nanoGEM - Nanostrukturierte Materialien: Gesundheit, Exposition, Materialeigenschaften

Assessment of Exposure to Nanomaterials through Consumer Products

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Consumers are exposed to chemicals directly and indirectly every day by handling of consumer products. Several hundreds of products containing engineered nanoparticles are currently available in Europe such as sunscreens, food packaging, and textiles. The exposure of consumers to nanoparticles by these products and possible resulting health effects are not fully understood. It is generally assumed that nanoparticles exhibit different physicochemical properties compared to materials of the same chemical composition at larger sizes. In case of human exposure to nanoparticles it is hypothesised that stronger or even new physiological effects might occur. For a comprehensive risk assessment it is therefore important to accurately determine the exposure of consumers to nanoparticles experimentally and/or using modelling approaches. Nanoparticles preferentially deposit within the alveolar region of the lung. In the alveoli they may induce inflammatory responses. Therefore inhalation is seen as the most critical route of exposure.
We investigated the applicability of known modelling applications to understand the extend of inhalation exposure to nanoparticles contained in or generated by a consumer spray and its dependence on the external aerosol and particle concentration. To this end, five applications, "ECETOC TRA", "ConsExpo", "SprayExpo", "Stoffenmanager Nano", and "MPPD" were compared. The two first order applications "ECETOC TRA" and "Stoffenmanager Nano" yield very conservative results. For example, using "Stoffenmanager Nano" silver, SiO_2, ZrO_2, and boehmite are grouped into a high hazard class. This results in a moderate risk even at very low assumed concentrations. Conversely, "MPPD" allows for detailed exposure scenarios and provides models of airways of adults and children. Relating the exposure levels modelled using "MPPD" to results of hazard assessments of specific nanomaterials will improve the risk assessment of consumer sprays containing nanoparticles.

Comparison of the exposure models

Five models were investigated (Fig. 1). ECETOC TRA and Stoffenmanager Nano are exposure models of the first order, while ConsExpo, SprayExpo, and MPPD require detailed data input. The different models can be assigned to three categories. ECETOC TRA and ConsExpo are consumer models that provide different categories of consumer products. The workplace models SprayExpo and Stoffenmanager Nano are optimised to compute exposure scenarios typical for work routines. Finally, Stoffenmanager Nano and MPPD are nanoparticle models that include computations specific for nanoparticles. However, additional properties such as surface modifications, coating, or crystallinity are not considered in the latter models.

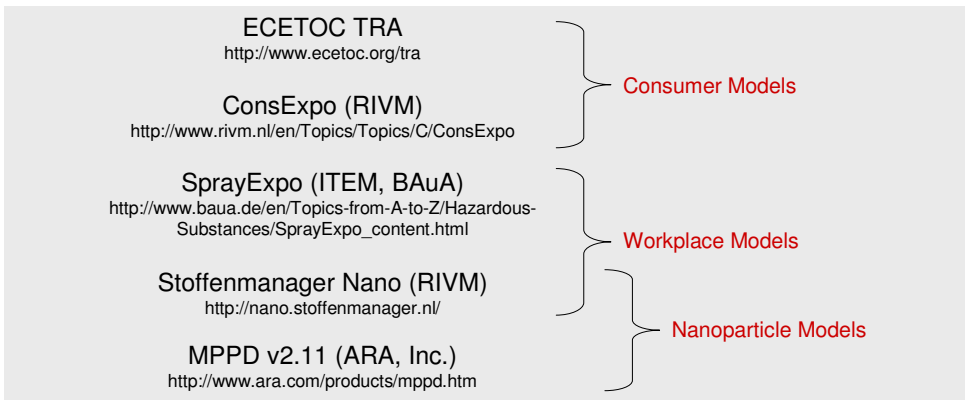

Fig. 1: Sources of the five tested exposure models.

Determination of input parameters

Several input parameters were determined experimentally using a consumer spray advertised with "Nano" in its name (Table 1). Most importantly, an aerosol mass concentration of 310 mg/m³ was observed. Using ECETOC TRA, the aerosol mass concentration for this product category with otherwise similar parameters was 347 mg/m³, providing a conservative estimate of the same magnitude to the measured values. No nanoparticles were found in the investigated product. Therefore, where required rounded data of comparable published studies were used.

Mass Generation Rate	0.666 g/s
Droplet Diameter	1.2 – 2.5 µm
Aerosol Mass Concentration	
at a distance of 20 cm	310 mg/m³
at a distance of 30 cm	230 mg/m³
Nanoparticles	none

Table 1: Experimentally determined parameters of a consumer spray product advertised with "Nano" in its name.

Risk assessment of a putative spray containing silver nanoparticles using Stoffenmanager Nano.

Table 2 shows a summary of data generated by Stoffenmanager Nano v1.0.6 for a spray that is applied approximately once a month for 1-30 minutes. As a consumer related scenario, a room of <100 m³ without general ventilation and absence of personal protective equipment are used as parameters.
As a possible ingredient, silver nanoparticles are grouped into hazard class D by Stoffenmanager Nano. As a result the weighted risk score does not fall below class II, middle, even for very low concentrations of silver nanoparticles in this infrequent-exposure scenario, while the weighted exposure class drops to 1, low. Note that also a number of other nanomaterials are grouped into hazard class D. Results for these materials are therefore identical to the table shown below.

Concentration of Nano-component [%]	Hazard Class	Time Weighted Exposure Class	Time Weighted Risk Score	Task Weighted Exposure Class	Task Weighted Risk Score
1	D	2	II	3	I
0.1	D	1	II	2	II
0.01	D	1	II	2	II
0.001	D	1	II	1	II
0.0001	D	1	II	1	II

Table 2: Risk assessment using Stoffenmanager Nano for a spray application containing silver nanoparticles. Hazard class: A, low; B, average; C, high; D, very high; E, extreme. Exposure class: 1, low; 2, average; 3, high; 4, very high. Risk score: III, low; II, middle; I, high.

Modelling of nanoparticle deposition using MPPD v2.11

Three different exposure scenarios were investigated (Fig. 2A). The general consumer scenario uses parameters suggested by the Federal Institute for Occupational Safety and Health (BAuA) for the workplace scenario. For two additional consumer scenarios, a specialised age-specific lung model was used. The 21 year old consumer was entered as leaning forward with a resting breathing pattern to simulate a putative spray application to a shoe. An upright 3 year old child simulates a bystander. The modelled regional deposition fraction plotted against the particle diameter (Fig. 2B) demonstrated that the relative deposition of particles of the size 1-100 nm is similar between the three scenarios. However, the deposited amounts differ because of the different tidal volumes of the scenarios (Fig. 2C). Note that MPPD v2.11 uses a linear relationship of lung deposition versus particle concentration.

A

Spray Application, Interior, Well Mixed Room
Inert Nanoparticles: 9 nm (CMD, GSD 1.5, ~35 nm MMAD), Density 5.68 g/cm³

	Consumer, Upright, (According to BAuA Workplace Suggestion)	Forward Leaning Consumer (21 Years)	Bystander (3 Years)
Breathing Frequency·min⁻¹	19	14	24
MPPD Lung Model	Yeh / Schum 5-Lobe	Age-Specific 5-Lobe	Age-Specific 5-Lobe
Total Lung Capacity	5358.07 ml	4765.11 ml	125.15 ml
Number of terminal airways	26624	26624	26624
Tidal Volume	1000 ml	477.2 ml	121.3 ml

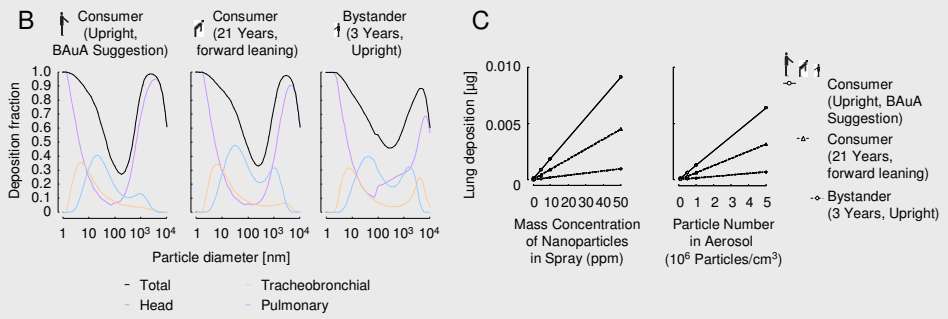

Fig. 2: Modelling of nanoparticle deposition using MPPD v2.11. A: Exposure scenarios, B: Effect of the particle diameter on the deposition in different regions of the airways, C: Effect of the nanoparticle concentration in the spray on the lung deposition.

Exemplary risk assessment for inert biopersistent nanoparticles

The data generated by MPPD allows for a preliminary risk assessment when a lung-specific adverse effect concentration is known. Here, the overload hypothesis is used. It postulates a breakdown in alveolar macrophage dust removal due to loss of mobility of the cells. Inert dusts have been suspected to be tumorigenic in rats under extreme overload conditions which are, however, not reached if OECD guided inhalation protocols are used. Furthermore, the overload hypothesis applies only to inert particles. Solubility and additional putative physiological effects such as cardiotoxicity, respiratory sensitisation, immunotoxicity, or target organ mutagenicity specific to the nanomaterial have to be assessed separately. Morrow (1988) estimated that the overload effect is initiated at particulate volumes exceeding 60 µm³ per alveolar rat macrophage. We use this value as lowest observed effect level (LOEL). Furthermore, a non-recurring application of a spray for five minutes was assumed. The employed particle concentration of $1 \cdot 10^6$ particles/cm³, corresponding to 2.2 µg/m³ for hypothetical 9 nm (CMD, GSD 1.5, ~ 35 nm MMAD) particles of the density 5.68 g/cm³, is an average aerosol particle concentration compared to literature data on various nanoparticles. Together with the data obtained by modelling using MPPD a margin of safety of >27,000 was extrapolated (Table 3).

Spray Application 5 min, $1 \cdot 10^6$ Particles/cm³

Consumer Scenario	Consumer, Upright	Consumer, Forward Leaning (21 Years)	Bystander (3 Years)
Deposition Per Macrophage (SED)	$13 \cdot 10^{-6}$ pg	$7 \cdot 10^{-6}$ pg	$3 \cdot 10^{-6}$ pg
$LOEL_{Rat}$ = „Overload“ (60 µm³/aMΦ)*			
*Morrow (1988) Fundam. Appl. Toxicol. 10, 369–384			
applies only to inert particles, solubility and additional physiological effects specific to the nanomaterial have to be assessed separately			
$NOEL_{Human}$ = $LOEL_{Rat}$ (pg/aMΦ) / 10 (Interspecies Variability) / 10 (Intraspecies Variability) / 10 (Extrapolation LOEL-NOEL)			
Margin of Safety $NOEL_{Estimate}/SED_{Modelled}$	$2.7 \cdot 10^4$	$4.7 \cdot 10^4$	$11 \cdot 10^4$

Table 3: Exemplary risk assessment using MPPD-derived data for a non-recurring application of a spray for five minutes. For input parameters see Fig. 2; aMΦ, alveolar rat macrophage; LOEL, lowest observed effect level; NOEL, no observed effect level; SED, systemic exposure dose.

Conclusions

- **Three different scenarios were simulated of consumers using a putative spray containing inert biopersistent nanoparticles of the density 5.68 g/cm³ for five minutes.**
- **The software application MPPD v2.11 was employed to compute the loading of nanoparticles per alveolar macrophage.**
- **Using this data together with the overload hypothesis for inert biopersistent particles, a safety margin of >27,000 was calculated.**
- **A margin of safety of >100 is considered safe for consumer products.**

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