Scaffold Public Documents – SPD7

Innovative strategies, methods and tools for occupational risks management of manufactured nanomaterials (MNMs) in the construction industry

FORMULATING OCCUPATIONAL EXPOSURE LIMITS VALUES (OELs) (INHALATION & DERMAL)

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1 EXECUTIVE SUMMARY

So far, no regulatory OELs specifically addressing nanomaterials have been given by the EU or by any national authority. However, some recommended limit or reference values for the concentration of nanomaterials in the workplace air have been proposed by a few institutes and agencies. A general framework for the development of OELs for nano-objects and their aggregates and agglomerates is under development in the International Organization for Standardization (ISO).

The Scaffold project aims at giving advice and practical tools for risk management related to the use and exposure to nanomaterials within the construction sector. As a part of this it is important to define recommendable occupational exposure limits.

On the basis of a thorough review (Scaffold Public Document SPD5) on the five nanomaterials included in Scaffold (titanium dioxide, amorphous silica, nanocellulose, carbon nanofibres and nanoclays) the available toxicological data was analysed and attempts were made to identify the critical effects and doses and to derive (health-based) occupational exposure limit values.

Based on the available data on the toxicological properties of the nanomaterials focused on in the Scaffold project the following recommendations for occupational exposure limit values were proposed:

Amorphous silicon dioxide

SiO_2 has been extensively studied. Experimental and epidemiological data were available, and all toxicological endpoints were covered. Mild, reversible, local lung effects were identified as the critical effects. The NOAEC for these effects in rats was 1.3 mg/m^3. From this, by converting animal exposure to occupational exposure 8 h/ day, and taking into consideration differences in respiratory rates between rats and humans and inter-individual differences (total assessment factor 5), the suggested **8 h OEL for the respirable fraction is 0.3 mg/m^3**.

Titanium dioxide

TiO_2 has during the last decade been one of the most studied NMs. Its critical effects are related to local inflammatory effects in the lungs after repeated inhalation, showing a NOAEC of 0.5 mg/m^3 in rats. By applying the same assessment factors as for SiO_2, an **8 h OEL of 0.1 mg/m^3** is suggested for TiO_2 (respirable fraction).

Carbon nanofibres and nanocellulose

The amount of data related to the potential hazards caused by carbon nanofibres and nanocellulose is still very low, and there are no valid studies which could be used for the derivation of an OEL. As there are some indications that biopersistent fibrous NMs (e.g., some types of carbon nanotubes) might be harmful when inhaled, an **OEL of 0.01 fibres/cm^3** is suggested for these materials, **based on the precautionary principle**.

We are aware of the fact that there is currently a lack of quantitative measurement methods for the estimation of exposure to carbon nanofibres or nanocellulose. Thus a minimization of

the exposure is recommended as long as reliable methods, allowing comparison of sample concentrations with the suggested OEL, are not available.

Nanoclays

Very limited amounts of data on the hazards related to nanoclays have been published. The term 'nanoclays' contains many different materials, which complicates the assessment. **No OEL** can be set for nanoclays at this stage.

General, low-toxicity dust

Within the construction sector, mixed exposure to different kinds of dust is extremely common. In addition to the substance specific OELs, our recommended 8 h OELs for general, inert dust are **0.3 mg/m^3 for the respirable fraction, and 4 mg/m^{3}for the inhalable fraction**. These values can also be applied to nanoclays.

The OELs proposed in this report will be included in the risk management toolkit produced within Scaffold.

2 OBJECTIVES AND SCOPE

The aim of the present work was to derive (health-based) occupational limit values for the nanomaterials included in the Scaffold project. The hazard assessment carried out in a previous step (Scaffold Public Document SPD5), i.e. identification of critical health effects and the levels of exposure at which they occur for each of the materials, served as a basis for the derivation of the limit values.

As there are not yet any generally accepted approaches for the setting of limit values for nanomaterials, the work started by collecting and comparing the different approaches presented by different instances. Also, the background information and the basis for the few available reference values proposed for the selected nanomaterials were evaluated.

3 INTRODUCTION

The Scaffold project focuses on five different types of manufactured nanomaterials (MNMs), namely silicon dioxide (amorphous silica, SiO_2), titanium dioxide (TiO_2), nanoclays, carbon nanofibres and nanocellulose. A thorough review of the available data on the toxicity and health effects of these MNMs was carried out in a previous step (Scaffold Public Document SPD 5). The focus of the present work was then to evaluate the data presented in SPD5, as well as the currently available information related to different types of limit values for occupational exposure to MNMs, proposed by different actors. On the basis of these evaluations, suggestions for occupational exposure limit values for the MNMs involved in the Scaffold project were made. The results of this work and the OELs proposed in this report will be included in the risk management toolkit produced within Scaffold.

4 METHODOLOGY

Background information on occupational exposure limits for nanomaterials was collected from the open literature. Based on the available data, the approaches for the derivation of OELs for the nanomaterials included in Scaffold were selected.

For the calculations and derivation of OELs, the toxicological data presented in the Scaffold Public Document SPD5 was used in order to define critical effects and doses, as well as data gaps related to the five materials.

5 RESULTS

5.1 Existing occupational reference values for nanomaterials

Occupational exposure limit values (OELs) are binding or guideline limit values for the concentrations of impurities, such as chemical substances, in the workplace air. Their primary purpose is to protect the workers from the adverse health effects of the impurities. OELs are set both at the EU level and at national level. Depending on the type of the OEL, the value may be strictly health-based, include socio-economic and/or technical feasibility considerations, or it may be based solely on technical feasibility.

So far, no regulatory OELs specifically addressing nanomaterials have been given by the EU or by any national authority (Gordon et al. 2014). However, recommended limit or reference values for the concentration of nanomaterials in the workplace air have been proposed, for example, by the Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung (IFA) in Germany, by the British Standards Institution (BSI) in the UK, and by the National Institute for Occupational Safety and Health (NIOSH) in the US (IFA 2014a; BSI 2007; NIOSH 2011; 2013). A general framework for the development of OELs for nano-objects and their aggregates and agglomerates is under development in the International Organization for Standardization (ISO 2014).

The applicable approaches for setting OELs, or other reference values, for nanomaterials depend mainly on the availability of toxicological data on the material (Schulte et al. 2010; Kumpel et al. 2012). When adequate data is available, traditional quantitative risk assessment, based on the dose-response data on the critical health effects, may be applied for setting a substance-specific OEL. However, when the toxicity data is limited, alternative approaches, often including grouping of the materials on the basis of their physico-chemical properties, need to be applied.

If there are no nano-specific limit values, the values proposed for the substances (in bulk form), e.g., national OEL or derived no effect levels (DNELs) given under the EU REACH legislation, have to be taken into account for example in the risk assessment.

5.1.1 Substance-specific reference values

For the materials included in the SCAFFOLD project, substance-specific limit values have been proposed for titanium dioxide (TiO_2) nanoparticles (NIOSH 2011; Gamo et al. 2011; Stone et al. 2011), silicon dioxide (SiO_2) in the form of synthetic amorphous silica or silica fume (DFG 1991) and carbon nanofibres (NIOSH 2013; Naganishi et al. 2011). The reasoning behind the proposed values is discussed below. Based on literature searches, no information was found on any proposals for limit values related to exposure to nanocellulose or nano clays.

To our knowledge, no dermal limit values have been proposed for any nanomaterials.

5.1.1.1 Titanium dioxide

Table 1 summarises the reference values suggested for TiO_2 nanoparticles. In the EU-funded ENRHES project (Engineered Nanoparticles: Review of Health and Environmental Safety), a DNEL value was calculated for TiO_2 nanoparticles (Stone et al. 2011), according to the guidance given by the European Chemicals Agency (ECHA 2012). Oxidative stress driven pulmonary inflammation, which may lead to other effects, including lung cancer, was identified as the critical health effect of TiO_2 nanoparticles. Point of departure for the suggested DNEL value, 0.017 mg/m^3 (8 h), was the *no observed adverse effect level* (NOAEL) of 0.5 mg/m^3 identified in rats exposed to TiO_2 nanoparticles at 0.5, 2 or 10 mg/m^3 for 13 weeks (Bermudez et al. 2004). A corresponding DNEL of 0.067 mg/m^3 (8 h) would result if the minimal to mild effects observed in the study at 2 mg/m^3 were assumed not to be adverse, leading to a NOAEL of 2 mg/m^3.

In a Japanese research project (Gamo et al. 2011), an OEL of 0.61 mg/m^3 (8 h) was suggested for TiO_2 nanoparticles based on the same study but applying different assessment factors for covering uncertainties related to interspecies extrapolation, individual variability and extrapolation of exposure periods.

In the evaluation of the NIOSH (2011), ultrafine TiO_2, including TiO_2 nanoparticles, was concluded to be a potential occupational carcinogen acting through a secondary genotoxicity mechanism related to chronic pulmonary inflammation. The mechanism was concluded to be common for low-solubility particles, and related to particle size and surface area. Based on the carcinogenicity data from three inhalation studies in rats (Heinrich et al. 1995; Lee et al. 1985; Muhle et al. 1991) and dose-response modelling, an exposure limit of 0.3 mg/m^3 (8–10 h) was recommended for ultrafine TiO_2, representing a level associated with 1/1000 excess risk of lung cancer over a working lifetime. For fine TiO_2 particles, NIOSH recommends a limit of 2.4 mg/m^3.

Table 1. Recommended reference values for titanium dioxide nanoparticles.

Ref.	Critical effect(s)	Key study	NOAEL of the key study (mg/m^3)	Corrected NOAEL for human exposure (mg/m^3)	Assessment factor(s) applied	Calculated BMDL for human exposure (mg/m^3)	Suggested reference value (mg/m^3)
Stone et al. 2011	Pulmonary inflammation	Bermudez et al. 2004	0.5–2	0.25–1.0	15	-	0.017–0.067[a]
Gamo et al. 2011	Pulmonary inflammation	Bermudez et al. 2004	2	1.8	3	-	0.61[a]
NIOSH 2011	Lung cancer	Heinrich et al. 1995; Lee et al. 1985; Muhle et al. 1991	-	-	-	0.29[b]	0.3[c]

BMDL: 95% lower confidence limit for the benchmark dose associated with 1/1000 excess risk of lung cancer. NOAEL: No observed adverse effect level.

[a] Time weighted average over 8 hours.

[b] Model average.

[c] Time weighted average up to 10 hours/day during a 40-hour work-week.

OELs have been given for TiO_2 (without specifying the size range) in many countries (IFA 2014b). The values given by the different national authorities range between 3 mg/m^3 and 15 mg/m^3. TiO_2 has also been registered under REACH. According to the publicly available information on the ECHA website (ECHA 2014), the DNEL for TiO_2 is 10 mg/m^3 (workers, long-term inhalation exposure).

TiO_2 is included in the current work-list of the EU Scientific Committee on Occupational Exposure Limit Values (SCOEL), meaning that the committee is evaluating the available data and might, based on the evaluation, give recommendations for TiO_2 OEL-values to be included in the EU list of Indicative Occupational Exposure Limits.

5.1.1.2 Silicon dioxide (amorphous silica)

The German MAK commission (Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area), has set a MAK value of 4 mg/m^3 of total dust (time-weighted average over 8 hours) for synthetic amorphous silicas, including pyrogenic and precipitated silica and silica gel (DFG 1991). The MAK value is defined as the maximum concentration of a chemical substance in the workplace air which generally does not have known adverse effects on the health of the employees. The value was based on the results of animal inhalation studies, particularly a 13 weeks inhalation study in rats exposed to pyrogenic silica at 1.3, 6 or 30 mg/m^3, which showed slight reversible inflammatory changes in the lungs at 1 mg/m3 and more pronounced effects at ≥6 mg/m^3 (Reutzel et al. 1991). In addition, a MAK value of 0.3 mg/m^3 (respirable dust; 8 h) was set to silica fume and other amorphous silicas which, in spite of being X-ray amorphous, were considered to possess short range crystalline order because of the conditions under which they originate (DFG 1991). A further reasoning for the values *per se* was not given.

A few other countries also have OELs for silica fume. The 8 h value for the respirable fraction of silica fume is in each of the cases 2 mg/m^3 (IFA 2014b). The OEL values for amorphous silica vary between 1 and 10 mg/m^3 and have mostly been given for the inhalable fraction.

The silica fume DNEL value given in the REACH registration for workers' long-term exposure is identical with the MAK value for respirable silica fume, 0.3 mg/m^3 (ECHA 2014).

5.1.1.3 Carbon nanofibres

NIOSH recently suggested a recommended exposure limit of 0.001 mg/m^3 for carbon nanotubes and carbon nanofibres (time-weighted average over 8 hours; measured as respirable elemental carbon) (NIOSH 2013). Working lifetime exposure at this level was calculated to result a 2.4–54% excess risk of minimal (grade 1) lung effects, and to a 0.23–16% excess risk of mild (grade 2) lung effects, based on the lung histopathological data of two inhalation studies on rats (Pauluhn 2010; Ma-Hock et al. 2009). In these studies, rats were exposed to multi-walled carbon nanotubes at doses ranging from 0.1 to 6 mg/m^3 for 13 weeks, followed by a post-exposure observation period of up to six months.

In a Japanese research project, an OEL of 0.08 mg/m^3 (8 h) was suggested for carbon nanofibres, based on the NOAEL of a four weeks inhalation study on rats (Naganishi et al. 2011). In the study, rats were exposed to multi-walled carbon nanotubes at 0.37 mg/m^3 for 4

weeks. As no consistent changes in the lung histopathology or inflammatory markers in broncho-alveolar lavage (BAL) were detected during a three months follow-up, the applied dose level of 0.37 mg/m^3, calculated to correspond to a human equivalent concentration of 0.50 mg/m^3, was determined to be the NOAEL of the study.

5.1.2 General reference values

General benchmark exposure levels for nanomaterials have been recommended by the BSI in 2007 and the IFA in 2009 (BSI 2007; IFA 2014a). The values recommended by the IFA were also adopted as provisional reference values for engineered nanomaterials by the Social and Economic Council (SER) in the Netherlands in 2012 (Table 2) (SER 2012). These values are also recommended as reference values for engineered nanomaterials by the Finnish Institute of Occupational Health (FIOH 2013).

The benchmark exposure levels of the BSI were based on the OEL of the bulk material, ranging from ≤0.1 x OEL for poorly soluble nanomaterials to 0.5 x OEL for soluble nanomaterials (BSI 2007). These values were intended as pragmatic guidance levels and were not assumed to be safe workplace exposure levels. As the values are based on an existing OEL, they are not applicable for materials for which an OEL has not been derived. Alternatively, a number-based level of 20.000 particles/cm^3 was suggested for poorly soluble particles on the basis of the level of urban air pollution in the UK (20.000–50.000 particles/cm^3). For fibrous particles, a value of 0.01 fibres/cm^3 was suggested, based on the limit value applied for asbestos removal.

The benchmark exposure levels recommended by the IFA and the SER are presented in Table 2. A value of 20.000 or 40.000 particles/cm^3 was suggested for biopersistent granular nanoparticles in the size range of 1–100 nm, depending on the particle density. These values were mainly based on experiences in exposure measurements and the detection limits of the available measurement methods, and were not substantiated toxicologically.

It is important to note that the number-based benchmark levels are restricted to particles in the size range below 100 nm. If larger aggregates or agglomerates appear, determination of the mass concentration may be necessary. For example, a mass concentration of 0.1 mg/m^3 of TiO_2, corresponding to 45.000 cm^{-3} of 100 nm TiO_2 particles, is equally achieved with only 360 cm^{-3} of 500 nm TiO_2 agglomerates (IFA 2014a). In the recommendations given by FIOH, a limit value of 0.3 mg/m^3 should be considered for nanomaterials occurring as aggregates or agglomerates.

The German MAK Commission recently set a MAK value of 0.3 mg/m^3 x density of the material (g/cm^3) for poorly soluble respirable particles in the size range above 100 nm without specific, composition-related toxicity (DFG 2012). The value was based on a common volume-based threshold level for impaired lung clearance and resulting inflammatory response observed in rat inhalation studies with different types of poorly soluble particles (Pauluhn 2011). As an example, the corresponding limit values for SiO_2 and TiO_2, with densities of 2.2 and 4.2 g/cm^3, would be around 0.7 mg/m^3 and 1.3 mg/m^3, respectively.

Table 2. Benchmark exposure levels for nanomaterials recommended by the IFA and the SER (IFA 2014a; SER 2012).

Nanomaterial	Benchmark exposure level	Comments
Rigid, biopersistent nanofibres for which effects similar to those of asbestos are not excluded	0.01 fibres/cm^3	
Biopersistent granular nanomaterial with density of > 6000 kg/m^3	20.000 particles/cm^3	Size range 1–100 nm.
Biopersistent granular nanomaterial with density of < 6000 kg/m^3	40.000 particles/cm^3	Size range 1–100 nm. Includes SiO_2, TiO_2, nanoclays, and nanofibres for which asbestos-like effects are excluded.
Non-biopersistent granular nanomaterials	applicable OEL	

5.2 Recommendations given based on the hazard assessment carried out in the Scaffold project

The recommendations for SiO_2 and TiO_2 follow the traditional scheme for proposing health-based OELs, namely 1) identification of critical effect; 2) identification of exposure level at which no effects occur (NOAEC); and 3) calculation of OEL, if needed by application of assessment factors in order to cover differences between animals and humans and/or variations between individuals.

For the other MNMs included in the Scaffold project it was not possible to derive health-based OELs due to the lack of robust and/or relevant data on their potential health effects. For these substances, recommendations were given based on the precautionary principle, and taking into account recommendations of different actors within the field of nano/chemical safety.

5.2.1 Silicon dioxide (amorphous silica)

Amorphous SiO_2 has been extensively studied, partly due to the fact that SiO_2 particles in the nano size-range have been produced and used for decades, already before the term “nanomaterial” was introduced. Experimental and epidemiological data are available, and all relevant toxicological endpoints are more or less covered.

Repeated SiO_2 exposure via inhalation has been shown to affect the lungs, resulting in lung inflammation, granulomatous lesions and interstitial fibrosis. However, as opposed to quartz, these changes in animal studieswere mostly reversible after the cessation of the exposure. The 13-week rat inhalation study of Reuzel et al. (1991) was identified as the key study. In the examinations, local lung effects were observed in animals exposed at 6 mg/m^3. The lowest dose, 1.3 mg/m^3, resulted only in very mild effects, which have been evaluated as non-pathological changes with low-grade severity (OECD 2004). The NOAEC of this study is thus 1.3 mg/m^3.

For the calculations of a limit value, the starting point, i.e. NOAEC, was first corrected in order to consider differences in exposure time (6 h versus 8 h / day and in breathing volume for rest versus light work) (ECHA 2012):

Corrected starting point= 1.3 mg/m^3 x (6 h/day / 8 h/day) x (6.7 m^3 / 10 m^3) = 0.653 mg/m^3

In order to cover the potential differences related to the sensitivity of different individuals, it was considered that a factor of 2.5 should be applied.

By applying the above mentioned factor, the calculations for an OEL for SiO_2 are as follows:

OEL = 0.653 mg/m^3 / 2.5 = 0.26 mg/m^3 ≈ **0.3 mg/m^3**.

The 8 hour OEL suggested for amorphous SiO_2 in the nano size-range is thus 0.3 mg/m^3. The value is applicable for the respirable dust fraction (including primary particles < 100nm, as well as their aggregates and agglomerates being in the respiratory size range). The suggested value is in fact identical with the DNEL given in the REACH registration of silica fume, as well as with the MAK value for the silica fume fine dust (ECHA 2014; DFG 1991).

No data allowing for determination of an OEL for dermal exposure were identified.

5.2.2 Titanium dioxide

Also for TiO_2 the critical effects are related to pulmonary inflammation, which has been observed in animal inhalation studies at various exposure durations. The study of Bermudez et al. (2004), was identified as the key study for pulmonary effects after repeated dose exposure. Rats, mice, and R hamsters were exposed to TiO_2particles for 13 weeks at concentrations 0.5, 2, or 10 mg/m^3) and pulmonary responses were assessed up to 52 weeks post-exposure. The results showed that pulmonary responses were stimulated by TiO_2 within mice and rats, but not in hamsters. High concentrations (10 mg/m^3) of particles impaired their clearance from lungs in rats and mice. Pulmonary inflammation was evidenced by increased numbers of macrophages and neutrophils and increased concentrations of soluble markers (total protein and LDH) in BALF in rats and mice exposed to 10 mg/m^3. In rats responses were also observed in animals exposed to 2 mg/m^3. Based on this, a no observed adverse effect concentration (NOAEC) of 0.5 mg/m^3 was identified.

The limit value was calculated as follows: First, the starting point, i.e. NOAEC, was corrected in order to consider differences in exposure time (6 h versus 8 h / day and in breathing volume for rest versus light work) (ECHA 2012):

Corrected starting point= 0.5 mg/m^3 x (6 h/day / 8 h/day) x (6.7 m^3 / 10 m^3) = 0.251 mg/m^3

In order to cover the potential differences related to the sensitivity of different individuals, it was decided to use the sameassessment factor of 2.5, as was used in the calculations for the SiO_2 OEL.

By applying the above mentioned factor, the calculations for an OEL for TiO_2 are as follows:

OEL = 0.251 mg/m^3 / 2.5 = 0.1005 mg/m^3 ≈ **0.1 mg/m^3**.

The suggested 8 hour OEL is thus 0.1 mg/m^3 and it can be concluded that it is in the same size range as the REL value (0.3 mg/m^3) proposed by NIOSH in the USA (2011). Their value was estimated based on a two-year carcinogenicity study. The DNEL values proposed for TiO_2in the ENRHES project report (Stone et al. 2011) used the same study of Bermudez as the critical study, but they applied markedly higher assessment factors, which explains why their values(0.017 mg/m^3 and 0.067 mg/m^3, see section 6.1.1.1) are markedly lower than the one derived in this current report.

Our recommendation is to apply the OEL when comparing exposure measurement data of the respirable fraction of the workplace air, including both primary nanoparticles (<100 nm) as well as their aggregates and agglomerates.

No data allowing for determination of an OEL for dermal exposure were identified.

5.2.3 Carbon nanofibres

Different types of fibrous carbon-based nanomaterials are currently within the focus of many nanosafety and nanotoxicology projects. However, so far, the majority of the studies have been done with various types of carbon nanotubes, and the amount of data related to possible hazardous effects of carbon nanofibres is still fairly limited. One issue, not making the hazard assessment of carbon nanofibres any easier, is the fact that there are a lot of different types of carbon nanofibres, which might not induce the same kinds of toxicological responses in exposed persons.

The few studies published so far on carbon nanofibres indicate a potential to induce inflammatory effects in the lungs after exposure by inhalation. In addition, studied with some types of carbon nanotubes indicate a strong potential for pulmonary, genotoxic and carcinogenic effects, and it has been discussed that some of the long, rigid nanofibres might behave in an asbestos-like manner. There are, however, a lot of different types of carbon nanotubes at the market, and it appears that the toxic potential may vary a lot depending on which type of material has been tested.

The limited studies on carbon nanofibres, in combination with the varying structures of different kinds of fibres, makes it, in our opinion, impossible to identify any NOAEC, or to derive any health based limit value.

Due to the potiential hazardous effects of carbon nanofibres we do recommend to minimize the occupational exposure. In line with other recommendations (IFA 2014a, SER 2012), we propose, **based on the precautionary principle, a limit value of 0.01 fibres/cm^3(8 h)** for occupational environments.

We are aware of the challenges related to the measurement of airborne exposure to carbon nanofibres. At the moment, to our knowledge, the methods for quantification of carbon nanofibres from air samples are very limited. As long as quantitative methods are not available, it is recommendable to take actions in order to check and improve the risk management methods, if these kinds of fibres are observed in the workplace air, although it might perhaps not be possible to calculate the concentrations.

No data allowing for determination of an OEL for dermal exposure were identified.

5.2.4 Nanocellulose

The amount of data related to the potential hazards caused by nanocellulose is still very low, and there are no valid studies which could be used for the derivation of an OEL. As there are some indications that biopersistent fibrous NMs might be harmful when inhaled, we recommend to apply the precautionary principle. Our suggestion for an 8 hour OEL value is thus the same as for carbon nanofibres, i.e. **0.01 fibres/cm^3**.

As for the carbon fibres, also for nanocellulose there is a lack of quantitative measurement methods. Thus a minimization of the exposure is recommended as long as reliable methods, allowing comparison of sample concentrations with the suggested OEL, are not developed.

5.2.5 Nanoclays

Very limited amounts of data on the hazards related to nanoclays have been published. Furthermore, the term 'nanoclays' includes many different materials, which complicates the assessment.

Due to the lack of substance specific data, or data on related substances, **no OEL** can be set for nanoclays at this stage.

For nanoclays we recommend to follow limit value for general dust, as proposed in section 6.2.6.

5.2.6 General reference value for dusts

Within the construction sector, exposure to different kinds of dust is extremely common. In fact, in the majority of applications it is likely that the exposure to mixed types of dust, originating from the construction materials etc., result in much higher exposure levels and pose a larger health risk than the exposure to the nanomaterials included in the construction materials. The dust occurring in the workplace air is likely to consist both of so called low toxicity, inert dust particles, but also of particles with a known toxicity (e.g. certain metals or crystalline silica). The exposure to all of these has to be taken into account in the risk assessment at the workplace.

There are indications that repated exposure to low-toxicity, inert dust, resulting in particle accumulation in the airways, may induce pulmonary effects (Pauluhn 2011, DFG 2012). In order to protect workers from these kinds of health hazards we propose (as modified from DFG 2012) the following limit values for non-toxic, inert dust, covering also granular nanomaterials occurring as aggregates or agglomerates for which no substance specific limit values have been given:**0.3 mg/m^3 for the respirable fraction** and **4 mg/m^{3}for the inhalable fraction**.

These values can for example be applied for nanoclays as long as no substance-specific data useful for the derivation of (health based) limit values for those materialsare available.

6 CONCLUSIONS

So far, no regulatory OELs specifically addressing nanomaterials have been given by the EU or by any national authority. However, some recommended limit or reference values for the concentration of nanomaterials in the workplace air have been proposed by a few institutes and agencies. A general framework for the development of OELs for nano-objects and their aggregates and agglomerates is under development in the International Organization for Standardization (ISO).

Based on the available data on the toxicological properties of the nanomaterials focused on in the Scaffold project the following recommendations for occupational exposure limit values were proposed:

Amorphous silicon dioxide

SiO_2 has been extensively studied. Experimental and epidemiological data were available, and all toxicological endpoints were covered. Mild, reversible, local lung effects were identified as the critical effects. The NOAEC for these effects in rats was 1.3 mg/m^3. From this, by converting animal exposure to occupational exposure 8 h/ day, and taking into consideration differences in respiratory rates between rats and humans and inter-individual differences (total assessment factor 5), the suggested **8 h OEL for the respirable fraction is 0.3 mg/m^3**.

Titanium dioxide

TiO_2 has during the last decade been one of the most studied NMs. Its critical effects are related to local inflammatory effects in the lungs after repeated inhalation, showing a NOAEC of 0.5 mg/m^3 in rats. By applying the same assessment factors as for SiO_2, an **8 h OEL of 0.1 mg/m^3** is suggested for TiO_2 (respirable fraction).

Carbon nanofibres and nanocellulose

The amount of data related to the potential hazards caused by carbon nanofibres and nanocellulose is still very low, and there are no valid studies which could be used for the derivation of an OEL. As there are some indications that biopersistent fibrous NMs (e.g., some types of carbon nanotubes) might be harmful when inhaled, an **OEL of 0.01 fibres/cm^3** is suggested for these materials, **based on the precautionary principle**.

We are aware of the fact that there is currently a lack of quantitative measurement methods for the estimation of exposure to carbon nanofibres or nanocellulose. Thus a minimization of the exposure is recommended as long as reliable methods, allowing comparison of sample concentrations with the suggested OEL, are not developed.

Nanoclays

Very limited amounts of data on the hazards related to nanoclays have been published. The term 'nanoclays' contains many different materials, which complicates the assessment. **No OEL** can be set for nanoclays at this stage.

General, low-toxicity dust

Within the construction sector, mixed exposure to different kinds of dust is extremely common. In addition to the substance specific OELs, our recommended 8 h OELs for general, inert dust are **0.3 mg/m^3 for the respirable fraction, and 4 mg/m^{3}for the inhalable fraction**. These values can also be applied to nanoclays.

According to the literature review in SPD5, no data were available based on which dermal limit values could have been derived.

7 REFERENCES

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8 LIST OF FIGURES AND TABLES

Table 1. Recommended reference values for titanium dioxide nanoparticles.

Table 2. Benchmark exposure levels for nanomaterials recommended by the IFA and the SER.