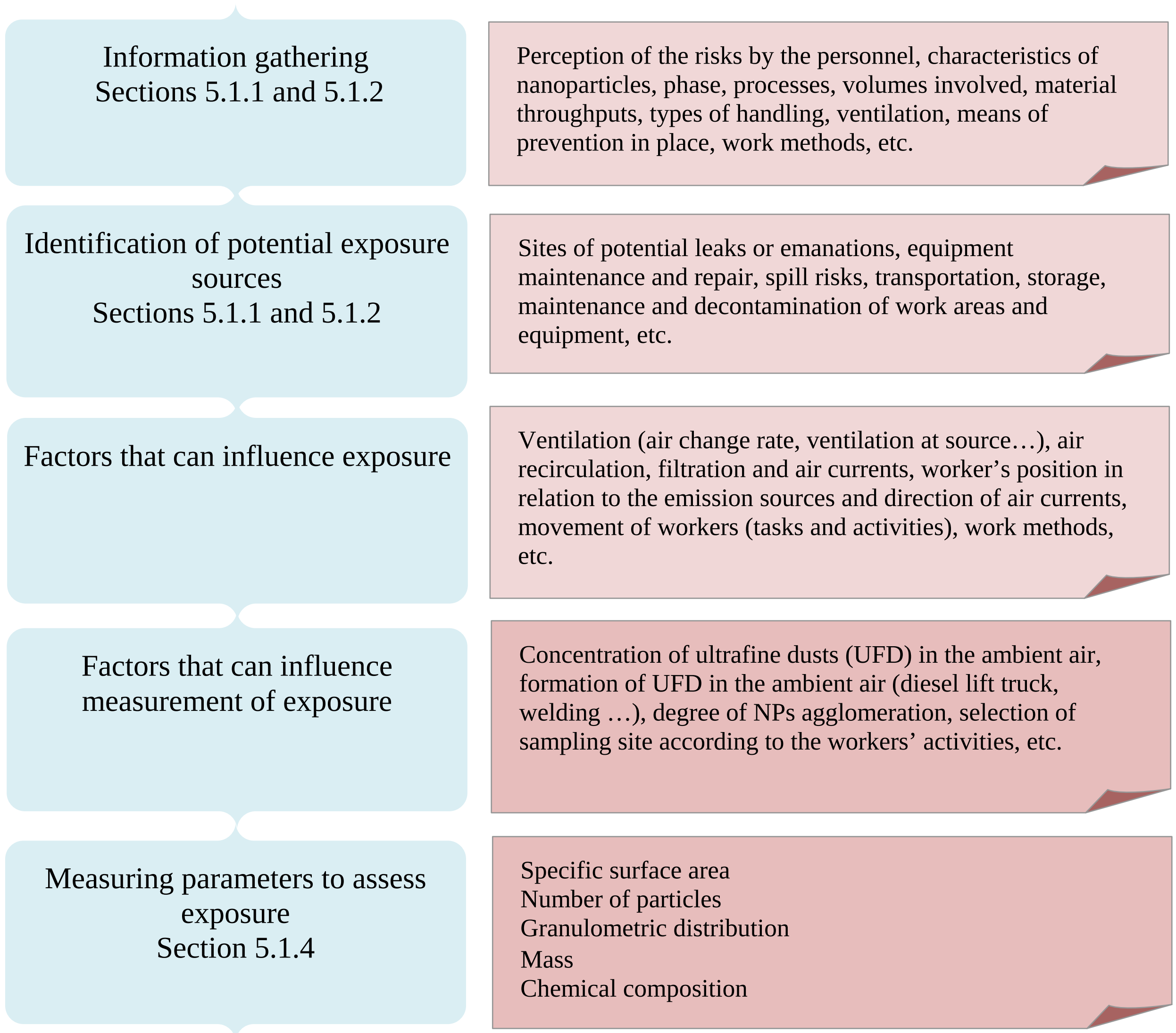


Figure 9: Synthesized nanoparticle exposure assessment strategy

Nonetheless, any good assessment strategy will integrate the limits of this approach. Several organizations, including the IRSST, recommend the use of a sampling strategy that will incorporate several measurement methods seeking to determine the mass, specific surface area, number of particles, granulometric distribution and the shape of the particles. Table 3 brings together various techniques for estimating these parameters.

Table 3: Examples of instruments and techniques allowing characterization of NPs aerosols

Parameter	Instruments	Remarks
Mass and granulometric distribution	Cascade impactors	Berner or micro-orifice cascade impactors allow gravimetric analysis of stages finer than 100 nm during individual assessment.
	TEOM	The Tapered Oscillating Element Microbalance (TEOM) preceded by a granulometric selector determines the mass concentration of nanoaerosols.
	ELPI (Electrical Low Pressure Impactor)	The Electrical Low Pressure Impactor (ELPI) allows real-time detection according to size of the active surface concentration and gives a granulometric distribution of the aerosol. If the charge and density of the particles are known or assumed, the data then can be interpreted in terms of mass concentration. The samples at each stage then can be analyzed in the laboratory.
	SMPS (Scanning Mobility Particle Sizer)	Real-time detection according to size of the particle number concentration gives a granulometric distribution of the aerosol. Knowledge of the shape and density of the particles then allows estimating of the mass concentration.
Number and granulometric distribution	CNC	Condensation nucleus counters (CNC) allow particle number concentration measurements in real time within the particle diameter detection limits. Without a granulometric selector, the CNC is not specific to the nanometric field. P-Trak offers screening with an upper limit of 1000 nm. TSI model 3007 is another example.
	SMPS	The Scanning Mobility Particle Sizer (SMPS) allows real-time detection according to the electrical mobility diameter (related to size) of the particle number concentration.
	Electron microscopy	Offline electron microscopic analysis can provide information on granulometric distribution and on the aerosol's particle number concentration.
	ELPI	Real-time detection according to size and active surface concentration gives a granulometric distribution of the aerosol. If the charge and density of the particles are known or assumed, the data then can be interpreted in terms of particle number concentration. The samples at each stage then can be analyzed in the laboratory.
Specific surface area and granulometric distribution	Diffusion chargers	Commercially available diffusion chargers allow real-time measurement of the active surface of the aerosol and have a response in relation to the active surface of particles smaller than 100 nm. These instruments are NP-size specific if they are used with an appropriate pre-separator.
	ELPI	The ELPI allows real-time detection of the aerodynamic diameter according to size and active surface concentration. The samples at each stage can then be analyzed in the laboratory.
	Electron microscopy	Electron microscopic analysis can provide information on the surface of particles in relation to their size. Transmission electron microscopy provides direct information on the projected surface of the particles analyzed, which can be linked to the geometric surface for certain forms of particles.
	SMPS	The SMPS allows real-time detection according to the electrical mobility diameter (related to size) of the particle number concentration. Under certain conditions, the data can be interpreted in terms of specific surface area.
	Parallel use of SMPS and ELPI	The differences in the aerodynamic diameter and electrical mobility measurements can be used to deduce the fractal size of the particles, thus allowing a particle surface estimate.

Another major challenge, beyond the deficiencies of the instruments at our disposal, is the assessment of exposure and adequate characterization of aerosols and synthesized NPs. The indoor and outdoor air of industrial facilities is already an often complex mixture of nanoscaled ultrafine dusts (UFD) of natural origin (viruses, smoke from volcanoes and forest fires…) or human origin (incinerator fume fractions, welding fumes, thermal power plant exhaust, polymer fumes or petroleum product combustion fumes, etc.). This means that during NPs characterization, this background noise from a mixture of different granulometries and diverse compositions will be added to the instrument readings. Some industrial operations (movement of personnel and vehicles, welding fumes and other related operations, etc.) are also likely to produce new UFD, increasing the concentration of interferences.

In such a context, **the first step in measuring the NPs dust level is to document the basic pollutants already existing in the ambient air or generated by other processes before the NP-related operations begin, so that the results obtained can be compared with this background noise.** This is an essential approach, given that the instruments we currently have available are not NP-specific and provide results for all of the aerosols present.

The measuring instruments must be placed strategically at the fixed stations to obtain the most accurate possible idea of the workers' exposure. They vary in complexity but nonetheless can provide invaluable information for assessment of occupational exposure and the total dust level, particularly in terms of NPs size, granulometric distribution, mass, specific surface area, particle number concentration or shape and degree of agglomeration. It is important to document the performance and limits of these instruments well, especially regarding their sensitivity, their specificity and the granulometry range to which they respond.

> Note that when this guide was written, the IRSST had no instrument that could be used by workplace professionals that would specifically evaluate NPs exposure. Furthermore, no workplace NPs evaluation has been done to date by its researchers.

5.1.5 Quantitative Assessment of the Toxic Risk

After gathering and interpreting all the available information on NPs toxicity and on the occupational exposure conditions prevailing in the work environments, it should be possible to estimate the toxic risk. Despite the fragmentary state of the knowledge, several studies have shown various toxic effects in animals (section 4.1). In the vast majority of situations, the data are insufficient to be able to predict the precise effects related to their exposure, especially in a context where the majority of studies have shown certain toxic effects in animals with acute exposure. There is almost no knowledge of the chronic risks associated with NPs. In a context of major uncertainties regarding the specific toxicity of NPs and the total lack of occupational exposure data, the quantitative risk assessment is actually impossible in most cases. In such a situation, ***a preventive approach, even a precautionary approach,*** must be put in place

> It is essential to remember that risk does not only depend on the toxicity of a product but on the combination of toxicity and exposure. Thus, risk can be expressed by:
>
> Risk = toxicity x exposure

and occupational exposure must be circumscribed at the lowest technically attainable level, according to the *ALARA* principle[6]. The main information necessary to assess a toxicological risk of NPs is summarized in Figure 10.

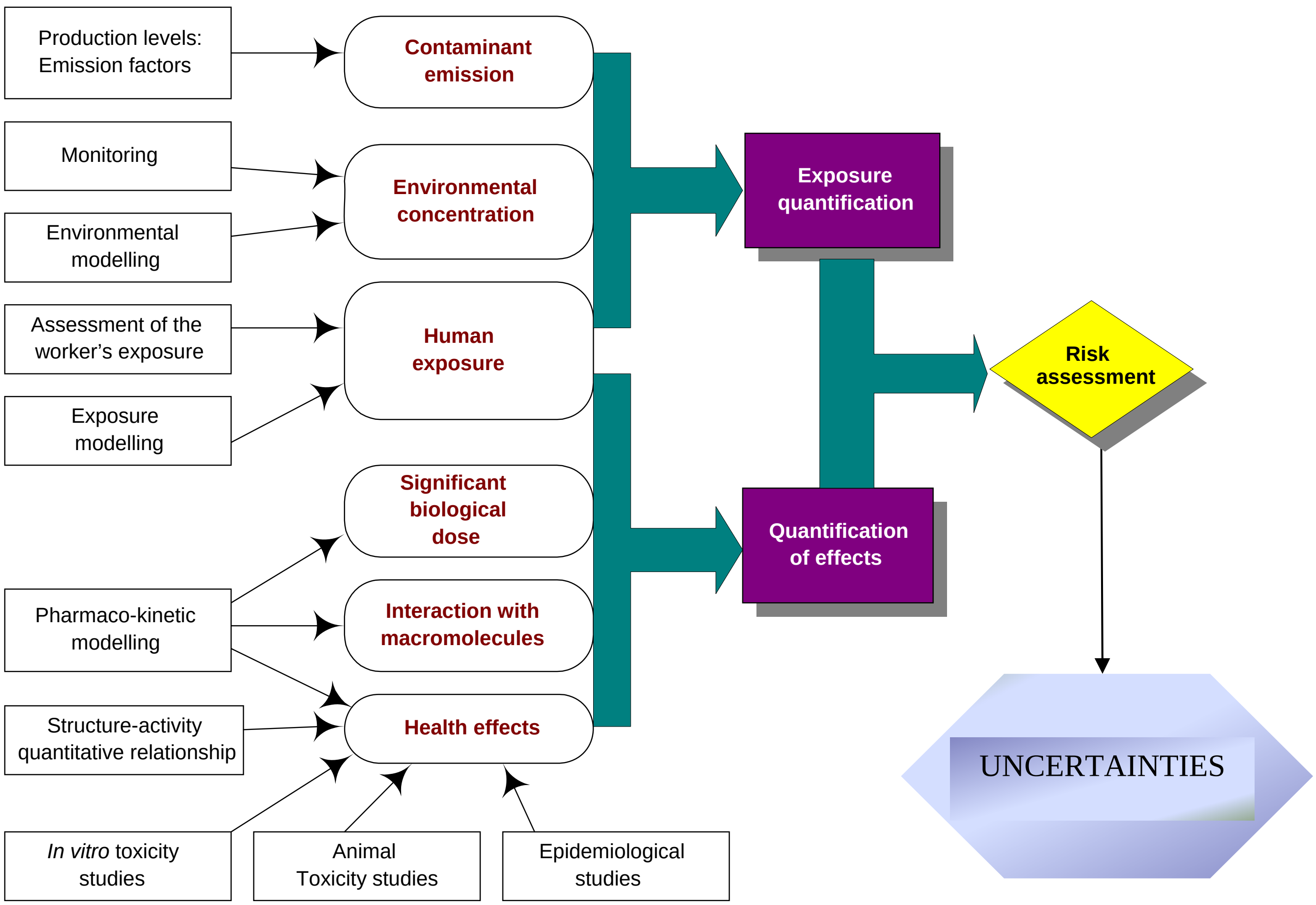


Figure 10: Toxicological risks of nanoparticles [7]

The following section will present an alternative approach to quantitative risk assessment where the level of control is adapted to the estimated level of risk. This approach targets the implementation of safe but realistic means of control in relation to the risk, even in a context of multiple uncertainties.

5.1.6 Qualitative Assessment of Toxic Risk: the "Control Banding" Approach

The lack of information on the toxicity of many NPs as well as on the exposure level, together with a lack of specific standards, often makes us unable to quantify the risk in a situation

[6] ALARA: This principle specifies that the exposure level must be "As Low As Reasonably Achievable".

[7] Adapted from Kandlikar *et al*., 2007

involving many uncertainties. This type of situation is not unique to the field of nanotechnologies. However, to be able **to implement safe but realistic means of control in relation to the risk**, a new approach was developed in Great Britain some ten years ago. Its use is becoming increasingly widespread: it is "*Control Banding*" (CB).

This approach has already been successfully applied in various workplaces, but Paik *et al*. (2008) are, to our knowledge, the first to propose such an approach adapted to the situation of NPs. This simple but effective tool makes it possible to take into account all the available information (toxicity, exposure level) and to develop logical hypotheses on the missing information.

When the available information required for a quantitative risk assessment is insufficient, it is recommended that the approach of the "control banding" (CB) model be used.

CB will determine the safe but realistic means of controls to be implemented.

The model is based on the use of a limited number of factors for evaluating the risk level in order to reduce the complexity and increase the applicability for non-experts. The control strategy is limited to three levels or bands of engineering controls (referring to *control banding*) based on solid foundations in occupational hygiene to which is added a fourth control band (cb) that requires the intervention of a specialist for the most hazardous situations. Each control band can then be estimated from an overall score to be determined for each task and that takes into account severity aspects (score related to toxicity) and probability aspects (score related to the probability of exposure or the potential exposure level). Table 4 presents the different control bands with the associated scores.

5.1.6.1 Determination of the severity score

In the context of NPs, a decision must first be made about the score associated with an unknown. While the most conservative approach would have been to consider any unknown risk as a high risk, Paik *et al*. (2008) concluded that this position would put undue pressure on controlling the exposure. These authors instead recommend that 75% of the maximum value be assigned to an unknown factor. This would therefore imply that in a situation in which no knowledge exists, the work should be carried out in a closed circuit. In this scenario, if one of the factors could potentially be high, the work should be done in control band 4, namely the maximum level of control.

The applicability of CB to NPs is based on the fact that the factors retained in the model proposed for determining the severity scores are established from the current scientific knowledge specific to NPs.

Table 4: Matrix of the control bands in relation to severity and probability (Paik *et al.*, 2008)

Probability

Severity	Extremely unlikely (0-25)	Less likely (26-50)	Likely (51-75)	Probable (76-100)
Very high (76-100)	cb 3	cb 3	cb 4	cb 4
High (51-75)	cb 2	cb 2	cb 3	cb 4
Medium (26-50)	cb 1	cb 1	cb 2	cb 3
Low (0-25)	cb 1	cb 1	cb 1	cb 2

Control bands:

cb 1: General ventilation

cb 2 : Fume hoods or local exhaust ventilation

cb 3 : Containment

cb 4: Seek specialist advice

Since toxicological studies suggest that several parameters seem to link exposure to the toxic effects observed, the main parameters are considered in the model. Mainly included are the capacity of NPs to deposit at different sites in the respiratory tract, their capacity to penetrate or to be absorbed by the skin, and their capacity to induce biological responses in different organs, as well as their translocation property.

Table 5, which is used to calculate the severity index, lists the parameters considered and the scores assigned in relation to the type of information available for each. Also, it is important to note that a maximum number of factors among those retained should be documented and that the new available information should be regularly updated in order to reduce the number of hypotheses and to determine as precisely as possible the score to be given to a specific situation. The severity score obtained (maximum of 100) will then be used with the probability score (also a maximum of 100) in order to determine the control band required according to Table 4.

Table 5: Calculation of the severity index of NPs as proposed by Paik *et al*., (2008)

Parameter to consider	Low	Medium	*Unknown*	High
Surface chemistry, reactivity and capacity to induce free radicals	0	5	***7,5***	10
Shape of the nanoparticle	0 if spherical or compact	5 if different shapes	***7,5***	10 if tubular or fibrous
Diameter of the nanoparticle	0 if 40 à 100 nm	5 if 11-40 nm	***7,5***	10 if 1 à 10 nm
Solubility of the nanoparticle		5 NP soluble	***7,5***	10 NP insoluble
Carcinogenicity of the nanoparticle	0 not carcinogen		***5,625***	7,5 potential
Reproductive toxicity of the nanoparticle	0 no risk		***5,625***	7,5 with risk
Mutagenicity of the nanoparticle	0 no		***5,625***	7,5 yes
Dermal toxicity of the nanoparticle	0 non toxic		***5,625***	7,5 toxic to the skin
Toxicity of the parent material *	2,5 if TWA from 11 to 100 μg/m³	5 If TWA from 2 to 10 μg/m³	***7,5***	10 if TWA from 0 to 1 μg/m³
Carcinogenicity of the parent material	0 not carcinogen		***3,75***	5 carcinogen
Reproductive toxicity of the parent material	0 non toxic		***3,75***	5 toxic
Mutagenicity of the parent material	0 no		***3,75***	5 yes
Dermal toxicity of the parent material	0 no		***3,75***	5 yes

* The parent product refers to the product of the same chemical composition but of larger size for which standards often exist. The score is 0 if the time-weighted average exposure value (TWA) is greater than 100 $\mu g/m^3$.

5.1.6.2 Determination of the probability score

The probability score determines the potential of NPs to become airborne and therefore, inhalable by the worker or absorbable through his skin. Table 6 summarizes the proposed estimation parameters as well as the score assigned for each of the situations.

Table 6: Calculation of the probability score as proposed by Paik *et al*., (2008)

	Low	**Medium**	***Unknown***	**High**
Estimated amount of nanomaterial used during the task	6,25 if < 10 mg	12,5 if 11 to 100 mg	***18,75***	25 when > 100 mg
Dustiness/mistiness *	7,5	15	***22,5***	30
Number of employees with similar exposure **	5 if 6-10	10 if 11-15	***11,25***	15 if >15
Frequency of operations	5 less than monthly	10 weekly	***11,25***	15 daily
Duration of operations ***	5 30 to 60 minutes	10 1 to 4 hours	***11,25***	15 if > 4 hours

* The dust level can be more easily determined by using a condensation particle counter, by knowing about the process, by observing the work surface contamination and the state of the NPs (powders or suspensions).

** A score of 0 is given for 5 employees or less.

*** A score of 0 is given for less than 30 minutes.

The insertion of severity and probability scores into Table 4 will lead to essential information in the choice of the minimum means of exposure control to be implemented.

Nevertheless, Chapter 7 will demonstrate that additional measures are just as essential in order to ensure continuous and effective exposure control.

6. LAWS, REGULATIONS AND OBLIGATIONS OF THE PARTIES

The laws and regulations governing the protection of human health, safety and physical integrity apply to all workers. The Act respecting occupational health and safety (AOHS) and the Regulation respecting occupational health and safety (ROHS) cover the general aspects of the obligations, in particular, in terms of development of prevention programs specific to the company and control of contaminants in the work environment in Québec. More specifically, job organization, methods and work techniques must protect workers' health and physical integrity.

The current knowledge of NPs toxicity is insufficient to propose new standards that would protect workers effectively.

Several chemical substances, constituting NPs, are already specified in Schedule I of the ROHS, which defines permissible exposure values (PEV). This regulation does not account for particle granulometry or the possibility of different toxicity based on size. Yet the preceding sections clearly showed that these parameters are very important to NPs absorption and toxicity in humans.

The Workplace Hazardous Materials Information System (WHMIS) obliges suppliers to label chemicals and write Material Safety Data Sheets (MSDS) describing the different substances: composition, health risks and safety, main characteristics and means of protection. Normally it is not possible to obtain exhaustive Material Safety Data Sheets specific to NPs. The existing MSDS generally do not account for size and deal with the largest particles.

The majority of Material Safety Data Sheets currently available do not allow the necessary preventive measures to be taken in relation to the actual risk, which is often unknown or underestimated.

Indeed, the information on new nanoscaled products is often incomplete, and even nonexistent. The new Globally Harmonized System (GHS) will specify and standardize the information on hazardous products. It can be hoped that NPs will be given a more prominent place, but for the time being, GHS will improve WHMIS, which will continue to apply nonetheless. Several other provincial or federal laws, particularly the Transportation of Dangerous Goods Act (TDG), can apply to NPs, just as they apply to other chemical substances. To our knowledge, however, no Québec or Canadian law deals specifically with NPs. The same situation prevails regarding the environmental effects of NPs.

Until we answer the fundamental questions on NP toxicity and until permissible exposure values have been established, exposure of workers and the public must be kept as low as possible.

Then, when adopted, everyone should ensure to respect the permissible exposure values.

7. CONTROL OF RISK FACTORS

Chapters 4 and 5 exposed the many scientific uncertainties and current practices related to the explosibility, fire and toxicity risks of NPs and to the occupational exposure levels. Chapter 6 showed the total lack of regulatory reference values specific to NPs. In a context in which quantitative risk assessment is impossible and these substances reveal unique nanoscaled properties, NPs should be considered as their own entity or as new compounds, and not as a miniaturization of substances for which the risks, particularly the toxicological risk, are well known and documented in advance.

In a context of multiple uncertainties regarding risks and the occupational exposure level, the authors of this document recommend the greatest prudence in applying a preventive approach based on the precautionary principle. This principle stipulates that, when faced with a high degree of scientific uncertainty, a precautionary approach should be adopted and the possible negative impacts reduced by minimizing occupational exposure, among other factors. This applies to the workstations where NPs are handled or are likely to be present.

Special attention must be paid to the NPs that involve major or little-known health risks and that have low or zero solubility. In such a context, the *control banding* approach (section 5.1.6) could represent a very precious tool because it can be used to establish safe but realistic means of control to implement, even in a context where required informations are incomplete.

To ensure that the right decisions are made to minimize the exposure risks and for safety, a prevention program specific to the facility should be developed, implemented, reassessed regularly and improved as needed. The example of such a program, mainly based on control of the occupational exposure, will be presented in the next chapter. The actual chapter will then cover the different preventive measures to the control of dust level and worker's exposure in occupational settings.

The authors recommend that the means of control used allow circumscribing as much as possible NPs dispersion in the air and on equipments to avoid any workers' exposure. The means of controlling exposure must consider all the work-related aspects: installations, processes, equipment, activities, tasks, workstations and workers' movements.

The principal elements of each of the three main risk control categories are illustrated in Figure 11. Note that engineering techniques are normally more effective than administrative measures and personal protective equipment, because they are independent of the workers' behaviour and prevent the possibility of contact between the pollutant and the worker.

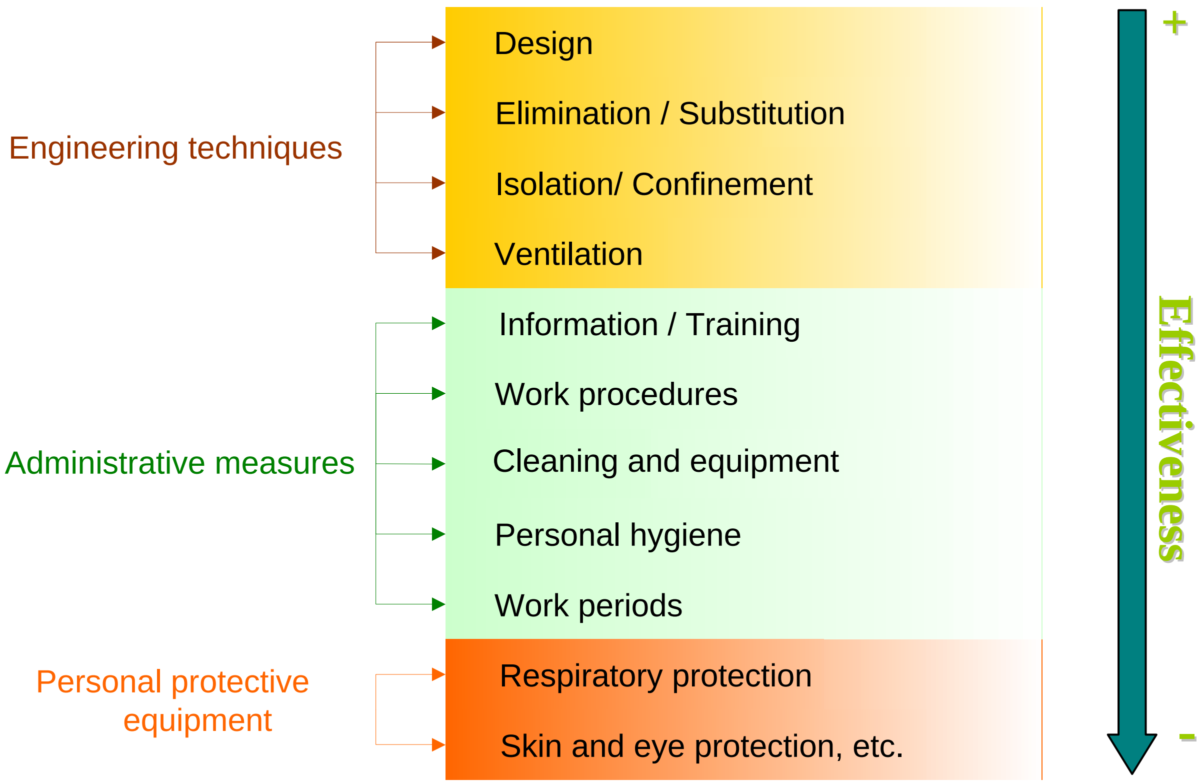


Figure 11: Risk control hierarchy

7.1 Engineering Techniques

The principal engineering techniques are 1) design, 2) elimination or substitution, 3) isolation or confinement, and 4) ventilation.

Design

Design allows development of building plans, organization of production, and installation of various ventilation, procurement, production, storage, shipping and other systems. In addition to accounting for all of the health and safety risks, regulatory requirements and production imperatives, safe workstation layouts must be planned to eliminate high-risk situations, both for the process and the equipment and for the workers. In case of a leak in the production systems, diffusion will favour dispersion into the environment. The designer therefore must account for the properties of the chemicals used and provide for control systems to limit NPs emissions in the work environment, such as confinement or local ventilation. If the use or synthesis of explosive dusts is anticipated, it is necessary to provide for the appropriate equipment and building structure.

Design is the first and most determining of the steps of organizing production in a company. It contributes decisively to prevention.

When design is deficient, it is often difficult and very costly to modify the process, the equipment or workstations to reduce (or eliminate) toxic or dangerous emissions.

Elimination/substitution

Elimination of toxic or dangerous NPs is to be preferred wherever possible. However, it will be impossible to eliminate NPs from the work environments when seeking to synthesize them or incorporate them into products to improve their performance. Substitution, another means of risk control, can find numerous applications in nanotechnology. This substitution involves:

- modifying the type of process (for example, replacing a dry process with a wet process);
- modifying the steps of the process to automate or eliminate certain high-risk operations, such as transfilling or transfer;
- replacing the most toxic or dangerous substances with less dangerous or less reactive substances;
- replacing equipment that is obsolete or too old to reduce potential leaks or ignition sources.

When applicable, elimination and substitution represent very effective approaches to risk control in the work environment.

Closed circuit, isolation and confinement

High-risk operations must be performed in some processes. Equipment then can be isolated in separate rooms, ventilated and equipped with independent ventilation systems, thus avoiding any possibility of workstation contamination and worker exposure. The worker can also be isolated in controlled environment booths or rooms for remote observation of the process.

Carbon black, silica fumes, nanoscaled TiO_2, metals and nanometric metal oxides normally are synthesized in closed circuit. Whenever possible, a closed circuit process is the main NPs production method capable of controlling emissions effectively. However, some operations that are not performed in an airtight closed circuit can be confined.

> Closed circuit (control band # 3 of the *control banding* approach), isolation and confinement normally should be effective to avoid contact between the worker and NPs. However, maintaining these installations will necessitate specific procedures, because some workers will have to enter these environments.

Ventilation[8]

Sporadic or accidental airborne NPs emanation is possible in certain processes or operations, because they all not always perform in a failsafe, airtight closed circuit. The ventilation system to be installed then will depend on the capacity to predict the NPs emanation site.

Airborne NPs emanation during open-circuit bag opening, transfer, mixing, and recovery, bagging or weighing of dry NPs is foreseeable. Capture of the contaminants at the source (local ventilation, control band # 2 of the *control banding* approach) then is an ideal method to control workstation contamination. However, observation of such a situation suggests considering modifications to the equipment to avoid NPs emanation.

Capture at the source involves:

- installing local ventilation as close as possible to the emission source, exclusive ventilation for isolated process or hoods near processes at risk of propagating particles;
- setting systems speed to capture all NPs that escape the process by considering their behaviour (similar to a gas or a vapour);
- treating emissions before they are vented into the environment;
- cleaning and maintaining the ventilation system regularly.

However, failures and leaks are usually unpredictable. The general ventilation then can dilute the ambient air by discharging the contaminated air outdoors (control band # 1 of the *control banding* approach). Environmental regulations could also require that the air be scrubbed before its release into the atmosphere. For energy saving reasons, several ventilation systems filter part of the air and return it to circulation after treatment. In the case of certain substances, this recirculation may be prohibited by the regulations in force.

General ventilation must not be considered an effective means of elimination of toxic NPs from a work environment, unless the risk could be quantified and it is proved that this technique, coupled with a fresh air intake, is enough to maintain ambient concentrations well below the quantities representing a significant risk.

[8] Schemes of the different ventilation systems described in this section can be found in Encyclopedia Britannica Inc. 2000, available on the internet

The ventilation system's performance is closely linked to:

- the quality of its design and its efficiency;
- its maintenance;
- and often, the work methods.

The efficiency of the new ventilation systems should always be assessed to ensure their performance. The specifications and the quality of the systems should be similar to those used for gases and vapours.

To our knowledge, there are no studies in the scientific literature regarding evaluation of the performance of the ventilation equipment used in applications with synthetic NPs. On the other end, the literature clearly shows the efficiency of different ventilation systems to remove ultrafine particles, of dimensions similar to NPs.

However, the literature informs us that significant exposure to nanoscaled particles are documented frequently in the production of carbon black, because the systems are not designed, maintained or used appropriately. The same is true of welding fumes, for which the source capture systems are often deficient. The design quality and especially the verification of capture efficiency, along with regular maintenance, are essential factors to ensure adequate protection of workers. Ventilation systems should always be vacuum cleaned, using HEPA (High Efficiency Particulate Arrester) filters and explosion-proof devices if explosive dusts are handled.

The air of the work environments, regardless of whether it comes from general or local ventilation, must be scrubbed before venting into the external environment. To be efficient, the scrubbing system must be operated with high-performance filters, such as HEPA (99.97% minimum filtration efficiency for 300 nm particles) or ULPA (*Ultra Low Penetration Air*, 99.999% minimum filtration efficiency for 120 nm particles) filters. Particles much smaller than the filter mesh are captured by various mechanisms, particularly diffusion, interception, impaction, gravitational sedimentation and electrostatic forces. Brownian diffusion, stimulated by collisions between air and NPs, creates random motion of NPs, thus increasing the path length and the probability that they will strike the filter. This is the dominant filtration mechanism for NPs. All these mechanisms ensure that efficient filtration can be achieved, even with very small diameter particles, which, when they adhere to the filter fibres, are mainly retained by Van der Waals forces.

HEPA and ULPA filters are used mainly in high-safety laboratory hoods for treatment of viral species, and in clean rooms. They should be used efficiently in the treatment of NPs contaminated gaseous effluents. The filtered air then would be vented outside at minimal risk to populations and the environment.

Wet scrubbing allows efficient contact between the aqueous solution sprayed inside the scrubber by high-pressure jets. A wetting agent can be added to the solution to favour NPs capture, mainly if the NPs have hydrophobic behaviour. However, this technique, which is efficient for capturing gaseous effluents, needs to be evaluated for very fine particles, such as NPs, where its effectiveness is unproven.

Electrostatic precipitation involves high voltage applied to closely spaced metal plates. Electrical charging of the particles by the corona effect occurs when the polluted air flows into an electrical discharge zone. The capture plates have an inverted polarity to the charged particles, which greatly increases capture of fine particles. The plates are cleaned periodically by water jets. The water is recovered in a sedimentation tank and recirculated after filtration. Normally, this principle is effective for fine particles. However, the maintenance and operating costs are high and regular maintenance is necessary to ensure optimal operation.

A *conventional baghouse scrubber* with pneumatic discharge of clogged masses can also be considered. This type of equipment can be effective with tightly woven bags of a good thickness. Usually, for HEPA filtration, cartridge filters with pleated filtration media are used to increase the filtration surface and thus reduce the filtration unit load.

7.2 Administrative Measures

Some administrative measures must absolutely be implemented

Other administrative measures must complement engineering techniques when such techniques are not achievable or cannot completely control the risk factors, or while waiting for these techniques to be put in place. They must never substitute for engineering techniques executed according to standard practices.

With the goals of reducing the risks of accidents and occupational exposure and favouring optimum work methods, the main administrative measures develop and ensure the implementation of:

- programs to inform and train workers and their supervisors in the ways to perform their work efficiently, while knowing the associated risks, and in preventive measures (health risks, fire and explosion risks, reading Material Safety Data Sheets and labels, work procedures, use of equipment, preventive measures during NPs manufacturing, handling, transfer, packaging, storage and shipping, during cleaning of equipment and workplaces, during waste treatment and during a spill, use and maintenance of personal and collective protective equipment, safety measures in place, personal hygiene, prohibition of smoking, drinking, eating or applying makeup in the work areas, emergency preparedness …);
- regular updates of the training and information program and regular transmission to the employees to help in efficient takeover of the occupational health and safety aspects;
- optimum work procedures with a view to minimizing generation and airborne suspension of NPs. These procedures must be explained and management must ensure that they are understood and applied;
- reduction of work periods;

- minimization of the number of exposed workers;
- access to NPs synthesis or handling sites always strictly limited to authorized personnel who have received appropriate training. Every access door must bear an explanatory sign conveying a message such as “Authorized personnel only”;
- standardization of all work surfaces, which should be non-porous and easy to clean;
- dry nanomaterials should be transferred in closed containers;
- measures for cleaning and scheduled preventive servicing and maintenance of equipment according to standard practices and the specificities of the business and the products that can accumulate in the workplaces; for example, all equipment should be padlocked before maintenance and cleaned thoroughly; the work areas should be cleaned at least once a shift with vacuum cleaners equipped with HEPA filters for any operation involving powdered NPs. In the case of explosive NPs, this equipment should be explosion-proof. Never use compressed air or clean with brushes, brooms or other methods that allow airborne resuspension of NPs. Moist fabric must be used for decontamination after ensuring that the solvent used is compatible with the NPs and does not cause a risk of incompatibility. These contaminated fabric then will be deposited in sealed bags for disposal with the other products containing NPs;
- measures promoting good personal hygiene in and outside the workplaces; among other measures, washbasins and showers must be installed to allow decontamination of workers, particularly before drinking, eating, smoking or returning home. In some situations, it would be advantageous to install locker rooms to avoid mixing work clothes and street clothes. Finally, work clothes should be cleaned in a manner that considers the risks related to their contamination by NPs and should not be taken home.

> All methods likely to trigger resuspension of particles are to be prohibited (for example, use of a broom or compressed air) during regular maintenance of the premises or after spills or leaks.

The administrative measures are well known and readers who want to know more can consult the reference books such as Roberge *et al.*, 2004. Nonetheless, it remains important for the facility to develop and implement work procedures regarding leaks and accidental spills. When these incidents occur, the cleanup must be performed immediately with a vacuum cleaner equipped with HEPA filters, then by wet cleaning or in a way that reduces resuspension or the possibilities of fire or explosion. Safe procedures must be established according to the risks and to reduce the exposure of the worker or workers. The particles could be sucked up with an explosion-proof vacuum cleaner designed with insulating materials, a ground or an explosion vent to prevent production of ignition sources (sparks or static electricity). It is also possible to use an electrical mobile vacuum cleaning system with an induction motor (to avoid sparks).

> **One essential administrative measure is to document in detail all information regarding the occupational health and safety aspects: dangers identified, risk assessment, means of control and efficiency, training, etc.**

7.3 Personal Protective Equipment

Personal protective equipment must only be used as a ***last resort***, when the engineering techniques and administrative measures are unsatisfactory to protect the workers.
Particular attention must be paid to the specific needs of maintenance personnel who often have access to locations where the exposure level could be significant.

Never forget that the effectiveness of protection decreases as an organization moves from engineering techniques to administrative measures to personal protective equipment (Figure 11).

In a NPs handling context, respiratory protection and skin protective equipment are the most important protection to be considered specifically.

Respiratory protection

In situations when it is necessary to wear respiratory protection, the ROHS provides for the obligation to develop and implement a respiratory protection program (RPP) for the persons concerned. Respiratory protective equipment is required for tasks identified as high-risk and must be selected according to the estimated risk level and the desired protection. The main high-risk tasks are maintenance of work areas and equipment, collection of control samples, tasks performed in the case of leaks, spills or aerosol projection, and any other situation in which particles may be released into the air or resuspended. For a good seal, the facepiece must fit tightly against the face. A preliminary fit test is required for this purpose. Given their very small size, NPs can pass through small interstices and penetrate a facepiece that does not fit tightly. This equipment must also be maintained regularly and appropriately. It must be stored under good conditions without risk of contamination.

When respiratory protective equipment is required, it is recommended that workers wear, at least, a positive-pressure respirator, such as a PAPR (Powered Air-Purifying Respirator) equipped with P100 filters and used with a flexible screen that covers the head, the shoulders and the upper torso, or with a properly adjusted full face shield. In most situations, these devices offer an adequate protection factor. Nonetheless, an expert opinion is recommended to ensure a sufficient level of protection according to the specific risk. It is not advisable to wear negative-pressure respirators, because a poor adjustment would allow introduction of NPs into the respirator. The use of a surgical mask, which is not considered as respiratory protective equipment, should be proscribed, because several studies have shown that it offers little protection against NPs.

When respiratory protective equipment is required, a respiratory protection program must be developped and implemented. Through the program, workers are trained and the protective equipment is selected according the the specific risks.

An air intake system will certainly offer excellent protection but it is much less easy to use. Use of a less efficient respirator, such as an N95, may be acceptable in cases where the risk could be quantified and is relatively low. On the other hand, this system's performance decreases in situations requiring a lot of exertion. For more information on selection of a respirator, see the IRSST guide to selection and user of respirators, available at the following addresses: www.irsst.qc.ca/fr/_publicationirsst_673.html and www.prot.resp.csst.qc.ca .

Skin protection

Skin protection generally can be summed up as outerwear and gloves. Given that NPs can penetrate through very small spaces, the outerwear must be designed to leave as little room for penetration as possible. It currently can allow particles to enter, mainly through the stitches, zippers and extremities. The type of outerwear material can also be permeable to particles. In a context where we have no NP-specific information, the usual protective outerwear is recommended, such as hooded coveralls, lab coats and Tyvek® shoe covers. It is possible to make some modifications to this outerwear to reduce the risk of production of static electricity and thus reduce attraction of NPs. Since the necessary information for maintenance of anti-NP protective outerwear does not exist, use of disposable material is recommended.

Regarding gloves offered in a wide range of sizes, and their resistance to various chemicals, cuts and perforations, some studies suggest that nitril gloves could be effective for short handling and two pairs could be worn, one over the other, for long handling. However, it is possible to use other types of gloves. Selection of the gloves will have to account for their permeability to the solvent used.

Finally, NPs exposure risk areas must be identified clearly and separated from the so-called clean areas, such as locker rooms and lunch rooms. It is important to remove protective clothes in a sequence that reduces the potential for contamination of street clothes and clean areas. The work clothes must be removed from the production areas in duly labelled and hermetically sealed bags. They will have to be treated as hazardous materials, according to the regulations in force. For less risky areas where protective outerwear is not required, the work clothes must be cleaned and washed in the workplace and not at home, because of the risk of transporting NPs.

In conclusion, the literature does not make it possible to determine the real effectiveness of such skin protective equipment, but because of the small size of NPs, there is a high probability that the effectiveness of some of this equipment is limited.

7.4 Current International Practices

Although the different approaches to the control of risk factors have already been described in the first part of this section, it seems interesting to inform the reader on the current work practices in research laboratories and industrial plants in other countries. After a vast worldwide consultation of researchers and companies operating in the field of nanotechnology, the International Council On Nanotechnology report (ICON, 2006) relates that the principal means of controlling exposure are broken down as follows, expressed as a percentage of the companies or research laboratories for each of the means mentioned: 43% use laboratory hoods, 32% glove boxes, 23% vacuum systems, 23% white rooms, 20% closed circuits, 15% laminar flow ventilation tables, 12% biosafety cabinets and 12% glove bag. Most companies or laboratories use more than one means of emission control, which is why the total exceeds 100%.

This same report mentions different other means of control and work methods in operation. In particular, we learn that several reactors are equipped with sealed containers in enclosures to collect the synthesized NPs. By the same approach, NPs users can feed their production line to eliminate any generation of NPs aerosols in the work environment. These systems allow vacuum cleaning of the enclosure before recovering the container. Automatically ventilated or burner-equipped systems allow self-cleaning of all residual material. Liquid suspensions are transferred with a portable peristaltic pump to avoid spatters and spills. A device is used to open a closed circuit and disperse the solid NPs directly into it, feeding a process that incorporates NPs into a mixture and eliminating any generation of airborne NPs aerosols in the work environment. The use of an isolated control room is also reported and allows remote operation of equipment. The workers only intervene for maintenance and cleaning by well-trained workers wearing personal skin and respiratory protective equipment. Use of alarm systems and sensors responding to process control modifications is also reported. If a sensor is activated, the equipment is closed automatically to limit the potential NPs emissions. All these means were developed to control the specific risks and are the result of an optimized design, accounting for all the variables to be considered.

Moreover, the ICON report (2006) mentions that 41% of the organizations say they use lab coats (cotton, nylon), 7% of them disposable, while 26% use coveralls, 7% of them disposable, that offer better protection than lab coats. In addition, 11% mention the use of shoes reserved for the laboratory and 9% have their own laundry service. Different types of gloves are used, but the types most commonly used are made of nitril, latex or rubber. The use of PVC, polyethylene, neoprene and leather gloves is also reported. Several organizations use long gloves that cover the wrists, double pairs of gloves or gloves that offer protection against wrist exposure. For most of the respondents to this survey, the choice of gloves is mainly dictated by the solvents used and not by the NPs. Some facilities reported the use of antistatic shoes and bonnets when the NPs exhibit explosive properties.

7.5 Control of Safety Risks

The safety risks, such as particle explosions and fires, and the reduction of their occurrence and consequences, must be characterized to favour protection of the workers.

7.5.1 Explosion Risks

A satisfactory knowledge of the characteristics of the NPs used (sizes, composition, state, minimum activation energy…) and the environmental conditions (ambient temperature, space available…) can reduce the explosion risk. In workplaces where explosion or fire risks exist, it is essential to develop and implement an emergency preparedness plan. Risk reduction depends on control of the main factors (quantity of airborne particles, ignition source and oxygen concentration).

- **The number of particles released** can be reduced by:
  - engineering techniques (modification of the type of process used, reduction of transfilling, reduction of the number of equipment stops and starts, addition of confinement and local ventilation…);
  - regular maintenance of the equipment and the premises to ensure that there are no particle deposits, avoiding resuspension of particles (by ventilation, pipe vibration and displacement) and ensure that there is no accumulation of particles in a small space;
  - storage designed to limit the release of airborne NPs.
- **The presence of an ignition source** is one of the factors constituting the explosion triangle. Thus, it is important to:
  - ensure that the quantity of particles in the cloud is not too high, because the cloud itself can become an ignition source;
  - identify the different possible points of origin of heat, flames or sparks. Once these points are identified, measures will be taken to prevent the formation of energy sources, for example, by modifying the processes, adding explosion vents and a ground, or replacing certain materials with non-electrically conductive materials. The electrical equipment should be sealed against vapours and gases;
  - ensure that the machines are in good working order;
  - reduce the ambient temperature and increase the water concentration in the particles whenever possible.

The presence of solvents or other substances in which the NPs are dissolved facilitates ignition of the explosive reaction.

- **Reduction of oxygen concentration** to 5% (by increasing the carbon dioxide or nitrogen rate) mitigates the possibilities of an explosion in the places at risk. However, if there are workers in these places, they must be protected against asphyxia.

Reduction of consequences

Closed systems that produce, transfer or store these nanoscaled particles must be equipped with safety devices conforming to NFPA (National Fire Protection Association) standards. The consequences of an explosion can also be reduced by installing explosion vents (panels or surfaces yielding under a pressure less than the resistance capacity of the walls or structure of closed enclosures), and systems for detecting increased pressure (that emit a signal announcing an explosion) and for explosion suppression. Flame front deflectors, rotary airlocks and the reinforcement of the structures of production equipment components are other examples of safety devices for reducing the devastating effects of an accidental explosion of very fine particles. In the event of an explosion, an emergency evacuation procedure for workers must already be in place and well understood by the workers in order to limit injuries or losses of life.

7.5.2 Fire Risk Reduction

Fire protection requires a thorough study of all the products used in the manufacturing processes (synthesis and uses). Special attention must be paid to the susceptibility of a product to burst into flames and the compatibility of the different products used or stored. The conditions of their storage also represent a way to limit the occurrence of fires (in the presence of an inert gas or in anhydrous conditions, by coating NPs with a protective layer of salts or different polymers that can be eliminated before using the product). Moreover, identification of the probable activation sources of a fire (heat source, flame, electrical source [see section 4.2.2]) can allow action on these sources, as discussed in the previous section. After they are identified, reduction depends on:

- replacement of the flammable or reactive products with other products less likely to burn or isolating them from the other substances;
- modification of the type of process used, isolation of ignition sources, use of other materials or addition of cooling sources to control the heat sources;
- isolation of electrical equipment against dust (and sometimes against vapours).

In addition, fire risks can be reduced:

- by controlling the environmental factors: oxygen rate (reducing the rate can decrease the fire risk), temperature…;
- by instituting regular maintenance of equipment and installations;
- by positioning the fire protection installations adequately;
- by storing products in hermetically sealed containers labelled as prescribed in WHMIS and ensuring their compatibility;
- by following the regulations in force for all installations.

Reduction of consequences

Rapid detection of a fire is important, given the potential severity of the damage. This can be done by smoke detectors or heat detectors, which could help anticipate the fire before its outbreak.

Reduction of the consequences of a fire depends on rapid suppression of the fire by using sprinklers, extinguishers (or another method) and by installing obstacles to its propagation. The use of fire-stop (fire-resistant) materials allows isolation of the fire or slowing of its propagation. However, attention must be paid to the incompatibility of the substances used. For example, some metal dusts are incompatible with water and produce hydrogen when they come into contact with it. This hydrogen can then catch fire or explode. To extinguish such a fire, chemical powders must be used.

When extinguishing a fire, care must be taken not to create air movements, because resuspension of combustible or easily oxidizible particles can cause an explosion. A NPs cloud can trigger a deflagration in contact with flames or heat. The fire must be thoroughly extinguished or the premises must be evacuated as soon as possible before the arrival of the firefighters or other emergency services. It is also imperative to inform the fire department in advance of the presence of these dangerous substances.

7.6 Control of Environmental Risks

Control of risks for the environment and their effects mainly involves limiting NPs emissions into the environment and the terrestrial and aquatic ecosystems. In fact, it is practically impossible to track the progression of NPs in the environment and there are no methods for eliminating them from the media (air, water and soil) where they eventually could reconcentrate via the food chain.

It is essential to dispose of wastes (particularly including filters, absorbent fabrics or paper, cleaning fluids and materials, disposable clothing and respirators) according to best practices. Solid wastes should be stored in closed and sealed containers until their treatment and disposal. These wastes and liquid effluents, including scrubber sludge, must be considered as NPs and the compatibility of the different wastes requires special attention. Different waste stabilization or incineration methods exist and the best approach is chosen case by case.

It is also important to limit emissions by ensuring that plant releases have been filtered or treated in advance (see section on ventilation) according to standard practices and follow the procedures required in the provincial and federal regulations on hazardous wastes, their storage and their disposal/treatment.

8. WORKING SAFELY WITH NPs IN A FACILITY: PROPOSAL FOR A PRACTICAL APPROACH

The previous chapters showed that industrial production of NPs or their integration into a production line definitively represents specific risks to workers' health (poisoning, occupational diseases) and safety (fires, explosions, chemical incompatibility, electrical risks, high temperatures) due to the unique properties of nanoscaled particles and the processes implemented. Indeed, in the vast majority of situations, the scientific literature has shown greater toxicity of NPs compared to larger-scaled products of the same chemical composition. The large specific surface and the high number of these NPs per unit mass also increase the fire and explosion risks.

It is essential to mention that risk management involves the search for balance between achievement of gains and minimization of losses. It should be an integral part the philosophy and business practices of any organizational culture, because it is an essential factor in good corporate governance. In practice, risk management is a step-by-step process, based on a logical sequence, with an iterative approach that allows continuous improvements in decision-making, while facilitating constantly improved performance. The authors of this guide consider that organizations that manage their risks effectively are more likely to achieve their objectives, and at lower costs.

The absence of takeover and effective management of the specific risks related to nanoparticles could have human, financial and corporate image repercussions with serious consequences for the company.

The preceding chapter showed that scientific knowledge and the technologies currently available allow effective management of NP-related risks. This chapter proposes a practical approach for implementing different elements of prevention within the facility.

Responsible management of nanotechnology development inevitably depends on the preparation, implementation, monitoring and continuous improvement of an industrial accident and occupational disease prevention program in the work environment, based on a precautionary approach, with the goal of minimizing risks when they cannot be determined precisely.

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

1) occupational health and safety represent an action priority;
2) the management and all employees are fully committed to it;
3) the necessary efforts are made to achieve the prevention objectives.

Moreover, in different fields and at the international level, risk management has become a key component of the business process, in both the public and private sectors.

At the time this guide is written, the number of Québec companies producing NPs on a large scale is still limited and we do not know what companies incorporate NPs into their process. Consequently, this chapter will only be partially based on the observations during industrial visits. Instead, it will propose a practical, step-by-step approach, adaptable to multiple situations in facilities by integrating information gathered in the few Québec plants visited.

- With incomplete knowledge of the toxicity and behaviour of NPs and their effects in the body,
- With totally unknown occupational exposure levels,
- With a total lack of regulation specific to NPs,

strict measures should be put in place to reduce the pulmonary and cutaneous exposure risk as much as possible.

In this sense, the information presented in the previous sections is used to determine the appropriate measures to be implemented.

8.1 Industrial Prevention Program

Figure 12 provides an example of prevention program content that could be applicable in a facility, regardless of whether it synthesizes NPs or incorporates them into a process to produce value-added goods with distinct characteristics.

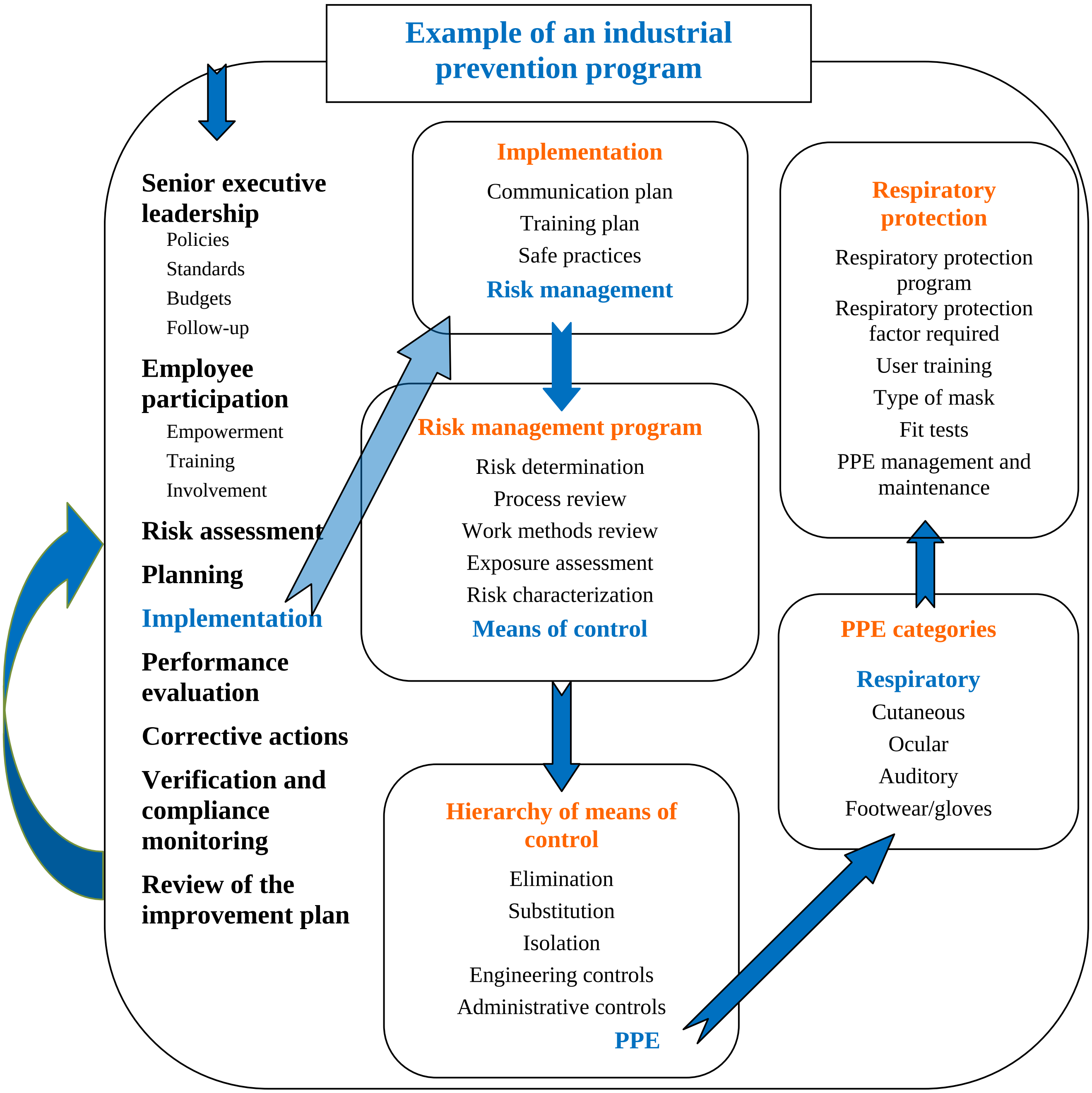


Figure 12: Principal components of an industrial prevention program.

The left-hand column of Figure 12 summarizes the main essential steps of the prevention program: senior executive leadership, employee participation, risk assessment, planning, implementation, performance evaluation, corrective actions, verification, compliance monitoring and review of the improvement plan. **This approach puts the emphasis on the necessity of continuous improvement of the prevention program by iterative integration of the new information into the risk assessment.** The centre and right-hand parts of the figure document a specific aspect of this program in more detail – implementation.

Senior executive leadership

The employer manages and supervises the workers, the equipment and the work methods. Consequently, the employer has the obligation to observe all the laws and regulations in force and take all reasonable means to ensure that its employees work safely.

Beyond regulatory obligations, prevention should be part of the fundamental values of any company. In this sense, a prevention program should be prepared, implemented, evaluated and constantly improved through an iterative documentation process.

Non-absenteeism due to illness or accident is likely to be transformed rapidly into a competitive advantage by limiting production costs while favouring good labour relations.

Senior executive leadership must materialize through the development of clear and known policies and the allocation of the necessary budgets for an effective assumption of responsibility for occupational health and safety (OHS). Upper management must appoint a person in charge of the prevention program, who will ensure compliance with all the laws and regulations in force and implementation of the decisions made. This manager is required to do regular follow-up of OHS and ensure the effectiveness of the measures put in place. By his continuous involvement, he will remind the employees that OHS represents a priority for the organization. In this capacity, he has to establish clearly the distinct responsibilities of the individuals mandated to ensure implementation and follow-up of his decisions.

The OHS manager, accountable to upper management, should have the leeway and the decision-making authority to perform his mandate adequately. In particular, he must establish clearly the responsibilities of the different people and ensure the continuous commitment and support of upper and middle management and the other OHS committee members.

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

- **Senior executive leadership**
  and
- **Employee participation**

→ **Therefore, an OHS committee should be instituted, composed of representatives of the employer, including the manager responsible for OHS, and the workers.**

Employee participation

Employees are the people primarily exposed to risks in the facility. To favour implementation of the best means of prevention, and to develop and apply safe work methods, they must collaborate with the members of the OHS committee or with any other prevention structure adapted to their work environment. They should also take the training made available to them and apply the safe work methods developed for them. **Each worker has obligations or responsibilities regarding safe work**. Not only are workers required to comply rigorously with the instructions received but they must report any risky situation they identify and propose a solution if possible.

Risk assessment

Danger is an inherent property of a substance or a situation with the potential to cause effects when an organism, a system or a population is exposed to this agent.

Risk is the probability that effects will occur on an organism, a system or a population in specific circumstances of exposure to a dangerous agent.

→ ***In the presence of a dangerous agent, the risk is zero if there is no exposure***

Each workstation should be the subject of a risk assessment, either quantitative (sections 5.1.3 and 5.1.5) or based on the *control banding* approach (section 5.1.6). In fact, the means of prevention to be implemented will be directly related to the results of the risk assessment: the more precise the risk assessment, the more likely the exact determination of the means of protection to be implemented at the best cost, while properly protecting the workers. Furthermore, to carry out the most precise risk assessments achievable, it is important to document as much as possible and continuously all of the real conditions encountered in an establishment.

The overall approach that led to the risk assessment provides all of the elements for determining the devices and procedures to be implemented for proper protection of workers, equipment and workplaces.

In some situations, a medical surveillance program for the workers could be useful and should be considered.

Based on the information available and carefully documented, a decision must then be made about the actions that should be carried out and that will ensure a safe workplace.

Planning

Planning represents a critical phase because it will determine the steps to be executed and will lead to choices for carrying out the decisions that were made in order to ensure that the work with NPs can be performed safely.

Planning must take into account each and every step in the manufacturing process, from the laboratory to shipping, and including procurement, synthesis, use, storage, maintenance, transportation and industrial waste of NPs. Planning also has the objective of establishing each person's responsibilities, as well as the strategies and means for achieving the established objectives. It determines precisely the work to be carried out, by whom, the specifications of the equipment, the criteria to be met, as well as the implementation schedule.

In the same way, the planning stage determines the specific programs to be implemented, such as the respiratory protection program, the content of basic training and refresher training, information dissemination strategies, schedules and good work practices, the access zones limited to authorized personnel, and even the personal protection to be used and the best decontamination strategy for contaminated clothing. It takes into account the specific characteristics of the products used, synthesized or handled and, the processes, as well as the procedures during the planning of the emergency plan and first aid, and the procedures to be developed for asphyxia, electrocution, accidents, spills, etc.

Implementation

Implementation is accomplished according to the steps laid out in the prevention plan. It represents the practical implementation of all the preliminary work that allowed identification of all the risks and the means of control.

Figure 12 illustrates different elements contained in the risk management program and details examples necessary to the success of the approach. If it is necessary to resort to respiratory protective equipment, for example, this will guarantee adequate protection only if it is properly selected, if the workers know how to use it and ensure a tight fit, and if it is maintained correctly and replaced when required.

Performance evaluation

A step often forgotten, performance evaluation is an essential aspect that ensures effectiveness

Once implementation is completed, it is essential to ensure the performance of the improvements made in the work environment. Thus, each change, whether it pertains to equipment or individual responsibilities, must be evaluated to ensure that it meets the initial objectives. Performance evaluation should furthermore be the subject of a planned regular verification program.

Corrective actions

Corrective actions should be taken promptly after any performance evaluation that does not meet the initial objectives. These corrective actions should also be evaluated and the process repeated until the objectives are achieved.

Verification and compliance monitoring

The compliance monitoring represents a long-term guarantee of the effectiveness sought

Management must ensure regularly that the different elements of the prevention plan are still effective and meet the initial objectives. The authors have observed, through different research projects, that the main factors contributing to reduce the effectiveness of the means of prevention over time included modifications to the processes without adjustment of work methods, installation of new equipment without the necessary assessment and information on the associated risks, arrival of inadequately trained new employees, poorly maintained ventilation systems, instructions forgotten by foremen and employees, etc.

Review of the improvement plan

A prevention program is a dynamic entity that continually requires updating in order to improve and to take into account new information that has become available. This updating is done through an iterative process on a regular basis.

We have mentioned several times that the scientific data on NP-specific risks are only partially known. The same is true of exposure in most work environments. However, the prevention program provides for documentation of the occupational exposure level without accounting for the emergence of new scientific knowledge. The content of the suppliers' Material Safety Data Sheets should also be improved. Over time, the facility develops, new production lines are put in place, workers are hired, and medical monitoring may have identified new risks that were initially unsuspected.

In short, the prevention program established may no longer perfectly meet the initial objectives and take into account new scientific knowledge. This is why it should be evaluated and modified regularly, as needed, to integrate new scientific knowledge, the new elements to be implemented or elements already implemented that must be improved. In an iterative approach, this means going back to the risk assessment step after ensuring the commitment of upper management and the employees. This review of the improvement plan should be designed in advance and be part of any prevention program.

Access to specialized resources

In situations where the facility does not have all the necessary expertise, it is always possible to resort to experts. They can be very helpful in establishing an effective prevention program adapted to the work environment. In Québec, the CSST prevention network, the parity sectorial associations, the health and social services agencies, the prevention mutuals and certain consultants are able to assist the organization in taking charge of its risks.

8.2 Particularities in University Research Laboratories

Section 8.1 discussed an approach applicable to ***any work environment, including research laboratories***. However, within the context of writing this guide, visits to Québec research laboratories active in the NT field, mostly in university settings, provided an opportunity to take note of certain challenges specific to these work environments.

This information does not claim to cover every imaginable situation in the research environment. The aim of the current section is solely to raise awareness about certain realities and to provide ***additional information*** adapted to these workplaces in relation to certain specific situations identified.

In the case of a laboratory, the researchers are interested in synthesis of new nanoparticles (NPs), and the development of enhanced products containing nanometric structures. To do so, researchers use precursors, produce intermediate products and generate NPs containing wastes.

Table 7 identifies some challenges observed in ***certain*** university research laboratories. These are not generalized situations for all university laboratories, since most educational institutions have established teams of health and safety specialists to assist the research professors in aspects of prevention. Nevertheless, some situations seem to be the rule rather than the exception.

Table 7: Some challenges identified during visits to university research laboratories regarding the prevention plan proposed in Figure 12

Senior executive commitment	
	It can be difficult to influence senior university administrators directly regarding the allocation of the necessary budgets for purchasing and maintenance of prevention equipment.
Chain of transmission of OHS concerns	
	Several hierarchical levels exist. Moreover, concerning OHS, each professor enjoys great freedom in supervising students. The conditions are not always in place for students to know the risks and take the appropriate preventive actions. The empowerment and involvement of some professors may vary according to the laboratory's culture, which is why some students have never heard of the risks related to their laboratory experiments.
Assessment of the risks specific to laboratory operations	
	Specialized OHS resources who can contribute to risk assessment are limited. There are also continual changes in experimental conditions, resulting in constantly evolving risks (toxicity, catalysis, fire, explosion and MSDS specific to NPs or, failing this, the known risks of larger-scaled products of the same composition), which makes all this information difficult to document. Exposure is assessed only in exceptional situations.
Prevention planning and implementation	
	The university's prevention management can offer general courses on laboratory best practices and, in some cases, provide solutions to problems specific to a laboratory. On the other hand, new students are arriving constantly and training them adequately upon their arrival represents a major challenge. No laboratory visited had named a prevention officer. New laboratories are usually well designed for the research that will be conducted there and the OHS aspects are taken into account. However, research orientations evolve over time, so that the mission of some laboratories may change substantially. General and local ventilation are likely not to be adapted to the new needs. Moreover, different constraints may prevent a laboratory upgrade. For example, to our knowledge there is no grant program allowing a professor to apply for funds to review the general ventilation or to replace an obsolete laboratory hood. Written safe work methods do not exist in all laboratories, and the selection of personal protective equipment is often left up to the student, who does not have the necessary knowledge.
Performance evaluation	
	In the laboratories visited that had a research assistant with more than five years of experience, none of them had any memory that the effectiveness of the hoods had been verified and that their performance had been evaluated. These best practices should be applied at least once a year.

The main aspects that can contribute to preventive management of OHS risks in a research setting **are identical** to those for any other establishment.

In this specific environment, an attempt must be made to find practical solutions to the challenges listed in Table 7 and that identify an aspect for improvement in a given laboratory.

Even if some aspects are normally outside the control of the research professor (for example, the commitment of upper management), he can nevertheless act at several levels and implement solutions for some situations. He can first develop a prevention culture in his laboratory. Naming a person in charge of the health and safety aspects in his laboratory is one example of his possible area of action, just like ensuring that any new student is trained in good general safe work practices in the laboratory, applicable to all laboratories that handle chemical substances, as well as in the specific requirements related to the handling and management of NPs. He can ensure that all equipment used to synthesize or handle NPs is decontaminated before it is used for some other purpose, for maintenance or is disposed of. These few examples illustrate that the university research professor can act directly on several of the challenges identified during our visits.

9. CONCLUSION

This best practices guide for handling of NPs was produced jointly by the IRSST, which assumed responsibility for it, the CSST and NanoQuébec. The three organizations combined their efforts to achieve a common objective: *promote the safe development of nanotechnologies in Québec* by developing and disseminating a tool to take over the health and safety component in the research laboratories and in the institutions producing or using NPs.

The nanotechnology field is rapidly expanding and the number of workers potentially exposed to NPs is constantly increasing. However, some NPs can involve dangers of fire or explosion or dangers to workers' health. Although research on health risks has increased significantly in the past few years, many questions remain unanswered. It is also currently difficult to assess occupational exposure with parameters (number of particles, specific surfaces, granulometric distribution…) that can link exposure to the health risks. In such a context, quantitative risk assessment is practically impossible, but *control banding* offers an interesting alternative in determining some minimum prevention measures to be implemented.

It then becomes particularly important to support safe development of nanotechnologies in Québec. The purpose of this guide, dedicated to researchers and companies, is to summarize the state of knowledge and provide information and recommendations for takeover and control of risks in order to prevent the occurrence of accidents or the development of occupational diseases.

The authors recommend adopting a preventive approach, even a precautionary approach, to avoid any NPs exposure. They undertake to update this guide when more specific information becomes available from research projects or from documentation of situations in the research or industrial environments.

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[9] To make the best practices guide more readable, only a few references are included. A detailed list of relevant references is available in the synthesis documents published by Ostiguy *et coll*. in 2006 and 2008, available at www.irsst.qc.ca.