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Review

# Sustainability and environmental ethics for the application of engineered nanoparticles

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ABSTRACT

The production and use of Engineered Nanoparticles (ENPs) or materials containing ENPs has increased astonishingly, leading to increased exposure to workers and consumers. The invention and applications of new materials either create new opportunities or pose new risks and uncertainties. The uncertainties concerning application of ENPs are posing disturbances to the ecosystem and human health. This review first addresses in vitro and *in vivo* studies conducted on the toxicity of ENPs to animals and humans. Ethical justifications are provided specially with reference to Intergenerational Justice (IRG-J) and Ecological Justice (EC-J). The social benefits and burdens of ENPs are identified for present and future generations. Some mitigation approaches for combating the potential risks posed by ENPs are proposed. Finally, suggestions for the safe handling of ENPs in future are proposed in the review.

## 1. Introduction

The term nanotechnology refers to the science of investigating and manipulating materials at atomic, molecular and macromolecular scale (Sudarenko, 2013). Nanoparticles (NPs) are known to occur naturally (e.g., volcanic ash and forest fires), accidentally (i.e., unintended human activities) and anthropogenic (e.g., cosmetics and other consumer products) (Buzea et al., 2007; Sudarenko, 2013). Engineered nanomaterials (ENMs) or engineered nanoparticles (ENPs) are man-made materials produced deliberately for different industrial applications and most commonly having dimension from 1 to 100 nm (Auffan et al., 2009). It is widely acknowledged in the scientific community that ENPs have enormous potential to transform industrial processes in the future thereby shaping how the society and the global economy will function. They have several industrial and domestic applications in consumer products, cosmetics, agriculture, soil and groundwater remediation, electronics, energy storage, biomedical and transportation (Besha et al., 2018; Boldrin et al., 2014).

The applications of ENPs in hundreds of consumer products is making life simple from time to time (Vance et al., 2015). For instance, nano-electronics has created several advances such as, faster & smaller portable electronics with more data storage (Roco et al., 2011). Ultra-high definitions screens use nanotechnology to create vibrant colours and improve energy efficiency (Roco et al., 2011). Nanotechnology is also behind small materials that are being introduced in medical applications (e.g., capsule endoscopy camera to take picture in the digestive tract) (Koulaouzidis et al., 2015). The use of ENPs, however is not without risk to human and the environment. Laboratory and real case investigations revealed that ENPs could pose potential environmental and human health risks (Journeay and Goldman, 2014; Pietroiusti and Magrini, 2014; Trop et al., 2006). Moreover, unethical and uncontrolled use of ENPs have also created an ongoing debate amongst the scientific community.

Several European Union regulatory agencies have established frameworks to regulate the production and use of ENPs. The most strongest of these regulations is the framework known as Registration, Evaluation, Authorisation, and Restriction of Chemicals (REACH) effective on 18 December, 2006) (Technology, 2017). However, the implementation of regulations and frameworks to ensure the sustainable use of ENPs also relays on a person's or organization's ethics and moral values. Several reviews have been published on the applications of ENPs, their fate, and toxicity (Eduok et al., 2013; Peters et al., 2016; Srivastava et al., 2015; Stark et al., 2015). However, no review has yet been published on the ethics of the sustainable use of ENPs.

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The main objective of this review is to evaluate the ethics regarding the sustainable use of ENPs for their intended applications. ENPs have already been detected in wastewater influent and effluents, surface water, groundwater, foods, consumer goods, soils, biosolids and other media (Bäuerlein et al., 2017; Carboni et al., 2016; Peters et al., 2018; Yang et al., 2016b, 2014). Ethical issues or decisions are claimed to be justified when potentially good environmental and ecological outcomes are obtained through the applications of ENPs, especially from the Ecological Justice (EC-J) and Intergenerational Justice (IRG-J) points of view. Considerations on whether the application of ENPs is sustainable, without any damage to humans and the ecosystems, are discussed. The social burdens and benefits associated with these considerations are also discussed. The review provides mitigation approaches to effectively tackle the challenges associated with the applications of ENPs and concludes with suggestions for future research.

## 2. Applications of ENPs

According to the Woodrow Wilson International Centre for Scholars and the Project on Emerging Nanotechnologies and Nanotechnology Consumer Products Inventory (CPI), there are more than 1800 consumer products containing ENPs produced currently by 622 companies in 32 countries (Vance et al., 2015). $TiO_2$, $SiO_2$, and ZnO ENPs are the most widely produced on a mass basis. Silver-based Ag-NPs represent only 2% of the overall production of nanomaterials. Although the exact annual production of ENPs is not known, Piccinno et al.(Piccinno et al., 2012) estimated the production of $TiO_2$ was as high as 10,000 tonnes/year, while that of $CeO_2$, $FeO_x$, $AlO_x$ and CNT was between 100 and 1000 tonnes/year in 2012. The estimated turn-over of nano-products for nanotechnology global market was claimed double-digit billions of US dollars in 2003 (Kaluza et al., 2012), which is estimated to be worth more than US$173 billion by 2025 (Technology, 2017). Recently, UNESCO has also stated that nanotechnology is a research priority for several countries (Baskaran, 2017). The wide range of applications of CNT, $CeO_2$, $SiO_2$, $TiO_2$, ZnO, Ag-NPs, fullerenes, nZVI and other ENPs are summarized in several reviews (Table 1).

Nanotechnology have been applied across biomedical, optical, electronic, mechanical and chemical fields as well as consumer products such as food and cosmetics (Coles and Frewer, 2013; Koulaouzidis et al., 2015; Peters et al., 2016; Roco et al., 2011). ENPs are applied in food manufacturing & processing to improve the texture of dairy products such as yogurts and ice- cream (Coles and Frewer, 2013; Peters et al., 2016). As a food packaging, nano-silver is used as microbicide to keep food fresh for long period of time and to prevent contamination (Coles and Frewer, 2013; Peters et al., 2016; Srivastava et al., 2015). Also, nano-encapsulation through nano-crystals increased bioavailability of omega-3 fatty acid where it is needed (Coles and Frewer, 2013). Because of ENPs have the ability to cross biological barrier, nanomedicine is investigated for drug delivery such as liposomal doxorubicin (Doxil®/Mayocet ™) for breast cancer treatment (Mu and Sprando, 2010). $TiO_2$ and ZnO ENPs are used as sunscreen lotions (i.e., to protect the skin from UV-light attack) and toothpaste (Mu and Sprando, 2010; Srivastava et al., 2015). Nano-sensors, for instance, carbon nanotube-based sensors is used to measure the levels of capsaicinoids in chili peppers (Sozer and Kokini, 2009). In the electronic sectors, tin oxide ($SiO_2$) nanoparticles area employed in solar cells and transparent conducting glass (Srivastava et al., 2015).

## 3. Ecological and human health concerns of ENPs

The widespread applications of ENPs raise concerns about the potential risks they may pose once discharged into environment. It is imperative to determine the level of exposure when assessing the risks. The physical and chemical properties of ENPs such as size, shape, surface area, charge, solubility, reactivity and many other properties are directly linked to the toxic effects of ENPs. ENPs move faster than other contaminants in aquifers and soils due to their smaller size. They may act as a “Trojan horse” by carrying hazardous chemicals and dispersing them in the environment. For instance, CNT adsorbs polycyclic aromatic hydrocarbons (PAHs) and enhances the toxicity of PAHs (Musee, 2011). Different levels of toxicity in humans, animals and plants can be induced by ENPs. The exact impacts of ENPs on humans and the environment are not yet fully understood with contradictory results documented. The sources, fate and toxicity of ENPs in the environment are summarized in Fig. 1. The major effects of ENPs on humans and the natural environment are reviewed in the following sections.

ENPs enter wastewater treatment plants (WWTPs) following discharge from industrial/domestic applications (Fig.1). They can cause problems in the performance of WWTPs, systems (Besha et al., 2017). Untreated ENPs can enter surface water (e.g., a river) from WWTPs effluents (Markus et al., 2018). ENPs may affect a range of populations such as microalgae in rivers. ENPs can enter soil and leach to groundwater, which may affect plants and crops when the river water is used for irrigation. Wastewater sludge derived from WWTPs and organic waste treatment plants (OWTPs) may contain large amounts of ENPs. When sludge is applied as landfill and biosolids, soil bacteria, and other biota can be seriously harmed by ENPs attached to sludge (Chen et al., 2017). Incinerated sludge may still contain ENPs in the bottom and fly ash. These ENPs could leach and find their way to surface water, soils and groundwater when bottom ash is utilized for landfill purposes (Mitrano et al., 2017). ENPs for agricultural applications in the form of nano-agrochemicals such as pesticides, insecticides, and other biocides can directly accumulate in the food web and affect the growth of plants

**Table 1**
The applications of ENPs.

| Nanoparticles | Applications | References |
|---|---|---|
| $TiO_2$ | Food additive, flavour enhancer, and food supplement, antimicrobial agent together with other ENPs, personal care products, energy storage and photovoltaics, photo-catalysis, photoxidation of dyes, self-cleaning of windows, nano-composite membranes, polymeric membranes, an adsorbent for heavy metals and organic dyes | (Besha et al., 2019; Coles and Frewer, 2013; Ghosh et al., 2017; Peters et al., 2016) |
| ZnO | Plastics, ceramics, paper, glass, cements, paints, food packaging, UV-filters, sunscreens, batteries, potential use in phenols, dyes and heavy metal removal; photo-catalysts and polishing agents | (Peters et al., 2016) (Ghosh et al., 2017; Sozer and Kokini, 2009) |
| Fullerenes | Organic photovoltaic, sensors, lubricants in skin care, cosmetics and optical devices | (Besha et al., 2019; Srivastava et al., 2015) |
| $SiO_2$ | Coatings, drug delivery & biomedical purposes and cement | (Darr et al., 2017; Singh et al., 2014) |
| $CeO_2$ | In diesel fuel to reduce particulate emissions | (Rogers et al., 2010) |
| CNTs | Electrode materials, hydrogen storage, panel displays, sports equipment, nanometer-sized electronic devices, sensors & probes, memory chips and automobile parts | (Baughman et al., 2002) |
| Ag - NPs | As an antimicrobial membrane, food packing, plastics coating, toothpastes, soaps, foods & textiles, coatings & paints, textile, electrode materials, batteries and energy storage | (Haider and Kang, 2015; Peters et al., 2016) |
| nZVI | To remediate soils and groundwater contaminated with petroleum and polycyclic hydrocarbons; removal of chlorinated and nitoaromatic organic compounds, heavy metals, nitrate, arsenic, dyes and phenols | (Besha et al., 2018; Fu et al., 2014) |

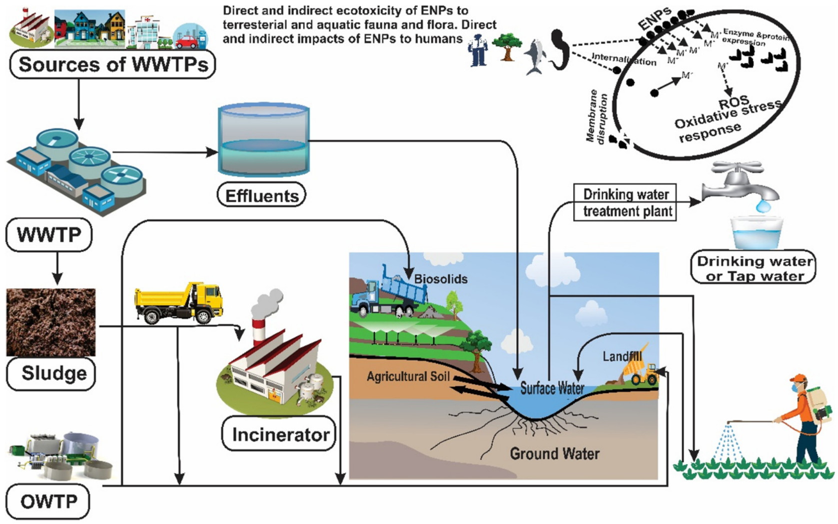


**Fig. 1.** The possible occurrence and fate of ENPs in the environment.

(Simonin et al., 2018). They affect soil bacteria and in turn the germination process. Humans and animals are potentially exposed to ENPs via the food chain (Gardea-Torresdey et al., 2014).

### 3.1. Ecological concerns of ENPs

Little is understood about the toxicity of ENPs on plants, microorganisms, and animals, especially once the particles encounter cell membranes or the proteins surrounding a cell. However, in vitro and in vivo studies indicated that, ENPs in the μg/L to mg/L concentration range induced toxicity, including oxidative stress, and cell membrane damage to bacteria (Auwerter et al., 2017; Cervantes-Avilés et al., 2017; He and Feng, 2017); fish (Hou et al., 2018); plants and algae (Gardea-Torresdey et al., 2014; Hou et al., 2018); crustaceans (Picado et al., 2015) and mammalian cells (Ivask et al., 2014). The interaction between particles and cellular components resulted in the generation of reactive oxygen species (ROS) through radicals, transition metals and other chemicals. Other mechanisms may play a role in the ecotoxicity of ENPs. For this reason, further research on ecotoxicity is needed to understand the ecological risks of ENPs.

#### 3.1.1. Sewage sludge

ENPs can complicate the removal of nitrogen during wastewater treatment by inhibiting key bacterial enzymes required for nitrification and denitrification (Auwerter et al., 2017; Cervantes-Avilés et al., 2017; Dahle and Arai, 2015; Guo et al., 2015). $TiO_2$ NPs (5–25 mg/L) with size ranges 20–50 nm) decreased the denitrification capacity of *Pseudomonas stutzeri* CFY1, which was isolated from activated sludge (Li et al., 2016). Almost complete inhibition of biogas production by $CeO_2$ NPs (García et al., 2012) and inhibition of respiration rates by $TiO_2$ NPs (Zhou et al., 2015) in municipal wastewater activated sludge were observed. The oxygen flux of the bacteria fell to 30, 26 and 42% with exposure to 1, 10 and 100 mg/L $TiO_2$ NPs, respectively, after 4.5 h (Zhou et al., 2015). It was also evident that $TiO_2$ NPs were toxic because of the release of dissolved $Ti^{4+}$ ion and generation of reactive oxygen species (ROS). In another study, long-term exposure of wastewater bacteria to $TiO_2$ (50 mg/L) and ZnO (50 mg/L) NPs with size ranges from 80 to 100 nm adversely affected the microbial communities and changed the relative abundance of key functional bacteria like ammonia oxidizing bacteria (Zheng et al., 2015). Moreover, inhibition of respiration by ZnO NPs (50 mg/L) immediately after its addition was seen when the oxygen flux was dropped to 4.5 h.

#### 3.1.2. Soils

It is reported that addition of $TiO_2$ (0.5, 1, and 2 mg/g soil) reduced both, microbial biomass and diversity in a soil in 60 days (Li et al., 2016). Other studies revealed that nZVI induced intracellular oxidative stress in soil bacteria (Fajardo et al., 2015; Sacca et al., 2014) and wastewater bacteria (Zhou et al., 2017). Different concentrations of $TiO_2$ (0.1, 0.5, 10, 100 and 500 mg/kg dry soil) reduced nitrification in the soil. However, there was a lack of a classical dose-response to determine the usual ecotoxicological metrics (EC50, IC50 or LC50) (Simonin et al., 2017).

#### 3.1.3. Aquatic microorganisms

Living cells have the capacity to take up NPs and the toxicity of ENPs to plants and algae depend on the size, dose and exposure time (Dahle and Arai, 2015; Manzo et al., 2013; Thunugunta et al., 2018; Zhang et al., 2016). For instance, the 48 h EC50 values for exposure to nano ZnO (50 nm) and bulk ZnO (1 μm) of the marine microalgae *Skeletonema costatum* were 6.4 mg/L and 8.3 mg/L, respectively (Zhang et al., 2016). Additional toxic effects include oxidative stress to the aquatic macrophyte *Hydrilla verticillata* (Spengler et al., 2017); chronic toxicity to green algae (*Pseudokirchneriella subcapitata*) (Picado et al., 2015); and damage to the DNA of marine algae *Dunaliella tertiolecta* by ZnO NPs (Schiavo et al., 2016). Fullerenes (nC60) at a sub-lethal concentration (0.09 mg/L), induced photosynthetic toxicity to the phytoplankton organism *Scenedesmus obliquus* (Tao et al., 2015). The photosynthetic products (protein, lipid and polysaccharide) and pigments (chlorophyll *a* and *b*) decreased due to the inhibition of the algal $Mg^{2+}$ ion.

#### 3.1.4. Plants and crops

A recent study reported that the accumulation of ZnO NPs (average particle size 35 nm) inhibited the growth of eggplant seedlings (Thunugunta et al., 2018). The toxicity of ZnO NPs was not primarily due to the generation of $Zn^{2+}$ ion, but most likely related to the peculiar character of the nanoscale compared to the bulk material (Manzo et al., 2013; Schiavo et al., 2016). Other studies have reported that cell membranes and the roots of onion and cucumber plants were destroyed by exposure to Ag-NPs (Gardea-Torresdey et al., 2014). Toxic effects of Ag NPs (0–1.6 mg/L) were observed in cowpea and wheat (Wang et al., 2015a). Enhanced uptake of Ag-NPs was due to the ruptures formed in the roots of cowpea. However, the toxicity of Ag NPs can be reduced by sulfidation (conversion to $Ag_2S$) (Doolette et al., 2013; Kaegi et al., 2013). Gardea-Torresdey et al. (Gardea-Torresdey et al., 2014) reported that the exposure of *Arabidopsis thaliana* to fullerenes prompted

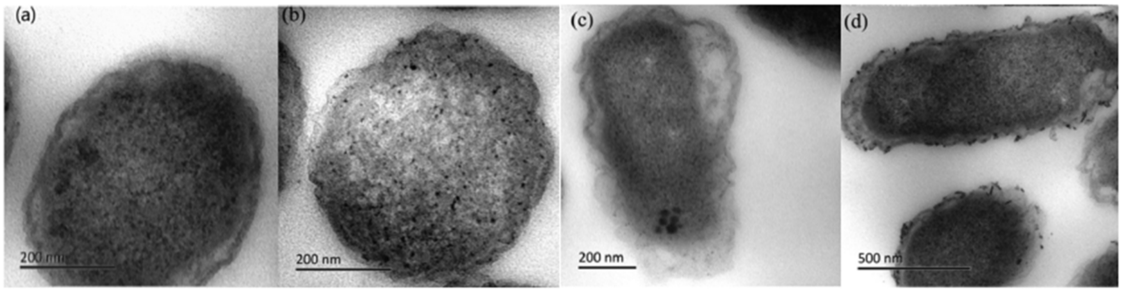


**Fig. 2.** TEM images of a) control, (b, c) treated *E. coli* with nZVI and (d) 0.4 wt % CMC- nZVI for 1 h (concentration of nZVI or CMC- nZVI was 500 mg/L). (a) Native *E. coli* with well-preserved cellular surface; (b) harsh membrane damage and decomposition by nZVI; (c) black dots showing nZVI entered, accumulated and created aggregates inside the cell indicating cellular internalization; and (d) outer shell of a layer of nanoparticles (CMC- nZVI) attached around the outer membrane and no cellular internalization was observed. Reprinted and reproduced with permission from (Dong et al., 2016). Copyright (2016) Elsevier.

abnormal cell division in the roots through the distribution of auxin. Reduction of the root length and height of rice seedlings (*Oryza sativa L.*) (Ji et al., 2017) and stunted growth of wheat (Du et al., 2011) were revealed by exposure to $TiO_2$ NPs. Further information on uptake, translocation, accumulation, and phytotoxicity of ENPs in plants can be found in the latest review (Tripathi et al., 2017). A decrease in yields in crops has been discussed extensively in the review by Rizwan et al. (Rizwan et al., 2017). The detrimental impacts of ENPs on crops and soil microorganism was demonstrated by He and Feng (He and Feng, 2017). The implications of ENPs entering the food chain is still largely unknown and it needs further investigation.

### 3.1.5. Crustaceans

ENPs induced acute and chronic toxicity to species of crustacean (*Daphnia Magna*) (Lopes et al., 2014; Picado et al., 2015; Zhu et al., 2010). For example, $TiO_2$ induced modified acute (72 h) and chronic (21 days) toxicity in one particular crustacean (Zhu et al., 2010). The 72 h EC50 and LC50 values were 1.62 mg/L and 2.02 mg/L, respectively. Minor acute toxicity identified for the traditional 48 h exposure indicated that exposure time can be a controlling factor for the toxicity of ENPs. Severe growth retardation, mortality and reproductive defects were observed after chronic exposure of upto 21 days even at a concentration as low as 0.1 mg/L. The type of NP and their size play a role in the toxicity inflicted on *Daphnia Magna.* For example, small-sized anatase $TiO_2$ (10 nm) triggered a larger amount of intercellular ROS and malondialdehyde in *Daphnia Magna* compared to the larger rutile $TiO_2$ (Lin et al., 2014). Conversely, studies on vertebrates and invertebrates revealed that dissolved zinc ions rather than particle size played a significant role in the toxicity of ZnO NPs. The 48 h LC50 of 30 and 80–100 nm ZnO NPs to *Daphnia magna* were 1.02 and 1.10 mg/L, respectively (Lopes et al., 2014). In another study, the toxicity of soluble Zn in *Daphnia Magna* demonstrated an LC50 of 1.01 mg/L for Zn $(NO_3)_2$ (Bacchetta et al., 2016). The toxicities of ZnO NPs and soluble zinc were very similar due to similar mechanisms caused by the $Zn^{2+}$ ion.

### 3.1.6. Fish

ENPs are toxic to fish under a range of circumstances (Chen et al., 2016; George et al., 2014; Osborne et al., 2015; Zhao et al., 2016). Exposure to ZnO NPs at higher concentrations (10, 30, 60, 90 or 120 mg/L) of zebrafish (*Danio rerio*) embryos for 96 h resulted in acute toxicity and developmental abnormalities by increasing heart beat and reducing the rate of embryo hatching (Zhao et al., 2016). Moreover, ZnO NPs induced oxidative damage and apoptosis in zebrafish, and apoptosis was accelerated via the p53 mitochondria caspase mediated pathway. Ag-NPs (25, 50 and 100 μg/L) inhibited a number of bacterial colony forming units and bacteria growth in *Danio rerio*'s mucus surface (Bacchetta et al., 2016). Fullerenes (nC60) accumulated in the liver, increased the cholesterol level, and induced oxidative stress in common carp (*Cyprinus carpio*) in 10 days (Chen et al., 2016). Exposure to ZnO NPs (50 and 500 mg/kg of feed) for 6 weeks followed by 2 weeks recovery period revealed that juvenile common carp experienced chronic dietary toxicity (Chupani et al., 2018).

Photo-induced transformation of ENPs resulted in greater cytotoxicity and embryonic toxicity to fish under light rather than dark conditions (George et al., 2014). For instance, $TiO_2$ and Ag-NPs under artificial light triggered oxidative cell damage in blue-gill sun fish, and mortality in the embryo of zebrafish (George et al., 2014). This indicated that the toxicity of NPs to organisms may vary due to environmental conditions. Once NPs enter the environment, their physical and chemical properties can be significantly influenced by a variety of factors (e.g., surface coating by natural organic matter) which can change the toxicity of the NPs. Therefore, the toxicity tests of NPs to microorganism should consider environmental conditions (e.g., sun light, natural organic matter, etc.) since ambient laboratory conditions may underestimate or exaggerate the toxicity of NPs.

### 3.1.7. Other toxicity tests

Toxicological studies showed that nZVI quickly inactivates bacteria such as *Pseudomonas fluorescens* and *Bacillus subtilis var. niger* (Wang et al., 2017). Acute toxicity of nZVI ($\geq$ 500 mg/kg soil) to earthworms in soils (*Eisenia fetida* and *Lumbricus rubellus*) was observed and the toxicity declined with aging (El-Temsah and Joner, 2012). The toxicity of nZVI was mainly due to its ability to catalyze the formation of hydroxyl radicals (• OH) from superoxide ($O_2^-$) and $H_2O_2$ (Chen et al., 2012). Up to 0.5log reduction of nZVI after 30 min and nearly 0.7log reduction after 1 h were observed after exposure of *E. Coli* to 100 ppm nZVI (Dong et al., 2016). The toxicity of nZVI towards microbes can be reduced by coating carboxymethyl cellulose (CMC) on the surface (Fig. 2). CMC reduces aggregation and sedimentation, and inhibits close contact between bacteria and nZVI, and therefore, CMC can serve as a stabilizer during environmental remediation applications. Exposure of the invertebrate *Chironomus riparius* to fullerenes in artificial sediments resulted in acute and chronic toxicity (Waissi et al., 2017). With rapid uptake of C60, oxidative stress in the tissues, changes in the cell structure, and unbalanced emergence rate in female and male *Chironomus riparius* were observed. Both multi-walled carbon nanotubes (MWCNT) and singled-walled carbon nanotubes (SWCNT) induced toxicity in animals, plants, microorganisms and humans through the underlying mechanisms of inflammatory response, oxidative stress, malignant transformation, DNA damage and mutation, the formation of granulomas and interstitial fibrosis (Liu et al., 2012).

The toxicity of ENPs depends on contact time, type of species, concentration, test environment (presence of dissolved oxygen, total suspended solids and natural organic matter), physical and chemical properties of ENPs (size, surface area, surface charge, tendency of aggregation/agglomeration and hydrophobicity/hydrophilicity); and type of test being conducted (in vitro or in vivo). For example, rod-shaped ZnO NPs are more toxic than spherical ones (Hou et al., 2018). Exposure methods and exposure medium also affect toxicity. The spatial distribution of ENPs (in the case of biofilms - to what extent the NPs penetrate the biofilms) is crucial in determining the ecotoxicological data of ENPs.

### 3.2. Potential human health concerns of ENPs

People are exposed to ENPs during occupations, research activities, use or misuse of personal care products (PCPs). The distributions and clearance of ENPs in the body depend on the type, properties, concentration of ENPs and the age and health status of exposed persons (e.g., young children, people with pre-existing health conditions) (Tang et al., 2015). The current risks to humans from domestic and industrial uses of nano-products are largely unknown and unquantified. However, in vitro and in vivo tests revealed that ENPs are toxic to cells in the brain, immune and circulatory, reproductive & developmental systems (Tang et al., 2015). Real scenario cases and deaths from exposure to ENPs in the workplace were also reported in different countries (Pietroiusti and Magrini, 2014).

Exposure of humans to ENPs can arise through inhalation, ingestion, intravenous injection or dermal contact from contaminated air, food or drinking water, or directly from nano-products (Liu et al., 2012; Smolkova et al., 2015; Tang et al., 2015; Vance et al., 2015; Vance and Marr, 2015). ENPs can induce toxicity to humans by inhalation around construction sites (e.g., release of $SiO_2$, ZnO and $TiO_2$) (Van Broekhuizen et al., 2011), during indoor use of sprays containing nano-aerosols (e.g., emission of Ag from throat spray) (Vance and Marr, 2015) and through the release of carbon black NPs and CNT from recycled padding of vehicles (Novak, 2012). ENPs may be ingested through nanofoods (e.g., $TiO_2$ from candies, sweets, gums and cookies) (Weir et al., 2012); via the food chain (e.g., bioaccumulation of ZnO in edible plants) (Gardea-Torresdey et al., 2014); through deposition of airborne NPs on food and drinks (Vance and Marr, 2015); via maternal-foetal transmission through the placenta, and exposure during breast feeding (Tang et al., 2015). Dermal contact with ENPs can occur through the use of cosmetics and sunscreen lotions on the skin and hair (e.g., $TiO_2$ and ZnO release) (Vance et al., 2015); via clothing (application of nano Ag in textile industries as an antimicrobial agent) (Tang et al., 2015) and during unintentional touching of surfaces and products containing ENPs (e.g., computer processors containing Si NPs) (Vance et al., 2015; Vance and Marr, 2015). Vance et al. (Vance et al., 2015) investigated the most probable exposure routes of ENPs from consumer products containing ENPs listed in the CPI (Fig. 3). Skin is the primary exposure route (58% of the products); 25% of the products are probably inhaled and the remaining 16% are ingested. The toxic effects of ENPs on the respiratory system, gastrointestinal tract and skin are summarized in the following sections.

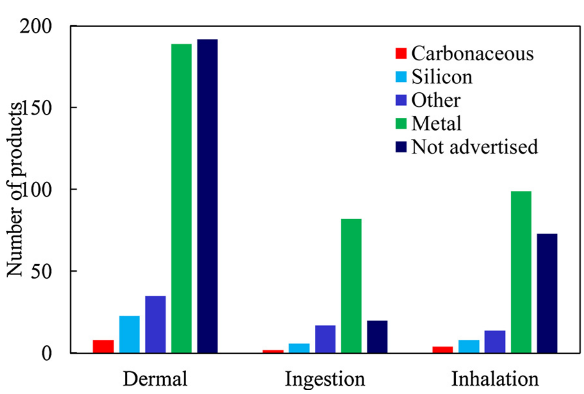


**Fig. 3.** Potential exposure pathways from the expected normal use of consumer products, grouped by major nanomaterial composition categories Reprinted and reproduced with permission from (Vance et al., 2015). Copy right (2015) Open access platinum.

#### 3.2.1. Respiratory tract/system

The human respiratory tract may be affected immediately when people misuse aerosolized sprays containing ENPs. People in the immediate vicinity are most likely exposed. There are no regulations regarding indoor exposure of nanomaterials. Thus, it is important to be ethical when utilizing nano-aerosol sprays. Deposition of ENPs in the respiratory tract depends on size and shape of the nanomaterials. Smaller nanomaterials penetrate deeper into the lungs than the larger ones (Technology, 2017). Consumer products, which have the potential to aerosolize ENPs in indoor environments, are released in shops, shopping malls, day-care centres, and schools, and have the potential to affect the respiratory tract. The majority of potentially aerosolized nanomaterials listed in the CPI comprise metal or metal oxide nanoparticles (Ag, Au, $TiO_2$, $CeO_2$, ZnO, $Al_2O_3$, Mg, $WS_2$, C, and Si) (Project, 2018). The CPI lists more than 190 products that have the potential to aerosolize (both wet and dry aerosols having ultrafine and fine range size) ENPs resulting in inhalation during use (e.g., sprays and hair dryers). Emissions of aerosols from products containing Ag NPs and nanofilm products containing $TiO_2$ have been reported (Nazarenko et al., 2014).

Case reports of long-term exposure of people to ENPs revealed serious health outcomes for their lungs and other aspects of the respiratory system. Exposure to polyacrylate spray for seven young female Chinese workers led to deaths for two of them and unusual pleuropulmonary symptoms for all (Song et al., 2009). ENPs were identified in pulmonary and pleural cells. In 2011, Song et al. (Song et al., 2011) later reported that the spray paints contained silica ENPs. A 38-year old male died 13 days after inhaling Ni nanoparticles and Ni NPs $< 25$ nm were found in his lung macrophages (Phillips et al., 2010). The Ni NPs had caused adult respiratory distress syndrome. In another report, a 58-year old man experienced Bronchiolitis obliterans, an inflammatory condition affecting the bronchioles after three months of exposure to a polyester powder paint containing $TiO_2$ NPs (Cheng et al., 2012). A 26-year old female chemist handling nickel nanoparticle powder developed throat irritation, a flushed face and a nasal congestion condition ("post nasal drip") (Journeay and Goldman, 2014). Another case reported that a 33-year old female who was exposed to toner dust experienced abdominal pain, weight loss and diarrhoea (Theegarten et al., 2010). Submesothelial aggregates of carbon nanoparticles (CNPs) with size range from 31-67 nm were found in tissue specimens. Inhaled ENPs are able to be transported along the lymphatic and blood vessels and affect other organs such as the kidneys (Theegarten et al., 2010). Although these case reports do not confirm or exclude a particular risk posed by ENPs, they do indicate that ENP exposure in the workplace must be recognized.

#### 3.2.2. Gastrointestinal tract (GIT) and the skin

If products containing ENPs are ingested, they may affect the GIT (Esch et al., 2014; Tang et al., 2015). For instance, ENPs can enter the GIT if mucus is cleared. Both direct ingestion (e.g., food) and indirect ingestion (e.g., NPs dissolution from food containers) can lead to ENPs exerting toxic effects on the GIT (Bergin and Witzmann, 2013). However, intestinal mucus can act as a barrier to NP uptake. $TiO_2$ ingested in food (as a food colorant), oral exposures to Ag NPs sourced from fish in water and exposure to silica NPs utilized for clearing alcoholic beverage and anti-caking agents may affect the GIT (Bergin and Witzmann, 2013). Food-grade $SiO_2$ NPs exhibited adverse effects on a cell model (microvilli) of the human gastro-intestinal tract and evidence of $SiO_2$-mediated production of ROS was revealed (Yang et al., 2016a). ENPs found in certain foods can affect epigenetic pathological processes in humans; however, their ability to induce disease requires further analysis in the future (Smolkova et al., 2015). Similar to this, $TiO_2$ particles were detected in human liver and spleen, with more than 24% in nanosize range ($< 100$ nm) (Heringa et al., 2018). With this data, it was concluded that health risks associated to oral exposure to $TiO_2$ could not be ruled out. A recent review on the exposure, toxicity and impact of nanomaterials on human health has been presented by Pietroiusti et al. (Pietroiusti et al., 2018).

Development of lesions after ENPs entered the skin was reported (Trop et al., 2006). For instance, a 17-year old boy with a 30% mixed depth burn developed hepatotoxicity and argyria-like symptoms, and a greyish face after treatment with a Ag-containing wound dressing (Trop et al., 2006). The silver levels in plasma (107 μg/kg) and in the urine (28 μg/kg) were elevated. A chemist who handled Ni nanoparticles in the laboratory experienced new skin reactions to her earrings and belt buckle (Journeay and Goldman, 2014). $CeO_2$ (< 25 nm) NPs induced toxicity to human skin melanoma cells (A375), creating oxidative stress by generating ROS and superoxide dismutase and decreased glutathione levels (Ali et al., 2015). One in vivo study documented the penetration of $TiO_2$ (4 and 60 nm) NPs in pig ear where it accumulated in the deep layer of the epidermis (Wu et al., 2009). Similarly, $TiO_2$ NPs induced toxicity to mice after penetrating in their hairless skin (Wu et al., 2009).

Nanotechnology has the potential to diagnose, treat and cure diseases that were previously untreatable and will represent a huge advance in nanomedicine when therapeutic nanomaterials are ready for application. While the creation of lighter weight and durable medical implants using nanotechnology is inevitable, their safety is still not fully known due to the limited research on the toxicity of nanomedicine. During treatment of a particular disease or condition, a nanomedicine can cross the cell membrane and potentially damage cells. An in vitro test was undertaken to investigate the mechanisms of toxicity of ZnO NPs to human liver cells (HepG2) (Sharma et al., 2012). With the addition of 14 and 20 μg/ml of ZnO NPs, mitochondrial activity fell to 53% and 43%, respectively, after 24 h. Ag ions and Ag-NPs are used in medical devices because of their antibacterial, antifungal and antiviral properties. However, the release of Ag ions and Ag-NPs from medical devices (e.g., catheters) can induce toxicity to the liver, kidneys, spleen, lungs, brain and skin (Faunce and Watal, 2010).

## 4. Ethical issues and sustainability

Ethics involves the identification and assessment of hazardous risks in the environment. It also requires the need for non-maleficence (non-harming), autonomy (self-determination) and justice (fairness in distribution of risks) (Schulte and Salamanca-Buentello, 2007). According to the *Stanford Encyclopaedia of Philosophy*, environmental ethics refers to moral relationships of human beings (anthropocentric view) to, and also the value and moral status of, the environment, and its non-human (non-anthropocentric view) content (Stanford, 2018). It sets values and actions that need to be carried out to protect sustainable biodiversity and ecological systems. In assessing the sustainability of ENPs for different applications, identification of the distributive justice over time with reference to environmental ethics is vital. In the following sections, both ethical concerns of EC-J and IRG-J are discussed by examining the main areas relevant to the sustainability of ENPs (Table 2).

### 4.1. Intergenerational Justice (IRG-J)

Risks linked to ENPs raise several concerns of environmental ethics. One of these is IRG-J, which is defined as justice between generations or the welfare the present and future generations (Thompson, 2010). Fair IRG-J occurs when each generation does its fair share of enabling members of succeeding generations to satisfy their needs, to avoid serious harm, and to have the opportunity to enjoy things of value. It is the responsibility of the present generations to keep our ecosystem safe and what happens to future generations partially depends on what we do now (Wolf, 2003). Table 2 lists the sources of the main important ENPs that are potentially a concern for human health as well as the exposure routes, ethical issues and the mitigation approach.

The applications and release of ENPs in the environment should be evaluated carefully in terms of IRG-J. For example, sludge incineration plants may release ENPs in bottom ash and fly ash that could affect the welfare of present and future generations. Thus, indirect exposure of human to ENPs via the food chain is inevitable due to applications of sludge for agricultural purpose (Pradas del Real et al., 2016). Additionally, people could be exposed to ENPs during transportation and application of the sludge in the land. In North Carolina, South Carolina and Virginia, people responded in interviews revealing that they felt physical symptoms and bad odour during sludge land application events (Lowman et al., 2013). People also responded the lack of notifications of land applications in the neighbourhoods, reporting concerns to public officials and influencing decisions about how the practice is conducted where they live. Several of them questioned the fairness of disposing urban waste in rural neighbourhood. This is against the definition of environmental justice given by United States Environmental Protection Agency (EPA). Fairness requires identification of the risks, by whom these risks are borne, those exposed to such risks should be aware of them and people who are exposed to the highest risks should get the highest benefit.

Any ethical issues concerning ENPs affecting animals and humans are the targets of IRG-J. IRG-J considers the potential risk of people to nano-agrochemicals (e.g., nano pesticides) and agriculture-related risks through indirect exposure to ENPs in the food chain (Gardea-Torresdey et al., 2014). Animals can directly drink water from rivers where effluents containing ENPs are discharged into the river. The seepage of ENP from the sludge disposed into landfill can contaminate surface water and the surrounding areas, affecting the people nearby. Nano sieves used as nanofiltration in the food manufacturing and processing industry may have detrimental effect on human. The food packages containing Ag NPs are disposed as waste, leached and accumulated in the environment where it kills microorganism and complicates biological wastewater treatment installations. One of the most important concern of IRG-J for ENPs in food and agriculture is the non-maleficence (i.e., the safety of the food and the process). This is exceptionally prominent due to the level of unknown risks associated with this technology, including potential unforeseen risks to biological organisms, environment, and future generations.

Furthermore, bioethical issues are very important for IRG-J when applying nanomaterials in the healthcare sector (i.e., biomedical equipment and nanomedicine applications). Bioethical issues include the obligation to disclose enough information on the production and applications of nanomedicines for consumers to understand the benefits and any risks associated with nanomedicine or medical tools. The bioethical problems in nanomedicine can be viewed from four different principles of Beauchamp and Childress (Beauchamp and Childress, 2001) including autonomy, beneficence, non-maleficence and justice. These principles are generally well acknowledged, and any ethical considerations in the nanomedicine applications such as nanosurgery, tissue engineering and drug delivery can be answered by these principles. Especially, respect for human nature is crucial to frame the development of nanomedicine and to solve ethical issues. As well, sound regulations in healthcare and medical policy, and fair and responsible personnel are keys to attain sustainable utilization of nanotechnology.

Human dependence on natural resources will continue in the future in spite of the advances made in technologies in the last few decades. The use of ENPs needs to be sustainable, and the scale and nature of ENP associated risks are rapidly evolving. The production of most common ENPs, as found in consumer products (e.g. personal care products), is increasing at an alarming rate. The public are now exposed to ENPs, either directly and indirectly, and this requires great attention to human health. Basically, the ecological and social welfare of the future generations is the concern of IRG-J. Therefore, fair and equitable sharing of benefits (welfare) and burdens (threat) among generations is a crucial issue when considering IRG-J. This is in line with the definition offered by Thompson where ecological sustainability develops without affecting the needs of society in the future (Thompson, 2010).

**Table 2**
Sources of ENPs with environmental and human concerns, possible exposure routes, ethical issues and mitigation approaches.

| Sources of ENPs | Examples | Acceptors | Possible exposure routes | Possible environmental/ ecological & human concern | Ethical issue | Mitigation approaches/requirements | References |
|---|---|---|---|---|---|---|---|
| Leakage during production | Metal, metal oxides and carbon-based ENPs, etc., | Human, aquatic and terrestrial microorganisms | ENPs may be inhaled, ingested or contaminate the skin; ENPs reach soils and surface water and then finally reach groundwater | May adversely affect the respiratory system of humans; inhibition of nitrification-denitrification process in sewerage system | EC-J, IGR-J | Use adequate protection, e.g., gloves, evaluate the hazards posed by nano-aerosols, good workplace practices and identify potential sources of leakage areas (e.g., exhaust ventilation system) | (Faunce and Watal, 2010; NIOSH, 2009) |
| Occupational | Nano-aerosols (materials suspended in a gas) e.g., $SiO_2$, $TiO_2$, Ni, etc., | Humans | Inhalation and ingestion in the workplace. For example, during transport, storage or waste treatment, construction, automobile and aerospace industry, drug delivery and chemical industry; Handling of powder | Respiratory organs (lungs, nose) irritation and inflammation, dermal contact, pleuropulmonary symptoms and gastrointestinal problems | IGR-J | Set a limit to ENPs exposure in the workplace, use personal protective equipment (e.g., gloves, clothes and respirator), evaluate the hazards posed by nano-aerosols, good workplace practices and use exhaust ventilation system and hood | (Groso et al., 2010; NIOSH, 2009; Pietroiusti and Magrini, 2014; Technology, 2017) |
| Sludge Incineration | NPs in the form of fly ash and slag/bottom ash (e.g., nano $CeO_2$ $TiO_2$, $SiO_2$, and CNT) | Humans, soils, water, and organisms | The possible exposure pathway is during transportation of the slag or ash for example, if there is the recovery of metals. During landfill, the slag containing NPs reaches soils. Additionally, NPs may leach from uncontrolled landfill sites and be distributed throughout the environment | The slag or the ash will end up in a landfill. This may affect soil bacteria and further the NPs seepage into groundwater; health issue is a concern if the slag is recycled (i.e., processing of the slag) and environmental issues occur if the slag is used for road construction (i.e., potential leaching) | IRG-J, EC-J | Fabric filters, electrostatic scrubbers, and wet electrostatic scrubbers have the potential to partially remove NPs from incinerator plant. Develop environmentally friendly biodegradable ENPs. Also, it is important to recycle waste containing ENPs before they are incinerated and applied for landfill purposes | (Andersen Lizzi et al., 2014;US et al., 2019 (Holder et al., 2013) |
| Biosolids | nano- Ag, ZnO, $TiO_2$, etc., | Organisms in the soils and water and indirect effect on humans | Through applications of biosolids for agricultural purposes, ENPs reach in the soil. During seedling and plant growth, ENPs reach the edible parts of plants. Potential contamination of food chain for both humans and animals | Effect on bacterial community diversity, a decrease in the activity of soil bacteria, and above ground plant biomass. However, in the sludge, most of the time Ag is found as $Ag_2S$, ZnO as ZnS which are less toxic. Moreover, ENPs may accumulate and indicate less mobility in the soil | EC-J, IRG-J | Though the sulphide form is less toxic, applications of biosolids containing these compounds may still pose problems in the soils. Therefore, regulations and controls may be applied in the case of biosolids for agricultural purposes. | (Colman et al., 2013; Fayiga and Saha, 2017; Ma et al., 2013; Yang et al., 2014) |
| Landfill | ZnO nano-Ag, $TiO_2$, nano Cu, etc., | Mainly soil microorganisms and the hydrosphere | Landfill sludge containing NPs or certain types of solid non-recyclable construction waste and landfill after incineration of solid waste containing ENPs | Sludge containing ENPs in the soil wields an impact on plants and microorganisms. Potential leaching of NPs from the waste to the leachate. May impact on methanogenesis and biogas production | IGR-J, EC-J | Further research is needed for biosolids before they are applied to landfill, especially the microscopic structural investigation of the NPs. | (Andersen Lizzi et al., 2014; Bolyard et al., 2013; Mitrano et al., 2017; Yang et al., 2014) |
| Nano agrochemicals nano-fertilizers, nanobiocides & nanopesticides | Chitosan, Ag, nano-encapsulate, ZnO and Fe etc., | Humans, plants, animals, and hydrosphere | Inhalation, dermal contact, and ingestion during spraying. ENPs may evaporate during spraying of nano-pesticides; during rain, nano-fertilizers could be washed and join surface water and ultimately make a contact with groundwater | If nano-pesticides are taken up by plants, they may have a detrimental effect. Nanoagrochemicals may inhibit the growth of roots and the toxic outcome is dose-dependent | IRG-J, EC-J | Governments should develop legislation and regulations for nano agrochemicals before they are sold on the market. Their ecotoxicological effects need to be much more clearly understood and explained | (Kah, 2015; Makarenko et al., 2016; Parisi et al., 2015; Peters et al., 2016) |
| Wastewater influents | $TiO_2$, ZnO, $CeO_2$, fullerenes etc., | Microorganism | After a number of applications, ENPs joins surface water that ends up in WWTPs influents. These include: washed off personal-care products; detergents and other cleaning products; releases from fabrics during washing; surface run-off of spilled lubricants, oils and fuels; and releases from paints | Different lab-scale experiments reported that ENPs affect the various processes of WWTPs, for instance nitrification-denitrification, phosphorus removal, etc., by being toxic to wastewater bacteria | EC-J | Appropriate use of ENPs and their distributions; regulations from governmental bodies to limit the presence of ENPs entering surface waters | (Wang et al., 2017) |

(*continued on next page*)

**Table 2** (*continued*)

| Sources of ENPs | Examples | Acceptors | Possible exposure routes | Possible environmental/ ecological & human concern | Ethical issue | Mitigation approaches/requirements | References |
|---|---|---|---|---|---|---|---|
| Wastewater effluents | $TiO_2$, ZnO, Ag, $CeO_2$, fullerenes, etc., | Hydrosphere, terrestrial and aquatic animals | The effluents of wastewater treatment joins surface water, for example, rivers after treatment | Wastewater effluents confirmed the presence of ENPs. It joins the river may affect aquatic animals. Indirect detrimental effect on terrestrial animals | EC-J | Development of WWTPs intended for the removal of ENPs is one option; Regulations should be in place to limit the amount of ENPs in the effluents of wastewater. | (Bäuerlein et al., 2017; Brar et al., 2010; Carboni et al., 2016; Peters et al., 2018) |
| Airborne ENPs | $TiO_2$, ZnO, $CeO_2$, Ag, Au, etc., | Atmospheric organisms, humans, and indirectly to terrestrial and aquatic animals | During the industrial process of different materials, ENPs may leak, and when found in the fly ash, for example, lead to the combustion of fossil fuels. They are also released from vehicles. Aerosolized materials containing ENPs can be sprayed indoors and be transported over long or short distances | Airborne NPs may be inhaled, ingested, contacted dermally and irritate the eyes, skin and respiratory organs. ENPs can end up in water bodies after they are washed and join surface waters and then affect fish and microorganisms | IRG-J, EC-J | Use of Venturi scrubbers, fabric filters and safe work practices in the industry; Recirculating air filtration inside automobiles and homes, create adequate ventilation, reduce the sources of airborne NPs | (Ellenbecker and Tsai, 2015; Pui et al., 2008; Vance and Marr, 2015) |
| Nanowaste | Any materials containing ENPs and which are discarded as waste | Atmosphere, humans, hydrosphere, and soils | Items released during the end use phase such as personal care products, cosmetics detergents, lubricants catalysts host waste materials that contain different ENPs. Materials released from nonpoint sources of spillage, leakage, vehicles, during landfilling, incineration. These joins wastewater influents, river, etc | Both treated and untreated waste streams affect both human and ecological systems (fish, wildlife). Hazards caused by nanowaste in the environment are based on the nanowaste class. Class I nanowaste (e.g., memory chips) is non-toxic while class V nanowaste (e.g., sunscreen lotion) is very/extremely toxic | IRG-J, EC-J | Reduce intentional disposal of nanowaste, but the best way to control nanowaste is recycling, development of biodegradable ENPs, segregations, and collection of nanowaste and appropriate treatment | (Ganzleben et al., 2011; Musee, 2011) |
| Nanomedicine and medical tools | Ag-NPs, $SiO_2$, etc., | Humans | Through the applications of nano-enabled medicine, small medical implants | Nanomedicine can penetrate the cell membrane and cell wall. They may traverse the placenta and pose health risks | IRG-J | Though nanomedicines are currently stilll being developed, they will soon be on the market. However, their toxicological impacts should be disclosed | (Faunce and Watal, 2010; Wang et al., 2015b) |
| Food, beverage and food packaging | Al, $TiO_2$, Ag, CNT, ZnO, Fe, $SiO_2$, etc., | Humans | Food packaging may contaminate the food and adsorb it; ENPs directly added as preservatives and flavoring agents. Nano sieves for filtration purpose | People eat food, which has ENPs in it. Though ecotoxicological data is not yet understood for ENPs in food, the potential is there for ENPs in the food to endanger people's health. | IGR-J | Label all foods containing ENPs and their concentration range. Regulations and other types of government controls are another option | (Coles and Frewer, 2013; Peters et al., 2016; Smolkova et al., 2015) |

### 4.2. Ecological Justice (EC-J)

The other major theme is Ecological Justice EC-J which deals with damage to the ecology, including consequential toxicity (damage) to terrestrial and aquatic flora and fauna, surface water, sediments, aquifers and any beneficial non-living matter that could be adversely affected by ENPs. Ecological justice is concerned with the release of large amounts of ENPs that may severely impact the ecosystem. For instance, the presence of a coal fired power plant and an incinerator increased the amount of fullerenes (C60) in soil samples in the Netherlands (Carboni et al., 2016). Markus et al. (Markus et al., 2018) reported presence of relatively large quantities of nano Zn in the upstream of River Dommel in Eindhoven due to the former zinc smelter operated along the nearby Belgian border to the south. Applications of nZVI for remediation of contaminated soil is a common practice specially in the USA (Mueller et al., 2012); however, the potential release of nZVI from the soil being treated would cause potential accumulation of NPs in the groundwater (Coles and Frewer, 2013).

The applications of ENPs for different purposes and its subsequent toxicity to lifeforms other than humans has led to a debate regarding whether this is just or unjust. For instance, in some countries including Switzerland and Denmark, household and similar waste from commerce is incinerated and applied to landfill (Andersen et al., 2014). Some ENPs could release as landfill gas and leachate. This may have negative impacts on the environment and directly related to EC-J. It was confirmed that low concentration of Ag NPs (0.14 mg Ag/kg soil) in a single dose produced adverse effects in plants and microorganism during sewage biosolids applications in realistic field scenario (Colman et al., 2013). Nano pesticides (having small size and solubility) can contaminate soils waterways and food chain across a wider area (Coles and Frewer, 2013). Moreover, nanoencapsulated pesticides applied for the vaccinations of fish release nanoparticles where their destination is unpredictable.

The release of ENPs into the environment is undoubtedly increasing with unknown implications for the food chain. It is demonstrated that ENPs could accumulate in crops, have a detrimental effect on the productivity of plants, and can compromise the nutritional value of food crops and transfer dangerous chemicals and/or toxins throughout the food chain. Sustainable emerging nanotechnologies should be considered to ensure the intergenerational and ecological equity. Different social aspects such as culture, tradition, religion, and people's moral values can be used to justify both EC-J and IRG-J. The relationship between humans and other lifeforms due to the outcome of ENPs should lead us to maintain or create a healthy environment for all lifeforms so that, the present and future generations can benefit.

## 5. Burden benefit balance (equilibrium)

Burden/benefit balance is a crucial ethical consideration. The concept of distributive justice maintaining the benefits and the burdens between generations need to be fairly distributed. The dilemma is how the benefits of ENPs can be balanced or realized while minimizing the risk to the environment and humans. As described in section 3, ENPs can have adverse health effects on people and damaging the ecosystem (bacteria, soils, water). Therefore, products containing ENPs should show minimal risks to end users, animals, the environment and the future generations. Complete transparency and burden/benefits communication about potential risks and benefits to consumers provide free and informed choice.

Being ethical is to have a convincing moral value that can motivate others to aim for sustainability, and can therefore, be considered to foster sustainability. Other sustainability criteria such as ecological welfare, public welfare, and social equity can be achieved by moral values (Fig. 4a). It has been flagged that there is the need for rapid regulatory responses to avoid harm posed to human health and the environment, especially by the unfair management of waste containing nanomaterials (Ali et al., 2015). However, the production of nanomaterials and the potential exposure of humans and the environment to nanomaterials through waste streams have escalated (Musee, 2011). Consequently, achieving IRG-J will not be an easy task.

Emissions of materials containing ENPs (e.g., nanowaste) from various sectors in developed nations is by far greater than that of developing nations. To limit this burden benefit constraint, some have argued that developing nations should generate higher emissions due to the increase in their economic capacity, or there should be a reduction of emission from developed countries (Tufa, 2015). For instance, equal distribution of waste sites across territories or equal per capita distribution of carbon consumption must be shared between countries (Peters, 2015).

To achieve sustainability in terms of intergenerational justice, an agreement can set up between relevant bodies (Fig. 4b). For instance, one such agreement can refer to treaties between developed and developing nations. Additionally, key regulatory frameworks and legislation regarding the production, application and release of ENPs into the environment must be agreed. In the burden-benefit balance process, international agreements and laws designed to protect the environment can decrease the danger of ENPs.

## 6. Mitigation approaches

Although enough information is lacking on the risk of ENPs to humans and the environment, some scientific results have been reported. As a result, we recommend some precautionary measures that can be applied to ENPs for its safe use. Responsible entities such as research and scientific institutes, and the industrial sector must develop and implement preventative and protective measures appropriately so that the potential risk of ENPs can be minimized. For instance, the Ecole Polytechnique Fédérale de Lausanne (EPFL) outlined safety measures that have been accepted by its chemical laboratories dealing with nanomaterials (Groso et al., 2010). EPFL classified nanomaterials into three hazard classes based on a schematic decision tree. Then they provided technical, organizational and personal mitigation strategies for each hazardous nanomaterial. We recommend that other research institutions follow similar or modified mitigation approaches in their internal regulations to curtail the hazards posed by ENPs.

### 6.1. Risk mitigations in the workplace

Employees and other personnel have the rights to know about toxic or hazardous substances to which they have been exposed in the workplace. The protection of workers who are both, directly and indirectly involved in the production of ENPs should be a common practice. It is important to ensure all labelling of products is clear and safety data sheets and safety procedures are fully documented and updated (Groso et al., 2010). Deposited airborne nanomaterials will most probably affect workers, if the dust collection systems are not cleaned properly. Continuous maintenance of production and manufacturing systems, including cleaning and proper disposal of materials is crucial to reduce the risk of ENP exposure of people in workplaces (NIOSH, 2009; Pietroiusti and Magrini, 2014). The US National Institute for Occupational Safety and Health (NIOSH) recommends precautionary measures that minimize exposure to ENPs (especially nanoaerosols(NIOSH, 2009). Extensive precautionary control of exposure to ENPs in the workplace has been commented on by Pietroiusti and Magrini (Pietroiusti and Magrini, 2014). These include, but not limited to, evaluating hazards posed by nanomaterials, assessing workers' job tasks, educating and training workers, developing proper protective equipment (e.g., gloves), evaluating control methods, good work practices (e.g., cleaning work areas) and working on criteria and procedures for installing and assessing engineering controls (e.g., exhaust controlling system). To control nano-aerosols, an efficient ventilation system should reduce exposure. Laboratory fume hoods can

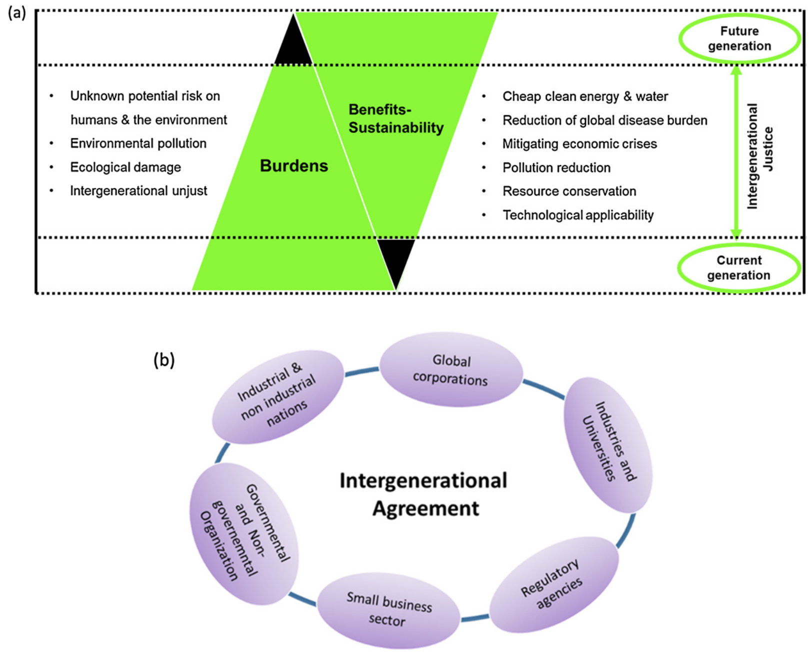


**Fig. 4.** (a) The burdens and benefits of ENPs, (b) Intergenerational agreement which is considered to be the baseline for burdens and benefits that present and future generations must establish in order to achieve sustainable development.

significantly reduce workers' exposure if they are well designed with varied air flow patterns (Vance and Marr, 2015).

The Organisation for Economic Cooperation and Development (OECD) established a list of ENPs that is very relevant to modern workplaces ,OECD, 2008a Several Occupational Exposure Limits (OELs) have been proposed by different national organizations to control ENPs in the workplace. The OELs are based on the type of ENP and their size but, criteria set by organizations for the same ENPs may vary. For example, the German Social Accidental Insurance (IFA) limits particles to 1–100 nm range in the workplace IFA, 2019 . Elsewhere, Safe Work Australia (SWA) limits particles to a size > 100 nm including aggregates and agglomerates (Morawska et al., 2012). The recommendation provided by US NIOSH for biopersistant granular ENPs to have a density < 6 kg/L, for example $TiO_2$ NPs is 0.3 mg/m$^3$, whereas the Japanese New Energy and Industrial Technology Development Organization (AIST) limits it to 0.61 mg/m$^3$ (Pietroiusti and Magrini, 2014). The Occupational and Health Administration (OSHA) of the USA limits silver to 100 μg/m$^3$ for a 40 h workweek OSHA, 2019 Respecting the precautionary measures and the OEL in the workplace reduces the risk of exposure to ENPs.

### 6.2. Regulations and controls

There are several relevant EU and other regulatory legislations that can be applied to control the production and use of nanomaterials; however, they are not equally strong (Technology, 2017).

These are horizontal and product-specific legislation in place in the European Union:

**Horizontal legislation**: apply only to public bodies to impact private rights.

- Regulation (EC) 1907/2006: **Registration, Evaluation, Authorisation, and Restriction of Chemicals** (REACH) (Prinz, 2014). This legislation is applied to imported or manufactured chemical substances in the EU. Currently, the European Commission is preparing modifications to some of the REACH annexes to address nanomaterials related specific issues.
- Regulation (EC) 1272/2008: **Classification, Labelling, and Packaging** (CLP) (Prinz, 2014). Hazardous nanomaterials must be classified and labelled. The manufacturers, importers, and users shall identify the physical state of the substance in which it is placed for sale and distributed for use.
- EU framework Directive 89/391- addresses measures to protect workers' health and safety and **EU framework Directive** 98/24 which documents the hazards related to chemical substances (Technology, 2017).

**Product-specific legislation**:

- Regulation (EC) 1223/2009: **Cosmetics Products -** the EU Commission must be notified about cosmetic products containing nanoparticles six months prior to selling or marketing them, and include toxicological and safety data (Prinz, 2014). For instance, the presence of nano $TiO_2$ in sunscreen lotions must be reported.
- Regulation (EU) 1169/2011: **Food Information to Consumers -** it is mandatory to provide nutrition information for food EU, 2018b . This regulation combined two directives (2001/13/EC and 90/496/EEC) into one piece of legislation. One of the key changes in this regulation is now the mandatory requirement to list engineered nanomaterials in food ingredients.
- Regulation (EC) 1333/2008: **Food Additives -** food additives which change in particle size after being added to certain foodstuffs; a change in specification shall be provided before it is ready for sale Rules, 2019
- Regulation (EU) 528/2012: **Biocidal Products Registration** (BPR). A risk assessment is needed for biocidal products containing ENPs and product labeling will reflect that it comprises nanomaterials EU, 2018a .

However, the effectiveness of current regulations and legislation for controlling ENPs are unsure. In principle, nanomaterials are covered by the scope of many of the existing legislative frameworks. However, it is quite unsure if the current legislations are actually applicable when it comes to specific nanomaterials and their diverse applications (Hansen and Baun, 2012). The reasons for this could be the lack of eco-toxicological data and the minimum values and occupational exposure limits are not established with the existing methodologies. Effective legislations and regulations for the production, sale, use, and disposal of products containing ENPs are currently needed. Regulations and monitoring measures can be implemented by governments, other regulatory agencies and manufacturers if concerns exist for nanomaterial products and any associated risks. The products should only be sold with controllable risks to people and the environment, and after controlled intensive environmental and health impact assessments of nanomaterials have been executed and documented. There are several relevant EU and other regulatory legislations (Park, 2012) that can control the production and use of nanomaterials; however, they are not equally strong (Technology, 2017).

### 6.3. Safe disposal and recycling of nanowaste

The disposal of nanomaterials or materials containing ENPs requires special care to minimize potential health risks posed by the release of nanomaterials. Hazardous, toxic or chemically active nanomaterials must be neutralized before they pose a serious health risk to humans or affect the ecosystems. Whenever necessary, nanomaterials should be recycled before they are disposed of. There are different classes of nanowaste (Musee, 2011); consequently, a ‘one size fits all’ type of procedure for disposal of these nanowastes will not be enough. Therefore, it is important to understand the properties of particular nanowastes and implement specific disposal procedures. Standardized nanowaste disposal procedures are yet to be implemented worldwide (Faunce and Kolodziejczyk, 2017).

### 6.4. Safe design and development of biodegradable ENPs

Research and development scientists have responsibility to design safe ENP products (Vance and Marr, 2015). Robust coatings can minimize abrasion related emission of ENPs. A narrow spray nozzle can reduce nano-aerosol dispersion and can have limited impact in the environment. Development of suitable nanowaste containers that are able to help with segregation of nanomaterials will make nanowastes easy to recycle. The innovative concept of “safe by design” can minimize hazards and consumers’ exposure when ENPs are applied (Kraegeloh et al., 2018). This type of concept ensures that ENPs are user and environmentally friendly, less toxic and biodegradable, and contribute to the sustainability of EC-J and IRG-J. Novel strategies in drug delivery for the treatment of cancer through the safe-by-design approach were envisioned recently (Chuan et al., 2015; Movia et al., 2014). Furthermore, synthesis of nanomaterials from biowaste and industrial waste material are good initiatives (Samaddar et al., 2018).

### 6.5. Creating awareness

Increasing consumer and the wider community’s awareness of the ability of nanotechnology to solve current challenges, when used appropriately, is needed. When nanomaterials are inappropriately employed, they can pose risks to the public and the environment by creating irreversible problems. Awareness of the public should be enhanced through campaigns, dialogues, and education by governmental, non-governmental organizations and official bodies so that communities know the hazards caused by nanomaterials, and what to do when this happens. Makers of products containing nanomaterials must clearly label products and all levels of risk must be disclosed to consumers. Additionally, consumers should be informed on the safe handling of products containing ENPs, and the basics of risk management should be articulated by the manufacturers. Preparing guidelines, sharing experiences, and knowledge transfer and in general, a more unified and collaborative approach at all levels, are vital to address this fast-growing aspect of the use of nanomaterials and the hazards that could occur. Due to manufacturer’s secrecies and nondisclosure policies, important information concerning production, extraction and refining, manufacturing, use and final disposal of the products could be unavailable (Hansen and Baun, 2012). It would be ethically unjust if manufacturers benefited from new technology while all associated risk information to the consumers are limited or uncertain. In 2007, an organization like NIOSH and OECD established a NIOSH-led project to raise awareness on exposure and risk mitigation when using nanomaterials (OECD, 2008b).

### 6.6. Preliminary risk assessment based model and experimental results

When a material changes from bulk to nano form, its chemical and physical properties are also changed. For examples, gold in its bulk form does not absorb visible light; however, the nano form of gold absorbs visible light and can be used as a catalyst. Because of the change in chemical reactivity, gold nanoparticles can show associated toxicity and health concerns. Therefore, materials containing ENPs must be assessed for their toxicity and health hazard before they engage for applications. Ecotoxicological data for new and emerging ENPs are vital and must be provided by the manufacturer before the ENPs is commercialized. For instance, asbestos posed a serious health risk worldwide due to the lack of preliminary toxicity information and health hazard assessment (Boffetta, 1998). Risk assessment supported by both modelling and experimental approaches could be applied to minimize the negative impacts of ENPs in the environment. Most in vivo and in vitro studies employ pure and unprocessed ENPs; however, transformation products may also be toxic. Hence, it is necessary to consider the transformation products of ENPs when conducting toxicity tests. It should be noted that current toxicity tests performed with ENPs are not yet fully standardized for all ENPs (Hund-Rinke et al., 2016). Standardized measurements for determining the toxicity of ENPs to humans and other lifeforms is important to understand the overall toxicity of ENPs. Others measures, such as good characterization techniques of ENPs, and identifying the distribution of ENPs in products with both modelling and experimental approaches is vital. Furthermore, long term impacts of ENPs in the environment should be properly explained, backed up by effective policies and regulations that limit the minimum/threshold of toxicity of ENPs.

## 7. Conclusion and future outlook

With the advancement of technologies, NPs are becoming an increasingly important part in our daily lives. Currently, there are uncertainties about the risks of utilizing ENPs and these risks are yet to be fully understood and quantified. There are uncertainties concerning the use of ENPs appropriately in an ethical way in order to preserve our environment in a sustainable fashion. For example, to what extent drug companies and all concerned parties, including physicians, follow the rules and be ethical in producing and using nanomedicine properly?

There is lack of consideration of environmental ethics in the way that ENPs are currently applied. Available in vitro and in vivo studies demonstrated that ENPs have an adverse effect on the ecosystem and health of humans. Some cases leading to human deaths from exposure to ENPs were described in this review. Ethical queries related to IRG-J and EC-J pertaining to environmental and ecological welfare for present and future generations and sustainability highlighted the potential risks if nanomaterials are continually used without proper control. Appropriate mitigation strategies will be feasible after careful analysis of toxicity data (if available) and risks posed by ENPs. This step involves identification and communication of hazards and risks by governments and scientists, and the selection of the best management controls for ENPs.

To overcome all ethical dilemmas, the appropriate methodologies are to be implemented to protect people and ecology to minimize adverse effect. Apart from conventional engineering measures and protective personal equipment, ethics plays a major role in protecting our environment from the risks posed by ENPs. Such ethical considerations include both IRG-J and EC-J concerning the core applications and practices of ENPs. A fair use of nanomaterials would benefit current and future generations. Knowledge transfer and interpretation regarding scientific data is challenging to the governments, agencies, industries, and public. It is thus necessary for scientists to use appropriate qualifiers in published papers and pay attention to scientific results. Risk mitigation approaches are proposed in this review considering the ethical practices of different shareholders. However, the sustainability of application for nanomaterials requires all efforts and ethical considerations from different parties, in particular the initial interpretation and research activities by scientist.

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