ENVIRONMENTAL HEALTH AND SAFETY: THE ICT SECTOR

This section presents an analysis of the human health and safety aspects of eight of the more commonly used materials for ICT: gallium arsenide, gallium nitride, molybdenum disulphide, tungsten selenide, silica (amorphous and crystalline), graphene and silver. The selection was based on their common usage and/or likely future usage in ICT. It was not intended that the review be exhaustive and more materials can be added at a later date if required.

The basis for the evaluation was “Stoffenmanager Nano” application[1, 2], 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.

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.

Hazard assessment of nanoparticles

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 ICT 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.

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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 prioritization 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 prioritization of airborne manufactured nano objects. Ann. Occup. Hyg. 56, 525-541.

Hazard bands for the specified nanoparticles

Nanoparticles	Hazard band	Source
Gallium arsenide	D	This report
Gallium nitride	n/a	no data
Graphene	E	This report
Molybdenum disulphide	C	This report
Silicon dioxide (silica), synthetic amorphous	C	le Feber et al. (2014)
Silicon dioxide (silica), crystalline	E	van Duuren et al. (2012)
Silver	D	le Feber et al. (2014)
Tungsten selenide	n/a	no data

Details of the hazard bands derived for each material are given below, except for silica. The hazard banding of silica nanoparticles has already been reported[8] [9].

GALLIUM ARSENIDE

No toxicity studies on nano-GaAs were encountered in public literature. According to data from the REACH dossier of GaAs, (powdered) GaAs has limited solubility in water (based on released As3+ ions). GaAs is marketed as an article made from very pure (99.9999%) crystalline bulk material, predominantly in the shape of wafers[10], implying an even lower water solubility. Therefore, applying the methodology of van Duuren et al. (2012), the hazard characteristics of the parent material are used.

GaAs is classified as carcinogenic, but not mutagenic (based on sufficient evidence) by the EU. It should be noted that the classification for carcinogenicity was based on inhalation studies with micronised powdered GaAs, and that the relevance of these studies for human exposure to crystalline GaAs is questioned[11]. Based on the classification of the bulk material, nanoGaAs is attributed hazard band D.

GALLIUM NITRIDE

No relevant toxicity studies on nano-gallium nitride were encountered in public literature. Gallium nitride wafers are virtually insoluble in water, even in dilute acid[12], and therefore, applying the methodology of van Duuren et al. (2012), the hazard characteristics of the parent material are used.

Gallium nitride is not classified for any toxicity by the EU. However, this absence of classification was based on the lack of data. Besides the gallium ions, which are not considered relevant for gallium nitride since it is insoluble in water[13], only one

8 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.

9 M.F.J., Tielemans, E., Fransman, W., 2012. Stoffenmanager Nano version 1.0: a web-based tool for risk prioritization of airborne manufactured nano objects. Ann. Occup. Hyg. 56, 525-541.

10 Bomhard, E.M., Gelbke, H.-., Schenk, H., Williams, G.M., Cohen, S.M., 2013. Evaluation of the carcinogenicity of gallium arsenide. Crit. Rev. Toxicol. 43, 436-466

11 Ibid

12 Jewett, S.A., Makowski, M.S., Andrews, B., Manfra, M.J., Ivanisevic, A., 2012. Gallium nitride is biocompatible and non-toxic before and after functionalization with peptides. Acta Biomater. 8, 728-733

13 Foster, C.M., Collazo, R., Sitar, Z., Ivanisevic, A., 2013. Aqueous stability of Ga- and N-polar gallium

structurally-similar compound was found using the on-line ChemID database: gallium phosphide, which was characterised as being 80% similar with gallium nitride. For this compound also no relevant toxicity data were found, meaning read-across could not be employed. Therefore, no hazard banding could be derived.

Graphene

Graphene is composed of sp2-hybridized 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)[14].

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[15].

Currently, limited information about the *in vitro* and *in vivo* toxicity of graphene is available (Seabra, et al. 2014). 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 (Nezakati, et al. 2014).

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.

Intratracheal instillation of 50 µg GO in mice caused severe pulmonary distress after inhalation causing excessive inflammation, while the amount of non-functionalised graphene instilled did not[16]. Single intravenous (i.v.) injection of graphene oxide into mice at a dose of 10 mg/kg bw accumulated in the lung resulting in pulmonary oedema and granuloma formation, with NOAEL of 1 mg/kg bw[17]. Furthermore, surface functionalised graphene (PEGylated) appears to be far less toxic: no toxic effects after single i.v. injection of 20 mg/kg bw (Yang, et al. 2011). In mice, PEGylated GO materials showed no uptake via oral administration, indicating limited intestinal

nitride. Langmuir 29, 216-220.

14 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.

15 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.

16 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.

17 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

absorption of the material, with almost complete excretion. In contrast, upon i.p. injection in mice, PEGylated GO was found to accumulate in the liver and spleen[18].

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 (Seabra, et al. 2014). Generalisations are therefore hard to make, but graphene nanostructures are not fibre-shaped and theoretically may be assumed to be safer than carbon nanotubes (Seabra, et al. 2014).

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.

Molybdenum disulphide

No relevant toxicity studies on nano-molybdenum disulphide were encountered in public literature. It is insoluble in water and therefore, applying the methodology of van Duuren et al. (2012), the hazard characteristics of the parent material are used. Molybdenum disulphide is not classified for any toxicity by the EU. Based on this absence of classification, the nanoforms should be assigned hazard band C, the lowest category a nanoparticle can be assigned just based on toxicity data for its non-nano parent compound[19].

Tungsten selenide

No relevant toxicity studies on nano-tungsten selenide were encountered in public literature. Tungsten selenide is also not classified for any toxicity by the EU. However, this absence of classification was based on lacking data. Also on the top five similar compounds retrieved by ChemID (rhenium selenide, tantalum selenide, tungsten telluride, manganese selenide and molybdenum selenide, similarity ranging from 85 to 95%) no relevant toxicity data were found, meaning read-across could not be employed. Therefore, no hazard banding could be derived

Exposure assessment

Manufacturing of the applied nanomaterials in ICT is a crucial phase regarding health and safety, due to relatively high potentials for exposure of employees. However, the production phase was earlier described in the sector “manufacturing” and will not be evaluated in this sector report.

Most of the engineered nanomaterials are present in the products as part of a matrix. During the manufacture of ICT products engineered nanomaterials may be used and are applied mainly as coatings. For the majority of these coatings, only a low percentage of engineered nanomaterials are present. Some of the identified substances may not necessarily be engineered nanomaterials.

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18 Yang, K., Wan, J., Zhang, S., Zhang, Y., Lee, S.-., Liu, Z., 2011. In vivo pharmacokinetics, long-term biodistribution, and toxicology of pegylated graphene in mice. ACS Nano 5, 516-522. (Cited in Seabra, et al. 2014)

19 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 prioritization of airborne manufactured nano objects. Ann. Occup. Hyg. 56, 525-541.

The production phase of ICT products on industrial scale consists mainly of automatic processes, with employees only engaged in product quality control or system engineering. In addition, most processes are performed in cleanrooms and/or under well-controlled conditions, as dust is a major threat to the quality of the products. Nevertheless, spray scenarios for coating normally result in high exposure concentrations, so potential exposure cannot be neglected. In the situation of a manual process without proper exposure control measures (e.g. local exhaust ventilation, cleanroom), employees may be exposed to relatively higher concentrations. Lastly, during the end-of-life phase several metals may be present in the ICT product, which can be worthwhile to recycle. Recycling of these metals may involve, for example, shredding of ICT products, and any engineered nanomaterials could become airborne. However, as the shredded products only will contain a small amount of engineered nanomaterials, potential exposure to engineered nanomaterials during this process will be relatively low.

In conclusion, the use of nanotechnology ICT products results in exposure band 1 (consumers and workers), whereas during the production of nanotechnology ICT products exposure band 2 (workers) is believed to be realistic. Furthermore, during the end-of-life phase an exposure band 1 (workers) is realistic.

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).

Priority bands in the Stoffenmanager system

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

Key:

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 ICT sector are listed the table below.

Priority bands for the ICT sector

		Exposure band	
		Production phase of ICT product	Use and end-of-life phase ICT products
Nanoparticle	**Hazard band**	**2**	**1**
Gallium arsenide	D	2	2
Gallium nitride	n/a	n/a	n/a
Graphene	E	1	1
Molybdenum disulphide	C	2	3
Silicon dioxide (silica), synthetic amorphous	C	2	3
Silicon dioxide (silica), crystalline	E	1	1
Silver	D	2	2
Tungsten selenide	n/a	n/a	n/a

The highest priority is for graphene and crystalline silica during the production, use and end-of-life phases, while gallium arsenide and nanosilver have intermediate priority in those phases. Molybdenum disulphide and amorphous silica also have intermediate priority in the production phase, but low priority during use and end-of-life phase in view of a lesser potential of exposure in those phases. For gallium nitride and tungsten selenide no adequate data were available to perform hazard and exposure banding.

EHS References

Bomhard, E.M., Gelbke, H., Schenk, H., Williams, G.M., Cohen, S.M., 2013. Evaluation of the carcinogenicity of gallium arsenide. Crit. Rev. Toxicol. 43, 436-466.

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.

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.

Foster, C.M., Collazo, R., Sitar, Z., Ivanisevic, A., 2013. Aqueous stability of Ga- and N-polar gallium nitride. Langmuir 29, 216-220.

Jewett, S.A., Makowski, M.S., Andrews, B., Manfra, M.J., Ivanisevic, A., 2012. Gallium nitride is biocompatible and non-toxic before and after functionalization with peptides. Acta Biomater. 8, 728-733.

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.

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.

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

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.

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 prioritization of airborne manufactured nano objects. Ann. Occup. Hyg. 56, 525-541.

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.

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

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.