ENVIRONMENTAL HEALTH AND SAFETY: ENVIRONMENT

1 Introduction

Not much is known about exposure of humans to nanomaterials in the environment sector. CNT was identified for use in water filtration systems and nanosensors implemented to monitor environmental parameters. Also other nanomaterials (e.g. Ni, Pt, Au, Si, InP, GaN) are used in nanosensors. Nanosensors were evaluated as part of the ICT sector (see NanoData Landscape Compilation: ICT), and are therefore not further discussed here. Furthermore, nano-remediation was identified as an important environmental application. Various nanomaterials, such as nanoparticles, tubes, wires, fibres, function as adsorbents and catalysts and their composites with polymers are used for the detection and removal of gases (e.g. SO_2, CO, NO_x), chemical contaminants (e.g. arsenic, iron, manganese, nitrate, heavy metals), organic pollutants (aliphatic and aromatic hydrocarbons) and biological substances, such as viruses, bacteria, parasites and antibiotics[1]. Examples of nanomaterials applied are cobalt manganese oxide nanoparticles, synthesised *in situ* in pressurised reactors for the supercritical water oxidation process to clean waste water of organics; zero-valent iron in permeable reactive barriers and silver, iron, gold, iron oxides and titanium oxide in polymeric membranes to remove metals and other contaminants from wastewater; nanofibres (silica, dendrimers, CNTs) in nanofibre media and membranes used for filtration; nano-zeolites and dendrimers functionalised with inorganic nanoparticles, used as sorbents to remove heavy metals from wastewater[2]. Another nanomaterial used in remediation, is nano-calcium peroxide, which is applied in *in situ* chemical oxidation (ISCO) of contaminated ground water, sediment or soil in order to destroy the contaminants by converting them to innocuous compounds[3].

The basis for the evaluation was the "Stoffenmanager Nano" application[4] [5], a risk-banding tool developed for employers and employees to prioritise health risks occurring as a result of respiratory exposure to nanoparticles for a broad range of worker scenarios. This tool combines the available hazard information of a substance with a qualitative estimate of potential for inhalation exposure. "Stoffenmanager Nano" does not contemplate the dermal and oral routes of exposure. The respiratory route is the main route of exposure for many occupational scenarios, while the oral route of exposure is considered minor and sufficiently covered, from a safety point of view, by good hygiene practices established in production facilities as prescribed through general welfare provisions in national health and safety legislation in EU countries[6]. The dermal route may be the main route of exposure for some substances or exposure situations, and cause local effects on the skin or systemic effects after absorption into the body[7]. However, nanoparticles as such are very unlikely to penetrate the skin[8], and consequently nano-specific systemic toxicity via the dermal route is improbable. Therefore, when evaluating nano-risks for the respiratory route, the most important aspects of

[1] Khin, M.M., Nair, A.S., Babu, V.J., Murugan, R., Ramakrishna, S., 2012. A review on nanomaterials for environmental remediation. Energy Environ. Sci. 5, 8075. doi:10.1039/c2ee21818f

[2] Ibid

[3] Khodaveisi, J., Banejad, H., Afkhami, A., Olyaie, E., Lashgari, S., Dashti, R., 2011. Synthesis of calcium peroxide nanoparticles as an innovative reagent for in situ chemical oxidation. J. Hazard. Mater. 192, 1437–40. doi:10.1016/j.jhazmat.2011.06.060

[4] Marquart, H., Heussen, H., Le Feber, M., Noy, D., Tielemans, E., Schinkel, J., West, J., Van Der Schaaf, D., 2008. 'Stoffenmanager', a web-based control banding tool using an exposure process model. Ann. Occup. Hyg. 52, 429-441

[5] Van Duuren-Stuurman, B., Vink, S., Verbist, K.J.M., Heussen, H.G.A., Brouwer, D., Kroese, D.E.D., Van Niftrik, M.F.J., Tielemans, E., Fransman, W., 2012. Stoffenmanager Nano version 1.0: a web-based tool for risk prioritisation of airborne manufactured nano objects. Ann. Occup. Hyg. 56, 525-541

[6] ECHA, 2012. Chapter R.14: Occupational exposure estimation in: Anonymous Guidance on Information Requirements and Chemical Safety Assessment., Version: 2.1 ed. European Chemicals Agency, Helsinki, Finland.

[7] Ibid

[8] Watkinson, A.C., Bunge, A.L., Hadgraft, J., Lane, M.E., 2013. Nanoparticles do not penetrate human skin - A theoretical perspective. Pharm. Res. 30, 1943-1946

occupational safety are covered.

Currently version 1 of Stoffenmanager Nano is being updated with recent data and insights. The hazard of six metal oxide nanoparticles has been reassessed and their hazard bands have been updated. This revision is based on more recent toxicity data to attribute the hazard bands according to the methodology described in the ISO guideline on the use of the control banding approach in occupational risk management of engineered nanomaterials[9] [10]. It has been published in a TNO-report[11]. Hazard bands for the nanoparticles listed in the table below are taken by preference from this report and, if not available in that report, from van Duuren-Stuurman et al. (2012). If a nanoparticle in the list has not been evaluated in either publication, data were collected from public literature to derive its hazard band, as described in the section on hazard assessment below.

2 Hazard assessment

In the ISO guidelines the available hazard information is used to assign specific nanoparticles to one of five hazard bands, labelled A to E (A= low hazard, E= highest hazard). In essence, it applies the toxicity classification rules of the Globally Harmonised System (GHS)[12] to establish the hazard band. The table below lists the criteria to allocate hazard bands per toxicity endpoint.

The highest toxicity endpoint hazard for a given nanomaterial is attributed to that material. Details of the hazard bands derived for each material are given below.

CALCIUM PEROXIDE NANOPARTICLES

In contact with water, CaO_2 dissolves to form H_2O_2 and $Ca(OH)_2$, liberating a maximum of 0.47 g H_2O_2/g CaO_2 (Khodaveisi et al., 2011). The rate at which it decomposes is higher for nano-calcium peroxide than for micro-calcium peroxide[13]. No data on the toxicity of the nano-form have been found in public literature, and since it decomposes into soluble compounds in water, its hazard should be evaluated using Stoffenmanager for bulk compounds. Calcium peroxide is not classified for toxic hazards by the EU, but the majority of REACH registrants has classified it with Skin Irrit. 2 (H315), Eye Irrit. 2 (H319) and STOT SE 3 (H335). Based on the last classification calcium peroxide is allocated hazard band C.

[9] This approach is very similar to the Stoffenmanager version 1.0 approach.

[10] ISO, 2013. Nanotechnologies -- Occupational risk management applied to engineered nanomaterials -- Part 2: Use of the control banding approach, ISO/PDTS 1. ed. International Organisation for Standardisation, Geneva, Switzerland. doi:http://www.iso.org/iso/catalogue_detail.htm?csnumber=53375

[11] Le Feber, M., Kroese, E.D., Kuper, C.F., Stockmann-Juvala, H., Hyytinen, E.R., 2014. Pre-assigned hazard bands for commonly used nanoparticles.

[12] UN, 2015. Globally Harmonized System of Classification and Labelling of Chemicals (GHS). United Nations, New York, USA and Geneva, Switzerland

[13] Khodaveisi, J., Banejad, H., Afkhami, A., Olyaie, E., Lashgari, S., Dashti, R., 2011. Synthesis of calcium peroxide nanoparticles as an innovative reagent for in situ chemical oxidation. J. Hazard. Mater. 192, 1437–40. doi:10.1016/j.jhazmat.2011.06.060

Table: Allocation of hazard bands per toxicity endpoint to nanomaterials insoluble in water

Toxicity category	Hazard band				
	A No significant health hazard	B Slight Hazard	C Moderate Hazard	D Serious hazard	E Severe hazard
Acute toxicity: LC_{50} inhalation 4H (mg/m^3) (Aerosols/particles)	Low >5000	Acute tox 4 1000-5000	Acute tox 3 500-1000	Acute tox 1-2 <500	-
Severity of acute (life-threatening) effects		STOT SE 2-3; Asp. Tox 1	STOT SE 1	-	-
Respiratory Sensitization	Negative	-	-	-	Prevalent moderate to strong respiratory allergic reactions Resp. Sens. 1
Mutagenicity/ genotoxicity	Negative	-	-	-	Muta 2, Muta 1A-1B
Irritant/ corrosiveness[a]	None to Irritant Eye Irrit.2: Skin Irrit 2 EUH066	-	Severe Irritant skin/eyes Irritant to respiratory tract STOT SE 3: Eye Dam. 1 Corrosive Skin Cor. 1A-1B	-	-
Carcinogenicity in combination with mutagenicity[b]	Negative	Negative	Some evidence in animals Carc. 2	-	Confirmed in animals or humans. Carc. 1A-1B
Carcinogenicity without mutagenicity[b]	Negative	Negative	Some evidence in animals Carc. 2	Confirmed in animals or humans. Carc. 1A-1B	-
Developmental/ reproductive toxicity	Negative	Negative	Negative	Reprotoxic defects in animals and/or suspected or proved in humans Repr. 1A/B or 2	-
Likelihood of chronic effects Adverse effects per respiratory route (mg/m^3/6h/day) (90 day chronic study with dusts/mists/ fumes)[d]	Unlikely Not adverse effects seen at CS < 200[e]	Unlikely Not adverse effects seen at CS < 200[e]	Possible, STOT RE 2 Adverse effects seen at 20 < CS < 200	Probable, STOT RE 1[c] Adverse effects seen at CS < 20	-

Table modified from the ISO guidelines (ISO, 2013)

CARBON NANOTUBES, SINGLE- AND MULTI-WALLED (CNT)

Carbon nanotubes have often been demonstrated to have severe toxicity; however, this seems to be largely dependent on the dose, the degree of agglomeration and the route of administration. Differences in toxicity are also expected between single and multi-walled CNTs and are presumably dependent on their aspect ratio[14].

Upon inhalation, single walled carbon nanotubes (SWCNTs) have shown various chronic inflammatory responses in rat and mice, depending on type of exposure (inhalation, oral administration)[15] [16] [17]. For example, while no tumours were reported in the case of short to medium term pulmonary exposures to SWCNTs or MWCNTs in rodents, several studies have shown the potential for MWCNTs to act like the persistent fibres of asbestos, causing thoracic inflammation and fibrosis. Additionally, MWCNT have been shown to penetrate the alveolar region of the lung and to cause inflammation. These biological events have been shown to lead to the cancer mesothelioma[18], although MWCNT have not been demonstrated to *de facto* cause mesotheliomas. Still the weight-of-evidence for certain types of MWCNT (e.g., those with high aspect ratios) is increasing. In conclusion, flexible, rigid, high-aspect-ratio MWCNT may cause cancer in a similar fashion to asbestos and may be as potent in this respect.

Based on the data summarised above, there are indications that carbon nanotubes are mutagenic and carcinogenic while some can be classified as persistent fibres. Therefore, they are consigned to the highest hazard band, E.

COBALT MANGANESE OXIDE NANOPARTICLES

These particles are formed *in situ* and react *in situ* in closed reactors and as such will not constitute a human safety issue and are therefore not further discussed here.

COBALT-PLATINUM NANO-CATALYST (CO PT ALLOY)

No data on the toxicity of the alloy, be it in bulk or nano-form, have been found in public literature, hence it will be evaluated based on the properties of its constituent metals. The table below lists the classifications published by ECHA: cobalt has a globally harmonised classification and platinum only self-classifications. The most serious classification is that of cobalt for respiratory sensitisation code 1, on which basis the nanoparticle is attributed hazard band E.

Table: Classification of cobalt and platinum for human health hazards as listed by ECHA

Hazard class and code	Hazard statement code	Cobalt (GHS) classification?	Platinum (self-classification) # classified/total notifiers
Skin Sens. 1	H317	yes	56/317
Resp. Sens. 1	H334	yes	9/317
Skin Irr. 2	H315	no	1/317
Eye irr. 2	H319	no	1/317

Source: http://echa.europa.eu/information-on-chemicals/cl-inventory-database

COPPER TUNGSTATE ($CuWO_4$)

No toxicity data on copper tungstate, be it in the bulk or nano-form, have been retrieved from public

[14] El-Ansary, A., Al-Daihan, S., Bacha, A.B., Kotb, M., 2013. Toxicity of novel nano-sized formulations used in medicine. Methods Mol. Biol.

[15] Ibid

[16] Zhao, J., Castranova, V., 2011. Toxicology of nanomaterials used in nanomedicine. J. Toxicol. Environ. Heal. - Part B Crit. Rev. 14, 593–632.

[17] Yildirimer, L., Thanh, N.T.K., Loizidou, M., Seifalian, A.M., 2011. Toxicological considerations of clinically applicable nanoparticles. Nano Today 6, 585–607.

[18] http://www.mesothelioma.com/mesothelioma/

literature. Copper tungstate is virtually insoluble in water[19]. Nano-copper tungstate is used for its photocatalytic activity[20] and has a band gap energy of 3.5 eV[21]. In several respects, it is comparable to titanium dioxide, namely it is also insoluble in water, is photocatalytic and has a similar band gap energy of 3.0 (rutile) or 3.2 eV (anatase)[22]. Therefore, tentatively and in view of the uncertainties of this read-across, copper tungstate is attributed one hazard band higher than titanium dioxide, i.e. band D.

DENDRIMERS

The most successful early dendrimeric constructs were synthesised using classical linear, random coil polymers, such as polyethylene glycol (PEG), N-(2-hydroxypropyl) methacrylamide (HPMA) copolymers, poly(glutamic acid) (PGA), poly(ethyleneimine) (PEI) and dextrin (a-1,4 polyglucose), while more recently polyamidoamine (PAMAM; Starburstk) dendrimers and poly propylenemine) (also called PPI, DAB; AstramolR) dendrimers have gained commercial success[23].

Many in vitro studies have shown toxic effects for almost all of dendrimeric nano-polymers, depending on particle size, shape, coating and many other factors[24] [25]. When they display clear toxicity, it is mostly associated with cationic dendrimers disrupting the cell membrane, e.g. the 5.0G PPI dendrimer has a 24h-EC_{50} for HEPG2 cells between appr. 10 and 1 µg/mL and a 72h-EC_{50} < 1 µg/mL (Jain, et al. 2010). At concentrations around 1 mg/mL, also clear haemolytic effects were observed in vitro (4 h incubation) with uncoated dendrimers, but not with coated ones (Jain, et al. 2010). Via the i.p route LD_{50} of 7.0 G PAMAM dendrimers is between 40 and 160 mg/kg in mice, while sub-chronic administration of 2.5 and 10 mg/kg bw did not result in mortality nor in renal damage. Based on the available data, no clear conclusion can be drawn with respect to dendrimer toxicity, but based on their membrane disruptive effects, it cannot be excluded that they may cause serious health effects, especially after respiratory exposure. Since there is no indication of mutagenic effects, and they also do not seem probably as these polymers destroy the cell membrane thus killing the cell, this nanoparticle is assigned the one but highest hazard band, D.

FULLERENES (C60)

Classified by Stoffenmanager Nano in hazard band D[26].

GRAPHENE AND GRAPHENE OXIDE

Graphene is composed of sp2-hybridised carbon atoms arranged in a two-dimensional structure. The various forms of graphene include few-layer graphene, reduced graphene oxide, graphene nano-sheets and graphene oxide (GO)[27].

The UK government body, the Medicines and Healthcare Products Regulatory Agency (MHRA), and the US Food and Drug Administration (FDA) are now reviewing all forms of graphene and

[19] Grobler, S.R., Suri, S.K., 1980. Solubilities of the molybdates and tungstates of silver and copper(II) in water by ion-selective electrodes. J. Inorg. Nucl. Chem. 42, 51–53. doi:10.1016/0022-1902(80)80042-X

[20] Gouma, P.I., Lee, J., 2014. Photocatalytic nanomats clean up produced water from fracking. Transl. Mater. Res. 1, 25002.

[21] Jovanović, D.J., Validžić, I.L., Mitrić, M., Nedeljković, J.M., 2012. Synthesis and structural characterisation of nano-sized copper tungstate particles 59, 70–74

[22] Li, W., Bak, T., Atanacio, A., Nowotny, J., 2016. Photocatalytic properties of TiO2: Effect of niobium and oxygen activity on partial water oxidation 198, 243–253. doi:10.1016/j.apcatb.2016.05.044

[23] Duncan, R., Izzo, L., 2005. Dendrimer biocompatibility and toxicity. Adv. Drug Deliv. Rev. 57, 2215–2237.

[24] Ibid.

[25] Jain, K., Kesharwani, P., Gupta, U., Jain, N.K., 2010. Dendrimer toxicity: Let's meet the challenge. Int. J. Pharm. 394, 122–142.

[26] Van Duuren-Stuurman, B., Vink, S., Verbist, K.J.M., Heussen, H.G.A., Brouwer, D., Kroese, D.E.D., Van Niftrik, M.F.J., Tielemans, E., Fransman, W., 2012. Stoffenmanager Nano version 1.0: a web-based tool for risk prioritisation of airborne manufactured nano objects. Ann. Occup. Hyg. 56, 525–541. doi:10.1093/annhyg/mer113

[27] Seabra, A.B., Paula, A.J., De Lima, R., Alves, O.L., Durán, N., 2014. Nanotoxicity of graphene and graphene oxide. Chem. Res. Toxicol. 27, 159-168.

functionalised graphene oxide (GO) because of their poor solubility, high agglomeration, long-term retention, and relatively long circulation time in the blood[28].

Currently, limited information about the *in vitro* and *in vivo* toxicity of graphene is available[29]. The toxicity profiles of graphene and graphene oxide (GO) nanoparticles remain difficult to separate, since their characterisation, bulk and chemical composition are very similar at the nanometre length scale[30].

In vitro graphene has been demonstrated to be cytotoxic, be it overall to a lesser degree than carbon nanotubes (Seabra, et al. 2014). However, the reliability of this conclusion can be doubted since Seabra et al. stated that graphene showed an inverse dose-relationship, being more cytotoxic than carbon nanotubes at low concentrations. The only elaborate comparative study reported by Seabra et al., refers to genotoxicity towards human fibroblast cells. GO proved to be the most potent genotoxic agent compared to iron oxide (Fe304), titanium dioxide (Ti02), silicon dioxide (Si02), zinc oxide (ZnO), indium (In), tin (Sn), core—shell zinc sulphate-coated cadmium selenide (CdSe(3)ZnS), and carbon nanotubes.

GO has been shown to cause severe pulmonary distress in mice after inhalation causing excessive inflammation, while non-functionalised graphene[31]. Single intravenous (i.v.) injection of graphene oxide into mice accumulated in the lung resulting in pulmonary oedema and granuloma formation[32]. Furthermore, surface functionalised graphene (PEGylated) appears to be far less toxic: no toxic effects after single i.v. injection[33]. In mice, PEGylated GO materials showed no uptake via oral administration, indicating limited intestinal absorption of the material, with almost complete excretion. In contrast, upon intra-peritoneal (i.p.) injection in mice, PEGylated GO was found to accumulate in the liver and spleen[34].

The toxicity of graphene is dependent on the graphene surface (the chemical structure or the nature of the functionalised coatings), size, number of layers, cell type, administration route (for *in vivo* experiments), dose, time of exposure, and synthesis methods[35]. Generalisations are therefore hard to make, but graphene nanostructures are not fibre-shaped and theoretically may be assumed to be safer than carbon nanotubes[36].

Based on the scarce available evidence, it cannot be excluded that some forms of graphene will be as potent a toxicant as carbon nanotubes. Therefore, graphene and graphene oxide are assigned to hazard band E.

IRON NANOPARTICLES

[28] Begum et al. 2011 cited in Nezakati, T., Cousins, B.G., Seifalian, A.M., 2014. Toxicology of chemically modified graphene-based materials for medical application. Arch. Toxicol. 88, 1987-2012.

[29] Seabra, A.B., Paula, A.J., De Lima, R., Alves, O.L., Durán, N., 2014. Nanotoxicity of graphene and graphene oxide. Chem. Res. Toxicol. 27, 159–168.

[30] Nezakati, T., Cousins, B.G., Seifalian, A.M., 2014. Toxicology of chemically modified graphene-based materials for medical application. Arch. Toxicol. 88, 1987–2012

[31] Duch, M.C., Budinger, G.R.S., Liang, Y.T., Soberanes, S., Urich, D., Chiarella, S.E., Campochiaro, L.A., Gonzalez, A., Chandel, N.S., Hersam, M.C., Mutlu, G.M., 2011. Minimising oxidation and stable nanoscale dispersion improves the biocompatibility of graphene in the lung. Nano Letters 11, 5201-5207.

[32] Zhang, X., Yin, J., Peng, C., Hu, W., Zhu, Z., Li, W., Fan, C., Huang, Q., 2011. Distribution and biocompatibility studies of graphene oxide in mice after intravenous administration. Carbon 49, 986-995

[33] Yang, K., Wan, J., Zhang, S., Zhang, Y., Lee, S.-T., Liu, Z., 2011. In vivo pharmacokinetics, long-term biodistribution, and toxicology of pegylated graphene in mice. ACS Nano 5, 516–522.

[34] Yang, K., Gong, H., Shi, X., Wan, J., Zhang, Y., Liu, Z., 2013. In vivo biodistribution and toxicology of functionalised nano-graphene oxide in mice after oral and intraperitoneal administration. Biomaterials 34, 2787–95. doi:10.1016/j.biomaterials.2013.01.001 cited in Seabra, A.B., Paula, A.J., De Lima, R., Alves, O.L., Durán, N., 2014. Nanotoxicity of graphene and graphene oxide. Chem. Res. Toxicol. 27, 159–168.

[35] Seabra, A.B., Paula, A.J., De Lima, R., Alves, O.L., Durán, N., 2014. Nanotoxicity of graphene and graphene oxide. Chem. Res. Toxicol. 27, 159–168.

[36] Seabra, A.B., Paula, A.J., De Lima, R., Alves, O.L., Durán, N., 2014. Nanotoxicity of graphene and graphene oxide. Chem. Res. Toxicol. 27, 159–168.

Classified by Stoffenmanager Nano in hazard band D for sizes ≤50 nm (C for sizes >50 nm). Since the size distribution of the iron nanoparticles used may include sizes below 50 nm, the highest risk band is used in the risk assessment applied here.

IRON OXIDE NANOPARTICLES

Classified by Stoffenmanager Nano in hazard band D for sizes ≤50 nm (C for sizes >50 nm). Since the size distribution of the iron oxide nanoparticles used may include sizes below 50 nm, the highest risk band is used in the risk assessment applied here.

GOLD NANOPARTICLES

Classified by Stoffenmanager Nano in hazard band D for sizes ≤50 nm (C for sizes >50 nm). Since the size distribution of the gold nanoparticles used may include sizes below 50 nm, the highest risk band is used in the risk assessment applied here.

MICELLES

Micelles in aqueous environments are globular aggregates of amphipathic molecules with their hydrophobic tails facing inwards and their hydrophilic heads facing outwards[37]. In the environment nano-micelles may be used to clean polluted water from metals and organic pollutants[38]. There are many chemically different nano-micelles, that may differ in toxicity. However, most likely in the application envisaged here their toxicity may principally depend on the pollutants they sequester and concentrate inside themselves. Therefore, it is not feasible to derive a hazard band for nano-micelles in general without taking into account their chemical composition and the pollutants they are supposed to remove from the environment.

NANOCLAY

Classified by Stoffenmanager Nano in hazard band D for sizes ≤50 nm, and in band C for sizes >50 nm. Since the size distribution of the nanoclay nanoparticles used may include sizes below 50 nm, the highest risk band is used in the risk assessment applied here.

NANO-POROUS MATERIALS

The description of the role of nanotechnology for environmental purposes in chapter 2 mentions the use of nanocrystals to capture carbon dioxide. Sneddon et al. (2014) reviewed the use of nano-porous materials, amongst others materials with a crystalline structure, in carbon dioxide capture. None of these are already applied at an industrial scale and it is doubtful that they ever will be in view of their higher costs in comparison to the absorbent usually applied in the capture and subsequent geological storage of carbon dioxide[39]. Technically, metal-organic frameworks (MOFs) and mesoporous[40] silicas and ordered mesoporous activated carbon functionalised with amine groups are the most likely candidates for carbon dioxide capture. Since all these materials themselves are not nano-sized, but only contain nano-sized pores, their toxicological properties will be mainly determined by their bulk chemical properties. MOFs often contain toxic metals (e.g. Cu) and/or heterocyclic or aromatic organic compounds, making it likely more hazardous than e.g. mesoporous silicas and activated carbon. However, the nature of amine compounds ligated to the silicas and activated carbon in order to confer carbon dioxide capturing properties to them, may introduce hazardous properties to these rather inert bulk chemicals. Concluding, based on the scant information available and great variety in materials applied, no realistic estimate of the hazard band to be attributed to nano-porous materials

[37] Stryer, L., 1988. Introduction to biological membranes, in: Biochemistry. W.H. Freeman and Company, New York, USA, pp. 280–312.

[38] Noh, S. Il, Shim, J.K., Kim, J.Y., 2008. New amphiphilic polymer nanoparticle-enhanced UF process for removal of organic pollutants and metal ions 14, 480–486. doi:10.1016/j.jiec.2008.02.007

[39] Sneddon, G., Greenaway, A., Yiu, H.H.P., 2014. The potential applications of nanoporous materials for the adsorption, separation, and catalytic conversion of carbon dioxide 4. doi:10.1002/aenm.201301873

[40] The designation “mesoporous” refers to nano-sized pores.

can be made.

NANO-COATED HYDROPHOBIC SAND

The description in this report of the role of nanotechnology for environmental purposes mentions nano-coated hydrophobic sand to create an artificial water table in the soil in order to address water scarcity. Since the sand will consist of macroscopic grains and is chemically inert, possible toxicological hazards of this material will depend on the nature of the nano-coating used and human exposure to it will largely depend on the ease with which it may get detached from the sand when coming in contact with the skin. Due to lack of information in these respects, no realistic estimate of the hazard band to be attributed to nano-coated hydrophobic sand can be made.

SILICON NANOWIRES

Silicon nanowires are high-aspect ratio filamentary crystals of silicon, which implicates these nanowires may cause asbestos-like toxicity upon inhalation[41]. Fibres may induce lung inflammation and fibrosis that progress over time after exposure and may eventually lead to tumour formation. Whether this process occurs will depend on the dimensions of the fibres (length and width), and their durability (bio-persistence). Particles less than 3 µm in width deposit more readily in the respirable region of the lung; long fibres with lengths greater than 15 µm frustrate phagocytosis and clearance by alveolar macrophages. Roberts et al. (2012) performed an in vivo experiment in rats to test whether silicon nanowires do cause asbestos-like toxicity. They found indications for the fibre paradigm being valid for these nanowires, but the evidence was not conclusive, a.o. because of the scarcity of long fibres ultimately reaching the alveoli. In view of the physical properties of the silicon nanowires and the fact that some evidence points to them following the fibre paradigm, hazard band E is attributed to them, in accordance with the Stoffenmanager Nano approach.

SILVER NANOPARTICLES

In an update on silver and some metal oxide nanoparticles hazard band D was attributed to nanosilver[42].

SINGLE ENZYME NANOPARTICLES (SENS)

The description of the role of nanotechnology for environmental purposes in chapter 2 mentions the use of SENs in water remediation. Immobilising enzymes on nanoparticles will allow increased concentrations of the enzyme and convey a broader working pH and temperature range and a higher thermal stability. Many different nanoparticles may be used, like alumina nanoparticles, cellulose-coated magnetite nanoparticles, Fe_3O_4 nanoparticles, gold nanoparticles, poly-methyl methacrylate (PMMA) nanoparticles, polystyrene nanoparticles, silica coated nickel nanoparticles, silica nanoparticles, zeolite-gold nanoparticles and ZnO nanoparticles, as well as single and multi-walled carbon nanotubes and graphene oxide nanomaterials[43] [44]. Not only the nature of the nanoparticles employed but also that of the enzyme immobilised on it will determine the hazardous properties of single enzyme nanoparticles, since enzymes are bioactive compounds. Concluding, based on the scant information available and great variety in nanoparticles and enzymes applied, no realistic estimate of the hazard band to be attributed to SENs can be made.

[41] Roberts, J.R., Mercer, R.R., Chapman, R.S., Cohen, G.M., Bangsaruntip, S., Schwegler-Berry, D., Scabilloni, J.F., Castranova, V., Antonini, J.M., Leonard, S.S., 2012. Pulmonary toxicity, distribution, and clearance of intratracheally instilled silicon nanowires in rats 2012. doi:10.1155/2012/398302

[42] Le Feber, M., Kroese, E.D., Kuper, C.F., Stockmann-Juvala, H., Hyytinen, E.R., 2014. Pre-assigned hazard bands for commonly used nanoparticles.

[43] Ansari, S.A., Husain, Q., 2012. Potential applications of enzymes immobilised on/in nano materials: A review. doi:10.1016/j.biotechadv.2011.09.005

[44] Campbell, A.S., Dong, C., Meng, F., Hardinger, J., Perhinschi, G., Wu, N., Dinu, C.Z., 2014. Enzyme catalytic efficiency: A function of bio-nano interface reactions 6, 5393–5403. doi:10.1021/am500773g

TITANIUM DIOXIDE NANOPARTICLES

In an update on some metal oxide nanoparticles hazard band C was attributed to titanium dioxide nanoparticles[45].

3 Exposure assessment

For the environmental applications where information on the application process or conditions is available, the nanomaterials are either present in a closed system or in a solid matrix (e.g. membrane, filter, grid). For such applications the exposure potential during the use phase is low (1). It may be assumed this is also the case for the other applications mentioned. However, a number of applications mentioned are still being investigated at the laboratory scale only, and consequently their exact use condition at an environmental scale are yet uncertain. Furthermore, during the production phase of these systems or matrices the exposure potential may be higher (3). Also during the end-of life phase, exposure is not expected to be very high, but somewhat higher than during the use phase (2).

4 Risk assessment

The hazard and exposure bands are combined to yield so called priority bands, according to the scheme depicted in the table below. A high priority implies that it is urgent to apply exposure control measures or to assess the risks more precisely, and a low priority implies that it is not very urgent to apply exposure control measures ort to establish the risk involved with more precision. It should be emphasised that because of the scarcity of available information, the scheme is set in a conservative way (according to the precautionary principle).

Table: Priority bands in the Stoffenmanager

exposure band \ hazard band	A	B	C	D	E
1	3	3	3	2	1
2	3	3	2	2	1
3	3	2	2	1	1
4	2	1	1	1	1

Hazard: A = lowest hazard and E = highest hazard; exposure: 1 = lowest exposure and 4 = highest exposure; overall result: 1 = highest priority and 3 = lowest priority (Van Duuren-Stuurman, et al. 2012).

Risks based on the hazard and exposure banding applied to the environmental sector are listed in the table below. Carbon nanotubes, dendrimers, graphene and graphene oxide have a high priority (1), indicating the need to apply exposure control methods or to assess the risks more precisely. All other materials have an intermediate priority, except calcium peroxide and titanium dioxide in the in-use phase, for which they have a low priority.

[45] Le Feber, M., Kroese, E.D., Kuper, C.F., Stockmann-Juvala, H., Hyytinen, E.R., 2014. Pre-assigned hazard bands for commonly used nanoparticles.

Table: Priority bands nanotechnology environmental sector

		Exposure band	
		In-use exposure	End-of-life exposure (occupational)
Nanoparticle	**Hazard band**	**1**	**2**
Calcium peroxide	C	3	2
Carbon nanotubes, single- and/or multiwalled	E	1	1
Cobalt manganese oxide	n/a	n/a	n/a
Cobalt-platinum nanocatalyst	E	1	1
Copper tungstate ($CuWO_4$)	D	2	2
Dendrimer	E	1	1
Fullerenes (C60)	D	2	2
Gold	D	2	2
Graphene and graphene oxide	E	1	1
Iron	D	2	2
Iron oxide	D	2	2
Micelles	n/a	n/a	n/a
Nanocoated hydrophobic sand	n/a	n/a	n/a
Nanoclay	D	2	2
Nanoporous materials	n/a	n/a	n/a
Silicon nanowires	E	1	1
Silver	D	2	2
Single enzyme nanoparticles (SENs)	n/a	n/a	n/a
Titanium dioxide (titania, rutile, anatase)	C	3	2