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Research paper

First order risk assessment for nanoparticle inhalation exposure during injection molding of polypropylene composites and production of tungsten-carbide-cobalt fine powder based upon pulmonary inflammation and surface area dose

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ABSTRACT

Inhalation exposure to low toxicity and biodurable particles has shown to induce polymorphonuclear neutrophilia (PMN) in the lungs, which is a strong indicator for lung inflammation. Recently, Schmid and Stoeger (2016; http://dx.doi.org/10.1016/j.jaerosci.2015.12.006) reviewed mice and rat intratracheal instillation studies and assessed the relation between particles dry powder BET surface area dose and PMN influx for granular biodurable particles (GBPs) and transition metal oxides. In this study, we measured workers alveolar lung deposited surface area (LDSA) concentrations ($\mu m^2\ cm^{-3}$) during injection molding of polypropylene (PP) car bumpers and production of tungsten-carbide-cobalt (WCCo) fine grade powder using diffusion chargers. First order risk assessment was performed by comparing the doses calculated from measured LDSA concentrations during an 8-h work day with the $NOEL_{1/100}$, the one hundredth of no observed effect level, assigned for GBPs ($0.11\ cm^2\ g^{-1}$) and transition metal oxide particles ($9 \times 10^{-3}\ cm^2\ g^{-1}$). During the injection molding of PP car bumpers, LDSA concentrations varied from 23 to 39.8 $\mu m^2\ cm^{-3}$. During 8-h exposure PP, particle doses were at a maximum of $1.4 \times 10^{-3}\ cm^2\ g^{-1}$, which was a factor 100 lower compared to the $NOEL_{1/100}$ assigned for GBPs. In the WCCo fine powder production plant, the LDSA concentrations were below 18.7 $\mu m^2\ cm^{-3}$, which corresponds to the 8-h dose of $2.7 \times 10^{-3}\ cm^2\ g^{-1}$. This is 3 times lower than the $NOEL_{1/100}$ assigned for transition metal oxide particles. The LDSA concentrations were generally low compared to urban background levels of 44.2 $\mu m^2\ cm^{-3}$ in European cities.

1. Introduction

In an occupational environment, particle concentrations in air can be highly elevated compared to the background due to high energy processes and use of chemicals that lead to particle formation (Hämeri et al., 2009). Process generated particles and increasing use of engineered nanomaterials (Vance et al., 2015) present new challenges to understand exposure, hazard and risk management in occupational environments (Hämeri et al., 2009; Pietroiusti and Magrini, 2014; Bekker et al., 2015).

Currently, only few occupational exposure limit values exist for particulate matter (PM) and are usually given in inhalable (PM_{10}; $D_p \leq 10$ μm) or respirable ($PM_{4.0}$; $D_p \leq 4.0$ μm) mass concentration (Cherrie et al., 2013; Kuempel et al., 2014). However, many studies have shown that PM_{10} or $PM_{4.0}$ mass concentration is only a rough indicator for a biologically effective dose of the complex mixture of airborne particles (Oberdörster, 2000; Maynard and Kuempel, 2005; Borm et al., 2007; Wittmaack, 2007; Gebel, 2012; Simkó et al., 2014; Schmid and Stoeger, 2016; Braakhuis et al., 2016). There is a need to develop risk assessment techniques where PM exposure and dose assessment is closely related to the biological response (Pietroiusti and Magrini, 2014).

For regulatory purposes and efficient hazard assessment, nanomaterials can be grouped according to their intrinsic physical properties and biological interactions (Arts et al., 2014, 2015, 2016; Braakhuis et al., 2016; Dekkers et al., 2016; Godwin et al., 2015). Granular biodurable particles (GBPs) are the largest material group considering their material production volumes and use (Piccinno et al., 2012). GBPs are classified as low toxicity particles (Moreno-Horn and Gebel, 2014; Arts et al., 2016) although all GBPs may cause inflammation depending on the deposited dose. Ongoing inflammatory processes may cause secondary mutagenicity that may finally lead to lung cancer

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(Gebel et al., 2014). The total particle surface area (cm^2) that is deposited in the lung (lung deposited surface area; LDSA) is recognized to be a relevant dose metric to describe toxicological outcomes for a range of different sizes of GBPs of the same chemical composition and morphology after inhalation (Oberdörster et al., 2005; Stoeger et al., 2007, 2009; Waters et al., 2009; Braakhuis et al., 2016; Schmid and Stoeger, 2016).

An influx of polymorphonuclear neutrophils (PMNs) in the lungs is a hallmark of the onset of inflammation after PM exposure (Grommes and Soehnlein, 2011). Lung inflammation is expected to be associated with the dose in the alveolar region of the respiratory tract (Nieboer et al., 2005) which is why LDSA is expected to more accurately define the dose-response relationship (Lison et al., 2014). For example, for TiO_2 particles of two different sizes with the instilled dose expressed as mass, nano-sized particles induce a greater inflammatory response in the lung than micron-sized particles. However, with the dose expressed as particle surface area, the neutrophil responses fitted the same dose-response curve (Oberdörster et al., 2005).

In this study, we measured workers exposures in a factory producing polypropylene (PP) car bumpers with injection molding and in a tungsten-carbide-cobalt (WCCo) fine grade powder production plant. The PP was colored using organic pigment nanoparticles and WCCo is classified as nanomaterial. In both facilities the exposure to engineered nanomaterials cannot be ruled out, therefore a Tier 2 exposure assessment was performed (OECD, 2015). PM concentrations were measured from near field (NF) and far field (FF) with two miniature diffusion size classifiers and airborne particles were collected for Transmission Electron Microscopy (TEM) analysis. A first order risk assessment for inhalation exposure based on pulmonary inflammation was performed by assuming that the PMN surface area dose-responses assigned by Schmid and Stoeger (2016) can be compared to the doses calculated from measured LDSA concentrations during 8-h exposure.

2. Materials and methods

2.1. Injection molding

An injection molding machine (Engel, 2500 tons, Engel Austria GmbH, A-4311 Schwertberg) was used to manufacture PP components with a weight of 1.59 kg. Three different PP materials were molded:

- Natural color PP (PP_0; KSR4525, Borealis AG, Vienna, Austria)
- PP containing 20 wt% mineral filler (PP_H; Hifax TRC 221P/2 G14008 OTOPHT, Mat no.: 19301A42, LyondellBasell, Ferrata, Italy)
- PP containing 0.2 wt% organic pigment (PP_{OP}; di-keto-pyrrolo-pyrrole pigment, CAS-Nr. 84632-65-5, SUN FP-7 project provided by BASF Schweiz AG, Switzerland; see also Sotiriou et al., 2016)

Injection molding was performed in a naturally ventilated industrial hall (area > 2500 m^2; T = N/A; RH = N/A; Fig. 1a). In addition to the injection molding, an electric forklift was used occasionally. During the second, day painting was performed in a paint booth approximately 30 m from the injection molding area. A blow torch was used occasionally to smooth PP bumper holder parts which were cut off with a knife.

2.2. Sieving and milling

WCCo fine powder was manufactured by fragmenting *ca.* 1 cm^3 WCCo pieces with a high energy ball mill (technical information N/A). The high energy ball mill was located in a ventilated cabin (air exchange ratio N/A) where the replacement air was unfiltered outdoor air from the production hall (Fig. 1b). After milling, the WCCo powder was sieved using a vibrating sieve with a 38 μm pore size. The material was added to the sieve *via* an open feed funnel which had local exhaust ventilation (volume flow N/A). The sieve was switched off when the bucket with sieved powder was replaced with an empty one. The sieve was located in a partly closed room located in the production hall (Fig. 1b). During the measurements, Iron-based, Nickel-based and Titanium-based powders were milled and handled in other parts of the facility. During the work tasks, workers wore filtering facepiece respirators (type FFP2, manufacturer N/A).

2.3. Measurement strategy

Particle concentrations were measured with two Miniature Diffusion Size Classifiers with a 0.7 μm pre-separator (DiSCmini, Matter Aerosol AG, Wohlen, Switzerland). During the injection molding, concentrations were measured simultaneously 1.5 m from the mold and from a workstation (Fig. 1a). In the WCCo fine powder production, concentrations were measured simultaneously 0.5 m from the sieve and from in the process hall or the high energy mill cabinet and the process hall (Fig. 1b).

The DiSCmini instrument functions through unipolar charging of particles and detection of their carried charge in two electrometer stages. In the first stage, the diffusion stage, where particles are detected mainly due to their inherent Brownian motion. In the second stage, the filter stage, the remainder of the particles is detected. Based on the ratio of the two electrometer signals, an average particle size, D_p, can be calculated as smaller particles undergo larger Brownian motion and will thus be more likely to be detected in the first stage (Fierz et al., 2011). This average particle size can then be used to calculate a number concentration, assuming a Geometric Standard Deviation (GSD) of 1.7, from the summed measured currents as the efficiency of the charging

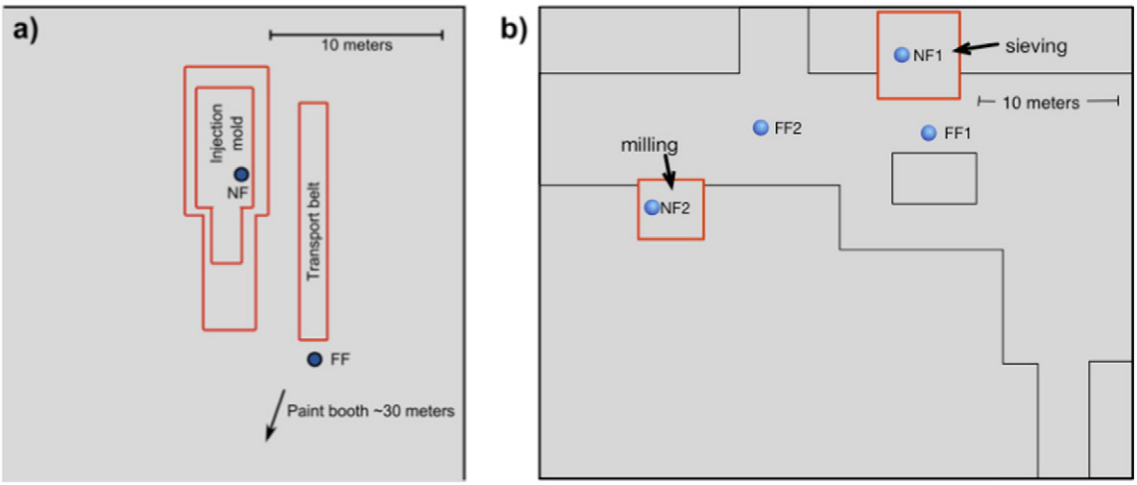

Fig. 1. Layout of the process areas a) in the injection molding and b) in the WCCo sieving and milling.