

Chapter 9

Nanotoxicity and Nanoethics

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1. Introduction

Nanotechnology (NT) involves studying and applying matter at extremely small scales, typically between 1 and 100 nanometers (nm), where one nm equals one billionth of a meter. At this scale, materials can exhibit new physical, chemical, and biological properties (Litter & Ahmad, 2023). For example, gold, silver, carbon, titanium dioxide, and iron oxide behave differently at the nanoscale, with changes in colour, strength, surface area, mobility, and reactivity. These unique properties make NT valuable in medicine, agriculture, electronics, water purification, energy, and food packaging. However, these same changes can also introduce risks. Therefore, NT must be approached with caution (Amin et al., 2024).

Nanotoxicity (NTox) refers to the harmful effects of nanomaterials (NMs) on living systems, including human and animal cells, plants, bacteria, fish, soil organisms, and entire ecosystems. NTox does not mean all NMs are toxic; it means their safety must be evaluated. Nanoparticles (NPs) can enter cells, circulate in the bloodstream, and accumulate in organs such as the lungs, liver, brain, or reproductive system. They can also move through soil and water. Toxic effects depend on factors such as size, shape, dose, surface charge, solubility, coating, and exposure duration. NTox research measures which doses cause harm, which organs are affected, and how long effects persist (Demir, 2021).

Nanoethics (NE) examines ethical considerations in NT, including who benefits, who faces risks, who controls data, who ensures safety, and who is responsible if harm occurs. NE also considers how the public can trust scientists and companies. While NT advances drug delivery, water purification, materials, and sensors, it can also lead to hidden exposures and unequal distribution of benefits. NE links scientific progress with responsibility, focusing on measurable risks, informed consent, access, justice, and public safety (Swierstra & Rip, 2007).

Nanotechnology can remove heavy metals from water, deliver drugs to targeted cells, increase solar cell efficiency, improve wound dressings, and enable rapid diagnostic tools. These applications are proven and measurable. However, innovation without thorough risk assessment can cause future harm. A material may appear safe in one test but unsafe in another. A nanoparticle may be stable in storage but reactive in lung fluid. A coating may initially prevent toxicity but degrade over time. Therefore, risks must be evaluated alongside benefits. (Emerich & Thanos, 2003).

This chapter outlines how nanoparticles (NPs) behave in the body and the environment. It describes the physical and chemical properties that influence toxicity and discusses health risks to the lungs, brain, and reproductive systems. The chapter also addresses impacts on soil, water, and air; bioaccumulation; safety testing; regulation; ethical principles; social access; case studies; and future developments. The objective is clear: to demonstrate why small particles require significant

responsibility. The chapter also shows that safe NT is achievable when science, regulation, ethics, and society collaborate.

2. Fundamentals of Nanotoxicity

The foundation of NTox is physicochemical properties (PCP), which are the measurable characteristics of a material. These include size, shape, surface area, surface charge, surface chemistry, crystal form, solubility, coating, and aggregation. These properties determine how a nanoparticle (NP) moves and reacts. For example, a 10 nm particle has more surface area per gram than a 100 nm particle, which can increase reactivity and potentially lead to greater oxidative stress (OS). A stable, coated NP may be less reactive. Therefore, while size is important, it is not the only factor to consider (Isibor et al., 2024).

Shape of the nanoparticles also influences toxicity. Spherical NPs may behave differently than rods, fibres, tubes, or plates. Long, rigid carbon nanotubes (CNTs) can act like thin fibres in lung tissue, and some fibre-shaped materials are harder for immune cells to remove. Sharp or needle-like forms can damage cell membranes, while plate-like graphene oxide (GO) interacts strongly with membranes due to its large surface area. Shape also affects how particles settle in water, enter cells, or block biological channels. Therefore, each study should measure shape (Zhao et al., 2017).

Surface chemistry is critical in NTox, as the surface interacts with cells, proteins, enzymes, soil, and water. Surfaces can be positively, negatively, or neutrally charged. Positively charged NPs may bind strongly to negatively charged cell membranes, increasing uptake and potentially damaging membranes. Surface coatings can reduce this effect. For example, polyethylene glycol (PEG) coatings can extend blood circulation time in some medical NPs. However, coatings may change after contact with proteins, forming a new protein layer called the protein corona (PC), which can alter the NP's identity in the body. As a result, the NP entering the body may differ from the one produced in the lab (Liu et al., 2017).

Solubility is a key factor, NPs dissolve and release ions, while silver nanoparticles (AgNPs) can release zinc, killing bacteria; on the other hand, they can also disrupt functioning and inhibit other cells. Titanium dioxide nanoparticles (TiO₂NPs) are less soluble. Still, they can produce reactive oxygen species (ROS) under light. At the same time, iron oxide nanoparticles (IONPs) can be used in magnetic imaging, but iron balance in the body must be controlled, so each NM needs its own measured study (Aliakbari et al., 2019; Sirelkhatim et al., 2015).

NPs interact with biological systems upon first contact. In humans, exposure can occur through inhalation, ingestion, skin contact, injection, or medical implants. In the environment, exposure may result from wastewater, soil sludge, air dust, product washing, or industrial release. After contact, NPs may remain on surfaces, pass through mucus, enter cells, or move into the bloodstream. The pathway depends on dose, particle size, and barrier strength. Lung alveoli are

very thin, allowing inhaled NPs to reach deep lung areas. Intestinal cells can absorb some NPs after oral exposure. Even with the skin's strong barrier properties, damaged skin can allow NP entry (Mu et al., 2014).

Cells take up NPs through several processes: endocytosis (the cell engulfs the particle), phagocytosis (immune cells ingest larger particles or clusters), diffusion, or as a result of membrane damage. Once inside, NPs may move to lysosomes, mitochondria, the nucleus, or the cytoplasm. If NPs damage mitochondria, cellular energy decreases. If NPs or ROS damage DNA in the nucleus, the risk of mutation increases. These are measurable changes (Emerich & Thanos, 2003).

Tissues and organs respond differently to NPs. Lung tissue may show inflammation, liver tissue may exhibit enzyme changes, kidney tissue may experience filtration stress, brain tissue may show nerve cell stress, and reproductive tissue may display changes in sperm count or hormone levels in animal studies. However, organ toxicity depends on the exposure route. Injected NPs follow a different pathway than inhaled NPs. Swallowed NPs encounter acid, enzymes, bile salts, and gut bacteria, while skin-applied NPs interact with sweat, oil, and the outer skin layer. Therefore, a single safety test is not sufficient for all applications (Emerich & Thanos, 2003; Liu et al., 2017).

The primary mechanism of toxicity is oxidative stress (OS), which occurs when reactive oxygen species (ROS) production exceeds antioxidant defences. ROS include superoxide, hydroxyl radicals, and hydrogen peroxide. At low levels, ROS serve as normal signalling molecules, but at high levels, they damage lipids, proteins, and DNA. NPs can generate ROS through surface reactions, metal ion release, light activation, or immune responses. OS can trigger inflammation and reduce cell viability. Many NTox studies measure ROS levels, glutathione (GSH), malondialdehyde (MDA), catalase (CAT), and superoxide dismutase (SOD) as markers (Emerich & Thanos, 2003; Isibor et al., 2024; Swierstra & Rip, 2007).

DNA damage is another important mechanism. Damage can occur directly, such as when nanoparticles reach the nucleus, or indirectly through reactive oxygen species. Researchers measure DNA strand breaks with the comet assay and assess chromosome damage with the micronucleus test. Changes in gene expression can be detected by polymerase chain reaction (PCR) or sequencing. DNA damage does not always lead to cancer, as cells have repair mechanisms. However, repeated damage, poor repair, or prolonged exposure raise concerns, highlighting the need for long-term testing (Ameixa & Bald, 2024).

Inflammation is also a key mechanism. It is the body's response to injury or foreign substances and can be protective. However, prolonged inflammation may damage tissue. Nanoparticles can activate macrophages, neutrophils, and epithelial cells, which then release cytokines. Common cytokines include interleukin-6 (IL-6), tumour necrosis factor alpha (TNF-alpha), and interleukin-1 beta (IL-1 beta). Elevated cytokine levels indicate immune activation. In the lungs, chronic inflammation can sometimes cause fibrosis-like changes, while in blood

vessels, it may increase cardiovascular risk. Thus, inflammation serves as both a defence and a potential risk (Ameixa & Bald, 2024; Bhabra et al., 2009) as shown in Figure 1.

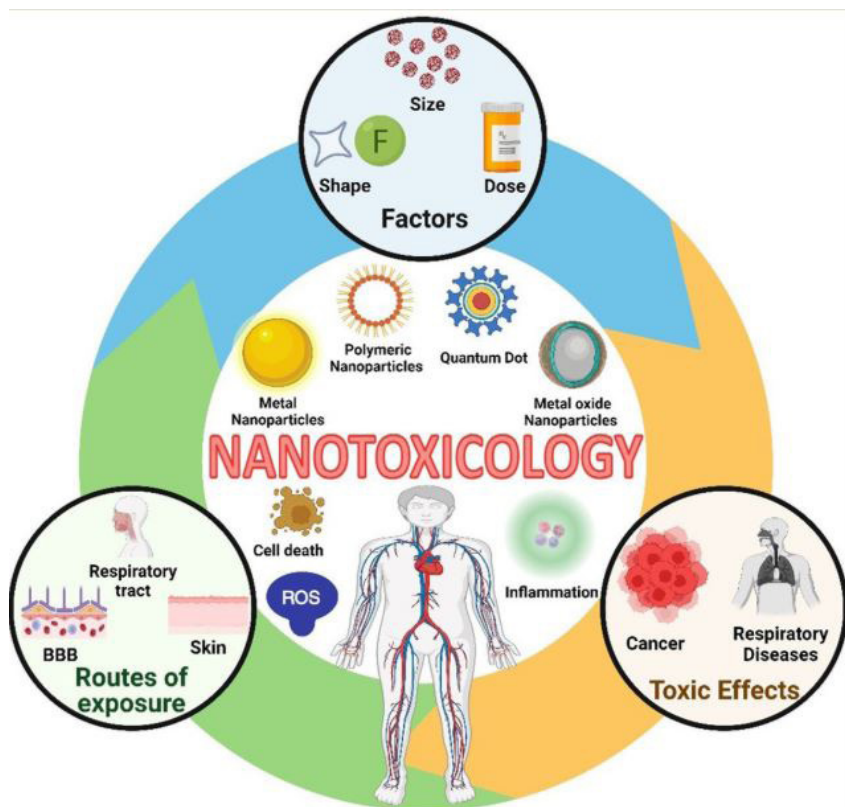


Figure 1. Impact of nanotoxicity on human health

3. Health and Environmental Impacts

The human health risk from nanoparticles (NPs) depends directly on exposure. Factory workers may inhale dry nanopowders, while patients can receive nanomedicine by injection. Consumers may encounter NPs in cosmetics, textiles, sprays, food packaging, and electronics. Although public exposure is generally lower than worker exposure, it is often more varied. Risk depends on both hazard and exposure; a highly toxic NP poses little risk with zero exposure, while a low-toxicity NP can become a risk with frequent, prolonged exposure (Dreher, 2003).

Respiratory risk is among the most studied areas. The respiratory system includes the nose, throat, airways, and lungs. Small NPs can reach the alveoli, which are tiny air sacs where oxygen enters the blood. Particles deposited in the alveoli may be removed slowly. Some NPs can cross the air-blood barrier in small amounts, while others remain in lung tissue. Lung cells may exhibit oxidative stress, inflammation, reduced viability, and tissue thickening. Workers handling powders require masks, ventilation, wet methods, and exposure monitoring. Spray products also require careful design, as they can generate inhalable droplets (Dreher, 2003; Emerich & Thanos, 2003).

Neurological risk is more complex. The neurological system includes the brain, spinal cord, and nerves. Some NPs may reach the brain through the bloodstream if they cross the blood-brain barrier (BBB), or through the olfactory nerve after nasal exposure. The BBB protects the brain from many substances, but very small particles, surface-coated particles, or inflamed tissues may alter NP movement. Potential effects include oxidative stress in nerve cells, changes in neurotransmitter levels, and microglia activation. Microglia are the brain's immune cells. Evidence remains mixed, with many findings based on animal and cell models. Long-term human data are limited (Cattaneo et al., 2010; Dreher, 2003).

Reproductive risk is also important. The reproductive system includes testes, ovaries, placenta, uterus, sperm and eggs. Some animal studies show that certain NPs at high doses can reduce sperm movement, change hormone levels, or cause placental stress. The placenta is not a simple wall. It is an active organ. It can allow or block different materials. NP size, coating and dose decide movement. More data is needed for real human exposure. Still, precaution is needed in products used by pregnant women, infants and reproductive-age individuals. Skin risk is generally lower when the skin is healthy, as the outer layer serves as a strong barrier. Many NPs in creams remain on the surface or in hair follicles. However, damaged, burned, or diseased skin may permit greater entry. Sunscreens use titanium dioxide nanoparticles (TiO₂NPs) and zinc oxide nanoparticles (ZnONPs) to block ultraviolet (UV) light and reduce UV exposure. These products must be tested for penetration, photoreactivity, and long-term use (Cattaneo et al., 2010; Guseva Canu et al., 2018).

Ecotoxicity refers to toxic effects on ecosystems, including soil, water, and air, which can receive NPs from factories, waste, sewage sludge, product washing, tyre wear, paints, and medicine waste. The NPs can bind to clay, organic matter, roots, and microbes, reducing movement and changing microbial activity. Soil microbes are important for the nitrogen cycle, carbon cycle, and plant growth; if AgNPs reduce harmful bacteria, they may also reduce useful bacteria at certain doses. Soil worms can also take up particles. Their survival, growth, reproduction, and enzyme activity can be measured (Dreher, 2003; Emerich & Thanos, 2003).

In water, NPs may remain dispersed, settle, dissolve, or form aggregates. Freshwater, seawater, and wastewater differ in salt content, pH, and organic matter, which influence NP behavior. Fish, algae, daphnia, and bacteria are commonly used as test organisms. Silver nanoparticles (AgNPs) can reduce algal growth and affect fish gills at certain doses. Titanium dioxide nanoparticles (TiO₂NPs) can generate reactive oxygen species under light and impact aquatic organisms. Zinc oxide nanoparticles (ZnONPs) can dissolve and release zinc ions. However, organic matter in natural water may reduce or alter toxicity, so laboratory and field results can differ (Emerich & Thanos, 2003; Isibor et al., 2024).

Air exposure happens through dust, spray, combustion or industrial release. Airborne NPs can travel with wind. They can deposit on leaves, soil, water and buildings. Airborne nanomaterials are hard to measure because many natural and human-made ultrafine particles already exist in air. Instruments measure particle number concentration, mass concentration, size

distribution and surface area. For worker safety, real-time monitoring and filter sampling can be used. The main issue is not only total mass. For NPs, particle number and surface area may be better dose metrics in some cases (Cattaneo et al., 2010; Isibor et al., 2024).

Bioaccumulation refers to the buildup of a substance in an organism over time, while biomagnification is the increase in concentration through the food chain. Many NPs do not biomagnify like persistent organic pollutants, but some NPs or their released ions can accumulate in organs. Aquatic organisms can absorb particles from water or food, and plants can take up small particles or ions through their roots. Animals may then consume these plants. The final risk depends on dissolution, transformation, excretion, and tissue storage. Long-term exposure is important, as even low daily doses can have measurable effects after months or years (Dreher, 2003; Guseva Canu et al., 2018).

Long-term exposure is a significant concern as nanotechnology is expanding across many sectors. Short-term studies of 24 or 48 hours cannot capture chronic risks. Chronic exposure can alter immune response, fertility, microbiome, organ weight, enzyme levels, and gene expression, and may cause delayed effects. Some nanomaterials can transform after release; for example, silver nanoparticles (AgNPs) can become silver sulfide in wastewater. This form may be less toxic than free silver ions but still contributes to environmental load. Therefore, life cycle assessment (LCA), which tracks a product from raw material to disposal, is necessary (Cattaneo et al., 2010; Emerich & Thanos, 2003) as shown in Figure 2.

4. Risk Assessment and Regulation

Risk assessment (RA) is a stepwise process that identifies hazards, measures exposure, studies dose-response, and describes risk. For nanomaterials (NMs), RA is more complex than for larger chemicals. The same chemical formula can present different risks in various nanoforms. Factors such as size, shape, coating, and surface charge can alter outcomes. Therefore, a single material name is insufficient. A safety file must include detailed characterisation, specifying mean size, size range, shape, surface area, zeta potential, purity, crystal form, coating, solubility, and aggregation state. Without these data, toxicity results are unreliable (Fan & Alexeeff, 2010).

Current safety testing includes cell studies, animal studies, environmental studies, and new approach methodologies (NAMs). Cell studies are rapid and controlled, measuring cell death, ROS, cytokines, DNA damage, and barrier integrity. Animal studies assess whole-body and organ-specific effects. Environmental tests evaluate algal growth, daphnia survival, fish embryo development, earthworm reproduction, and plant growth. NAMs encompass organ-on-chip systems, computational models, high-throughput screening, and read-across methods. These tools can reduce animal use and increase efficiency, but they require validation (Guseva Canu et al., 2018; Roig, 2018).

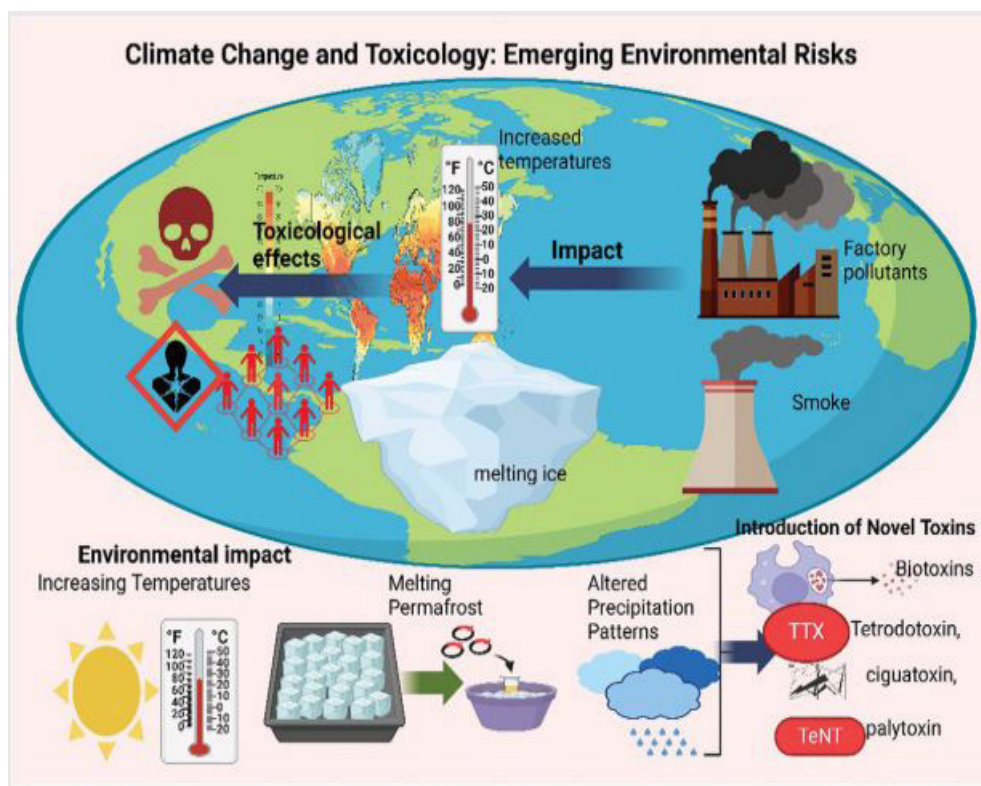


Figure 2. Impact of Nanotoxicity on the environment

Sample preparation presents significant challenges. Nanoparticles (NPs) can agglomerate, forming larger clusters. For example, a test may begin with 20 nm particles, but cells may receive 300 nm aggregates. The delivered dose may differ from the intended dose, as particles can settle on cells, adhere to plastic tubes, or react with culture media. Therefore, dose measurement must reflect what cells or organisms actually receive. While mass per millilitre is useful, additional metrics such as particle number, surface area, ion release, and delivered dose are often necessary (Fan & Alexeeff, 2010).

Regulatory systems vary by country. The European Union (EU) uses Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), which covers chemicals and nanoforms. In the United States (US), agencies such as the Food and Drug Administration (FDA), Environmental Protection Agency (EPA), and Occupational Safety and Health Administration (OSHA) apply existing laws. The FDA uses a product-based approach for drugs, cosmetics, food, and medical devices. The International Organisation for Standardisation Technical Committee 229 (ISO/TC 229) sets standards for terminology, measurement, testing, and health safety practices. The Organisation for Economic Co-operation and Development (OECD) provides test guidelines and guidance for manufactured NMs (Roig, 2018).

While these frameworks are valuable, several gaps remain. The first is a data gap: many NMs lack comprehensive chronic toxicity, reproductive, developmental, and neurotoxicity data.

The second is exposure data, as it is difficult to determine real-world NP exposure for workers and consumers. The third is environmental fate data, since NPs can transform in wastewater, soil, and sunlight. The fourth is mixture data, as individuals are exposed to combinations of dust, chemicals, microbes, and NPs. Mixture effects can be additive, less than additive, or more than additive (Fan & Alexeeff, 2010; Guseva Canu et al., 2018).

Predictive models remain limited. While models can estimate toxicity based on size, charge, solubility, and surface area, they require large, reliable datasets. Many studies use varying methods, report only nominal doses, omit coating information, or use different cell lines and exposure times, making comparisons difficult. Machine learning (ML) can assist, but its effectiveness depends on data quality. Poor data leads to poor predictions, making data quality an ethical concern as well (Guseva Canu et al., 2018).

Regulatory challenges are global, as NMs are traded internationally. Products manufactured in one country may be used in another, where testing capacity may be limited, and workers may lack adequate protective equipment. Informal recycling can release NPs from electronics and coatings, and labels may not indicate nano content, leading to unequal risk. International guidelines help, but enforcement happens locally. Effective regulation should include training, monitoring, laboratory capacity, and public reporting (Roig, 2018).

5. Nano-ethics: Principles and Frameworks

NE starts with responsibility. Scientists and companies must act before harm occurs, not only after damage. Responsible research and development (RRD) requires integrating safety from the outset. Researchers should assess potential risks, companies should test exposure before launching products, governments should set clear standards, and universities should teach safety and ethics. Responsibility does not hinder innovation; it protects it from failure and public concern (Allhoff, 2007).

The precautionary principle (PP) is essential in NT. PP allows for limiting actions when there is a potential for serious risk and data is incomplete. It does not require halting all NT, but calls for safer design, limited release, improved labelling, and additional testing when uncertainty is high. For example, medical NPs injected into the bloodstream require rigorous testing, dry powders used in factories require worker protection, and NPs in spray products require inhalation studies. PP serves as a practical safety tool (Biroudian et al., 2019).

Transparency requires open, clear information. The public should be informed when NMs are present in products with potential exposure. Workers need to know the materials they handle, regulators need full details on nanoforms, and medical patients should understand the benefits and risks of nanomedicine. Transparency builds trust, while withholding information undermines it. If a company conceals nano content and harm occurs, public backlash can be significant. Clear labelling and accessible safety data help reduce fear (Nurock, 2020).

Accountability ensures that someone is answerable for outcomes. If a product causes harm, the manufacturer cannot claim ignorance and avoid responsibility. Accountability involves documentation, safety files, traceability, post-market monitoring, recall plans, and independent review. Self-reporting alone is insufficient; third-party testing increases confidence. Public funding agencies may also require ethics reviews and safety plans. Accountability is demonstrated through action, not promises (Allhoff, 2007; Nurock, 2020).

Public trust is fragile. Many people cannot see NPs and may hear that NT is invisible and powerful, which can cause concern. Trust increases when scientists communicate clearly and address public concerns early. Public engagement should go beyond advertising and include two-way discussions. People may ask about safety, employment, religion, the environment, privacy, and cost. These questions are valid, and effective NT policy should address them (Biroudian et al., 2019; Nurock, 2020).

6. Societal and Global Perspectives

Equity requires a fair distribution of benefits and risks. Nanotechnology can assist both wealthy and poor communities by enabling low-cost water filters, improved vaccines, clean energy devices, and soil sensors. However, initial benefits may reach wealthier markets first, while poorer communities may receive waste or lower-quality products. This raises ethical concerns. When nanotechnology is publicly funded, the benefits should be widely shared. Planning must include affordable access. Safe water technology has limited value if poor villages cannot afford it (Ferrari, 2010).

Access is also critical in medical nanotechnology. Nanomedicine can enhance cancer therapy, imaging, vaccine delivery, and gene delivery, but these treatments may be expensive. If only wealthy patients can access them, health inequality may increase. Clinical trials should include diverse groups, as drugs tested in one population may not have the same effects in another. Factors such as age, sex, pregnancy, liver or kidney disease, and nutrition can influence responses. Ethical medical nanotechnology requires fair trial design and equitable pricing (Allhoff, 2007b).

Ethical dilemmas in medical NT are serious. Drug-delivery NPs can target tumours or cells and reduce side effects. But they can also stay in organs. Long circulation time can increase exposure. Implants with nano coating can reduce infection. But they may release particles after wear. Brain nanodevices can help diagnosis or treatment. But they can raise privacy and consent issues. A patient must understand risks. Consent must be clear and not forced. We must weigh benefits against harm (Dalton-Brown, 2012).

Nanoelectronics also raises ethical concerns. Smaller devices can enhance computing, sensors, and communication, but may contribute to increased electronic waste. E-waste can expose workers to metals and nanomaterials during informal recycling. Tiny sensors can monitor

the environment and health, but may also be used to monitor individuals without consent. Therefore, nanoelectronics involves not only toxicity, but also issues of privacy, labour, waste, and power (Chauhan et al., 2021).

Environmental justice means that no group should bear an unfair share of environmental risk. Vulnerable populations, such as children, pregnant women, older adults, sick workers, low-income communities, and those living near factories or waste sites, may face higher exposure and less protection. While factories may provide jobs, they can also release dust or wastewater. Ethical nanotechnology requires exposure monitoring near production sites, worker training in local languages, and safety sheets that are simple and easy to understand (Dalton-Brown, 2012; Ferrari, 2010).

A global perspective also requires research capacity. Many countries use imported nanomaterials, but not all have the instruments needed to measure size, surface charge, or aggregation. Without proper measurement, regulation is weakened. International cooperation can support laboratories, training, and shared databases. This is important for safe trade and for building trust (Allhoff, 2007b).

7. Summary

This chapter provides a clear overview of nanotechnology (NT), nanotoxicity (NTox), and nanoethics (NE). NT involves manipulating matter at the 1 to 100 nanometer (nm) scale, where particles exhibit altered size, mass, surface area, charge, solubility, and reactivity. These properties make nanomaterials (NMs) valuable for drug delivery, water treatment, crop sensors, electronics, energy devices, and food packaging. However, the small size and high surface area also increase exposure, organ uptake, cellular entry, and environmental release. Nanoparticles (NPs) can enter cells, circulate in the bloodstream, accumulate in organs such as the lungs, liver, brain, and reproductive system, and disperse in soil, water, and air. The chapter discusses how factors such as size, shape, surface chemistry, charge, coating, solubility, concentration, and exposure duration influence toxicity. It outlines key toxicity mechanisms, including oxidative stress (OS), DNA strand breaks, lipid damage, enzyme alterations, and inflammation. The chapter also addresses respiratory, neurological, reproductive, skin, and dose-response effects. It covers risk assessment (RA), safety testing, response data, regulation, data gaps, and limitations of predictive models. NE is discussed in terms of consent, labelling, exposure reporting, safety data sharing, and risk management. Case studies include silver nanoparticles, sunscreens, carbon nanotubes, nanomedicine, and nanoelectronics. The chapter concludes that safe NT requires thorough testing, robust regulation, safer design, and public monitoring for future applications.

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