

# N A N O M A T E R I A L S

Current situation and prospects  
in occupational health and safety



NANOMATERIALS

C O N T E N T S

04

Nanomaterials :  
a priority  
for prevention

06

What are  
nanomaterials?

08

Where are  
nanomaterials found ?

10

What are the health  
effects of nanomaterials?

14

What is known  
about exposure  
to nanomaterials?

20

Is there any  
effective protective  
equipment against  
nanomaterials?

24

What risk management  
for nanomaterials?

28

Publications  
& Abbreviations

## NANOMATERIALS: A PRIORITY FOR PREVENTION

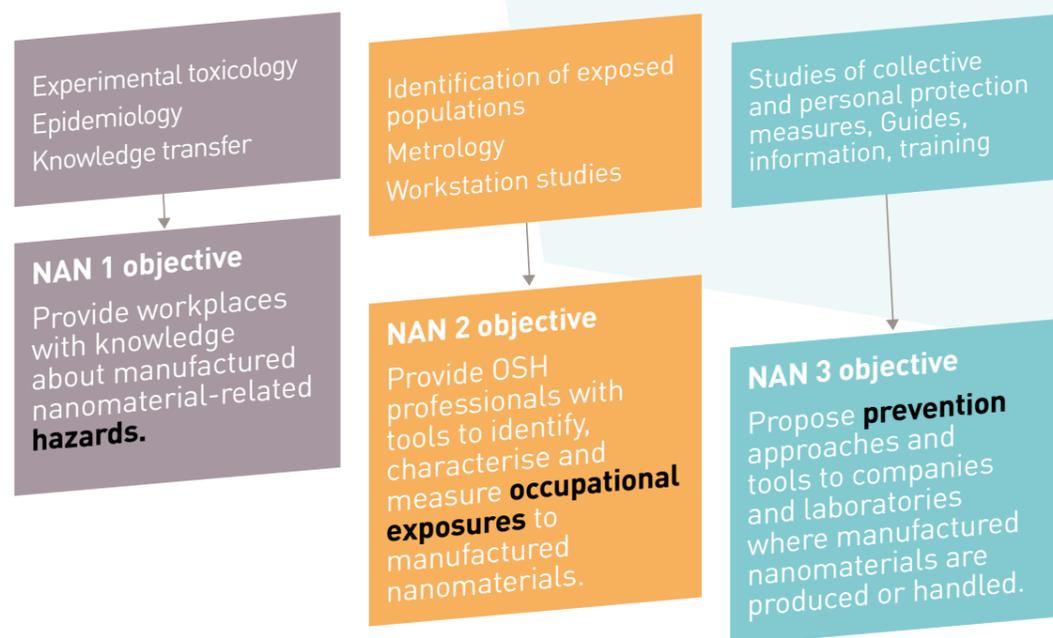
→ **The development of manufactured nanomaterials entails exposure of increasing numbers of workers.**

Since the early 2000s, even though concerns have been expressed about the health effects of nanomaterials, huge budgets have been devoted to research into new applications all over the world. Nanomaterials have a growing impact not only in cutting-edge sectors such as electronics, aeronautics and alternative energies, but also in traditional sectors such as the chemical, plastics, automotive, building, food and cosmetics industries. However, most funding is oriented towards the development of applications, while very little goes to occupational health and safety issues. According to

various estimates, some 300,000 to 400,000 people are currently employed in the nanotechnologies in Europe. In France, over 5,000 workers in companies and 7,000 laboratory researchers might be exposed.

Anticipating and controlling nanomaterial-related risks are among the priorities of most occupational health and safety organisations. In the US, NIOSH is undertaking a considerable research effort in this field. INRS has been working hard for several years to provide solutions and make them available to those in charge of risk prevention in the workplace. In this respect, INRS was one of the first organisations to turn the spotlight on the

### Objectives of the INRS Nano programme



occupational health issues of nanoparticles in an expert opinion published in 2007 [4]. It was found that there was a considerable need for research and an urgent need to develop prevention measures appropriate for nanoparticles.

In 2008, INRS set up an action programme for nanomaterial-related risks. This is currently continuing as part of its 2013-2017 strategic plan, and is organised around three goals designed to provide some answers to the challenges raised by nanomaterials.

The programme builds both on INRS's multidisciplinary teams, which bring together toxicologists, chemists, physicists, air flow experts, physicians and epidemiologists, and on external partnerships. Much of the work is carried out within the context of doctoral theses and cooperation, both nationally (CARSAT/CRAM, ANSES, CNRS, Universities, engineering schools, IRSN, InVS, INERIS, CEA, etc) and internationally (European projects, PEROSH network, OECD, the European Agency for Safety and Health at Work in Bilbao, ISSA, etc). The primary aim of this work is to enhance knowledge (laboratory research and field studies) and transfer it to the workplace (assistance, information and training).

The programme includes the acquisition of new equipment and the setting up of safe testing facilities: recently, INRS has set up a new laboratory that brings together research activities relating to the toxicity, metrology and characterisation of nanomaterials and to the efficiency of protective equipment.

In April 2011, the scientific conference on nanoparticle- and nanomaterial-related risks organized by INRS in Nancy in partnership with the PEROSH network was attended by over 450 people, enabling them to share state-of-the-art knowledge and discuss research needs in the field [10]. Over the past decade much effort has gone into developing standards, guides of good practice and methodologies for risk assessment and control. Although progress has been achieved, many questions remain.

This document aims to present nanomaterial-related occupational health issues as well as the resources deployed by INRS to find solutions, share them and disseminate them to various target audiences.



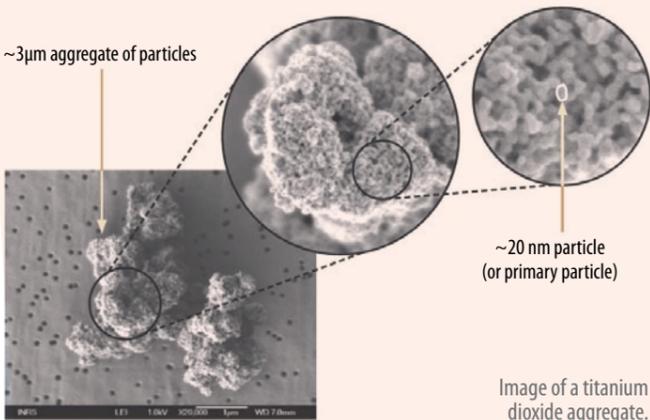
## A new Nanomaterials Research Unit at INRS

This new laboratory, with an area of approximately 600 m<sup>2</sup>, brings together a range of means for research into nanomaterial-related risks. It includes:

- an area reserved for toxicology studies, nanoparticle generation and exposure of animals (rodents) by inhalation, meeting the regulatory requirements for animal testing;
- an ISO class 5 clean room initially dedicated to work on collective protection equipment;
- a zone including an area for the CAIMAN experimental facility and four areas equipped with safety cabinets and controlled environment chambers, for activities relating to nanoparticle characterisation and metrology, and respiratory protective devices.

This research unit responds to the need to carry out inhalation studies. It enables facilities, measuring equipment and human resources to be pooled, and fosters synergies between different disciplines. It has been laid out and equipped according to INRS recommendations for prevention in laboratories where manufactured nanomaterials are handled (ED 6115).

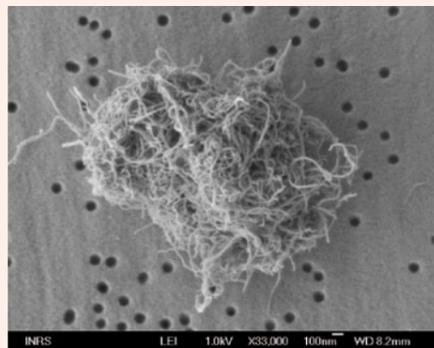
# WHAT ARE NANOMATERIALS?



~3µm aggregate of particles

~20 nm particle (or primary particle)

Image of a titanium dioxide aggregate.

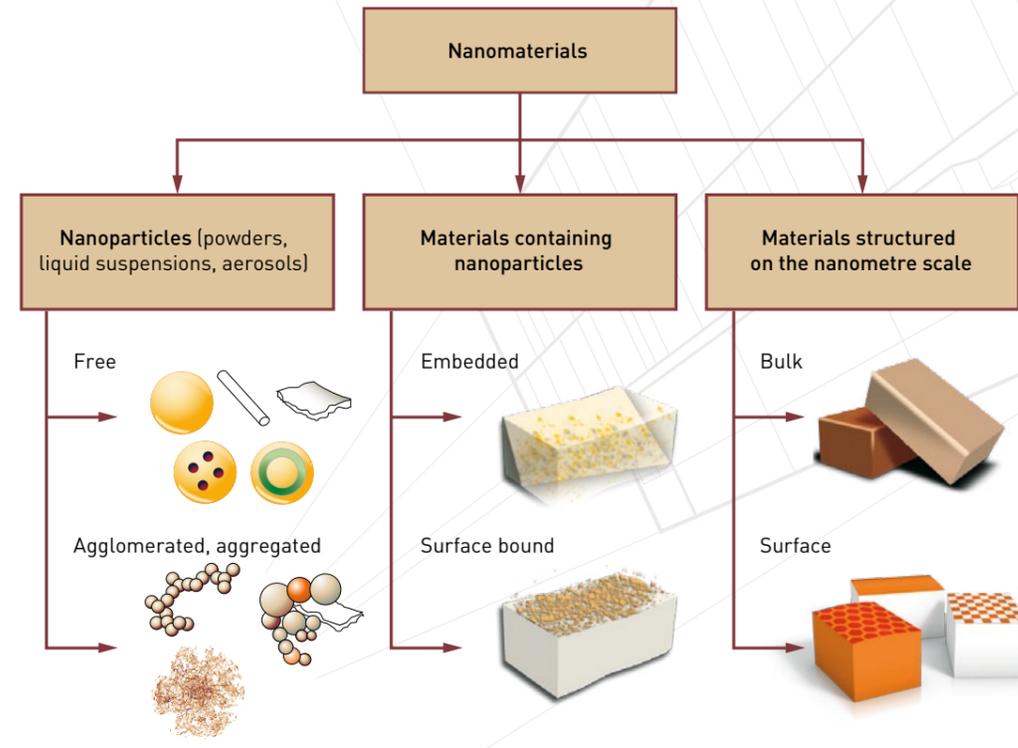


Multi-walled carbon nanotubes seen through a transmission electron microscope.



The term 'nanotechnologies' covers tools, manufacturing techniques and spinoff products that make use of the properties of matter and phenomena at the nanometre ( $10^{-9}$  metre) scale. Within this broad category, manufactured nanomaterials make up a family of chemicals with extremely diverse properties, and it is principally this diversity that makes it so difficult to assess the risks. The potential for innovation of these materials made up of nanometre-scale particles is based on the fact that matter at these scales has specific (mechanical, electrical, optical, catalytic, etc) properties that are different to those of materials with the same chemical composition but made up of larger particles. However, it is these same properties, especially those related to particle surface characteristics, that also cause concern about their health effects.

It is especially difficult to define the precise boundaries between the 'nano' and 'micro' domains. The scientific community agrees that the dimension at which novel or improved properties appear is in the region of 100 nm. A number of national and international organisations such as ISO, OECD and the European Commission have proposed definitions for the term 'nanomaterial'. Most of these definitions are based on the size range of the constituent building blocks (1 to 100 nm) or on the specific surface area by volume<sup>1</sup>. These building blocks (nano-objects or, generically, nanoparticles) are not usually of uniform size: their population is said to be polydisperse (as opposed to monodisperse). That is why some definitions also propose a threshold for the numerical size distribution of the primary particles: beyond this threshold, the material is considered to be a nanomaterial (the values proposed for this threshold lie between 0.15 and 50% in number). From a practical point of view, measuring the size and size distribution of the primary particles requires the use of sophisticated techniques, and there is as yet no standardised method. It should be stressed that these definitions are based on a categorisation of particles by size and do not include any aspects related to their chemical properties or their hazards.



Different categories of nanomaterials. Adapted from Hansen et al. (2007)

Depending on the type of material, nano-objects can have various shapes: more or less spherical (nanoparticles), more or less flat (sheets), or with a relatively large length-to-diameter ratio (nanotubes, nanofibres). Such nano-objects are rarely found in an unbound state but tend to aggregate<sup>2</sup> or agglomerate<sup>3</sup> in clusters whose external dimensions can easily reach several thousand nanometres (several µm). The state of agglomeration/aggregation varies in particular according to the manufacturing process and the medium in which the particles are found (air, biological liquid, etc).

As well as their external structural characteristics, nanomaterials can be distinguished by their chemical properties. Various processes such as coating or functionalisation of particles by polymers or other molecules can alter their properties, giving rise to increasingly sophisticated materials (active nanostructures able to respond to external stimuli, known as 'second-generation nanomaterials'). All these processes lead to a new material whose properties are fundamentally different from those of the original material.

This document deals with nano-objects, their agglomerates and aggregates (NOAAs) intentionally produced industrially

or in research laboratories. There are also many occupational situations where workers are exposed to **nanometre-scale particles**, known as ultrafine particles, unintentionally released by thermal or mechanical processes. It should also be remembered that every day we are in contact with micro- and nanometre-scale particles naturally present in the atmosphere or of anthropogenic origin (pollution related to human activity).

<sup>1</sup> Ratio of the surface area of a particle or of a material to its volume. One of the important characteristics of nanomaterials is the magnitude of their specific surface area per unit volume. The smaller the size, the greater the surface area/volume ratio. For instance, a specific surface area of 60 m<sup>2</sup>/cm<sup>3</sup> corresponds to a monodisperse population of particles smaller than 100 nm.

<sup>2</sup> An aggregate is a cluster of particles held together by strong chemical bonds (covalent bonds).

<sup>3</sup> An agglomerate is a cluster of particles either held together by weak physical bonds (such as van der Waals forces) or entangled (this is the case for nanotubes for instance). An agglomerate can be broken up by a low energy source (shaking, ultrasound).

## WHERE ARE NANOMATERIALS FOUND?



Prefabricated external facing of a building in photocatalytic concrete (with inclusion of stainless steel discs).

### Examples of nanomaterial applications

In most known final applications, nanomaterials are either embedded into an organic matrix (composites, cosmetics) or bonded to a surface (electronics, self-cleaning glass):

- **synthetic amorphous silica:** rubber reinforcing agent (tyres), additives for high performance concrete, coatings, paints, inks, paper, plastics, cosmetics, food
- **carbon black:** rubber reinforcing agent (tyres), pigment (inks, toners)
- **titanium dioxide:** photocatalysts, component of dirt-resistant coatings (glass, cement for building), paints and varnishes, inks, ceramics, cosmetics, textiles
- **zinc oxide:** rubber, cement, cosmetics, pharmaceutical products
- **cerium dioxide:** diesel fuel additive, polishing agents
- **calcium carbonate:** reinforcing agent (rubber, plastics, paper, coatings)
- **nanosilver:** bactericide (textiles, medical equipment)
- **carbon nanotubes:** mechanical strengthening and lightening agent for nanocomposites (sports equipment, aerospace and automotive industries, textiles)
- **quantum dots:** medical diagnosis.



Nanomaterials can take the form of a powder, a colloidal suspension, a deposit on the surface of another material (such as glass or a textile) or be incorporated in a matrix, usually a polymer (nanocomposites based on polycarbonate, polyamide, etc).

The issue of occupational risks can arise at various points in a product's life cycle:

- when nanomaterials are **manufactured:** chemical industry, start-ups, research and development laboratories;
- when nanomaterials are **processed** or incorporated into products: laboratories, formulation and processing industries (such as construction and civil engineering, the cosmetics industry, the plastics industry and paint manufacture);
- when products containing nanomaterials are **used:** cars, construction and civil engineering, etc;
- **at the end** of a product's life when it is processed and recycled: e.g. electronic waste.

Nanomaterial technology is not new. Some of the most common manufactured nanomaterials have sometimes existed for decades, and most of them are manufactured in large quantities (titanium dioxide, synthetic amorphous silica, carbon black, calcium carbonate, cerium dioxide, zinc oxide, silver). Others are more recent and still little used (carbon nanotubes, fullerenes, graphene, etc).

Since 2006, INRS has carried out studies on identifying exposed populations [5, 11]. Carried out as mail surveys, such studies systematically came up against the difficulty companies have in identifying a chemical as being a nanomaterial (safety data sheets not filled in, staff untrained in such identification). The results nonetheless established the existence of 20 production sites, i.e. 2,000 – 4,000 potentially

exposed workers. Except for carbon nanotubes, these mostly concerned the traditional nanomaterials mentioned in the previous paragraph. In 2010, a survey of over 1,000 companies belonging to the chemical, paints, inks and varnishes, and plastics industries gave an estimated figure of around 4,700 potentially exposed workers in these sectors (production and downstream user establishments). Lastly, an additional field survey on the use of nano titanium dioxide in activities connected to building and civil engineering showed that consumption was still low in this sector, with exposure mainly confined to establishments producing prefabricated components [12].

Recently, a study commissioned by the French General Directorate for Competitiveness, Industry and Services identified 130 – 180 companies genuinely focused on nanomaterials R&D and/or marketing activities, over half of which are SMEs. A significant number of low-profile start-ups produce nanomaterials. The survey confirms that the category of innovative products (carbon nanotubes, fullerenes, quantum dots, etc) is still at a pre-industrial stage. Workers currently exposed to these products are therefore most likely to be found in research laboratories (around 7,000 people in France) or in start-ups.

The fact remains that the diversity and continuous development of applications for nanomaterials, together with the lack of a standardised definition, make it extremely hard to make an accurate assessment of the number of exposed workers. While developments are expected in many sectors, especially in construction and civil engineering, chemicals, plastics, electronics, the automotive and aerospace industries, energy, healthcare, cosmetics and textiles, **the system in France that now makes it compulsory to declare all substances in a nanoparticulate state**, which came into force on 1 January 2013, should improve knowledge about nanomaterials and their uses, and facilitate the identification of potentially exposed populations.

## WHAT ARE THE HEALTH EFFECTS OF NANOMATERIALS?



Microscopy observation of a cell culture being treated with nanoparticles.



### → The health effects of ultrafine particles caused by air pollution or welding processes have long been studied.

Epidemiological studies and human trials under controlled exposure conditions suggest in particular the possibility of respiratory and cardiovascular effects. Although epidemiological studies have been carried out on workers exposed to carbon black or titanium dioxide, it is difficult to draw any conclusions from this work since the size of the dust particles is never clearly established. Consequently, today there exist practically no studies on the specific effects of manufactured nanomaterials on humans. There are several obstacles to carrying out such studies, such as inadequate information about exposure, lack of knowledge of early effects to be measured, and restricted access to companies. In France, the EpiNano monitoring system for workers potentially exposed to nanomaterials set up by InVS could serve as a basis for future epidemiological studies.

Although the experimental toxicity of nanomaterials has been the subject of much research, the findings are often of limited significance: *in vitro* studies on cellular models that are difficult to extrapolate to humans, *in vivo* studies on animals using exposure routes that are not representative of occupational exposure, short exposure periods, insufficient physicochemical characterisation and a wide variety of tested materials. Such studies rarely involve inhalation even though this is the exposure route of most concern for workers.

The goals of **nanotoxicology** are, on the one hand, to study the ability of nanoparticles to penetrate the body, their fate in the body and how they are eliminated, and on the other, to identify their effects both at the site of deposition and at a distance from it. It is also important to determine the dose-response relationship as well as the kinetics of biological responses. This is a complex task due to the diverse physico-chemical characteristics of nanomaterials, which affect their behaviour at the molecular, cell and organic level. The size and distribution of nanoparticles, the extent of agglomeration and aggregation, their ability to produce oxidants, and their shape, surface characteristics and solubility all play a key role in determining their toxicity.

One of the prerequisites in nanotoxicology is therefore the physicochemical characterisation of materials to be tested, not only before exposure but also in the exposure environment. Nanoparticles have specific surface properties (electric charge, porosity, crystal structure, etc) that govern their interaction with the environment in which they are present. This can allow them to adsorb onto their surface macromolecules found in biological media, building a protein or lipidic corona that can affect the distribution and behaviour of the particles in the body. Recent research in this field shows that, in addition to the intrinsic characteristics of nanomaterials, it is also necessary to take into account their biological environment, which adds an extra layer of complexity. Lastly, surface alterations, especially by coating of particles or functionalisation, can modulate these interactions.

### Penetration into the body

In the workplace, inhalation and skin contact are the main possible contamination routes. The penetration of insoluble nanomaterials through the skin has been the subject of a few studies. Percutaneous penetration seems unlikely, and only appears to be significant if the skin's stratum corneum is damaged. Inhalation is the predominant penetration route into the body. There are a number of validated theoretical models that can be used to estimate the likelihood of deposition of inhaled particles according to their size. Particles with a diameter between 10 and 100 nm are mostly deposited in the pulmonary alveoli, in a significantly higher proportion than for micrometre-scale particles. Smaller particles are mainly deposited in the upper airway and, to a lesser extent, in the tracheobronchial region.

### Fate in the body and biological activity

Particle **size** not only determines the site of deposition but also the efficiency of pulmonary clearance<sup>4</sup> systems. In the pulmonary alveoli, clearing cells called macrophages usually take care of the elimination of insoluble contaminants via a phagocytosis mechanism<sup>5</sup>. However, the phagocytosis capacity of these macrophages is weaker with regard to nanoparticles than to larger particles. This may result in a significant accumulation of nano-objects in the pulmonary alveoli as well as greater interaction with the alveolar cells. This overload is likely to cause inflammation that may eventually lead to the development of lung diseases.

It has been shown that in certain cases nanoparticles are able to cross tissue barriers that are considered to have low permeability. Once inhaled, they can cross the alveolar wall, migrate to the pleura and to the lymph node structures, reach the bloodstream

and lymphatic system, and attain various organs such as the spleen, liver, heart, central nervous system and bones. When some nanomaterials such as manganese oxide and titanium dioxide are deposited in the nose they may migrate and accumulate in certain parts of the brain after crossing the blood-brain barrier.

For particles of identical chemical composition and shape, reducing their size causes (at equal mass) an increase in their specific surface area and in the number of reactive groups likely to interact with biological media. Several studies have shown that titanium dioxide, a substance supposed as having low toxicity, has a far greater inflammatory effect on the lungs at the nanometre scale than at the micrometre scale, for a dose of equivalent mass and identical crystal form. In these studies, the dose expressed as surface area was better correlated with the observed effects than the dose expressed as mass.

Some nanoparticles, especially metal oxides, can produce **reactive oxygen species** (ROS, also known as free radicals) on their surfaces or cause them to be produced by cells. This situation can result in toxic phenomena. Induction of oxidative stress is certainly a critical parameter for the determination of nanoparticle toxicity: the connection between the ability of nanoparticles to produce oxidising species *in vitro* and the onset of inflammatory effects *in vivo* has been clearly demonstrated for various nanoparticles.

As well as their chemical composition, the **shape** of nano-objects is a determining factor in their biological activity. Several *in vivo* studies have compared the effects of fibrous and spherical titanium dioxide and carbon nanoparticles, and concluded that, at equivalent doses, the fibrous form causes greater inflammatory effects. The extremely large length-to-diameter ratio of carbon nanotubes, combined with their biopersistence, has raised concern about their ability to trigger pulmonary reactions similar to those caused by asbestos.

Lastly, just as for micrometre-scale particles, the **solubility** of nanoparticles can have an impact on biological effects. Slow dissolution with release of hazardous compounds such as toxic ions can become a major factor of toxicity: then the solubilised nano-objects are transferred from the lungs to the bloodstream.

<sup>4</sup>Pulmonary clearance: a measurement of the ability of the lungs to eliminate a substance (amount of substance eliminated per unit time).

<sup>5</sup>A mechanism that enables certain specialised cells (macrophages, neutrophil granulocytes) to ingest foreign particles.



**There is a considerable need for research into nanomaterial toxicity. Answers are urgently required in the following areas:**

- **evaluating toxic effects after exposure of laboratory animals by inhalation:** inhalation studies appear to be the most relevant for the early assessment of nanomaterial-related hazards; an INRS study will focus on the effect of agglomeration on pulmonary toxicity and the toxicokinetics of titanium dioxide. Another study, carried out as part of the European project **NANoREG**<sup>6</sup>, and where principal INRS partners are NRWCE and PHE, will focus on toxicity by inhalation of carbon nanotubes;
- **studying the effect of physico-chemical parameters on the biological activity of nanomaterials**, with the aim of proposing new approaches to predicting effects and developing safer products;
- **studying the effect of the method of administration**, by comparing the effects observed after exposure by inhalation and after intratracheal instillation;
- **determining the parameter (metric) best correlated with observed effects:** mass, number of particles, surface area, etc;
- **evaluating the ability of nanoparticles to migrate from the lungs to other organs** or biological compartments such as the blood, heart and brain, and the effects on these organs;
- **looking for toxic effects** on the immune system;
- **proposing the most suitable *in vitro* and *in vivo* test methods** for nanomaterials and strategies to reduce animal testing;
- **studying the penetration of insoluble nanomaterials through healthy skin**, since the results of published studies do not completely rule this out;
- **conducting epidemiological studies as early as possible:** in the near future INRS plans to launch a study whose aim will be to look for early respiratory effects in an exposed population. Other effects could be studied, such as cardiovascular effects. The prospective cohort set up as part of the EpiNano surveillance system could be of significant help in identifying companies that work with nanomaterials [32]. This is one of the goals of the cooperation agreement on epidemiological surveillance and studies, specific to manufactured nanomaterials, signed in 2012 by INRS and InVS.

<sup>6</sup> The goal of the NANoREG project funded by the European Commission is to provide answers to the technical questions posed by the application to nanomaterials of European regulations such as REACH.

Since 2007, INRS has been helping to improve knowledge in the field of nanotoxicology. The materials studied are selected from among those produced or used in large quantities, and those for which there is cause for concern, such as iron oxides, titanium dioxide, synthetic amorphous silicas and carbon nanotubes. The goals of the studies, carried out *in vitro* or *in vivo*, are in particular to discover whether there exists a different toxicological profile depending on whether the particles are in micro- or nanoparticulate form, to specify the determining physicochemical characteristics, and to propose test methods suitable for nanomaterials.

The results show that biological effects, such as inflammatory potential [18] or the immunosuppressive effect of iron oxide particles [15] studied in rodents by the intratracheal route, are greater for most of the nanoparticles tested than for their micro-sized counterparts. In a study in rats on potential translocation into the central nervous system via the olfactory route, no cerebral translocation was observed for any of the nano-alumina studied [21].

Because of its ability to give advance warning of carcinogenic effects, genotoxicity is a major research area in nanotoxicology, and has been the subject of several studies at INRS [16, 17, 19, 20], especially as part of the European Joint Action **Nanogenotox** coordinated by ANSES. The results reflect the inconsistency of current data in this field, since they are heavily affected by experimental conditions, dispersion method, type of cell line, and type of particle (size and/or specific surface area, crystal form, presence or absence of coating, etc).

The overall results, compared with those available in the literature, show that it is not possible to formulate a general hypothesis about nanomaterial toxicity. Every nanomaterial, including those which share the same chemical composition, has its own toxicological profile, and must be evaluated on a case-by-case basis. To date it has not proved possible to predict the potential effects of a nanomaterial due to the large number of parameters affecting its toxicity.



Treatment of cell cultures with nanoparticles in suspension.

## Focus on... The potential health effects of two insoluble nanomaterials: ultrafine titanium dioxide and carbon nanotubes

**Titanium dioxide** exists in different forms, basically sub-micron forms (fine or pigmentary TiO<sub>2</sub>) and nanometre forms (ultrafine TiO<sub>2</sub>). Ultrafine TiO<sub>2</sub> is one of the most widely used nanomaterials. It is marketed either in its original form or, more commonly, in modified form following treatment of the particle surfaces.

Titanium dioxide was long considered an insoluble, inert material with low toxicity, and categorized among dusts said to have no specific effects. However, as the particles become increasingly fine, the material takes on new properties that can alter its biological activity.

Many toxicological studies using a single intratracheal instillation or repeated dose inhalation have shown pulmonary inflammatory effects that were more pronounced with ultrafine TiO<sub>2</sub> than with fine TiO<sub>2</sub>. These effects are dose-dependent when the dose administered is expressed as surface area, and their intensity depends on a large number of parameters such as exposure level and duration, size, crystal structure, and particle surface characteristics.

In long-term studies carried out on rodents exposed by inhalation, ultrafine TiO<sub>2</sub> caused

persistent pulmonary inflammation and increased frequency of pulmonary tumours at especially high doses. These observations have led the International Agency for Research on Cancer (IARC) to categorize titanium dioxide in Group 2B, agents that are possibly carcinogenic to humans, on the basis of sufficient evidence from animal testing. However, epidemiological data in humans does not provide conclusive evidence.

For many authors, carcinogenic activity is not a specific effect of the material but rather a generic effect of poorly soluble, low-toxicity particles, related to a secondary (or indirect) genotoxicity mechanism associated with persistent inflammation that appears at sufficiently high doses. Further studies are needed to confirm this hypothesis.

**Carbon nanotubes** (CNTs) are a crystalline form of carbon whose structure can be represented by one or more sheets of graphene rolled up on themselves or around each other (single-walled or multi-walled). The diameter of these cylinders varies from a nanometre to a few tens of nanometres (100 nm) and their length from a micrometre to a few millimetres. These dimensions give them a high elongation (length-to-diameter) ratio. CNTs exist in many varieties that differ by the number of sheets, size, and composition (presence of metal catalyst residues, functionalisation). They are already used in a number of applications and are reported to be especially promising nanomaterials in terms of technological innovations.

CNTs have already been the subject of many toxicological studies that show that they are a source of serious health concerns if inhaled. Available data include biokinetic studies, sub-chronic 90-day inhalation studies, and studies carried out using other routes with variable exposure times. Some studies on animals have shown that (single- and multi-walled) CNTs can reach the alveoli, penetrate the pulmonary interstitium and reach the subpleural tissue.

Only multi-walled nanotubes have been reported to reach the intrapleural space. Several studies on rodents have shown pulmonary effects at relatively low mass doses, including inflammation, granulomas and fibrosis. The effects appear rapidly and persist or progress after the end of exposure. They are observed whatever the type of CNT, whether purified or not. The extent of agglomeration appears to be an important factor in determining the deposition site and the pulmonary response. In studies where CNTs were compared to other fibrogenic materials (silica, asbestos, carbon black), the effects of CNTs were similar to or greater than the effects of such materials.

In addition, it has been shown that intraperitoneal injection of a single dose causes mesotheliomas in rodents. These effects are observed with multi-walled nanotubes with a length of over 5 µm and a rigid structure, suggesting a 'fibre' type mode of carcinogenic action for certain CNTs.

Extrapolating these results to humans remains difficult. In the current state of knowledge it is not possible to draw any conclusions about the long-term effects of inhaling CNTs. Further studies by this route are necessary, especially to understand the factors that may play a role in causing cancer (biopersistence, size, extent of agglomeration, etc). Results concerning the genotoxicity of CNTs continue to be contradictory and also need to be explored further.

## WHAT IS KNOWN ABOUT EXPOSURE TO NANOMATERIALS?



Adjusting the settings of the CAIMAN facility for the generation of metal nanoparticle aerosols.



There is only a limited amount of data relating to occupational exposure to manufactured nanomaterials. Blame is especially attributed to the lack of consensus regarding measurement criteria, a host of mostly unsuitable instruments, and non-standardised measurement strategies [22, 23, 24]. For nearly ten years, INRS has been working on this issue, focusing on four highly interdependent topics: generation of test nanoaerosols, aerosol metrology, workplace exposure, and nanomaterial characterisation [2, 3].

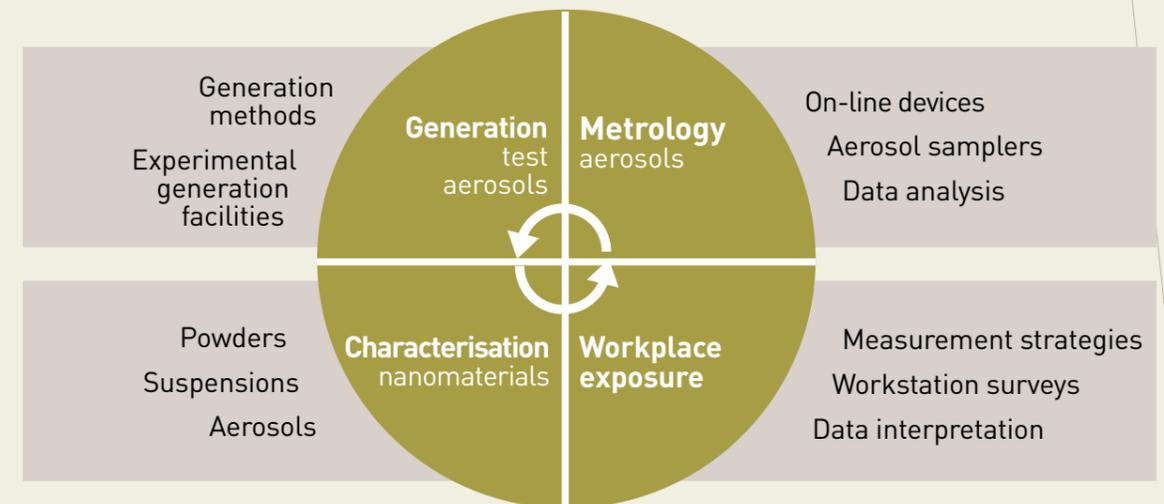
### Generation of test aerosols

In order to study aerosol measuring instruments and develop physicochemical test methods, laboratories need to be equipped with facilities that can generate stable and reproducible test aerosols. It was with this in mind that the CAIMAN<sup>7</sup> experimental facility was developed. Validated for use in the European Nanodevice<sup>8</sup> project, CAIMAN is now regarded as a reference facility in Europe. Aerosols of nanoparticles of different chemical composition, shape, electrical charge, size distribution and concentration level can be obtained [25, 26]. Optimum protection for workers is provided during tests, since the enclosure of the facility was incorporated right from the design stage.

### Aerosol metrology

Many recently available measuring instruments can be used to characterise exposure to nanoaerosols. However, little is known about their efficiency. Evaluating their efficiency is the principal goal of the metrology studies carried out by INRS [27, 28]. Of the instruments studied, some carry out real-time measurement of number, surface-area and mass

## INRS Nano programme: Topics and subjects addressed regarding exposure to nanomaterials

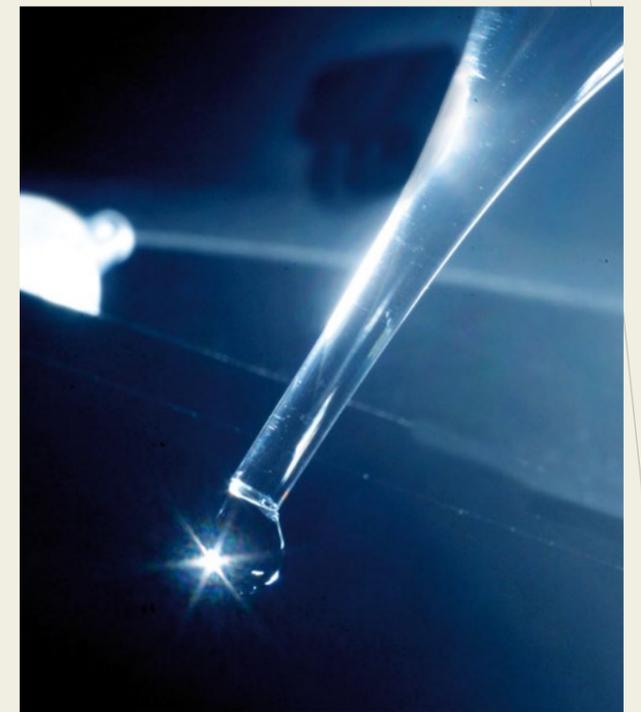


concentrations, while others are designed to collect the aerosol and require further off-line analysis before results can be obtained (electron microscopy or physico-chemical analysis). Several prototypes have been studied in the laboratory, particularly as part of the **Nanodevice** project.

Data analysis plays a key role in the process of exposure characterisation. Therefore, as well as testing the efficiency of different instruments, it is also necessary to produce and test support tools for users. In this context, INRS has developed a modular programme for analysing data from cascade impactors, a family of instruments that produce information for each class of particle size [29, 30]. A specific version of this tool allowing the inversion of data has also been developed for the Electrical Low Pressure Impactor (ELPI).

<sup>7</sup> Characterisation of Nanoparticle Aerosol Measuring Instruments

<sup>8</sup> FP7 project funded by the European Commission, bringing together 26 partners and coordinated by Finland's FIOH institute. The main goal of this project was the study of portable, easy-to-use devices for the characterisation of exposure of workers.



Deposition of a drop of a nanoparticle suspension for particle-size analysis by dynamic light scattering (DLS).



Characterising the exposure of a worker at an emptying station for bags of powdered nanomaterials.

### Workplace exposure

For a worker to be exposed there must be emission of nanoparticles into the air (in other words, formation of a nanoaerosol at source), followed by dispersion into the nearby environment and transfer to the breathing zone. The handling of nanomaterials in powder form is an obvious potential source of exposure. Although exposure is likely to be reduced if the nanomaterial is embedded into a matrix or firmly attached to a surface, emission may also occur in the event of physical attack by processes such as cutting, machining, sanding, wear, etc. Exposure scenarios are therefore many and varied, and can only be identified by carrying out workstation surveys in companies and laboratories.

It is essential to define a **measurement strategy** before carrying out a workstation survey. Drawing on its expertise in measuring aerosols, INRS very early on put forward recommendations regarding characterisation of potential emission and occupational exposure to aerosols. The recommendations were discussed by a working group made up of experts from INERIS, CEA and INRS, and were issued as a joint publication [13]. The strategy differs significantly from that used for traditional aerosols and comprises two levels of intervention. The first level is a basic characterisation intended for people with experience in atmospheric metrology and assessment of occupational exposure to aerosols, and with a basic understanding of nanomaterial-related risks. The second level is an expert assessment aimed at specialists in nanoaerosol metrology.

Given the emerging nature of knowledge in the field of exposure to nanomaterials, there will be changes in this approach, particularly with the prospect of international harmonisation

and standardisation. Such changes are likely to concern the characteristics of the target aerosol to be measured, especially the metric (the parameter that is the best correlated with health effects, used to define the threshold limit values), since progress in toxicology has not yet been sufficient to achieve a consensus on this point. It will also be necessary to standardise measurement strategies with regard to instruments, physico-chemical test methods and interpretation of results.

INRS is implementing this strategy in field studies. Workstation evaluations have been carried out in laboratories and in establishments producing or using nanomaterials such as titanium dioxide, carbon nanotubes and nanosilver. Some of these studies were carried out in partnership with our European counterparts and with the CARSATS. The results obtained to date show that, for most of the activities observed, emissions and/or exposure exist. However, generally speaking, working situations and the corresponding exposures are poorly documented.

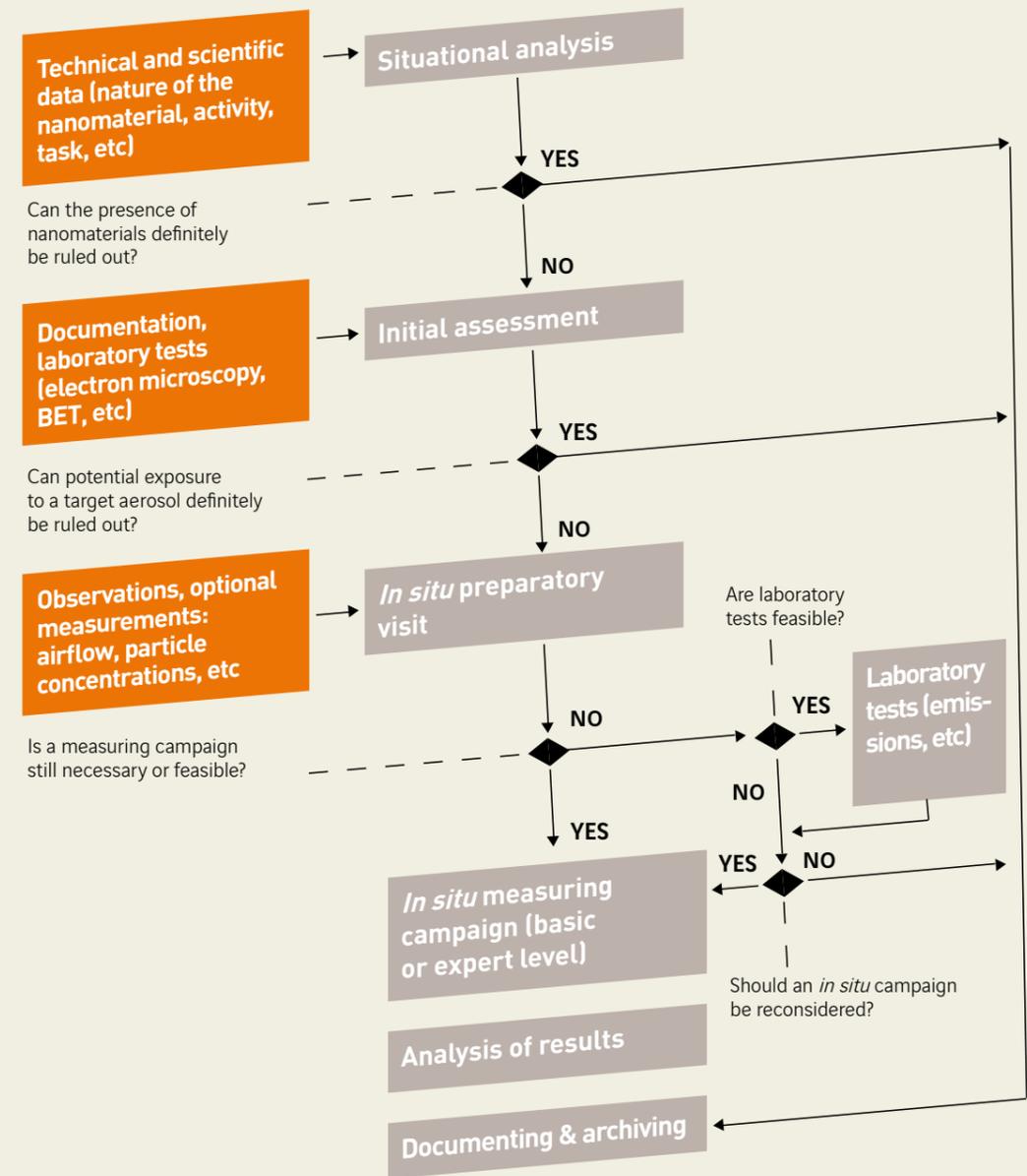
In this context it appeared advisable, as part of the exchanges between PEROSH network institutes, to work towards the development of a nanomaterials-related **occupational exposure database** to be standardised and shared internationally. The project, called NECID<sup>9</sup>, is led by IFA and involves researchers from eight European organisations specialised in occupational health and safety, including INRS. A first version of this database including measurement data obtained as part of other projects or activities specific to these institutes should be completed by end 2013.

<sup>9</sup> Nano Exposure and Contextual Information Database



An example of the real-time measuring devices used to characterise nanoparticle aerosol emissions and exposure in the workplace environment.

## Diagram: Overall flow chart of a strategy\* for characterisation of potential emission and occupational exposure during operations involving nanomaterials



\* Drawn up by CEA, INERIS and INRS experts



Preparing a test on aerosol emission from a nanopowder in the Nanoduster facility.

### Characterisation of nanomaterials

The physico-chemical characterisation of nanomaterials is essential, both to understand what workers are exposed to in their jobs and to better understand the behaviour of nanomaterials in toxicological studies. A large number of parameters need to be taken into consideration, such as particle size and morphology, size distribution, chemical composition, crystal form, density, specific surface area, fractal dimension<sup>10</sup>, and dustiness<sup>11</sup>. For all these parameters, the aim is to have robust characterisation methods and to set up protocols that are able to meet regulatory requirements and eventually be included in reference documents. A number of fundamental and applied research teams are working to develop such methods, some of which are based on combining relatively recent techniques.

For instance, work is being carried out at INRS on developing expertise in determining particle size and morphology using electron microscopy. Since 2013, the Institute has been equipped with a new facility (STEM<sup>12</sup>) which is used to carry out elementary mapping at nanometre scales. Another key parameter under study is the specific surface area. As part of a thesis cofunded by INRS and IRSN, a method that enables the specific surface area of aerosols to be estimated by analysing transmission electron microscope images has been

developed and compared with the conventional BET<sup>13</sup> method [31]. Protocols have been developed in other areas such as the fractal dimension or the particle-size distribution of nanoparticles in suspension.

INRS's expertise in the field of nanomaterial characterisation has been put to good use especially in the **Nanogenotox** Joint Action. The work carried out in this context, in particular with CEA and NRCWE, has helped to define a generic dispersion protocol implemented in the project's toxicological studies.

**Dustiness** is an important factor in risk assessment. The current standardised methods (EN 15051) do not apply to nanoparticles. INRS has designed and tested two new methods, named 'nanoduster' and 'nanodrum', the latter resulting from the systems developed by NRCWE. The methods were applied to various nanomaterials as part of the **Nanodevice** and **Nanogenotox** projects, and have for several years been the subject of joint work between five PEROSH network institutes with a view to developing a standard approach that could be used to classify powders on the basis of this parameter. This work, led by INRS, will continue as part of a **CEN project (Mandate 461)**, in order to achieve five new standards in this field.

<sup>10</sup> Parameter representing the arrangement of primary particles in an agglomerate.

<sup>11</sup> Propensity of powders to emit an aerosol under the effect of a mechanical stimulus.

<sup>12</sup> Scanning Transmission Electron Microscope.

<sup>13</sup> Brunauer, Emmet, Teller.



Despite the progress achieved, there is still a major need for knowledge in the field of occupational exposure to nanomaterials. Efforts need to continue, drawing on the work already carried out:

- **developing and providing OSH professionals and companies with new tools to assess exposure:** sampling systems and measuring instruments appropriate for use in the field, protocols for tests and use of measuring instruments; protocols for the physico-chemical characterisation of powders and aerosols;
- **developing and standardising the measurement strategy internationally;**
- **documenting real emissions and exposure in companies** and developing exposure scenarios;
- **developing the Nano Exposure and Contextual Information Database (NECID);**
- **developing aerosol generation** from powdered nanomaterials in order to carry out inhalation toxicology studies.

INRS actions in this field will be carried out in collaboration with partners pursuing the same goals: PEROSH network institutes, INERIS, CEA, Universities and CNRS. INRS is taking part in the **CEN Mandate 461** projects (2013 – 2018), which aim to achieve European standards in the general area of nanomaterial characterisation and exposure measurement. INRS is also participating in the European **NANoREG** project (2013 – 2016), one of whose objectives is to develop reference methods for the identification and characterisation of manufactured nanomaterials and of exposure to such chemical agents with regard to regulatory requirements. Lastly, in France, INRS is taking part in exposure characterisation as part of the systems for monitoring workers exposed to nanomaterials set up by InVS.

### INRS research into unintentionally produced ultrafine particles

In the field of occupational health, exposure of workers to ultrafine particles (UFP) generated by industrial processes such as welding smoke, thermal projection of metals, diesel engine emissions, metal polishing, etc, has long been well known. Circumstances in which workers are exposed to UFP are much more frequent than for manufactured nanomaterials. Although these are the subject of prevention measures commensurate with the risks, such risks do raise questions. While some of these processes generate very large quantities of highly toxic UFP, very few have until now undergone an assessment adapted to the nanometre fraction of the aerosol to which the workers are exposed.

It is therefore important to avoid restricting research to manufactured nanomaterials alone [1]. INRS carries out specific studies with a view to better correlating health effects and exposure to UFP and to defining appropriate prevention measures. These studies especially concern the development of methods for the characterisation and measurement of UFP aerosols, the improvement of techniques to unclog filters used to filter metallisation fumes, and the study of solutions other than fibrous media for the separation of metallic UFP. And lastly, INRS contributes its expertise to the construction of a job-exposure matrix for UFP (MatPUF programme led by ISPED).

## IS THERE ANY EFFECTIVE PROTECTIVE EQUIPMENT AGAINST NANOMATERIALS?



Seeking effective prevention measures against nanomaterials has proved tricky, not only because there is generally no threshold value guaranteeing adequate protection, but also due to the especially high levels of protection that may be required for nanomaterials presenting a proven health risk. Nonetheless, it is vital to monitor the efficiency of the equipment used, building on the state of the art and currently available knowledge. As for all particulate pollutants, prevention measures are based on ventilation and air purification. Air purification involves both air extraction systems and respiratory protective equipment. In this context, the studies carried out aim to:

- find out whether nanomaterials have any distinctive features with regard to existing prevention measures;
- carry out a quantitative assessment of the effectiveness of such prevention measures with respect to nanomaterials.

### Predictive ventilation<sup>14</sup>

In workplace atmospheres, nanoaerosol transport remains largely dominated by air flow. However, such aerosols have certain specific features that need to be taken into account, such as:

- a significantly greater deposition rate, which is likely to cause contamination of surfaces, especially inside equipment;
- rapidly changing particle size due to agglomeration.

Agglomeration can occur either through self-agglomeration of nanoparticles or through agglomeration of nanoparticles on larger particles, such as those present in natural atmospheric aerosols or resulting from other processes taking place in the vicinity.

Since 2009, INRS, in partnership with the LEMTA laboratory, has been studying the impact of these specific features on the behaviour of nanoaerosols (transport, deposition, agglomeration). The goal is to develop and validate models [33] that simulate the changing characteristics of nanoaerosols over time, from emission to inhalation. Understanding such changes is crucial if we wish to determine worker exposure and design air cleaning systems.



Synthesising and collecting carbon nanotubes in a laboratory safety cabinet.



This work needs to continue until a numerical simulation method (predictive ventilation) is developed that is able to predict the transport of nanoaerosols in workplace atmospheres.

### Collective protective devices

Ventilated chambers such as laboratory safety cabinets and cytotoxic safety cabinets (CSC) are widely used in laboratories for the handling of nanomaterials. These devices are not generally designed specifically for such use, while some are targeted at the nanomaterials sector even though their effectiveness has not been independently assessed.

INRS, in collaboration with IRSN, studied the containment efficiency of a CSC with regard to various nanoaerosols and under a variety of working conditions [34]. The study tested three methods that can be used to evaluate containment: two tracing methods, one based on a fluorescent nanoparticle tracer and the other on a gas tracer, and a method whereby nanoparticles escaping from the chamber are directly counted in a clean room. The results showed that nanoaerosol containment is quantitatively similar to that of a gas, although aerosols are slightly better contained due to deposition on walls and to agglomeration. However, they demonstrated the extreme sensitivity of containment to air flow disturbances (draughts, inadequate installation or handling), as well as the crucial importance of the pollution source (position, intensity, etc).

In addition, the containments obtained might not be consistent with the very low threshold limit values that may apply to some nanomaterials.

From the point of view of prevention, these studies confirm that rules of good practice, generally defined for the use of laboratory safety cabinets or other types of ventilated chamber<sup>15</sup>, must be applied as strictly as possible when it comes to protection from nanoaerosols.



Containment test of a laboratory safety cabinet in a clean room.



With regard to collective protective devices, further work needs to be carried out. INRS will undertake comparative studies of the efficiency of various air flow systems (conventional laboratory safety cabinets, class II microbiological/cytotoxic safety cabinets<sup>16</sup>) with regard to nanoaerosols, and will evaluate their appropriateness for the operating environment and above all for the process they are supposed to make safe.

→ Ultimately, the goal pursued is to propose a suitable containment test for such pollutants which could be used as the basis for the definition of a standardised test. On the basis of the results of this standardised test and of a workstation survey, it would then be possible to supervise the choice of a ventilated chamber from among the various systems on the market.

In connection with this goal, INRS is involved in work on standardising laboratory safety cabinets and will be taking part in the component of the European NANoREG project that deals with the effectiveness of risk-management measures.

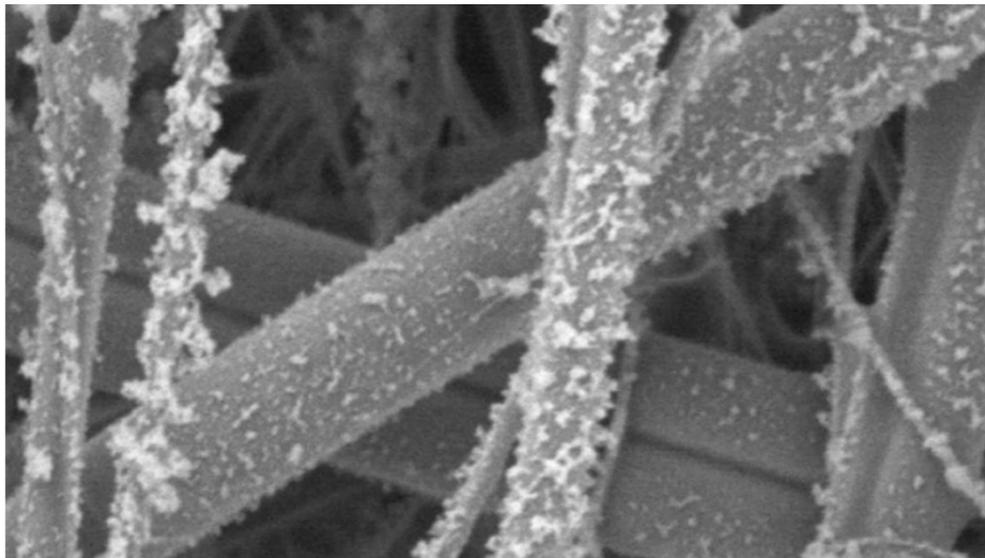
<sup>14</sup>The principle of predictive ventilation consists in using a computer simulation to test the effectiveness of local or general ventilation, with the possibility of exploiting these results when designing facilities.

<sup>15</sup>"Sorbonnes : guide pratique de ventilation", Ed. INRS ED 795, 2009.

<sup>16</sup>The distinctive feature of class II safety cabinets lies in the ventilation of their operating space. Some are now specifically designed for nanomaterials.

### Filtration of nanoparticles

Protective facilities against aerosols usually make use of filters. This is the case for general ventilation systems, ventilated chambers, and source capture systems, which filter the air before discharge outside the workplace, and for respiratory protective equipment, which purifies the ambient air before inhalation. Since 2005, INRS has been working on the measurement of nanoparticle filtration efficiency, in collaboration with the LRPG laboratory. It has been shown that fibrous filters are an effective barrier to particles with a diameter exceeding 1 nm. Below this size, detection limits are reached [6, 35]. Thermal rebound<sup>17</sup>, which may be a reason for reduced filter efficiency, should only occur below this threshold. In the specific case of electrically charged filters, a dramatic increase in filtration efficiency was observed.



Carbon nanoparticles caught in a HEPA filter.



**Other questions related to filtration remain to be addressed:**

- **Effect of nanoparticle morphology on filtration efficiency.** US researchers have shown that filters are more effective when particles have an elongated morphology (nanofibres, nanotubes).
- **Filter clogging since it can lead to a deterioration of the ventilation system.** Actually, the greater the specific area of the particles, the more the clogging ability of the layer of particles retained in the filter increases.

### Respiratory protective equipment (RPE)

Penetration of nanoparticles into filtering RPE can occur via two routes: penetration through the filtering medium or penetration by leakage, especially at the head/facepiece interface. Penetration of nanoparticles by leakage has been studied very little. Research at INRS has shown that significant consequences are to be expected in the event of leakage, and that the effect of a leak is all the greater if the filter equipping the facepiece initially had high filtration efficiency [34]. Studies have therefore been carried out to measure the filtration efficiency of RPE with regard to nanomaterials, concerning both filtration and leakage impact. The work initially focused on two types of commonly used masks (filtering half masks). It was carried out in collaboration with LRGP and IRSN on an experimental facility that attempted to reproduce as closely as possible real operating conditions by using an artificial head connected to a breathing machine [14, 36]. The results showed that for this type of RPE the protective factor varies very little with particle size. No deterioration in respiratory protection was observed. This work made it possible to develop a methodology for the determination of protective factors with regard to nanoparticles. However, many other issues remain to be explored.

A document to help in the choice of the most appropriate RPE in situations of exposure to nanomaterials has been published by INRS (ED 138). In the current state of knowledge, recommendations largely depend on the specific case (nature of nanomaterials, concentration emitted during the process or operation, and duration) and can only be based on existing standardisation.

<sup>17</sup>Theory that states that filtration efficiency could decrease below a certain particle diameter, due to the excessive speeds of such particles.



The efficiency of respiratory protective equipment (seen here, air line breathing apparatus) is tested with regard to particles. The mask is placed on a standardised head, put inside a chamber. A breathing machine is used to simulate human breathing. The aerosol is generated inside the chamber, and the concentrations outside and inside the mask are monitored according to particle size.



**Research into respiratory protective equipment needs to continue.**

- **INRS will especially focus on the efficiency of equipment with a high protective factor** (filtering equipment such as powered or unpowered air-purifying full face masks as well as breathing apparatus), and on the effect of particle morphology (aggregates, nanotubes, etc) on the protective factor.
- **The findings may lead to a possible amendment of standardised protocols** used to test RPE in the event of a specific use of nanomaterials.

## WHAT RISK MANAGEMENT FOR NANOMATERIALS?

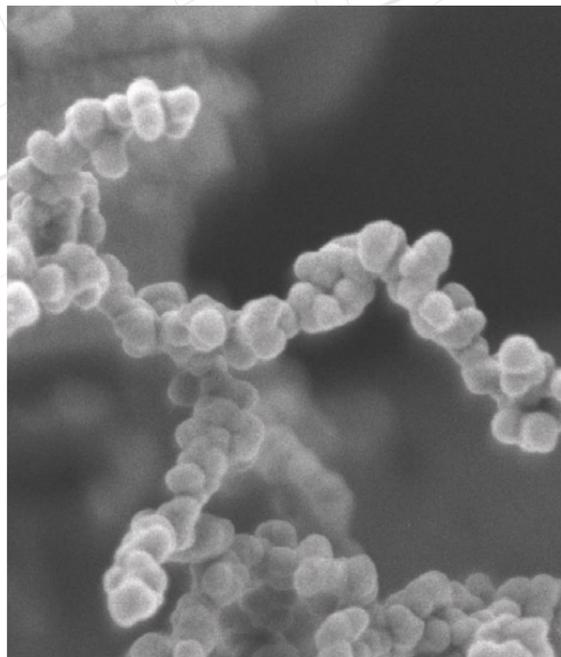


Although much uncertainty remains, there is enough experimental data to make it clear that the toxicological behaviour and reactivity of nanomaterials represent a potential hazard to health. Just as for micrometre-scale particles, the parameters of biopersistence<sup>18</sup> (in particular due to low solubility) and of shape (elongated nano-objects) might significantly increase their pulmonary toxicity after inhalation. An INRS study that provides a sociological interpretation of the management of nanoparticle-related risks in industry and in research laboratories, carried out in collaboration with the PACTE laboratory, shows that risk perception in this field is especially unclear. Prevention generally requires risks to be fully understood and properly assessed [8]. However, lack of knowledge and a tendency to confuse nanotechnology-related risks with nanomaterial-related risks can lead either to denial or, conversely, to excessive measures.

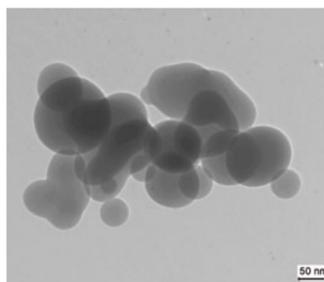
For nanomaterials, as for any chemical agent, it is important to remember that responsible risk management in the workplace is primarily based on the identification of working situations where workers are potentially exposed, and on a rigorous risk assessment.

The identification stage can sometimes be tricky: in fact, INRS's inquiry into the industrial use of nano-objects showed that the data transmitted to users, especially in material safety data sheets and factsheets, are generally incomplete or even lacking altogether, and that workers often handle nanomaterials without even being aware of it. This lack of information impedes prevention. It is therefore important to upgrade safety data sheets and undertake further investigation with the aim of improving knowledge about the sectors involved and the exposed populations. INRS will shortly publish sheets to help identify and recognise nano-related risks in companies.

There is still insufficient toxicological data about nanomaterials to determine dose-response relationships, which therefore restricts the definition of occupational exposure limits. Threshold limit values defined for dust reputed to have no specific effect<sup>19</sup>, which is sometimes described as inert, are not applicable to nanomaterials that have a specific toxicity.



Electron microscope images of nanostructured particles



Some of INRS's counterpart organisations such as NIOSH and IFA already propose indicative threshold values for nanomaterials. These provisional values are based on incomplete toxicological data or on an extrapolation from values set for better-known particles. These organisations make it clear that complying with these values does not constitute a guarantee against developing an adverse effect, but that they are simply an aid to decision-making. Waiting until objective toxicological data is available in order to set exposure limits is likely to take a long time: this approach is in keeping with improved protection for workers, although it remains tricky to implement without a standardised strategy and measurement tools that are fully validated and easy to use by companies.



Symbol proposed by INRS to indicate risk of exposure to nanomaterials.

In addition to health risks there may also be fire and explosion risks, as for ordinary dust. Very few nanomaterials have been specifically assessed with regard to such risks. However, it may be assumed that since nanopowders are more reactive they will tend to be more dangerous than coarser powders with the same chemical composition.

In this context, carrying out a quantitative risk assessment in the workplace is usually impracticable. That is why qualitative methods making use of easily accessible information and based on a certain number of hypotheses have been developed. The main aim of such methods, which should help to alleviate current deficiencies regarding nanomaterial risks, is to rank such risks and prioritise preventive action. Most of these methods use an approach based on a classification into 'bands' of hazards and exposures (control banding). Such methods have not been validated and their effectiveness in companies remains uncertain. Given that it is necessary to make assumptions in order to apply them, it is essential that the user has in-depth expertise in the field of chemical risk prevention and nanomaterials.

Rather than waiting for comprehensive knowledge to become available, it is therefore important to develop a pragmatic approach based on available parameters that can impact the level of risk for workers throughout the whole product life cycle.

→ **Through its information, assistance and training activity, INRS recommends that, for nanomaterials, prevention measures should be implemented on a case-by-case basis, appropriate to the product and the exposure scenario, with the aim of avoiding, or at least minimising, exposure.** These recommendations are based on the general prevention principles defined in the French Labour code (article L 4121-2) and are broadly similar to those applying to any activity involving exposure to hazardous chemicals, namely:

- substitute or modify the process (work in the liquid phase for instance),
- optimise the process to obtain the lowest possible dust level (use a closed circuit process, capture pollutants at source, filter air in the workplace),
- wear personal protective equipment if capture is insufficient,
- implement waste collection and disposal,
- train and inform workers.

→ **Studies have shown that conventional means of protection from aerosols and compliance with good work practices** (in particular, suitable design and maintenance in good working order of equipment) can lead to a significant reduction in exposure to nanomaterials.

→ **Similarly, applying procedures aimed at preventing the risk of explosion of ordinary clouds of dust** should reduce the risk of explosion of nanomaterials.

<sup>18</sup>Biopersistence: characteristic related to the residence time or retention time of a particle or fibre in tissue or in an organ. Biopersistence is a concept that depends on several parameters, such as solubility in a biological medium, clearance potential, size and composition of particles or fibres, etc.

<sup>19</sup>Dust with negligible solubility, causing no serious systemic toxicity, and whose only effect, if the dose is great enough, is that of pulmonary overload. In France, these values, namely 10 mg/m<sup>3</sup> (inhalable fraction) and 5 mg/m<sup>3</sup> (respirable fraction) were laid down in 1984 (article R-4222-10 of the French Labour code). They correspond to dust levels now considered excessive by occupational health and safety experts.

→ INRS proposes and disseminates various information products about nanomaterials in order to assist companies and laboratories in their prevention approach (see page 27), and recommendations regarding medical surveillance [9]. These tools were developed on the basis of state-of-the-art research carried out at INRS or published by other organisations in France and in other countries. They are available on the INRS website and are aimed at a wide audience (from workers to OSH professionals specialised in chemical hazards). Some of them were drawn up in close collaboration with national partners such as CARSATs/CRAMs and CNRS.



→ In addition, INRS regularly takes part in awareness-raising and information days (organised for instance by regional occupational health services or as part of conferences on prevention). Since 2009 it has offered three-day **training courses** aimed at a wide variety of audiences, including researchers, engineers, OSH professionals and industrial medical officers concerned by activities involving nanomaterials. By the end of 2013, around 140 people will have attended the courses.

→ These recommendations will be regularly revised as and when increasingly reliable information is published about nanomaterial hazards and exposure levels.

New information products will be made available to OSH professionals, occupational health services, workers and employers.

→ The prevention approach recommended by INRS will be laid down in a guide for workplace intervention intended for OSH professionals and in a guide for waste disposal.

→ Other points concerning risk management currently under discussion will form the basis of further tools intended for companies, especially small enterprises.

These will include guidelines for drawing up material safety data sheets, development of an approach aimed at classifying nanomaterials on the basis of their physico-chemical properties and of the resulting potential hazards, and integrating risk prevention through process design (new production methods aimed at reducing nanomaterial toxicity, improved monitoring of the evolution of materials throughout their life cycle, limiting exposure, etc).

## INRS information products (available at [www.inrs.fr](http://www.inrs.fr))

→ Nanomatériaux. Filtration de l'air et protection des salariés, ED 138 (2011).

→ Nanomaterials: definitions, toxicological risk, characterisation of occupational exposure and prevention measures, ED 6050 (2012).

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→ Les nanomatériaux : risques pour la santé et mesures de prévention, ED 6064 (2012).

→ Dioxyde de titane - Fiche toxicologique, No 291 (2013).

→ Aide au repérage et à la prise en compte du risque nano en entreprises, to be published in 2013.

→ Nanomatériaux. Assainissement de l'air des locaux de travail, Fiche pratique, to be published in 2014.

→ Dioxyde de titane - Guide technique, to be published in 2014.

## Traceability of exposures and medical surveillance of workers

INRS receives many enquiries from occupational health services. Should workers potentially exposed to nanomaterials be subject to specific medical surveillance? Because of the gaps in our knowledge about the health effects of nanomaterials, there is at present no consensus about the content and methods of medical surveillance [9]. Determining levels of inflammatory markers or of pro-inflammatory proteins in biological media (blood, urine, breath) is one avenue of research, although this is not yet at a stage that allows it to be proposed as a routine method. Medical surveillance must therefore be adapted on a case-by-case basis, and its main objectives should be to determine workers' aptitude for the job and inform them about risks and protective measures. Keeping a record and ensuring traceability of all the information collected concerning health events, results of additional tests and exposures is of fundamental importance. This information should be kept so that it can be made use of at a later date, especially for epidemiological investigations.



Weighing a sample of nanopowder under safe conditions, using a special ventilated chamber.

## INRS's contribution to expert work

INRS contributes its expertise on nanomaterials to several expert committees and specialised working groups working with national and international bodies:

→ The 'Nanotechnologies-Nanomaterials' expert group led by INRS, which brings together around a dozen representatives from CARSATs/CRAMs and CNAMTS, and whose main goal is to draw up and formalise a coherent action plan for the 'Prevention' network. Discussion in this group has led to the appointment by each CARSAT/CRAM of a nanomaterials officer in charge of implementing action in the field. INRS also contributes its technical and scientific support to the CTNs.

→ Regarding standardisation, INRS takes part in the work of the AFNOR X 457 'Nanotechnologies-Nanomaterials' commission and follows the activities carried out in the ISO TC 229 and CEN TC 352 commissions. It is also present in the CEN/TC137 'Workplace Atmospheres' commission and took part in drawing up the first normative document on exposure to nanomaterials (FD ISO/Tr 27628, 2007).

→ INRS specialists regularly participate in ANSES assessments and working groups on nanomaterials. Two experts take part in the permanent 'Nanomaterials and Health' working group.

→ INRS takes part in the 'Risk Assessment' and 'Exposure Measurement and Exposure Mitigation' groups in the OECD's programme on manufactured nanomaterials, and in the ICOH 'Health of workers exposed to nanomaterials' committee.

→ INRS has contributed to several reports on nanomaterials for the Topic Centre for Occupational Health and Safety at the European Agency for Safety and Health at Work in Bilbao.

→ INRS participates in an expert group at the Observatoire des Micro et Nano-Technologies (OMNT).

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## TABLE OF ABBREVIATIONS



### [ANSES]

Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail

### [CARSAT/CRAM]

Caisse d'assurance retraite et de la santé au travail / Caisse régionale d'assurance maladie

### [CEA]

Commissariat à l'énergie atomique

### [CNRS]

Centre national de la recherche scientifique

### [CTN]

Comités techniques nationaux

### [ICOH]

International Commission on Occupational Health

### [IFA]

Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, Germany

### [INERIS]

Institut national de l'environnement industriel et des risques

### [InVS]

Institut de veille sanitaire

### [IRSN]

Institut de recherche en sécurité nucléaire

### [ISO]

International Organisation for Standardisation

### [ISPED]

Institut de santé publique, d'épidémiologie et de développement, Université de Bordeaux

### [ISSA]

International Social Security Association

### [LEMETA]

Laboratoire d'énergétique et de mécanique théorique et appliquée, Université de Lorraine & CNRS

### [LRGP]

Laboratoire réactions et génie des procédés, Université de Lorraine & CNRS

### [NIOSH]

National Institute for Occupational Safety and Health, United States

### [NRCWE]

Nationale Forskningscenter for Arbejdsmiljø, Denmark

### [OECD]

Organisation for Economic Co-operation and Development

### [PACTE]

Laboratoire Politiques publiques, Action politique, Territoires, Université de Grenoble & CNRS

### [PEROSH]

Partnership for European Research in Occupational Safety and Health ([www.perosh.eu](http://www.perosh.eu))

### [PHE]

Public Health England, UK

### [R&D]

Research and development

### [SME]

Small and medium-sized enterprise



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