

**Advancement in Quebec Research on the Prevention of Risks
Related to Occupational Exposure to Nanomaterials**
**Avancement des recherches au Québec sur la prévention des
risques liés à l'exposition professionnelle aux nanomatériaux**
**Avances de la investigación en Quebec sobre la prevención de
los riesgos vinculados a la exposición profesional a los
nano-materiales**

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Résumé de l'article

Cet article présente les orientations de recherche priorisées et les réalisations
des membres de la communauté de chercheurs en nanotoxicologie dans ces
cinq thématiques : la toxicologie, l'épidémiologie, la métrologie/caractérisation,
le comportement aérodynamique/ventilation et les équipements de protection.
Par exemple, la section toxicologie présente des résultats portant sur les effets
respiratoires des nanoparticules de dioxyde de titane (TiO₂) *in vivo* et des
nanotubes de carbone (NTC) *in vitro* et *in vivo*. En ce qui concerne l'étude de
l'exposition professionnelle aux nanoparticules, les recherches réalisées
incluent des évaluations des concentrations en masse et en nombre, des
mesures de distributions granulométriques ainsi que la caractérisation en
microscopie électronique des particules de taille nanométrique. Dans le
domaine des équipements de protection, des études sont menées pour mesurer
la pénétration des nanoparticules à travers les gants et les vêtements de
protection dans des conditions simulant leur utilisation en milieu de travail.
Par ailleurs, une expertise sur la mesure d'efficacité des filtres des systèmes de
ventilation et des appareils de protection respiratoire a été mise en place au
laboratoire de l'IRSST. La performance des filtres a été étudiée sous différents
régimes de débit constant ou variable. L'article se termine par une description
des retombées directes de la formation du regroupement dans le domaine de la
prévention des risques liés aux nanomatériaux.

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Advancement in Quebec Research on the Prevention of Risks Related to Occupational Exposure to Nanomaterials

Patricia Dolez, Yves Cloutier, Alexandra Noël, Lyes Tabet, Denyse Gautrin, Maximilien Debia, Gilles L'Espérance, Stéphane Hallé, Ali Bahloul and Ludwig Vinches

The nanotechnology field is a growing industry, particularly in Quebec: occupational exposure risks already exist and should increase exponentially. In recent years, work has been undertaken in Quebec to develop knowledge for improving the prevention of nanomaterial-related risks. In particular, a group of researchers, professionals and students involved in the nanotechnology field was created in 2006 under the aegis of the Quebec Occupational Health and Safety Research Network. Its aim is to share the expertise of the different stakeholders in this field in order to promote multidisciplinary collaboration and more rapid advancement in research.

KEYWORDS: advancement in research; risk prevention; occupational exposure; nanomaterials

Introduction

The nanotechnology field is rapidly expanding. Between 2001 and 2008, the number of discoveries and inventions, R&D funding programs, manufactured products, and workers in this field has increased on average by 25% per year (Roco, Mirkin and

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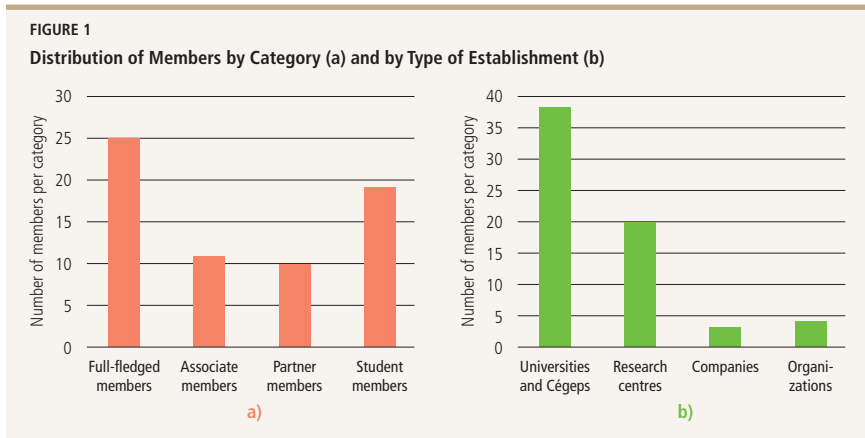
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Hersam, 2011). Risks of occupational exposure to nanoparticles therefore exist and could increase exponentially. It has been estimated that the number of workers worldwide in the nanotechnology field will double every three years to reach 6 million in 2020. In Quebec, there are currently 265 university professors working in the field of nanotechnology, with 30 holding Canada Research Chairs (NanoQuébec, 2010). Despite the fact that nanomaterials are and will be increasingly present in commercial products and workplaces, considerable uncertainty remains about their potential toxicity and their possible effects on human health and the environment.

To share the expertise of the different stakeholders in this field and coordinate research efforts in order to answer these questions more rapidly, a community of nanotoxicology researchers (www.rrsstq.com/fra/nanotoxicologie.asp) was created in 2006 within the Quebec Occupational Health and Safety Research Network (QOHSRN) with the support of the Institut de recherche Robert-Sauvé en santé et en sécurité du travail (IRSST, Occupational Health and Safety Research Institute) (Truchon *et al.*, 2008a). The group includes researchers, professionals and students interested in the nanotechnology field and working within universities, research centres, companies and organizations in various disciplines such as toxicology, epidemiology, chemistry, engineering, metrology, industrial hygiene, ventilation and protective equipment. More precisely, the objectives of this nanotoxicology group within the QOHSRN are to take stock of the available knowledge and research needs, to implement mechanisms for sharing knowledge, to contribute to the training of future scientists, to stimulate and facilitate multidisciplinary collaboration, and to establish a common research program on the effects of nanomaterials on workers' health in order to avoid duplication of research and to help in submitting grant applications with different funding agencies.

This nanotoxicology group currently consists of 65 members from numerous public organizations and private companies: AGY Consulting, Collège Ahuntsic, Commission de la santé et de la sécurité du travail (CSST), École de technologie supérieure (ÉTS), École Polytechnique de Montréal, CTT Group, Hôpital Sacré-Cœur de Montréal, IMAC Inc., Institut Armand-Frappier (INRS), IRSST, Ministère de l'intérieur français, NanoQuébec, Solutions Environnement Inc., Concordia University, the Université de Montréal (UdeM), Université de Sherbrooke, and the Université du Québec à Montréal (UQAM). Their breakdown by category of member and home institution is illustrated in Figure 1. The nanotoxicology group's activities are coordinated by a committee consisting of two co-leaders (Yves Cloutier [IRSST] and Patricia Dolez [CTT Group]) and one student in charge of logistics and communication (A. Noël [Université de Montréal]). The members meet regularly to share their research results, to discuss the needs for research in this field, and to find partners for carrying out collaborative multidisciplinary work.



This article includes a presentation of the research orientations in five prioritized areas: toxicology, epidemiology, metrology/characterization, aerodynamic behaviour/ventilation, and protective equipment. It also describes the progress made by the different research teams in these five areas. It ends with a description of the impacts the group had on prevention related to nanomaterial risk.

Priority Research Orientations

Right from its creation, the group worked on establishing a research program (Truchon *et al.*, 2008b), which is available in French and in English on the nanotoxicology group's site (www.rrsstq.com/fra/nanotoxicologie.asp). This program was developed from an analysis of data from the literature from different research groups around the world and from existing published data on the toxicity of nanoparticles and ultrafine particles. These allowed the existing gaps in this field to be identified. The proposed research avenues were grouped according to the five following themes: toxicology, epidemiology, metrology/characterization, aerodynamic behaviour/ventilation, and protective equipment.

For the toxicology theme, the priority is to study the relationship between exposure-dose-response at certain doses and exposure levels characteristic of workplace conditions in order to ensure direct applicability of the new research. The chosen approach includes inhalation studies on laboratory animals using doses representative of workplace reality, mechanistic studies to determine the characteristics of the dose best correlated to the effects, toxicokinetic studies of nanoparticles to identify the target organs, *in vitro* validation tests with doses representative of *in vivo* exposures, and chronic toxicity studies. To support occupational health practitioners in the prevention of the health effects associated with nanoparticle exposure and to offset the lack of metrology methods, the research program recommends the development of effect and exposure biomar-

kers. The very nature of the recommended research strategy also involves a consolidation of the infrastructures for generating and measuring nanoparticles as well as for animal exposure.

For the epidemiology theme, it is recommended that an inventory be carried out of the companies and research laboratories in Quebec whose personnel are exposed to nanoparticles in order to maximize the spin-offs of the research for Quebec. First, the strategy recommended for achieving this objective includes the mailing of questionnaires, the holding of meetings, and walk-through-type industrial hygiene investigations. Second, a nano-epidemiological study is proposed to determine whether relationships exist between the exposures specific to the environments involving nanotechnologies and selected symptoms and/or diseases. Such a study could be carried out on populations of nanotechnology apprentices (students/learners) according to a model developed by the researchers in the respiratory health research group at Hôpital du Sacré-Cœur de Montréal (Gautrin *et al.*, 1997); this would allow a comparison of the health profile before and after a more or less long period of exposure to nanoparticles.

In metrology and characterization, the development of expertise for evaluating workplace exposure and characterizing nanoparticles and nano-aerosols has been identified as a priority. The first step in this work, which requires investments for consolidating laboratory infrastructures, involves the implementation of sampling techniques, in particular those relating to nanoscopy (TEM, SEM, etc.). Research efforts will also have to focus on the development of computer tools, for example to determine the correspondence between animal and human doses, to evaluate the exposure doses from the nanoparticle size distribution, and to calculate, when necessary, the surface concentration from the available data, such as the number concentration.

The aerodynamic behaviour/ventilation theme includes the characterization of the efficiency of local exhaust systems and general ventilation, and the measurement of workers' exposure. In parallel, the development of numerical models paired with tools for modeling flows in confined environments is targeted in order to predict the exposure levels and the efficiency of ventilation control systems. The application of this approach requires a better characterization of the aerodynamic behaviour of nanoparticles, in particular the determination of their diffusion coefficients, the quantification of their interactions, and the evolution in aerosol particle size over time.

Finally, respiratory and skin protection are the research areas focused on in the protective equipment theme. For respiratory protection, in order to complete the work being carried out elsewhere in the world on filtration aspects, it is recommended that the effect of conditions of use of devices be evaluated, in particular the questions of fit and the risk of penetration at the gaps and interface with

the skin. The projects pertaining to skin protection relate to 1) the development of methods for measuring the effectiveness of equipment, including the case where the nanoparticles are in powder form or in colloidal solution and where mechanical stresses are applied simultaneously on the protective clothing; 2) the measurement of the effectiveness of standard protective clothing against nanoparticles; and 3) the study of the impact of the presence of the liquid carrier of the colloidal solutions and the actual conditions of use of the protective equipment, particularly those conditions including the mechanical stresses and the microclimate inside protective equipment, on the penetration of nanoparticles through the materials used for skin protection.

Progress in the Toxicology Theme

Compared to materials of identical chemical composition but of larger size, nanoparticles acquire new physicochemical properties at the nano-scale. The toxic potential of these nanomaterials is attributed to these same properties. However, documentation on the human health effects resulting from exposure to nanoparticles remains fragmentary and incomplete. Nanotoxicology is therefore a priority research area due to the increased uses of nanotechnologies in the fields of medicine, electronics, as well as pharmaceutical and consumer products. The health issues raised by exposure to nanoparticles are similar to what is associated with ultrafine particles in the literature. In this section, studies on the toxicity of TiO₂ nanoparticles and CNTs are briefly described. The choice of these particles is motivated by their important current or expected industrial use.

Titanium Dioxide

Inhalation is considered as the most probable occupational exposure pathway for nanoparticles. A large number of studies have shown that the toxic potential of inhaled nanoparticles can be linked to parameters associated with size, including the surface area and the degree of agglomeration (Kim *et al.*, 2010). In fact, the phagocytic activity of alveolar macrophages is optimal for micrometric particles, but seems less efficient for nanometric particles (Geiser *et al.*, 2008). Hence, small agglomerates (< 100 nm), which seem to escape the macrophages, are more likely to interact directly with biological material. In a recent study by the nanotoxicology group members on rats, comparisons were made of the relative pulmonary toxicity induced by inhaled 5-nm TiO₂ nano-aerosols showing two different agglomeration states, namely smaller than or larger than 100 nm, at mass concentrations of 2 and 7 mg/m³ (Noël *et al.*, 2012). The results showed that at 7 mg/m³, the aerosol consisting of large agglomerates induced an inflammatory response, while exposure to the aerosol consisting of small agglomerates suggests cytotoxic and oxidative stress responses. These results clearly indicate

that biological responses to nanoparticles could depend on the dimension of the agglomerates and on the mass concentration of the aerosols. Other members of the nanotoxicology group are also working on the *in vitro* and *in vivo* inflammatory properties of TiO₂ (Gonçalves and Girard, 2011).

Carbon Nanotubes

The first studies carried out in 2000 on the biosafety of CNTs attributed their toxicity to their tubular form similar to asbestos fibres. Later studies showed that different parameters may be involved, such as: size, aggregation, surface reactivity, etc. Thus, Poland *et al.* (2008) showed that only long (~ 15 µm) multi-walled CNTs (MWCNTs) presented carcinogenic effects similar to those of asbestos fibres in the mouse. Similarly, Warheit *et al.* (2004) observed that exposure of rats to single-wall CNTs (SWCNTs) resulted in a 15% mortality of the animals within 24 hours. The authors attributed this mortality to a mechanical blockage of the animals' upper respiratory tract following agglomeration of the CNTs. A recent study by the nanotoxicology group showed that the effects of MWCNTs coated with a carboxylic polyacid-type polymer are relatively similar to those of bare CNTs, while CNTs coated with polystyrene showed no effect *in vitro* or *in vivo* (Tabet *et al.*, 2011). These changes could be due to differences in surface reactivity. In conclusion, the diversity of CNTs, the few data available, and the contradictions between the studies make it harder to reach a consensus on the toxicity of these nanoparticles.

Progress in the Epidemiology Theme

The sectors affected by nanotechnologies as well as the materials involved are still poorly documented in Quebec and elsewhere globally. Furthermore, despite a significant number of *in vitro* and *in vivo* toxicological studies, knowledge about the human health effects is limited and no epidemiological study on workers exposed to nanomaterials has yet been published.

The need for creating exposure registers has been expressed by several authors worldwide since 2008, for evaluating the size of the populations of workers at risk and for planning epidemiological studies and developing medical monitoring programs (Nasterlack, Zober and Oberlinner, 2008; Schulte *et al.*, 2008). In France, an epidemiological investigation with the implementation of an exposure register is planned, as well as a medium- and long-term monitoring program including a prospective cohort study and cross-sectional studies on workers producing or using nanomaterials in their work (Boutou-Kempf *et al.*, 2011). Other groups of researchers in Italy and the United States are focusing their attention on evaluating the health risks associated with specific exposures, for example TiO₂ nanoparticles (Iavicoli *et al.*, 2011) and CNT (Schubauer-Berigan, Dahm and

Yencken, 2011). Exposure registers will also allow the planning of multicentre studies when the numbers of workers exposed to specific nanomaterials are too low in a single centre (Nasterlack, Zober and Oberlinner, 2008).

Furthermore, even though toxicological studies on animals and epidemiological studies on the consequences of exposure to the ultrafine particles resulting from some industrial processes or to atmospheric pollution indicate potential effects on the respiratory and cardiovascular systems, the present lack of knowledge on the human health effects of exposure to nanoparticles represents a significant challenge when establishing monitoring programs. Nevertheless, French researchers propose monitoring several respiratory system disorders such as pulmonary inflammation and the incidence or exacerbation of chronic obstructive diseases, and cardiovascular system disorders such as myocardial infarction, strokes, thrombosis and arrhythmia (Boutou-Kempf *et al.*, 2011).

In the province of Quebec, a preliminary epidemiological component was included in a telephone survey carried out in 2007 by E&B Data for NanoQuébec (Truchon and Cloutier, 2008). Of the 62 companies contacted, 19 answered a questionnaire: 4 were active in production only, 10 used nanotechnologies in their work processes, and 10 combined production and use. Based on the information provided by 14 of these companies, 308 workers were at risk of exposure, with 68% having a university degree. Of these 308 workers, 30% were in direct contact with nanomaterials and all wore protective equipment. To complete this initial work, and inspired by a proposal in 2008 for the description of the researchers, companies and workers involved in the nanotechnology field in Quebec (G. Truchon, personal communication), a project for nanotechnology mapping in Quebec is currently being carried out, thanks to the support of the IRSST (Endo, Emond and Ostiguy, 2011). Its aim is to produce a portrait of the nanotechnology situation in Quebec, by documenting the sectors, companies and researchers working with nanoparticles.

In conclusion, despite the need expressed in several countries for epidemiological studies, these studies are taking time to be implemented. The main difficulties mentioned are: 1) the fact that the industrial sectors and exposed workers are still poorly identified, and the lack of specific population registers, 2) the choice of an appropriate methodological approach, and 3) the fact that knowledge about the potential health effects of exposure in humans is still too fragmentary to precisely define the outcomes to be monitored.

Progress in the Metrology/Characterization Theme

Due to the uncertainties about the health effects resulting from exposure to nanoparticles, exposure assessment and control appear to be essential elements in the risk management process. However, 1) the lack of a harmonized approach

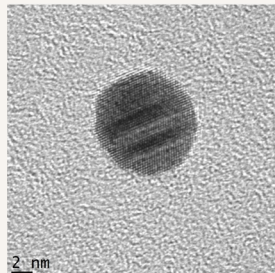
to the strategies and instrumental methods, the parameters measured, the dimension ranges used, and the data analysis procedures, 2) the lack of information about the uncertainty and the limits of detection of the instruments, and 3) the lack of precision about the contribution of other sources to the measured concentrations are deficiencies associated with metrology and characterization, which hinder the implementation of nanoparticle risk management (Kuhlbusch *et al.*, 2011). However, the literature shows that evaluations of the number and mass concentrations of nanoparticles, and of their particle size distribution, their specific surface area, and chemical composition, are necessary.

As an alternative to the different sophisticated nanoparticle detection instruments (which are difficult to transport and rather inaccessible by occupational hygienists), work carried out by members of the nanotoxicology group explored the effectiveness of microscopy techniques in characterizing the structure of nanoparticles or nanomaterials. Among these techniques, analytical transmission electron microscopy (ATEM) is particularly useful. In addition to its atomic resolution (Figure 2), it allows the particles or regions of interest in manufactured products to be directly observed in order to determine the size, quantity (volume fraction), morphology, chemical composition, and crystalline structure. Such observations also make it possible to distinguish individual particles from agglomerates and aggregates and to obtain particles sizes by number (as opposed to particle sizes by mass). In addition, work carried out with industrial partners from Quebec confirmed what was predicted by theory, that a very large number of very small particles constitutes a very small fraction of the sample weight (unless that sample only contains very small particles).

Other work has focused on the development of sampling techniques paired with different types of impactors (Noël *et al.*, 2013; L'Espérance *et al.*, 2008). The results show that samples can be collected for subsequent microscopic observations without any modification of the samples, for example by deposition on

FIGURE 2

Analytical Transmission Electron Microscopy (ATEM) Image of a Gold Nanoparticle Showing the Presence of Crystallographic Twins



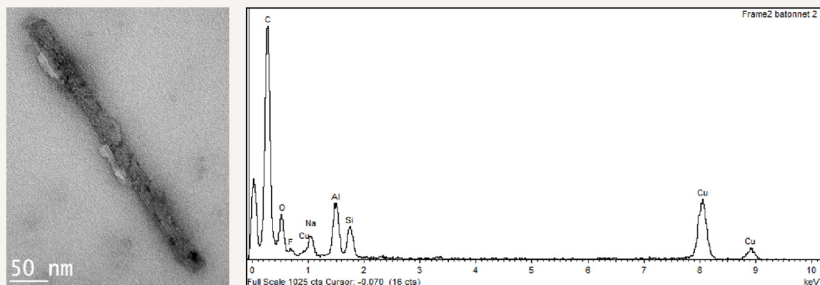
3-mm grids directly usable in electron microscopy. Filter deposition techniques for electron microscopy analysis have also been developed. Moreover, these studies have shown the importance of analyzing a significant number of particles in order to determine the characteristics by electron microscopy, whether in powder form or by deposition on filters or on solid substrates in impactors.

Other examples of recent work in Quebec by the group's members include evaluations of occupational exposures to nanoparticles, both manufactured and unintentionally produced, in two welding schools, in one aluminum plant, in one thermoplastic material processing company, and in three laboratories producing and/or using nanoparticles (Debia *et al.*, 2012a, 2012b; Cattin *et al.*, 2012). The research has revealed that aluminum plant workers, welders, and workers in the thermoplastic material processing industry can be exposed to high concentrations of unintentionally produced nanoparticles (Debia *et al.*, 2012b). An ATEM analysis of the nanoparticles emitted in an aluminum plant shows the presence of spherical and fibrous nanoparticles that can be isolated or agglomerated and that mainly contain the elements Al, Na and F (Figure 3). In the research laboratories, the evaluations did not show major concentrations of nanoparticles. Only one nanoparticle production process involving crushing in liquid nitrogen generated detectable concentrations of nanoparticles. The manipulation of nanoparticles in glove boxes in the other two laboratories seemed to adequately prevent worker exposure.

Since there is no exposure limit assigned to nanoparticles, and the implementation of such limits presents important technical and scientific challenges, the metrology and characterization results should not be interpreted using the quantitative conventional approach of exposure evaluation, but instead by using a semi-quantitative hybrid approach whose purpose is to implement prevention measures adapted to each situation. The metrology and characterization of nanoparticles are therefore complementary and will evolve in the light of new knowledge.

FIGURE 3

Particle Collected in the Air of an Aluminum Plant and Associated with an Approximate Aerodynamic Diameter of 28 nm



Progress in the Aerodynamic Behaviour/Ventilation Theme

In the workplace, the main exposure route recognized by interventionists is the inhalation of aerosol nanoparticles. As a result, particular attention must be paid to the effectiveness of exposure control systems such as general ventilation and local exhaust systems. In a context in which nanoparticle exposure measurements are relatively complex, the development of numerical models for predicting the concentration of a nano-aerosol in a confined space becomes particularly important. These models, paired with flow modeling tools, will be capable of predicting the workplace exposure levels for several ventilation scenarios and thus contribute to the development of effective and efficient collection systems.

The purpose of the work carried out at the École de technologie supérieure is to develop and validate numerical models for predicting the spatiotemporal evolution of a nano-aerosol's concentration in relation to airflow conditions, the aerodynamic diameter of the nanoparticles emitted, and their rate of emission per unit of time. More specifically, the aerodynamic behaviour research activities focus on 1) the evaluation of the deposition coefficients of nanoparticles in an enclosure, 2) the modeling of the transport and diffusion of a nano-aerosol in an inhalation chamber, and 3) the implementation of a diffusion-inertia Eulerian model in an open object-oriented source code.

Due to the small size and low inertia of nanoparticles, their aerodynamic behaviour can be modeled using a Eulerian model in which a single concentration equation describes the aerosol's behaviour. While it is impossible to obtain the particle field velocity with this approach, it considerably reduces the number of equations to be solved. Deposition by particle diffusion is considered by imposing a mass fraction of zero on the solid walls. The passive scalar transport equation coupled with the Navier-Stokes equations was solved numerically to predict the deposition coefficients of TiO_2 nanoparticles in an asymmetric airflow in a duct (Morency and Hallé, 2013), and in the airflow of a cubic exposure chamber (Morency *et al.*, 2008). The results of these models compare favourably with the deposition coefficients obtained using the Brockmann (2001) and Crump, Flagan and Seinfeld (1983) relationships. This approach was also used to predict the concentration of a TiO_2 nano-aerosol in an inhalation chamber in relation to the ventilation conditions (Morency and Hallé, 2010). The aim of this work was to verify the uniformity of the concentration of a TiO_2 nano-aerosol for a study on the pulmonary toxicity of this aerosol in rats exposed by inhalation. The numerical results compared to the experimental measurements obtained using an ELPI cascade impactor showed that, for low concentrations, the solving of a single concentration equation would suitably represent the transport, diffusion and deposition of a nano-aerosol on the walls. This modeling also showed the importance of the mesh concentration on the solid walls. In fact, since the

concentration boundary layer thickness is much less than the velocity boundary layer thickness, particular attention must be paid to the mesh in order to suitably capture the high concentration gradients at the walls.

Work is also being carried out to validate a diffusion-inertia model. This model, valid for low inertia particles, is based on the solving of a passive scalar transport equation, modified to take into account particle sedimentation. This model's predictions are actually compared to particle size distribution measurements provided by an EEPs spectrometer.

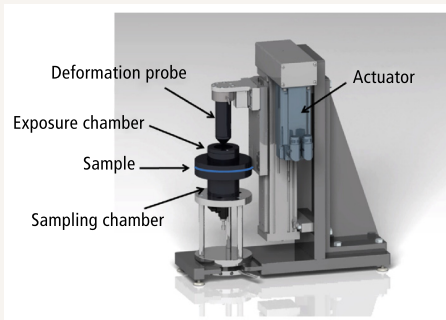
Progress in the Protective Equipment Theme

An increasing number of studies show that skin can be permeable to nanoparticles (Wu *et al.*, 2009). However, some research has focused on protective gloves and clothing against nanoparticles. The work carried out by nanotoxicology group members at the École de technologie supérieure has led to the development of a method for studying the penetration of nanoparticles through protective materials under conditions simulating workplace use (Dolez *et al.*, 2012). In particular, nanoparticles can be applied in solution or in powder form. At the same time, material samples are simultaneously subjected to the application of mechanical deformations simulating what happens at joints in the body, for example when opening and closing the hand (see Figure 4). Different environmental conditions can also be applied during the tests in order to simulate the microclimate inside protective clothing (temperature, humidity, and contact with perspiration).

The initial results obtained with disposable nitrile gloves showed the passage of powder TiO_2 nanoparticles after sixty successive deformations (Vinches, Dolez and Vu-Khanh, 2012). In the presence of a colloidal solution, the phenomenon occurred after only thirty deformations. The amplification of the phenomenon is

FIGURE 4

Schematic Representation of the Experimental Device for Measuring the Penetration of Nanoparticles through Protective Materials

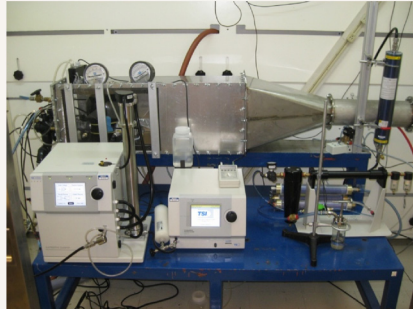


attributed to the swelling of the elastomer membrane by the colloidal solution liquid carrier. In the case of butyl rubber, no passage of nanoparticles was detected. For protective clothing, the results show the passage of TiO_2 nanopowder after 60 deformations with a polyethylene/polypropylene non-woven fabric, and after 20 deformations with a cotton/polyester woven fabric used for labcoats. These initial results demonstrate the need for continuing these investigations so that more precise information can be provided on the levels of protection offered by protective gloves and clothing in the event of exposure to nanoparticles and in order to guide the workers' choice.

N95 filters are the ones most used in respiratory protection. Their effectiveness under different conditions (breathing rate, humidity, duration of their exposure to nanoparticles) is the subject of studies at the IRSST to 1) develop and validate a test bench for generating nanometric size particles under controlled experimental conditions (Figure 5), and 2) evaluate the effectiveness of N95-type filtering facepieces exposed to nanoparticles (Mostofi *et al.*, 2011, 2012).

FIGURE 5

Test Bench for Measuring the Effectiveness of N95 Filters



The results show that for an airflow of 85 L/min, the penetration of nanoparticles through the N95 filters was less than 5%, which is consistent with NIOSH standard 42CFR part 84. The most penetrating particles (MPPS) are between 30 and 50 nm in size. High airflows (> 85 L/min) considerably reduce the efficiency of these filters. Furthermore, the efficiency of N95 filters increases with the duration of use because of a clogging effect as well as the dimension of the most penetrating particles. Finally, the study on the efficiency of N95 filters in cyclical flow mode simulating human breathing confirms the conclusions obtained in constant flow mode (Mahdavi *et al.*, 2012). It should be noted that one original feature of the work carried out by the group's members is in the method used to calculate the filtration efficiency, namely with a polydisperse aerosol, contrary to the methods used elsewhere, which are based on monodisperse aerosols.

Impacts

Since its formation in 2006, the nanotoxicology group has had major impacts on the training of future scientists. Students and postdoctoral fellows represent close to 30% of the members. Some have benefitted from direct financial support with, for example, eight \$800 scholarships being awarded in 2009. Support was also provided in 2011 and 2012 to enable a doctoral student to present his research work at the International Conference on Nanotechnology: Fundamentals and Applications. Students and postdoctoral fellows are regularly invited to describe the progress of their work at scientific events or gatherings, for example within the quarterly scientific meetings of the nanotoxicology group. Finally, it is worth mentioning that some of these students were recently rewarded for their efforts: Alexandra Noël, doctoral student at the Université de Montréal, received one of the three awards for the best student communication at the 2012 colloquium of the QOHSRN, and Ludwig Vinches, doctoral student at the École de technologie supérieure, received the 2011 *Prix de la Relève* award from the CTT Group.

The group has also contributed to the establishment of a solid laboratory infrastructure in nanotechnology, in particular through a grant of \$1.8 million from the Canada Foundation for Innovation in 2009 for a project entitled “Xenobiotics and nanoparticles: new approaches for characterization, expology and biological monitoring.” This project, conducted by the Université de Montréal, includes equipment at the leading edge of technology for generating and detecting nanoparticles as well as an ultramodern facility for exposing small rodents to nanoparticles by inhalation. Other pieces of equipment have also been acquired to strengthen the nanotoxicology infrastructure for the group, for example a nanosizer obtained through an NSERC equipment grant awarded in 2011 to UQAM.

Another important impact of the nanotoxicology group involves the collection and dissemination of information in this field. For example, a database of references relating to the toxicology of nanoparticles was developed and is accessible by group members. It is indexed through key words. A list of commercially available nanoparticles has also been compiled. It includes information on the physical properties of nanoparticles as well as an indication of their price. Finally, a technology watch service is offered through e-mails sent to the group’s members about published articles and reports that are relevant in this field or announcing conferences or any other event of potential interest to them.

The networking between the group’s members has also contributed to the development of several collaborative research projects. These include four projects carried out in the framework of an IRSST-NanoQuébec competition organized in 2009 on the impact of nanoparticles, metrology and means of control:

- Development of a method for measuring the penetration of nanoparticles through glove materials under conditions simulating workplace use, with researchers from the ÉTS, IRSST, UdeM, École Polytechnique, and Harvard University in the United States;
- Procedure for measuring and controlling manufactured nanoparticles, with researchers from the ÉTS and the IRSST;
- Development of procedures for measuring the effectiveness of filters in capturing nanoparticles, with researchers from Concordia University, the IRSST, and NIOSH in the United States;
- Characterization and control of occupational exposure to nanoparticles, with researchers from UdeM and Health Canada.

This collaborative work between the group's members has led to numerous publications. Between 2006 and 2012, there were more than 25 articles in scientific journals and in conference proceedings, 11 peer-reviewed reports, 7 articles in technical journals, and more than 60 oral presentations and poster presentations at national and international events.

The group was also the initiator of several scientific events. In particular, besides the scientific activities organized in conjunction with the group's quarterly meetings in which some of the members present the results of their work, the group contributed to the participation of Dr. Guillemin, former director of the Institute for Work and Health in Switzerland, at the opening of the 31st AQHSST Conference in 2009. A Symposium entitled "The infinitely small in action: Research on nanoparticles and ultrafine particles in an OHS context" was also organized during the 2012 ACFAS conference. Its program included seven oral presentations, with one by Benoit Balmana, president of NanoQuébec, and a round table discussion on the evolution of needs in the group's five priority themes.

Finally, the nanotoxicology group has also had major impacts on international cooperation. In particular, The International Team in Nanosafety (TITNT) was created by members, with the support of the Quebec Ministère du Développement Économique, Innovation et Exportation and the Canadian Institutes of Health Research (www.titnt.com). Its team consists of researchers from France, Germany, Japan, the United States and Canada, including several group members. Other partnerships have also been established, among others those with the Laboratoire de nanochimie et sécurité des nanomatériaux of the Commissariat à l'énergie atomique et aux énergies alternatives (CEA) and the Laboratoire Santé Travail Environnement of the Université de Bordeaux in France, and with the Harvard School of Public Health and the National Institute for Occupational Safety and Health in the United States.

Conclusions and Prospects

Since the nanotoxicology group's launching in 2006, it has resulted above all in the creation of research teams in several institutions in Quebec. These multidisciplinary teams continue to be active in the nanotoxicology field and in the occupational health and safety aspect of nanotechnologies. New members are joining regularly and continue to submit grant applications, to carry out projects, and to disseminate their findings.

In addition, the early integration of students from all levels into these teams and the important role that they can play there due to the egalitarian status created by the group's climate, help to train and prepare these future scientists in a gradual and informal way. Furthermore, some of the students that were involved in the group at the outset are now active as researchers. This therefore perfectly fulfills one of the most important mandates of the QOHSRN.

Moreover, the quality and importance of the research carried out by the group's members can be attributed to the establishment, right from the group's creation, of a research program that continues to be relevant today, as well as to the multidisciplinary nature of the group's members. This observation is furthermore supported historically by the group's members receiving almost all of the research funds in the public call for proposals made by NanoQuébec and the IRSST in 2008. It is important to mention that all these applications were peer reviewed at the international level.

Finally, the nanotoxicology group's research and partnership platform has demonstrated its effectiveness in contributing to the advancement of knowledge in this field and is perfectly able to meet the still present research needs. It is nevertheless important for this community of researchers to continue to receive encouragement and support so that it remains a dynamic place of exchange with numerous direct and indirect scientific impacts.

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SUMMARY

Advancement in Quebec Research on the Prevention of Risks Related to Occupational Exposure to Nanomaterials

This article includes a presentation of the research priorities and achievements of the members of this nanotoxicology researcher group in the five following themes: toxicology, epidemiology, metrology/characterization, aerodynamic behaviour/ventilation, and protective equipment. The toxicology section includes a presentation of results relating to the respiratory effects of titanium dioxide (TiO₂) nanoparticles *in vivo* and carbon nanotubes (CNT) *in vitro* and *in vivo*. Regarding occupational exposure to nanoparticles, studies that have been carried out include evaluations of mass and number concentrations, measurements of particle size distributions, as well as electron microscopy characterization of nanometric-sized particles. In the field of protective equipment, studies are being carried out to measure the penetration of nanoparticles through protective gloves and clothing under conditions simulating their use in workplaces. Furthermore, expertise has been developed at the IRSST on the measurement of filter efficiency in venti-

lation systems and respiratory protective equipment. Respiratory filter efficiency performance was evaluated under constant and variable airflows. The article ends with a description of the direct impacts on nanomaterial risk prevention related to the nanotoxicology researcher group.

KEYWORDS: advancement in research, risk prevention, occupational exposure, nanomaterials

RÉSUMÉ

Avancement des recherches au Québec sur la prévention des risques liés à l'exposition professionnelle aux nanomatériaux

Cet article présente les orientations de recherche priorisées et les réalisations des membres de la communauté de chercheurs en nanotoxicologie dans ces cinq thématiques : la toxicologie, l'épidémiologie, la métrologie/caractérisation, le comportement aérodynamique/ventilation et les équipements de protection. Par exemple, la section toxicologie présente des résultats portant sur les effets respiratoires des nanoparticules de dioxyde de titane (TiO₂) *in vivo* et des nanotubes de carbone (NTC) *in vitro* et *in vivo*. En ce qui concerne l'étude de l'exposition professionnelle aux nanoparticules, les recherches réalisées incluent des évaluations des concentrations en masse et en nombre, des mesures de distributions granulométriques ainsi que la caractérisation en microscopie électronique des particules de taille nanométrique. Dans le domaine des équipements de protection, des études sont menées pour mesurer la pénétration des nanoparticules à travers les gants et les vêtements de protection dans des conditions simulant leur utilisation en milieu de travail. Par ailleurs, une expertise sur la mesure d'efficacité des filtres des systèmes de ventilation et des appareils de protection respiratoire a été mise en place au laboratoire de l'IRSST. La performance des filtres a été étudiée sous différents régimes de débit constant ou variable. L'article se termine par une description des retombées directes de la formation du regroupement dans le domaine de la prévention des risques liés aux nanomatériaux.

Mots-clés : avancement des recherches, prévention des risques, exposition professionnelle, nanomatériaux

RESUMEN

Avances de la investigación en Quebec sobre la prevención de los riesgos vinculados a la exposición profesional a los nanomateriales

Este artículo presenta las orientaciones de investigación priorizadas y las realizaciones de los miembros de la comunidad de investigadores en nano-toxicología relativas a cinco temáticas: la toxicología, la epidemiología, la metrología/caracte-

rización, el comportamiento aerodinámico/ventilación y los equipos de protección. Por ejemplo, la sección toxicología presenta ciertos resultados sobre los efectos respiratorios de las nano-partículas de dióxido de titanio (TiO₂) in vivo y de los nanotubos de carbono (NTC) in Vitro e in vivo. En lo que respecta al estudio de la exposición profesional a las nano-partículas, las investigaciones realizadas incluyen evaluaciones de concentraciones en masa y en cantidad, medidas de distribución granulométricas así como la caracterización en microcopia electrónica de partículas de talla nano-métrica. En cuanto al campo de los equipos de protección, se llevan a cabo estudios para medir la penetración de nano-partículas a través los guantes y la vestimenta de protección en condiciones que simulan su utilización en los medios de trabajo. De otro lado, la pericia en la medida de eficacia de los filtros de sistemas de ventilación y de aparatos de protección respiratoria se ha desarrollado en el laboratorio del IRSST. Se ha estudiado el rendimiento de los filtros bajo diferentes regímenes de cadencia constante o variable. Para terminar, el artículo presenta una descripción de las repercusiones directas de la formación de reagrupamientos en el campo de prevención de riesgos vinculados a los nano-materiales.

PALABRAS CLAVES: progreso de las investigaciones, prevención de riesgos, exposición ocupacional, nano-materiales