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Estimation of health risks and safety margins due to inhalation of ultrafine particles and nanoparticles in selected occupational, consumer and environmental settings

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Abstract. Nanoparticles exhibit properties different from those of the same bulk materials leading to unknown toxicological implications that have evoked concern for (1) occupational, (2) consumer and (3) environmental safety.
The current work utilizes epidemiological and toxicological data for screening level assessment of these risks using various suggested health relevant dose metrics (mass, particle number and surface area) to (i) quantify the potential risk levels and to (ii) compare the properties of these alternative risk assessment methods.

1. Materials and methods

Low toxicity low solubility (LTLS) particles (*e.g.* carbon black, polystyrene, and titanium dioxide) have been shown to exhibit similar toxicity, especially per particle surface areas doses [1, 2] and the toxicological data for these particles are used for a baseline risk assessment. The upper limit of particle-related health risks is estimated by using the dose-response function of quartz, a known high toxicity compound with 60 times higher toxicity than the LTLS particles [1].

Besides toxicological studies, epidemiology has shown that especially mass concentrations of urban ambient particles are associated with relative mortality risks for long-term exposures ($PM_{2.5}$; RR_{mass}=10% per 10 µg m^{-3}) and daily exposures (PM_{10}; RR_{mass}=0.6% per 10 µg m^{-3}) [3]. Recently Stölzel *et al.* [4] showed that also particle number concentrations of ultrafine (<100 nm in diameter) particles are associated with mortality (RR_{number}=2.8% per 10^4 cm^{-3}). For application of the epidemiology on ambient particles to other types of LTLS nanoparticles (<100 nm in at least one dimension), we assume that the mortality in the general population is caused by the retained alveolar dose of the non-soluble fraction of ambient particles. Subsequently, the risk factors per ambient particle concentration were converted into risks per accumulated dose of non-soluble particles in the alveolar lung region by using an attenuation model [5- 7], respiratory physiological data, an alveolar

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particle deposition model [8] and an exponential model for particle clearance from the lungs [9]. The obtained dose-response relationships are reported in more detail in a parallel paper [10].

Occupational concentrations of ultrafine particles (or nanoparticles) at 62 workplaces in various industries were measured by Möhlmann [11], using standard aerosol measurement techniques. In addition to particle number concentrations (size-resolved between 14 nm and 673 nm) and mass concentrations of the respirable fraction, there were mass size distributions from 17 workplaces. The particle number concentration levels at the workplaces ranged from 5.9×10^{3} cm^{-3} to 5.6×10^{6} cm^{-3} (mean 3.5×10^{5} cm^{-3}, sd 3.1×10^{5} cm^{-3}). To provide information on particle surface area, either the particle number or the mass size distribution was used assuming spherical particle shape (and a density of 2 g cm^{-3} for conversion from mass) Particle intake values were calculated using 8-hour working day and inhalation rate of 9.6 m^3 per 8 hours (*i.e.* 1.2 m^3 h^{-1}) and converted into uptake values using the ICRP model [8] and assuming that no protective equipment was employed.

Exposure levels to printer generated nanoparticles were estimated using the particle emission rates of high emissions printers (27% of the 63 laser printers studied by [12]) and a mass-balance model [13, 14] for occupational settings in an office and for consumers in the case of home use of laser printers assuming 8 hours (office), 4 hours (home office) and 14 hours (family member) exposure times with 10% and 1% (office and home, respectively) printing times. More detailed presentation of the methods regarding the printer particles is given in a parallel full-length paper [15].

Environmental exposures to carbon black from tires were estimated using emission data from a road simulator study (emissions from 300×10^{9} to 3000×10^{9} nanoparticles per vehicle-km [16]) and a traffic volume model for Germany (706×10^{9} km a^{-1} divided into rural, urban and highway fractions, [17]). The average particle intake was estimated from weighted intake fractions for rural, urban and highway emissions [18- 23]. The intake values were converted into alveolar deposition using the ICRP deposition model [8].

Risk characterization: Two different methods, toxicological and epidemiological risk assessment, are used and the results are compared. Toxicological risk is given as the ratio of the alveolar doses in a given exposure scenario to the lowest observed effect level (LOEL) as estimated from the toxicological studies using allometric scaling to convert the cell [24] and animal-based toxicological data into human equivalent values. Toxicological data is available for particle surface and mass doses, but no experimental data was found for particle number doses. Epidemiological data is used to estimate daily and annual excess mortality risks expressed as percentages and cases per million for the printer and tyre carbon black particles. Environmental epidemiology is not applied to the occupational exposures because of the differences in the exposed population characteristics (including age structure and health status). Epidemiological data was not found for particle surface concentration exposures.

2. Results

(1) The occupational exposure risk was expressed as the ratio of the 8-hour working day uptake to the human toxicological LOEL measured as particle mass or as particle surface area. The resulting 8-hour alveolar uptakes were on the average 71.2 times higher than the mass-based observed effect level for LTLS particles (Table 1), indicating a significant risk. Corresponding mean surface area risk measure was 1.8. Potential high toxicity of specific ultrafine particles was estimated using the high known particle toxicity of quartz; the uptake levels were 4.3×10^{3} and 1.1×10^{2} times higher than the lowest observed effect levels for quartz mass and surface metrics, respectively (Table 1).

(2) Consumer and office exposures of laser printer users and risks were calculated using three methods; epidemiological (i) particle number concentration (PNC) and (ii) particle mass, and (iii) toxicological LOEL. The highest risks were modelled for the occupational office and home office. Epidemiological relative mortality risks were 0.43% and 0.08% using the PNC and mass metrics, respectively, corresponding to 34 and 6 annual deaths per million users. Toxicological risk levels were 2.9×10^{-3} and 1×10^{-3} for mass and surface area metrics, respectively (Table 2).

(3) Environmental exposures to carbon black nanoparticles from tyres were estimated for Germany. Additional relative mortality from particle number exposures was estimated to be 0.03% (annual

mortality in Germany 218 deaths) and from daily mass exposures 0.0004% (3 deaths in Germany). Annual mass exposures were estimated to be associated with 7 deaths. Toxicological risk levels were 2×10^5 and 1×10^5 for mass and surface area metrics, respectively.

Table 1. Toxicological assessment of occupational potential risk levels and comparison of mass versus surface based measures on human 8-hour working day uptake (62 industrial working places). Assuming no protective equipment used.

Toxicological measure	**Relative toxicity**	**Statistics on the ratio dose/LOEL** Mean	sd	min	max	**R<1[b]** n
Mass	LTLS[c]	71.2	213	1.6	1010	0
Suface area	LTLS[c]	1.8	4.8	0.001	25.0	50
Mass	High tox[d]	4273	12765	94.3	60577	0
Suface area	High tox[d]	107.1	286	0.08	1499	6

[a] Lowest observed effect level as expected on humans based on allometric scaling
[b] R=dose/LOEL; n=number of workplaces (out of 62) where dose <LOEL (i.e. ratio R< 1.0)
[c] Low toxicity, low solubility nanoparticles [d] High toxicity as estimated using quartz as positive control

Table 2. Population risks associated with laser printers and carbon black particles from tyres.

Risk assessment type		**Exposure to laser printer particles in Offices**	**Homes or home offices Singe room**	**Full residence**	**Exposure to particles from tyres**
1 Daily NC[a] epidemiology					
Daily uptake (number)	10^9 d^{-1}	3.13	3.13	1.09	0.24
Epidemiological RR (number)	%	0.43 %	0.43 %	0.15 %	0.03 %
Annual mortality per million[b]	cases	34	34	12	3
In Germany	cases	[c]	[c]	[c]	218
2 Daily MC[a] epidemiology					
Daily uptake (mass)	µg d^{-1}	0.21	0.21	0.07	0.001
Epidemiological RR (mass)	%	0.08 %	0.08 %	0.03 %	0.0004 %
Annual mortality per million[b]	cases	6	6	2	0.03
In Germany[d]	cases	-	-	-	3
3 Long-term MC[b] epidemiology					
Annual uptake (mass)	µg a^{-1}	[e]	[e]	[e]	0.419
Epidemiological RR (mass)	%	[e]	[e]	[e]	0.0011 %
Annual mortality per million[c]	cases	[e]	[e]	[e]	0.09
In Germany[d]	cases				7
4 Toxicological risk as mass dose					
Daily uptake (mass)	µg d^{-1}	0.21	0.21	0.07	0.001
Ratio to toxicological LOEL[f]	1	0.29 %	0.29 %	0.10 %	0.002 %
5 Toxicological risk as surface dose					
Daily uptake (surface)	cm^2 d^{-1}	0.16	0.16	0.06	0.002
Ratio to toxicological LOEL[f]	1	0.10 %	0.10 %	0.04 %	0.001 %

[a] NC=number concentration; MC=mass concentration [d] Fraction of population exposed to printers not estimated.
[b] Assuming annual background mortality rate of 0.8%. [e] Daily printer use pattern for annual exposures not estimated.
[c] Number of printer users in Germany not estimated. [f] [Uptake]/[Allometrically scaled observed effect level], %

3. Conclusions

Toxicological risks found for occupational settings (R > 1.6 (mass) and 1×10^{-3} (surface area)) were significantly higher than for consumer (printer) and environmental (tyre) scenarios (R < 2.9×10^{-3} (mass) or 1×10^{-3} (surface area)). For consumers and environmental settings the risks are smaller, but based on the epidemiological risk estimates still significant, warranting technological and policy development for exposure reduction especially for the printer particles.

The general linear no-threshold epidemiological risk model projects population level effects below the toxicological thresholds. In the current study the allometric scaling from laboratory experiments to

humans was selected specifically for producing highest risks. Nevertheless, all observed toxicological LOEL values correspond to mortality risks, which are substantially higher than $1{:}10^6$, and therefore either risk coefficients from epidemiological studies or toxicological safety factors have to be considered in a risk assessment.

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