ENVIRONMENTAL HEALTH AND SAFETY: TRANSPORT

1 Introduction

Exposure to nanomaterials in the transport sector may be quite diverse. Three categories of subsectors were identified within the NanoData project – use in infrastructure, use in vehicles and use in operations (e.g. catalysts and sensors).

This section presents an analysis of human health and safety aspects of the more commonly used materials for transport including aluminium oxide, carbon (in the form of nanotubes), cerium oxide, cobalt oxide and titanium dioxide. The selection was based on their common usage and/or likely future usage in transport. It was not intended that the review be exhaustive and more materials can be added at a later date if required and if information is available. One additional material was identified, magnesium/aluminium or magnalium in the form of nanoparticles, but there were no data available on this alloy so no assessment could be made. All other combinations of nanoparticles and sectors were evaluated.

The basis for the evaluation was "Stoffenmanager Nano" application[1, 2], a risk-banding tool developed for employers and employees and used to prioritise health risks occurring as a result of respiratory exposure to 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[3]. 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[4]. However, nanoparticles as such are very unlikely to penetrate the skin[5] 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 selected nanoparticles of the transport sector and their hazard bands, either taken from le Feber et al. (2014)[6] or van Duuren et al. (2012)[7] or derived in this project[8]. In essence, it applies

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[1] 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.

[2] 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.

[3] 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.

[4] Ibid

[5] 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

[6] 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.

[7] 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.

[8] Derived according to the methodology described for "Stoffenmanager Nano" in van Duuren-Stuurman et al. (2012). In essence, it applies the toxicity classification rules of EU Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures.

the toxicity classification rules of EU Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures. Further information is given in the annex. The hazard banding of the nanoparticles with identified significant use in the transport sector is assessed below.

Table: Hazard banding of transport-related materials

Nanoparticles	Hazard band	Source
Aluminium	C	This report
Aluminium oxide/ alumina	C	Le Feber et al. (2014)
Calcium carbonate	A	EFSA (2011)
Carbon nanotubes	E	This report
Cerium oxide	C	Le Feber et al. (2014)
Cobalt oxide	E	Van Duuren et al. (2012)
Magnesium hydroxide	C	Van Duuren et al. (2012)
Nanoclays	D	Van Duuren et al. (2012)
Silica (amorphous)	B	Le Feber et al. (2014)
Silica (crystalline)	E	Van Duuren et al. (2012)
Titanium dioxide (titania/ rutile/ anastase)	C	Le Feber et al. (2014)

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

ALUMINIUM NANOPARTICLES

Toxicity data on aluminium nanoparticles are very scarce as the focus is more usually on aluminium oxide. A SCOPUS literature search revealed one relevant toxicity study: Braydich-Stolle et al. (2010)[9] compared the *in vitro* toxicity of aluminium and aluminium oxide nanoparticles and found no significant difference between the cytotoxicity of both nanoparticles. Based on this, it may be assumed that aluminium and aluminium oxide nanoparticles are equitoxic. Therefore aluminium nanoparticles are attributed the same hazard band as aluminium oxide nanoparticles: band C (see below).

ALUMINIUM OXIDE NANOPARTICLES

In an update on some metal oxide nanoparticles, Stoffenmanager Nano has attributed hazard band C to aluminium oxide nanoparticles[10].

CALCIUM CARBONATE

The substance calcium carbonate has been registered under REACH. The registrant has indicated that the substance has a nanoform and has provided separate information on the nanoform. Calcium carbonate, including its nanoform, has not been classified as hazardous by any route of exposure. EFSA, the European Food Safety Authority, has given a scientific opinion on re-evaluation of calcium carbonate (E 170) as a food additive. This opinion, concluded that *"the available data are sufficient to conclude that the current levels of adventitious nanoscale material within macroscale calcium carbonate would not be an additional toxicological concern"*[11]. In view of this lack of toxicity, nanocalcium carbonate is not classified and therefore assigned hazard band A.

CARBON NANOTUBES (CNTS), SINGLE-WALLED (SWCNTS) 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.

[9] Braydich-Stolle, L.K., Speshock, J.L., Castle, A., Smith, M., Murdock, R.C., Hussain, S.M., 2010. Nanosized aluminium altered immune function. ACS Nano 4, 3661–70. doi:10.1021/nn9016789
[10] 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
[11] EFSA, 2011. Scientific Opinion on re-evaluation of calcium carbonate (E 170) as a food additive. EFSA J. 9, 2318. doi:10.2903/j.efsa.2011.2318.

Differences in toxicity are also expected between single and multi-walled CNTs and are presumably dependent on their aspect ratio[12].

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)[13] [14] [15]. 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 into the alveolar region of the lung and to cause inflammation. These biological events have been shown to lead to the cancer mesothelioma[16], 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.

CERIUM OXIDE NANOPARTICLES

In an update[17] on some metal oxide nanoparticles hazard band C was attributed to cerium oxide nanoparticles.

COBALT OXIDE NANOPARTICLES

Stoffenmanager Nano has attributed hazard band E to cobalt oxide nanoparticles[18].

MAGNESIUM HYDROXIDE NANOPARTICLES

No relevant toxicity studies on nano-magnesium hydroxide were identified in publicly-available literature. It is not very soluble in water (solubility approx. 9 mg/L) and therefore, applying the methodology of van Duuren et al. (2012)[19], the hazard characteristics of the parent material are used. Magnesium hydroxide has no harmonised classification in the EU[20] and it is also not classified by 400 notifiers[21] nor in the registration dossier[22], based on sufficient information. Based on this lack of classification, the nanoforms should be assigned hazard band C, the lowest category a nanoparticle can be assigned, based on toxicity data for its non-nano parent compound[23].

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

[13] Ibid

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

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

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

[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] 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

[19] Ibid

[20] http://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/13362

[21] Companies or consortia of companies that notified that the product was being produced or imported by them.

[22] http://echa.europa.eu/registration-dossier/-/registered-dossier/16073/7/6/2

[23] 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

NANOCLAYS

These are classified by Stoffenmanager Nano in hazard band D for sizes ≤50 nm (C for sizes >50 nm). Since the size distribution of the nanoclay nanoparticles used may include sizes below 50 nm, the risk band used in the risk assessment applied here is D. [24]

SILICA

Synthetic amorphous silicon dioxide nanoparticles

In an update on some oxide nanoparticles, hazard band B was attributed to synthetic amorphous silica nanoparticles[25].

Crystalline silicon dioxide nanoparticles

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

TITANIUM DIOXIDE NANOPARTICLES

In an update on some metal oxide nanoparticles[27], hazard band C was attributed to titanium dioxide nanoparticles.

3 Exposure assessment

NANOTECHNOLOGY IN INFRASTRUCTURE

Nanomaterials (titanium dioxide) are used in/on glass and other surfaces in transport for self- cleaning and other properties and to reduce the intensity of sunlight and heat entering vehicles. If the nanomaterial is in glass, the exposure potential is low (use phase, 1). Handling powder titanium dioxide to produce the glass results in the highest exposure potential (manufacture phase, 4).

Paints or coatings are frequently used in transport to protect the surface from wear and to make the surface more attractive in appearance. 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 in coating forms for self-cleaning properties, better water resistance, etc. In the manufacturing 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, then the exposure potential is high (4). If the coating is on the surface the exposure potential is again low (use phase, 1).

NANOTECHNOLOGY IN VEHICLES

Carbon nanotubes are being applied to existing materials to increase strength and to reduce weight in the structure and interior of vehicles including materials used in the aerospace sector. In addition, carbon nanotubes are used in engines to improve the heat-transferring properties which can affect the performance, emission and durability of the engine. Furthermore, nanoadditives are added to fuel to reduce the soot emissions (e.g. cerium oxide nanoparticles; aluminium nanoparticles; magnesium-aluminium (magnalium) and cobalt oxide nanoparticles).

Regarding the exposure potential, based on expert judgement we believe a relative low exposure (1) is expected for the nanomaterials in these products. However, during the vehicle manufacturing phase, when handling nanomaterials, the exposure potential can be high (4). In the end-of-life phase shredding maybe a realistic scenario to recycle the nanomaterial, resulting in a relatively low exposure

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[24] Ibid

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

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

potential (2).

NANOTECHNOLOGY FOR OPERATIONS

In this subsector, catalysts and sensors are predominantly represented in the products with nanomaterials that are currently available. Although some nanomaterials are widely applied (e.g. MWCNTs, TiO_2) most are only produced on a nanoscale (e.g. using lithography). Similarly to the other subsectors, a high exposure potential is expected for the occupational phase handling nanomaterials, while low exposure potential is foreseen during the use phase. In the end-of-life phase, shredding may be a realistic scenario to recycle the nanomaterial, resulting in a relatively low exposure potential (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 emphasized that because of the scarcity of available information, the scheme is set in a conservative way (according to the precautionary principle).

For transport infrastructure (construction of roads, etc.), roughly four phases can be discerned in the life cycle of construction materials: production, building, use and demolition. Roughly three phases can be discerned in the life cycle of transport vehicles and nano-enabled products used in operations: production, use and end-of-life. 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

hazard band / exposure 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).

As seen in the table below, due to the high expected exposure all nanomaterials reach the highest risk priority during the production phase, except calcium carbonate (intermediate priority). In the use phase, aluminium (oxide), calcium carbonate, cerium oxide, magnesium hydroxide and titanium dioxide have a low risk priority, nanoclay has an intermediate priority, while carbon nanotubes and cobalt oxide have the highest 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 end-of-life phase, risk management/evaluation of transport materials containing carbon nanotubes and cobalt oxide should receive the highest priority, while the materials containing the remainder of the listed nanomaterials should receive intermediate priority.

Table: Priority bands for the transport sector

Nanoparticle	Hazard band	Exposure band		
		Production/ building/ application phase	Use phase	End-of life phase
		4	1	2
Aluminium/aluminium oxide	C	1	3	2
Calcium carbonate	A	2	3	3
Carbon nanotubes, single- and multiwalled	E	1	1	1
Cerium oxide	C	1	3	2
Cobalt oxide	E	1	1	1
Magnalium	n/a	n/a	n/a	n/a
Magnesium hydroxide	C	1	3	2
Nanoclay	D	1	2	2
Silica (amorphous)	B	1	3	3
Silica (crystalline)	E	1	1	1
Titanium dioxide (titania, rutile, anatase)	C	1	3	2