

THE NANOTECHNOLOGIES: APPLICATIONS AND MANAGEMENT OF THE NEW RISKS FOR THE HEALTH OF THE WORKERS

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■ **KEYWORDS:** Nanotechnology, Nanomaterials, Risk management from nanoexposure at work

ABSTRACT

Nanotechnology represents one of the emerging technologies used in recent years in a more or less widespread way in the world of research, study and work, and especially in the latter sector the risks associated with the production and use of nanomaterials are still largely unknown. To date, there is a substantial imbalance of knowledge between the application of nanotechnologies and their impact on health; the information currently available on the health effects and risk assessment of nanomaterials in the workplace is limited; systematic methodologies to assess exposure are not yet known and, given the intensive and highly diversified use of nanomaterials by industry in recent years, it is difficult to estimate the number of workers exposed and the effects on their health.

It is well known that the research and development activity currently underway in the nanotech sector, both at public and private level, covers a wide spectrum of thematic areas such as chemistry and materials (structural and functional), nanoelectronics and photonics, bio(nano)sciences, medical and instrumentation. The potential application effects concern fundamental productive sectors ranging from pharmaceuticals and development of electromedical devices, to cosmetics, electronics and information technology, from transport to environment and energy, but also sectors that typically involve small and medium-sized enterprises, such as textiles and fashion, footwear, food, construction materials, advanced mechanics and the preservation of cultural heritage. The healthcare sector is not exempt from being affected by nanotechnology as well, and this generally poses a greater risk for worker exposure to nanomaterials within its work and professional settings. Specifically, nanotechnology and nanomaterials in healthcare, with their applications can certainly offer significant advantages, for example techniques and approaches of miniaturization through chemical synthesis and control of molecular assembly which represent indispensable opportunities in the prevention, diagnosis and treatment of diseases. However, although there are still ongoing studies and research in this area, the field of nanotechnology is developing faster than the generation of knowledge on health and safety aspects of nanomaterials. Living and working environments, in fact, can be exposed during all stages of the entire production cycle of substances in nanoform: during production, transport and storage, or during use and disposal.

However, the lack of information on the behavior of nanomaterials in the environment makes it difficult to assess their risks in different sectors.

The present research work aims to explicate the areas of development of nanotechnologies, and to explain how workers might encounter nanomaterials in their workplaces when performing their daily activities.

There will be a focus on exposure from nanomaterials, on the assessment and management of potential risks of these new forms of materials, on the knowledge and / or study of the hazardous properties of substances in nanoform and their safe use with a view to verify how to currently try to contain the potentially harmful impacts on the environment and the health of workers and contribute to the implementation of the legislation of the sector although aware that the risk of exposure to nanomaterials is a toxicological issue still being explored by medical science.

The use of nanomaterials, in fact, may represent an emerging health and safety risk that must be assessed and managed through a specific approach, particularly within the complexity of work environments. Therefore, an attempt will be made to indicate the prevention and protection measures to reduce the impact on workers' health and safety, also by referring to the relevant legislation and the precautionary principle.

■ INTRODUCTION

Nanotechnology, a neologism like the Internet was in its early days, then the term became commonly used and the Net entered everyday life. Will the same happen for nanotech? It is a new basic science, which is not confined to a niche market like biotechnology, but is transversal with repercussions on all industries. It was the American engineer Kim Eric Drexler who ‘patented’ this term and used it in his book ‘*Engines of creation: The coming Era of Nanotechnology in 1986*’, but the first references to these new methods certainly date back to a few decades earlier, and the term “nanotechnology” was first used by Norio Tan-

iguchi of the University of Tokyo in 1974, although the trailblazer on this topic was the American physicist Richard Phillips Feynman (Nobel Prize in Physics in 1965 thanks to his studies on quantum electrodynamics), in 1959 he gave a lecture on molecular studies entitled ‘*There is plenty of rooms at the bottom*’, during which he introduced the paradigm of nanotechnology, a new concept of physics and chemistry for which it was possible to manipulate the properties of materials at the atomic and molecular level, a method later called ‘scale down’; This method involved designing machine tools at a scale of 1: 10, and then using them for the next generation of tools at a scale of 1:100...

and so on, up to today's 1:1,000,000,000 (one-billionth) or to a millionth of a millimeter with Nanotechnology whose name comes from nanometer, the prefix "nano" referring to a Greek prefix meaning "dwarf" or something very small. Richard Feynman predicted a future in which scientists, by manipulating atoms and molecules, would be able to build materials and structures of greater strength, lighter weight, greater control of the light spectrum, and greater chemical reactivity. Like the Web, nanotechnology originated in the military, thanks to government funding for the U.S. defense industry, and is now spreading to other sectors. Unlike the Internet, however, they do not follow the "all for free" philosophy, but have a value that can be defended with patents. They also require uncommon skills, as evidenced by the fact that many Nobel Prize winners sit on the boards of entrepreneurial companies. Finally, it is a very pervasive technology because it can be applied in any field of activity. In fact, in recent years, research in the field of microtechnology is evolving at a dizzying pace with applications now evident and consolidated in many sectors (microelectronics, telecommunications, sensor technology, textiles, environmental and biological). This research in recent years is experiencing a metamorphosis under the impetus of a new and strong development tending to decrease in scale, the use of materials on nanoscopic scales (molecular and / or atomic), through which we discover the amazing properties of quantum physics, not found on macroscopic scale, for which the matter has "unusual characteristics". Therefore through the cross-fertilization of different disciplines and branches of pure and applied research, under the drive to find new materials, new processes, new applications and to the realization of innovative products we are witnessing a rapid transition from microtechnology to nanotechnology [1]. Hence the development of nanoscience, engineering and technology at the nanoscale (billionth of a meter), fields of research and study in which manipulation of matter at the atomic, molecular and supramolecular level takes place, in order to obtain materials and systems with significantly improved characteristics. Nanotechnology is therefore the technological science capable of controlling and manipulating matter at the atomic and molecular scale (US EPA, 2007), deals with the creation and use of structures, devices and systems with new properties and functions at the nanoscale, approximately from 1 to 100 nanometers (nm). To better understand the meaning of this scale consider that 1 nanometer is obtained by dividing 1 millimeter into a million equal parts, so, a cubic micron of water contains about 90 trillion atoms, taking into account that the nanometer is a thousandth of a micron. The red blood cells that have an average diameter of 7 microns have, for example, a diameter of 7000 nanometers. So nanomaterials can be even 10,000 times smaller than the width of a human hair. With this in mind, it is possible to design and build new materials or machines that were previously inoperable.

According to the definition of the Recommendation 2011/696/EU of the European Commission (EC), *nanomaterials are natural, incidental or engineered materials containing particles in the free, aggregated or agglomerated state, and where, for at least 50% of the particles in the number size distribution, one or more external dimensions are in the range of 1 nm to*

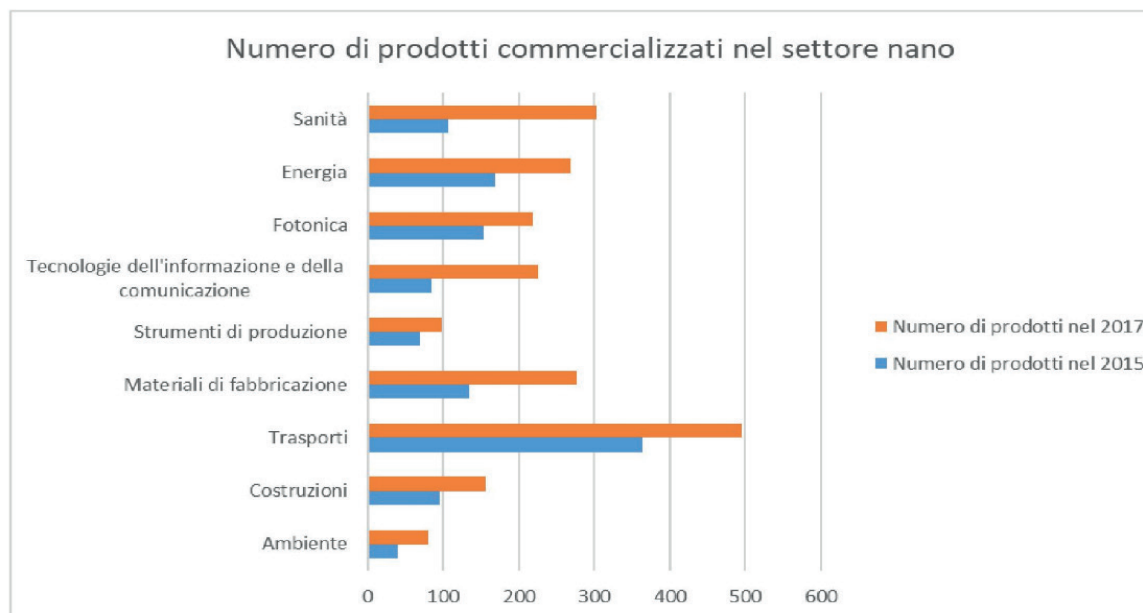
100 nm. To date, the production and/or fabrication of engineered nanomaterials is a rapidly developing area, with a wide range of applications in many different sectors, hence the development of Nanotechnology as one of the emerging sectors that is growing as a technology in the global economy and is expected to represent the a new industrial revolution, may have various applications for the improvement of daily life and for greater sustainability, and is gradually attracting the attention of the whole world for its enormous development prospects as well as the space available for its commercial extension.

Unfortunately, only 1% of total government and private funding in nanotechnology R&D is dedicated to research on nanotechnology-related health risks and nanomaterial exposure in the workplace. This imbalance also affects scientific production: in 2006, only 5% of publications on nanoparticles, nanomaterials and nanotechnology focused on aspects related to health and occupational exposure [2]. The situation at national level is photographed in the "Second Census of Nanotechnology in Italy", carried out by AIRI/Nanotec IT in 2006. The document highlighted the existence in the country of a substantial activity involving about 180 public research facilities and companies.

The activity is distributed throughout the country, with about 57% of facilities located in the North, 28% in the Centre and the remaining 15% in the South. Numerous initiatives have been undertaken in recent years with the aim of improving the use of resources, increasing overall operational efficiency and strengthening commitment: centers of excellence for nanotechnology have been created in various universities; research activities, even located in different places, have been linked by directing them towards common objectives; some Technology Districts have made nanotechnology a priority area for research.

While globally, the global market for nanotechnology products was valued at \$22.9 billion in 2013 and increased to about \$26 billion in 2014. This market reached approximately \$64.2 billion by 2019; a compound annual growth rate (CAGR) of 19.8% from 2014 to 2019. The global nanotechnology-enabled printing technology market was estimated to total \$14 billion in 2013. The global nanotechnology market is expected to grow at a CAGR of around 17.5% from 2016-2022.

In the most recent research survey, "Global Nanotechnology Market Outlook 2022," the analyst conducted a segmented research on the nanotechnology industry and explained the key market trends to clearly highlight the areas that offer promising opportunities for industries to scale up their development. Nanotechnology contributes to almost every field of science, including physics, materials science, chemistry, biology, computer science, and engineering. In particular, nanotechnology has been applied to human health in recent years with promising results, especially in the field of cancer treatment. At present, the biomedical industry is one of the largest sectors where nano-enabled products have made a crucial contribution, mainly in the healthcare sector, with significant growth in other topics such as electronics and energy (**Figure 1**). The unique properties of materials manipulated at the nanoscale enable innovative applications in many manufacturing sectors; however, precisely because of their novel characteristics, nanomaterials may pose an



Fonte: Elaborazione MATTM da dati *European Commission – “NanoData Impact Assessment Energy, Health, ICT, Manufacturing, Photonics” Synthesis Report (ottobre 2017)*

Fig. 1 - Number of products marketed in the nano sector

emerging health and safety risk that must be assessed and managed through a specific approach, particularly within the complexity of work environments.

METHODOLOGY AND MATERIALS

This “sector study” was based on careful and critical reading of books and journals on nanotechnology as well as consultation of policy documents prepared by the European Commission [3-4] and the National Science Foundation [5], followed by the vision and consultation of websites on researches and studies carried out by the university world and by research and development (R&D) organizations belonging to the private/public entrepreneurial world and to further in-depth analysis carried out on websites dealing with the issues concerning the development and applications of nanomaterials, a study that has allowed to carry out an accurate meta-analysis on the state of the art of the use of nanomaterials in contemporary society. At the same time, a study was carried out on the regulations in force both at European and Italian level, in order to verify the existence or not of a regulation on the emerging risks related to nanotechnology, for the protection of the environment and human health, and to verify the adoption of the possible measures of prevention and protection with respect to the possible harmful effects of nanoexposure. The documents and/or sites consulted are cited in the bibliographical references to which reference is made for any further information.

Nanotechnology and Nanomaterials

Nanoparticles have existed in nature forever, for example, milk contains nanoscale droplets of fat and every cell in the body relies on nanometer-sized protein complexes to function. Nanoparticles are also manufactured or produced as a byproduct of many long-standing processes, such as fires, diesel engines, and high-energy manufacturing processes such as welding or grinding. Nanomaterials have been used commercially since the 1930s. One example is silver

used in photographic film. Another important nanomaterial that has been produced in large volumes for a long time is carbon black. Annual production of carbon black is more than 10,000,000 tons and its use is widespread. Almost all black paint contains carbon black, and the substance is also used to improve the mechanical strength and protection of plastics from sunlight, as well as in the production of automotive tires and rubber products.

Meyya Meyyappam (director of nanotechnology research at NASA) in a meeting with Silicon Valley investors (reported in the *Sole 24 Ore* of December 2, 2004) said: “..... nanotechnology is the creation of useful or functional materials, processes, devices and systems through the control of matter at the nanometer level and the exploitation of innovative phenomena and properties (physical, chemical and biological) at that scale of magnitude So far there has been much nanoscience and little nanotechnology”.

Therefore, nanotechnology produces and acts on matter in nanometric form. Since chemicals in nanoform have chemical and physical properties that differ from those of the corresponding substances in non-nanoscale, they might have different biological activity with potential harmful effects on health and environment. For this reason, *nanotoxicology* is defined as the discipline that studies the effects of nanomaterials on living organisms, and *nanoeotoxicology* as the science that studies the effects on the biosphere and ecosystems.

The European Scientific Commission on Emerging and Newly Identified Health Risks (SCENIHR, 002/05) in its 2006 Opinion, defines *nanoscience* as the science that studies the phenomena and manipulation of materials at atomic, molecular, and macromolecular scales with properties that differ significantly from those of dimension major, and defines *nanotechnology* as the design, characterization, manufacture, and application of structures, devices, and systems limiting shape and size at the nanoscale.

On this topic it is considered necessary to provide the

following definitions:

- **nanotechnology:** a term that can be attached to a process or product only if the following conditions are met: o development of research and technology at the atomic, molecular or macromolecular level, at a size scale ranging approximately from 1 to 100 nanometers o creation and use of structures, devices and systems that have innovative properties and functions due to their size o ability to control and manipulate matter at the atomic scale [6]. It follows that the use of nanotechnology allows the deliberate and intentional modification of the properties of a material by bringing it to the nano-scale to give it new functions;
- **nanoscience:** the result of interdisciplinary cooperation between physics, chemistry, biology, biotechnology, materials science and engineering with the aim of studying the phenomena and manipulation of materials at the atomic and molecular scale, whose properties differ significantly from those of larger dimensions [7].

Four generations of new nanotechnology products and processes are identified for potential development between the year 2000 and 2020:

1. **Passive nanostructures** (first prototype creation: 2001): product of the primary research on nanostructured materials and instruments for measurement and control of processes at the nanoscale, such as nanoparticles, nanomaterials and carbon nanotubes.
2. **Active nanostructures** (creation of first prototypes: 2005): devices and systems for energy storage and conversion; instruments for molecular medicine and food systems; nanoelectronics; 3D instrumentation and manufacturing at the nanoscale.
3. **Nanosystems** (early prototyping: 2010): heterogeneous nanostructures and engineered supramolecular systems, such as artificial tissues and sensory systems; quantum interactions within nanoscale systems; nanoscale electromechanical systems; cell-focused therapy with nanodevices.
4. **Molecular nanosystems** (first prototype creation: 2015): manipulation at the atomic level for the design of molecules and supramolecular systems; single molecule dynamics; molecular machines; design of large and heterogeneous molecular systems; controlled interaction between light and matter with relevance to energy conversion.

From the experimental point of view, nanotechnology and nanoscience began to appear around the eighties through two major lines of development: the birth of cluster science (*clusters are aggregates of a few atoms*) and the invention of Scanning Tunnel Microscopy. But remember that already in 1974 the first molecular electronic device was patented by IBM. Moving in this direction, in a nanotechnological context, we first came to the discovery of fullerene in 1985 and then to carbon nanotubes. Interest in single-electron devices began to emerge, devices based on DNA and molecular electronics.

Subsequent developments have led to study with great interest nanocrystals and quantum dots. Nowadays, the interest of nanotechnology has been mainly focused on biology (nanosensors and manipulators of biological matter), medicine (markers, detectors, drug dispensers), new materials, information, computation and

quantum computing (quantum computing, memories, flexible organic LED displays) and on stochastic and deterministic approaches with which to manipulate single molecules and atoms superficially on a material. Nanomaterials have emerged from the application of materials science to nanotechnology revolutionizing countless manufacturing sectors, so much so that they are defined “*as the indispensable technological basis of a whole range of manufacturing applications that may change our lives in the future, offering potentially enormous benefits to society, industry, the environment and health*”. Nanotechnologies are counted among the six *Key Enabling Technologies (KETs)*, as well as considered a key tool of the European Commission’s Horizon 2020 program [8] atomic and molecular. They aim to build materials and products with special chemical and physical properties, different from those of the same materials with larger structure. Therefore, nanotechnology and nanomaterials can help us improve our quality of life and respond to some of the key issues of the day, such as climate change, by reducing greenhouse gas emissions. Other potential benefits include contributions to improved energy storage and efficiency, better diagnosis and treatment of disease, faster computer systems, and the cleanup of polluted air, soil and water.” The development of nanomaterials is based on the assumption that elements, when brought to nanometer size, acquire special chemical and physical properties that are different from the corresponding conventional materials. The reasons can be traced to the change in the laws of quantum mechanics active at this scale and to the fact that the surface assumes a fundamental role. For this reason, the properties of a specific material can be designed by managing the size of the nanometric units that constitute it. This discovery has triggered a real revolution that has made it possible to act on the magnetic and electrical properties or on the melting temperature, without changing the chemical composition of the material.

Review of Nanomaterials

Nanomaterials are classified into:

- *natural nanomaterials*, widespread in the environment, they result from biological and geological processes, such as natural combustion processes or volcanic eruptions;
- *accidental nanomaterials*, they are produced unintentionally, for example they derive from vehicle traffic, diesel engines, industrial incinerators, welding operations and laser printing processes of photocopiers;
- *engineered nanomaterials*, are intentionally produced at the laboratory level for scientific and industrial purposes and have a well-defined chemical composition.

Nanomaterials have unique physical, chemical, electrical, and mechanical properties that change as they decrease in size. These properties are different from the corresponding original materials (not in “nano” form) and depend on the increased surface-to-volume ratio that results in increased reactivity, higher electrical conductivity and resistance, and potentially greater biological activity. It is these characteristics that make nanomaterials particularly attractive for use in a variety of application areas; they have been in use for decades now, and new generations of nanoform materials continue to develop rapidly, so much so that their

market is expected to grow. They differ in chemical composition, shape, and structure. The analysis and data reported in this section are based on Roadmaps [9] and [10].

For simplicity, nanomaterials have been classified thus classified into 8 main non-exhaustive categories:

- Carbon based Nanomaterials (e.g. carbon nanotubes, graphene, fullerenes, Nano diamonds, graphite.)
- Nanoparticles and Nanocomposites
- Metals and alloys (metal oxides and dioxides, e.g. gold, silver, aluminum, titanium, copper, cerium, iron, platinum)
- Biological Nanomaterials
- Nanopolymers
- Nanoglass (nanocellulose)
- Nanoceramics
- Nano-porous materials

and for each category are reported: **-Definition -Properties -Application Perspectives.**

Generally, nanomaterials are classified in relation to the number of nanometric dimensions they present (Figure 2).

In fact, there are:

- **zerodimensional structures** (*quantum dots*), in which all dimensions are at the nanoscale, such as nanoparticles (oxides, metals, semiconductors, fullerenes, etc.);
- **one-dimensional structures**, with only one finite dimension, such as *nanowires* (full one-dimensional structures), nanotubes (hollow one-dimensional structures);
- **two-dimensional structures**, with only two finite dimensions, such as thin films (*monolayer, multilayer or self assembled monolayers* etc.).
- **Carbon-based Nanomaterials**

Definition - Materials in which the nano-component is pure carbon. Thus, polymers do not fall into this category (Figure 3 and 4) [9]

Properties: They are therefore of great potential interest for the storage of electricity and hydrogen. They have excellent properties as electron emitters so they

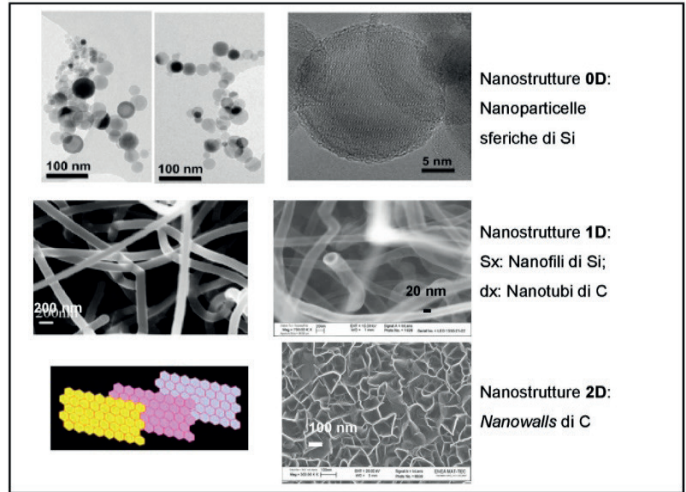


Fig. 2 - Examples of nanostructures produced at the Department of Physical Technologies and New Materials of ENEA in Italy

could be used for displays and in microscopy (as tips or sources). Other applications are in the medical field (e.g. needles to deliver active agents into living cells). Composites of the carbon nanotube/polymer type have potential applications for cold cathodes, LEDs and as ultra-strong materials. Other promising materials are carbon-based nanofilms (Si, N, B or Ti carbides and diamond-like carbon) with applications related to their unique mechanical properties (low coefficient of friction, high toughness, abrasion and scratch resistance). The R&D activity on fullerenes, cage-shaped materials made of pentagonal or hexagonal carbon rings (Figure 6) with extraordinary electronic, mechanical and adsorptive properties related to their peculiar molecular architecture, is in its waning phase.

The most promising industrial applications [9] for CNTs (*Carbon Nano Tubes*) are in the energy field (*hydrogen and energy storage*), in bio-sensors and in the medical sector (recently the prospects of applications for tissue engineering and implantology are surpassing those for *drug delivery* systems). The applications of

Elenco dei nanomateriali a base di carbonio maggiormente studiati

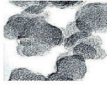
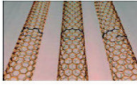
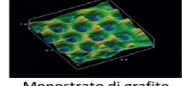
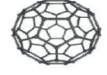
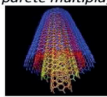
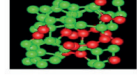
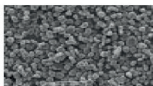
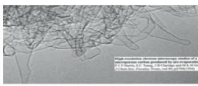
Elenco dei nanomateriali a base di carbonio maggiormente studiati		
Nanostrutture singole a base di carbonio		Film, rivestimenti, superfici nanostrutturate, materiali massivi nano strutturati
Nanoparticelle	Nanotubi di carbonio (CNT-Carbon NanoTubes))	
Carbon Black (fuliggine o nerofumo) 	SWCNT: Single Wall CNT (CNT a singola parete) 	Film a base carbonio  Monostrato di grafite
Fullereni Materiali a forma di gabbia costituiti da anelli di carbonio 	MWCNT: Multi Wall CNT (CNT a parete multipla) 	DLC (Diamond Like Carbon) materiale a base di carbonio amorfo con le proprietà del diamante 
Nanoparticelle di grafite 	CNT a singola parete di forma irregolare, ricurvi (Nanohorns) 	Carbonio nanoporoso: Materiale a base di C amorfo, ad elevata superficie specifica e con pori nanometrici, a ridotta distribuzione delle dimensioni Carbon Aerogel: Materiali a base di carbonio con bassissima densità e pori nanometrici, a ridotta distribuzione delle dimensioni

Fig. 3 - List of the most studied carbon-based nanomaterials

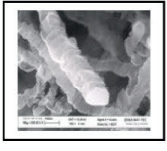

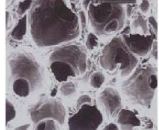
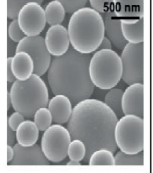
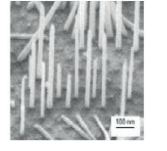
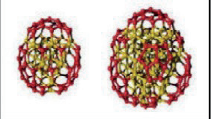
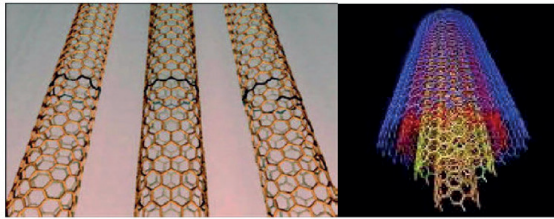
Elenco dei nanomateriali a base di carbonio maggiormente studiati		
Nanostrutture singole a base di carbonio		Film, rivestimenti, superfici nanostrutturate, materiali massivi nano strutturati
Nanoparticelle	Nanotubi di carbonio (CNT-Carbon NanoTubes))	
Nanocluster di carbonio (nanoaggregati costituiti da 100-10000 nanoparticelle cristalline di carbonio) 	Nanofili a base di C 	Nanoschiuma carbonica o Carbon Foam: allotropo a bassissima densità 
Nanoparticelle di carbonio 	Nanorod (strutture con due dimensioni laterali su scala nanometrica) 	Nanocristalli di carbonio (Nanodiamante) 

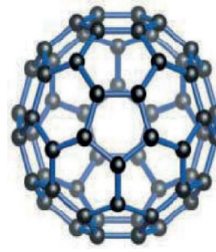
Fig. 4 - List of the most studied carbon-based nano-materials



Sinistra: nanotubi di carbonio a singolo strato;
a destra: nanotubi di carbonio a multistrato

Fig. 5 [9]

Left: Single-layer carbon nano tube / **Right:** multilayer carbon nanotube



Molecules with cages of $C_n (n \geq 60)$ carbon atoms take the collective name of fullerenes. They represent a new allotropic state of carbon, different from graphite and diamond]

Fig. 6

CNTs as electron emitters also appear to be extremely interesting, but at the moment the limitation of the reduced stability of the material, whose electrical properties degrade rapidly, remains to be overcome. Samsung has realized a prototype of FED (*Field Emitting Diode*) display with nanotubes, but there are still many technical problems to overcome. Finally, there are possible applications as materials for lighting and microwave amplification. Carbon-based films also have application prospects and have the largest number of new patents.

– Nanoparticles and nanocomposites

Definition: Nanoparticles are particles with typical sizes ≤ 100 nm. The most common are spherical in shape (**Figure 2**) and are made of metallic, semiconductor, or ceramic materials (oxides and non-oxides). Nanocomposites are composite materials in which one of the two phases (or both) are at the nanoscale (in the second case we speak of nano-nanocomposites) (**Figure 7**).

The presence of a second phase (or both) at the nanoscale significantly improves the properties of the material and/or gives it new functions. For example, the presence of nanodispersoids in ceramic matrices can give the ceramic material superplasticity properties (exceptional ability to stretch when subjected to stress) typical of metals (**Figure n. 8**).

Properties - The materials considered most promising for applications are:

1. Matrices additivated with nanoparticles or fibers.

- Polymer matrices additivated with nano-clays, fibers, carbon nanotubes, metal nanoparticles or ceramics.

- Ceramic matrices additivated with nanocarbon, nanopolymers, nanoparticles.
 - Metal matrices additivated with nanopolymers.
- #### 2. Nano-nanocomposites
- Nanoparticles coated with a core-shell of different materials.
 - Carbon nanotubes-nanopolymers
 - Carbon nanotubes-nanoceramics
 - Nanoparticles linked to DNA chains
 - Nanopolymers linked to DNA chains.

Application perspectives - Nanocomposites have application perspectives in a variety of sectors.

In the energy sector:

- *Energy storage:* polymer nanocomposites have good application prospects, but current reliability and durability characteristics must be improved.
- *Energy saving:* nanocomposites with good electrical conductivity characteristics can be used to manufacture higher quality electrical cables.
- *Energy applications:* fuel cells and batteries.

In the bio-medical sector:

- Nanocomposites for the controlled release of drugs (*drug delivery*) such as core-shell nanoparticles (e.g. the inner core, called core, contains the drug and the outer shell, is made of macromolecules that perform the function of recognition of the target organ).
- Bio-imaging (nanoparticles with peculiar optical and magnetic properties that are manifested at the nano-scale: they can allow the visualization of cells, tissues, organs, etc.).
- Tissue engineering (active and passive implantology): hydroxyhepatite, calcium

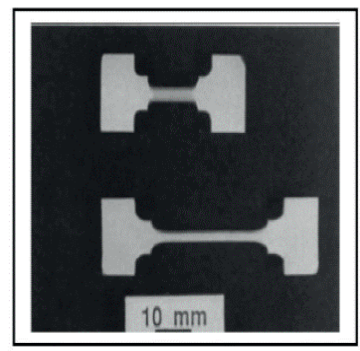
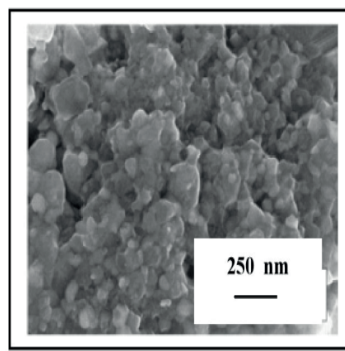
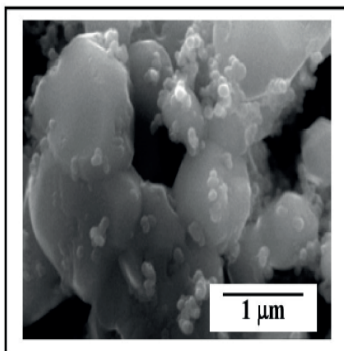


Fig. 7 - (Results from the NANOMAT Network)

[Left: Alumina/SiC nanocomposite in which the matrix (alumina) is at the micrometer scale and the second phase (nano SiC “Silicon Carbide” produced at ENEA’s Department of Physical Technologies and New Materials in Italy) is at the nanometer scale;

Right: alumina (40%)/zirconia nanocomposite in which both phases are at the nanoscale]

Fig. 8

[Superplastic Elongation of Si_3N_4/SiC Nanocomposite]

carbonate, nanoceramics.

- Bio-nanocomposites, Nanocomposites for dental care.
- Nanosensors.

In the transport and space sector:

- Lightweight and strong nanocomposites.
- Polymeric nanocomposites.
- Coatings.

Metals and alloys Definition

Metals are divided into two categories: *ferrous and non ferrous*.

Properties - In this category, the most promising nanomaterials for industrial applications are:

1. Nanopowders and metal nanomaterials of:

- Ti, Ti-Al
- Ti and transition metal alloys (Fe or Ni or Cu)
- Mg-Ni
- Fe-Cu-Nb-Si-B alloys
- Fe alloys and transition metals (Co, Ni, Cr, Cu, Zr)
- Al alloys and transition metals (Fe, Ni, Ti, Zr)
- Al, Mg, Al-Mg alloys

2. Noble metal nanopowders:

- Ag
- Au
- Pt
- Pd

Nanostructured and nanocrystalline metallic materials offer radical improvements in mechanical properties and/or new functions that make them extremely promising for innovative technological solutions and the manufacture of highly competitive products. This is evidenced by the ever-increasing number of patents, particularly on metal nanopowders, whose properties are related to increased specific surface area. The second rapidly expanding field is that of nanostructured light metals with properties mechanical properties superior to conventional materials (strength, ductility, corrosion and wear resistance, etc.).

Metal nanopowders find use in health protection (e.g. Ag nanopowders have anti-bacterial properties), as catalysts and as getters. Coatings based on nanostructured metal alloys have superior tribological properties compared to conventional materials, such as high corrosion and wear resistance, low coefficient of friction, etc.

Al, Mg, and Ti based alloys have superior mechanical properties due to a change in the deformation mechanism when going to the nanoscale.

Nanostructured materials based on Mg and its alloys (both in bulk form and nanopowders) are of extreme interest for hydrogen storage because of the increase in hydrogen diffusion coefficient and solubility limit. Finally, a field on which much of the research has focused is magnetic nano materials. Magnetic properties vary on the nano-scale and a magnetic material can become "soft" thus allowing a decrease in energy losses in components such as the core of a transformer.

Application Perspectives - The most promising application perspectives for metallic nanomaterials, according to Nanoroadmap 2015 [9] concern applications in electronics, *energy storage*, telecommunications, medicine, catalysis, mechanics (production of mechanical micro-components), micro-systems (such as MEMS (Micro - Electro - Mechanical Systems), bio-MEMS, nano-electromechanical systems, electrochemical, multifunctional sensor systems).

Biological Nanomaterials

Definition - The category of bio-nanomaterials is defined in this study (in accordance with the reference documents) as those materials of biological origin that are used for applications in nanotechnology. Conversely, bio-compatible materials are materials of non-biological origin that are used for medical applications (e.g., alumina for implantology). The most studied are:

- protein-based nanomaterials (2D/3D proteins, nano-containers, functional protein units, etc.);
- peptides (nanostructured peptides in the form of nanofibers, nanocrystals, nanotubes, etc.);
- viruses (nanostructured materials using viruses as structural components...);
- lipids (nano-containers, nano-supports, etc.);
- DNA (hybrid structures, 3D cages and networks, nanowires, etc.);
- composites.

Properties

- The characteristics of greatest application interest for bionanomaterials are:
- self-assembly properties (e.g., molecular components may have the ability to self-organize into ordered structures);
- the capacity for molecular-specific recognition.

Current Applications

- There is already a substantial number of patents [9] covering the following topics/applications of bio-nanomaterials:
- self-assembling systems
- actuators
- molecular motors
- sensors
- systems for controlled drug delivery
- information storage devices

[Peptides (macromolecules consisting of chains of amino acids) can self-assemble into nanotubes due to the charges (positive or negative) on the top of the chain and the non-polarity of the tail].

Most applications appear to be still in the early stages and patents are at the *proof of principle level*.

Prospective applications - Most applications are related to the medical-health sector (*chips* for DNA or protein screening, *drug delivery*, etc.), but important applications are also expected in the field of sensors (traditional bio-sensors have received a boost from the advent of nanotechnology) and in the energy sector (biological complexes to capture solar energy, fuel cells that include bio-molecules for electricity production, etc.).

Nanopolymers

Definition - Polymers are materials characterized by the repetition of units of atoms (monomers) in chains that may not be the same length in the same material.

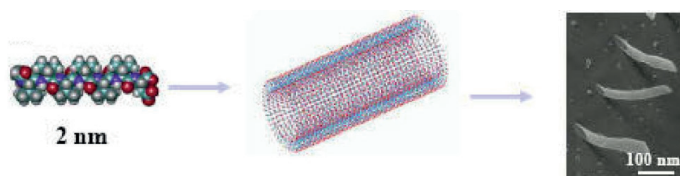
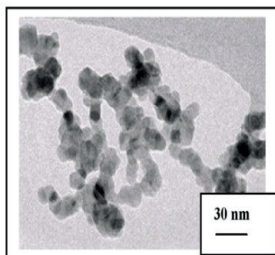


Fig. 9 - [S. Zhang, *Nature Biotechnology* 21, 1171 (2003)].



SiC (Silicon Carbide) nanoparticles produced by laser pyrolysis at the Department of Physical Technologies and New Materials of ENEA in Italy

Fig. 10

Nanopolymers are nanostructured polymers to which the nanostructure imparts substantial changes in intrinsic properties. They are obtained by nanolithography techniques (nano-imprint, electron beam lithography, etc.). *Polymer nanocomposites* (PNCs) are polymers in which a second phase is dispersed at the nanoscale (nanoparticles, nanotubes, nanoplatelets, etc.).

Properties - The attractive forces between the polymer chains determine the properties of the materials giving them high tensile strength and high melting point. Nanostructure and/or dispersion of a second nanoscale phase can improve the polymer properties giving excellent physical, mechanical and thermal properties.

Application Perspectives - Industry studies ^[9] show that *nanopolymers* are currently considered as the most promising nanomaterials for applications in medicine and energy and materials science. The key to achieve success in industrial applications of nanopolymers is to be able to predefine the composition and morphology of the material, control the interfaces and interactions between components (*building blocks*). The main obstacles to the industrialization of nanopolymers are currently the cost and the lack of reproducibility in performance and the lack of stability of the final material.

Nanoglass

Definition - The glass nanomaterials considered in this study are silica, ITO (Indium Tin oxide), metallic and electrochromic glasses, nanoporous glasses, glasses for photonics, and nanoresistors.

Properties - A myriad of new functional properties have been observed in nanoglass. The combination of nanotechnology (*nanoprocessing*, etc.) and photonics has given rise to a new branch called *nano-optics* that studies the phenomena that take place when light interacts with nanostructures. Recent advances are related both to the manipulation of nanomatter (shape and composition of nanostructures) through *processing* techniques at the nanometer level (nanolithography, laser ablation, dip-penlithography) and to the control of light fluxes on small dimensions. The study and exploitation of the properties that appear when electric fields are confined (and intensified) in nano-matter will have an impact in fields such as high-resolution optical microscopy, optical data storage, optical communications, non-linear optics, etc..

Prospective applications - Nano-optics opens new horizons in photonics (and therefore in the field of communications) where limitations related to the materials currently used could be overcome by the use of new materials and / or exploitation of new phenomena observed on the nano-scale. The fusion of

nano-optics and nano-materials is expected to lead to the development of new sensors. However, the most promising developments in nano-optics are expected (*in high-density optical data storage*), near-field optical microscopies (AFM-Atomic Force Microscope, confocal, optical, tunneling microscopy), and MEMS (micro-electrical-mechanical systems) for molecular-level measurement and nano-positioning systems (e.g., for mirrors).

Nano-ceramics

Definition - The ceramic materials considered in this study are ceramic oxides and non-oxides, silicates and composites. The most interesting for applications are:

- Tungsten Carbide-WC (already in use);
- Oxides of Al (alumina), Zr (zirconia), Ti (titania), Si (silica), Zn: they are all already produced on a large scale, but there is much interest in the synthesis of nano-titania in particular crystal configurations for applications as a catalyst and in cosmetics.
- Silicon nitride, oxides of Mg (magnesia), iron, cerium (ceria), yttrium, silicon carbide, boron nitride: currently produced on a laboratory scale.
- Hydroxyapatite [mineral having chemical composition $\text{Ca}_5(\text{PO}_4)_3(\text{OH})$]; it is the main mineral constituent of bone tissue).

Hydroxyapatite has a variety of uses in medicine that could benefit from the nano structure.

Properties - Nano-crystalline ceramic materials (monolithic and nano-composites) have potential mechanical (increase in strength, hardness, ductility, decrease in density and elastic modulus...), thermo-mechanical (increase in coefficient of thermal expansion, decrease in thermal conductivity, increase in specific heat...) and functional (increase in electrical resistance) properties superior to conventional (*coarse-grained*) materials. The inherent brittleness of ceramics is expected to be counteracted by the presence in nano-composites of a relevant fraction of grain-edge nanoparticles. Superplasticity properties have been shown for some nano-ceramics (**Figure 8**). In principle, increased diffusivity should result in improved sinterability of crystalline nanopowders.

Prospects for applications - Some products are already on the market (ceramics consisting of oxides of nanomaterials, pigments, coatings in the form of thin films, light filters, etc.) others are expected to get there in the short term, however, analysts' opinions on development prospects are divergent. The factors that still make the prospects for application of nano-ceramics uncertain are:

- the difficulty of scaling-up of synthesis systems (from laboratory scale to industrial prototypes);
- the poor reproducibility of results (in terms of morphology of nanopowders);
- the excessive cost of production;
- the lack of satisfactory methodologies (at industrial level) for processing and consolidation of nanopowders.

With regard to the latter point, it is necessary to develop industrial-level techniques for the disagglomeration of nanopowders that make it possible to reduce defects in the sintered material due to the presence of aggregates in the starting powders (**Figure 11**).

Market-relevant applications of nanoceramics are expected in almost all technological sectors and in

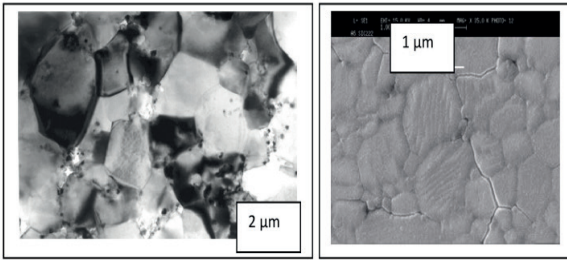


Fig. 11 - (Results of IRTEC-CNR of Faenza - Italy in the European Network NANOMAT)

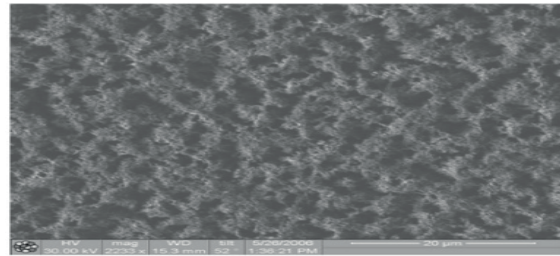


Fig. 12 - (Porous silicon made at the Department of Physical Technologies and New Materials of ENEA of Italy)

particular in optics, precision mechanics, analytical chemistry, mechanical engineering, pharmaceuticals and biology.

[Left: TEM microscopy image of a SiC alumina-nanopowder nanocomposite in which defects (voids) due to the presence of nanoparticles agglomerated at the grain boundaries are evident.

Right: SEM microscopy image of the same nanocomposite showing intergranular microfractures originated by the presence of agglomerated SiC nanoparticles in the starting poor].

Other promising applications for nanopowders are expected in the fabrication of sensors, membranes, catalysts, and filters. Currently, only oxides (such as silica and titanium oxide) are produced on a commercial scale, while non-oxides have not yet crossed the laboratory production scale.

In the medium term, after solving the difficulties of powder aggregates illustrated in **Figure 10** above, vast market scenarios for ceramic nanomaterials with exceptional mechanical and thermo-mechanical properties can be envisioned.

Nanoporous Materials

Definition - Nanoporous materials are natural (zeolites and clays) or synthetic (alumino-silicates, phosphates, etc.), organic or inorganic or hybrid materials with holes less than 100 nm in diameter. They can have open (interconnected) or closed pores and amorphous, crystalline or semi-crystalline structure (*framework*). Nano porous materials are commonly divided into massive (*bulk*) and membrane nano porous materials. Examples of materials that can be both bulk and membranes are carbon (see Par. Carbon-based nanomaterials), silicon, silicates, polymers, metal oxides, hybrids (consisting of inorganic units connected by organic ligands acting as spacers), while specific for membranes are zeolites (crystalline alumino-silicates formed by tetrahedra interconnected to form three-dimensional lattices).

Properties - Nano-porous materials combine the advantages derived from the porous structure with the functionality (physical, chemical and/or biological) typical of the material itself, whose properties can be varied by going to the nano-scale. A well-known example is offered by the nano-porous silicon that is a good emitter of light in the visible, unlike the silicon in massive form that emits a weak radiation in the IR (infrared).

The characteristics of nano-porous materials that are most interesting for applications are:

- the increase in surface adsorption capacity (including selective);
- the possibility of fine filtering (“molecular sieves”);

- the weight reduction
- the thermal insulation;
- the photonic properties.

Prospects for applications - Nano-porous materials offer interesting prospects for applications in a wide range of sectors, from catalysis to membranes for fuel cells and the petrochemical industry, from gas separation to sensors and finally to medical applications.

Some examples of nano materials on which there is a lot of focus: one of the most famous nanomaterials is graphene which is made up of a single layer of carbon atoms with a two-dimensional ultra-thin structure. It is very resistant and rigid, about 100 times more than steel, and has an incredible flexibility as well as a higher electrical conductivity than any other substance. Reasons that make it a very versatile material with numerous applications. In January 2017, a research team from the Massachusetts Institute of Technology (MIT) managed to compress small graphene flakes into specific geometric shapes. The result, published in the journal *Science Advances*, is the strongest and lightest material ever made, boasting a density of just 5 percent of steel and a strength that is as much as ten times greater. Graphene, however, is not the only nanomaterial with incredible potential. Recently a team of researchers from Rice University in Houston, USA, published a study in the scientific journal *Journal of the American Chemical Society* that illustrates the amazing properties of **boron**. According to scholars, in fact, this material arranged in one-dimensional chains of atoms is able to conduct electricity without resistance, becoming an antiferromagnetic semiconductor. A characteristic that opens up very promising applications for information technology.

Analysis of the main application areas of nanomaterials and nanotechnology: Current status and future developments

Nanostructured materials, produced by the science and physics of matter operating at the nanoscale, on the push of requests coming from the scientific and industrial world have been successfully used in various products that are more efficient, more advantageous from an economic point of view, more innovative and avant-garde than those currently in use. These are, as mentioned in the previous paragraph, polymeric, metallic, ceramic, semiconductor, magnetic nanostructured materials, or the nanostructuring of massive materials or surface with physical-chemical processes. The studied materials find mechanical, biomedical, photonic, sensor, catalytic, energetic applications, etc.....

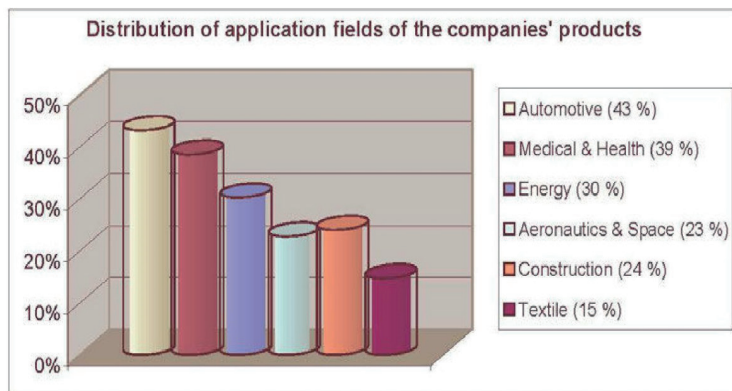


Fig. 13

[European Survey on Success, Barriers, Needs for the industrial uptake of nanomaterials in SME-Small Medium Enterprises]

The main industrial sectors that benefit from nanotechnology are chemical, transport and communication, electronic, computer, textile, pharmaceutical, biomedical, agro-food, aerospace.

Figure 13 shows that currently the largest number of nanoproducts is found in the automotive industry, followed by the medical-health sector, energy, aerospace, building construction, textiles and so on.

In detail we analyze the sectors in which there is a prevalent use of nanomaterials:

- *cement production*, through the use of synthesized amorphous silica;
- *production of paints and wall coatings*, making surfaces easy to clean, scratch-resistant and resistant to microbial attack, thanks to their stain-resistant properties and high resistance to water penetration. The nanomaterials most commonly used in this field are titanium dioxide, silicon dioxide and silver in nanoform;
- *manufacture of tires* (especially carbon black and silica-based nanomaterials) to reinforce rubber and extend its life;
- *fabrication of some computer components*, to make them lighter, reduce energy consumption, increase the speed at which they work, and increase data storage capacity (e.g., development of carbon nanotubes that can quickly convert light into electricity, or enable dramatic improvements in computer performance through faster processors and batteries that last longer);
- *inkjet inks and toners*, where the nanoform increases the quality of print colors and reduces the risk of clogging printer nozzles;
- *textile production*, including children's clothing, to attribute the characteristics of antibacterial protection (*with nano-silver an antimicrobial used in fabrics "for example in beachwear" and medical applications*) UV resistance and waterproofing to fabrics (for example in mountain clothing or tablecloths). An example of new materials in the textile field: Smartshirt System (T-shirt with integrated sensor and grid with conductive fiber that connects with a PC or cell phone with bluetooth).
- *production of sports equipment* (such as tennis rackets, golf clubs and bicycle frames) to make them lighter and, at the same time, stiffer. Carbon

nanotubes are the most popular material, being lighter, having great flexibility and very high tensile strength compared to some metals used in industry. The use of nanotubes is widespread due to their properties of mechanical strength, low weight, heat dissipation and electrical conductivity in applications such as electronics, energy storage, spacecraft and automotive structures and then also in sports equipment;

- *sunscreens and moisturizers*, hair care products and makeup, in sunscreens, in particular, nanomaterials based on titanium dioxide and zinc oxide (as sunscreens) prevent the product, once applied to the skin, to appear white as it happens with sunscreen products with high sun protection. These nanoparticles make the product transparent, so the person tends to apply it frequently, achieving greater UV protection. Silver-based nanomaterials are used for their natural antibacterial activity;
- *inks for tattoos and permanent makeup*, which may contain nanomaterials based on titanium dioxide, aluminum oxide, zinc oxide and iron oxides in order to improve the aesthetic appearance of pigments;
- *in the production of products for the diagnosis and treatment of diseases* (nanomedicine discipline). Some nanomaterials, such as barium sulfate, for example, being opaque to X-rays, are used as a contrast medium for X-rays; others can be applied to improve the properties and therapeutic action of a drug. If, for example, a drug taken by mouth (oral route) has difficulty distributing itself in the body, it can be encapsulated in a more soluble and absorbable nanomaterial that facilitates its distribution in the body. In addition, the use of nanomaterials facilitates the selective and specific delivery of the drug to the organ where it is most needed to act. For example, some anticancer drugs are very toxic to the entire body, but by using nanoform materials as drug delivery vectors, it is possible to promote drug release only in the tumor area and not in the healthy area, limiting the toxic side effects associated with chemotherapy;
- *manufacture of food packaging and storage products*, and in the food itself, as components of additives to increase the shelf life and yield of food. Packaging containers are in most cases made of plastic, a material poorly suited to prevent gases, such as oxygen, from penetrating and reaching the food; the addition of nanomaterials, such as nanoargles and titanium dioxide, can make the plastic lighter and stronger, preventing gases and light from entering the package and causing spoilage during long storage periods. Recently, "smart" packaging is being designed that uses nanosized sensors to monitor the condition of food. These are nanoparticle-based sensors, which give a visual alert when a contaminant is present in the food. Silver in nanoform is used to coat surfaces of refrigerators and food containers for known antibacterial properties
- *improve the purity and potability of water and the healthiness of soils*, are used to restore water contaminated by heavy metals and to remove pollutants from the exhaust of transport vehicles. Let's analyze in more detail some of these applications.

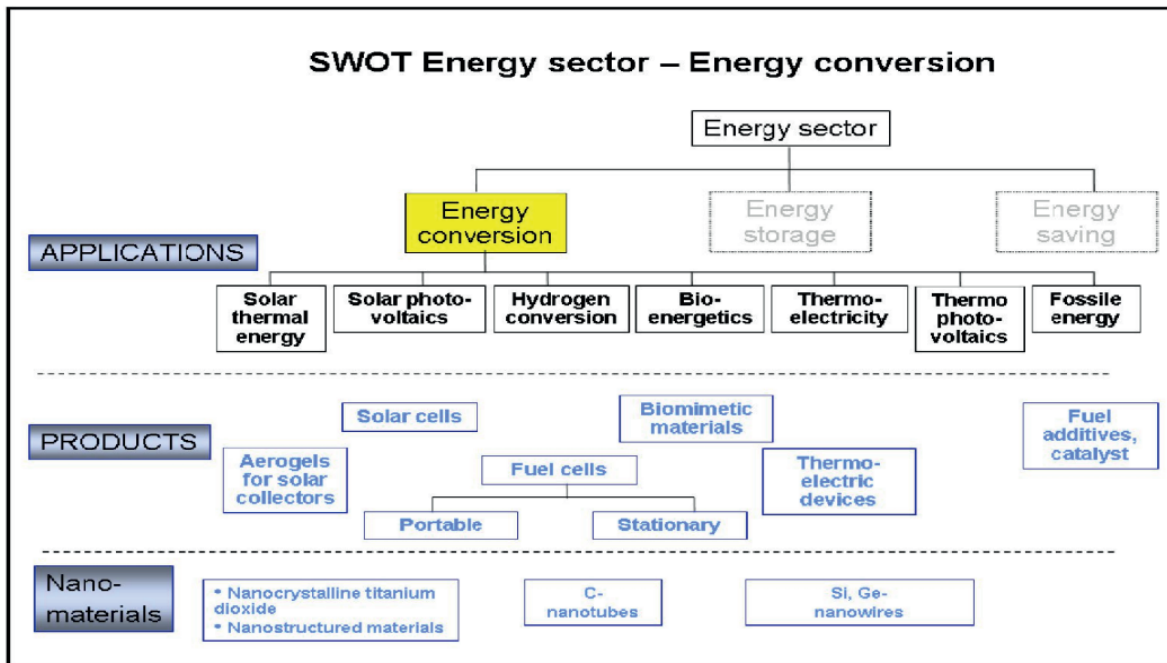


Fig. 14 - ^[11]- Applications and products in the energy conversion domain

Nanobiotechnology

Another sector being colonized by nanotechnology is the biological one. We are witnessing the development of innovative bio-sensors and systems for the intelligent distribution of drugs. Developing bio-sensors means doing molecular analysis; it is necessary to realize devices able to interact with complex organic molecules and give recognition signals, in real time, related to the type of molecule and its concentration. This requires the development of highly integrated systems capable of rapidly and automatically performing multiple complex biochemical examinations.

It is a multidisciplinary activity, in fact, it needs to integrate scientific and technological sectors in very different fields such as micro and nano-electronics, micro and nano-processing, materials science, physics and surface chemistry, computer science, biochemistry and biology. However, drastically new technological perspectives and application potentials will open up for the analysis of DNA, RNA, proteins and other biological molecules or even cells. The end-user sectors are those of biomedical therapeutics and diagnostics, pharmacology and agro-food analysis.

Energy

There is a growing need to reduce dependence on fossil fuels and decrease heat generation from energy sources. Nanotechnology offers potential benefits in all segments of the energy sector, from production to transmission, distribution, conversion and utilization of energy as it enables solutions alternatives for generating, storing and saving energy. In each of the above applications nanomaterials offer potential advantages in all technologies related to renewable energy sources (**Figure 14**) and also allow the reduction of pollutants. According to the sources consulted ^[10,11] the most promising applications of nanotechnology in this domain are in photovoltaics (solar cells), hydrogen conversion (fuel cells) and thermoelectric (thermo-electronic devices).

Nanotechnology research in the energy sector can be summarized in three guidelines.

1. the study of nanostructured materials for the production of photovoltaic energy,
 2. fuel cells,
 3. hydrogen storage.
1. Producing “photovoltaic energy” with nanotechnology essentially means “copying nature” and producing nanostructured materials that in the solar cell simulate the chlorophyll process present in plants. The materials considered most promising are quantum dots, carbon nanotubes, fullerene, nanowires, dendrimers, nanoparticles.
 2. As far as fuel cells are concerned, devices that separate the electron from the proton in hydrogen atoms and thus produce an electric current, nanotechnologies all reside in the heart of the device: “the membrane”, which is responsible for separating hydrogen into protons and electrons.
 3. One of the basic problems with using hydrogen fuel lies in the safe storage of the thick hydrogen. Nanotechnology holds great promise with the ability to safely store hydrogen in nanostructures such as carbon nanotubes, zeolitic type materials or nanopowders. In all cases, these are nanometer-sized structures that have extremely high specific surfaces/volumes available for hydrogen trapping as a consequence of the nanoscale of the problem.

Nanoelectronics

As far as nanotechnological applications to the field of electronics are concerned, there are two main axes along which research is proceeding, in line with top-down and bottom-up technological approaches; These are, respectively, the evolution of microelectronics towards the nanoscale and molecular electronics. In the first case, pushing to extreme limits the techniques of material reduction and circuit etching (in jargon lithography), without substantial

paradigmatic changes in the manipulation of the flow of matter, it was possible to realize objects with critical dimensions. At these dimensional scales, classical physics gives way to quantum mechanics and a device must be redesigned to function properly - with the advantage of being able to exploit an extended range of incredible new capabilities.

Example of this category of devices is the SET, single electron transistor, a component capable of injecting in a nanometer volume a single electron, which then governs a current flow through the repulsive Columbian forces that it exerts on the other traveling electrons. Molecular electronics on the other hand has required a real technological break-through, aiming to study the conduction properties of single molecules. A single molecule has the advantage of being able to be crammed into a very small space and especially to be designed to have certain characteristics. Molecular diodes and transistors are already a reality.

Agribusiness

Food products must be carefully controlled, both to protect their quality and for consumer safety. Quality control, traceability, storage status, and product adulteration can be verified through the use of a nano-sensor selective for a chemical species related to food spoilage or contamination.

The use of highly specific nanosensors allows for real-time, online analysis along the production chain or even in situ on the finished product.

The introduction of analysis protocols based on “*labs on chip*” (sensors and biosensors) provides considerable advantages, both for quality control and safety. Through the use of these new technologies, it is possible to improve the sensitivity of the measurements and at the same time considerably reduce the time required to carry them out. In particular the electronics, where possible, should be integrated to transfer the data with the highest signal-to-noise ratio to the data-sending interface and potentially use wireless communication protocols.

Another sector of strategic importance where nanotechnology can play a priority role is that of “*smart packaging*”. The role of food packaging is radically changing from passive, i.e. simple packaging that serves to separate the content from the outside, to active, i.e. packaging that acts on the product and with

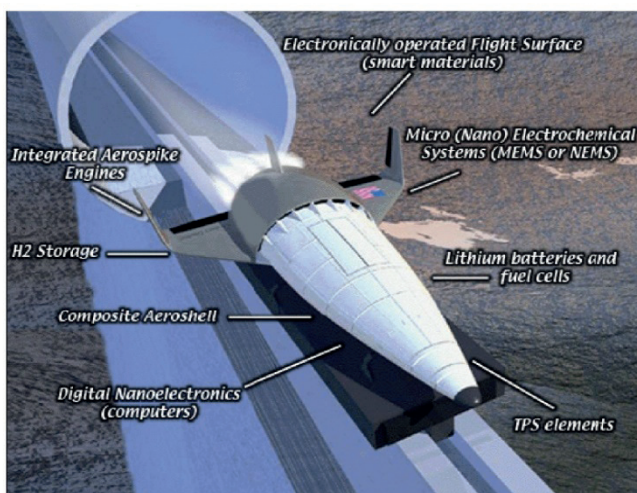


Fig. 15 - [12]

Application examples for nanomaterials in the aerospace industry

the consumer, becoming a dynamic system, where food and packaging communicate and interact with each other and with the outside world. The development of innovative solutions also based on nanotechnology for the “*smart packaging*” of food products, responds to a very wide range of needs along the entire food chain, from production to distribution, through the processes of processing, storage and transport.

Aero-space

The main objectives of the European **aviation industry** to remain competitive are [12]:

Decrease travel rates by acting on reducing the costs of:

- aircraft purchase (by 35%)
- maintenance (by 25%)
- fuel consumption (by 20%)

Improving engines to reduce:

- CO₂ emissions (by 50%)
- NOx emission (by 80%)
- noise level in aircraft (by 50%).

Regarding the first three points, it can be assumed that the use of multifunctional nano composite materials with thermo mechanical properties superior to conventional materials can allow a reduction in costs thanks also to the reduced need for maintenance. The reduction in aircraft weight as a result of the use of low-weight nano-structured materials, together with the use of more efficient engines, should lead to a reduction in fuel consumption. The use of nanomaterials that can work at temperatures 100 to 200 °C higher than in current engines should lead not only to greater efficiency, but also to a reduction in NOx emissions.

The most promising materials for aircraft structures are nano-composites such as glass fibers/polymer matrices reinforced with nanoparticles that release a liquid that promotes polymerization around any fractures or nano-clays for structural reinforcement and increased thermal resistance in nanocomposites. Regarding the development of new “light” materials (to decrease consumption without compromising safety and performance) the most promising candidates are *polymer nanocomposites reinforced with carbon nanotubes and boron nitride and epoxy resins reinforced with nanoclays*. In fact, these materials offer a high ratio of toughness to weight, impact resistance, and radiation protection.

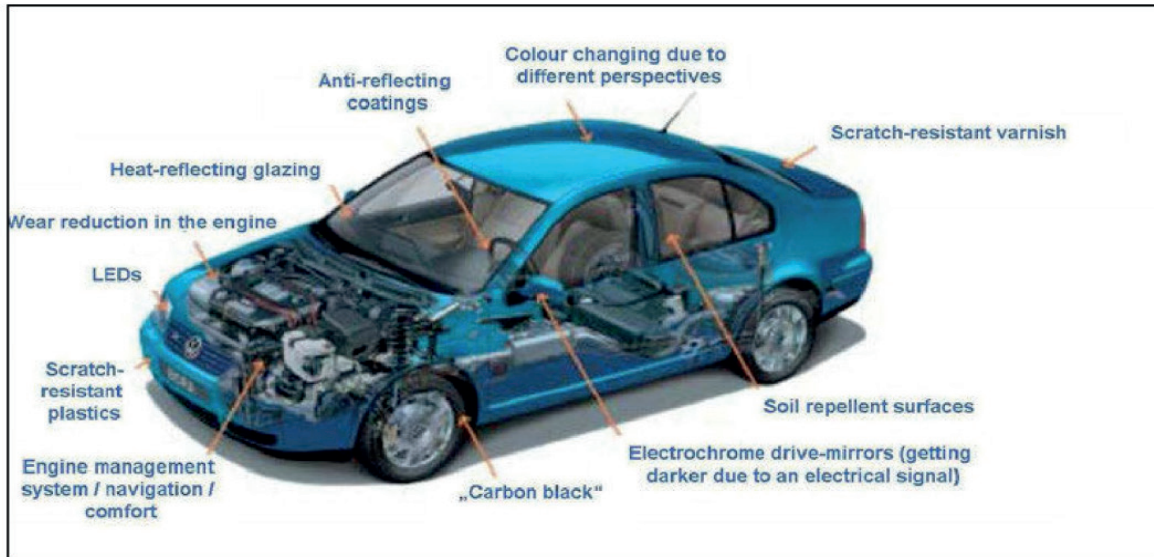
Nanostructured metals find applications in the parts most subject to corrosion and wear (landing gears, brakes, etc.). Finally, coatings (in the form of thin films) that incorporate nanopowders can be used as self-cleaning or anti-glare layers for windows.

Coatings are attracting interest in the aeronautical sector because of the possibility of:

- increase resistance to corrosion, wear and abrasion;
- Reduce pigment degradation under UV radiation (decreasing repainting frequency);
- improve the thermal barrier;
- reducing turbulence.

Finally, there is a lot of focus on nano-materials for use in seat and interior coatings as the addition of nano-clays reduces flammability. In addition, nano materials for coatings are potentially lighter and more hygienic (due to the addition of antimicrobial particles) than conventional materials.

At the European level, **the use of nanotechnology**



(da: Nanomobility initiative of the German Ministry for Education and Research – BMBF, www.nanotruck.net)

Fig. 16 - [14] Potential benefits of nanotechnology to automotive component development.

in space is seen as a long-term development area and prominent fields of interest include communications, energy production and storage, and propulsion systems. Recently, ESA AURORA program (dedicated to long-term strategy for solar system exploration) has considered the use of nano-crystalline materials, nano-composites, and bio-mimetic materials for space applications. In the U.S., there is greater investment in nanotechnology for space. In fact, NASA already in 2004 invested about \$31 million in basic and applied research in this field ^[13], setting long-term goals mainly related to a vision of intelligent, evolutionary and adaptive space systems resulting from the convergence of nanotechnology, biotechnology and information technology.

The driving force for the use of nanotechnology in the space sector is related to the possibility of helping to achieve the critical goals of this sector:

- decreased costs
- risk reduction
- flexibility during missions
- increased potential.

Also for the aeronautical and space industry, as for energy, the main element of success related to the use of nanotechnology is related to material properties (followed by the improvement of product quality) and the major barrier is the development of technologies and the production process (followed by the cost/benefit ratio).

Automotive

The main objectives of the automotive industry are:

- the reduction of environmental pollution
- reduction of vehicle weight
- recyclability
- safety
- increased efficiency and performance of engines (fuel saving)
- vehicle aesthetics
- lengthening of maintenance cycles.

As far as the *bodywork and passenger compartment*

are concerned, polymer nanocomposites are already being used to make both internal and external parts. Greater use will be possible when the difficulty of painting them with products on the market (electrostatic paints) is overcome. Looking ahead, new high-strength, safe and recyclable nano-composites are being developed for interiors and exteriors.

Nanocomposites consisting of nanoparticle-reinforced polymers can be a viable alternative to metals for *engine components* because they are lighter, corrosion-resistant, sound-absorbent, and recyclable. In addition, future fuel injectors for diesel engines could be coated with nano-diamond to increase wear resistance. The main technological barrier to the use of nanocomposites is the need to develop methods to improve the dispersion of nanoparticles in plastics and to fine-tune industrial techniques for processing nanomaterials.

Many industries already make coatings in which nanoparticles are incorporated to achieve surfaces that are more resistant to scratching and corrosion, self-cleaning, more durable, and smoother. Adding nano particles to coatings can also make them iridescent, anti-static, block UV components, etc.

Nanotechnology-based lubricants reduce friction between moving parts and minimize wear, reducing maintenance costs and increasing performance. At the industry level, there is considerable attention to the possibility of replacing *carbon black* in tires with nano-clays and nanopolymers to increase wear resistance and improve eco-friendliness. There are also plans to use nano-soot as an additive to conventional materials to increase tire life, reduce friction and reduce fuel consumption. Certainly, the greatest impact of nanotechnology in the automotive sector is expected from the development of new miniaturized sensors and integrated systems. In particular :

Night vision systems:

- polymers additivated with nanoparticles for components with high transmissivity in the IR;
- sensors for IR.

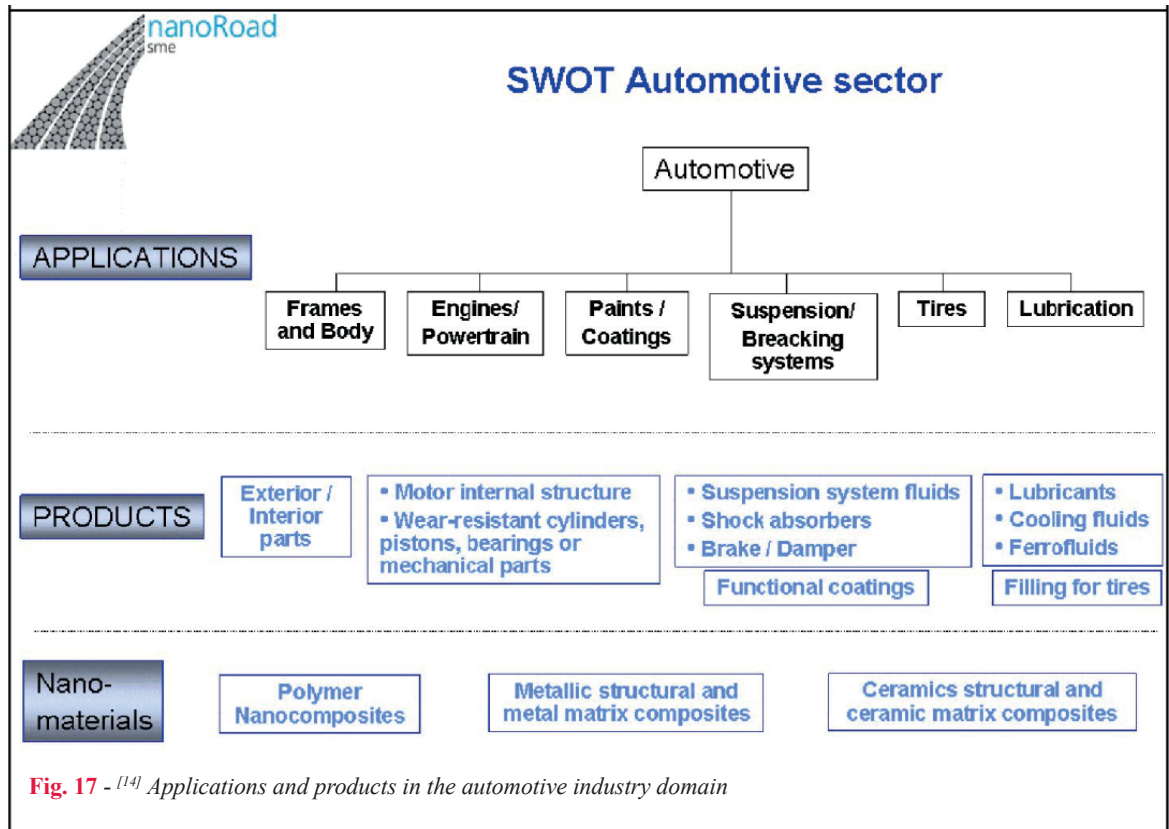


Fig. 17 - ^[14] Applications and products in the automotive industry domain

Sensors:

- cabin air quality monitors;
- harmful emissions detection.

Control panel:

- thin-film display;
- interactive glasses;
- carbon nanotube-based micro-switches.

Lighting systems:

- new light sources;
- optical switches or electro-optical films.

Nano Medicine

The field of bio-medical and health care is, and will increasingly be, influenced by “nano-bio-technologies,” an area that interfaces between chemical, biological, and physical sciences ^[10,15]. To understand the relationships between the world of bio-materials (made by nature) and the world of nanomaterials (made by humans), it is instructive to take a look at the dimensions of biomaterials (**Figure 18**): it becomes apparent that the world of nanomaterials has typical dimensions Nano Medicine.

(10-100 nm) comparable with proteins and viruses. The investigation of proteins (proteomics) is at an early stage (after genomics). On the other hand, most diseases occur at the cellular level and selective in-

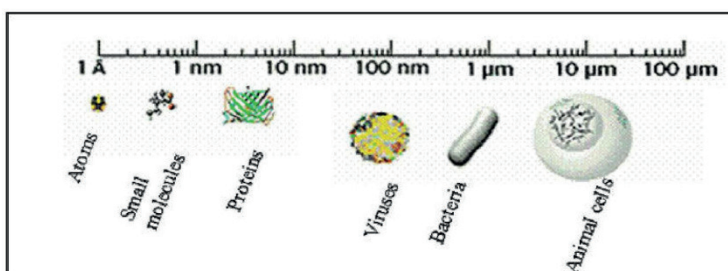


Fig. 18 - Bio material dimensions

terventions on cellular parts and functions are hardly possible today and represent a challenge for tomorrow to which nanobiotechnology could contribute. Therefore, nanotechnologies applied to health research are able to offer solutions in a certain sense revolutionary with applications in the field of clinical therapies and diagnostics as well as in surgical sciences that could lead to the development of a nano-medicine that operates with minimal invasion, based on integration with fourth industrial revolution (4IR) technologies, the possible integration of modern 4IR tools such as artificial intelligence (AI), robotics, machine learning, ZigBee technology and the internet of things (IoT) or combining nanotechnology with pure sciences such as biology and chemistry. Early detection, “smart” treatments, and the activation of self-healing mechanisms are among the main goals on the road to health evolution.

The main application areas of nano materials in the bio-medical and health sectors are shown in **Figure 19**. ^[15]

For each application, several products can be identified in which nanomaterials play or may play an important role.

One very lively area is *drug delivery* for the benefit of chemotherapy, nanomedicine would allow the use of polymerized nanoparticles to combine with specific markers in cancer cells. The nanoparticles circulate in the blood vessels until they reach the target cells and only then the drug is released affecting and only the cancerous tissues and not the neighboring ones. This method would therefore allow the administration of higher and more effective drug doses while preserving healthy cells. In the field of “*drug delivery*” the current research and development activity focuses on:

- formulation of drugs by means of nanoparticles that can improve their solubility, increase their

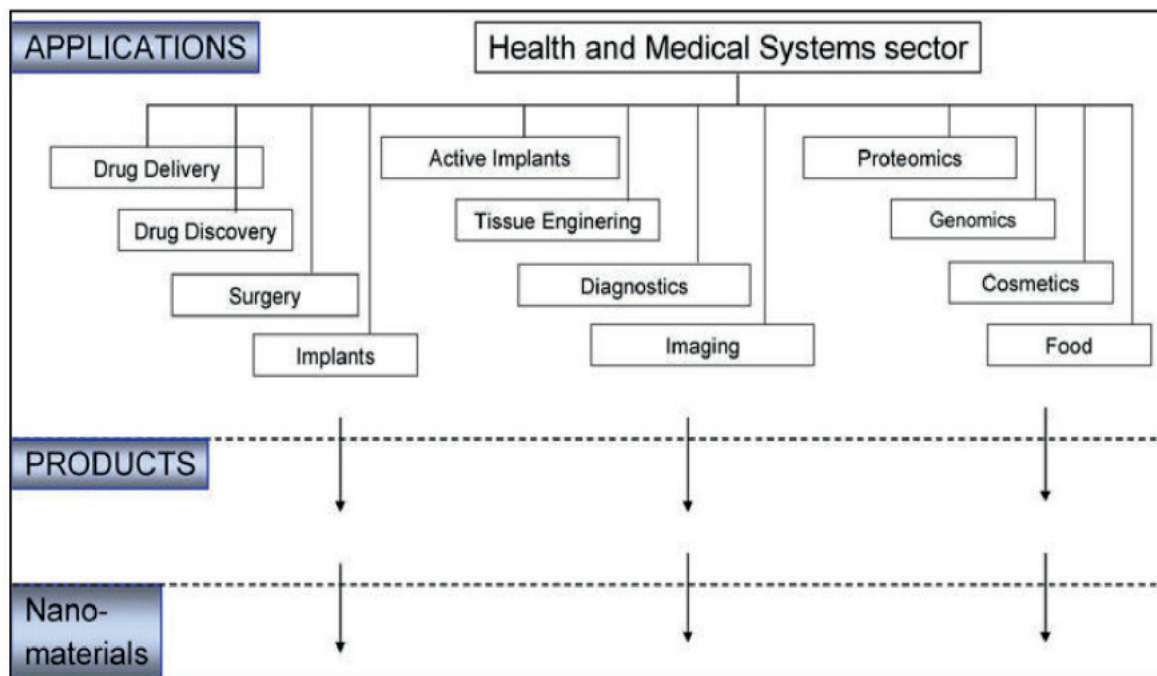


Fig. 19 - Main areas of application of nanomaterials in the bio-medical and health domains

resistance to stomach acids and enzymes, allow a controlled release;

- new formulations and routes of administration to deliver drugs to sites in the body previously inaccessible to drugs;
- release of the right drug in the right place at the right time;
- personalized drugs.

This opens up the vast prairie of nanoparticles and so-called “*smart drugs*”, a boundless army of tiny drug transporters designed to travel through our bodies and release their precious therapeutic cargo when programmed conditions occur. The theoretical advantages of nanoparticles, which have uncommon properties that can be exploited to modify the kinetics of a drug, are related to increased solubility, longer duration of drug exposure, exposure of the drug trapped in the nanoparticle at the target site, higher therapeutic index, and the potential to develop less resistance in chronic use. Nanomedicine can also be very effective in combating sepsis as treating bacterial infections that are resistant to many drugs is a major challenge for medicine. Thus, the pervasiveness of nanotechnology is total, and nanomedicine is one of the “hottest” areas currently.

Nanomedicine is evolving, clearly ranging from nanoparticles for molecular diagnostics to imaging, to micro and nano-therapies and integrated medical systems with the goal of performing complex repair actions at the cellular level within the body in the near future. It is well established that nano particles will have a major impact on bio-imaging techniques in the near future. For example:

- the nuclear contrast agent Technetium-99 can be attached to nano particles (perfluorocarbon) capable of delivering it to specific blood vessels;
- new contrast agents for MRI (*Magnetic Resonance Imaging*) are being developed by means of nano-bio-technologies, such as gadolinium compounds encapsulated in nanoparticles (perfluorocarbon), holmium compounds in fullerenes or nanoparticles

of ferrous oxides;

- semiconductor quantum dots are extremely promising candidates for in vitro and in vivo bio-visualization as they emit size-dependent color radiation under optical stress.

A revolutionary aspect is represented by the possibility of being able to “mark” and “track” cells with nanoparticles.

However, there is also **Nanodiagnostics** with the ultimate goal of identifying the disease as early as possible, ideally at the level of its manifestation in a single cell, nanotechnology can offer diagnostic tools with characteristics of better sensitivity, specificity and reliability, as well as the possibility to record several measurements in parallel or to integrate different analytical steps, from sample preparation to detection in a single miniaturized device. Thanks to micro- and nanotechnology, the device could contain enough “intelligence” and automation on board to be used by the patient himself and provide a multitude of information to the physician.

So in the field of diagnostics, it can be said with conviction that the development of bio-nanotechnology will be a useful support for the identification of samples (e.g. small amounts of antibodies in body fluids, DNA, etc.), validation of new drugs, in vitro modeling. The *driving force* will be represented by analysis technologies based on miniaturization (*from microarray to nanoarray*) and on the transition from MEMS to NEMS also thanks to nano-lithographic techniques. For example, the *Lab-on-a-Chip* is a miniaturized device that employs a network of channels and wells etched on glass or polymer chips to create miniature laboratories. The use of pressure or electrokinetic forces causes small volumes (pico or nanoliter) of fluid (containing the biological samples to be analyzed) to move through the channels in a controlled manner and then send them to the *microarray/nanoarray* sensors. This miniaturization technology allows speed of analysis, low consumption of samples and reagents and high reproducibility. Currently there are already

products at industrial level.

Some futuristic examples: there is the *respirocita* a *nanorobot* that behaves like a tiny tank capable of storing oxygen and carbon dioxide at 1000 atmospheres, releasing them in a controlled manner (thanks to nanosensors and nanorotors integrated into its structure). It has a spherical shape, about one micron in diameter, and a hull composed of carbon atoms, similar to diamond.

It mimics the red blood cell, but in an enhanced way: the nanorobot is able to store and release 200 times more oxygen. A saline solution of 5 cm³, could replace the entire blood system of the human being (which on average has at its disposal more than 5 liters of blood). Imagine to undergo a “transfusion” of a liter of *respirociti*: you could stop breathing for about 4 hours or sprint at your maximum speed for 15 minutes without taking a breath of oxygen! This is a nanorobot theorized and designed a few years ago by Robert Freitas Jr. (a researcher at the IMM in Palo Alto, California). This is not science fiction. It is the current vision of one of the frontiers of nanomedicine. Nanomedicine is an area where the technology is still being developed. Nanorobots are one of the most pragmatic applications and among the first to be postulated. Nanorobots will become reality in a future that many of us will probably see.

As for the *nanosensors* mentioned above, or chemical or biological sensors that convey information at the molecular level, being able to note changes in volume or concentrations or displacement and gravitational forces or electrical or magnetic or pressure or thermal of cells, they could recognize the cells among them, highlighting in particular the cancerous ones. The use of microelectronics-derived technologies has enabled the miniaturization of *nano-bio-sensors*, which has led to the development of arrays of highly integrated sensors, capable of extracting information from small samples and performing several measurements in parallel on a single sample. These therapeutic nanoparticles aim at a more efficient delivery of a therapeutic drug (chemotherapeutic) to the site of pathology, avoiding its accumulation in healthy organs and tissues, and are mainly based on the “*Enhanced Permeability and Retention*” (EPR) effect. Advances in microelectromechanical technology (Mems) have allowed the development of sensors that involve the transduction of mechanical energy based primarily on mechanical phenomena. This very interesting research area in the field of microdevices that can accumulate the drug and release it on demand, possessing a very small microchip containing a sensor, will offer an unprecedented potential for the development of mass production of extremely sensitive sensors and for the rapid analysis of chemicals and different biological species at low cost. Therefore, nanoparticles represent an innovative tool in research and therapy due to their self-assembly, small size, increased stability, biocompatibility, tumor-specific targeting of antibodies or ligands, encapsulation and delivery of anticancer drugs, and increased contact surface area between cells and nanomaterials. Active targeting of nanoparticles through conjugation with cell surface markers can increase the efficiency of nanoparticles in delivering various agents to the tumor area, significantly reducing toxicity to living systems. Nanoparticles can use multiple biological pathways to achieve specific delivery

to cellular and intracellular targets, including transport across the blood-brain barrier that many anticancer drugs cannot circumvent. This is further confirmation that nanotechnology offers many advantages in various fields of science. In this sense, nanoparticles are the cornerstone of nanotechnology. Recent advances in nanotechnology have shown that nanoparticles have great potential precisely for medical applications.

Also in the US, *peptide nanoparticles* have been developed that can treat infections that do not respond to conventional antibiotics. Biological nanofactories are being engineered to send communication between different populations of bacteria since the nanofactories can fight bacteria that may lead to infection before the cells bacterial proliferate in such a way as to become dangerous. In other words, it would create a natural immune system response capable of blocking bacterial infection without the use of drugs.

Viewed from the perspective of the nanoscale, silver can be used to fight infection in a wide variety of ways. In fact, silver ions can easily reach the germ’s nucleus where the vital gene chain is located. When silver ions combine with these genes, they become paralyzed and therefore unable to replicate. More recently, it has been discovered that silver, when bound to oxygen, can electrocute the germ. The use of nanotechnology can also be applied to catheters treated with antiseptics and coat them to prevent the spread of infection. Nanoantibiotics can also be used as a superior alternative for existing treatments in brain infections. In fact, the brain membrane is not penetrable by most conventional antibiotics because the molecular structure of most drugs is too large to cross the blood-brain barrier while peptide nanoparticles can cross it without difficulty and thus act as a carrier for both hydrophobic (i.e. rejected by water) and hydrophilic (i.e. binding to water) drugs, allowing the nanoantibiotic to reach the infected areas of the brain that require treatment.

Regarding surgery, nano materials could be used for the fabrication of tools (e.g., scalpels) with special mechanical properties and characteristics such as biocompatibility, sterility, anti-toxicity, wear resistance, etc..

Finally, regarding genomics and *proteomics*, it is currently very difficult to identify the impact of nanomaterials in these areas and to draw a “roadmap” [15].

Regarding *implantology*, research in the field of bio-nano-technologies focuses on the use of nanomaterials to improve bio-compatibility (titanium alloys), achieve better adhesion between cells and implant, realize bio-active coatings, decrease toxicity and flammability, improve sterility (coatings based on Au and Ag ions), elasticity, corrosion resistance and half-life. In addition, the possibility of nano-structuring surfaces to promote cell adhesion is explored.

The application of bio-nanotechnology to biological *tissue engineering* is at a very early stage (basic research) and could have an impact on the reconstruction of biological tissues by culturing patient cells on *scaffolds* (artificial supports) made of bio-materials that promote cell proliferation and are eventually resorbed (e.g. biodegradable polymers).

One of the most mature sectors is undoubtedly represented by the application of nano materials to *cosmetics*, as shown by the high number of patents filed and products already on the market. Nano materials under development or already in production are used

in toothpastes, skin creams, sunscreen creams (based on nano particles of zinc oxide that absorbs UV radiation), perfumes, gels, lipsticks.

Research in Italy

Among the most important and far-reaching initiatives for the support of “Nanotechnological” innovation in Italy, we would like to point out the one adopted in 2005 by MIUR (Ministry of Education, University and Research of Italy) through the research funding tool consisting of FIRB funds. Were then funded 4 initiatives in the scientific area of Nanobiotechnology for innovative devices and sensors for genomics and post-genomics, 4 public-private National Laboratories that were enhanced or generated through the call. The reference locations are Genoa (University of Studies), Lecce (National Nanotechnology Lab, NNL), Venice (ABO Oncology Association) and Turin (Polytechnic). The last Laboratory was later named Latemar^[16]. Today Latemar is in its fourth year of activity. It has carried out 8 lines of research (from Lab-on-a-chip, to advanced and integrated sensors in microfluidics, to innovative characterization techniques), with results witnessed by more than 60 publications in international journals, more than 70 presentations in Conferences, some patents and the creation of spin-offs that are going to commercially exploit the products of the research. It has hired and trained more than 20 young researchers with strongly interdisciplinary contents. Since 2009 it organizes the Alp Nanobio International School^[17], an International Training School on nano-biotechnologies.

Hazard Scenarios of Nanomaterials

The risk of exposure to nanomaterials represents to date a toxicological issue still being explored by medical science. While the expansion of the nanotechnology sector has aroused great interest for the obvious economic and social benefits that derive from their use, there are many concerns about the possible negative effects of these materials on the environment and human health. Eric Drexler one of the fathers-pioneers of nanotechnology already in his time described that nanoorganisms will come to compete and blend with natural life forms.

What is unknown about atomic technology poses incalculable risks, ranging from environmental contamination, to health risks, to the construction of new weapons of mass destruction. In the field of health, the major concern that has nanotechnologists debating is the fear that nanoparticles could penetrate the human body and cause unknown damage. Human organisms have always been exposed to a large amount of nanoparticles that our bodies have learned to live with. The fear is that a development of nanotechnology and related industrial production will result in the creation of new particles with dangerous health consequences. Where nanoparticles are firmly attached to a supporting material, such as automotive paint, products raise less concern than where nanoparticles move freely in the environment. These free-moving nanoparticles can be inhaled through the lungs or absorbed through the skin. If today many particles cause the most diverse respiratory diseases, such as asthma or cardiovascular pathologies, tomorrow the diffusion of nanotechnologies could multiply these harmful effects.

Also with regard to the environmental impact there are

many open points in relation to a possible risk to the environment attributable to nanoparticles and nanotechnology products. Many synthetic particles are unknown to the environment in type and quantity. They could constitute a new class of harmful and non-biodegradable substances. One example is the aluminum oxide nanoparticle. According to a recent report by an environmental scientist at the New Jersey Institute of Technology (NJIT), recently published in “Toxicology Letters,” aluminum oxide nanoparticles slow root growth in five plant species: corn, cucumber, cabbage, carrot and soybean. Aluminum oxide nanoparticles are commonly used for abrasion-resistant layers, sunscreen lotions that provide ultraviolet protection, and environmental catalysts that reduce pollution. “Prior to this study, plants were considered totally immune to nanoparticles; instead, it has been shown that seeds can interact with nanoparticles such as aluminum oxide nanoparticles, which slow and damage the growth process,” says Daniel J. Watts, of NJIT, an author of the study. In the real world, nanoparticles can be in the air, coming from tailpipes, smokestacks, or chimneys, can mix with rain and snow, and then reach the ground. Even the application of nanotechnology to the field of warfare can be foreshadowed as a dangerous mixture. In fact they would not only allow to build more destructive conventional weapons at a reduced cost, but also weapons of mass destruction that self-replicate, as viruses do when they attack the human body. Two examples of this are the strong investments of the state of Israel and the United States in projects aimed at the realization of innovative means of warfare. The Jewish state is financing a project for the realization of a “*bionic bumblebee*”, a new form of robot-killer with unprecedented capabilities: assembled with pieces as small as a millionth of a millimeter, these nano-weapons should be able to face Palestinian missiles, capable of intercepting suicide bombers and efficient in countering the most creeping war tactics. The United States, on the other hand, are already producing the “*wasp*”, a micro airplane of 41 centimetres and weighing only 275 grams, already in reconnaissance in Afghanistan. It is controlled by a radio control and is almost imperceptible so much so that it can approach the target without being noticed. It is able to creep into enemy camps where it can release contaminants or explosive material.

Environment, Nanotechnology and Eco-Nanotoxicology.

In the last decades, the development of materials science and in particular the study of nano-structured materials has been able to respond not only to pressing technological needs but also to an increased sensitivity and legislative requirements of an environmental nature. For applications such as those in the textile industry, decorative or functional coatings for the automotive sector, traditional chemical processes with a strong environmental impact (finishing or dyeing processes, or galvanic coatings) are and will be replaced by innovative technologies of deposition of thin films in high vacuum or plasma treatments at atmospheric pressure with much less environmental impact. Or anti-stain treatments, or for the increase of dyeability, anti-wear or high hardness coatings, surface activations for adhesion between different materials (e.g. metals/polymers), or deposition of polymeric films

with hydrophilic or hydrophobic functionalities, deposition of films with high biocompatibility, anti-ignition treatments, gas barrier films. This incomplete list of properties can be obtained through surface treatments with an extension of the order of nanometers: it is possible to modify the energy and the surface properties of treated materials (both inorganic and organic) without changing their massive properties, obtaining stable properties and technological performances higher than those resulting from traditional chemical processes, the latter certainly having a more invasive impact on the surrounding environment.

The wide use of nanotechnology, interest aroused by the obvious economic and social benefits on the other hand, there are concerns about the possible negative effects of these materials on the environment and human health. Since this is a particularly complex technology, developed in recent times, it has been necessary to develop a risk assessment process for nanomaterials in order to investigate, in particular:

- the relevance of exposure pathways to humans and the environment;
- the exposure measurement systems;
- the translocation mechanisms and degradation potential of nanoparticles within the human body;
- the mechanisms of toxicity to humans and the environment.

This evaluation process takes into account the particular size and shape of nanoparticles that as such can come into contact with different organisms, affecting the entire food chain.

The environmental fate of nanoform substances depends on the specific characteristics of the substance, such as shape, solubility in water, overall size, ability to agglomerate, etc. Once in the environment, nanoparticles give rise to numerous processes of chemical-physical interaction with various biotic and abiotic components and can remain intact or undergo the following processes:

- dissolution;
- speciation (i.e. association with other dissolved chemicals in ionic or molecular form)
- degradation (biological or physicochemical transformation into other substances and/or complete mineralization);
- agglomeration;
- deposition.

In this regard, it is also appropriate to perform an environmental risk assessment on engineered nanomaterials in the biosphere and their effects on ecosystems, an activity defined as eco-nanotoxicology or science that studies the release of nanomaterials into the air, water and soil, and see how they come into contact with different organisms and how they can affect the entire food chain.

The evaluation of nanomaterials relies on the use of standardized testing guidelines to ensure that they are performed uniformly and provide relevant and reliable data. An overview of the testing guidelines to be used for risk assessment of nanomaterials is available on the European Union Observatory for Nanomaterials (EUON) website. The database contains over 300 nanomaterials currently on the market in the Union, some of which have been registered under the REACH Regulation.

European Chemicals Agency (ECHA) is currently working to integrate the Guide to Registration and

Identification of Substances with a specific appendix for substances in nanoform. The latest available version of that appendix is from September 2019. In addition, an update to Chapter R.6 of the Guidance on IR & CSA Requirements for substances in nanoform is underway. The latest version available is September 2019. The final versions of these documents will soon be available on ECHA's website.

With Regulation (EU) 2018/1881, the provisions already provided for the chemical safety assessment are also applied to substances in nanoform: hazard identification, description of the different nanoforms, exposure assessment for humans and the environment, description of degradation, transformation or reaction processes and environmental fate for each substance in nanoform. In this way, an effective implementation of the REACH regulation is guaranteed also for substances in nanoform, ensuring a high degree of protection of human health and the environment.

Eco-nanotoxicology and nanotoxicology (the latter science will be discussed in the next paragraph) have a primary role in preventing risks to the environment and human health, as well as for a complete and correct information to consumers.

However, the lack of information on the behavior of nanomaterials in the environment makes it difficult to assess their risks in the various sectors.

Emerging Occupational Safety Risks from Nanomaterials and Nanotoxicology

Any technology can cause both positive and negative effects. The attention of the doctrine^[18] and of national^[19], European and international institutions^[20], has thus focused on the potential risks to the health of workers arising from the use of these technologies. These risks are sometimes not directly attributable to the technological tool, but rather to the way in which the work is carried out that results from their use. The use of nanomaterials may represent one of these emerging risks for health and safety at work, and as such it must be assessed and managed with a specific approach for known hazardous factors and with a precautionary approach for unknown ones, especially within the complexity of the work environment.

The study of the potential harmful effects of nanomaterials on human health is called nanotoxicology (the study of the effects of nanodevices and nanomaterials on living organisms). This is a new discipline of fundamental importance, which deals not only with evaluating the effects of nanomaterials but also with assessing whether the methods and tools used so far to study chemicals not in the form of nanomaterials (nanoform), can also be used for nanomaterials to ensure a targeted health risk assessment and reduction.

Nanomaterials entering the body through different pathways can be absorbed, distributed, and transformed (metabolized). Involvement of the body's defense system (immune system) as well as induction of oxidative stress seem to be some of the main mechanisms of action of many nanomaterials.

So-called nanospecific hazards may occur when emissions of nanoparticles occur and are absorbed by living beings or the environment. Possible health and environmental risks arise in particular from free particulate and fibrous nanomaterials. These can exist as dust, dust, or in dispersions or as aerosols, or they can be released in bound forms. The possibility of such re-

leases must be considered throughout the life cycle of the nanomaterial or nanoparticle. Since man-made nanomaterials can be released into the air, water and soil, they can come into contact with a variety of organisms and affect the entire food chain. Nanotoxicology is the discipline that studies the potential environmental and human health effects of nanomaterials and nanoparticles.

Currently there is a paucity of accurate information on human exposure, exposure pathways to nanomaterials, their fate in the human body, and their ability to induce undesirable biological effects such as the generation of oxidative stress. There are not many data available on in vitro, animal and human studies, there is some inhalation study for only a few nanomaterials. So far, no long-term adverse health effects in humans have been observed. This means that exposure to nanomaterials must be minimized, despite the uncertainty about adverse health effects, when there are reasonable indications to do so, it is necessary to always have a precautionary approach towards potential emerging risks such as nanotechnologies in order to avoid careless exposure of people.

Currently, there is also no specific dedicated legislation and/or regulations on nanomaterials, but there are specific provisions in existing legislation to be used by analogy. Due to the growing demand for information and transparency, some European states have developed national registries, through which they monitor nanomaterials produced, imported and distributed on the market. At the same time, however, companies are already implementing internal guidelines in order to ensure responsible management of nanomaterials and worker safety.

Considering the current widespread use of nanomaterials, all people are directly or indirectly exposed to them, and this is intuited by recalling the definition of the Recommendation 2011/696/EU of the European Commission (EC), which in simpler language defines nanomaterials as tiny particles invisible to the human eye, present in our daily lives in commonly used products such as food, cosmetics, electronics, and pharmaceuticals, and workers in this context represent the main potential exposures at each stage of the life cycle of nanomaterials ^[21], furthermore as the use and production of nanomaterials increases, so does the potential exposure of the workers involved ^[22].

According to one source, the volume of nanomaterials in the market can be classified as follows ^[23]:

1. carbon black (9.6 million t)
2. synthetic amorphous silica (1.5 million t)
3. aluminum oxide (200 000 t)
4. barium titanate (15,000 t)
5. titanium dioxide (10 000 t)
6. cerium dioxide (10,000 t)
7. zinc oxide (8000 t)
8. carbon nanotubes (CNT) and carbon nanofibers (CNF), (100-3000 t)
9. silver nanoparticles (20 t).

Therefore, in the workplace, exposures can often be higher than the known risks because the risks and consequently the management measures for nanotechnology are not certain ^[24].

It is therefore a true emerging risk as defined by the European Risk Observatory: "An emerging risk in the field of Occupational Health and Safety is any risk that is new and growing." ^[25].

New means that:

- the risk did not exist before (and is caused by new processes, new technologies, new types of workplaces, or social or organizational transformations);
- a problem that has been known about for some time that is newly considered a risk due to a change in social or public perception;
- a risk recognized as such because of new scientific knowledge.

Risk is increasing if:

- the number of hazards driving the risk is increasing;
- the probability of exposure is increasing (level of exposure and/or number of people exposed);
- the effect of the hazard on worker health is increasing (severity of health effects and/or number of people affected).

The possible hazards of nanomaterials can be traced to their nanometric structures, which often exhibit "altered" chemical and physical properties compared to analog substances of the nonnanometer size. An important characteristic of nanomaterials is their large surface area to volume ratio (= high value of surface-to-volume ratio). This can often result in increased reactivity as well as increased bonding capacity. Many nanomaterials have a very strong tendency to form agglomerates or aggregate, which can lead to changes in their properties. However, the large surface area relative to volume may persist. In addition to their external structural attributes, nanomaterials can also be differentiated chemically. While some nanomaterials consist of chemically homogeneous substances or compounds, others are purposely modified to make them more functional. It is also possible that residues of auxiliary substances used during the production process may be found on the surface or inside the nanomaterial in the form of impurities that affect its properties. As such, nanomaterials are an emerging hazard and of considerable concern due to their potential health effects. Not all nanomaterials necessarily have a toxic effect, but a proper assessment of potential effects requires a case-by-case approach and research is still ongoing. According to the Health and Safety Executive, the UK's public health and safety body, the small size of nanoparticles can penetrate the body and our cells and even cross the blood-brain barrier, with potentially harmful consequences for our health. Inhalation exposure is the first and most important route of entry of nanomaterials into the body, and there are numerous studies on the potential effects of nanomaterials on the respiratory system. Some types of carbon nanotubes can have effects similar to those of asbestos, cross biological barriers and reach, in addition to the lungs, other organs and tissues (liver, spleen, kidneys, heart, brain and soft tissues in general). The most important effects found during epidemiological and scientific studies, is in the lungs and include, among others, inflammation and tissue damage, fibrosis and tumor generation. Nor can the cardiovascular system be affected. Where nanomaterials have uncertain or not clearly defined toxicology and unless, or until, robust evidence is available on the hazards from inhalation, ingestion, or absorption, a precautionary approach to risk management should always be adopted because nanomaterials in the environment can be absorbed and/or ingested by various animal and plant organisms and then spread through

the food chain, which is a major route of exposure for humans. The environment can be contaminated during the production, transport, storage, use and disposal of products containing nanomaterials. Once in the environment (air, water, soil), nanomaterials can remain intact, or they can be transformed into other chemicals, join together to form aggregates, or be deposited. This depends on their chemical and physical characteristics, but also on the characteristics of the environment with which they interact: therefore, it is complex and difficult to assess the risks in different environmental sectors.

Human exposure to nanomaterials may depend on the work performed, for example workers involved in their production and/or handling; or it may be accidental, consuming and/or using products in which they are contained.

The aim of this bibliographic research is to monitor the state of the art of the evolution of the European and national regulations in force for the management of risks from nanomaterials, to know the specific risks and to verify the good practices and/or the best existing procedures in order to better protect the health and safety of workers and the community through the identification of the right prevention and protection measures.

European and National Regulatory Framework on Risks from Nanomaterials

Currently, there are no specific officially recognized occupational exposure limits (OELs) for nanomaterials. Recently, ISO/TR 18673:2016 “Nanotechnologies-Overview of Available Frameworks for the Development of Occupational Exposure Limits and Bands for Nano-Objects and their Aggregates and Agglomerates (NOAAs)” has been adopted by UNI.

The Standard provides a collection of methods and procedures useful for determining occupational exposure limits and bands (OELs/OEBs) for manufactured nano-objects and their aggregates and agglomerates (NOAAs). Such data, as is indicated in the standard, are useful for occupational health and risk management. In addition, the IARC (International Agency for Research on Cancer) is evaluating a possible classification in Group 2B (possible carcinogenic to humans) for Multi-Walled Carbon Nanotubes (MWCNT-7) and in Category 3 for Single-Walled Carbon Nanotubes.

In order to ensure at this stage an adequate protection of health and environment, both at European and international level it is recommended to apply the precautionary principle so as to minimize the potential risks of exposure to nano materials.

European framework: on October 18, 2011, the Commission adopted the Recommendation on the definition of a nanomaterial. According to this Recommendation, a “Nanomaterial” is defined as:

a natural, incidental, or manufactured material containing particles, in the unbound state or as an aggregate or agglomerate and in which, for 50 percent or more of the particles in the number size distribution, one or more external dimensions fall within the size range 1 nanometer - 100 nanometer. In specific cases and where justified by environmental, health, safety, or competitive concerns, the 50 percent number size distribution threshold may be replaced with a threshold between 1 and 50 percent.

Notwithstanding the above, fullerenes, graphene flakes, and single-walled carbon nanotubes with one

or more external dimensions less than 1 nm should be considered nanomaterials. The definition will be used primarily to identify materials for which special provisions (e.g., for risk assessment or ingredient labeling) might apply. These special provisions are not part of the definition, but part of specific legislation in which the definition will be used. A material that falls under this definition (as the regulatory definition of a nanomaterial adopted by the European Commission) is not automatically hazardous, and a material that does not fall under this definition is not necessarily low risk. If the hazard level of any material you are using is unclear, you should take a precautionary approach to risk management.

There is currently a new Regulation in place for the evaluation of substances in nanoform. The European Commission, in its second regulatory review of nanomaterials [COM(2012) 572 final], concluded that the REACH Regulation provides the best possible framework for managing risks related to nanomaterials, whether they are present as forms of substances or mixtures. However, more specific requirements are needed as nanoforms can have peculiar toxicological profiles and exposure patterns and therefore require specific assessment and appropriate risk management measures. Based on the impact assessment carried out by the Commission [SWD(2018)474], the need to clarify registration requirements for nanomaterials emerged.

Therefore, in 2017, the process of amending the annexes of the REACH Regulation began to clarify the requirements for registration of substances in nanoform and the obligations for downstream users. This process was concluded on December 4, 2018 with the publication of Regulation (EU) 2018/1881, which provided for the amendment of certain annexes of the REACH Regulation.

Regulation (EU) 2018/1881 entered into force on January 1, 2020, and from that date, manufacturers and importers of nanomaterials are required to register these substances according to the new requirements of the Regulation (Article 2).

The information to be provided on the safety of nanomaterials under the new requirements of the regulation allows companies and competent authorities to systematically assess the hazardous properties of nanomaterials, how they are used, and what risks they may pose to human health and the environment. The changes introduced by the new regulation affected Annexes I, III, VI, VII, VIII, IX, X, XI and XII, establishing information requirements for nanoform substances. Based on Regulation (EU) 2018/1881, manufacturers and importers of a substance in nanoform will need to demonstrate that the risks associated with identified uses of the substance are adequately controlled. The regulation specifies the changes made to the REACH Regulation regarding the standard information requirements and the conditions under which experimental tests are required. In particular, the regulation introduces new provisions on nanomaterials in the annexes of the REACH Regulation:

- Annex I: specific parameters for chemical safety assessment are included;
- Annexes III and VI-XI: requirements for registration information are defined, such as composition characteristics of substances, additional or replacement tests specific to substances in

- nanoform or conditions for exemption;
- Annex XII: The obligations of downstream users are defined, e.g. when a use is not covered by the safety data sheet.

Italian national framework: Article 41 of the Italian Constitution (1947) states first of all that “Private economic initiative is free. It cannot take place in contrast with the social use or in such a way as to damage security, freedom, human dignity”.

There is also art. 2087 of the Civil Code that requires: “The entrepreneur is required to adopt in the exercise of the enterprise the measures that, according to the particularity of the work, experience and technique, are necessary to protect the physical integrity and moral personality of the workers.”

It is also found in the Law n. 833/1978 “Reform Law of the National Health Service of Italy” the achievement and maintenance over time of adequate levels of protection and the provision of preventive and curative services. With this law, Italy has chosen to link the activities related to health and safety - including, in general, the inspection competences in this field (attributed to the Local Health Authorities and only in relation to sectors with a particular risk of accidents, to the peripheral structures of the Ministry of Labour and Social Policies) - to the health services of prevention, diagnosis and treatment guaranteed to all citizens. The legislative framework of reference is Council Directive 89/391/EEC of 12 June 1989 on the application of measures to encourage improvements in the safety and health of workers in the workplace, now transposed in Italy by Legislative Decree 81/08, the so-called “Consolidated Law on Health and Safety at Work” (consisting of 306 articles - divided into 13 titles - and 51 technical annexes), which clearly and comprehensively sets out the protective measures to be adopted in every workplace. This directive is fully applicable to nanomaterials. Employers must therefore carry out a risk assessment and, if a risk is identified, take the necessary measures to eliminate it, and/or prevent accidents and illnesses of an occupational nature, must take all measures that experience has shown to be necessary, feasible according to the state of the art and appropriate to the operating conditions [see art. 18, paragraph 1, lett. q) of Legislative Decree 81/08 and subsequent amendments and additions, which imposes on the employer and manager to “*take appropriate measures to avoid that the technical measures adopted may cause risks to the health of the population or deteriorate the external environment by periodically verifying the continued absence of risk*”]. Obligation that automatically is to be extended legitimately also to the use of nanomaterials.

Finally, the activities of the INAIL NanOSH Italia network, which have been underway for several years in compliance with the existing competences (for example, the national authority for REACH at the Ministry of Health) and with the existing activities at European level, are aimed at an in-depth study of health and safety issues deriving from the use of nanomaterials, which may lead to significant results in the near future. While on the subject of environmental protection there is Legislative Decree no. 152 of April 3, 2006 (environmental protection law consisting of 89 articles and 9 annexes that regulate the management and disposal of waste), where the production of waste must be pre-

vented as far as possible and the waste must be disposed of in an environmentally friendly manner and, as far as possible and reasonable, within the national territory. In this context, the recycling of waste is to be placed at the forefront. These principles also apply to wastes with nano-specific properties, but there are greater restrictions if such wastes are to be classified as hazardous waste. In view of the above, and in view of the apparent absence of specific reference legislation for risks from nanomaterials, the Organisation for Economic Co-operation and Development (OECD) has determined that in general the Guidelines to be used for risk assessment of chemicals can also be used for nanomaterials, but that some of them need to be adapted or replaced to take into account the specific properties of nanomaterials.

Exposure limits for nanoparticles

Currently, there are no European or internationally recognized exposure limit values for engineered nanoparticles (PNI). While the Association of American Industrial Hygienists (ACGIH) currently considers data insufficient to determine specific limit values for PNI, the US National Institute for Occupational Safety and Health (NIOSH), in late 2005, proposed an exposure limit value for fine Titanium Dioxide (TiO₂) particles of 1.5 mg/m³ (the weighted average concentration over 40 hours of work per week) and ultrafine particles (< 100 nm) of 0.1 mg/m³. Toxicological knowledge is still insufficient, apart from special cases related to particles produced by diesel engine combustion and carbon black, to establish occupational exposure limit values. The wide heterogeneity of engineered nano-materials (NMI) reduces the number of specific occupational exposure limits (OELs) that can likely be developed in the near future.

But occupational exposure limits for engineered nanomaterials can be developed more rapidly using dose-response data obtained from animal studies for specific nanoparticles across categories of nanomaterials with similar properties and modes of action. When adequate dose-response data from animal and human studies are available, application of risk-assessment methods may provide an estimate of the risks from exposure to nanomaterials to worker health and, in conjunction with workplace exposure data, provide the basis for determining specific exposure limits. Thus, in the absence of adequate quantitative data, the qualitative approach to risk assessment, exposure control, and the application of best practices is an appropriate and prudent measure to reduce the risks to workers from exposure to engineered nanomaterials.

Recommendations on the protection of workers from the potential risks of manufactured nanospecific materials ^[26].

Guiding Principles: In general, for conducting an appropriate risk assessment from exposure to nanomaterials, in the absence of a specific legislative reference regulating this area of risk, it is necessary to use a precautionary approach as one of its principles of good practice. This means that exposure should be reduced, despite uncertainty about adverse health effects, when there are reasonable indications to do so (*focus exposure control on preventing inhalation exposure with the goal of reducing it as much as possible*). In addition another important guiding principle,

the hierarchy of controls must be considered, it means that when there is a choice between control measures, those measures that are closer to the root of the problem should always be preferred to those that put more burden on workers, such as the use of personal protective equipment (PPE) [89/656/EEC - Title II D. 81/08 - Chapter I] (*According to this principle, engineering controls should be used when there is a high level of inhalation exposure or when there is no or very little toxicological information available. In the absence of appropriate scientific evidence, PPE, particularly respiratory protection, should be used as part of an airway protection program regardless that includes fit-testing*).

The decision to use PPE should be based on professional judgment, risk assessment, and risk management practices. In Italy, the use of personal protective equipment is regulated by Legislative Decree No. 81 of April 9, 2008 (Title III, Chapter II). In particular, Standard UNI 10720 (*Guide to the selection and use of respiratory protective equipment*) establishes guidelines on the criteria for the selection, use and maintenance of respiratory protective equipment. The ISO (International Organization for Standardization) has published the standard ISO/TR 12885:2008 Nanotechnologies - Health and safety practices in occupational settings relevant to nanotechnologies, now under revision, where measures and control criteria are suggested in working environments characterized by exposure to engineered nanoparticles.

It is also suggested to prevent skin exposure through occupational hygiene measures such as surface cleaning and the use of appropriate gloves.

The risk assessment of exposure to specific nano substances is good practice to perform it with the same approach used for chemical substances through the implementation of an evaluative and preventive process distinct in phases and precisely:

- hazard identification and characterization;
- exposure estimation;
- identification of the consequent risk.

For a correct hazard identification of nanomaterials, a fundamental step is to know their chemical properties (chemical composition, surface charge and reactivity, solubility, stability/dissolution, hydrophobicity/hydrophilicity) and physical properties (size/dimensional distribution, crystal structure, surface area, aggregation/agglomeration). These properties are crucial for the assessment of the biological activity of nanomaterials and, consequently, for the evaluation of their potential toxicity to human health and the environment. Each of the steps described above will in the future make use of well defined (standardized) procedures in order to prepare adequate prevention and protection measures for human health and the environment. These procedures will refer in a short-term scenario to guidelines to be developed by the Organisation for Economic Co-operation and Development (OECD). This process in a general sense at the moment at Community level will be implemented in cooperation between all Member States and industry and will see the involvement of the international scientific community. To this end, the European Community has recently decided to finance the development and/or revision of some OECD Guidelines and in recent years, within several European and national projects (e.g., NANO-

REG, NanoReg 2, RINNOVARENANO), methods have been studied and developed that take into account the specific properties of nanomaterials for a proper assessment of potential health and environmental risks related to their use.

Managing Risks Associated with Nanomaterials in the Workplace

In the workplace, employers are obliged to ensure the safety and health of workers in all work-related aspects by regularly carrying out risk assessments, as specified in Framework Directive 89/391/EEC [27], including risks that may arise from nanomaterials. Furthermore, Directive 98/24/EEC (Title IX of Legislative Decree. 81/08 - Chapter I) on chemical agents in the workplace [28] imposes stricter provisions on the management of risks arising from hazardous substances to which one is exposed at work, particularly with regard to a hierarchy of prevention measures in which priority is given to elimination or substitution measures, they also apply to nanomaterials as they fall under the definition of "substances" contained in the REACH Regulation [30] and as such must also comply with the CLP Regulation (on classification, labelling and packaging of substances and mixtures) [31]. If a nanomaterial, or macro-scale material with the same composition, is carcinogenic or mutagenic, it is necessary to also comply with the obligations arising from Directive 2004/37/EEC (Title IX of Legislative Decree 81/08 - Chapter II) on carcinogens and mutagens in the workplace [29]. In any case, it is necessary to refer to national legislation, which may provide for stricter provisions, and in any case, even for nanomaterials it is possible to follow an approach to risk assessment that incorporates that already in use for substances that expose workers to chemical risk. Despite ongoing research, the field of nanotechnology is evolving faster than the acquisition of knowledge about the health and safety aspects of nanomaterials. Several knowledge gaps remain to be filled regarding the health and safety implications of nanomaterials for workers and risk assessment methods.

With regard to workers, possible exposure steps to nanomaterial hazards include:

- **during manufacturing processes**, as nanoparticles may be released into the air that may pose a potential health risk to workers, especially if protective equipment is not used;
- **during equipment maintenance**;
- **during cleaning and waste disposal**.

Operations that may increase the risk of exposure include the following:

- working with nanomaterials in a liquid without adequate protection (e.g., gloves);
- working with nanomaterials in a liquid during pouring or mixing operations or where a high degree of agitation is required;
- generation of nanomaterials in the gas phase in open systems;
- handling (e.g., weighing, mixing, spraying) with powders of nanostructured materials;
- maintenance of equipment and processes used to produce or fabricate nanomaterials;
- cleaning or waste disposal;
- cleaning of dust collection systems used to capture nanoparticles;
- sanding, drilling of nanomaterials, or other mechanical processing that may lead to

aerosolization of nanoparticles.

For risk management of nanomaterials in general work environments it is recommended as follows:

- identify the hazard classes assigned to nanomaterials according to the Globally Harmonized System (GHS) of Classification and Labeling of Chemicals indicated in the MSDSs and group them into nanomaterials that are with specific toxicity, nanomaterials that are fibers, and nanomaterials that are biopersistent granular particles;
- educate and train workers on the specific health and safety issues of nanotechnology materials;
- involve workers in all phases of risk assessment and control.

CONCLUSIONS

Risk assessment is “a complex and iterative operation that necessarily requires, for each environment or workplace considered, the identification of the sources of risk of exposure to nanomaterials present in the work cycle, the identification of the consequent potential risks of exposure to nanomaterials in relation to the performance of work, and the estimation of the magnitude of the risks of exposure to nanomaterials associated with the situations of preventive interest identified”.

In general, exposure to toxic substances should be prevented by avoiding, as far as reasonably possible, the use of hazardous substances. If, however, this is not possible, exposure should be controlled through the application of appropriate prevention and protection measures consistent with the order of priority shown in Figure 1, which describes the hierarchy of control of exposure to hazardous substances.

According to the precautionary principle, it is necessary to “minimize exposure, and this is possible both by reducing the duration of exposure and/or the number of people exposed, and by reducing the concentration of the nanomaterials themselves, through the implementation of appropriate prevention and protection measures.”

These measures should follow the “scale of priorities from the elimination of nanomaterials, to their replacement with non-hazardous materials, to isolation/confinement or segregation of the source of exposure, to technical measures to capture, limit and expel nanomaterials, to changes in work organization and the use of PPE as a supplement to technical measures.”

Here, then, is a list of prevention and protection measures available to date:

- **substitution:** replace pulviscular preparations with others that contain nanoparticles in a bound matrix and thus prevent their diffusion (dispersions, pastes, granulates, compounds, etc.); replace

spray applications with others with little aerosol formation (brush application, immersion);

- **source segregation:** use closed-loop equipment; automation - robots;
- **environmental protection interventions:** fume hoods; ventilation of work environments; localized suction; alarm systems; correct use of production systems; filtration of exhaust air (HEPA filter in case of air recirculation in the work room); eventual separation of the work room and adaptation of the ventilation system (slight depression)”.

These then the possible measures of safety and organization of work:

- minimize the duration of exposure;
- minimize the number of people exposed;
- limit access to the work environment;
- no smoking;
- operations away from flames, heat sources and sparks;
- training/information on hazards and protective measures;
- labeling;
- Material Safety Data Sheets;
- safety signs;
- safety services (emergency showers, eye wash, first aid intervention notes for the substances used).

Finally, the measures in relation to personal protection and hygiene interventions: “gloves; masks and respirators; correct use of laboratory equipment and instruments; propipettes; automatic pipetting machines; disposable materials; availability of containers for temporary storage of waste”.

The White Paper also provides some examples of best practices, such as an example of a proper approach to risk estimation, based on the “control banding” approach.

The example, “valid for both laboratory research and industrial production activities, once the preparatory steps of identifying risk sources and risks of exposure to nanomaterials have been conducted, is characterized by the following ten parameters:

1. numerosity of exposed workers;
2. frequency of exposure;
3. frequency of direct handling;
4. size of nanomaterials;
5. nanomaterial behavior (e.g., dispersion or agglomeration);
6. effectiveness of PPE used;
7. work organization and procedures;
8. toxicological characteristics of substances;
9. Fire and explosion hazards;
10. Suitability of work spaces and equipment”.

Therefore, in practice, the right approach to risk assessment of nanomaterials in the workplace is to follow the method already in use for toxic/harmful substanc-

Eliminate
Replace
Contain
Use control systems
Apply control procedures
Use personal protective equipment

Tab. 1- Hierarchy of control of exposure to hazardous substances

es. That is, to take preliminary information from the Safety Data Sheets (SDS), as an important information tool for the prevention of risks from hazardous substances in the workplace. However, the information on the presence of nanomaterials and their characteristics, risks to workers, and prevention measures contained in these sheets is generally scarce or non-existent [32-33]. Organizations are therefore encouraged to contact suppliers directly to request additional information. Amendments to Annex II of REACH [34], which provides the legal framework for safety data sheets, and European Chemicals Agency (ECHA) guidance on the compilation of safety data sheets [35], which provide additional advice on claims about the characteristics of nanomaterials, are expected to improve the quality of information contained in SDSs. The Organization for Economic Cooperation and Development (OECD) guidelines [36] help identify possible sources of airborne nanomaterial emissions from various types of processes and work practices.

Preliminary guidance suggests that, when assessing exposures, particular attention should be paid to the following workplace activities and practices, which should therefore be prioritized for risk management:

- activities in which nanomaterials with the following properties are used:
- nanomaterials with known specific toxic effects (e.g., arsenic and cadmium and related compounds or crystalline silica), or for which the same material on a macro-scale is known to have specific toxic effects;
- biopersistent, non-fibrous (such as titanium dioxide and aluminum oxide) and fibrous (such as carbon nanotubes) nanomaterials;
- soluble materials for which health hazards have been identified or for which no health hazard is demonstrated.
- any situation in which nanomaterials may become airborne, such as loading and unloading nanomaterials or chemicals containing them from crushing or mixing equipment, placing chemicals in containers, sampling manufactured chemicals, and opening systems for product recovery;
- the cleaning and maintenance of facilities (including closed manufacturing systems) and hazard reduction devices, such as filters in local exhaust ventilation systems;
- the research and development of substances containing nanomaterials, such as composite materials;

- the handling of powders and spray mixtures containing nanomaterials; powders may present a higher risk of explosion, spontaneous combustion, and electrostatic charge and thus create safety concerns. In addition, dust clouds may form resulting in inhalation exposure;
- mechanical or thermal treatment of articles containing nanomaterials that could be emitted as a result of processes such as laser treatment, grinding, or cutting;
- waste treatment operations that include articles containing nanomaterials.

In principle, all activities involving nanomaterials performed outside of a hermetically sealed facility may be considered critical because they present an exposure risk to workers. However, exposures are also possible with hermetically sealed systems, e.g., in case of leaks or during cleaning and maintenance activities, and this should be considered in the risk assessment and application of preventive measures.

Toxicological evidence indicates that exposure to some nanoparticles may cause adverse health effects in laboratory animals, but there are no specific studies on exposed workers. Current knowledge about possible health risks from occupational exposure to engineered nanoparticles is scarce. If, following the application of nanomaterial exposure control measures, levels remain elevated, the use of protective respirators, clothing, and gloves can reduce exposure. Certified respirators have been shown to provide good levels of protection from exposure to nanomaterials, making them an important tool for a risk management strategy in those cases where source emission control is not feasible. There is a need to develop in vivo or workplace laboratory studies to measure the total internal leakage (PTI) of respirators used as protection for exposure to nanoparticles.

In this regard, however, there are guides and tools available to facilitate the management of risks from nanomaterials in the workplace and at the time of writing the European Commission has commissioned Risk & Policy Analysts Ltd [37], together with IVAM UVA BV [38], to prepare practical guidance aimed at ensuring safe conditions in workplaces where synthetic nanomaterials and nanotechnology are used, as part of a larger study conducted with the aim of ascertaining the possible impact of nanomaterials and nanotechnology in the workplace and assessing the scope and requirements for possible changes in EU occupational health and safety legislation (more information [39]).

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- [39] <http://ec.europa.eu/social/main.jsp?catId=148&langId=en&callId=311&furtherCalls=yes>; <http://osha.europa.eu>;