ENVIRONMENTAL HEALTH AND SAFETY: CONSTRUCTION

1 Introduction

Exposure to nanomaterials in the construction sector may be quite diverse. Seven categories of categories of construction materials were identified within the NanoData project. All combinations of nanoparticles and sectors were evaluated. The basis for the evaluation was "Stoffenmanager Nano" application[1, 2, 3], a risk-banding tool developed for employers and employees to prioritise health risks occurring as a result of respiratory exposure to hazardous nanoparticles for a broad range of worker scenarios.

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[4]. In view of the nature of the products in this sector, oral exposure of consumers is also considered to be minor.

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[5]. However, nanoparticles as such are very unlikely to penetrate the skin[6] and consequently nano-specific systemic toxicity via the dermal route is improbable. Therefore, when evaluating risks from nanotechnology for the respiratory route, the most important aspects of occupational and consumer safety are covered.

2 Hazard assessment

In Stoffenmanager Nano, 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). The table below presents an overview of nanoparticles (selected for their use in the construction sector) and their hazard bands, either taken from le Feber et al. (2014)[7] or van Duuren et al. (2012)[8] or derived in this project.

Table: Hazard bands for the specified nanoparticles

Nanoparticles	Hazard band	Source
Carbon nanotubes	E	This report
Carbon nanofibres	D	This report
Copper	D	This report
Graphene	E	This report
Graphite nanoparticles	E	This report

[1] Le Feber, M., Kroese, E.D., Kuper, C.F., Stockmann-Juvala, H., Hyytinen, E.R., 2014. Pre-assigned hazard bands for commonly used nanoparticles. TNO2014 R11884.

[2] 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.

[3] 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.

[4] 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.

[5] Ibid

[6] 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

[7] Le Feber, M., Kroese, E.D., Kuper, C.F., Stockmann-Juvala, H., Hyytinen, E.R., 2014. Pre-assigned hazard bands for commonly used nanoparticles. TNO2014 R11884.

[8] 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.

Nanoparticles	Hazard band	Source
Iron oxide	D	This report
Molybdenum	C	van Duuren et al. (2012)
Silicon carbide	C	This report
Silicon dioxide (silica), crystalline	E	van Duuren et al. (2012)
Silicon dioxide (silica), synthetic amorphous	C	le Feber et al. (2014)
Titanium dioxide	D	le Feber et al. (2014)
Tungsten oxide	E	van Duuren et al. (2012)
Vanadium pentoxide	E	van Duuren et al. (2012)
Zinc oxide	B	le Feber et al. (2014)

Details of the hazard bands derived for each material are given below.

CARBON NANOTUBES (CNTS), SINGLE- AND MULTI-WALLED (MWCNTS)

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.

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). 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. In addition, MWCNT have been shown to penetrate into the alveolar region of the lung and to cause inflammation. These biological events have been shown to lead to the cancer mesothelioma, although MWCNTs 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.

CARBON NANOFIBRES (CNFS)

CNFs are related to CNTs[9, 10]. The former consist of stacked graphite platelets, while the latter consist of graphite platelets rolled up in cylinders. Due to their graphitic structure, CNFs are highly insoluble, and thus highly bio persistent, and are not expected to be broken down when inhaled[11]. The *in vitro* toxic properties of CNFs have been summarised[12] in comparison with carbon black, an extremely fluffy fine powder with a large surface area composed of elemental carbon (IARC, 2010), and CNTs. The most important observations are mentioned below.

Several studies show that the cytotoxicity of CNFs is very low. The sequence of increasing potency for

[9]Fubini, B., Fenoglio, I., Tomatis, M., Turci, F., 2011. Effect of chemical composition and state of the surface on the toxic response to high aspect ratio nanomaterials. Nanomedicine (Lond). 6, 899–920. doi:10.2217/nnm.11.80

[10] NIOSH, 2013. Current Intelligence Bulletin 65. Occupational exposure to carbon nanotubes and nanofibres. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, Washington DC, USA.

[11] Fubini, B., Fenoglio, I., Tomatis, M., Turci, F., 2011. Effect of chemical composition and state of the surface on the toxic response to high aspect ratio nanomaterials. Nanomedicine (Lond). 6, 899–920. doi:10.2217/nnm.11.80

[12] Ibid

carbon black, CNTs and CNFs is: carbon black < CNFs < CNTs.

Carbon nanofibres also have a low inflammatory potential. While CNTs induced a dose-dependent increase in DNA damage at all dose and treatment times, CNFs induced DNA strand breaks and chromosomal damage in human bronchial epithelial only after a long time of treatment with no dose dependence. However, CNFs containing iron impurities (<1.4% wt) showed a genotoxicity comparable with asbestos and stronger than SWCNTs[13]. Exposure to CNFs can cause respiratory effects similar to those observed for CNTs. CNFs are a less potent inflammatory agent than MWCNTs and of comparable potency as carbon black.

Concluding, CNFs appear to be of comparable toxicity with carbon black and are less toxic than MWCNTs. Since MWCNTs are attributed to hazard band E and carbon black to hazard band D in Stoffenmanager Nano (Van Duuren-Stuurman et al., 2012), carbon nanofibres are placed in hazard band D.

COPPER

No *in vivo* inhalation toxicity studies adequate for toxicological risk assessment of metallic copper nanoparticles were identified in public literature. As metallic copper is insoluble in water, classification of the bulk material could be used to derive a hazard band for metallic copper nanoparticles. Bulk copper is not classified for human toxicological endpoints, which would mean it should be attributed hazard band C (Van Duuren-Stuurman et al., 2012). However, the ECHA registration dossier explicitly mentions the classification is only applicable to copper powders, with particle size > 10µm and <1 mm. Furthermore, like e.g. silver nanoparticles, copper nanoparticles are antimicrobials whose effectiveness increases with decreasing size[14, 15] suggesting that nanocopper, like nanosilver, is more toxic than its bulk counterpart. Comparative *in vitro* evaluation of cytotoxicity showed nanocopper to even be slightly more cytotoxic than nanosilver[16]. Nanosilver has been attributed hazard band D[17] and based on the comparison mentioned above, nanocopper is attributed the same hazard band.

GRAPHENE

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 nanosheets and graphene oxide (GO)[18].

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 functionalised graphene oxide (GO) because of their poor solubility, high agglomeration, long-term retention, and relatively long circulation time in the blood[19].

[13] Fubini, B., Fenoglio, I., Tomatis, M., Turci, F., 2011. Effect of chemical composition and state of the surface on the toxic response to high aspect ratio nanomaterials. Nanomedicine (Lond). 6, 899–920. doi:10.2217/nnm.11.80

[14] Nuñez-Anita, R.E., Acosta-Torres, L.S., Vilar-Pineda, J., Martínez-Espinosa, J.C., de la Fuente-Hernández, J., Castaño, V.M., 2014. Toxicology of antimicrobial nanoparticles for prosthetic devices. Int. J. Nanomedicine 9, 3999–4006. doi:10.2147/IJN.S63064

[15] Schrand, A.M., Rahman, M.F., Hussain, S.M., Schlager, J.J., Smith, D.A., Syed, A.F., 2010. Metal-based nanoparticles and their toxicity assessment. Wiley Interdiscip. Rev. Nanomed. Nanobiotechnol. 2, 544–68. doi:10.1002/wnan.103

[16] Lanone, S., Rogerieux, F., Geys, J., Dupont, A., Maillot-Marechal, E., Boczkowski, J., Lacroix, G., Hoet, P., 2009. Comparative toxicity of 24 manufactured nanoparticles in human alveolar epithelial and macrophage cell lines. Part. Fibre Toxicol. 6.

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

[18] 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.

[19] 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.

Currently, limited information about the *in vitro* and *in vivo* toxicity of graphene is available[20]. 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[21].

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[22]. Single intravenous (i.v.) injection of graphene oxide into mice accumulated in the lung resulting in pulmonary oedema and granuloma formation[23]. Furthermore, surface functionalised graphene (PEGylated) appears to be far less toxic: no toxic effects after single i.v. injection[24]. 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[25].

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[26]. Generalisations are therefore hard to make, but graphene nanostructures are not fibre-shaped and theoretically may be assumed to be safer than carbon nanotubes[27].

Based on the scarce available evidence, and in spite of its theoretical advantage in relation to carbon nanotubes, it cannot be excluded that some forms of graphene will be as potent a toxicant as carbon nanotubes. Therefore, graphene is assigned to hazard band E.

GRAPHITE NANOPARTICLES

Graphite is one of only three naturally-occurring allotropes of carbon (the others being amorphous carbon and diamond) and has a honeycomb lattice structure. For some researchers, nanographite is

[20] 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.

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

[22] 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. Minimizing oxidation and stable nanoscale dispersion improves the biocompatibility of graphene in the lung. Nano Letters 11, 5201-5207.

[23] 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

[24] 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.

[25] 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.

[26] 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.

[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.

synonymous with graphene[28], while others[29] make a distinction between graphene and graphite nanoplatelets, without being specific on how the one is distinguished from the other, both possessing the hexagonal graphite structure at the molecular level. As long as the distinction between nanographite and graphene is not clear, it is considered to be one of the many forms of graphene and evaluated in that category (see section above).

IRON OXIDE

Classified by Stoffenmanager Nano in hazard band D for sizes ≤50 nm (C for sizes >50 nm)[30]. 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.

MOLYBDENUM

No relevant toxicity studies on nano-molybdenum were identified in public literature. It is insoluble in water and therefore, applying the methodology of van Duuren et al. (2012)[31], the hazard characteristics of the parent material are used. Molybdenum is classified by a considerable number of CLP-notifiers as a suspected reprotoxicant (category 2) (affecting reproduction) as confirmed by the WHO[32]. Based on the self-classification of (bulk) molybdenum as a reprotoxicant, nanomolybdenum should be placed in hazard band E according to the criteria of Stoffenmanager Nano[33].

SILICON CARBIDE (SiC)

SiC occurs in several forms: (spherical) particles, fibres, and whiskers. SiC particles are manufactured (mostly for use as industrial abrasive) mainly by the Acheson process, with SiC fibres being unwanted by-products. SiC fibres are generally poly-crystalline and of variable length and diameter. They may include fibres that are indistinguishable from whiskers. SiC whiskers are intentionally produced by different processes as durable industrial substitutes for asbestos; they are physically homogeneous and monocrystalline, and their dimensions are similar to asbestos amphiboles[34].

SiC nanoparticles were not genotoxic in an *in vitro* Comet assay nor were they cytotoxic[35]. However, SiC nanoparticles did cause oxidative stress reactions in vitro as well as inflammatory responses[36, 37].

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[28] Figarol, A., Pourchez, J., Boudard, D., Forest, V., Akono, C., Tulliani, J.-M., Lecompte, J.-P., Cottier, M., Bernache-Assollant, D., Grosseau, P., 2015. In vitro toxicity of carbon nanotubes, nano-graphite and carbon black, similar impacts of acid functionalisation. Toxicol. In Vitro 30, 476–85. doi:10.1016/j.tiv.2015.09.014

[29] Ma-Hock, L., Strauss, V., Treumann, S., Küttler, K., Wohlleben, W., Hofmann, T., Gröters, S., Wiench, K., van Ravenzwaay, B., Landsiedel, R., 2013. Comparative inhalation toxicity of multi-wall carbon nanotubes, graphene, graphite nanoplatelets and low surface carbon black. Part. Fibre Toxicol. 10.

[30] 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

[31] Ibid

[32] WHO, 2011. Molybdenum in Drinking-water, Background document for development of WHO Guidelines for Drinking-Water Quality. Geneva, Switzerland.

[33] 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.

[34] Grosse, Y., Loomis, D., Guyton, K.Z., Lauby-Secretan, B., El Ghissassi, F., Bouvard, V., Benbrahim-Tallaa, L., Guha, N., Scoccianti, C., Mattock, H., Straif, K., 2014. Carcinogenicity of fluoro-edenite, silicon carbide fibres and whiskers, and carbon nanotubes. Lancet. Oncol. 15, 1427–1428.

[35] Barillet, S., Simon-Deckers, A., Herlin-Boime, N., Mayne-L'Hermite, M., Reynaud, C., Cassio, D., Gouget, B., Carrière, M., 2009. Toxicological consequences of TiO2, SiC nanoparticles and multi-walled carbon nanotubes exposure in several mammalian cell types: an in vitro study. J. Nanoparticle Res. 12, 61–73. doi:10.1007/s11051-009-9694-y

[36] Ibid

[37] Pourchez, J., Forest, V., Boumahdi, N., Boudard, D., Tomatis, M., Fubini, B., Herlin-Boime, N., Leconte, Y., Guilhot, B., Cottier, M., Grosseau, P., 2012. In vitro cellular responses to silicon carbide nanoparticles: impact of physico-chemical features on pro-inflammatory and pro-oxidative effects. J. Nanoparticle Res. 14, 1143. doi:10.1007/s11051-012-1143-7

Long and short CNTs were also investigated as well as different nanoTiO_2 compounds[38,]. SiC nanoparticles were less potent than all the other particles on a per weight basis. The degree to which SiC nanoparticles caused these toxic reactions depended on surface area, crystallite size, nature of crystallite phase, and iron content[39].

The carcinogenicity of SiC fibres was investigated in two studies on workers who were exposed to fibrous and non-fibrous SiC, quartz, and cristobalite while involved in the production of SiC nanoparticles via the Acheson process. Based on these studies, occupational exposures associated with the Acheson process were classified IARC as carcinogenic to humans (Group 1) on the basis of sufficient evidence in humans that they cause lung cancer[40]. Since the correlation between exposures to SiC fibres and cristobalite made it difficult to disentangle their independent effects, IARC concluded that fibrous SiC is possibly carcinogenic to humans (Group 2B)[41]. No data on humans exposed to SiC whiskers were available. In experimental animals, there was sufficient evidence for the carcinogenicity of SiC whiskers for IARC to classify SiC whiskers as probably carcinogenic to humans (Group 2A), on the basis that the physical properties of the whiskers resemble those of asbestos and erionite fibres, which are known carcinogens. In addition, the results of available mechanistic studies were consistent with proposed mechanisms of fibre carcinogenicity[42], although carcinogenicity of SiC nanoparticles was not explicitly discussed.

Since SiC fibres and whiskers are persistent fibres and are suspected carcinogens, they should attributed hazard band E, according to Stoffenmanager Nano[43]. SiC nanoparticles are not genotoxic, be it based on scant evidence, but exhibit characteristics (ROS formation, inflammatory responses) similar to e.g. titanium dioxide nanoparticles. In an update on some metal oxide nanoparticles hazard band C was attributed to titanium dioxide nanoparticles[44], consequently the same hazard band is attributed to SiC nanoparticles.

SILICON DIOXIDE NANOPARTICLES, CRYSTALLINE

Classified by Stoffenmanager Nano in hazard band E[45].

SILICON DIOXIDE NANOPARTICLES, SYNTHETIC AMORPHOUS

In an update on some oxide nanoparticles hazard band B was attributed to synthetic amorphous silicon dioxide nanoparticles[46].

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[38] Barillet, S., Simon-Deckers, A., Herlin-Boime, N., Mayne-L'Hermite, M., Reynaud, C., Cassio, D., Gouget, B., Carrière, M., 2009. Toxicological consequences of TiO2, SiC nanoparticles and multi-walled carbon nanotubes exposure in several mammalian cell types: an in vitro study. J. Nanoparticle Res. 12, 61–73. doi:10.1007/s11051-009-9694-y

[39] Pourchez, J., Forest, V., Boumahdi, N., Boudard, D., Tomatis, M., Fubini, B., Herlin-Boime, N., Leconte, Y., Guilhot, B., Cottier, M., Grosseau, P., 2012. In vitro cellular responses to silicon carbide nanoparticles: impact of physico-chemical features on pro-inflammatory and pro-oxidative effects. J. Nanoparticle Res. 14, 1143. doi:10.1007/s11051-012-1143-7

[40] Grosse, Y., Loomis, D., Guyton, K.Z., Lauby-Secretan, B., El Ghissassi, F., Bouvard, V., Benbrahim-Tallaa, L., Guha, N., Scoccianti, C., Mattock, H., Straif, K., 2014. Carcinogenicity of fluoro-edenite, silicon carbide fibres and whiskers, and carbon nanotubes. Lancet. Oncol. 15, 1427–1428.

[41] Ibid

[42] Ibid

[43] 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

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

[45] 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.

[46] Le Feber, M., Kroese, E.D., Kuper, C.F., Stockmann-Juvala, H., Hyytinen, E.R., 2014. Pre-assigned hazard bands for commonly used nanoparticles. TNO2014 R11884.

TITANIUM DIOXIDE

In an update on some metal oxide nanoparticles, hazard band C was attributed to titanium dioxide nanoparticles[47].

TUNGSTEN OXIDE

Nano tungsten oxide is insoluble in water[48]. No toxicity studies on it were identified in public literature. Due to this lack of data, it needs to be hazard banded based on the hazardous properties of its bulk parent compound[49]. There is no official EU classification for tungsten oxide and most registrants have not (self)classified tungsten oxide, while some have classified it as possibly carcinogenic. In the registration dossier published by ECHA, no data supporting one or the other conclusion has been submitted. ATSDR[50] has published a toxicity profile for tungsten as well as an update of the earlier profile[51]. Its sodium salt (sodium tungstate) is not mutagenic in the Ames test nor did it cause chromosome aberration *in vitro,* but it did prove to be mutagenic in the Chinese hamster lung V79 cell HGPRT forward mutation assay[52]. Sodium tungsten dehydrate was negative in *in vivo* micronucleus tests in rats and mice, but positive in in vivo Comet assays in mice[53]. Alloys with cobalt and tungsten carbide are carcinogenic when implanted in mice. It is unclear whether cobalt or tungsten is the causative agent. A drinking water carcinogenicity study with sodium tungstate dehydrate has been performed by the NTP[54] but so far the results have not been published[55]. Epidemiological studies did not show an association between tungsten exposure (as measured by urinary tungsten levels) and carcinogenicity, however the power of the studies was too low to draw definitive conclusions[56]. Concluding, there are indications tungsten oxide may be a mutagenic carcinogen and therefore tungsten oxide nanoparticles should be attributed hazard band E according to the criteria of Stoffenmanager Nano[57].

VANADIUM PENTOXIDE (DIVANADIUM PENTOXIDE)

No toxicity studies on nanovanadium pentoxide were found in public literature. It is soluble in water and can therefore be hazard banded based on the hazardous properties of its bulk parent compound[58]. Vanadium pentoxide is classified in the EU as reprotoxic and mutagenic and should therefore be assigned to the highest hazard band, E.

ZINC OXIDE NANOPARTICLES

In an update on some metal oxide nanoparticles, hazard band B was attributed to zinc oxide nanoparticles[59].

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[47] Ibid

[48] ATSDR, 2005. Toxicological profile for Tungsten. Agency for Toxic Substances and Disease Registry, Atlanta, USA.

[49] 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

[50] ATSDR, 2005. Toxicological profile for Tungsten. Agency for Toxic Substances and Disease Registry, Atlanta, USA.

[51] ATSDR, 2015. Addendum to the Toxicological Profile for Tungsten. Agency for Toxic Substances and Disease Registry, Atlanta, USA.

[52] ATSDR, 2005. Toxicological profile for Tungsten. Agency for Toxic Substances and Disease Registry, Atlanta, USA.

[53] ATSDR, 2015. Addendum to the Toxicological Profile for Tungsten. Agency for Toxic Substances and Disease Registry, Atlanta, USA.

[54] Ibid

[55] NTP site last checked on March 7, 2016

[56] ATSDR, 2015. Addendum to the Toxicological Profile for Tungsten. Agency for Toxic Substances and Disease Registry, Atlanta, USA.

[57] 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

[58] Ibid

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

3 Exposure assessment

Cement/lime concrete and mortars and other derivatives

Concrete is widely used in the world. An ordinary concrete is a mixture of cement, sand, gravel and water. Additives are used for special properties, e.g. to increase strength, hardness or corrosion resistance. Among these additives, silica fumes are very important materials. By adding microsilica, high performance concrete is produced, but by using nanosilica ultra-high performance concrete is formed, which is used increasingly. In addition, nanotitania particles have been added to concrete for self-cleaning properties at the surface.

Furthermore, CNTs and CNFs are being incorporated in concrete, as both of them can fill the pore spaces in concrete more effectively than more conventional fillers like sand. CNFs are considered to be superior to CNTs for this because their stacked structure has exposed edges, increasing surface area and thus improving bonding characteristics.

In "Stoffenmanager Nano" sets of exposure scenarios are assigned to exposure bands labelled 1 to 4 (1=low exposure, 4= highest exposure). As explained in the introduction, only respiratory exposure is considered here.

The likelihood of exposure to nanoparticles while handling cement, concretes etc. is highly dependent upon the type of process and the type of equipment involved in the process. Nevertheless, the usage (building phase e.g. mixing, dumping, transferring) of powder materials results in the highest exposure potential (4). If the nanomaterial is included in a liquid mixture (the cement/concrete, building phase) the exposure potential is highly reduced (2). If the nanomaterial is in a matrix (use phase, hardened cement/mortal) the exposure potential is low (1). During abrasive activities (demolition phase) on the cement/concrete the worker can be exposed to nanomaterials but the exposure potential is still relatively low (2). The most common applications are considered below.

Steel: nano-modified steel and nano-additions to steel

In addition to carbon and iron, some compounds like copper, vanadium oxide and molybdenum may be added to steel as nanoparticles. The likelihood of exposure to nanoparticles during the handling of nano-additions in powder form results in the highest exposure potential (building phase, 4). If the nanomaterial is in the steel the exposure potential is low (use phase, 1). Abrasion of an object which includes nanomaterial may result in exposure to steel aerosols which include nanomaterials, resulting in a relative low exposure potential (demolition phase, 2).

Glass: self-cleaning, energy-saving windows

Nanomaterials (titanium dioxide) are used in glass for self-cleaning properties and to reduce the sunlight and heat entering a building. When the nanomaterial is in the glass, the exposure potential is low (use phase, 1). Handling powder titanium dioxide to produce the glass results in the highest exposure potential (building phase, 4).

Heat insulation materials

The use of nanomaterials (e.g. nanoscale silica, graphite or silicon carbide) here includes aerogels and vacuum insulation panels for heat insulation. In the occupational setting, powder nanomaterials may be handled, resulting in the highest exposure potential (building phase, 4). If the nanomaterial is in the matrix of the insulation material the exposure potential is low (use phase, 1).

Coatings and paints

Paints or coatings are frequently used in construction to protect the surface from harmful weathering

commonly used nanoparticles.

effects (e.g. in the case of wood, for durability, water resistance, fungi resistance). They can also make surfaces more attractive. Paints are composed of base; vehicle or binder; solvent or thinner; drier and colouring pigments. In addition, several nanomaterials (e.g. TiO_2, ZnO, SiO_2) are applied as coatings for self-cleaning properties, better water resistance etc. Naturally, silica dioxide can be present as amorphous or crystalline nanoparticles, but in most applications the amorphous form is used[60]. In the building phase, the exposure potential is relatively low (2) since the nanomaterial is dispersed in the coating, except when the coating is sprayed on a surface, when the exposure potential is high (4). When the coating is on the surface, the exposure potential is again low (use phase, 1).

4 Risk assessment

The hazard and exposure bands discussed above 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 or to establish the risk involved with more precision. It should be emphasised that, because of the general scarcity of available information, the scheme is set in a conservative way (according to the precautionary principle).

Roughly four phases can be discerned in the life cycle of construction materials: production, building, use and demolition. If in a phase different degrees of exposure may occur, the highest exposure scenario is taken into account in the risk assessment (worst case scenario).

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).

Within the construction industry, since it does not manufacture the nanomaterials itself, the building phase generates the highest exposure (worst case exposure, band 4), the use phase the lowest (exposure band 1) and the demolition phase intermediate (exposure band 2). The resulting risk priority bands are listed in the table below.

Table: Priority bands for the construction sector

		Exposure band		
		Building phase	Use phase	Demolition phase
Nanoparticle	**Hazard band**	4	1	2
CNTs/CNFs	E	1	1	1
Copper	D	1	2	2
Graphene / nanographite	E	1	1	1
Iron oxide	D	1	2	2
Molybdenum	E	1	1	1

[60] Kaiser, J.-P., Zuin, S., Wick, P., 2013. Is nanotechnology revolutionizing the paint and lacquer industry? A critical opinion. Sci. Total Environ. 442, 282–9. doi:10.1016/j.scitotenv.2012.10.009

		Exposure band		
		Building phase	**Use phase**	**Demolition phase**
Silicon carbide, fibres & whiskers	E	1	1	1
Silicon carbide, spherical particles	C	1	3	2
Silicon dioxide (silica), crystalline	E	1	1	1
Silicon dioxide (silica), synthetic amorphous	B	1	3	3
Titanium dioxide (titania, rutile, anatase)	C	1	3	2
Tungsten oxide	E	1	1	1
Vanadium pentoxide	E	1	1	1
Zinc oxide	B	1	3	3

Due to the high expected exposure, all nanomaterials reach the highest risk priority during the building phase.

In the use phase, amorphous silicon dioxide, titanium dioxide, spherical SiC and zinc oxide nanoparticles have a low risk priority while carbon nanotubes, molybdenum, nanographite, silicon carbide fibres and whiskers, crystalline silicon dioxide, tungsten oxide and vanadium pentoxide have the highest risk priority and the remainder of the nanomaterials have an intermediate risk priority. It should be noted that in the use phase all nanomaterials are contained in a solid matrix, meaning exposure will be negligible and thus health risks will be low.

In the demolition phase, risk management/evaluation of building materials containing carbon nanotubes, molybdenum, nanographite, silicon carbide fibres and whiskers, crystalline silicon dioxide, tungsten oxide and vanadium pentoxide should receive the highest priority, while amorphous silicon dioxide and zinc oxide have a low risk priority. The building materials containing the remainder of the listed nanomaterials should receive intermediate priority during the demolition phase.