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NANOTECHNOLOGY: REFLECTIONS ON HEALTH BENEFITS AND RISKS

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Abstract. There is a constant increase in the demand for engineers who can transform nanotechnology from a scientific result into a commercial solution. However, new technologies often caused conflicts between those who want to exploit them as soon as possible and those who are waiting to receive absolute proof of safety. Certain types of nanoparticles are well studied and recommended for use in medicine, biology, chemistry, cosmetology, etc. Some nanoparticles are proven to be extremely toxic, with drastically different properties from the same volume compounds. The risks associated with using nanotechnologies and products containing nanoparticles cannot be minimized in the absence of regulations, which would allow adequate control to protect the environment and the population's health. Companies are also extremely careful in investing in this field as long as there is no transparent regulation, as the ultimate goal is to protect the surrounding environment and society. In this paper, we present an overview of the benefits of nanotechnology in areas that affect human health, as well as the risks that may arise from the early use or ill-will of nanotechnologies.

Keywords: *nanotechnology, applications, biomedical engineering, impact, risk, regulation.*

Rezumat. Există o creștere constantă a cererii pentru ingineri care pot transforma nanotehnologiile din rezultate științifice în soluții comerciale. Dar tehnologiile noi totdeauna au generat conflicte între cei care doresc să le exploateze cât mai repede posibil și cei ce sunt în expectativă să primească dovezi absolute de siguranța lor. Anumite tipuri de nanoparticule sunt bine studiate și utilizate sau recomandate pentru utilizare în medicină, biologie, chimie, cosmetologie. Multe nanoparticule se dovedesc a fi extrem de toxice, cu proprietăți radical deosebite de aceiași compuși în starea de volum mai mare. Riscurile legate de utilizarea nanotehnologiilor si a produselor care conțin nanoparticule nu pot fi minimizate în lipsa unor reglementări ce ar permite un control pentru a proteja sănătatea populației și mediului. Companiile sunt extrem de precaute în a investi în domeniul nanotehnologiilor atât timp cât nu există reglementări transparente deoarece este vorba de protecția oamenilor și mediului care-l înconjoară. Prezenta lucrare este o trecere succintă în revistă a beneficiilor nanotehnologiei în domeniile ce influențează sănătatea omului, precum și a riscurilor ce pot apărea din utilizarea precoce sau din rea-voință a nanotehnologiilor.

Cuvinte cheie: *nanotehnologie, aplicații, inginerie biomedicală, impact, risc, reglementare.*

1. Introduction

Nanoscience is the convergence of physics, materials science, and biology, which deals with handling materials on an atomic and molecular scale. Nanotechnology and nanoengineering represent the ability and process to measure, manipulate, assemble, control, and manufacture nanoscale matter. This science is relatively new and consists of known processes, as well as new unknown processes. Therefore, it is not surprising that there is no clear public perception of this topic: on the one hand there is the fear of the unknown as a potential source of danger, and on the other hand is the potential for good. The ability to deal with the matter at the atomic or molecular level allows for a deeper understanding of physical phenomena and control over the functionality of new devices.

In the paper [1] there is a mention, that time ago M.C. Roco predicted the following four stages in the development of nanotechnology products:

- passive nanostructures, passive properties of nanomaterials, including nanotubes and nanolayers, which provide more opportunities to renew products in everyday life;
- active nanostructures, which can change their state during use in a predictable way;
- nanosystems - nanorobotics, nanobiotechnologies, information nanotechnologies;
- molecular nanosystems are the most advanced by the intelligent design of devices at the molecular, atomic, and quantum effects level.

Nanotechnology, nanoengineering, and their microscopic universe are the globalization product with large investments for research and development around the world, already representing a huge industry. The global nanotechnology market was estimated at $1.76 billion in 2020, increasing to $100 billion in 2030. Nanomaterials offer a wide range of functionalities due to their physical and chemical properties manifested in their new state. These offer new methods in diagnosis, therapy, and in healthcare monitoring, with opportunities to solve unanswered medical problems. The applications of nanotechnology in energy, agricultural, food, consumer products, transport, logistics, and environmental sectors are also growing rapidly. The fastest growing domains are expected to be health, nanoelectronics, energy, aerospace, and defense. The USA, Brazil and Germany are expected to lead the nanotechnology industry in 2024, with a significant presence in the top countries such as Japan, China, South Korea and India.

Regarding the rapid development of nanotechnologies, we note that in 2019, over 40% of scientific publications on nanoscience came from China, followed by the USA and India. When it comes to patents, in 2019 the US had the most active market in the world for nanotechnology innovations (8900 patents filed), followed by the EU, China and South Korea.

From the dynamics of the infiltration of nanotechnologies in practically all the fields that influence our life, it is paramount that the regulations are aligned with the evolutions. The safety assessment of nanomaterials is an important process and we expect this to be safe by design. For these reasons, researchers, innovative engineers and regulators are best placed in developing guidelines for toxicological assessments and analytical methods to implement new definitions and various regulatory requirements.

2. Diversity of nanotechnology application in the vital area

To understand the impact of nanotechnology on human health, we analyze a predictable roadmap for nanotechnology (Figure 1). We note the usefulness of both phases, both the initial manufacturing process (obtaining new material, measurements and characterizations, attempts at technology transfer in various fields) and the final process of developing the architecture of nanodevices and possible applications (operating theories, modeling, formation of functional biochemical systems, new approaches).

The prospects for nanoscience, nanoengineering and nanotechnology are promising to the society and at the same time these achievements can be recognized as potential threats to humans in the lack of knowledge.

There are virtually no areas of activity that are not influenced by advances in nanotechnology and nanoengineering.

And all of them have an impact on human health, including those in the telecommunications, chemical, textile, automotive, etc. industries [2-8]. In our analysis we will refer exclusively to those areas (Figure 2), which we consider having a major impact on human health.

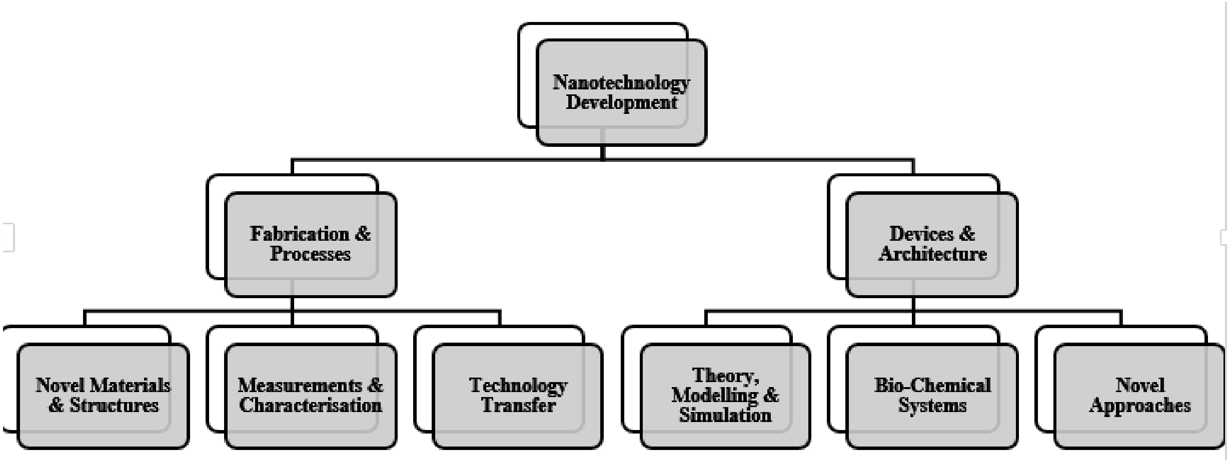

Figure 1. Predictable phases of nanotechnology development.

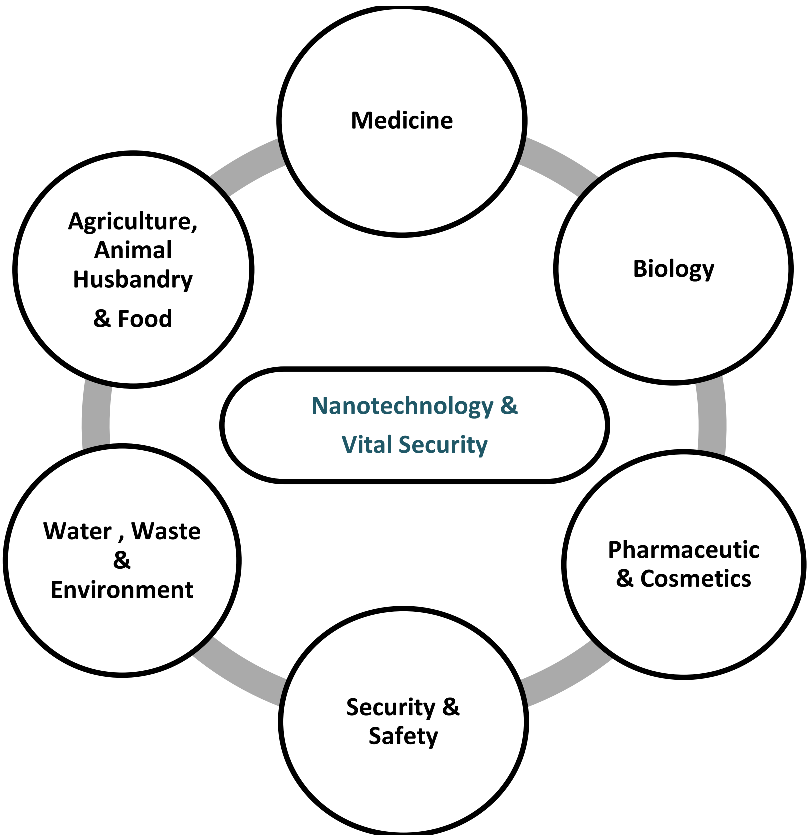

Figure 2. Nanotechnologies and vital security.

3. Nanotechnology and the environment

Nanoparticles (NPs) have been recommended as extremely useful for the protection and cleaning of the environment [8, 9]. There are applications of selective membranes that can filter contaminants or even salt from water, or nanostructured traps to remove pollutants from industrial effluents. Monitoring and characterization of the environment are performed using nanosensors, and nanostructured intelligent sensory systems (Figure 3). Nanomaterials contribute to significant reductions in the consumption of materials and energy, while the sources of pollution are maintained, and the need for industry maintenance determines increased opportunities for recycling [9]. Therefore, there is a potential to reduce environmental pollutants.

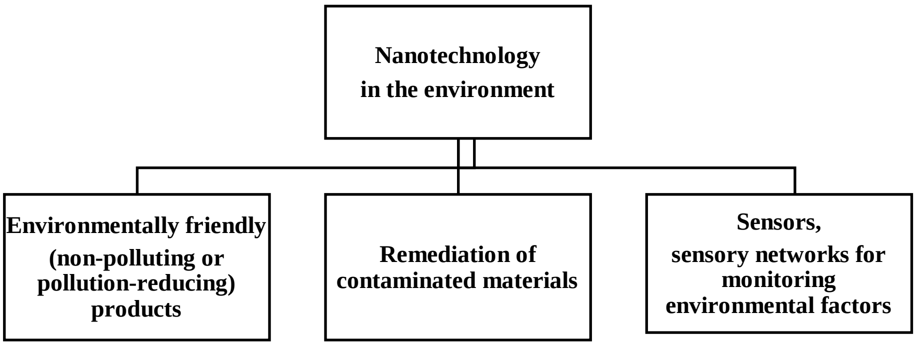

Figure 3. Nanotechnology in the environment.

However, we also identify the negative side due to reasons such as insufficient regulation, drastic growth of the nanotechnology industry, and the use of NPs in various fields that reside through the uncontrolled release of NPs into the environment. For these reasons, the assessment of the risk of NPs in the environment must be performed in terms of their mobility, reactivity, ecotoxicity and persistence. In the absence of rigorous control, nanoengineering applications increase the concentration of nanopollutants in groundwater and soil, which are the most common routes of exposure for environmental risk assessment.

Due to the high ratio of surface to mass NP, the distribution of the contaminant in the solid/water environment will be dictated by the absorption at the natural NP surface, the aggregation of the NP, or the co-precipitation at NP formation. The interaction of contaminants with NP is complex depending on the physicochemical characteristics such as size, chemical composition, morphology, porosity, state of aggregation/disaggregation, surface reactivity, surface loads, and surface passivation. In addition, environmental characteristics such as pH, temperature and light intensity affect the toxicities of some nanostructures. The same nanomaterial, but with different geometry: diameter, length, crystal structure and different surface modification, will have different toxicities.

The environmental pollution with nanoproducts represents a major problem with unpredictable consequences. Although many nanoproducts are considered harmless (e.g. nanoelectronics), their tiny size being scattered volens-nolens in the environment can cause serious consequences, which we do not know yet. Let's take a simple example, a drug in the form of nanopowder or nanodrage, useful for a person, but out of hand, or thrown away at the expiration of the easy time will pollute the atmosphere and cause unpredictable consequences for a healthy person. As a new source of pollution, nanotechnologies need to be given additional attention through appropriate regulations, following various research on ecological toxicity.

4. Nanotechnology, agriculture, and animal husbandry

The focus on sustainable agriculture argues for the implementation of the ecosystem method, in which abiotic-biotic living beings are in harmony with coordinated stability of food chains and their energy balances. Nanotechnology is one of the most effective solutions in achieving this goal by using nano- fertilizers, nanopesticides, nanoherbicides, etc. [13]. Water treated with nanotechnologies used for seed softening, irrigation, dilution of agrochemicals and fertilizer treatment positively influences the rate and condition of seed germination, seedling quality and crop yield and quality.

Plant genetic engineering leads to personalized benefits, such as increased crop yields currently achieved through the scientific application of NP chemicals. Nanotechnology is widely used in various ways (Figure 4) to improve agricultural production. Nanopesticides and nano-fertilizers have been shown to have little, or no toxicity due to much smaller and strictly dosed calculated amounts, while improving the effects [13, 19]. The control efficiency of biopesticides on a nanoscale is one to three times higher than that of regular pesticides when the dose was the same, reducing the cost by half.

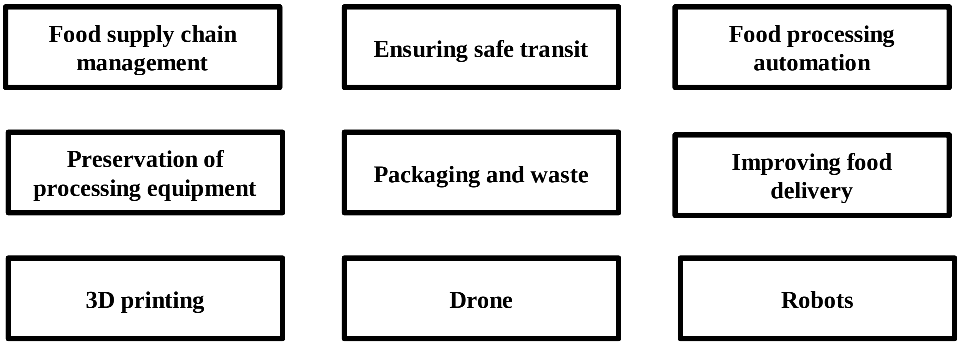

Figure 4. Nanotechnology in the food industry.

Nanofungicides and nanoinsecticides have considerable potential that was not yet been sufficiently explored in agriculture and nanotechnology-based delivery systems. Nanotechnologies have the increased ability to inhibit or kill various types of microbes and are useful in the environmental disinfecting. Also, NPs are useful for monitoring microelements in soil and plants, detecting soil toxins, detecting, and diagnosing crop diseases. The sensitivity of nanodevices can be used for the rapid, economical, and efficient detection of phytopathogens, thus reducing the chance of large-scale destruction of crops.

Nanotechnology is used in animal husbandry to improve the diagnosis, treatment, delivery of medicines, food preservation, reproduction, monitoring, and improvement of animal health, as well as for higher quality production [10, 14]. Nanobiocides are recommended to be effective in disinfection, disinsection, and rodent control procedures that contribute to sustainable and ecological agriculture.

5. Nanotechnologies in civil security

There is practically no civilian or military field in which nanotechnologies don't have applications. As research is the mainstay of identifying new applications of nanotechnology, it has become a key research priority since the EU's Sixth Framework Program for RTD (FP6, 2002-2006) containing projects targeting security applications. The applications of nanotechnology for civil security in FP6 covered four areas: detection, protection, identification, and assessment of societal consequences.

Direct or indirect detection (including imaging, sensory/sensory networks) of radiation, pathogens, and chemicals refers to the detection of viruses, bacteria, DNA, RNA, proteins, and nucleotides to prevent acts of bioterrorism, chemicals, industrial harmful gases, ionizing radiation, but also to other harmful electromagnetic waves, etc. [15-19, 45].

Detection devices for civil security were progressively influenced by the advances in nanotechnologies and we classify them arbitrarily into three categories:

- X-ray imaging, IR detection, and the emerging field of imaging at THz wavelengths;
- direct or indirect detection sensors of biological and chemical agents. We assign nanotubes and nanowires to direct detection sensors and electrical and electromechanical, colorimetric, quantum dots to sensors with indirect detection. Biological barcodes, consoles for the detection of biomolecules, and microorganisms we also assign to this category;
- polyfunctional smart miniature sensor networks (smart dust).

Referring to *protection devices* we note improved nanomaterials with new physical properties and functionalities, including higher strength and durability, built-in sensory capabilities and active materials.

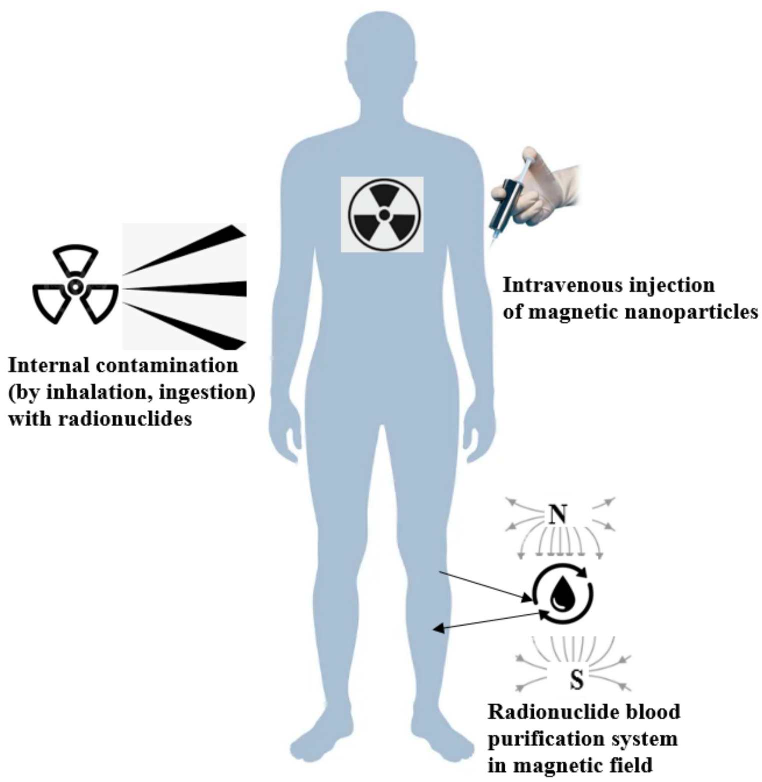

Figure 5. Example of blood purification of radionuclides with intelligent NP (adaptation from [45]).

In terms of civil security applications, nanodevice protection devices mainly benefit from the following functional materials:

- the advanced physical-mechanical, thermal, chemical resistance and low specific weight for flexible anti-ballistic textiles; reactive nanoparticle armor; shock absorber nanotubes; nanofibers, clothing and nano-coatings for biological products or chemical decontamination; switchable fabrics or materials to improve thermal control and fire protection etc.;

- smart, containing integrated nanosensors, reactive elements, intelligent materials for diffusion control and active transport of mass or electric charge control; smart NPs that recognize, capture, incorporate, eliminate, or destroy certain toxins or radionuclides. For example, at intravenous injection, biodegradable nanospheres circulate through the bloodstream, where surface proteins bind to targeted radionuclides. Nanospheres with identified and captured toxins are removed from the bloodstream through a small inserted into an artery shunt. The magnetic field applied to the shunt (Figure 5) immobilizes the Fe-based particles with radionuclides allowing the direction of the cleaned blood in the blood flow [45];
- shielding or absorption of electromagnetic interference in electromagnetic radiation fields, depending on wavelengths.

Nanotechnology is effective in the national security field by introducing smart weapons and nanosensors. But this also represents a major disadvantage of nanotechnology. Increasing the functionality or capability of weapons, such as miniaturization, can also constitute a threat. If this technology falls into the hands of terrorists or malicious actors, then we should be prepared for it as well, or we need adequate countermeasures and products that would protect people and the environment.

6. Nanotechnology and biomedicine

Interestingly, the colloidal solutions of iron sucrose NP were already in clinical use in 1949, 10 years before Feynman's (1960) call for the world of nano state. We can now confirm the realization of the idea of another scientist - Paul Ehrlich, who in his work on the concept of targeted therapy, stated the need for a "Zauberkugel" (magic bullet) - so a drug that would be specific and intended exclusively for the target without affecting normal host cells.

If we refer to the diversity of nano states of inorganic materials currently used in medicine (Figure 6), they all show some therapeutic, diagnostic, or delivery properties and markers [11-12, 15-20]. For example, antibody-functionalized nanostructured surfaces are used to detect specific proteins or cells resulting from the increased interaction surface and adhesion that give increased sensitivity in detection and NPs serve as markers for detecting biomolecules, pathogens, and MRI contrast agents.

Medical diagnosis with nanopores requires small volumes of evidence for counting and distinguishing a complex mixture of a variety of biological molecules by accessible electronic measurements. The simplicity, speed, and versatility of nanopore analyzes are promising for molecular diagnosis.

Quantum dots are another group of nano states, with a unique potential for clinical use, especially in diagnosis. The ability of quantum fluorescence points in different spectral regions would be useful for marking and imaging cells, cell structures, or biological pathogens, as well as observing processes in dynamics, which take place in cells, tissues, and the body as a whole.

Dozens of metal oxides in the form of NP are currently used in therapy (Figure 7), which shows, depending on the oxide, neuroprotective properties, antioxidants, antibacterial, antimicrobial, anticancer, drug carriers, etc. The most significant advances in nanotechnology in biomedicine are observed in cancer therapy, offering innovative solutions to overcome the limitations of chemotherapy and radiotherapy, through the targeted delivery of drugs, proteins, and polynucleotides. NPs based on micelles, liposomes, and polymers with "capture molecules" attached [11], along with single-walled nanotubes, are used as carriers of drugs for target delivery.

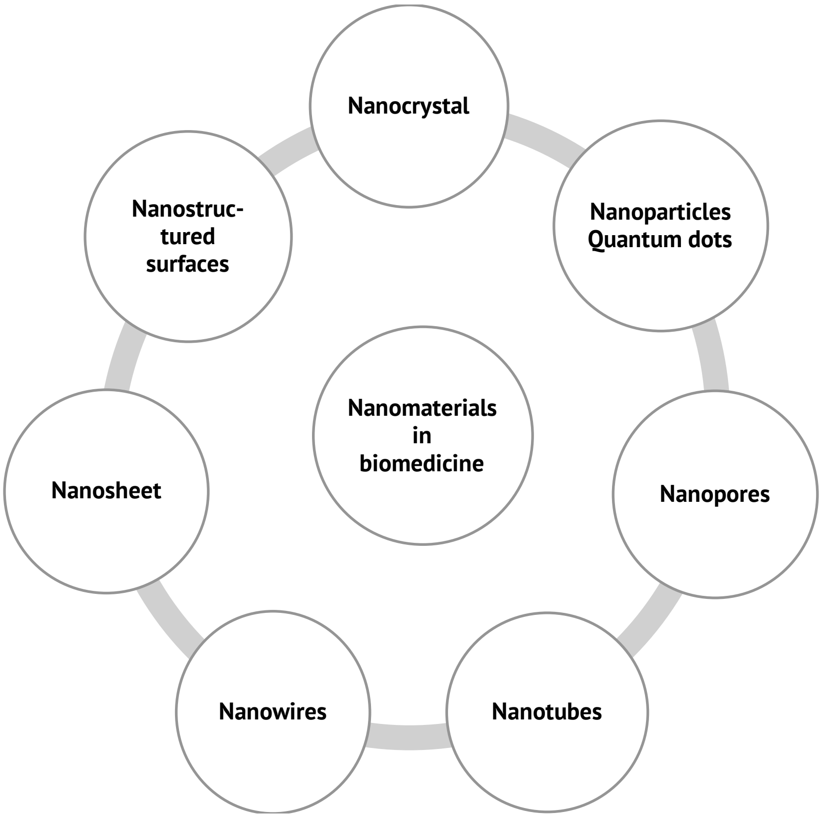

Figure 6. The diversity of nanostates used in biomedicine.

The unique form of NPs allows them to enter selectively through biological barriers by delivering drugs to the target in the minimum quantities necessary to obtain and maintain the therapeutic effect, thus reducing the possible toxicity of drug preparations. This is especially important in the case of very toxic and short-lived chemo- and radiotherapeutic agents [21-25].

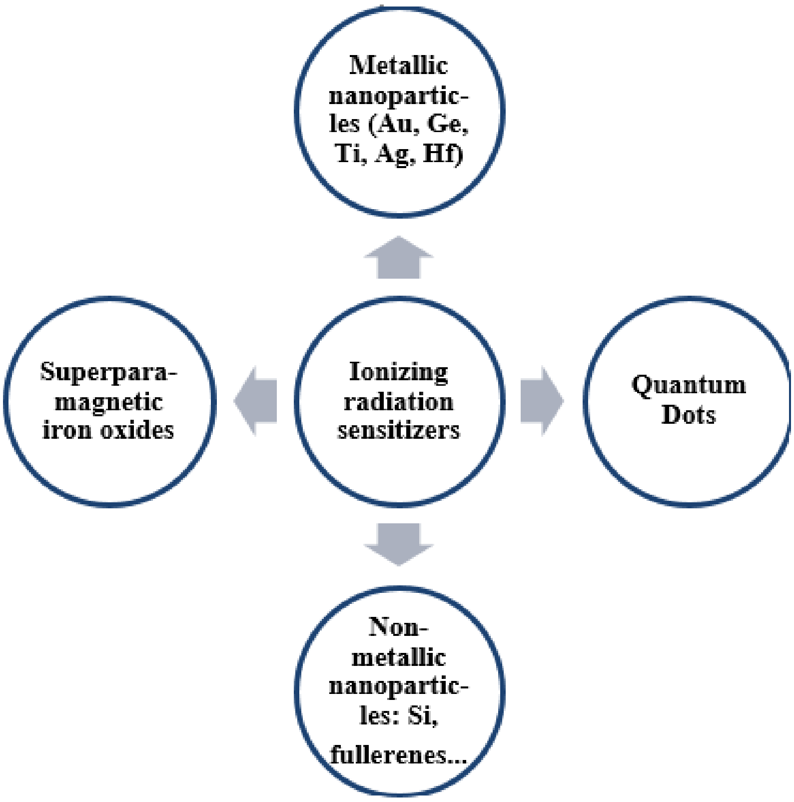

Figure 7. Nanoparticles types as sensitizers for medical purposes.

Another broad area of use of NPs in biomedicine is the design of biosensors for monitoring physiological parameters, as well as the detection of specific DNA fragments and regions or the identification of bacterial cells, etc. Thus, nanowires and Graphene oxide (GO-nS) are recommended to identify cellular interactions *in vivo* [26].

The potential of nanopores in the detection of direct sequencing of individual DNA molecules can provide useful information about an individual's genetic structure and determine the increased risk for certain diseases such as cancer. This nanopore-based detection sensor has potential for application in agriculture, security, defense, and evolving biology, where genomic information is useful.

Carbon nanotubes are being intensively investigated from the perspective of applications in therapy, especially in the treatment of cancer, but also for the development of new diagnostic agents and nanosensors. Carbon nanotubes can also be used for the targeted administration of drugs for the generation of new bone tissue.

The use of drugs in the form of nanocrystals facilitates absorption by the body. Nanocrystals are also used as markers of areas of interest in biomedicine for further studies, such as by immunofluorescence microscopy.

A report on the beneficial effects of NPs in thermoradio (immune) therapy, targeted delivery of pharmaceuticals, contrast agents, local amplification of the exposure dose [27-29], and the summary spectrum of the exposed benefits are represented in Figures 7 & 8.

Furthermore, NPs containing Ag in addition to antimicrobial and cytostatic effects useful in medicine serve as preservatives in the cosmetics industry.

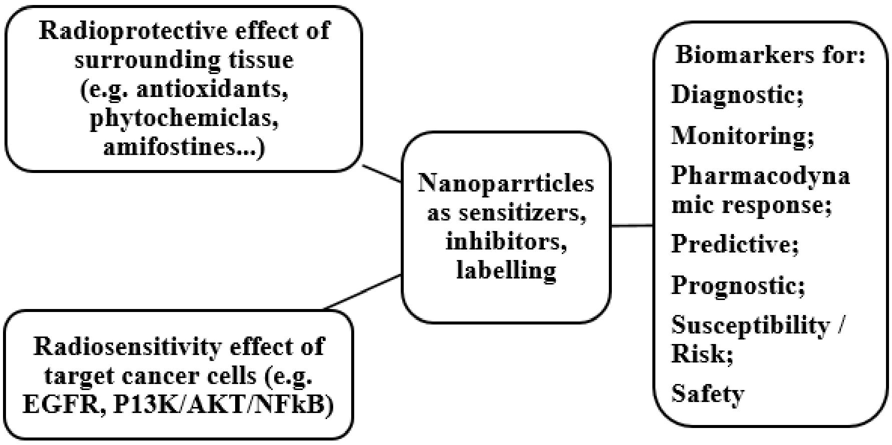

Figure 8. Nanoparticles as sensitizers, radioprotectors, or labelling of ionizing radiation for the treatment, diagnosis, and monitoring of cancer and other diseases (adaptation from [28]).

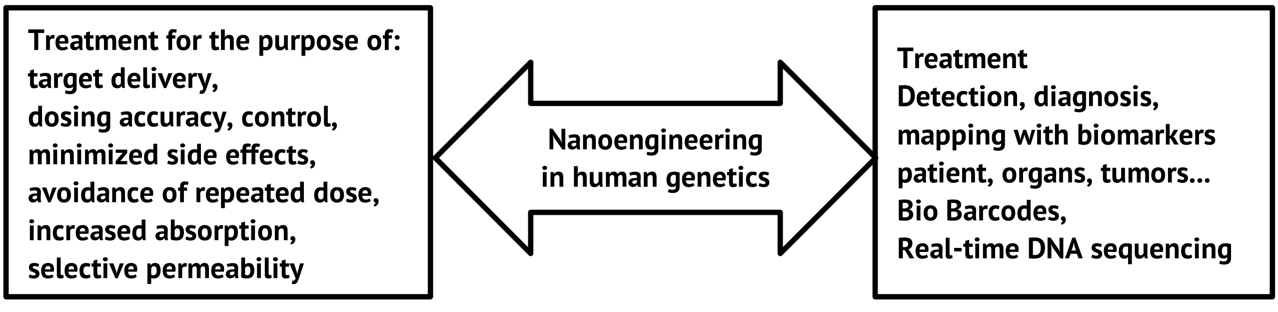

Figure 9. The usefulness of nanotechnologies in human genetics.

When we talk about the interrelationship between nanotechnology and biomedicine, let's not forget about the achievements [30-33] in the field of human genetic engineering (Figure 9). Without going into details, Figure 8 shows the benefits of nanotechnologies in treatment and diagnosis.

7. The nanotechnologies specifics risk

Various applications of nanotechnology expose people to potential dangers, such as potential toxicity. Uncontrolled exposure to NPs occurs through various pathways in the body: inhalation, ingestion, skin penetration, and intravenous injection [34, 35]. NPs reaching the extracellular fluid are conjugated with biomolecules present in the environment, which allows them to be internalized in cells by penetration directly or indirectly through known mechanisms, e.g. via phagocytosis, endocytosis or pinocytosis.

As a concern, we note with sufficient reasoning, that the skepticism of the usefulness of nanotechnologies is based on the lack of knowledge about their toxicity to humans and the environment. It is already established that we are not entitled to deduce the toxicity of a nanomaterial guided exclusively by its toxicity in macro form, as it is being a complex function of many parameters. Because of this, some are convinced that NPs are so risky that they require stopping research and applications in everyday life.

However, the precautionary principle cannot be used to stop nano-state research. We need to find a stable balance between the further development of nanotechnology and the need for research to identify potential dangers for establishing a scientifically susceptible database for risk assessment, with subsequent justified risk management procedures.

The small size of various shapes NPs gives a high penetration of epithelial and endothelial barriers in the lymph and bloodstream. This ensures the transport of NPs to all organs and tissues, including intercellular transport by transcytosis or simple diffusion across the cell membrane with adverse results in the penetration of cells by nanoparticles [36-39], such as physical damage to the membrane, structural changes in cytoskeleton components, disruption of transcription and oxidative DNA damage, mitochondrial damage, lysosome function disturbance, generation of reactive oxygen species, impaired membrane protein function and synthesis of inflammatory factors and mediators.

The penetration of NP into the bloodstream opens up to the possible penetration of the blood-brain barrier with consequences that are difficult to underestimate. Experiments that model NP toxicity on the body have shown that NP can cause thrombosis, inflammation of the upper and lower respiratory tract, neurodegenerative disorders, strokes, myocardial infarction, etc. What is certain is that NP, thanks to its size, can penetrate not only organs, tissues and cells, but also penetrate the cellular organs themselves (mitochondria and nuclei) which can drastically alert cellular metabolism and cause DNA damage, mutations and cell death.

We underline that public concerns about the increased toxicity of nanoparticles have a legitimate experimental basis for many years (silicosis, asbestosis, "black lung" disease, or anthracnosis) if we refer to their interaction with cells and tissues. Some scientific studies show the ability of the human body to clean itself of non-specific nanoparticles in the body, others - reiterate a tragic end of their action on the body through irreparable consequences or diseases. The ignorance of the interaction of the human body with the whole spectrum of nanoparticles does not allow us to say for sure about a total success story of nanotechnologies, and nanostructures, especially in biomedicine.

New technologies have always caused conflicts between those who want to exploit them as soon as possible and those who expect to receive reliable evidence. A particular concern of many is the likelihood that nanotechnology will spiral out of control to the detriment of humanity. These concerns relate to some advances in the ability of nanorobots to self-replicate and self-direct.

8. Risks associated with nanotechnology

Given the wide range of applications of the nanotechnologies mentioned above and the variety of industrial sectors affected, it is certain that the risks associated with nanotechnologies will be complex. The focus on the type of risks to be considered depends on the perspective of the particular entity involved in nanotechnologies. Suffice it to name just a few of these potential risks:

- political and economic,
- military (proliferation of WMD),
- societal impact,
- proliferation of bio-chemo-terrorism,
- environmental (uncontrolled release of NPs into the environment,
- nanoparticle harm risks/work hazards,
- risks of final ignorance of the interaction of the NPs with the biological environment or with other NPs,
- futuristic risks such as the nanotechnology of Homo sapiens, and the risk of the existence of Homo sapiens caused by the self-replication of nanomachines.

As with any new technology, risks can arise that we do not even intuit yet, which confirms the need for continuous and dynamic risk analysis. We risk saying that virtually all the safety issues addressed about nanotechnologies are related to the “free” uncontrolled nano state and less to the built-in, “fixed or immobilized” states of the already designed NPs. Of course, there are exceptions when products or materials with embedded NPs are thrown away, burned or destroyed in an uncontrolled manner by humans, thus causing risks that can be easily avoided.

From the risks outlined above, we draw attention to occupational hazards caused by the potential harm of nanoparticles. As shown in Figure 10, several conditions can be expected for potentially hazardous exposure of workers employed in nanotechnology research and innovation.

Nanotechnology activities	Examples of work tasks	Potentially hazardous exposures conditions	Potentially exposed workers
Innovation research activities	Sinthesizing & producing of NMs. Testing measurements involves toxicological & environmental impacts in *in vitro* & *in vivo* experiments	Handling nanopowders pouring & mixing nano-liquid suspensions; Cleaning spills or waste. Maintaining equipment	Reseurchers, engineers, technicians. Maintenance and waste handling personnel

Figure 10. Potentially hazardous exposure conditions for research and innovation workers (inspired from [6]).

Nanomaterials can present significant, often unknown, hazards to researchers, engineers, laboratory technicians, and support staff. In this regard, an analysis of the risk and impact of the life cycle of nanomaterials undergoing research on workers' health is needed.

Although during evolution the human body has developed a tolerance to most elements and molecules in their natural form of existence (dust, microparticles) with which it comes into contact, it has no natural immunity to new substances, new forms of existence (e.g. nano state) to identifying them as toxic, causing a reaction of the body's intolerance.

As mentioned, NP toxicity can be dictated by many factors (Figure 11) [34-38]. Moreover, NP size and surface area play an important role, largely determining the unique mechanism of NP interaction with living systems.

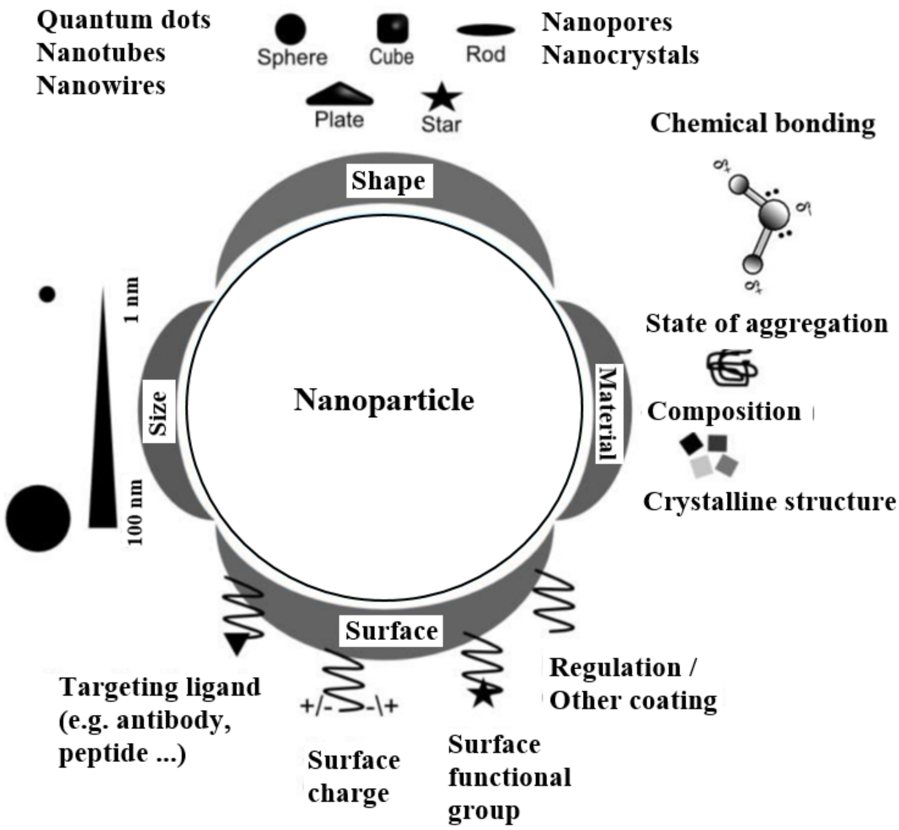

Figure 11. Determinants of nanoparticle toxicity (adaptation from [26]).

NPs are characterized by a very large specific surface area, which determines their high reaction capacity and catalytic activity. Dimensions from 1 to 100 nm are comparable to the size of protein cells (2−10 nm), the diameter of the DNA helix (2 nm), and the thickness of cell membranes (10 nm), which allows them to easily penetrate cells and organs [26]. For example, it is shown that gold NPs less than 6 nm penetrate easily into the cell nucleus, while the largest (10-16 nm) penetrate only through the cell membrane and are found only in the cytoplasm. This suggests that NPs of a few nanometers may be more toxic than NPs of 10 nm or more that cannot penetrate the nucleus. The toxicity dependence of gold NPs depends on their size in the range of 0.8 to 15 nm. It has been identified that 15 nm NP is 60 times less toxic than 1.4 nm NP for fibroblasts, epithelial cells, macrophages and melanoma cells. It is noteworthy that the 1.4 nm nanoparticles cause cell necrosis, while the 1.2 nm nanoparticles predominantly cause apoptosis. These data show us not only that NPs can penetrate the nucleus, but also that the correspondence of the geometric size of NPs (1.4 nm) with that of the major DNA groove allows them to interact effectively with the backbone of DNA. Sugar-phosphate loaded with negative sac and blocks the transcription.

The results of several studies show that carbon nanotubes, similar in shape to asbestos fibers, cause mesothelioma in the lungs. Also, inhaled carbon NP can weaken the immune system by affecting the T-cells responsible for its organization. On the other hand, it is shown that the harmfulness of nanocarbon is dictated by its durability, so its shape, the more durable it is, the more the behavior resembles asbestos particles.

The convergence of nanotechnology, synthetic biology and chemistry allows the creation of new agents and increases the resilience and lethality of existing ones. There is already talk of the possibility of editing various bacterial DNAs to create complex organisms and new chemicals.

New horizons of chemical-biological nano-generation delivery methods can create diagnostic and treatment impediments, reducing the body's immunity and causing ineffective diagnostic and treatment methods. As an example, carbon nanotubes can be used to supply only the lethal parts of the anthrax virus - without the imprinted protein that is recognized by the immune system.

9. Social impact and regulation

Exposure to nanomaterials is versatile and is achieved through production, transportation, storage, dissemination, use, and final disposal. Nanoparticles may not be recyclable or environmentally friendly, and when they lose control of their existence throughout their life, they could form a new category of non-ecological toxins and create a new threat to health, including through the environment. For these reasons, risk-based regulation of nanotechnologies is needed. Bowman and Hodge propose a model [40] that would argue for a complex regulation for nanotechnology (Figure 12).

This model takes into account product safety, civil society awareness, ethical and social issues, health, intellectual property rights, the international legal framework, including the environment. The soft and tough legal framework refers to various aspects of the consequences of nanotechnology and is applied in various fields: innovation research (through Codes of Professional Ethics) and, health, industry, pharmaceuticals, chemical industry, textile, automotive, etc.

We note that the governance system required for nanotechnologies does not differ substantially from the approach applied to other important environmental and public health issues. However, we mention that nanotechnologies come with specific challenges such as:

- the profound interdisciplinary character not previously encountered;
- high speed of development and enormous impact on industries and social benefits;
- low and delayed public awareness of nanotechnologies;
- the nature of the risks [41] created by some nanotechnologies;
- ethical, legal and social issues associated with some of the nanotechnologies.

The specific challenges and risks associated with some nanomaterials have posed questions to regulators, politicians, and researchers about the coverage of nanotechnologies and nanomaterials within the existing regulatory framework. To fill this regulatory gap, for example, the Commission of the European Communities has adopted a so-called *incremental approach* that recommends adapting existing legislation to the regulation of nanotechnologies and amending them.

This approach has led to some changes in European regulations and directives.

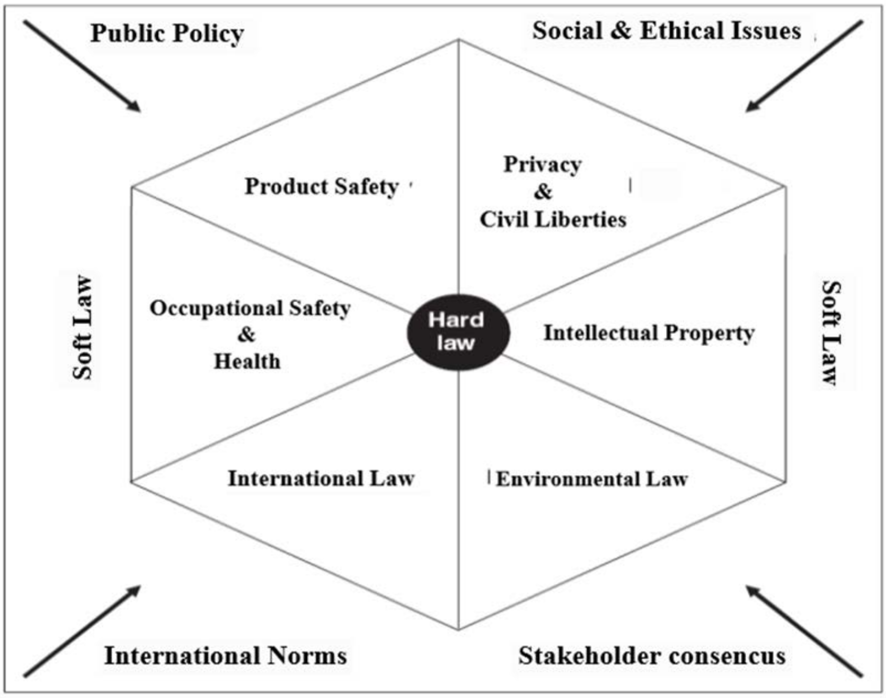

Figure 12. Bowman & Hodge nanotechnology regulatory model [40].

Thus, nanomaterials in the chemical, cosmetics, food, medical devices, plastic packaging for food, waste, and waste management are somehow indirectly regulated [42-44]. However, regulation by the incremental approach of the existing legal framework is characterized by several deficiencies.

10. Conclusions

Certainly, nanoelectronics is perhaps the most harmless nanotechnology with minimal adverse impact on human health. Exceptions may be due to non-compliance with the vital security in the technological process of obtaining as well as the uncontrolled discharge of technological waste into the environment.

Nanotechnologies in biomedicine represent dual-use technologies, which are characterized by both positive and negative impact from the current final ignorance of the mechanisms of interaction of nanoparticles with the biological environment.

The perspective of nanoparticles in medicine is primarily related to immunotherapy for diagnosis and clinical therapy depending on the type of nanoparticles. Immunotherapy combined with the targeted delivery of nanomedicines, characterized by high efficiency due to penetration, specific retention, and expected and predictable actions (destroying tumor cells) is under development for the treatment of various types of untreated diseases.

Nanoparticles have been shown to enter the human system in three ways: inhalation, ingestion, and penetration of the skin. Thus, it becomes extremely important to know the interaction of nanoparticles with cells, organisms, the biological environment, biomolecules, and other biosystems, but also the interaction with other nanoparticles parts of biosystems. These will determine the biocompatibility, toxicity and efficacy of nanoparticles in biological environments. This will ultimately allow the identification and design of non-toxic and beneficial nanomaterials in biomedicine.

Partially, in branches of the industry where nanotechnologies are used, nanoparticles are already regulated. Although nanotechnologies were not regulated by law in the recent past, their future in some areas must be largely determined by new regulations.

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