# Exposure Effects Related to Nanomaterial Life Cycles

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Nanoparticle-based biosensors are produced and utilized at different scales ranging from laboratory to industrial domains. While incorporating nanomaterials is beneficial to developing high-performance biosensors, at the stages of scale-up and disposal, it may lead to the unmanaged release of toxic nanomaterials. When considering the potential environmental impact and health safety of the scaled-up production of nano biosensors, it is necessary to examine the manufacturing, utilization, and end-of-life disposal of the nanomaterials used.

Keywords: dimensionality ; life cycle ; nanocomposite ; nanomaterial ; nanotoxicity ; surface chemistry ; toxicity ; transformation

## 1. Introduction

Nanoparticles are naturally occurring or engineered particles or materials less than 100 nm in size in at least one dimension. According to the European Commission, a Nanomaterial contains 50% or more particles in that size range [1]. At the nanoscale, particles often exist with unique physical properties distinct from the properties of their bulk form due to increased relative surface area per volume unit and the dominance of quantum effects [2][3]. The enhanced optical, magnetic, electrical, and catalytic properties of nanomaterials, including nanometals, nanometal oxides, carbon-based nanomaterials, and inorganic two-dimensional nanoparticles, have made them useful in various applications. Specifically, the field of nano biosensing has significantly expanded the frontiers for the development of high-performance sensing devices [4][5].

Biosensors employ biological or biomimetic recognition elements (e.g., antibodies, enzymes, molecularly imprinted polymers, aptamers, etc.) to selectively bind (and, in some cases, react) with target analytes potentially present in complex samples. Biosensor applications span a wide spectrum, including the fields of medicine, food safety, drug development, and environmental monitoring [6]. The biological elements typically utilized in biosensing platforms are often combined with nanomaterials with different compositions and dimensions [7] to facilitate or enhance the recognition and transduction processes of the operating mechanism of the biosensor device [8][9][10]. Generally, operation modes include electrochemical (measures changes in voltage, current, capacitance, impedance, etc.), electronic, optical (measures changes in fluorescence, luminescence, optical diffraction, etc.), piezoelectric, thermometric, acoustic, and colorimetric detection mechanisms. In most cases, nanomaterial-enabled technologies, such as biosensors and bioelectronics, are manufactured, used, and disposed of in a linear *end-of-life* fashion. Since the existing research on fate, transport, transformations, bioaccumulation, biomagnification, and toxicity of engineered nanomaterials is still in its infancy, there are significant knowledge gaps regarding the potential long-term health and environmental impacts of mass-produced nanoparticles used in novel technologies, such as biosensors.

## 2. Exposure Effects Related to Nanomaterial Life Cycles

When considering the potential environmental impact and health safety of the scaled-up production of nano biosensors, it is necessary to examine the manufacturing, utilization, and end-of-life disposal of the nanomaterials used. This type of risk assessment is considered a life cycle assessment (LCA). The life cycle includes the production of the nanomaterial-containing products, their use, disposal, and such end-of-life stages as reuse, recycling, recovery, and final disposal. Environmental impacts and health risks could be present at each stage and should be assessed [11].

At the production stage, nanomaterials can impact human health via direct occupational exposure. During the manufacturing process, individuals can be exposed to nanomaterials via the classical routes of exposure, i.e., inhalation, ingestion, and dermal contact. These exposures are of concern because nanomaterials often display enhanced toxicity different from that of their bulk counterparts. Inhalation of nanoparticles in an occupational setting can occur via exposure to dust-containing aerosolized nanoparticles. In the workplace, aerosolized nanoparticles can be generated through several manufacturing processes [12]. Workers can be exposed through nanoproduct harvesting, processing (handlining and packaging), and equipment cleaning [13]. Once inhaled, these nanoparticles can deposit in the lungs and respiratory tract, where they have been shown to accumulate and generate toxicity [14]. Dermal exposures to nanomaterials occur through skin contact with contaminated surfaces. In an occupational setting, dermal exposure to nanomaterials becomes especially problematic if nanomaterials have associated toxicities or contain impurities and if workers have compromised skin integrity [15][16].

Greater standardization of regulations related to exposure limits and safety controls (personal and engineer) is needed to overcome the toxicity concerns associated with nanomaterial exposure in occupational settings. Studies have shown that if employed correctly, process modification, engineered controls, and personal protective equipment can control nanomaterial exposure. However, the implementation of these controls is often lacking, and regulatory bodies do not have many set occupational exposure limits [17][18][19]. Unless these issues are addressed, the scaled-up production of biosensors will further contribute to the problem.

Potential environmental impacts associated with biosensors could also originate from the intentional and unintentional releases of nanoparticle-containing waste streams (atmospheric, waste solids, and waste liquids) during production [20][21][22]. For example, It has been reported that nanomaterials such as Cu, $TiO_2$, Ag, or $CeO_2$ could enter wastewater treatment plants (WWTPs), be eliminated mainly through the primary and secondary treatment, and then associated with the solid phases of sludge by over 80% by mass [23][24][25][26]. Dried sludge is then applied at a landfill resulting in the return of nanomaterial-contaminated sludge back to the environment. Many nanomaterials have antimicrobial properties. The initial concentration of nanomaterials present in wastewater or sludge may be low, but the accumulation of the nanomaterials in the wastewater stream and returned sludge could become problematic. It is also possible that the increased concentration of toxic nanomaterials could crash the WWTPs by killing the microorganisms essential for Biological Oxygen Demand (BOD) reduction.

A deeper understanding of the scale of environmental releases, and therefore potential environmental health concerns, is limited by the lack of consistent reporting of production quantities. While some efforts are being made by organizations such as the environmental protection organization (EPA) (premanufacture notifications (PMNs) and significant new use notices (SNURs)) more robust regulations and requirements on the reporting of production are needed to assess the true risk of nanomaterial production [27].

Once products are sold to consumers, further human and environmental exposures are possible. Nanomaterials are already widely applied in commercial products such as appliances, agricultural products, construction materials, cosmetics, foods, beverages, medical devices, and drug products [28][29]. As these products are used, they degrade, releasing nanomaterials into the surrounding environment [30][31]. Once in the environment, these nanoparticles, which are often engineered, persist much longer due to the modifications (capping, functionalization, etc.) used to stabilize the particles [32]. In general, the utilization of biosensors for point-of-care, laboratory detection, and clinical diagnostic purposes poses limited risks. However, implantable biosensors could pose more significant risks associated with their biocompatibility and toxicity with the biosensor materials. While several countries and institutions are attempting to establish regulatory frameworks, global regulations regarding nanomaterials in consumer products are lacking [28].

Nanomaterial waste from nano biosensors can also originate from the disposal of spent devices in landfills and the leachates associated with such a disposal method. Leachates containing nanomaterials can be generated from solid waste landfills, which could directly affect both the aerobic and anaerobic processes of WWTPs. Taylor et al. investigated the impact of three copper particles, micron-and nanoscale Cu particles, and a nanoscale $Cu(OH)_2$-based fungicide on the function and operation of a model septic tank. The results indicated that systems exposed to the three Cu particles caused distinct disruptions in septic tank function. Temizel et al. (2017) studied the effect of nano-ZnO on biogas generation from simulated landfills over one year. They demonstrated up to 99% of nano-ZnO was retained in the waste matrix, leading to a decrease in biogas production of 15% [33]. Incineration is one of the important strategies for sewage sludge management. The potential for air pollution due to aerosols generated during wastewater treatment and incineration could also pose risks to the environment and human health.

To mitigate possible risks associated with the disposal of nano biosensors, methods for reuse and recycling should be explored. Traditional techniques for the recycling of nanoparticles include separation techniques such as centrifugation and solvent evaporation. However, these techniques are energy intensive. Alternative methods include the application of molecular antisolvents, pH or thermal-responsive materials, and magnetic fields [34]. In batteries, the successful recovery of nanomaterials has already been demonstrated at the benchtop level for nanomaterials such as Zn and ZnO nanoparticles and Graphite-polyaniline nanocomposites via Inert gas condensation (thermal) and vacuum separation, hydrometallurgy and liquid-liquid extraction, and oxidative polymerization and precipitation [35]. Barriers to the effective recycling and reuse of nanomaterials arise from a lack of guidelines and strategies for the recovery and reuse of nanomaterials [34]. As researchers and regulatory bodies work to establish practical strategies and guidelines, the development of reusable biosensors should be prioritized [36][37].

Strategies to reduce and control the toxicity of nanoparticles are also needed to manage the negative impacts associated with exposure. Current strategies include the coating and encapsulation, loading, grafting, and doping of nanoparticles [38][39]. The development of new strategies requires further research into the mechanisms of nanoparticle toxicity as nanomaterials suitable for the fabrication of biosensors have associated scales of toxicity. A greater understanding of these factors can be leveraged to develop targeted strategies to modify nanoparticles used in the fabrication of biosensors.

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