Applicability of provisional NRVs to PGNPs and FCNPs

study within the frame of
the project Update of the NRVs

Pieter van Broekhuizen
Amsterdam 2017

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Title	**Applicability of provisional NRVs to PGNPs and FCNPs**
Date	April 2017
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This study was carried out on behalf of the Netherlands Ministries of Infrastructure and the Environment (I&M); Health, Welfare and Sport (VWS) and Social Affaires and Employment (SZW). The study was guided by the Risks of Nanothechnology Knowlegde and Information Centre (KIR nano) of the RIVM. The study was carried out within the frame of the project '*Update of the NRVs'* in cooperation with TNO. Further information: Pieter van Broekhuizen at pvbroekhuizen@kpnmail.nl	

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Summary

An essential point in occupational risk assessment of nanoparticles is that at many common workplaces the assessment cannot be restricted to the exposure to manufactured nanomaterials (MNMs) only. Simultaneous exposure to nanomaterials released from other sources, such as process-generated nanoparticles (PGNPs) and nanoparticles' fractions in conventional components (FCNPs), which may contain and release nanoparticles with similar (long-term) hazardous properties, should be taken into account as well for pro- and retrospective examination. This holds also for workplaces where only conventional, non-nano materials are used. Hazards of MNMs do not essentially differ from the hazards of PGNPs or FCNPs.
This study reviews general medium- and high-energy formation processes of PGNPs at industrial workplaces and the generated nanoparticles' number concentrations, their size, shape and composition. These are compared with the characteristics of ultrafine particles (UFPs) formed in the ambient atmosphere. Identified PGNP concentrations may mount up to as high as $5*10^6$ #/cm^3. Many processes are identified that can be characterized as having a permanent (full-shift) release of PGNPs. Prominent are heating and combustion processes and machining operations. Obviously, the characteristics of the PGNPs strongly relate to the processes and the materials used, but in general PGNPs can be characterized as a heterogeneous nano-sized mixture of organic decomposition products and inorganic oxides.
Also a limited inventory is made of FCNPs release in common non-nano compounds used in the manufacturing industry such as paints. Reporting in occupational hygiene literature of a release of this potential source from conventional compounds is rare. Release of FCNPs may result from low-energy processes such as filling, mixing, shovelling, sweeping.
A high exposure risk seems to occur in professions such as maintenance workers and cleaners

The question is discussed whether the current classification of provisional nano reference values (NRVs) may also be suitable for risk management of PGNPs and FCNPs. The answer to this question is positive. It is concluded that NRVs are a useful tool for precautionary risk management of PGNPs. For most common situations the NRV group 2b (for lower density granular nanoparticles) will be the appropriate NRV.
For risk management of FCNPs it is advised to use the OEL for the parent coarse material, and according to BSI (2007) and BAuA (Packroff 2015), to use a safety factor to this parent OEL. In case the parent coarse material does not have an established OEL, it is advised to apply the NRV as advised for PGNPs. For screening the full nanoparticles' exposure at workplaces, and as a trigger for nanoparticles' risk management it is advised to use the additivity rule.

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Preface

This study relates the results of an assignment by the RIVM in 2016 to elaborate on the need to update the Dutch provisional nano reference values (NRVs). Since 2012, when the NRVs were drafted for manufactured nanomaterials, quite some nano-specific knowledge was generated and the OEL for asbestos (one of the building blocks for the NRV group 1) was lowered. The assignment also included the question whether the current classification of provisional NRV values could be suitable as well for risk management of process-generated nanoparticles (PGNPs) and for the released fraction of nanoparticles in conventional products (FCNPs).

The first part of this study on updating of the NRV was carried out by Harrie Buist and Thies Oosterwijk of TNO (2017) and published in the report, titled "*Applicability of provisional NRVs to synthetic nanomaterials*".
The second part of the study on PGNPs and FCNPs was carried out by Pieter van Broekhuizen of Bureau KLB (2017) and separately published in this actual report, titled "*Applicability of provisional NRVs to PGNPs and FCNPs*".

The following 4 questions are addressed in the TNO report:

Q1. Which specific air limit values for nanomaterials are currently being proposed (worldwide) in scientific publications? Focus is on the nanomaterials for which previously provisional NRVs have been derived or other commonly used materials.
Q2. An overview of proposed (by authorities) substance-specific and non-specific air limit values for occupational exposure to nanomaterials.
Q3. How do the provisional NRVs from 2011 compare to current scientific knowledge and the recommended air limit values for occupational exposure in terms of height, dose metric and scientific basis?
Q4. a. Based on the current state of knowledge and understanding (questions 1-3), would adjustment of the provisional NRVs be recommended for synthetic nanomaterials?
b. In case adjustment of the current NRVs is recommended, what is needed to achieve this adjustment?

The following 2 questions are addressed in this Bureau KLB report:

Q5. Is the current classification of provisional NRV values suitable for process-generated nanoparticles (PGNPs) and for the fraction of nanoparticles in conventional products (FCNPs)?
Q6. a. Based on the current state of knowledge and understanding (questions 1-4), would adjustment of the provisional NRVs from 2011 be recommended for PGNPs and FCNPs?
b. In case adjustment of the current NRVs is recommended for PGNPs and FCNPs, what is needed to achieve this adjustment?

Applicability of provisional NRVs to PGNPs and FCNPs

1 Introduction

Exposure assessment to nanomaterials in industrial workplaces shows that the handling of Manufactured Nano Materials (MNMs) and nano-enabled products may give rise to exposure to primary MNMs and associates thereof (Brouwer 2010, Bekkers 2016). Simultaneously other sources may contribute to the total work-related nanoparticles' exposure. These include nanoparticles generated by industrial processes and equipment used, i.e. heating and combustion processes and high-energy mechanical machining of surfaces and articles (van Broekhuizen, 2012a); these particles are called *Process-Generated Nano Particles* (PGNPs). PGNPs may include as well nanoparticles released from the use of nano-enabled products and transformed by aging through the life cycle of nano-products (Mitrano, 2015). Other workplace-related sources may include nanoparticles released from conventional compounds of which some are known to contain a significant fraction of nano-sized particles that may be released when using the compounds as a dry powder; these particles are called *Fraction of NanoParticles in Conventional compounds* (FCNP). Additionally there is the airborne environmental background nanoparticles' concentration (BGNP), originating from natural processes and anthropogenic activities (such as traffic, industrial and domestic emissions), which in general is continuously exchanged with the indoor workplace air and as such may contribute as well to workplace nanomaterials' exposure.

In principle, monitoring and controlling BGNPs in the ambient air belongs to the jurisdiction of environmental authorities while monitoring and controlling (the release at the workplace of) MNMs, PGNPs and FCNPs belongs to the responsibility of the employer (c.q. the industry in general). That is a reason to distinguish BGNPs and the MNMs/PGNPs/FCNPs carefully. This does not mean BGNPs may not create health risks and in fact this indicates that while assessing the risks of exposure to nanomaterials the full exposure should be taken into account.

Definitions used

The study uses the (first part of the) definition for nanomaterials as advised by the European Commission (EC, 2011): *'Nanomaterial' means a natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm-100 nm.* […]
This, and according to the clarifying accompanying Question and Answers document (EC 2012), implies that PGNPs are considered to be 'incidental' nanomaterials and fully comply with the proposed definition. The same holds for FCNPs.

For the nanoparticles' types with different origins operational definitions are used:

MNMs: Manufactured NanoMaterials. MNMs are newly engineered nanomaterials and used in "commercial" products to give endproducts specific nanoproperties. MNMs meet the proposed definition for nanomaterials: 1-100nm and > 50% of the particles' number in the material. This implies that conventional materials (some of them may be at the market already long time) that meet this definition are regarded as nanomaterial, c.q. as an MNM. (It is obvious to note that for NPs measured in the air at the workplace or in the environment, the relative percentage as defined in the European definition (> 50%) is not relevant.

FCNPs: This is the fraction NPs contained in a conventional substance or component. (*Fraction of NanoParticles in Conventional compounds*). (If the conventional component contains >50% NPs (NP numbers) the component is by definition a nano-material). This means that a substance (e.g. a paint filler or dye) containing <50% of nanoparticles (1-100nm) (particles' number), is not a nanomaterial, but it might release NPs during 'low-energy' use. Examples are talc, calcium carbonate and several additives used in paint manufacturing.

PGNPs: Process-Generated NanoParticles are NPs, which are formed in heating and combustion processes, by electrical motors and high energy machining processes. Nanoparticles formed during machining (grinding, drilling, polishing, ..) of surfaces coated with a nanocoating are not necessarily identical to the original (pristine) MNMs in the nanocoating. The newly formed NPs may be clusters of MNMs + binder and other component contained in the coating. This means as well that during machining non-nanosurfaces PGNPs may be formed and released.

BGNPs: Background NPs. These include NPs formed during natural processes, such as volcanism, forest fires, erosion, etc. These include as well NPs with an anthropogenic origin emitted to the environment, such as those formed in domestically heating, industrial activities, road traffic, etc. By unfiltered workplace ventilation (open windows) BGNPs contribute to the concentration of NPs in the workplace. BGNPs are by definition identical to UFPs as used as name in atmospheric chemistry.

UFPs: Ultrafine particles are particulate matter of nanoscale size (<100 nm in diameter). In size they are identical to nanomaterials as defined by EC 2011. The name UFP is commonly used in environmental sciences and in air pollution policies.

Evidence shows that concentrations of PGNPs and FCNPs at workplaces may even dominate the airborne concentrations of released MNMs (van Broekhuizen et al. 2012b). It is obvious that the generation and release of PGNPs may take place at any conventional workplace using high-energy processes and that FCNPs may be released from 'low-energy' handling powdery raw materials at 'non-nano' workplaces as well.

Industrial processes (workplaces without any relation to nanotechnology and manufacturing or processing of nanomaterials) may generate airborne nanoparticles, sometimes up to levels of several millions of particles/cm^3. The potential hazard of the PGNPs and FCNPs, similar to MNMs, depends on factors like particles' size, surface, shape and composition and may be comparable to the anticipated and identified hazards for MNMs (SCENIHR 2009). Biopersistence is another important characteristic. As such the issue of occupational exposure to nanomaterials is a more widespread challenge, not related to the use of MNMs only. When carrying out a workplace risk assessment identification and characterization of PGNPs and FCNPs cannot be ignored (SER 2012, EU/US 2012). However characterization of this heterogeneous mix of airborne nanoparticles is complex and may complicate risk assessment.

The question at stake is whether the generic approach of the Nano Reference Values (SER 2012), as a tool for precautionary risk assessment, is suitable for risk management of PGNPs and FCNPs as well. The RIVM formulated their question as follows:

"Is the current classification of provisional NRV values suitable for process generated nanoparticles (PGNPs) and for the fraction of nanoparticles in conventional products (FCNPs)?"

To answer this question insight should be generated in common processes responsible for the formation/generation of nanoparticles, preferably classified in a few common groups allowing for more generic characterization of the nanoparticles' properties and allowing for ranking their hazards in the existing (or adapted) provisional nano reference values. Available Information related to particles' rigidity, shape, density, biopersistence/solubility and composition determining nanoparticles' characteristics could be used to further substantiate allocating PGNPs in the defined groups.

The NRV and the underlying philosophy

The philosophy behind the establishment of provisional Nano Reference Values (NRVs) in the Netherlands (SER 2012) was the need of actors in the social dialogue to have an operationalized tool for occupational risk management based on the precautionary principle: comprehensible for laymen, easy to use at different workplaces and pre-empting complex physical-chemical analysis and toxicity studies of airborne nanoparticles. The idea is that the generic NRVs are provisional and appropriate to serve as acceptable exposure limits as long as legal OELs for nanomaterials have not been derived. It should be noted that precaution is not identical to prevention. Precautionary action is indicated where risks are unknown but likely, while prevention is indicated where risks can be qualified and quantified and as a consequence focused measures can be designed.

The use of NRVs allows the industry to apply nanomaterials in innovative products, while designing an acceptable risk management plan for released nanoparticles, including as well the generated nanoparticles in workplace processes.

The NRVs (see table 1) distinguish between asbestos-like rigid biopersistent nanofibers reflecting on the current asbestos OEL, and biopersistent granular nanomaterials for which number-based benchmark levels are derived based on a mass concentration of 0.1 mg/m³ and standardized on a particles' diameter of 100 nm. For this the basic relation *weight = volume times density* was used for the conversion of mass concentrations into numbers concentrations, assuming nanoparticles to be perfect spheres (see Buist 2017 for further details):

$$W = \frac{\pi\, d^3\, \rho_p}{6\, 10^{15}}$$

in which W = particle weight (µg/particle), d = particle diameter (nm), ρ_p = particle density (g/cm^3).

For high-density granular nanomaterials this leads to a NRV of 20,000 nanoparticles/m^3, for low-density granular nanomaterials this leads to a NRV of 40,000 nanoparticles/m^3, which include as well entangled (non-rigid) nanofibers. For biodegradable or soluble nanomaterials the applicable OEL is used. (van Broekhuizen et al 2012c). The NRV is expressed as an 8-hours time weighted average concentration. It was advised to use the algorithm: NRV15min-TWA= 2 x NRV8hr-TWA for short-term high exposures of maximum 15 minutes (van Broekhuizen et al 2012c).

Class	*Description*	*NRV (8-hr TWA)*
1	**Rigid, biopersistent, insoluble, fibre form nanomaterials for which effects similar to those of asbestos are not excluded** • ***SWCNT or MWCNT or metal oxide fibres for which asbestos-like effects are not excluded by the manufacturer***	**0.01 fibres/cm³**
2a	**Non-biodegradable granular nanomaterials in the range of 1–100nm and density > 6 kg/liter** • ***Ag, Au, CeO_2, CoO, CuO, Fe, Fe_xO_y, La, Pb, Sb_2O_5, SnO_2,***	**20,000 particles/cm³**
2b	**Non-biodegradable granular nanomaterials in the range of 1–100nm and density < 6 kg/liter** • ***Al_2O_3, SiO_2, TiN, TiO_2, ZnO, nanoclay*** ***Carbon Black, C_{60}, dendrimers, polystyrene*** ***Nanotubes, nanofibres and nanowires for which asbestos-like effects are excluded by the manufacturer***	**40,000 particles/cm³**
3	**Biodegradable/soluble granular nanomaterials in the range of 1–100nm** • ***e.g. NaCl-, fats, flower, siloxane particles***	**Applicable OEL**

Table 1, Dutch nano reference values (NRV's) (SER 2012)

It should be emphasized that NRVs are not health-based values, and as such do not guarantee that exposure below this level does not cause harm. On the other hand it should be noted that the base level of 0.1 mg/m^3 (for nanoparticles with a 100 nm diameter) is a 'sharp' level taking into account that if the particles' diameter is smaller (<100nm) (which is commonly the case) the total mass of exposure (with the same particles number) is much lower than 0.1mg/ m^3.

Workplace nanoparticles' number-based concentrations are assessed with the NRVs, corrected for the existing background concentrations in the ambient air. For this the following traffic light scheme for workplace measurements was published (van Broekhuizen et al 2012c) (see figure 1). Since the NRVs were defined only for MNMs, the scheme distinguishes between MNMs and PGNPs, but takes addition of different nanoparticles into account if concentrations are lower than the NRV.

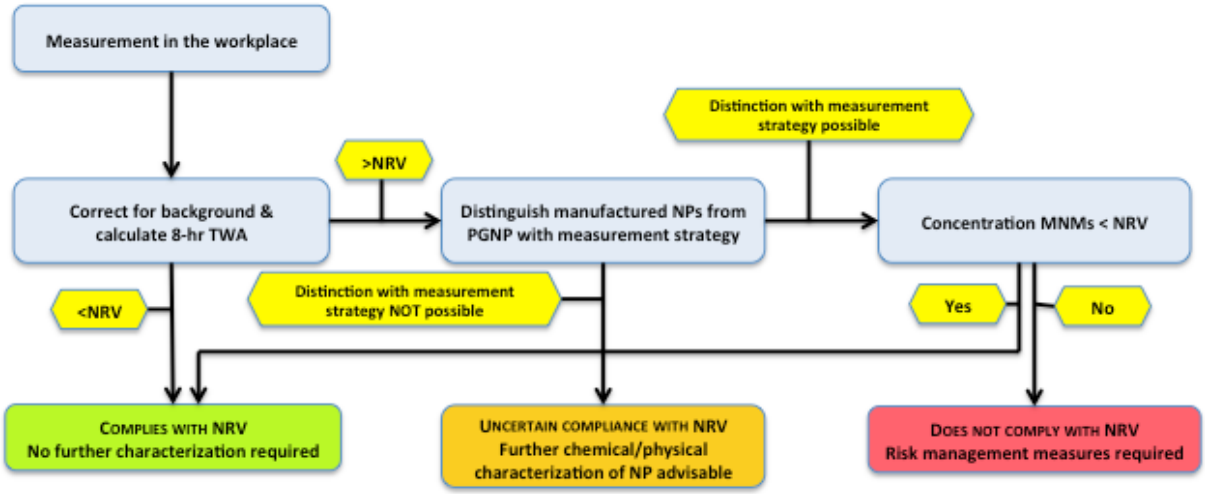

Figure 1, Traffic light scheme for characterizing nanoparticles and use of NRVs (from: van Broekhuizen et al.2012c)

2. Particles in atmospheric aerosols

For framing possible formation routes (generation and growth) of PGNPs and BGNPs some general findings from atmospheric chemistry can be used. In atmospheric chemistry models for particle formation and size distribution in the ambient air are extensively discussed (e.g. Whitby et al 1976; Finlaysson-Pitts et al, 2000; Calvo et al 2013). The atmospheric models frequently distinguish a fine particles range (< 2 µm) and a coarse particles range (>2 µm), of which the first may be sub-divided in ultra fine particles (or nucleation mode) (<10nm), transient nuclei or Aitken nuclei range (10-100nm) and an accumulation range (0,1-2µm). Frequently environmental models use the denomination 'ultra fine particles' for the range of particles with a diameter between 1-100nm (which include nucleation mode and the Aitken mode particles, and coincide with the definition for nanomaterials). Figure 2 shows an idealized size distribution and the hypothesized formation.

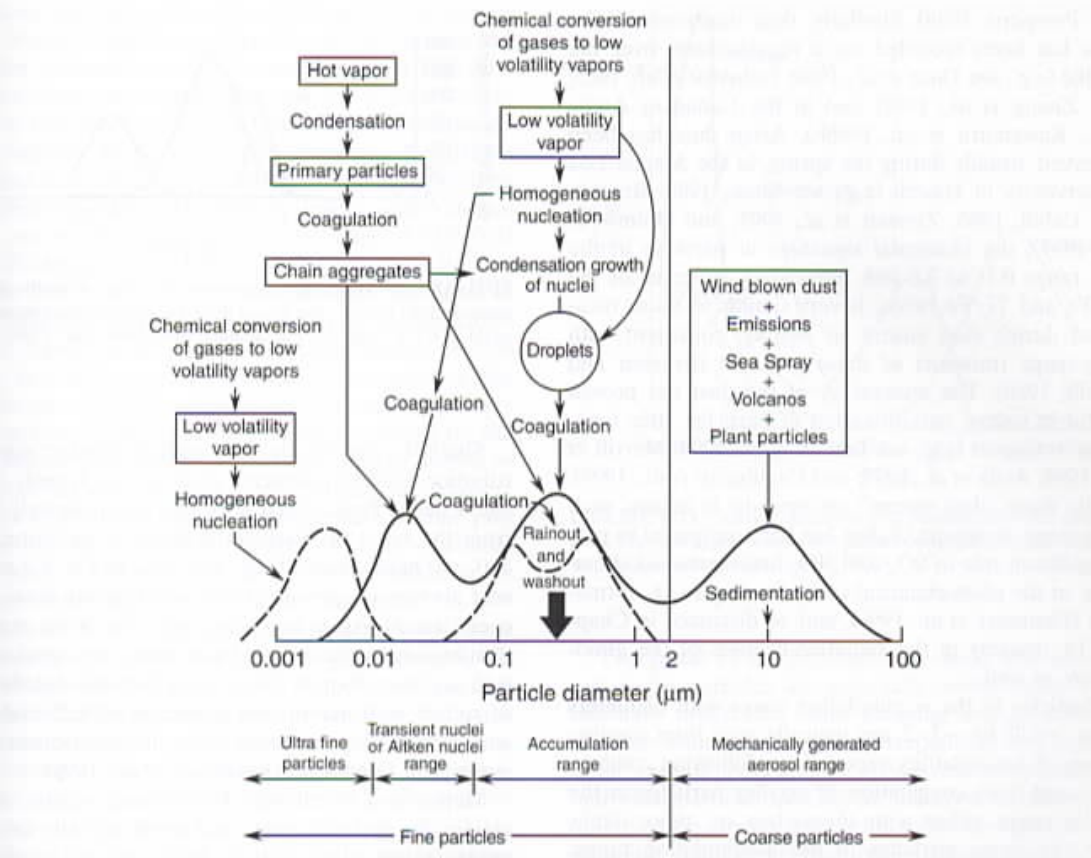

Figure 2 Idealized schematic of an atmospheric aerosol size distribution showing four modes, where the accumulation mode particles may also show a bimodal character as shown by the dashed line. Modes, sources, and removal mechanisms are indicated. (from: Whitby 1976 and adapted by Finlayson-Pitts, 2000).

High temperature combustion sources produce predominantly particles in the Aitken and the accumulation mode. The relative numbers of particles produced in the Aitken mode, compared to the accumulation mode depend on the nature of the combustion process (fuel, operation conditions) as well as the conditions of the dilution. The condensation of a low-vapour-pressure species to form a new particle is known as homogeneous nucleation. The vapour pressure of a substance over the curved surface of a droplet is greater than over a flat surface of the same substance. "The smaller the radius of the droplet, the higher is the vapour pressure over the droplet surface". Figure 3 shows an example of the surface distribution of particles produced by the combustion of several organic compounds, as well as by automobiles and a burning candle. The "dirtier" flames (e.g. candles, acetone) produced significant numbers in the accumulation mode, whereas the "cleaner" flames produce more Aitken mode nuclei (NRC 1979).

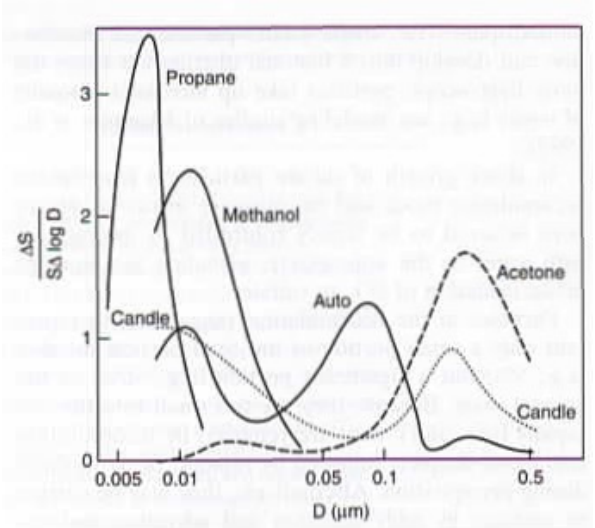

Figure 3 Surface distributions of particles from the combustion of several organics and from automobiles and a candle (from: Finlayson-Pitts, 2000)

Quantification

An overview of some 'common' environmental background concentrations of ultrafine particles is summarized in figure 4 (as summarized by van Broekhuizen 2012a).

Kreyling (2010) estimates that the daily dose of inhaled nanoparticles in humans is limited to a maximal nanoparticle aerosol concentration of 10^{12} m^{-3} (beyond that, coagulation changes the concentration rapidly within one minute under ambient air conditions), and the daily volume of air inhaled by an adult is ~15 m^3. Assuming a nanoparticle deposition probability of 0.3, the daily deposition amounts to ~5 × 10^{12} nanoparticles.

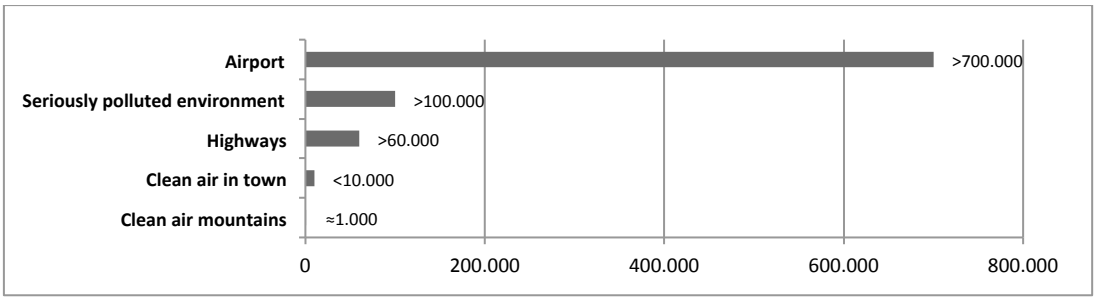

Figure 4 Indication of some "environmental" background concentrations, Ultrafine particles' concentrations (particles/cm^3)

Characterisation

Depending on their origin, atmospheric aerosols may be natural or anthropogenic. The main sources of anthropogenic particulate matter in the atmosphere lie in urban and industrial areas. Mentioned here are traffic (exhaust emissions, road surface abrasion, brake and tyre wear, particle resuspension from paved roadways), different industrial activities (emissions from power plants, oil refineries, mining), building (excavations, soil movement, demolitions) and emissions from housing (heating, food cooking). In rural areas, on the other hand, the main sources of aerosols are biomass burning and the emissions due to various farming activities.

Ultrafine material generated from the road-tyre interface has been reported to exhibit five major particle types, two of which are liquid (Dahl et al., 2006). The solid phase particles consist of single near-spherical particles and agglomerates of near-spherical particles, whose mobility diameters are between 10 and 100 nm. It is suggested that the spherical primary particles originate from carbon black used as a reinforcing filler though it is possible that small inclusions of ZnO or ZnS are responsible for the spherical morphology. The fractal structure of the agglomerates implies that they were detached under tensile stress rather than excessive heating, which would cause the chains to contract (Dahl et al., 2006).

Among the natural sources of particulate matter are the seas and oceans, deserts, soil, volcanoes, vegetation, wildfires and lightning. This wide range of sources generates particles with very different chemical compositions, commonly relating to their origin. Table 2 summarizes the main organic aerosol constituents and sources.
Inorganic marker elements associated with various emission sources or processes have been summarized in Table 3. Trace metals may be released by more than one technical process.

Main organic aerosol constituents and sources.

	Primary					Secondary		
	Fossil fuel combustion (e.g. vehicles)	Other anthropogenic processes (e.g. manufacturing, cooking)	Biogenic (e.g. vascular waxes) and bioparticles (e.g. spores)	Biomass burning	Soil	Gas-particle partition (adsorption and absorption)	Reactive condensation (e.g. acid catalysed reactions)	In-cloud processing
Alkanes, alkenes, alkanals, alkanoic acids, diacids	✓	✓	✓	✓		✓		?
Aromatics, PAHs	✓	✓		✓		✓	?	?
Hopanes, steranes, unresolved complex mixture (UCM)	✓							
Photochemical products (e.g. carbonyls, methyl tetrols, carboxylic acids, organosulphates)						✓	✓	✓
Sugars, polyols, polysaccharides			✓	✓	✓			
Levoglucosan				✓				
HULIS					?		?	?

Table 2 Main organic aerosol constituent and sources (From Calvo et al, 2013)
Hopanes = triterpenes; steranes = 4-cyclic compounds derived from steroids; HULIS = "humic-like substances" similar to humic substances from soil and water

Inorganic marker elements associated with various emission sources or processes.

Secondary aerosols		SO_4^{2-}, NO_3^-, NH_4^+
Sea salt		Cl, Na, Na^+, Cl^-, Br, I, Mg and Mg^{2+}
Crustal or geological tracers		Elements associated with feldspars, quartz, micas and their weathering products (mostly clay minerals), i.e. Si, Al, K, Na, Ca, Fe and associated trace elements such as Ba, Sr, Rb, and Li. In addition, there will be accessory silicates (notably zircon, titanite and epidote), and representatives from the minority non-silicate mineral groups, namely carbonates, sulphates, oxides, hydroxides and phosphates.
Technogenic tracers	Steel industry	Cr, Ni and Mo
	Copper metallurgy	Cu and As
	Ceramic industries	Ce, Zr and Pb
	Heavy industry (refinery, coal mine, power stations)	Ti, V, Cr, Co, Ni, Zn, As and Sb
	Petrochemical industry	Ni and V
	Oil burning	V, Ni, Mn, Fe, Cr, As, S and SO_4^{2-}
	Coal burning	Al, Sc, Se, Co, As, Ti, Th, S, Pb and Sb
	Iron and steel industries	Mn, Cr, Fe, Zn, W and Rb
	Non-ferrous metal industries	Zn, Cu, As, Sb, Pb and Al
	Cement industry	Ca
	Refuse incineration	K, Zn, Pb and Sb
	Biomass burning	K and Br
	Firework combustion	K, Pb, Ba, Sb and Sr
	Vehicle tailpipe	Platinum group elements, Ce, Mo and Zn
	Automobile gasoline	Ce, La, Pt, SO_4^{2-} and NO_3^-
	Automobile diesel	S, SO_4^{2-} and NO_3^-
	Mechanical abrasion of tyres	Zn
	Mechanical abrasion of brakes	Ba, Cu and Sb

Table 3 Inorganic marker elements associated with various emission sources or processes (From Calvo et al, 2013)

Metal boiling points and particles' size
The influence of the metal boiling point on their occurrence in certain type of aerosols is demonstrated by the research of Buonanno et al (2011) on waste incinerators. Waste combustion is one of the anthropogenic sources building up ambient background UFP concentrations. These emissions are normally efficiently filtered before they are spilled in the environment, but particles' formation and composition can be illustrative for the formation of PGNPs and the occurrence of specific elements in different size modes in combustion processes at workplaces. Buonanno et al

(2011) found maximum number concentrations of $2.7*10^7$ #/cm^3 and $2.0*10^3$ #/cm^3, respectively before and after the fabric filter showing a very high efficiency in particle removal by the fabric filter. The most abundant compounds found in samples collected before the fabric filter are Na–K–Pb oxides followed by phyllosilicates, otherwise, different oxides of comparable abundance were detected in the samples collected at the stack. With regard to heavy metal concentrations, the elements with higher boiling point present higher concentrations at lower diameters showing a not complete evaporation in the combustion section and the consequent condensation of semi-volatile compounds on solid nuclei. E.g. the elements As, Cd, and Zn decrease each contribution to the total fraction with the increasing of the diameter (from 50 nm to 200 nm) whereas Co, Cr, Fe, Sb, Sc, Sm, Th, Eu and Yb increase their contribution to the total amount with the increasing of the particle size. This different behaviour can be justified considering the boiling points that, for the first group elements, are lower than 1200 °C whereas they are higher than 1200 °C for the second group. Then, the distribution of elements with boiling points above 1200 °C is higher in 200 nm-particles than in 50 nm-particles.

UFPs and MNMs knowledge

Stone et al (2016) conclude that knowledge from environmental UFP research on particles' toxicity can be used to understand the mechanism of toxicity of MNMs and vice versa. Their summarized comparison of the physicochemical characteristics of ambient UFP with MNMs is shown in table 4. They illustrate the complexity of the composition of ambient UFPs as an agglomeration of different air polluting substances, including particles of inorganic and organic origin and volatiles (see figure 5).

Ambient UFP	Manufactured Nanomaterials
• Ambient air PM composition is complex, including coarse (2.5-10 µm), fine (<2.5 µm) and UF (<100 nm) particles. • Urban UFP derive mainly from combustion processes (e.g. traffic) and subsequent particle nucleation, coagulation and vapour condensation. • Urban UFP often contain transition metals or organic chemicals, i.e. complex composition (See figure 5). • Mixture of insoluble to soluble particles and droplets, possibly leading to the release of several constituents from one particle in lungs. • Vary over time and place in size distribution, particle morphology, chemical composition and concentration. • Although relatively large in terms of number, UFP contribute relatively little to the mass of PM compared to coarse particles. • Controlled exposures are impeded by the temporal variability, which complicates mechanistic studies. • Are always surrounded by gaseous pollutants.	• A number of definitions exist which usually stipulate that at least one dimension is in the nano-scale (1-100 nm). Many NM have three dimensions in the nano-scale, making them nanoparticles. • Often referred to as engineered or manufactured as they are designed and generated for a specific purpose. • Made in a wide variety of chemistries, consisting of single elements (e.g. carbon or metal), compounds (e.g. metal oxides or salts) or complex composites (e.g. core plus shell structure). • Can vary significantly in particle morphology and chemical composition but are well defined at production and close to production levels. • Spatial and temporal variance in airborne concentration may vary significantly. • Controlled exposures are possible, enabling detailed mechanistic studies. • Can be handled in a standardised manner, facilitating studies of defined properties.

Table 4 Ambient UFP and MNM physicochemical characteristics (from Stone et al 2016)

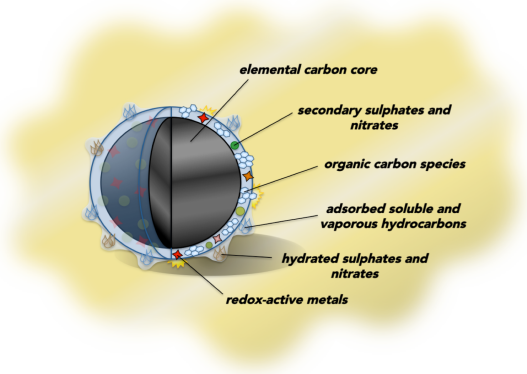

Figure 5 Schematic example of the complex composition of UFP (e.g. urban PM or particles in vehicle exhaust), which in urban air often have a carbon core coated with a diverse range of chemical species including reactive transition metals and organic hydrocarbons. Detail is not to scale. (figure from Stone et al 2016).

3. Aging and transformations through the life cycle of nano-products

Mitrano et al (2015) argue that nanomaterials exhibit the same chemical reactions as the bulk form of the materials undergoes, so traditional knowledge on metal and metal oxide chemistry can be broadly applied in many instances, with subtle adjustments concerning nano-specific reactions where appropriate. For example, the literature on corrosion is full of information on the transformation reactions of compounds such as Ag that are driven by thermodynamics, resulting in dissolution and phase transformation reactions. When extending this information to MNMs [and nano-enabled products], some of these reactions result in complete loss of the nano-properties, either because the particle has been dissolved or transformed into particles larger than 100 nm. In these cases, an assessment of the NP is no longer necessary but only of the metal it was composed of. On the other hand, some transformation reactions may only change the NP partially, for example the surface coating. Another likely transformation result is the aged and transformed nanoparticles' release from nano-enabled products as a result of the product life cycle processes, which particles can be qualified as PGNPs as well. Table 5 summarizes the main transformation identified reactions, the particle(s) they affect and the products categories for which it is important. For each transformation process, the main affected MNM and product categories are given. The main chemical or physical factors that govern the reaction are listed together with examples of the change of the MNM and the result of the transformation reaction. The final column indicates if the reaction leads to a more similar or more diverse set of particles.

Transformation process	MNM(s) affected	Main product category	Governing factors	Example(s) of MNM change	Result of transformation
Oxidation and reduction	Ag, Fe, CeO_2	All	• Element (oxidation, reduction or both) • Environmental factors (e.g. redox potential)	• Altered ratio of oxidized element in sample • Prerequisite to MNM dissolution	• Change to surface chemistry • Potential for further transformations (e.g. dissolution)
Photochemistry	TiO_2, ZnO, SiO_2, Ag, CNT	Cosmetics, textiles, coatings/surfaces, paints	• Light intensity • Ability of light to penetrate outer coating/layers	• Change to MNM coating • Oxidation state • Generation of reactive oxygen species (ROS) • Particle persistence	Change to surface chemistry, change of crystallinity
Dissolution	Ag, ZnO	Textiles, cosmetics	• Particle size • Capping agent • Composition • Solution chemistry	• MNM surface properties • Toxicity • Particle persistence	Loss of nano-identity, formation of secondary particles
Phase transformation	Ag, ZnO, SiO_2, CuO	All	• Particle size • Capping agent • Composition • Solution chemistry	• Sulfidation • Phosphatization	Change to particle surface chemistry, change to primary particle functionality
Absorption to MNM surface	All materials	All	Solution chemistry	• Agglomeration • Organic ligands may affect dissolution, charge, and stability	Changes to particle surface chemistry
Desorption from MNM surface	All materials	All	• Solution chemistry • Particle composition	Strongly affects the coatings of product-weathered MNM's, especially if capping agent loosely bound to MNM surface	Changes to particle surface chemistry
Exposure to extreme heat (Incineration)	CNT, ZnO, Ag Surface: All	All, at the end of life cycle	Disposal/waste stream differences that vary by country or region	• Complete combustion of material • Combustion only of surface coatings • Melting • Chlorination	Loss of nano-properties (CNT, ZnO, Ag) or change to surface properties (TiO_2, SiO_2)
Re-Precipitation	Ag, ZnO	All, after M^+ release from product	Solution chemistry Light	• Sunlight driven photo-reduction of Ag metal • Formation of Zn-carbonate after ZnO dissolution	New particle formation

Table 5 Main chemical transformation reactions during use and disposal of nano-products

4. Toxicity of PGNPs

The toxicity of combustion derived nanoparticles (CDNPs), as a 'subgroup' of the PGNPs was already extensively described by Donaldson et al (2005) in the 'early days' of the discussion on nanomaterials' risks. They illustrated the comparable pathway of the toxicological activity, especially the formation of ROS by oxidative stress for three types of PGNPs and one MNM (carbon black)(figure 6).

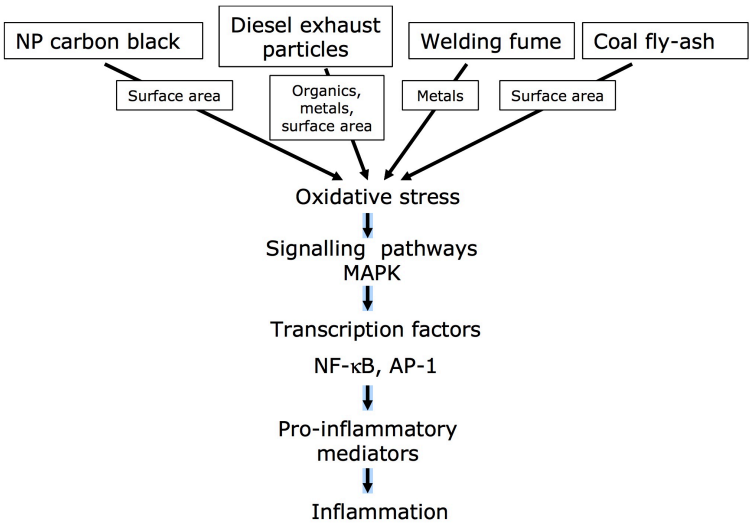

Figure 6 Different components of different CDNP can cause oxidative stress that acts through well-documented redox-sensitive pathways (illustration from Donaldson et al 2005)

Donaldson et al (2005) state that the different CDNP show considerable heterogeneity in composition and solubility, meaning that oxidative stress may originate from different components depending on the particle under consideration. Key CDNP-associated properties of large surface area and the presence of metals and organics all have the potential to produce oxidative stress. CDNP may also exert genotoxic effects, depending on their composition. CDNP and their components also have the potential to translocate to the brain and also the blood, and thereby reach other targets such as the cardiovascular system, spleen and liver. They conclude that CDNP therefore can be seen as a group of particulate toxins unified by a common mechanism of injury and properties of translocation, which have the potential to mediate a range of adverse effects in the lungs and other organs.

In general the toxicological properties of PGNPs are comparable to mechanisms and effects of manufactured nanomaterials. See for example Fadeel et al (2012); Luther et al (2013) and Stone et al (2016).

5. Sources of PGNPs at the industrial workplace

An indicative overview of a few sources of PGNPs and generated nanoparticles' number concentrations was summarized by van Broekhuizen (2012b). This was adapted with figures collected in this study (see figure 15). It is obvious that higher PGNP concentrations than 6-7*10^6 /cm^3 are rare in practice. This might relate to coagulation (agglomeration, aggregation) properties in the air and sedimentation of the larger associates (Kreyling 2010). Rim et al (2012) studied time-varying, size-resolved particle indoor UltraFine Particles (UFP) concentrations (particle size between 2 nm and 100 nm) and they observed the temporal change in the UFP size distribution for different indoor UFP sources (cooking, candles, hair dryers, and power tools). They conclude that the coagulation effect was higher with smaller UFP and higher number concentrations, and they emphasize the influence of ventilation. When the central fan was turned on, particle deposition loss was substantial and comparable with the coagulation loss. When it was turned off, deposition loss was not significant and coagulation was the primary cause for the shift of UFP size distribution. Compared with coagulation and deposition, air change was a minor effect in these tests.

5.1 Generic sources

PGNPs can be distinguished in three groups based on processes in which they are formed:

- Nanoparticles generated in heating and combustion processes
  - These include combustion products from ovens, burning fuels such as diesel and petrol (Donaldson, 2005). These include also nano-sized product generated with some electro motors, where sparks may induce nanoparticle formation. Furthermore, there are numerous heating and combustion processes generation nanoparticles: plasma cutting, welding, metal grinding, soldering, laser ablation, smoking food, iron casting, heating shrinking foil, etc.
- Nanoparticles generated in machining operations
  - These include different medium- and high-energy processes such as machining surfaces whether or not enriched with MNMs. Operations like abrasion, polishing, grinding, drilling, milling, extrusion, 3D printing
- Other processes
  - These include aging reactions, 'low-energy' wear processes, etc. (see also table 5)

NB: Low-energy processes include in general the handling (and cleaning) of materials, such as storing, conveying, filling, mixing, shovelling, sweeping (Shandilya 2014). Also FCNPs may be released by these operations.

5.2 Heating and combustion processes

Welding

For welding fumes (WF) social partners in the Netherlands agreed to use an 8hr time weighted average Occupational Exposure Limit (OEL) of 1mg/m^3. OELs used in some other EU member states (FR, AT, BE) for welding fumes are 5 mg/m^3. This mass based approach however does not give information on the risks of exposure to nanoparticles generated during the welding process, while environmental epidemiology indicate that for the adverse effect of inhaled particles not only particle mass is crucial but also particle size (Oberdorster et al, 2005). Welding processes with high mass emission rates (manual metal arc welding, metal active gas welding, metal inert gas welding, metal inert gas soldering, and laser welding) show mainly agglomerated particles with diameters above 100 nm and only few particles in the size range below 50 nm (10 to 15%). Welding processes with low mass emission rates (tungsten inert gas welding and resistance spot welding) emit predominantly ultrafine particles with diameters well below 100 nm (Brand et al 2013).

While the International Agency for Research on Cancer (IARC) categorizes welding fumes in Group 2B (possibly carcinogenic to humans), it has also noted that an as-yet unexplained reason for excess lung cancer risks still exists, which demands increased research focused on thorough characterization of specific welding fume components (IARC, 1990; Husgafvel-Pursiainen 2009).

For arc welding WF particles are usually classified into three types according to the mechanism of their formation (Jenkins et al., 2005; Sowards et al., 2008; Zimmer & Biswas, 2001): (1) ultrafine particles (less than 0.1 μm) formed by condensation from the gas phase, saturated with substances from both the electrode and weld metal; (2) coarse fume particles (larger than 1 μm) formed by mechanical means such as ejection of microscopic electrode material droplets (microspatter) from the arc or molten weld pool; and (3) particles (agglomerates of various shapes and densities) larger than 0.1–0.2 μm, which are mainly formed by coagulation of ultra-fine particles. When shielded metal arc welding (SMAW) is applied, the latter two types of particles mostly prevail (98–99% of WF mass) in the welder's breathing zone (Sowards et al., 2008). Most of the WF ultra-fine particles formed during SMAW consist of a core containing iron and manganese compounds (Fe_3O_4 and $MnFeO_2$) and a shell rich in silicon, calcium, potassium, sodium and fluorine (depending on the composition of the electrode coating) (Voitkevich, 1995). The chemical composition of coarse WF particles differs strongly from that of ultra-fine particles. Oprya et al (2012) analyzed for SMAW that particles with an average content of iron (agglomerates of ultra-fine particles) formed the largest group (over 70%) of inhaled particles in the WF. For each electrode type, their average elemental composition did not depend either on the size of the agglomerates, or on the heat input.

Brand et al (2012) shows that whereas welding techniques with high mass emission rates (MMAW, MAG, MIG, and Laser) show predominantly particles with diameters about 100–200 nm and few nanoscaled particles, so-called 'clean' techniques with low mass emission rates (TIG, and RSW) emit nearly exclusively particles smaller than 50 nm with number concentrations similar to other welding techniques (see table 6). Such particles are in respect to their potential toxicological properties of particular interest.

	***C* mean average (cm^{-3})**	**Standard deviation (cm^{-3})**	**Cmax average (cm^{-3})**	**Standard deviation (cm^{-3})**	***F* < 100 average**	**Standard deviation**	***F* < 50 average**	**Standard deviation**	**Mode average (nm)**
MMAW	2.6E + 06	4.5E + 05	6.5E + 06	1.2E + 06	0.24	0.02	0.10	0.02	143
MAG	2.1E + 06	1.1E + 06	4.7E + 06	2.5E + 06	0.54	0.02	0.16	0.02	108
MIG alu	5.0E + 06	1.6E + 06	1.2E + 07	4.7E + 06	0.35	0.03	0.13	0.06	124
MIG solder	2.1E + 06	1.6E + 06	5.1E + 06	3.9E + 06	0.44	0.01	0.15	0.02	124
Laser	5.0E + 07	3.8E + 06	1.2E + 08	8.6E + 06	0.42	0.02	0.12	0.01	114
TIG	2.4E + 06	4.5E + 05	3.3E + 06	4.9E + 05	0.99	0.01	0.90	0.05	16
RSW	2.0E + 06	9.3E + 05	4.7E + 06	2.2E + 06	1.00	0.00	0.98	0.01	11

Table 6 *Number Size Distribution of Fine and Ultrafine Fume Particles From Various Welding Processes*
Mean particle number concentration (C mean), maximum particle number concentration (Cmax), fraction of particles smaller than 100 nm (*F* < 100), fraction of particles smaller than 50 nm (*F* < 50), and mode of the distribution for the 7 welding techniques. Shown is the average and standard deviation (Std. Dev) of the five measured emission episodes for each technique (25 spots for RSW).
Manual metal arc welding (MMAW), Metal active gas welding (MAG), Metal inert gas welding on aluminum (MIG aluminum), Metal inert gas soldering on zinc plated base material (MIG soldering), Laser welding, Tungsten inert gas welding (TIG), Resistance spot welding (RSW)

The relation between particle diameters and number concentrations by welding technique measured stationary at 33 worksites in total, with >20 scans per worksite is shown in figure 7 (Lehnert et al 2012). TIG welding generated smaller particles most of which were <100 nm, whereas GMAW, FCAW, and SMAW yielded larger particle agglomerates that were mainly >100 nm, but nevertheless with a peak around ca. 200 nm.

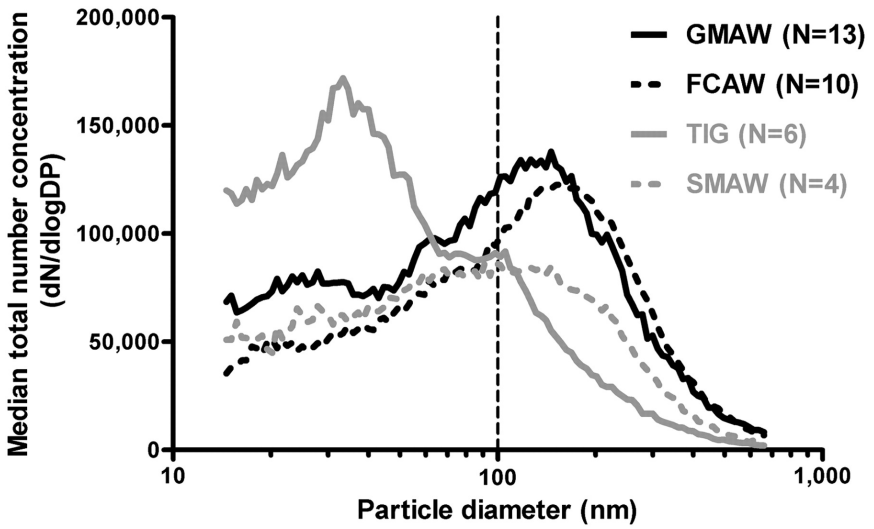

Figure 7 Particle size distributions measured by SMPS (number count versus particle diameter in the range 14–673 nm) averaged over the worksites for different welding techniques (GMAW, FCAW, TIG, and SMAW)

This Weldox study (Lehnert et al 2012) measured the exposures with and without the use of personal protective equipment (Powered Air Purified Respirators - PAPR), and including local exhaust ventilation (LEV). Concentrations were significantly higher when LEV was inefficient or when welding was performed in confined spaces. The efficiency of using PAPRs is illustrated in figure 8 albeit only expressed in mass and not in number concentrations.

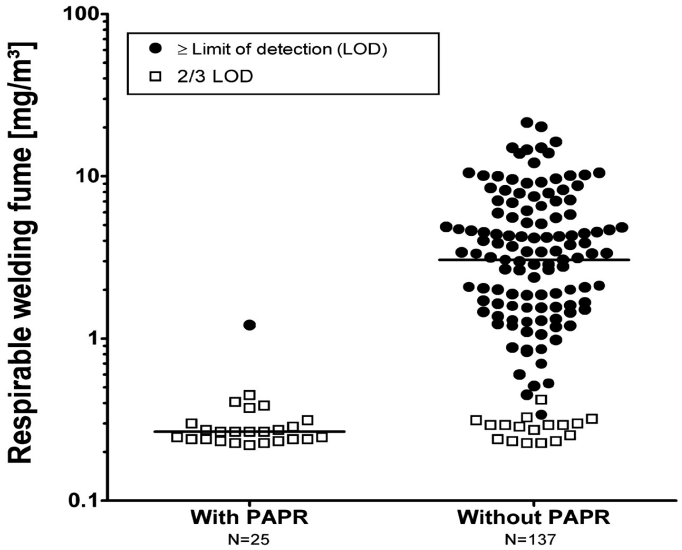

Figure 8 Respirable welding fume inside PAPRs and in welders without PAPR (excluding workers applying TIG and miscellaneous techniques during the shift. Welders did not wear PAPRs during TIG welding) (Lehnert et al 2012).

Graczyk et al (2016) confirm the high release of nanoparticles for TIG (also known as gas tungsten arc welding -GTAW). They report a mean particle number concentration at the breathing zone of $1.69*10^6$ particles cm^{-3}, with a mean geometric mean diameter of 45 nm. On average across all subjects, 92% of the particle counts at the breathing zone were below 100 nm. The elevated concentrations of tungsten were most likely due to electrode consumption.
For GTAW of stainless steel shows different types of agglomerates in the nanosize fraction of the GTAW aerosol (Miettinen et al 2016). The agglomerates that did not consist of iron oxide primary particles contained increased proportion of Ni compared to the proportion of (Cr + Mn) than the agglomerates that consisted of iron oxide primary particles. In the middle of the workshop, the number size distribution was unimodal with the geometric mean diameter (GMD) of 46 nm. Near the breathing zone the number size distribution was multimodal, and the GMDs of the modes were in the range of 10–30 nm. Two different agglomerate types existed near the breathing zone. The first type consisted of iron oxide primary particles with size up to 40 nm and variable amounts of Cr, Mn, and Ni replacing iron in the structure. The second type consisted of very small primary particles and contained increased proportion of Ni compared to the proportion of (Cr + Mn) than the first agglomerate type.

Cena et al (2015) demonstrated that mild and stainless steel welders using gas metal arc welding (GMAW) of mild and stainless steel and flux-cored arc welding (FCAW) are exposed to large concentrations of Mn, Cr, and Ni nanoparticles that will have the ability to deposit in the respiratory system. They indicate that most of the Cr and more than half of the Ni and Mn in the fumes were in the nano-fraction. Up to 5% of the deposited nano-sized Cr was in the Cr(VI) valence state.

GMAW studied in an automobile manufacturing factory shows that size distribution, morphology, and chemical compositions of welding particles are significantly different from indoor and outdoor background particles (Zhang et al 2013). A bimodal size distribution by mass and a unimodal size distribution by number for welding nanoparticles were observed. The cluster of nanoparticles, presented as chain-like structure, dominates the welding particle's morphology. Particle evolution involves three modes of size distributions, i.e., primary nanoparticles, agglomeration, and coarse particles. Working activities, sampling distance from sources, air velocity, background particles, and engineering control measures have significant influence on nanoparticle levels in workplace atmosphere. Zhang et al conclude that number and surface area concentrations are better exposure metrics for exposure assessment of nanoparticles than mass concentrations.

Nanoparticles formation is also influenced by the welding performance (Graczyk et al, 2016). ROS production was potential was significantly higher for apprentices that burned their metal during their welding task. It is likely that ROS production potentials are not influenced by one particular metal, but

rather, by the oxidation state of the welding particles. Welding performance in regards to the quality of the weld relates to the ROS generation potential of the fume, thereby signifying a potential determinant for exposure. As induction of ROS by NPs is a key event in toxicological cellular response and an important contributor to acute and chronic vascular and pulmonary diseases, it is imperative also with regard to health protection, and not only regarding quality of the weld, that proper welding techniques are used in order to avoid excess oxidation.

Plastic welding, extrusion and melting

Plastic welding for semi-finished plastic materials is described as a process of uniting softened surfaces of materials, generally with the aid of heat (except solvent welding). Welding of thermoplastics is accomplished in three sequential stages, namely surface preparation, application of heat and pressure, and cooling. Numerous welding methods have been developed for the joining of semi-finished plastic materials. Wake et al (2002) report on the relative high release of nanoparticles for plastic welding ($3.7*10^4$ with a median diameter 37 nm)

Thermal degradation products of polymers

The chemical nature of the thermal decomposition of polymers varies widely from one material to another. At its simplest it may consist of a complete breakdown to a single, and readily identifiable product, which is often a monomer. On the other hand a complex mixture of products may be obtained together with a relative stable intractable residue.

From the point of view of identification there are three types of thermal degradation.

- Firstly, substances of the molecular dimensions of monomer or less, of which a detailed analysis can usually be made.
- Secondly, substances are often produced which are volatile at the degradation temperatures but involatile at ordinary temperatures. These are usually polymer chain fragments, which are larger than monomer. Although they may be referred to as dimeric, trimeric, etc., their precise chemical structures have usually not been determined.
- Finally, the involatile residue, which often remains, is frequently insoluble although knowledge of the mechanism of the degradation reaction combined with spectral data can often give some information about this structure. The relative amounts of these three kinds of products can vary with the temperature of degradation although not a great deal of information of this kind is available.

Sealing and moulding plastic

Zilaout et al (2013) measured a high PGNP emission from the heating (with an open flame) of shrinking foil, used for the sealing and shipping of rubber in a rubber manufacturing site, with concentrations up to maxima of $1.4*10^6$ #/cm^3 and a mean diameter of 57nm of, as they suggest composed of plastic degradation products, probably mixed with combustion products.

Moulding of high-density polypropylene (HDPE) leads to high PGNP emissions of decomposition products with maxima of 600,000/cm^3 with a mean diameter of 83nm (Zilaout 2013).

3D printing

In fact 3D printing is a form of precise extrusion, and as such it is not unexpected that PGNPs are formed in this process. Stephens et al (2013) examined PGNP formation from the thermoplastic plastics ABS (acrylonitrile butadiene styrene) and PLA (poly lactic acid) and found emission rates of respectively $1.9*10^{11}$ #/min and $2*10^{10}$ #/min. This leads to concentrations of maximum $1.4*10^4$ #/cm^3 with a particles size distribution between 11 and 116 nm.

Soldering

There is evidence of intense nanoparticle generation from a low power (45 W) flux soldering unit (Gómeza et al 2013). This is a familiar device often used in daily life, including home repairs and school electronic laboratories. They demonstrate that metal-containing nanoparticles may reach high concentrations (ca. 10^6 particles/cm^3) within the breathing range of the operator, with initial size distributions centred at 35–60 nm The morphological and chemical analysis of nanoparticle agglomerates collected on TEM grids and filters confirms their multiparticle structure and the presence of metals.

Engines

Diesel motors

In 2013 the IARC classified diesel engine exhaust as carcinogenic to humans (group 1), based on the evidence of a causal association between diesel engine exhaust exposure and increased risk of lung cancer in humans, and an association with cancer of the urinary bladder (IARC 2013). Combustion-derived nanoparticulate appears to predominately mediate the adverse vascular effects of diesel exhaust inhalation (Mills et al 2011).

In 2012 the Dutch social partners in the tyres and wheels industry, the car body industry and the motor vehicles industry agreed to use an OEL of 7 µg EC/m^3 (TGG-8 uur, measured as respirable dust) (EC=elementary carbon) (Carrosseriebranche nd). In the Netherlands diesel engine exhaust is on the actively list of the Health Council to derive and OEL (GR 2017) and an advice is expected in 2017 or 2018. The GR will use the study of Taxell and Sartonen (2016) for their advice. This study also uses a mass based approach, i.e. EC/m^3 as metric, and based on this inventory it might be expected that the advice for a recommended health-based OEL might even be lower than 7 µg EC/m^3. None of these studies explicitly further elaborates on the specific effects of the generated nanoparticles in diesel exhaust fumes.

Hesterberg et al (2010) proposed to use diesel exhaust particulates (DEP) as a generic model to suggest limit values for toxic effects of nanoparticles. They state that DEP, as a complex mixture of ultrafine and coarse particles and a variety of gaseous components of toxicological relevance (e.g. nitrogen oxides, carbon monoxide, aldehydes), may bear similarities to e.g. fullerenes, carbon-based nanotubes and to sphere-shaped primary particles, whereas their physical structure (i.e., agglomerates of spherical primary particles) bears similarities to others that also have a strong tendency to agglomerate (e.g., titanium dioxides and other metal oxides). Typical size distributions for DEP were found for primary particles in the range of 15-40 nm, and for agglomerates in the range of 60-100 nm (Burtscher 2005). Swanson et al (2016) showed in the presence of Fe nuclei resulting from 36 ppm ferrocene doping, 4500 ppm of fuel sulphur produced CNT-like structures. The precursor concentrations required for high rates of CNT growth are comparable to those found in transportation fuels used in many regions of the world.

Hesterberg et al (2010) suggested a NOEL (no-observed effect level) for cardio-vascular effects for DEP at an exposure level between of 100 µg/m^3 $PM_{2.5}$ (3×10^4 particles/cm^3) and 200 µg/m^3 $PM_{2.5}$ (5×10^4 particles/cm^3). These levels are in the same order of magnitude as the levels for NRVs for biopersistent granular nanomaterials.

Taxell and Sartonen (2016) note that the accumulation mode contains most of the DEP mass. Nucleation mode particles account for more than 90% of the particles' number concentration, but less than 20% of the particulate mass of untreated diesel exhaust, see figure 9.

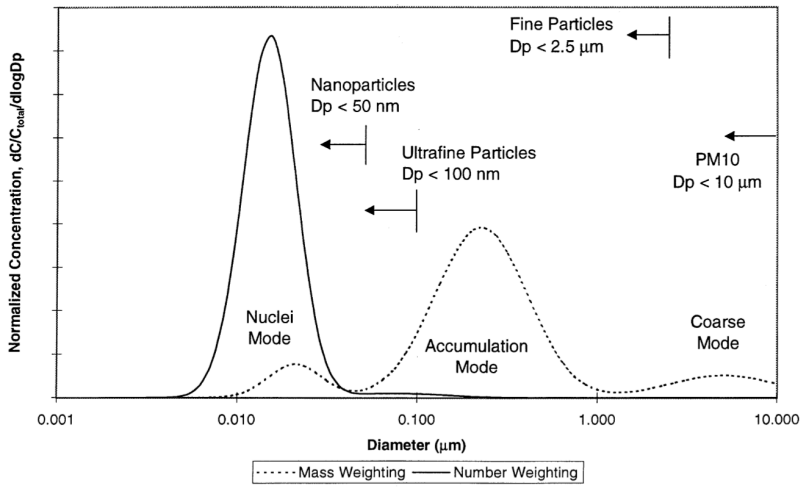

Figure 9: Typical mass and number size distributions of particles in untreated diesel exhaust. The mass or number concentration (C) of particles in any size is proportional to the area under the corresponding curve in that range (from Taxell and Sartonen2016)

Taxel and Sartonen (2016) state that the organic material associated with DEP is a complex mixture of linear, branched and cyclic hydrocarbons originating mainly from unburned fuel and engine lubrication oil, with small quantities of partial combustion and pyrolysis products. Polycyclic aromatic hydrocarbons and their nitrogen derivates may comprise up to 1% of the particulate mass of the untreated diesel exhaust.

Universal motors

Scymczak et al (2007) demonstrated that universal electrical motors emit nanoparticles with a high content of copper. Emissions up to 300,000 /cm^3, containing Cu are reported. During the operation of a universal motor, brushes made of graphite slide over commutator contact bars made of copper. This movement causes the formation of particles not only by mechanical abrasion, but also by brush sparks. Scymczak suggests that domestic appliances and electric power tools using power control by phase angle modulation can be a strong source of nanoparticles with a high content of copper. Recent models of brushless motors do not release nanoparticles (Kim et al 2014).

The use of a vacuum cleaner with a leak (caused by an inadequate sealing) was found to be the origin of nanosilica dispersion in the indoor air during nanosilica manufacturing (Kim et al 2014). While the particle size of the nanosilica that emitted into the air (during the handling of nanosilica by a worker) was mostly over 100 nm or several microns (μm) due to the coagulation of particles, the size of nanosilica that leaked out of vacuum cleaner was almost similar to the primary size (mode diameter 11.5 nm). Analysis of area samples resulted in 20% (60% in terms of peak concentration) less than the analysis of the personals sample. On the other hand, the structure of the vacuum cleaner itself caused leakage of nanoparticles due to the abrasion of the commutator and the carbon brush of the motor. Lioy et al (1999) studying the emission of fine particles (PM2.5) from residential vacuum cleaners also indicates the release of nanoparticles from certain vacuum cleaners and points at cleaning workers, e.g. in hotels as potential exposed population.

Koponen et al (2009) tested precoated MDF test plates painted with different nanocomposite paints (a 'carbon black paint and a nano-TiO_2 paint) with hand-held electrical sanding. They identified two smaller peaks of < 20 nm, a middle peak of about 200 nm and two of 1 and 2 **µ**m and they contribute the smallest two modes to the orbital sander's electrical motor, while the mid-sized mode (~200 nm) comprised a combination of electrical motor "spark-particles" and matrix debris (see also Koponen et al 2011).

Van Broekhuizen et al 2011 showed that concrete drilling machines generate high levels of PGNPs up to maxima of $8*10^4$ #/cm^3 with a median diameter of 44 nm, where the hardness of the concrete, i.e. the used force of the machine, influences the number of PGNPs: a larger force a large number of PGNPs.

Regarding possible formation of CNTs in PGNPs it should be noted that Kolosnjaj-Tabi et al (2015) showed that inhaled PM in Parisian ambient air contains CNTs. These CNTs are similar to those they found in dusts and vehicle exhausts (motor type not further described) collected in Paris, as well as to those previously characterized in ambient air in the USA, in spider webs in India, and in ice core. They conclude that these results strongly suggest that humans are routinely exposed to CNTs.

Laser techniques

Laser ablation for cleaning

Laser ablation is used for the conservation of artworks for laser cleaning of various materials such as paper, metals, stone, biological materials etc. for the cleaning of small works of art to even in restoration of complete building segments (Barcikowski et al. 2007). The technique is used in automatic scanners or by manually handling. In the latter case, the fumes are often not captured at all. The mean diameter and the dispersion of the particulate matter generated strongly depend on the laser parameters (fluence, pulse energy) and the cleaned material (gypsum, graphite, paper). The particulate matter which emerges during Nd:YAG[1] laser cleaning significantly decreases to the ultrafine particle diameter range (up to 75% with a diameter < 100 nm) if the fluence or the laser pulse energy is increased. Using shorter laser pulse duration, femtosecond laser ablation tends to the emission of finer particles.

[1] *Nd:YAG = "neodymium doped YAG-crystal" (Nd:$Y_3Al_5O_{12}$), where YAG is an yttrium-aluminium granate compound used as active medium for certain solid state lasers.*

At the highest laser fluence applied in the presented laser cleaning investigation, 78% of the PM is in the nanoparticle size range (30 - 100 nm). Lowering the fluence or pulse power results in a lower frequency of nanoparticles in the PM. It is notable, that femtosecond laser ablation ((Ti:Sapphire) causes finer particles then nanosecond laser ablation, which may be due to higher energy density compared to Nd:YAG laser ablation. Another significant difference of both ablation techniques is the emission rate which is one order of magnitude higher in the case of Nd:YAG laser ablation during laser cleaning

Laser engraving
Laser engraving used for coding serial numbers on aluminum tubes for personal care products in the cosmetics industry may generate high emissions of PGNPs (max: $2.9*10^6$ #/cm^3) (Zilaout et al 2013).

Lasers for medical surgery
Mowbray et al (2013) report about harmful surgical smoke generated by energy-based surgical instruments such laser. They identify that diathermy and laser produce respirable UFPs with exposure of the theater staff and they suggest that the produced smoke is potentially carcinogenic.

Laser techniques for ceramic tile sintering and ablation
High-powered CO2 lasers are used for industrial ceramic materials with advantages regarding the sintering process such as speed, temperature and enhanced durability and surface properties of structural materials. The high-energy nature of these laser processes implies a significant potential for the generation and emission of nanoparticles. The high temperatures applied in the furnace (up to 1195^oC) may cause chemical transformations in the raw tiles and the emission of particulate and/or gaseous pollutants into indoor air, which could be enhanced by the addition of the laser treatment. Laser tile sintering and laser ablation processes of ceramic materials in a pilot plant scale furnace generates high concentrations of nanoparticles (mean minute concentration up to $9.7*10^5$ #/cm^3 over 1.5 h), with mean diameter of 18 nm (Fonseca et al 2015). Two different temperature-dependent and tile composition-related emission behaviours were detected: thermally induced emission, and nanoparticle formation through nucleation. Nucleation occurred mostly during red clay tile sintering and probably due to S-bearing species in the raw material (e.g., $CaSO_4$). Ablation emissions were highest in terms of mass for all size ranges and highest in terms of particle size (mean diameter of 80 nm). The highest concentrations of metals (mainly Zn, Pb, Cu, Cr, As and Tl) were found in the ultrafine fraction <0.25 mm. Fonseca et al (2015 and 2016) use the Dutch NRV approach for their assessment and advices on risk management.
Industrial laser-based (high power CO2 laser) ceramic tile sintering indicates nanoparticle emission patterns strongly linked to temperature and tile chemical composition, and mainly independent of the laser treatment (Fonseca et al 2016). Also, new particle formation (from gaseous precursors nucleation) events were detected, with nanoparticles <30 nm in diameter being formed during the thermal treatment. The conducted TEM/EDX analyses of the samples show that quartz (SiO2) appears to be the main inorganic component released in both types of tiles. Other crystalline constituents found in both types of tiles were albite ($NaAlSi_3O_8$), metakaolinite ($Al2Si_2O_5$), and huntite ($Mg_3Ca(CO_3)_4$). Conversely, mineral phases such as microcline ($KAlSi_3O_8$) and hematite (Fe_2O_3) were only found in red clay tiles whereas augite ($CaMg(Fe, Al, Ti) (Si Al)_2O_6$ only in porcelain tiles. In addition, metal oxide nanoparticles of Zn, Cr, Al and Fe were also found, resulting from their use as opaque frits or pigments

Laser printing
Koivisto et al (2010) measured nanoparticles' number concentrations from laser printing activities after a print job to a maximum of $2.5*10^5/cm^3$, with a geometric mean diameter of 42 nm, which was 11 times compared to the background particle concentration. Koivisto et al (2010) refer to studies that indicate that nanoparticles from laser printers are secondary particles produced by the nucleation of volatile organic compounds originating from paper and toner. Wensing et al (2008) and Morawska et al (2009), based on studies on laser printing emissions conclude that nanoparticles emissions (d<100 nm) do not originate from toner but instead is related to the high-energy fuser unit. Wensing et al (2008) identified flame-retardant tri-xylyl phosphate, naphthalenes and siloxanes as possible constituents of the emitted printer aerosol and they do not exclude other chemicals to be identified as well.

Ceramics manufacturing

In traditional ceramics manufacturing in small-sized pottery studio significant concentrations are observed when the fired ceramics were painted/glazed (glaze firing) or not (bisque firing) (Voliotis et al 2014). Average nanoparticles' number concentrations during bisque firing of 1.4×10^5 cm^{-3} and during glaze firing of 2.5×10^5 cm^{-3} are measured, with a mean size of the nanoparticles varying between 30-70 nm during bisque firing and 15-40 nm during glaze firing. This indicates that the composition of the fumes leading to new particle formation is different in each case. The particles collected during both firing stages consisted mainly of Si, emitted by the clay. Particles from glaze firing also contained significant amounts of Pb, a Cu fraction and possibly C likely released from the pigments and the glazing applied on the surface of the ceramics.

Fluorescent tubes manufacturing

Van Broekhuizen et al (2012b) study the manufacturing of fluorescent tubes (with an internal coating of nano Al_2O_3) and they conclude that coating, sintering, drying and polishing, in which open fires are used, generate high numbers PGNPs, with a maximum of more than 10^6 #/cm^3 close to the emitting sources and a mean diameter of 26 nm (see figure 10). As an *expert guess* the authors suggest 'soot' to be the composition of these PGNPs. Soot is generally defined as a mass of impure carbon particles resulting from the incomplete combustion of hydrocarbons.

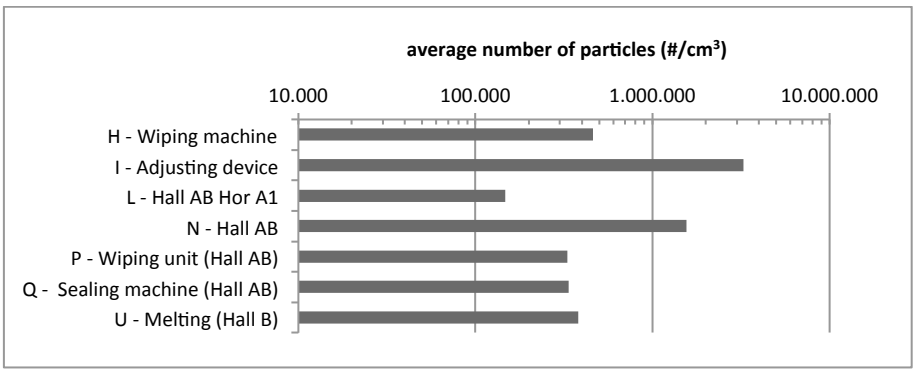

Figure 10 **Average concentrations of PGNP from equipment used for manufacturing fluorescent tubes**
The grey bars show the average levels of PGNP emitted during the operations of the indicated machines.

Average PGNP concentrations may reach a level of more than a 10^6 #/cm^3, with an assigned $NRV_{8hr\text{-}TWA}$ of 40,000 nanoparticles/cm^3 to these pollutions. Comparing the average NP-concentrations close to the (continuous) sources and the hall concentrations with the NRVs show for all the situations a strong exceeding of the NRV for workers in this area.

Rubber products manufacturing and extrusion

The reuse of shredded waste rubber tires for manufacturing rubber speed bumps and parking stops at 150°C emits rubber fumes during curing. Particle number concentrations are reported of $3*10^5$ cm^{-3}, 15min peak concentrations of $>5*10^5$ cm^{-3} and a CMD of 26nm (Kim et al 2013). Most of the rubber fumes were compact in shape. The composition analysis mainly detected C, Si and S; heavy metals such as Zn, Fe, and Mn were detected in some particles.

Zilaout et al (2013) make an inventory of MNM and PGNP emissions during rubber manufacturing and they conclude that weighing and milling activities do not lead to exposure of workers to nanoparticles; the used ventilation during these activities proves to be adequate. However, extrusion activities are characterized as a continuous daily exposure due to process generated nanoparticles. PGNP emissions of $>3*10^6$ #/cm^3, with a mean diameter of 46nm are observed, with a steady decrease in concentration at larger distances, but contributing to a continuous high background concentration in the working area (see figure 11). They also measure high continuous PGNP emissions leaking from heating ovens (vulcanization) in the working area, up to maxima of $1.8*10^6$ #/cm^3 with a mean diameter of 33nm.

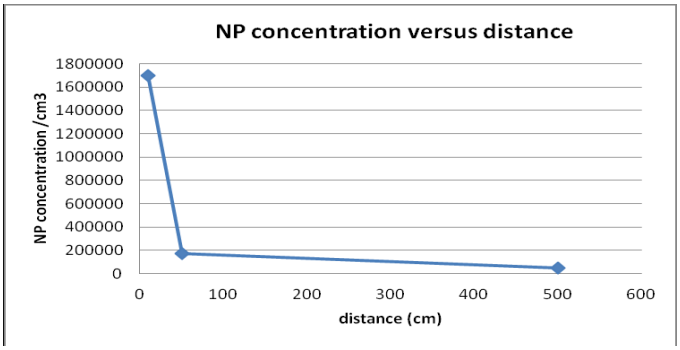

Figure 11 PGNP generation during rubber extrusion and dilution in the working room (fromZilaout 2013)

Foundry

Evans et al (2008) studied varying ultrafine particle number and respirable mass concentration generated within an automotive grey iron foundry. Respirable mass concentrations ranged from 0.001 to 1.07 mg/m^3 and the UFP number concentration ranged from $1.9*10^4$ to $3.5*10^6$ #/cm^3. Alloy melting and subsequent pouring operations were the primary sources of ultrafine particles within the foundry. Non-process foundry sources substantially influenced indoor ultrafine particle number concentration. Specific non-process aerosol sources included direct fire natural gas heaters, liquefied pro- pane-fuelled sweeper trucks and cigarette smoking.

Electronics industry

Manufacturing of chips for electrical equipment seems to generate metal-based fibre-like pollution inside the high-energy machine, which might generate exposure for cleaning an maintenance workers (van Broekhuizen, 2013)

5.3 Machining Operations

Safe Work Australia (Schutz et al 2013) studied PGNP formation from matrices including epoxy, polycarbonate, polyurethane, polymethyl methacrylates and polyamide. Nanomaterials used for reinforcing include silica, carbon fibres, carbon nanotubes and nanoclay. Machining processes investigated include wet and dry cutting, drilling, grinding, sanding and abrasion. From their review they conclude (Schutz et al 2013):

- The overall mass of emissions from the machining of composites containing reinforcing nano-objects is in most instances not significantly different from the machining of composites not containing nano-objects.
- High energy processes emit significantly higher numbers of particles and produce higher airborne mass concentrations than low energy processes.
- For some processes, lower emissions can be achieved by using wet machining in place of dry machining.
- Currently there is insufficient data to arrive at any conclusions about how emissions vary with material composition.
- A combination of; (a) nanoscale particles – nanoparticles from the matrix primarily but also free reinforcing nano-objects, (b) agglomerates or aggregates of nano-objects, and (c) matrix with nano-objects embedded are emitted. The machining of composites can result in nano-objects that are partially embedded in matrix fragments.
- Only one incidence of free individual carbon nanotubes (CNT) being detected has been reported (in the release from an abrasion experiment), while a number of studies examining the machining of CNT-containing composites did not find such a release. Free carbon nanofibres have also been detected in a machining study.
- As for emissions control generally, use of engineering controls with machining equipment can be used to significantly reduce worker exposure, if designed appropriately and maintained adequately.

Grinding

Grinding of several substrates (i.e. hard wood, aluminium, steel, PTFE, ceramic and granite) with a Dremel tend to generate a bimodal particle size distribution, with substrates showing distinct ultrafine and coarse modes (Zimmer et al, 2002). The results demonstrate that grinding of substrates produced ultrafine particles through vaporization or combustion of the substrate material, with maximum PGNP concentrations around 10 nm for the different substrates, except for hard wood, which has a maximum around 50 nm. (See figure 12). In the absence of a substrate (tool operating by itself) there was also evidence that the grinding tool led to the formation of ultrafine particles, albeit at lower concentration.

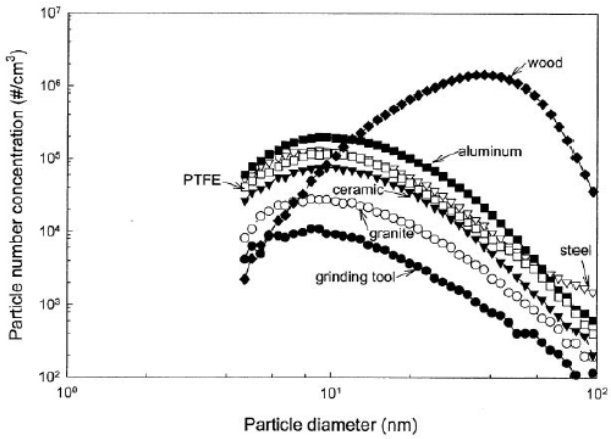

Figure 12 Nanoparticles concentrations experimentally generated with a high speed Dremel™ and various grinding substrates. (from Zimmer et al, 2002).

Abrasion, sanding

Professional sanding generates a considerable generation of nanoparticles up to concentration of $6*10^4$#/cm^3 (Gohler et al 2010). The generated nanoparticles are made up from matrix material, which contains the embedded additives (Gohler et al 2010; Vorbau et al 2009). There is no significant difference between coatings containing and not containing nanoparticle additives. Another study (Gohler et al 2013) shows that the sample material, the sample composition, the sample condition (e.g. weathering state) and the type of mechanical treatment have a strong effect on the particle release. For example artificial weathered coatings showed in the case of sanding a higher nanoparticle release as the non-weathered samples. In contrast, the artificially weathering of PP-composites led to a reduced release.

Despite occasional high numbers of released nanoparticles, no free nano-pigments were observed during independently performed SEM- and TEM-analyses of electrostatic precipitated aerosol particles. SEM-analyses of used abradants for sanding and dynamic friction showed the presence of pigment particles with dimensions significantly larger than the nanoscale for both the non-weathered and weathered samples.

Abrasive machining of composite systems containing carbon nanotubes (CNTs), micron-diameter continuous fibres (carbon or alumina), and thermoset polymer matrices shows that peaks in size distribution and surface area of generated particles (including size distribution) are not significantly different for composites with and without CNTs (Bello et al 2009). The nano-fraction contributed to ca. 10% of the surface area. Free CNTs were not identified. Dry cutting may give rise to concentrations of > 10^6 particles cm^{-3}. Bello et al used a graphite-epoxy system (aligned carbon fibres with an epoxy resin arranged in a layered laminate configuration) with aligned CNTs placed at the center ply interface. The second CNT–hybrid composite they used is a woven alumina (Al_2O_3) fiber cloth with aligned CNTs grown on the surface of the fibres, impregnated with an epoxy. Besides, the usual procedure is wet cutting did not produce exposures significantly different than background.

Koponen et al (2009) tested precoated MDF test plates painted with different nanocomposite paints (a 'carbon black paint and a nano-TiO_2 paint) with hand-held electrical sanding. They identified two smaller peaks of < 20 nm, a middle peak of about 200 nm and two of 1 and 2 **µ**m and they contribute the smallest two modes to the orbital sander's electrical motor, while the mid-sized mode (~200 nm) comprised a combination of electrical motor "spark-particles" and matrix debris. The largest two modes contain mostly nanocomposite debris.

Sanding of polyester parts leads to PGNP formation up to $2*10^6$ #/cm^3 with a diameter of average 38 nm (Zilaout 2013).

Fettling

Fettling of aluminium with a band saw at a relatively low speed results in a large number fraction of ultrafine particles (96%) as well as a high particle number concentration ($1.3*10^5$ cm^{-3}) (Elihn et al 2009). The authors speculate that processing of the metal aluminium at fettling may have given a higher particle number concentration at this job activity compared to iron processing due to the higher vapour pressure of aluminium.

Shredding

Shredding is a technique used for recycling of materials. The airborne release of nanoparticles from a thermoplastic nanoclay-reinforced nanocomposite was investigated: polypropylene resin with montmorillonite (Raynor et al 2012). They tested this material for shredding for recycling by using test plaques made from plain polypropylene resin, the same resin reinforced with talc, and the resin reinforced with montmorillonite nanoclay. Shredding was carried out under 'normal' (not-elevated) temperatures. (26-29^oC). All three materials generated airborne nanoparticles with a count median diameter of approximately 10–13 nm (see figure 13). The highest particle concentrations were generated during shredding of plain polypropylene test plaques. Fewer particles were generated by shredding the nanoclay-filled test plaques, but not as few as were generated during the shredding of the talc-filled test plaques. Because the nanoclay and talc reinforcing materials were larger than the majority of particles measured, most of the particles that were observed must have been generated by a mechanism other than the direct release of the nanoclay or talc. SEM imaging did not identify any nanoparticles that appeared to be nanoclay liberated from the nanocomposite.

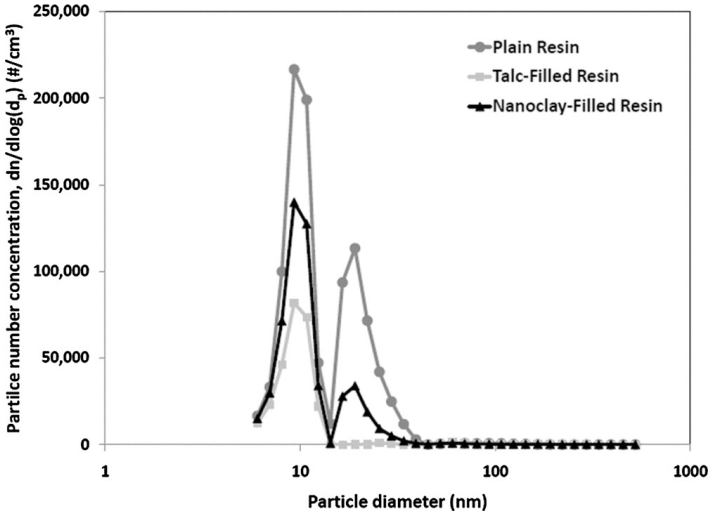

Figure 13 Particle size distribution by number measured by the FMPS as plaques made from plain resin, talc-filled resin, and nanoclay-filled resin were shredded by a granulator (from Raynor et al 2012)

Core making and moulding

Core making and moulding are activities where >90% of the particles are in the nano-range (GMD=22-48nm) (Elihn et al 2009). The generated particles, in concentrations from $2.5 – 7.5*10^4/cm^3$, are likely to originate from smelting and filling melted metal in moulds. Mass based concentrations (PM10) mount up to 0.3 mg/m^3.

Concrete working and drilling

Concrete cutting results in an average emission of $2.2*10^4$ $\#/cm^3$, with a GMD of 98 nm and peaks of $0.5*10^5 – 10^5$ $\#/cm^3$ (5-20min TWA) during the actual cutting (Elihn et al 2009).
Arzami et al (2014) also studied nanoparticles release during concrete cutting, drilling and mixing of fresh concrete (incorporating Portland cement with Ground Granulated Blastfurnace Slag, or Pulverised Fuel Ash). The cutting was found to produce the highest release of new particles in terms of both particles number concentration and particles number distribution ($> 6*10^5$ $\#/cm^3$ and 85% with a diameter 5-30 nm), followed by the drilling and mixing activities.
Drilling of nano-silica reinforced concrete and drilling non-nano-enabled concrete shows PGNP emissions up to maxima of $8*10^4$ $\#/cm^3$ with a median diameter of 44 nm. (van Broekhuizen et al 2011) The authors show that an idle running drilling machine generates higher levels of PGNPs than during actual drilling activities, while drilling in nanosilica reinforced concrete emits higher PGNP concentrations than the non-nano concrete. They conclude that it is the electrical drilling machine that is mainly responsible for the PGNPs while the hardness of the concrete is another trigger.

Asphalt road working

Asphalt workers are exposed to total dust, polycyclic aromatic hydrocarbon and NO_2, and simultaneously to nanoparticles. The nanoparticles originate mainly from asphalt paving activities and traffic exhausts; most however seemed to originate from asphalt fumes (Elihn et al 2008). During paving, a higher concentration was observed. A median particle concentration of $3.4*10^4$ cm^{-3} (interquartile range $1.3*10^4 – 7.5*10^4$ cm^{-3}) was measured close to the screedmen walking behind the paving machine. The geometric mean diameter of the number size distribution of particles (D *pg*) at the paving site was 70 nm (see figure 14). Traffic generates smaller particles, as reported from measurements in street canyons, in the order of 15 – 50 nm (Gidhagen et al 2005; Wehner et al 2002) Hot asphalt itself generates high concentrations of nanoparticles as measured at an asphalt manufacturing plant: when filling a carriage with hot asphalt peak concentrations between $1.5*10^5$ and $2.5*10^5$ cm^{-3} were observed during the measuring time of 1 hr. The composition of the nanoparticles was not assessed.

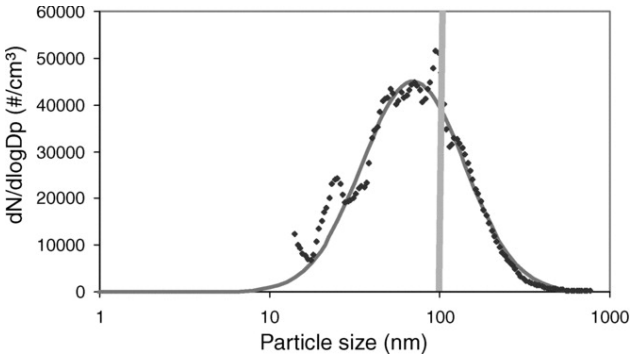

Figure 14 Nanoparticles release in asphalt work

The dotted line is the mean number size distribution of particles at a paving site during one day fitted by a lognormal size distribution. D_{pg} = 70 nm, GSD = 2. The percentage of UFPs (below 100 nm) was 74%.

5.4 Overview PGNP sources

As a summary of the chapters 5.2 – 5.4, an overview of the cited processes with PGNP release is given in figure 15. This figure combines the processes with released PGNPs, the measured mean particles' diameter, the analysed or assumed compositions of the release nanoparticles and the maximum particles' number concentrations.

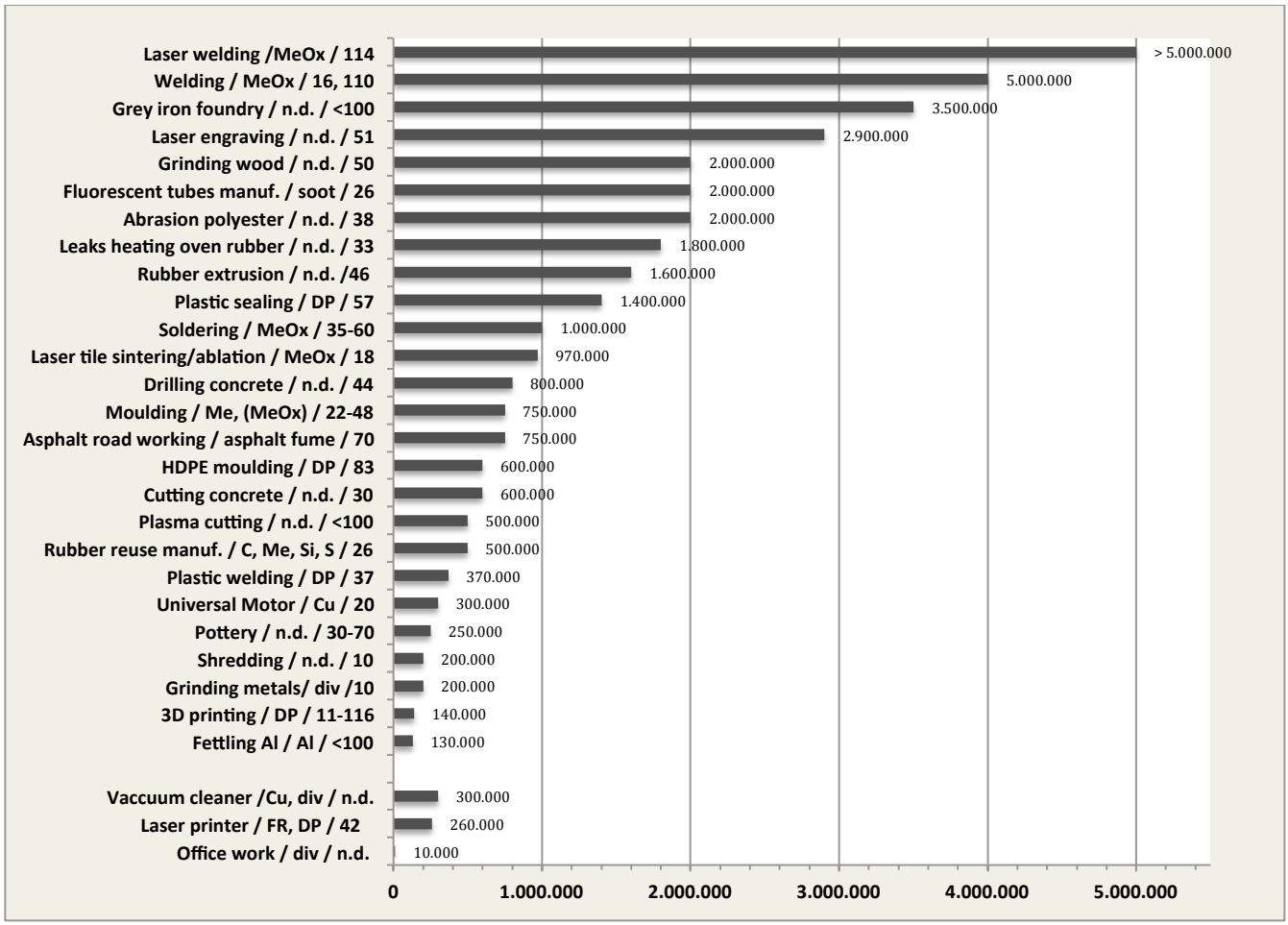

Figure 15 Summary of the maximum release of PGNPs, (nanoparticles' numbers/cm^3) as measured at different sources at common workplaces and cited in the text (chapter 2), including the mentioned particles' compositions and their mean particles' diameter. (Adapted from: van Broekhuizen (2012a). Y-axis: source / composition / mean diameter. MeOx = metal oxides; DP = Degradation products; n.d.= not determined; div. = diverse

6. Sources of FCNPs at industrial workplaces

FCNPs are predominantly nanoparticles released from conventional compounds that themselves are not classified as nanomaterials according to the EC definition (EC 2011). It appears that there are quite some different compounds used in industrial manufacturing processes that, although the technical qualifications do not demand for a nano-sized fraction in the total particles' size distribution, contain such a fraction anyway, due to specific manufacturing procedures. For some types the nano-fraction might be even essential to generate the desired properties, as is for example the case for some pigments. Obviously inhalatory exposure to an airborne nano-fraction is especially at stake when working with dry powders. Some industries, as for example the rubber industry, have been dealing traditionally with the issue of exposures to hazardous dry powders. Dustiness, as a measure of the ability of the material in bulk form to become airborne, is a well-recognized problem. Creative solutions, such as granulation and incorporating of the potentially dusty materials into a paste (or a wax) have realized a significant reduction in inhalatory exposures in the manufacturing industries, which resulted as well in preventing nanoparticles from these sources to be released in the workplace (Zilaout 2013).

Moreover, frequently the size distribution, especially the contribution of the nano-sized fraction to the total bulk, is not communicated in the production chain. Consequently, the end user of raw compounds may be ignorant and disregard a potential exposure to nanoparticles when dry powders are processed at the workplace.

An important characteristic of submicron particles is their agglomeration and aggregation behaviour, which may interfere with dispersion and emulsifying processes. To influence this particles' behaviour, but also to add other functionalities to the surface of particles, the surface is frequently functionalized (coated) to enhance their use in a range of industrial applications. This functionalizing may also influence the dustiness as shown by Burdet et al (2013). They studied the dustiness of six differently commercially available functionalized calcium carbonate nanopowder fillers: $CaCO_3$ uncoated, $CaCO_3$ for water-based latex paint, $CaCO_3$ for printing inks, $CaCO_3$ for rubber, $CaCO_3$ for adhesives, $CaCO_3$ for PVC plastics, $CaCO_3$ for PP/PE plastics. It was shown that the functionalization of the same calcium carbonate nanoparticles gave a large increase in dustiness compared to the uncoated particles. This finding may shed light on the properties of conventional functionalized particles as well.

Van Broekhuizen et al (2012b) studies nanoparticles' release in paint manufacturing of nano-paints and in conventional non-nano waterborne paints. It is notable that there is no airborne release of nanoparticles during the adding of nano-TiO_2. Contradictory there is a high release from the paint additives, the coarse TiO_2 and the fillers with mean diameters between 45-56 nm (talc is not shown in this figure, but shows an even higher release than CaCO3) (see figure 16). Based on their chemical identity the authors assigned all components a NRV of 40,000 #/cm^3 and they conclude that for the full period batch manufacturing the $NRV_{8hr\text{-}TWA}$ is not exceeded.

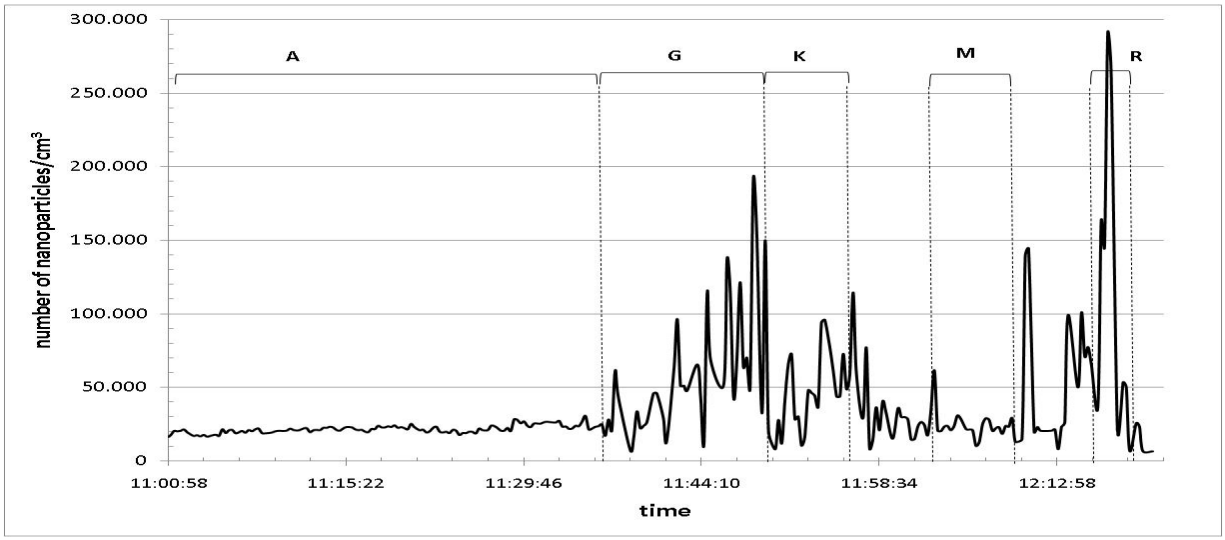

Figure 16 Nanoparticles' release pattern during paint mixing of a 'nano-paint'; the adding of different dry components to the paint mix (from van Broekhuizen 2012b). Note: the y-axis uses a logarithmic scale. A= background workplace, G= solid paint additives, K= coarse TiO_2, M= nano-TiO_2, R= filler $CaCO_3$ Sampling took place manually at a distance of 30 cm from the adding of the solid powders.

Manufacturing of a non-nano waterborne alkyd paint shows a comparable pattern (see figure 17). High NP emissions of $CaCO_3$ (period G) and talc (period F) are observed, with mean diameters between 38-58 nm. Also for conventional ('coarse') TiO_2 (d=72 nm) a slight emission of NPs might be observed (period H). The authors assigned all components a NRV of 40,000 #/cm^3. When it is assumed that the workers manufacture one batch per day the 8hr-TWA concentration remains well below the NRV. The authors conclude that when these activities would be carried out more than 3 times a day under the same conditions, the $NRV_{8hr\text{-}TWA}$ might be exceeded. For short-term exposure, especially for the adding of the talc and $CaCO_3$, the advised short-term levels are exceeded: $NRV_{15minTWA}$ (SER 2012a).

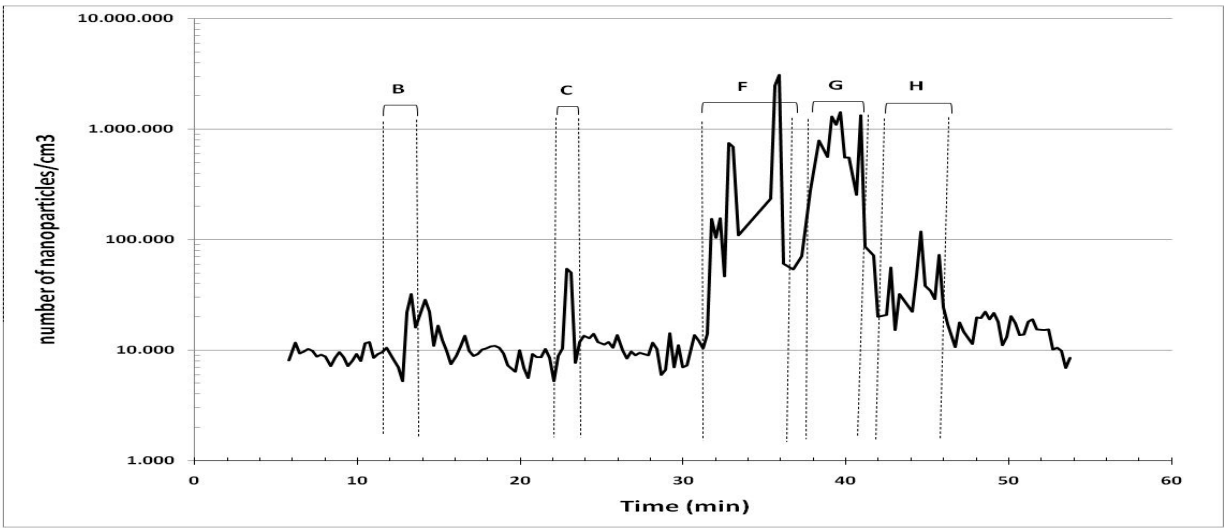

Figure 17 Measurement of nanoparticle concentration during production of "conventional" solvent borne white alkyd paint. (from van Broekhuizen 2012b). Note: the y-axis uses a logarithmic scale.
Solid components are added manually by pouring the content of paper bags into the agitator.
B = amide wax; C = clay mineral; F = talc; G = $CaCO_3$; H = TiO_2. Sampling took place manually at a distance of 30 cm from the adding of the solid powders.

Downstream knowledge on composition

Insight in the quantity of nanoparticles contained in 'non-nano' compounds and their potential release when using them as a dry powder is however not easy to achieve. This characteristic (particle size distributions including the nano-fraction) is generally not reported in risk oriented downstream communication.

The same holds for the functionalization of the surface of MNMs, and of conventional non-nano compounds (and consequently of FCNPs), which influences their potential dustiness. For commercial products (nano as well as non-nano) the composition of the actual functionalization material, and so the coating of the particles, is rarely communicated in risk-oriented downstream documentation.

7. Comparing common workplace concentrations of MNMs with BGNPs, PGNPs and FCNPs

This inventory of the character and release of PGNPs and FCNPs does not identify 'common' workplace concentrations of MNMs, applied control measures and consequential exposures to these MNMs. Nevertheless, based on the reporting in numerous scientific articles (Brouwer 2010, Piccino 2012, Brun 2012, van Broekhuizen 2012a, Bekkers 2016 and many others), the general impression is that the exposure to MNMs, as an 8-hrs-TWA, is low and generally well controlled. Exposures exceeding the NRV are rare. Manufacturing processes of nanomaterials are rare in the Netherlands and as such, these are not considered in this study. Downstream users of dry raw nanomaterials' powders, i.e. the manufacturing industry of 'nanoproducts' such as nano-enabled paints, -inks, -cosmetics etc., are usually well informed about the fact that they are using *nano*materials. The processes in which the dry nanomaterials are used in general have an intermittent character (batch processes) leading eventually to short-time release of MNMs. Measures taken at the workplace to control potential release are generally well considered, due to the generally existing awareness amongst this group of product manufacturers about the uncertain risks associated with the use of MNMs.
This does not hold for the users of nano-enabled end products from which nanomaterials may be released due to machining, heating of combustion of the products. The awareness amongst this group about the potential release of nanomaterials (MNMs or PGNPs) is low (amongst others: NanoDiode 2016). The reported NMs' release from nano-enabled products does not always consider the pure MNMs, but concerns generally the MNMs contained in the used matrices, i.e. some forms of PGNPs (van Broekhuizen 2012a).

Main characteristics from MNMs are compared with those from FCNPs, PGNPs and BGNPs in table 7.

Characteristic	MNM	FCNP	PGNP	BGNP
Formation	Manufactured for specific properties	Present in some existing coarse compounds	Generated in high-energy processes at workplaces	Released from traffic, and industrial and domestic activities
Use	For specific purposes and in nano-enabled products	As base material in conventional products	Not used as such	Not used as such
Composition	Unique	Identical to bulk	Depending on the process	Depending on the process
Size	1 – 100 nm by definition	1 – 100 nm by definition	1 – 100 nm by definition	1 – 100 nm by definition
Shape	Generally uniform, fiber or granular form	Generally uniform granular form	Different forms, granular, sometimes fibers	Different forms, granular, sometimes fibers
Surface	Generally with a specific coating	Sometimes with a specific coating	Without coating	Without coating
Density	For granular MNMs < or > 6,000kg/m^3	< or > 6,000kg/m^3	For most granular PGNPs: < 6,000kg/m^3	For most BGNPs: < 6,000kg/m^3
Toxicity	Oxidative stress, inflammation, genotoxic effects, ….	Oxidative stress, inflammation, genotoxic effects, ….	Oxidative stress, inflammation, genotoxic effects, ….	Oxidative stress, inflammation, genotoxic effects, ….
Biopersistence / solubility	Depending on the composition. For many: solubility <100mg/l (= insoluble)	Depending on the composition. For many: solubility <100mg/l (= insoluble)	Depending on the composition. May contain soluble and insoluble compounds	Depending on the composition. May contain soluble and insoluble compounds
Exposure dynamics	Intermittent, short-term, generally low exposure as 8hr-TWA	Intermittent, short-term, sometimes high exposure as 15min-TWA	Intermittent and chronic, possibly high exposure as 8hr-TWA and 15min-TWA	Generally diluted in ambient air. Peaks in traffic areas
Exposure levels	Maximum short-term levels during manufacturing nano-enabled products generally not exceeding 10^5 /cm^3.	Maximum short-term levels during products manufacturing may exceed 10^6/cm^3	Maximum levels chronic exposure exceeds frequently 10^6/cm^3	Average level in not too polluted industrialized western area 10,000 – 30,000 /cm^3

Characteristic	MNM	FCNP	PGNP	BGNP
Awareness	High for raw materials' and product manufacturers, low for downstream users	Almost zero at common workplaces	Almost zero at common workplaces	High for environmental authorities
Control	Frequently specific control measures	Rarely specific control measures	Rarely specific control measures	Rarely specific control measures
Responsibility	Employer for safe workplace Manufacturer/supplier for info	Employer for safe workplace Manufacturer/supplier for info	Employer for safe workplace Original Equipment Manufacturer for info	Environmental authorities
Existing OEL	NRV	OEL bulk material (but this is generally not nanomaterial specific)	None (general dust OEL, but this is not nanomaterial specific)	None (PM2,5, but this is not UFP specific)
Inclusion in occupational risk assessment	Increasingly recognized in RA	Generally ignored	Generally ignored	Generally ignored

Table 7 Comparison characteristics MNMs, FCNPs, PGNPs and BGNPs

8. Discussion and conclusions

Related to BGNPs

BGNPs (or UFPs as they are called in environmental sciences) may relate to PGNPs in terms of size distributions and composition and as such knowledge from environmental research can be used for occupational hazards and hygiene research and vice versa.

The most important point of distinction is the fact that BGNPs (UFPs) are formed in 'the environment', in natural and anthropogenic processes, and not (directly) influenced by indoor industrial activities. As such, BGNPs belong to the jurisdiction of environmental authorities and should be monitored and controlled by them. Monitoring and controlling (the release of) MNMs, PGNPs and FCNPs belong to the responsibility of the industry, c.q. the employer as laid down in European legislation. Therefore, a clear distinction in these different sources of nanoparticles at the workplace is essential.

Related to PGNPs

The not-limitative overview of different sources of PGNPs at professional workplaces shows that their contributions to the total number-based nanoparticles' workplace concentrations may strongly exceed nanoparticles' concentrations generated by the use of manufactured nanomaterials (MNMs) only. Number-based nanoparticles' concentrations may mount up to as high as $>5*10^6$ #/cm^3 (see figure 15). Higher concentrations are rarely observed, possibly due to coagulation and deposition phenomena and of course due to the use of adequate exhaust ventilation.

Sources of PGNPs can be characterized as high-energy processes such as heating and combustion processes and 'medium high' energy processes such as machining operations: cutting, drilling, grinding, sanding, abrasion, fettling, shredding, etc.
Low-energy processes including the handling of materials, such as storing, conveying, filling, mixing, shovelling and sweeping generally do not give rise to formation of PGNPs, although it must be emphasized that in jobs like cleaning and maintenance 'secondary' exposure to 'resuspended' PGNPs may occur.

Most prominent in generating high PGNP concentrations are welding activities. These activities are already long-time seriously scrutinized concerning the mitigation of hazardous particulate exposures, but an exclusive attention for nanoparticles' exposures seems not to be common practice. In this respect it is striking to identify the almost exclusive nanoparticulate exposure from TIG welding, which is a welding technique popular for its 'reduced exposures'. This emphasizes the contrast between a mass-based and a number-based metric for measuring exposures.

The size distribution of PGNPs in the nano-range seems to be dominated by two modes: the nucleation mode with a peak < 10 nm and the Aitken mode with a peak between 10 – 100 nm. These modes are mentioned as common modes in atmospheric chemistry, and it seems that these coincide as well with PGNPs. Accumulation mode particles (ca. 200-500 nm) are not frequently reported in 'PGNP-research', but it must be mentioned that this mode normally falls outside the scope of research on nanomaterials' risks, and as such are generally not detected with the used measuring equipment.

The composition of PGNPs depends strongly on the specific process in which the PGNPs are formed. For low- or medium-high energy machining activities of nano-enabled products the inventory shows that PGNPs frequently are composed of nano-sized matrix material with embedded pristine nanomaterials (and other additives). For high and medium high energy processes using organic base materials, these might be decomposition products from the organic structures. For machined plastics these are for example mono-, di- and short polymers including the in the matrix contained additives and reinforcement materials, and including as well oxidation and pyrolysis products from these materials. Frequently this mix is 'popularly' called soot in which also polycyclic aromatic hydrocarbons and sometimes also carbon nanotubes may be identified. The CNTs in this mix appear to be newly formed, and are not necessarily already contained in the original product.
In case inorganic materials are involved in the process, which is frequently the case as well, PGNPs will contain metal oxides. The finding that the metal boiling point influences the generated particle size is

of importance. Lower boiling metals have a higher contribution to smaller nanoparticles, while higher boiling metals predominantly contribute to larger particle sizes in waste incineration.

Again depending on the specific process it is assumed that PGNPs consist of a heterogenic mix of the mentioned decomposition products and associated air polluting substances from the workplace air (mixed with UFPs as exchanged with the outdoor air), comparable to what is schematically shown in figure 5.

Biopersistence of PGNPs is determined by the material(s) the PGNP is formed of. Consequently, this depends as well on the specific processes in which the PGNPs are formed and the association processes with other air polluting substances and particles. Within the nano risk assessment the property 'persistence' of inorganic nanomaterials is exchangeable used with the property 'solubility'. Soluble inorganic nanomaterials are supposed to be 'degradable'. For human toxicity however, the main factor seems to be not so much the solubility but rather the solubility rate. It is likely that the PGNPs from many processes in practice will only have a low solubility rate, making them rather biopersistent in terms of human risk assessment.

According to the used measuring equipment it is clear that for many industrial medium- or high-energy processes a significant fraction of nanoparticles may be released, which may lead to chronic exposures if these sources are not recognized as such and if control measures are omitted or not adequately designed for nanoparticles' mitigation.

Processes generating PGNPs may differ considerably in process duration. Some processes such as heating, combustion, extrusion, laser engraving, operating engines may operate a full working day, which may imply that PGNPs are continuously released, and without proper local exhaust ventilation may build up a high local nanoparticles' concentration in the workplace. This indicates the use of nano reference values (NRVs) for an 8hours time weighted average (8hr-TWA) period. For many machining operations with a shorter or an intermittent nature hazards might be better assessed by using an exposure limit for a short-term exposure: 15min-TWA. These operations may concern for example cutting, drilling, grinding, sanding and abrasion. Therefore it is suggested to use the $NRV_{15minTWA,}$ which is the NRV 8hr-TWA multiplied by 2 as proposed by van Broekhuizen et al. (2011a)

As a general tool for estimating whether formation of PGNPs at workplaces is likely the scheme as presented in the pilot Exposure registration working with nanomaterials (van Broekhuizen & Le Blansch 2015) might be useful (see figure 18)

As a general tool for workplace measurements the traffic light scheme for characterizing nanoparticles and use of NRVs as advised by van Broekhuizen et al (2012c) and presented in figure 1 might be used. This approach uses the addition rule for assessment and risk management provisionally, by adding all different granular nanoparticles' number concentrations, irrespective possible different origins (MNMs or PGNPs). If the $NRV_{8hr\text{-}TGG}$ or $NRV_{15min\text{-}TGG}$ is exceeded risk management measures should be applied to reduce the concentrations, or a more specific chemical analysis should be carried out to identify the hazardous nature of the exposure.

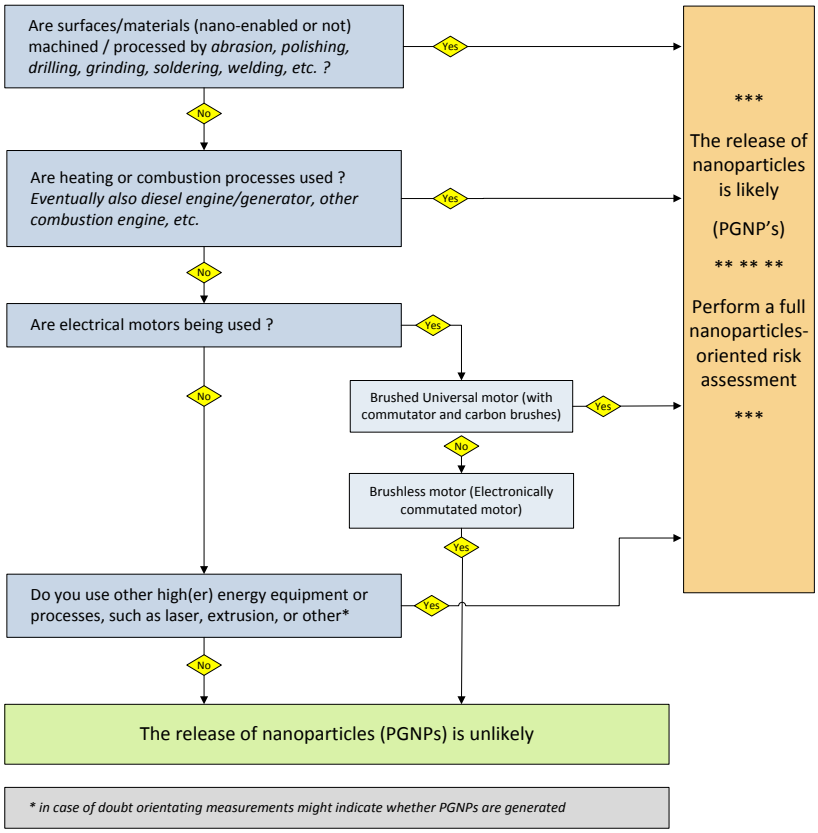

Figure 18 Guidance scheme identification PGNPs

Related to FCNPs

Inventories of FCNPs released from conventional 'non-nano' compounds used as dry powders in manufacturing of products show that their contributions to the total number-based nanoparticles' workplace concentrations may strongly exceed nanoparticles' concentrations generated by the use of manufactured nanomaterials (MNMs) only.

FCNPs are predominantly released in low-energy handling (and cleaning) of materials, such as storing, conveying, filling, mixing, shovelling, sweeping.

Regarding the chemical composition of FCNPs it may be concluded that it is, almost by definition, identical to the composition of the bulk. Therefore, should an OEL exist for the bulk compound and should its point of departure originate from an inhalation toxicity study, the possible nanotoxicity effects could be subsumed in this OEL, although it adds to the total nanoparticles' number concentration.

As a general tool for estimating whether release of FCNPs at workplaces is likely the scheme as presented in the pilot *Exposure registration working with nanomaterials* (van Broekhuizen &Le Blansch 2015) might be useful (see figure 19)

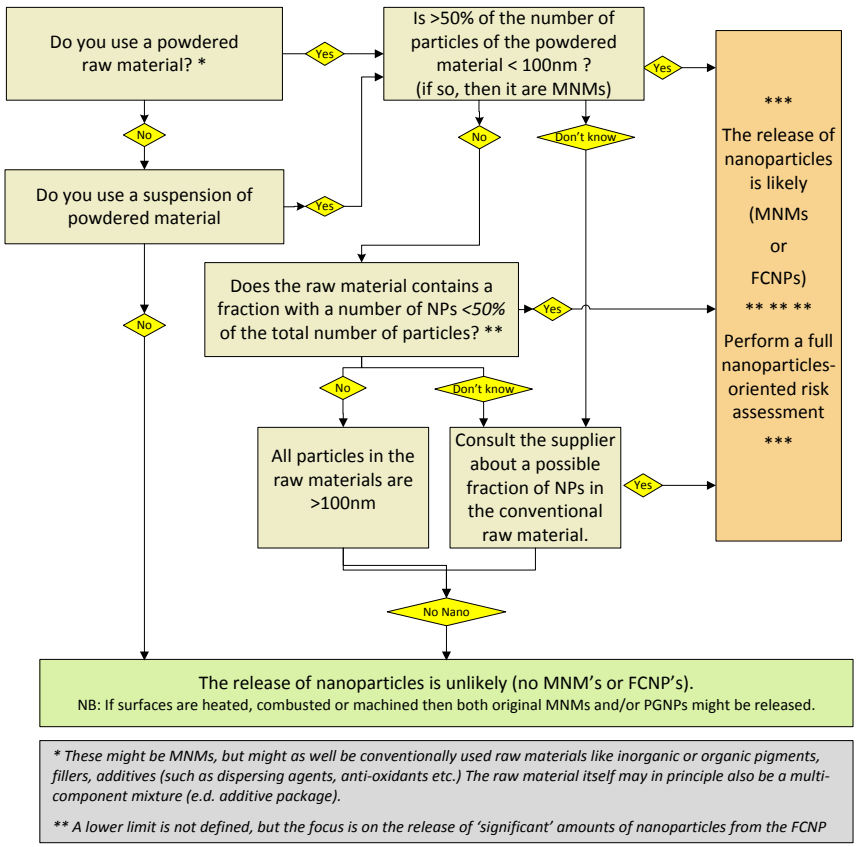

Figure 19 Guidance scheme identification MNMs and FCNPs

Related to classifying PGNPs and FCNPs in the existing NRVs

The actual inventory of 'common' workplace PGNP concentrations shows that it is desirable to have an OEL for PGNPs and FCNPs as well as for MNMs. Due to the generally poor characterisation of the heterogeneous PGNP-group of combustion, pyrolysis and decomposition products and the high analytical costs and consequentially low motivation (and possibilities) of individual companies to develop company-specific OELs, a generic precautionary approach, such as the NRV, may fill the existing gap in risk management.

While applying considerations regarding invoking the precautionary principle for risk management of poorly defined substances in terms of particles' size, shape and composition, as brought forward in the advice for the NRV (SER 2012), it can be concluded that the NRVs should be applicable as well to risk management of PGNPs and FCNPs.

For answering the question: *"Is the current classification of provisional NRV values suitable for process generated nanoparticles (PGNPs) and for the fraction of nanoparticles in conventional products (FCNPs)?"* it should be noted that the NRVs, as advised by the SER (2012), were declared to be applicable to the assessment of exposure to MNMs only. The Minister of Social Affairs adopted this (Asscher 2012). A later opinion-forming discussion of involved experts and policy advisors emphasized the desirability of declaring the NRVs also to be applicable to the assessment of exposure to PGNPs (Bennink 2013). Practice shows that the NRVs have been used as such in many reported risk assessment studies (e.g. van Broekhuizen 2012b; Fonseca 2016; Bekker 2016; Stockmann-Juvalla 2014).

The characteristics of FCNPs and PGNPs as listed in table 7 comply with the characteristics as defined for the MNMs under the NRV. Nevertheless it must be noted that the composition of PGNPs (and sometimes also of FCNPs) in practice is rarely thoroughly determined. Frequently only an indicative composition is suggested based on the used process and the anticipated release. Many authors report

the total nanoparticles' number concentrations and the mean particles' size distribution, but in general these sources can be characterized as 'poorly defined substances'.

An unambiguous use of NRVs for risk management of PGNPs exposure may thus face difficulties when non-experts have to select the appropriate NRV for the actual working situation. Characterisation and estimation of the actual PGNPs composition, size and shape, as indicators for the selection of the right NRV group, might not be possible without an extensive (and expensive) physical-chemical analysis.

A practical and acceptable approach is available, such as for example described in van Broekhuizen et al (2013a) for an assessment where PGNPs are not further characterized but are assessed as '*general biopersistent granular nanomaterials in the range of 1 and 100 nm*' (which is the NRV group 2 or 3). Selection between NRV group 2 and 3 is possible based on the processed or machined material: for high density material (density > 6,000kg/m^3) NRV group 2 could be used, while for low density materials (density < 6,000kg/m^3) NRV group 3 could be used. This last NRV group includes fiber-form nanomaterials for which asbestos-like effects can be excluded.

It should be noted that identified common workplace PGNP-concentrations seem rather high compared to the defined NRVs for the biopersistent granular nanomaterials (group 2a: 20,000 #/cm^3 and group 2b: 40,000 #/cm^3). Exceeding with a factor 10 and sometimes even a factor 100 is not uncommon even when taking into account that the NRVs should be applied as background corrected limit value. Moreover, for many used processes the emission of the PGNPs concerns a long-term or permanent (full-shift) source. At the same time a positive point is that for most of these processes in principal adequate 'conventional' emission control measures are available. Nevertheless installation requires acknowledgement of the need to control these potential hazardous exposure sources. A limited awareness for 'unconventional' PGNPs' sources such as for example the extruder was observed incidentally (Zilaout 2013). Furthermore the willingness of industrial managers to rank PGNPs exposures amongst serious workplace risks is another hurdle (van Broekhuizen 2013a).
This puts a serious demand on awareness raising activities.

The question whether complying with the NRVs for high-concentration PGNPs workplaces would face practical feasibility problems and consequently whether for PGNPs a higher (less stringent) NRV should be agreed, seems to be answered negatively, based on their potentially hazardous nature. After all the feasibility of low limit values for PGNPs should be assessed by comparing the actual process design to the actual state of the art of available exposure control techniques. For many actual situations it is known that measures are available. The current practice in the Dutch Social Economic Council regarding the setting of OELs for genotoxic carcinogenic and allergenic substances and negotiating the feasibility includes the possibility to allow for a (longer) transitional period to facilitate the industry to adapt exposure control measures when a low, non-feasible OEL is at stake (SER 2017). For carcinogenic substances the '*reasonably'* clause *excludes* economical arguments, and sets its focus on the technical feasibility. But the feasibility assessment for non-carcinogenic substances the '*reasonably*' clause includes technical, operational *and economical* reasons, which may be used for the assessment. I.e. too high costs are legally acceptable as argument to allow for lower control measures (although the WHO (2017) recommends for manufactured nanomaterials to implement the highest level of controls to prevent workers from any exposure in the absence of toxicological information). All policies include the 'occupational hygiene strategy' (EC 1998) stating a hierarchy of control with a source-oriented approach for risk management. This includes the preference not to use personal protective equipment (PPE) for regular, standard jobs. In this respect for example welding is an exception, because, so far, realizing exposures below the agreed welding OEL without PPE is not feasible. The low, precaution-based $NRV_{8\text{-hr-TWA}}$ and $NRV_{15\text{min-TWA}}$ are developed as an incentive to be used as a reference and to stimulate risk management for nanomaterials to assure a safe workplace (and in case a legal OEL is established these prevail over the NRV).

Comparison of emissions of high PGNPs-releasing techniques such as welding and diesel motors with the NRV requires some details of the actually used OELs for these substances. For welding the actual Dutch mass-based OEL is 1 mg/m^3 and dates back to 1993 (Wibowo 1993). It refers to 'inert' welding fume particles while the *nano*particles contained in the bulk (but not taken into account at that time) are not that 'inert'. The characteristic of the welding fume is that it contains particulates of all sizes,

large and ultrafine. Nowadays more information is available about the specific physical and chemical activity of nanosized metal oxides, which motivates special attention on this issue. As stated, the level of the NRV for granular nanomaterials was derived from a mass-based level of 0,1 mg/m^3, which is a factor 10 lower (more strict) than the actual mass-based welding OEL.

For the other high PGNP-releasing technique, the diesel motor, it was already stated that as yet there is no legal OEL established for diesel exhaust particulates (DEP), but based on a mass-based approach Dutch social partners agreed on a branch OEL of 7 µg EC/m^3 (TGG-8 uur, measured as respirable dust) (EC=elementary carbon) (Carrosseriebranche nd). As said, these approaches do not take the nano-particulate fraction into account as well, but according to Taxel and Sartonen (2016) the main part of the number-based particulate fraction (>90%) consist of nanoparticles. As such a number-based approach, besides the current mass-based approach, would be useful for DEP as well (see figure 9). Hesterberg (2010) suggested a NOEL (no-observed effect level) for cardio-vascular effects for DEP between $3*10^4$ particles/cm^3 and $5*10^4$ particles/cm^3), which is also in the same order of magnitude as the NRV.

Gebel (2012) compared the relative carcinogenic potency of nanosized granular biopersistent particles (GBP) with GBP micromaterials and indicates that a factor 4 or 5 higher for GBP may be a reasonable worst-case estimate, which includes a special emphasis on the dose metrics mass concentration. Subsequently Gebel (2012) argues that the tumor incidence is age dependent and that this has to be taken into account by using a factor of 2. According to Gebel this means that the difference in relative carcinogenic potency corrected for time to terminal section is not described best by a factor of 4 or 5 but by a factor of 2–2.5. This means that GBP nanomaterials would be 2- to 2.5-fold more potent carcinogens than GBP micromaterials when referring to the dose metrics mass concentration. As a first precautionary estimate the British Standard Institute (BSI 2007) used a safety factor of 10 of the existing OEL to derive nano *guidance values* for CMAR substances and a factor 15 of the existing OEL for other non-CMAR substances.
BAuA (Packroff, 2015) advises reference values for granular biopersistent particles (GBP) of respectively 0,5 mg/m^3 (respirable fraction) for GBP nanoparticles with *no* specific toxicity released from MNMs, and 0,1 mg/m^3 (respirable fraction) for nanomaterials with a specific toxicity, if a substance-related OEL doesn't exist. These are in the same order of magnitude as the existing NRVs. As stated, the level of the NRV for granular nanomaterials was derived from a mass-based level of 0,1 mg/m^3, which is a factor 10 lower (more strict) than the actual welding OEL.

The remaining question regards the likeliness of *rigid* nano-fibers to be formed in processes described. The actual scientific literature gives no indication for the formation of rigid nano fibers in heating and combustion processes or in machining activities. There might be one exception, i.e. certain laser ablation processes. Barcikowski et al (2013) describe the production of CNTs with laser techniques.

Conclusions

It is concluded that NRVs are a useful tool for precautionary risk management of PGNPs. For most common situations the NRV group 2b will be the appropriate NRV classification.
For rare cases where fibrous PGNPs are generated, especially the rigidity (besides the biopersistence and the size: aspect ratio > 3:1 and length > 5 μm) are indicators to decide whether the PGNP should be classified as rigid nanomaterials for which asbestos-like effects cannot be excluded and consequently be classified in NRV group 1.

Regarding the actual feasibility of classifying PGNPs in the NRV classes 2a and 2b for PGNPs and the expectation that not all PGNPs will have a genotoxic carcinogenic potential, and as such would allow for including economical arguments in the feasibility assessment, a more structural examination of the feasibility of the actual NRV classes 2a and 2b for 'problematic' situations is strongly recommended. This includes also 'conventional' workplaces where *no* manufactured nanomaterials are used. Welding and diesel motors are examples, but a focus should also be put on 'unexpected' sources such as extrusion, and modern techniques such as 3D printing.

For the use of 'conventional' raw materials a more systematic inventory of the nanosized fraction in these materials (FCNPs) and its potential release during use is also strongly recommended. This inventory could be combined with a feasibility study to find out whether actual procedures comply with existing OELs. For risk management of FCNPs it is advisable to use the OEL for the parent coarse material, although these generally do not assess the effects of the nano-fraction in the total particles' size distribution. Using a safety factor to this parent OEL between 5 to 10, as advised by BSI (2007) and BAuA (Packroff 2015), is advisable. In case the parent coarse material does not have an established OEL, application of the NRV as suggested for PGNPs is advised.

For screening purposes the additivity rule might be used for all workplace nanoparticles (i.e. not distinguishing between MNMs, PGNPs and FCNPs in the screening assessment).

It is recommended to use these two types of feasibility studies (PGNPs and FCNPs) as basis for a broader awareness campaign to inform involved stakeholders about the different sources of nanomaterials and the potential exposure.

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10. List of abbreviations

ABS	Acrylonitrile Butadiene Styrene
BAuA	Bundesanstalt für Arbeitsschutz und Arbeitsmedizin
BGNP	Background NanoParticle
BSI	British Standards Institute
CB	Carbon Black
CDNP	Combustion Derived Nanoparticle
CMAR	Carcinogenic, Mutagenic, Asthmagenic and Reprotoxic (substances/nanoparticles)
CMD	Count Median Diameter
DEP	Diesel Exhaust Particulates
DNEL	Derived No Effect Level
FCAW	Flux Cored Arc Welding
FCNP	Fraction of NanoParticles in Conventional compounds
GBP	Globular Biopersistent Particle
GMAW	Gas Metal Arc Welding
GMD	Geometric Mean Diameter
GSD	Geometric Standard Deviation
GTAW	Gas Tungsten Arc Welding
GTAW	Tungsten Arc Welding
HDPE	High Density Polypropylene
IARC	International Agency for Research on Cancer
LOAEC	Lowest Observed Adverse Effect Concentration
MAG	Metal Active Gas Welding
MIG aluminum	Metal Inert Gas Welding on aluminum
MIG soldering	Metal Inert Gas Soldering on zinc plated base material
MMAW	Manual Metal Arc Welding
MMD	Mass Median Diameter
MNM	Manufactured Nano Material
MWCNT	Multiple Walled Carbon Nanotube
Nd:YAG	Neodymium doped YAG-crystal (*yttrium-aluminium granate)*
NIOSH	National Institute for Occupational Safety and Health
NOAEC	No Observed Adverse Effect Concentration
NRV	Nano Reference Value
OEL	Occupational Exposure Limit
PAPR	Powered Air Purified Respirators
PGNP	Process Generated NanoParticle
PLA	PolyLactic Acid
PM	Particulate Matter
PNC	Particles' number concentration
RIVM	Netherlands National Institute for Public Health and the Environment
ROS	Reactive Oxygen Species
RSW	Resistance Spot Welding
SER	Dutch Social and Economic Council
SMAW	Shielded Metal Arc Welding
SWCNT	Single Walled Carbon Nanotube
SZW	Dutch Ministry of Social Affairs and Employment
TEM	Transmission Electron Microscopy

TIG	Tungsten Inert Gas Welding
TNO	Netherlands Organisation for applied scientific research
TWA	Time Weighted Average
UFP	UltraFine Particle
US	United States
WF	Welding Fumes