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ENGINEERED NANOMATERIALS IN OCCUPATIONAL ENVIRONMENTS: TOXICITY, RISK ASSESSMENT, EXPOSURE CONTROL, AND REGULATORY CHALLENGES

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ABSTRACT

Engineered nanomaterials (ENMs) are increasingly utilized in industrial, biomedical, agricultural, and consumer applications because of their unique physicochemical properties, including high surface area, enhanced reactivity, and nanoscale dimensions. However, these characteristics also raise concerns regarding occupational exposure and potential adverse health effects. Workers involved in the production, processing, handling, and disposal of ENMs represent the population at greatest risk, with inhalation serving as the primary exposure route, followed by dermal contact and inadvertent ingestion. Once internalized, ENMs can translocate to secondary organs, where they induce oxidative stress, inflammation, mitochondrial dysfunction, genotoxicity, apoptosis, and immune dysregulation, contributing to pulmonary, cardiovascular, hepatic, renal, neurological, reproductive, and dermal toxicity. This review summarizes current knowledge on occupational exposure pathways, toxicological mechanisms, biodistribution, persistence, and organ-specific health effects of engineered nanomaterials. It further discusses recent advances in risk assessment methodologies, including computational modeling, grouping strategies, control banding, and life-cycle assessment, together with existing regulatory frameworks and exposure control measures. Engineering controls, administrative practices, personal protective equipment, biological monitoring, and safe-by-design approaches are critically evaluated for minimizing occupational risks. Finally, current knowledge gaps and future research priorities are highlighted, emphasizing the need for standardized exposure assessment methods, validated biomarkers, long-term epidemiological studies, harmonized regulations, and sustainable nanotechnology practices to ensure safe industrial applications of engineered nanomaterials.

INTRODUCATION

Nanotechnology is an interdisciplinary field of science and engineering that contains design, synthesis, characterization, characterization and application of materials and devices that have very small dimensions [1]. Engineered nanomaterials are usually materials that have at least one external dimension or internal structural feature at the nanoscale, ranging from 1–100 nanometers.

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Due to their unique synthesis, physical and chemical properties, like high surface-to-volume ratio, electrical conductivity, increased surface chemical activity, the ability to tune optical behavior, and special mechanical features, engineered nanomaterials show characteristics that are different from their larger counterparts [2]. These properties and characteristics have made engineered nanomaterials a crucial part of modern nanotechnology, they have been rapidly adopted in various industrial and biomedical applications. Engineered nanomaterials are widely working across multiple sectors, including electronics industries, medical, environmental remediation, agriculture, and

advanced manufacturing. Metals and metal oxide-based nanomaterials, such as titanium dioxide, silver nanoparticles, and zinc oxide nanoparticles, are widely utilized in catalysts, protective coatings, cosmetics, antioxidant and personal care products. Similarly, carbon-based nanomaterials, with carbon nanotubes and graphene nanomaterial, have transformed the development of high-performance composites, nanoelectronics, sensors, and energy storage devices because of their mechanical strength and electrical conductivity performance. Rapid uses, commercialization and large-scale production of engineered nanomaterials have significantly increased their synthesis, characterization, manufacture, processing, transportation, binding and inclusion in consumer product and industrial invention [3]. As a result, concerns are growing about the potential negative effects on human health and the environment, especially in workplaces where people are working and being exposed for long periods. Direct contact with nanomaterials has become a vital public health issue, and occupational safety issue, as employees or individual working in nanoparticles industries are most likely to come into direct interaction with these materials. This kind of contact can happen throughout the entire lifecycle of nanoparticles, including synthesis, characterization, processing, balancing, packaging, transport, receiving, use, recycling, and waste disposal. In manufacturing services, activities like treatment, handling, weighing, mixing, grinding, drying, and packaging materials can produce nanoparticles or nano-aerosols in air, particularly during open system processes, increasing the risk of acquaintance through inhalation. (Figure 1) [4], [5].

Researchers and lab worker usually handle engineered nanomaterials in processed, liquid suspension, binding aerosol forms under experimental work, which don't always provide safety measures like those in industrial production facilities. Additionally, the growing use of nanotechnology in healthcare including targeted drug delivery, tissue engineering, biosensors, antioxidant and antimicrobial coatings has also introduced extra occupational contact situations for healthcare specialists, lab staff, and pharmaceutical hands. These changes highlight the importance of carrying out comprehensive professional risk assessments, exposure monitoring, and evidence-based prevention strategies to safely handle engineered nanomaterials in workplace [6].

Occupational exposure to engineered nanomaterials isn't just inadequate to their creation and manufacturing but spans their entire development. When products completed with nanotechnology reach the end of their service life, staffs involved in recycling, waste processing, clearance, and resource retrieval can come into contact with old, altered, or degraded nanomaterials whose physicochemical properties have altered. These changes can affect the environmental behaviour, bioavailability, and toxicological profile of engineered nanomaterials, making exposure and risk assessment more complex. Evidence from occupational monitoring studies (physical, chemical, mechanical, psychological and biological) shows that employees in various industrial settings are exposed to nanomaterials (Figure 2) [7].

For example, biomonitoring conducted in country found indium oxide nanoparticles in the blood plasma of workers at nanomaterial processing accommodations, with an average concentration of 10,371 particles/mL, while no nanoparticles were found in unaffected control persons. Similarly, lab-based exposure duties during nanoparticle synthesis found aerial concentrations of selenium, gold and silver nanoparticles to be 0.046 $\mu g/m^3$ to 0.077 $\mu g/m^3$, respectively [8]. Although these concentrations were below established industrial exposure limits, the results established measurable workplace exposure under standard operating circumstances. In addition, research on welders showed that about 79% of metallic nanoparticles in welding fumes are iron nanoparticles, and higher levels of iron in the blood were positively associated. These findings make it clear that occupational contact with nanomaterials happens in many industrial and research settings, and even when the atmospheric concentration is within current regulatory limits, it can still lead to measurable internal exposure. Such evidence highlights the need for comprehensive exposure monitoring, biomonitoring programs, and mechanistic toxicity testing to improve occupational risk assessment and to develop evidence-based strategies to ensure the safety of workers handling engineered nanomaterials [9].

Among the different exposure routes such as inhalation, ingestion and dermal contact, inhalation or aerosol is considered the main exposure pathway for occupational toxicity exposure. Due to their unique ultrafine size, airborne particles bypass upper respiratory defences, enter deep into the lung alveoli, and then pass through the alveolar capillary barrier into systemic circulation, where they can accumulate in other tissues. Moreover, the highly reactive surfaces of engineered nanomaterials can encourage and development of highly reactive oxygen species, leading to oxidative stress, antioxidant dysfunction, mitochondrial dysfunction, inflammation, inflammatory responses, DNA damage, and eventually cell injury [10].

Biological behaviour and toxicity of engineered nanomaterials are influenced by numerous physico-chemical parameters, such as particle size, shape, surface charge, surface functionalization, aggregation or

agglomeration state, crystallinity, solubility, and chemical composition. These features are dynamic and can alteration under different environmental or biological circumstances, leading to significant discrepancy in toxicity responses across different types of nanomaterials. As a result, traditional noxiousness approaches and commercially developed acquaintance assessment frameworks for conventional materials often fall short in accurately predicting the behaviour, exposure potential, and health risks of engineered nanomaterials [11]. This highlights the need for nano-specific risk assessment strategies that combine physico-chemical analysis with mechanical toxicity assessment. Although there has been a lot of improvement in specialized health and safety, traditional hazard assessment frameworks aren't fully proficient of dealing with the unique challenges posed by engineered nanomaterials. Conventional occupational acquaintance assessment mainly deliberates mass concentration as the primary exposure metric. But, due to their nanoscale magnitude, size and large specific surface area, engineered nanomaterials show biological activities that are mostly related to particle number concentration, surface area, particle size distribution, and surface awareness, not just mass [12]. Thus, mass-based exposure dimensions may underestimate the actual biological burden and the potential health risks associated with engineered nanomaterials exposure. Aerosol sampling and analysis methods often fall short of the sensitivity and specificity desired to distinguish engineered nanomaterials from ultrafine particles generated by combustion processes or environmental sources. On top of that, engineered nanomaterials go through dynamic characterization based on their chemical properties like aggregation, solubility, surface modification, and interactions with biological sources or matrices, which can significantly change their exposure and toxicological responses in real-world conditions [13].

Collectively, these limits display that commercial risk assessment approaches developed for conventional chemicals substance can't be directly pragmatic to engineered nanomaterials. The rapid evolution of nanotechnology has outpaced the development of uniform regulatory frameworks, exposure assessment methods, and evidence-based occupational security guidelines. So, to confirm safe and sustainable use of engineered nanomaterials in work surroundings, there's an urgent need to establish nano-specific monitoring techniques, validated exposure metrics, harmonized occupational exposure limits, and mechanism-based risk assessment approaches [14], [15]. Even though industrial use of engineered nanomaterials is increasing, the exposure to nanomaterials and the related occupational facets have not yet been adequately combined. Most available studies emphasis on nanotoxicity or environmental effects of explicit engineered nanomaterials, while occupational exposure routes, hazard assessment, and monitoring frameworks are often looked at separately [16], [17]. This dispersed information limits the development of comprehensive workplace risk management strategies. Therefore, this review provides a significant and integrated overview of workplace conditions related to engineered nanomaterials exposure. In particular, it summarizes the main workplace access routes and conditions, this review summarises the current exposure and risk assessment approaches, identifies existing challenges, therapeutic strategies and highlights future research priorities to strengthen workplace safety and evidence-based policy development.

Occupational exposure pathways of engineered nanomaterials

Contact with engineered nanomaterials depends on numerous factors such as source of emission, processes happening at the workplace, the materials characteristics, and the ways of contact. Different jobs have different levels of exposure and often, instead of continuous contact, there can be very high short-term exposures. This sector summarizes main ways of contact and workplace conditions based on evidence from field investigations, experimental studies, and occupational monitoring (Figure 3)[18], [19].

Sources and release mechanisms

Engineered nanomaterials can be released into workplace environment both through intentional manufacturing processes and accidental activities that occur during their production and use. Current evidence suggests that occupational exposure is mainly associated with handling, processing, and post-processing. A detailed analysis of 306 occupational exposure scenarios across 72 workplaces reported potential ENM exposure in 233 cases, with the highest incidents observed for carbon-based (83%), metal (73%), and nanoclay (100%) nanomaterials [20]. The study further identified material handling as the main source of exposure, where workers often came into contact with airborne agglomerates made up of nanoscale primary particles. Energy intensive industrial operations, such as thermal spraying, welding, grinding, and metal processing, are major sources of engineered nanomaterial emissions. These processes generate a large number of ultrafine particles, which are often rich in metals like nickel (Ni), chromium (Cr), and tungsten (W), and airborne particle concentrations often exceed 10^6 particles/cm^3. Studies have shown that nanoparticle concentrations in metal workshops are much higher compared to office environments, indicating that particle number

concentration is a better metric than mass concentration for measuring occupational nanoparticle exposure [19], [21].

Transport in occupational settings

The spatial distribution, persistence, and ultimate human exposure of engineered nanomaterials are determined by the dynamic transport processes they go through in work environments after being released. The predominant route is airborne transfer, especially for ultrafine particles that can stay suspended for long periods of time and have low settling velocities. Particle behaviour is largely influenced by aerosol dynamics, which include diffusion, coagulation, and agglomeration. According to studies, engineered nanomaterials are generally found in aggregates or agglomerates, which frequently range in size from tens of nanometers to several micrometers[22]. Agglomeration complicates exposure evaluation by affecting aerodynamic characteristics, deposition behaviour, and biological interactions. As evidenced by laser cutting operations, where insufficient airflow caused sluggish particle concentration decrease and longer exposure times, poor ventilation can result in prolonged airborne residence times. On the other hand, efficient engineering measures like gloveboxes, fume hoods, and local exhaust ventilation can keep particle concentrations close to background values. Nevertheless, short-term surges during particular jobs may still happen even in controlled surroundings, suggesting that ventilation is insufficient to completely [23] remove exposure. Another crucial factor to take into account is the spatial heterogeneity in particle distribution. Particle concentrations can differ considerably both vertically within the workspace and between near-field and far-field sites, according to studies. Exposure dynamics are further influenced by surface deposition and resuspension. Secondary exposure pathways can be created when particles that have been deposited on surfaces are re-entrained into the air due to human activity, cleaning, or mechanical disturbances. This is especially important in settings where there is a lot of manual labor or poor housekeeping procedures [24]. Transport behaviour is further influenced by interactions with co-pollutants and background aerosols. High background particle concentrations can occasionally encourage coagulation, which lowers the mobility of designed nanoparticles. Mixed particle systems, however, can change toxicological results and make exposure characterisation more difficult. In general, particle characteristics, ambient factors, and workplace behaviours interact to shape transport processes, which are highly dynamic and context-dependent. The degree to which released Engineered nanomaterials contribute to worker exposure is ultimately determined by these mechanisms [25].

Exposure routes

Inhalation, skin contact, and ingestion are the main ways that people are exposed to engineered nanomaterials at work; ocular and nasal exposure are less frequent but biologically significant routes. The physicochemical properties of engineered nanomaterials, workplace activities, engineering controls, and employee behaviour all affect each route's relative contribution. After internalization, engineered nanomaterials may move from the main site of exposure to distant organs via neural pathways or systemic circulation, raising the risk of multisystem toxicity[26], [27].

Inhalation

Since many industrial processes produce airborne nanoparticles and nanoaerosols, inhalation is commonly acknowledged as the primary route of occupational exposure. Because of their extremely small size, engineered nanomaterials easily get past the upper respiratory barriers and land in the alveolar region, where they may pass through the alveolar–capillary barrier and enter the bloodstream. Inhaled engineered nanomaterials can cause oxidative stress, inflammation, pulmonary fibrosis, and systemic toxicity, according to experimental and epidemiological data [28]. Patients with lung illnesses, especially idiopathic pulmonary fibrosis, have a high prevalence of occupational nanoparticle exposure, according to biomonitoring studies, which may indicate a link between long-term nanoparticle inhalation and respiratory disease. The significance of respiratory exposure in industrial contexts is shown by the fact that over 70% of inhaled ultrafine particles may lodge in the alveolar region in high-exposure jobs like metalworking and thermal spraying industries [29].

Dermal exposure

Direct contact with engineered nanomaterials or contaminated work surfaces during material handling, processing, or maintenance tasks causes dermal exposure [30]. While undamaged skin acts as an efficient barrier against the majority of nanoparticles, prolonged exposure, hair follicles, sweat glands, and damaged skin can all allow penetration. Dermal absorption is significantly influenced by elements such as particle size, surface chemistry, and skin integrity. As a result, using personal protective equipment insufficiently may raise the risk of systemic or localized exposure [31].

Ingestion

Intake of substances into the body through eating and drinking is generally considered a secondary exposure, and this mostly happens unintentionally through hand-to-mouth contact, eating or drinking in contaminated areas, or particles entering the digestive

tract from the respiratory pathway. Observational studies have shown that hand-to-mouth contact is quite common among workers, making it easy for nanoparticles accumulated on contaminated hands or workplace surfaces to enter the body, especially where cleaning measures are insufficient [32], [33].

Ocular and nasal exposure

Ocular and nasal exposure may potentially contribute to occupational uptake of engineered nanomaterials, albeit this is less often studied. Airborne nanoparticles can land on the surface of the eyes and then drain into the nasal cavity via the nasolacrimal duct, eventually reaching the gastrointestinal tract. Additionally, by moving along the olfactory and trigeminal nerves, nanoparticles deposited in the nasal cavity may avoid the blood–brain barrier and reach the central nervous system directly. By avoiding first-pass digestion, these exposure pathways may increase the bioavailability and toxicity of nanoparticles [34], [35].

In general, occupational exposure pathways are linked rather than separate. While resuspension of deposited particles prolongs breathing exposure, airborne nanoparticles can settle on working surfaces, raising the risk of skin contamination and eventual ingestion. The requirement for integrated exposure assessment and thorough occupational risk management is highlighted by the fact that the overall internal dose of engineered nanomaterials is determined by the combined influence of workplace conditions, material properties, engineering controls, and worker behaviour [36].

Physico-chemical properties of engineered nanomaterials that impact their uptake

Physico-chemical characteristics of engineered nanomaterials, which affect cellular absorption, biodistribution, persistence, and biological responses, play a major role in controlling their toxicity. Enhanced surface reactivity and a high surface area-to-volume ratio make engineered nanomaterials more biologically active than bulk materials. Particle size, shape, aspect ratio, surface charge, surface functionalization, chemical composition, solubility, crystallinity, and the capacity to produce reactive oxygen species are important factors that determine engineered nanomaterials toxicity. One important factor influencing biological interactions is particle size [37]. Compared to bigger particles, smaller engineered nanomaterials have stronger surface reactivity, deeper tissue penetration, and increased cellular absorption. Specifically, metal and metal oxide nanoparticles with diameters less than 20–30 nm frequently exhibit increased catalytic activity and ROS production, which increases their capacity to cause oxidative stress and cellular damage. Toxicological results are further influenced by particle shape. Certain carbon nanotubes and other high-aspect-ratio nanomaterials may avoid full macrophage phagocytosis [38], leading to fibrotic reactions, extended pulmonary retention, and persistent inflammation. Therefore, while identifying hazards and assessing occupational risk, both particle size and shape should be taken into account. In general, the chemical makeup of engineered nanomaterials cannot be used to predict their biological effects. To ensure the safe design and occupational use of engineered nanomaterials, thorough material characterisation and nanospecific risk assessment are essential. Toxicity, on the other hand, represents the combined influence of several physicochemical features [38], [39], [40].

The role of surface coating in engineered nanomaterials uptake and effects

Engineered nanomaterials quickly get coated in biological environments, mainly by proteins. Because of the high energetic adhesive forces near the surface, engineered nanomaterials can clump together and adsorb to the next available surface and other small molecules. It has been demonstrated that adding polyethylene glycol (PEG) to the surface of SWCNTs favorsuptake in tumors compared to normal organs, and adding PEG to poly (di-lactic acid-coated magnetic engineered nanomaterials increased their uptake by macrophages. To prevent engineered nanomaterials aggregation and/or affect their absorption and cellular effects [41], commercial providers and researchers frequently apply a surface coating. Mucus is produced by cells lining the airways. Pulmonary type II alveolar cells release surfactants (a mixture of 90% phospholipids and lung surfactant-speci fic proteins). Lung surfactants incorporate engineered nanomaterials. Mucus, which is released by goblet cells in the respiratory tract, eye, nasal cavity, stomach, and intes tine, entraps engineered nanomaterials. All of these surface coatings on engineered nanomaterials would be expected to impact their uptake and effects [42]

Engineered nanomaterials uptake from the initial site of exposure

Culture cells and other in vitro systems have been used to study engineered nanomaterials -induced effects and their mechanisms of action. These systems, however, are unable to simulate the intricacies of the entire organism, such as the restriction of uptake caused by barriers like the skin and first-pass metabolism, opsonization, metabolism that can either activate or inactivate a substrate, translocation to distant sites, activation of homeostatic defences, or inflammatory processes that release cytokines and other factors that can act at distant sites from their release [43], [44]. In order to address engineered nanomaterials absorption and translocation, this review mainly uses instances of

whole-animal research. Health impacts of airborne particles, particularly PM10 (thoracic fraction), PM2.5 (respirable fraction), PM1, and ultrafine particles (PM0.1), which are ≤ 10, 2.5, 1, and 0.1 μm (100 nm), respectively, have drawn a lot of attention. Due to their strong diffusion capabilities, a large proportion of one- to five-nm air-suspended engineered nanomaterials that enter the lungs are expected to deposit in the mucus-lined upper airways (tracheobronchial area) rather than the alveoli. However, about 45% of 10-nm, 50% of 20-nm, and 25% of 100-nm engineered nanomaterials settle in the alveoli. Exercise increases deposition. Alveolar particle deposition is reduced and tracheobronchial is increased in chronic obstructive pulmonary disease. One special mechanism for the direct delivery of engineered nanomaterials from the outside world to the central nervous system (CNS) is the olfactory pathway [26], [45]. After being deposited in the nasal cavity, olfactory sensory neurons may internalize the nanoparticles and use retrograde axonal transport to carry them to the olfactory bulb. The poliovirus (~30 nm) and colloidal silver-coated gold nanoparticles (~50 nm) have both been shown to exhibit this process. Similarly, within 1–7 days following exposure, about 35 nm ^13C-labeled nanoparticles were found in the olfactory bulb; lower amounts were later dispersed throughout the cerebrum and cerebellum. The olfactory bulb had a 3.5-fold increase in Mn accumulation following inhalation exposure to ~30 nm manganese (Mn) nanoparticle agglomerates, while several other brain regions showed substantial but smaller increases [46]. The distribution of Mn outside of the olfactory bulb raises the possibility that other transport mechanisms, such as cerebrospinal fluid circulation and translocation across the blood–brain barrier, may potentially play a role in the entry of nanoparticles into the brain. The olfactory route is a significant and frequently disregarded conduit for the uptake of minute amounts of engineered nanomaterials into the central nervous system since the nose cavity is the sole anatomical location where the nervous system is directly exposed to the external environment. Diffusion is the main process by which engineered nanomaterials are absorbed by the skin via intercellular, intracellular, and follicular channels. The main barrier is the stratum corneum, which permits tiny (<500 Da), lipophilic molecules to penetrate preferentially [47]. When engineered nanomaterials enter the stratum granulosum, they cause keratinocytes to release pro-inflammatory cytokines; when they enter the stratum spinosum, they activate Langerhans cells, which in turn cause immunological reactions. Engineered nanomaterials may reach the lymphatic and circulatory systems after passing through the epidermal barrier. According to available data, engineered nanomaterials penetration is often limited by intact human skin; however, uptake may be improved by hair follicles, injured skin, UV exposure, mechanical stretching or flexing, and intradermal delivery. While titanium dioxide and zinc oxide nanoparticles used in sunscreens exhibit little penetration through healthy skin, some engineered nanomaterials, such as quantum dots, have been found in the dermis and lymphatic system under these circumstances [48]. To lessen the toxicity caused by reactive oxygen species, surface modification (such as silica or alumina coatings) is frequently used. Further long-term safety studies are necessary because several engineered nanomaterials can cause local oxidative stress and inflammatory reactions, despite the apparent restricted systemic absorption after topical contact. Engineered nanomaterials are absorbed by the gastrointestinal tract via diffusion through the mucus layer, contact with enterocytes and microfold cells, and cellular translocation. Peyer's patches and other areas with reduced mucin concentration and poor epithelial integrity have higher absorption. According to experimental research, engineered nanomaterials can enter the bloodstream and build up in organs like the spleen, liver, blood, and bone marrow. Smaller nanoparticles are more bioavailable than bigger ones [49]. Urinary elimination seems to be modest, despite reports of biliary excretion. While there is still little data on buccal and sublingual absorption, current evidence suggests that GI absorption of engineered nanomaterials is size-dependent, with uptake increasing as particle size decreases. Engineered nanomaterials that are airborne, purposefully placed close to the eye (such as cosmetics), inadvertently sprayed onto the eye, or transferred from the hands during eye rubbing-which was found to happen in 37% of 124 adults every hour-can all cause ocular exposure. This method of exposure may cause engineered nanomaterials to be absorbed into the eye through the cornea or to leak into the nasal cavity through the nasolacrimal duct from the eye socket. This pathway has been mostly disregarded in investigations of engineered nanomaterials exposure, with the exception of one that discovered uptake of a polymer engineered nanomaterials into conjunctival and corneal cells [50].

The effects of engineered nanomaterials exposure on target organs

According to the dose-response principle, the intrinsic toxicity of engineered nanomaterials as well as the amount, duration, and mode of exposure determine the health risk. Since contemporary analytical methods can detect nanoparticles at quantities much below lethal limits, the presence of engineered nanomaterials in biological tissues does not always imply detrimental health impacts. Furthermore, before firm conclusions can be made, individual experimental results must be independently validated. The physicochemical characteristics of nanoparticles can change biological

reactions, therefore while toxicity data from ultrafine particles and bulk materials offer valuable insights, they are unable to accurately predict engineered nanomaterials toxicity. While highly soluble engineered nanomaterials like ZnO may largely cause toxicity through the release of metal ions, there are situations in which engineered nanomaterials are more poisonous than their dissolved components (such as cadmium-containing quantum dots). Therefore, rather of extrapolating from bulk materials or particular chemical ingredients, engineered nanomaterials risk evaluation should be based on properties unique to nanoparticles (Figure 4) [51], [52].

Pulmonary toxicity of engineered nanomaterials

Inhalation is the most frequent occupational and environmental exposure route; the respiratory system is thought to be the main target organ for exposure to engineered nanomaterials. After being deposited in the respiratory tract, engineered nanomaterials can interact with local immune cells, alveolar macrophages, endothelial cells, and epithelial cells while avoiding mucociliary clearance and penetrating the alveolar epithelium [53]. Their hazardous potential is increased by their small size, vast surface area, high aspect ratio, and surface reactivity, which encourage deep lung deposition and protracted retention. Engineered nanomaterials have been shown to cause oxidative stress, inflammation, genotoxicity, fibrosis, and pulmonary dysfunction in experiments using inhalation, intratracheal instillation, and in vitro pulmonary cell models. Rats exposed to Degussa P25 titanium dioxide nanoparticles for two years developed lung cancers, according to one of the first investigations on chronic inhalation [54]. In a similar vein, single-walled carbon nanotubes (SWCNTs) with residual transition metal catalysts caused more severe lung toxicity than ultrafine carbon black or quartz, as seen by epithelioid granulomas, chronic inflammation, and interstitial fibrosis. Because of their bigger diameter, higher aspect ratio, and greater ability to trigger innate and adaptive immunological responses, multi-walled carbon nanotubes (MWCNTs) typically show more pulmonary and systemic toxicity than SWCNTs, according to numerous animal studies [55]. Excessive production of reactive oxygen species (ROS), which causes oxidative damage to lipids, proteins, and DNA, is the main mechanism behind ENM-induced pulmonary toxicity. Pro-inflammatory cytokines including TNF-α, IL-1β, IL-6, IL-8, and TGF-β are expressed more when oxidative stress activates redox-sensitive signalling pathways such NF-κB, MAPK, and Nrf2. Extracellular matrix deposition, fibroblast activation, epithelial-mesenchymal transition (EMT), and finally lung fibrosis is all facilitated by persistent inflammation. Furthermore, engineered nanomaterials can damage antioxidant defence systems (GSH, SOD, CAT, and GPx), interfere with mitochondrial function, and trigger apoptotic pathways via caspase-dependent mechanisms. Carbon nanotubes, titanium dioxide (TiO_2), cerium oxide (CeO_2), zinc oxide (ZnO), silica (SiO_2), and other metal oxide nanoparticles have been shown in numerous studies to cause ROS overproduction, lipid peroxidation, DNA strand breaks, micronucleus formation, chromosomal instability, cell-cycle arrest, mitochondrial dysfunction, apoptosis, and decreased cell viability. These results suggest that engineered nanomaterials have a considerable potential for cytotoxicity and genotoxicity, which could be a factor in long-term respiratory disorders [56]. Due to their asbestos-like toxicity, high-aspect-ratio carbon nanotubes have also garnered a lot of interest. Granulomatous inflammation, mesothelial damage, and mesothelioma-like lesions were induced by intraperitoneal delivery of long, rigid MWCNTs, which closely resembled the pathological effects of crocidolite asbestos. Fiber length, stiffness, aspect ratio, and biopersistence all have a substantial correlation with toxicity. Variability between studies is caused by variations in particle size, aggregation state, surface functionalization, coating, crystallinity, dose, exposure time, and experimental exposure techniques, despite strong evidence of pulmonary toxicity. As a result, intratracheal instillation data could not always reflect human inhalation exposures that are realistic. However, recent research clearly shows that pulmonary exposure to engineered nanomaterials can cause oxidative stress, chronic inflammation, fibrosis, immune dysregulation, and genotoxicity. This emphasizes the significance of thorough long-term inhalation studies and risk assessment specific to nanoparticles for occupational and environmental health [57], [58].

Neuro-toxicity of engineered nanomaterials

Potential of metal oxide engineered nanomaterials to disrupt neuronal homeostasis following systemic exposure has raised concerns about their neurotoxicity. These nanoparticles can interact with glial cells and neural tissues after being absorbed, starting a series of cellular and molecular processes that impair regular brain function. Murine microglial cells exposed to TiO_2 nanoparticles (70% anatase: 30% rutile; primary particle size ~30 nm) significantly increased the extracellular generation of hydrogen peroxide and superoxide anions, accompanied by mitochondrial membrane hyperpolarization, indicating mitochondrial dysfunction and disruption of cellular redox balance, according to in vitro studies [59]. Reactive oxygen species and inflammatory mediators are then released by activated microglia, increasing oxidative damage in the neuronal microenvironment. Overproduction of reactive

oxygen species can oxidize proteins, nucleic acids, and membrane lipids, ultimately compromising the integrity and functionality of neurons. The neurotoxic potential of metal oxide engineered nanomaterials is further supported by in vivo evidence. In rats, intravenous administration of cerium oxide (CeO_2) nanoparticles significantly changed cerebral oxidative stress biomarkers and disrupted the activities of endogenous antioxidant enzymes, indicating disruption of the brain's antioxidant defence system. These changes in redox equilibrium may make neurons more vulnerable to oxidative damage, mitochondrial dysfunction, and apoptotic cell death [60].

Other organstoxicity of engineered nanomaterials

Dermal toxicity- Engineered nanomaterials are widely used in wound dressings, cosmetics, personal care items, textiles, and biomedical formulations, their dermato-toxicity has drawn more attention. While most engineered nanomaterials are effectively prevented from penetrating intact human skin, prolonged exposure, damaged skin, UV radiation, or mechanical stress can increase the penetration of nanoparticles into deeper layers of the skin. After internalization, engineered nanomaterials can interact with immune cells, fibroblasts, and keratinocytes to cause cellular malfunction and local inflammatory reactions [61]. Silver nanoparticles have been shown in experiments to dramatically lower the survival of human epidermal keratinocytes, showing direct cytotoxic effects on the epidermis. Excessive production of reactive oxygen species, mitochondrial malfunction, lipid peroxidation, DNA damage, and activation of apoptotic signalling pathways are some of the underlying processes. Furthermore, pro-inflammatory cytokines and chemokines are released in response to engineered nanomaterials-induced oxidative stress, which may cause skin irritation, inflammation, delayed wound healing, and damage to the integrity of the epidermal barrier. Similar dermato-toxic reactions have also been documented for a number of metal oxide engineered nanomaterials, especially under situations that encourage the production of reactive oxygen species, like UV exposure [31]. When taken as a whole, these results show that dermal exposure to engineered nanomaterials can cause cytotoxicity, oxidative stress, inflammatory reactions, and compromised skin homeostasis. This underscores the need for a thorough assessment of their long-term dermatological safety, particularly for products meant for frequent or long-term skin application [27].

Cardiovascular toxicity- engineered nanomaterials can interact with cardiac tissues and vascular endothelial cells by entering the systemic circulation through ingestion, inhalation, skin penetration, or intravenous delivery. Engineered nanomaterials cause endothelial dysfunction, oxidative stress, vascular inflammation, thrombosis, and increased vascular permeability, according to numerous studies [62]. Nitric oxide (NO) bioavailability is reduced by increased ROS generation, which impairs endothelial activation and vasodilation. Activation of inflammatory signalling pathways, including NF-κB and MAPK, stimulates the expression of adhesion molecules (ICAM-1 and VCAM-1) and pro-inflammatory cytokines, enabling leukocyte recruitment and vascular damage. Certain nanoparticles have also been associated with platelet activation, coagulation problems, cardiac oxidative stress, arrhythmias, and myocardial damage, suggesting an increased risk of cardiovascular disease following chronic exposure [63].

Hepatotoxicity- The liver plays a crucial role in systemic filtration and metabolism, making it a key location of ENM accumulation. Kupffer cells and hepatocytes effectively absorb ENMs after systemic distribution, where they cause oxidative stress, inflammatory reactions, and mitochondrial dysfunction. Hepatocellular damage is caused by increased ROS generation, which also activates apoptotic pathways, causes lipid peroxidation, protein oxidation, and DNA damage [64]. Elevated serum biomarkers of liver damage, such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and γ-glutamyl transferase (γ-GT), along with hepatic inflammation, steatosis, fibrosis, and histopathological changes, have been reported in experimental studies. Long-term exposure may affect metabolic balance and liver detoxification [65].

Nephrotoxicity- The renal system filters or removes a large number of circulating nanoparticles, making the kidneys another crucial target organ. Engineered nanomaterials can build up in tubular and glomerular epithelial cells, causing inflammation, apoptosis, oxidative stress, and mitochondrial malfunction. Experimental data shows elevated blood urea nitrogen (BUN), uric acid, and creatinine levels in addition to tubular degeneration, glomerular damage, and reduced renal filtration. Long-term exposure to disruption of renal antioxidant defence systems increases vulnerability to oxidative damage and leads to progressive renal failure [66].

Immunotoxicity- Depending on their physicochemical properties, engineered nanomaterials can influence both innate and adaptive immune responses. TNF-α, IL-1β, IL-6, and IL-8 are released as a result of engineered nanomaterials stimulating ROS generation and activating inflammatory pathways after being taken up by neutrophils, dendritic cells, and macrophages. Persistent

inflammation, granuloma development, hypersensitivity reactions, and tissue damage can all be facilitated by chronic immune activation [67]. On the other hand, some engineered nanomaterials inhibit the growth and activity of immune cells, which results in immunosuppression and diminished host defence. As a result, depending on particle size, composition, surface chemistry, and exposure circumstances, ENMs can have both immunostimulatory and immunosuppressive effects [68].

Reproductive toxicity- Numerous engineered nanomaterials have the ability to pass across physiological barriers, including as the placental and blood-testis barriers, which can impact fetal development and reproductive organs. Research on animals has shown that exposure to engineered nanomaterials affects ovarian follicular development, testosterone synthesis, spermatogenesis, sperm motility, and reproductive hormone balance[69]. Fetal oxidative stress, growth retardation, developmental defects, and altered organogenesis may result from placental transfer of nanoparticles during pregnancy. Within reproductive organs, oxidative stress, inflammation, mitochondrial malfunction, DNA damage, and apoptosis are the main culprits [70].

Genotoxicity- Many engineered nanomaterials have the potential to be genotoxic, either directly through contact with DNA or indirectly through oxidative damage caused by ROS. There have been reports of chromosomal abnormalities, micronucleus production, oxidative DNA lesions, DNA strand breakage, and poor DNA repair in both in vitro and in vivo settings. After prolonged exposure, persistent genomic instability may change gene expression, interfere with regular cell-cycle regulation, and raise the risk of carcinogenesis [71]. Oxidative stress is thought to be the primary mechanism driving engineered nanomaterials-induced toxicity, despite the fact that the toxicity of engineered nanomaterials varies with particle size, shape, surface charge, chemical composition, crystallinity, aggregation state, surface functionalization, dose, and exposure route. Inflammatory signalling, mitochondrial malfunction, apoptosis, fibrosis, and DNA damage are all triggered by excessive ROS formation, which eventually contributes to toxicity in the lungs, heart, liver, kidneys, brain, skin, immune system, reproductive system, and development. Therefore, before designed nanomaterials are widely used in biomedicine and industry, thorough toxicological evaluation and risk assessment specific to nanoparticles are crucial [72], [73].

Dose response assessment of engineered nanomaterials

When assessing the toxicological consequences of engineered nanomaterials, dose-response analysis is crucial. In contrast to conventional chemicals, engineered nanomaterials toxicity is frequently predicted more correctly by particle surface area, particle number, and surface reactivity than by mass or concentration alone. Several studies have shown that surface area has a stronger correlation with oxidative stress, cellular toxicity, and inflammatory responses than particle mass. For instance, when exposure was standardized to total particle surface area, the dose-response relationships for neutrophil infiltration, macrophage activation, and reactive oxygen species generation generated by TiO_2, silica, and carbon-based engineered nanomaterials were improved [74].

In spite of this, the majority of toxicological studies still describe exposure in terms of dose or concentration, and they typically show concentration-dependent increases in tissue accumulation, oxidative stress, inflammation, cytotoxicity, and nanoparticle uptake. However, due to particle aggregation or cellular saturation, these reactions could plateau at higher doses. Variations in particle size, shape, surface chemistry, aggregation state, exposure route, and exposure length further confound the interpretation of dose-response data. The majority of studies that are currently available have used acute, high-dose exposures, which are useful for identifying hazards but might not be a good representation of actual human exposure situations. In order to increase the accuracy of engineered nanomaterials risk assessment and establish biologically realistic dose-response correlations, long-term and repeated low-dose studies are necessary [75], [76].

Clearance, translocation and persistence of engineered nanomaterials

Based on their size, shape, solubility, surface chemistry, and biopersistence, engineered nanomaterials engineered nanomaterials go through clearance, systemic translocation, and tissue retention after exposure. While insoluble engineered nanomaterials are mostly cleared by macrophage-mediated phagocytosis in the alveoli and mucociliary clearance in the upper respiratory tract, soluble engineered nanomaterials easily dissolve and are removed through the blood and lymphatic systems [77]. Poorly degradable engineered nanomaterials, on the other hand, might linger in macrophages for extended periods of time, leading to sluggish clearance and persistent cellular reactions. Carbon nanotubes (CNTs) and other high-aspect-ratio nanomaterials generate frustrated phagocytosis, in which macrophages are unable to fully swallow the particles, resulting in ineffective clearance. Reactive oxygen species,

inflammatory cytokines, and chemokines are continuously produced as a result of this process, which promotes lung fibrosis, granuloma development, and chronic inflammation. Similar reactions to several high-aspect-ratio metal oxide nanoparticles have also been documented, highlighting the significance of nanoparticle shape in assessing toxicity [78]. A portion of engineered nanomaterials may move from the primary exposure site to secondary organs after ingestion, inhalation, cutaneous exposure, or systemic injection. Experimental research has shown accumulation in the liver, spleen, kidneys, lymph nodes, heart, brain, and bone marrow. Reticuloendothelial system cells, such as Kupffer cells, splenic macrophages, and microglia, are primarily responsible for uptake. In general, the systemic distribution of smaller nanoparticles is higher than that of bigger particles. Concerns about neurotoxicity, reproductive toxicity, and developmental toxicity are raised by the fact that certain engineered nanomaterials can also pass across biological barriers such the placental and blood–brain barriers [79]. One of the key factors influencing long-term engineered nanomaterials toxicity is thought to be biopersistence. Many metal oxide and carbon-based nanoparticles can stay in tissues for weeks, months, or even years following exposure due to their extreme resistance to degradation. Their extended retention increases the risk of delayed or long-term negative health effects by sustaining oxidative stress, inflammatory reactions, fibrosis, and tissue remodeling. Therefore, it is important to include clearance efficiency, systemic translocation, and persistence in the toxicological analysis and risk assessment of manufactured nanomaterials [80].

Risk assessment of engineered nanomaterials

Risk assessment of engineered nanomaterials is more complex than that of conventional chemicals because their small size, high surface area, and unique physicochemical properties influence exposure, toxicokinetics, and biological interactions. Therefore, nanomaterial-specific frameworks have been developed to improve hazard identification, exposure assessment, and risk characterization. The combination of exposure and risk determines engineered nanomaterials risk [81]. To enhance risk estimation under ambiguity, sophisticated techniques like risk banding and the Pythagorean Fuzzy Health Risk Assessment (PFHRA) incorporate material characteristics and exposure circumstances. These models show that while less hazardous elements can become dangerous at high exposure levels, extremely hazardous engineered nanomaterials may be low risk under controlled exposure. Bayesian Networks (BNs) and Weight-of-Evidence (WoE) techniques use physicochemical, toxicological, and exposure data to forecast engineered nanomaterials dangers. The BNs have stronger prediction potential by including causal linkages, whereas WoE offers clear evidence integration but leans more heavily on expert judgment and data quality. The QSAR and Nano-QSAR models estimate engineered nanomaterials toxicity using physicochemical parameters such as particle size, surface charge, and chemical composition [82]. These in silico technologies assist quick screening and safer nanomaterial creation, while their regulatory use remains constrained by lack standardized datasets. By comparing engineered nanomaterials with comparable physicochemical properties, grouping and read-across techniques estimate toxicity and eliminate the need for intensive experimental testing. Soluble, passive, active, and high-aspect-ratio nanomaterials are categorized using frameworks like DF4nanoGrouping. However, variations in particle size, coating, and surface chemistry can significantly impact toxicity, reducing the accuracy of predictions. Control banding (CB) is a useful screening method that recommends suitable workplace control measures by combining exposure and hazard data. Common tools include CB Nanotool, Stoffenmanager Nano, NanoSafer, and ANSES. Although beneficial for occupational risk management, these strategies are essentially qualitative and have little regulatory relevance [83]. While encouraging safe-by-design practices, life-cycle frameworks like GUIDEnano, SUND, NANoREG, and LICARA nanoSCAN assess engineered nanomaterials risks during production, use, and disposal. However, the absence of large-scale validation, uncertainty in environmental alterations, and the scarcity of long-term exposure data limit their application. Modern engineered nanomaterials risk evaluation integrates toxicokinetic modeling by evaluating absorption, distribution, accumulation, and persistence. Unlike conventional chemicals, engineered nanomaterials exposure is best characterized using multiple dose metrics, including mass, particle number, and surface area, to more accurately predict biological effects and internal exposure [84], [85].

Engineering control for occupational exposure to engineered nanomaterials

The main and most successful method for reducing occupational exposure to engineered nanomaterials is engineering controls. Because they prevent or lessen nanoparticle release at its source, these techniques are favored over administrative controls and personal protective equipment (PPE) in the hierarchy of exposure control. Process modification, source confinement, negative-pressure enclosures, worker isolation, robotic handling, designated work spaces, and local exhaust ventilation (LEV) are examples of common engineering controls. Since most engineered

nanomaterials lack specified occupational exposure limits, putting these controls in place is thought to be the best way to safeguard employees [86]. To stop airborne nanoparticles from escaping during synthesis and handling, process containment is frequently used. Engineered nanomaterials s are successfully isolated from workers and their surroundings by devices including glove boxes, chemical fume hoods, biological safety cabinets (BSCs), and externally ventilated enclosure systems. According to experimental research, properly constructed fume hoods effectively reduce aerosol dispersion into the breathing zone by containing nanoparticles produced during the handling of fullerenes, carbon nanotubes (CNTs), silver nanoparticles, and alumina nanoparticles [87]. Because they maintain steady airflow and lessen turbulence, constant-velocity fume hoods offer better containment than conventional and bypass hoods. Containment efficiency is significantly increased by optimal hood face velocities of roughly 0.4–0.5 m s^{-1} (80–100 ft min^{-1}), suitable sash height, cautious operator movement, and placing materials well inside the hood. During laboratory-scale nanoparticle manipulation, biological safety cabinets with HEPA filtration, low-turbulence ventilation, and enclosed workplaces offer extra protection [88].

Another crucial technical control for lowering airborne engineered nanomaterial concentrations is LEV. High-efficiency particulate air (HEPA) filters installed in well-designed LEV systems effectively catch nanoparticles before they enter the worker's breathing zone. By pushing polluted air higher and away from employees, air-displacement ventilation systems further enhance the quality of the air at work. Multi-walled carbon nanotube (MWCNT) concentrations in the air can be lowered to undetectable levels by enclosing processing equipment and using LEV, according to industrial research. Similarly, during reactor cleanout, portable LEV systems have decreased the release of silver, cobalt, and manganese nanoparticles by 75–96%, demonstrating their efficacy in limiting occupational exposure [89].

Engineering controls' effectiveness is influenced by both operational procedures and equipment design. While good ventilation design, routine maintenance, reduced hood clutter, and regulated worker motions greatly improve containment, poorly built hoods with little airflow or excessive turbulence may increase nanoparticle release. Workplace nanosafety programs should be built around well-designed engineering controls, especially process containment and HEPA-filtered local exhaust ventilation, which offer the most dependable and efficient ways to lower occupational exposure to engineered nanomaterials [90].

Figure 1: Exposure of engineered nanomaterials.

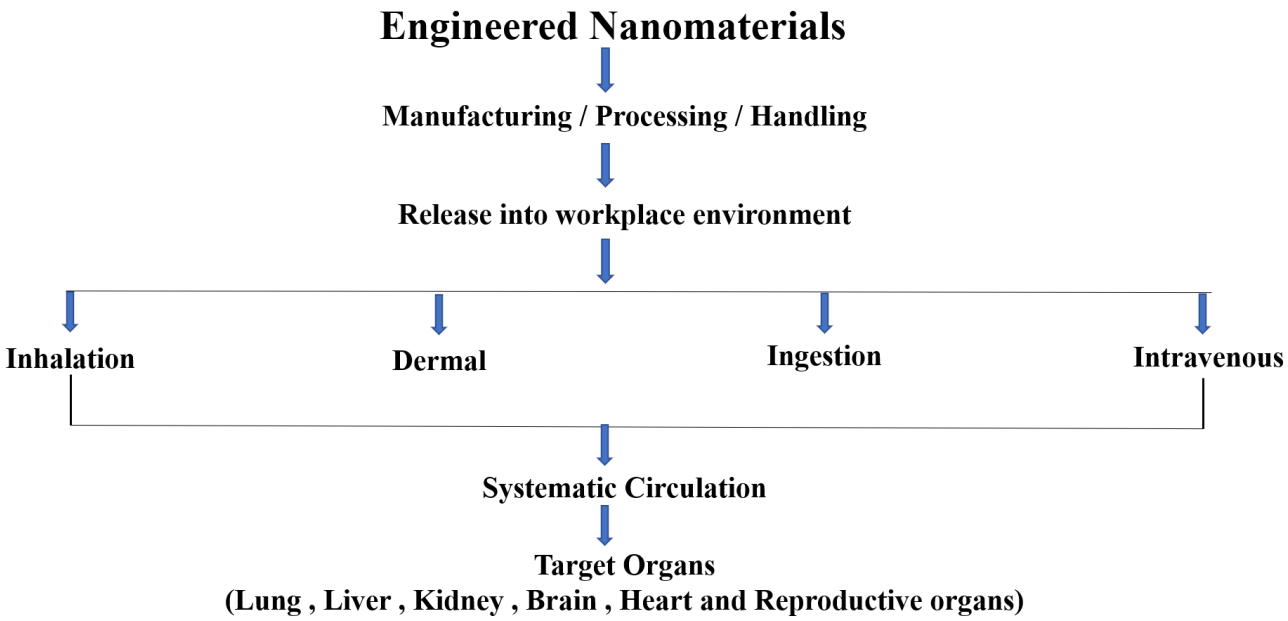


Figure 2: Types of occupational hazards.

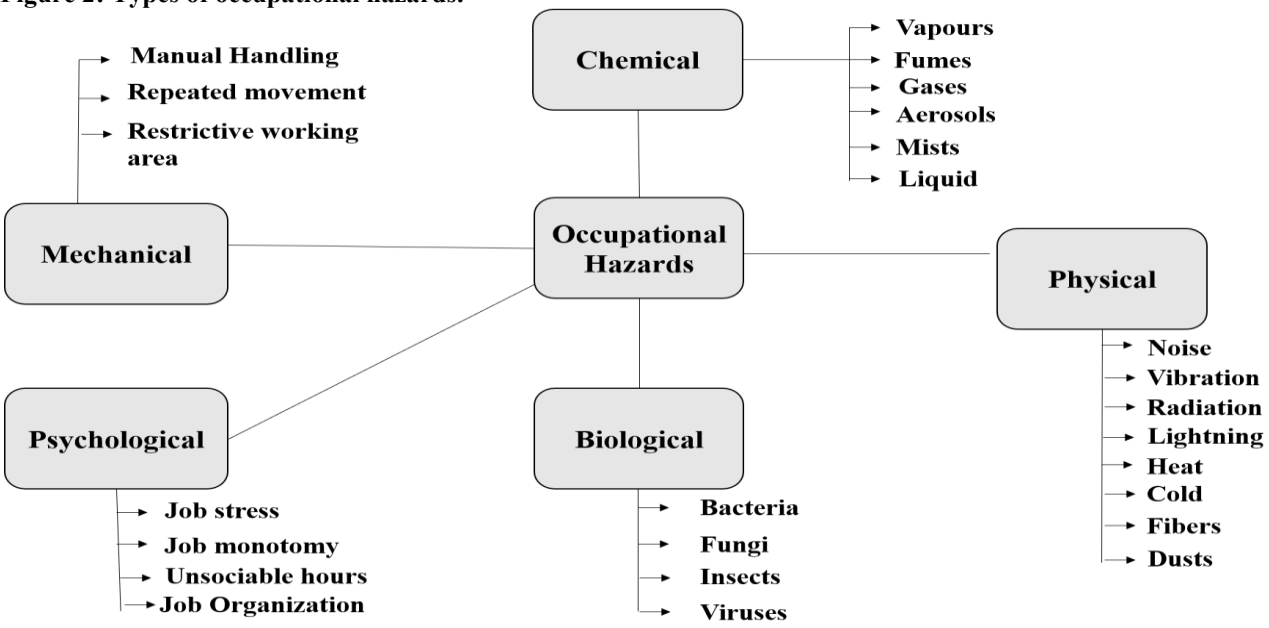
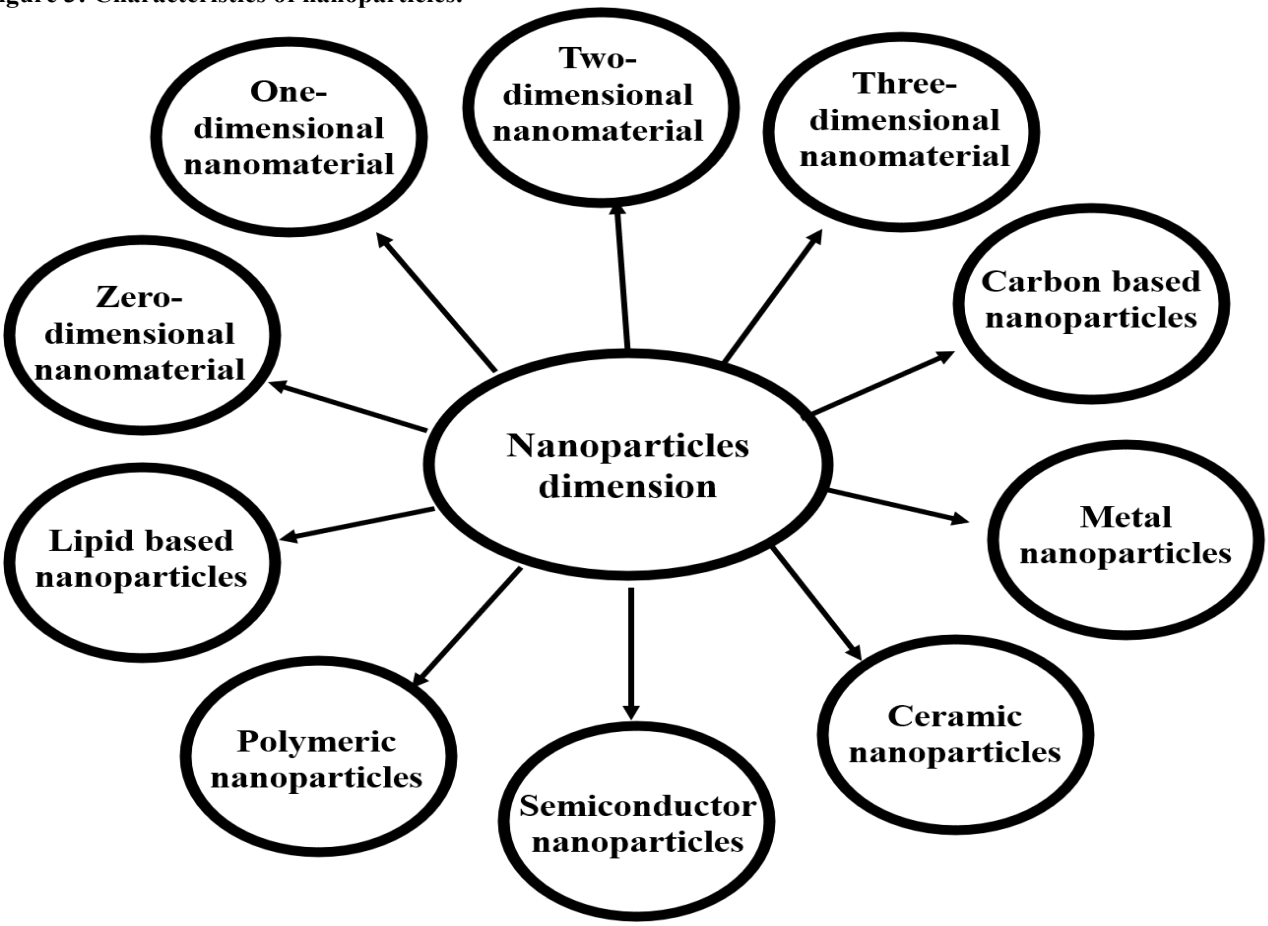


Figure 3: Characteristics of nanoparticles.



Administrative controls for reducing engineered nanomaterials

Administrative controls are a crucial backup plan for reducing occupational exposure to engineered nanomaterials (ENMs) when engineering controls are unable to completely remove exposure [91]. Instead, then removing the danger directly, these controls are made up of workplace practices, rules, and procedures intended to lessen the frequency, duration, and intensity of worker exposure. Implementing hygiene plans specific to nanomaterials, creating and enforcing standard operating procedures (SOPs), conducting frequent competency evaluations and worker training, limiting the length of exposure, rotating jobs, controlling access to ENM handling areas, and properly labeling and storing nanomaterials are all examples of effective administrative measures [92]. While dry sweeping and compressed-air cleaning should be avoided, good housekeeping techniques like regular wet cleaning or HEPA-filter vacuuming are advised to prevent nanoparticle accumulation and secondary aerosolization. Early identification of occupational exposure and possible health impacts is further supported by routine medical exams, biological surveillance, and workplace monitoring. Studies have demonstrated the efficacy of administrative interventions by showing that thorough cleaning and better housekeeping considerably lower airborne nanoparticle concentrations in nanocomposite production facilities. Administrative controls are essential to comprehensive occupational nanosafety systems, especially when combined with engineering controls and suitable personal protective equipment (PPE), even though they are typically less effective than engineering controls [93].

Personal protective equipment against engineered nanomaterials

When combined with engineering and administrative controls, personal protective equipment (PPE) serves as the final line of defence against occupational exposure to engineered nanomaterials. Respirators, gloves, and protective clothes are examples of PPE that lessen skin and inhalation exposure when handling engineered nanomaterial [94].

Respirators- When applied correctly, European FFP2 and FFP3 respirators and NIOSH-certified N95, N99, N100, and P100 respirators effectively filter out airborne nanoparticles. Particle size, airflow velocity, electrostatic interactions, and respirator fit all effect filtration effectiveness; particles between 40 and 50 nm in size have the highest penetration (most penetrating particle size, or MPPS). Fit testing and appropriate respirator use are crucial for successful nanoparticle management since increased breathing rates and inadequate face seals greatly diminish protection [95].

Protective clothing- Wearing protective clothing reduces cutaneous contamination and stops engineered nanomaterials from spreading outside of the workplace. Compared to woven materials like cotton or polyester, nonwoven textiles, especially Tyvek, offer significantly higher resistance to nanoparticle penetration. Choosing the right lab attire is crucial to lowering environmental pollution and worker exposure. Gloves- While stretching, wear, or microscopic flaws may enhance permeability, nitrile, latex, and neoprene gloves are generally good barriers against engineered nanomaterials. Because of their exceptional durability and chemical resistance, nitrile gloves are frequently advised. Although double gloving has not reliably shown decreased nanoparticle penetration, it may offer extra protection against unintentional contamination [95], [96].

Biological monitoring and medical surveillance- The goal of secondary prevention is to identify early health impacts in workers handling engineered nanomaterials through biological monitoring and medical surveillance. To assess workplace safety and the efficacy of control measures, occupational health surveillance combines exposure assessment, hazard monitoring, and recurring medical exams. However, surveillance should be focused on established workplace health programs and overall occupational risk rather than engineered nanomaterials-specific indicators alone, as there is currently insufficient data to support routine nanoparticle-specific medical screening [97], [98].

Therapeutic and environmental remediations

The health concerns associated with engineered nanomaterials, especially metal- and metal oxide-based nanoparticles, may be further mitigated by environmental cleanup and therapeutic interventions in addition to engineering controls, administrative measures, and personal protective equipment. Using plants to eliminate, stabilize, or detoxify metal pollutants from contaminated soil and water is an economical and environmentally benign method known as phytoremediation [99]. High capacities for accumulating metals like cadmium, lead, arsenic, chromium, nickel, zinc, and copper have been shown by hyperaccumulator plants like Brassica juncea (Indian mustard), Helianthus annuus (sunflower), Vetiveriazizanioides (vetiver grass), Pteris vittata (Chinese brake fern), Salix spp. (willow), Populus spp. (poplar), hemedismus indicus, curcumin, ellagic acid, and caffeic acid. When metal-based engineered nanomaterials are released during production, usage, or disposal, these plants may help lessen environmental pollution [100].

Chelation therapy may be a helpful medical intervention for people who have been shown to have been exposed systemically to hazardous metal ions

emitted from ENMs. Calcium disodium EDTA ($CaNa_2EDTA$), dimercaptosuccinic acid (DMSA; succimer), 2,3-dimercapto-1-propanesulfonic acid (DMPS), dimercaprol (BAL), deferoxamine (DFO), and deferasirox are examples of chelating drugs that bind free metal ions and help eliminate them by renal or biliary excretion. Lead, arsenic, mercury, iron, and aluminum toxicity can be effectively treated with these medications [101]. However, because many nanoparticles are poorly soluble, biopersistent, and maintained within tissues, their effectiveness against intact engineered nanomaterials is still restricted. As a result, chelation therapy should only be used when engineered nanomaterials release bioavailable hazardous metal ions and under proper medical care [102].

In general, chelation therapy and phytoremediation are complementary methods for controlling environmental pollution and metal-induced toxicity linked to engineered nanomaterials. However, the best way to reduce occupational and environmental dangers related to manufactured nanomaterials is still to prevent exposure through engineering controls, administrative controls, and suitable personal protective equipment.

Current challenges

The extensive use of engineered nanomaterials engineered nanomaterials in consumer, commercial, and industrial products has made risk assessment, regulatory oversight, and exposure assessment extremely difficult. Workplace practices, production procedures, and the characteristics of nanomaterials all have a major role in the wide range of occupational exposure. According to studies, engineered nanomaterial emissions are typically task-specific, with material handling, maintenance, cleaning, and post-processing activities-rather than enclosed production-releasing the most. Accurate exposure characterisation is challenging since ventilation efficiency, process automation, and engineering controls all affect exposure levels. The various modes of exposure, including as inhalation, cutaneous absorption, and accidental ingestion, present another significant obstacle [103]. The predominant occupational exposure route is still inhalation, especially for ultrafine particles (less than 100 nm), whereas secondary exposure is caused by hand-to-mouth transmission and skin contact. It is still challenging to distinguish manufactured nanoparticles from incidental or naturally occurring ultrafine particles produced by combustion or industrial processes, which limits source identification and accurate exposure assessment. Inadequate long-term exposure studies, a lack of standardized testing procedures, and a dearth of toxicological data further complicate the risk evaluation of engineered nanomaterials. Although hazard prediction has improved because to techniques like control banding, Bayesian network models, weight-of-evidence analysis, Nano-QSAR, and read-across methods, its dependability is still restricted by data quality, model uncertainty, and a lack of regulatory validation. Additionally, during their life cycle, engineered nanomaterials experience aging, surface modification, aggregation, and dissolution, which changes their physicochemical characteristics, bioavailability, and toxicity-all of which are frequently missed by traditional risk assessment techniques [104]. Harmonization of regulations continues to be a significant challenge. Many nations still regulate ENMs under traditional chemical laws, despite the European Union's introduction of nanoform-specific regulations and life-cycle considerations. As a result, the majority of engineered nanomaterials currently lack globally recognized testing methodologies, validated exposure measures, and regulated occupational exposure limits. Furthermore, use-phase, environmental release, recycling, and end-of-life disposal are still not sufficiently addressed in existing regulatory studies, which mainly concentrate on exposure during the production stage. Overall, addressing these challenges requires standardized exposure monitoring, harmonized international regulations, validated predictive models, comprehensive life-cycle assessments, and high-quality long-term toxicological and epidemiological data to support safe development and responsible use of engineered nanomaterials [105].

CONCLUSION

Engineered nanomaterials have transformed numerous industrial and technological sectors; however, their widespread use has raised significant occupational health concerns. Their small size, high surface area, and unique physicochemical properties influence absorption, biodistribution, persistence, and biological interactions, making conventional risk assessment approaches insufficient. Experimental evidence demonstrates that occupational exposure to ENMs can induce oxidative stress, inflammation, mitochondrial dysfunction, genotoxicity, immune dysregulation, and organ-specific toxicity affecting the lungs, cardiovascular system, liver, kidneys, nervous system, skin, and reproductive organs. Despite considerable advances in understanding nanotoxicity, significant uncertainties remain regarding chronic low-dose exposure, combined exposures, realistic workplace scenarios, and long-term health outcomes.

Recent developments in computational toxicology, Nano-QSAR models, Bayesian networks, grouping and read-across strategies, control banding, and life-cycle assessment have improved nanosafety evaluation, although their widespread regulatory implementation is still limited by insufficient standardized data and harmonized methodologies.

Effective occupational protection therefore relies on a hierarchy of controls, prioritizing engineering controls, administrative measures, appropriate personal protective equipment, exposure monitoring, and worker training. Future research should focus on establishing validated biomarkers of exposure and effect, standardized dose metrics, harmonized international regulations, and long-term epidemiological investigations. Integrating safe-by-design principles with sustainable nanotechnology and advanced predictive risk assessment will be essential for balancing technological innovation with worker health and environmental protection.

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Data Available Statements

The data that supports the findings of this study are available from the corresponding author upon reasonable request.

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