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The Validity and Applicability of Using a Generic Exposure Assessment Model for Occupational Exposure to Nano-Objects and Their Aggregates and Agglomerates

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ABSTRACT

Background: Control banding can be used as a first-tier assessment to control worker exposure to nano-objects and their aggregates and agglomerates (NOAA). In a second tier, more advanced modelling approaches are needed to produce quantitative exposure estimates. As currently no general quantitative nano-specific exposure models are available, this study evaluated the validity and applicability of using a generic exposure assessment model (the Advanced REACH Tool—ART) for occupational exposure to NOAA.

Method: The predictive capability of ART for occupational exposure to NOAA was tested by calculating the relative bias and correlations (Pearson) between the model estimates and measured concentrations using a dataset of 102 NOAA exposure measurements collected during experimental and workplace exposure studies.

Results: Moderate to (very) strong correlations between the ART estimates and measured concentrations were found. Estimates correlated better to measured concentration levels of dust ($r = 0.76$, $P < 0.01$) than liquid aerosols ($r = 0.51$, $P = 0.19$). However, ART overestimated the measured NOAA concentrations for both the experimental and field measurements (factor 2–127). Overestimation was highest at low concentrations and decreased with increasing concentration. Correlations seemed to be better when looking at the nanomaterials individually compared to combined scenarios, indicating that nanomaterial-specific characteristics are not well captured within the mechanistic model of the ART.

Discussion: Although ART in its current state is not capable to estimate occupational exposure to NOAA, the strong correlations for the individual nanomaterials indicate that the ART (and potentially other generic exposure models) have the potential to be extended or adapted for exposure to NOAA. In the future, studies investigating the potential to estimate exposure to NOAA should incorporate more explicitly nanomaterial-specific characteristics in their models.

KEYWORDS: exposure modelling; NOAA; validation

INTRODUCTION

The growing production and use in combination with the limited knowledge about the potential hazardous properties of nanomaterials raises questions and concerns about potential health effects. Especially for workers who handle these nanomaterials or the products they are incorporated in on a regular basis, it is essential to get insight into the potential levels of exposure to nano-objects and their aggregates and agglomerates (NOAA; ISO, 2012).

As it is often costly and time consuming to obtain sufficient numbers of measurements to adequately characterize exposure to NOAA, occupational exposure models can be useful tools in the exposure assessment process. At the moment, a few nano-specific control banding tools for inhalation exposure to NOAA are publicly available (ANSES, Ostiguy *et al.*, 2010; Control Banding Nanotool, Paik *et al.*, 2008; Zalk *et al.*, 2009; Precautionary Matrix, Höck *et al.*, 2008; Guidance on Working Safely with Nanomaterials, Cornelissen *et al.*, 2011; Stoffenmanager Nano, Van Duuren-Stuurman *et al.*, 2012; and Nanosafer, National Research Centre for the Working Environment, 2015). Control banding tools categorize both hazard and exposure into different bands indicating the level of risk. Therefore, control banding can be used as a pragmatic tool for a first-tier assessment (screening) to manage risk potential emerging from NOAA exposure. In a second tier, more advanced modelling approaches are needed to produce quantitative NOAA exposure estimates. However, second-tier NOAA exposure assessment models for occupational exposure are not (yet) available.

Generic, non-nano-specific, higher-tier quantitative exposure models to evaluate inhalation exposure to chemical substances at the workplaces have already been developed, e.g. Stoffenmanager (Marquart *et al.*, 2008) and the Advanced Reach Tool (ART) (Fransman *et al.*, 2011). These models have been developed for 'conventional' chemical air contaminants, and currently, there is no information available on the quality of the estimation regarding exposure to NOAA. However, these models might have potential to be extended or adapted for exposure to NOAA.

This article describes the evaluation of the performance of the ART, which serves as a generic, higher-tier model for occupational inhalation exposure assessment, to estimate exposure to NOAA. The ART framework incorporates a mechanistic model and (if) available exposure measurements from the user and/or a general database (note, to date no nano exposure data are included) using Bayesian methodology in order to produce more precise estimates for specific exposure scenarios (Fransman *et al.*, 2011). The mechanistic model follows a source–receptor structure comprising modifying factors representing the source, transmission compartments, and the receptor.

In this study, the performance of the ART was evaluated using measured NOAA exposure data from both experimental and field studies, in order to gain insight into the validity and applicability of using a generic exposure assessment model for NOAA exposure estimation and eventually risk assessment of working with (product embedded) NOAA.

MATERIAL AND METHOD

Data description

The dataset used to validate the ART contained 102 measurements collected during 3 experimental studies ($N = 73$) and 29 field studies at workplaces.

Three experimental studies were conducted in a room of 19.5 m^3 with well-controlled environmental and ventilation conditions. Activities involved dumping (Experiments 1 and 3) and simultaneously dumping and mixing (Experiment 2) of a ~100% nanopowder. The effect of various determinants was studied by systematically alternating one determinant, while the other determinants were kept constant. Determinants and number of measurements varied between experiments (Table 1). The experimental setup and results of the experiments are described in detail by Bekker *et al.* (2016).

Workplace measurements took place at various workplaces in the Netherlands and represent different exposure scenarios and exposure forms, i.e. handling of ~100% nanopowder ($N = 21$) and handling of liquid intermediates/ready-to-use products ($N = 8$). The workplace exposure data were collected during a broad scale exposure study described in detail by Bekker *et al.* (2015). In addition, some repeated measurements ($N = 8$) were conducted. More details about the workplace exposure measurements can be found in Supplementary material A, available at *Annals of Occupational Hygiene* online.

Table 1. Summary determinants and variables of conducted experiments

Study	Activity	Determinant	Variables
Experiment 1	Dumping SiO_2 powder	Dump rate	Single drop; continuous drop
$N = 13$		Dump mass	30; 65; 100 g
		Dump height	5; 27.5; 50 cm
Experiment 2	Dumping and mixing TiO_2 powder	Dump rate	Single drop; continuous drop
$N = 16$		Ventilation rate	0; 13 ACH
		Mixing speed (min^{-1})	36; 80
		Containment	Open; closed but breaching system
Experiment 3	Dumping SiO_2, TiO_2, Al_2O_3 powder	Moisture content	0.5–21.1
$N = 44$		Receiving surface	Water; container surface
		Drop height	30; 60 cm

ACH, air changes per hour.

Data collected during the experiments consisted of particle size distributions measured in real time with the Scanning Mobility Particle Sizer (SMPS; ϕ 10–500 nm, model 3080, TSI Inc.) in combination with the Aerodynamic Particle Sizer (APS; ϕ 0.5–20 μm, model 3321, TSI Inc.) covering a broad size range meeting the inhalation fraction estimated by the ART model. During the workplace measurements, a NanoID NPS500 (ϕ 10–500 nm, Naneum) was used instead of an SMPS since it is more portable and less bulky than the conventional SMPS and does not contain a radioactive source. The measurement devices were placed at a fixed location in the near field of the worker (<1 m) at breathing zone height. Whenever the worker moved around, the measurement devices were moved as well to keep the distance between the worker and the instruments <1 m. In general, the workers were in close proximity of the source (<1 m).

ART estimates

Based on the contextual information, median full-shift inhalable exposure estimates (mg m^{-3}) were obtained for each measurement using the online ART tool (https://www.advancedreachtool.com). The reliability of the ART estimates depends on the ability of the assessor to interpret the information for the ART parameters (Schinkel *et al.*, 2014). In order to ensure a good reliability of the ART estimates, the online ART tool was filled in by the same person who also gathered the experimental and field data ensuring a good understanding of measurement circumstances. Subsequently, the model input was reviewed by two developers of the ART ensuring that the input parameters were correctly interpreted. Inconsistencies between the assessors regarding input parameters (5 of the 102 measurements) were discussed until consensus was reached. When two or more activities occurred during a measurement, a time-weighted average was calculated for all the activities during the measurement period.

Information about the moisture content of the powders was not provided by the suppliers of the nanomaterials. An internal study (unpublished data), during which the moisture content of 14 commonly used powders was tested right after opening the factory package, showed that most nanopowders had a moisture content between 1 and 3%, with the exception of silica nanopowder which had a moisture content of 9%. Based on these results, the assumption was made that all silica nanopowders used during the workplace and Experimental studies 1 and 2 had a moisture content between the 5 and 10% and all other powders <5%. During Experiment 3, the moisture contents were measured (range 0.5–21.1%).

In reporting the development of ART, Schinkel *et al.* (2011) defined an uncertainty factor (UF) for each module of ART, where the definition of the UF stated that 90% of the geometric means (GMs) for individual datasets are within a factor 4.4 (dust) or 5.8 (liquid aerosols) lower or higher than the ART estimated GM (90% confidence interval). It was evaluated whether this assumption could be extrapolated to NOAA.

Metric conversion

The ART model estimates exposure levels expressed in median inhalable mass concentrations (mg m^{-3}), while the measured NOAA concentration levels are expressed in particle number concentration (# cm^{-3}). In order to compare the ART estimates with the measured NOAA concentrations, the raw particle size distribution data from the SMPS/NanoID and APS were converted into mass concentrations using the following equation, based on Hinds (1982):

$$C_{\mathrm{m}} = 10^{-15} \cdot \rho_{\mathrm{p}} \cdot C_{\mathrm{n}} \cdot \frac{\pi}{6} \cdot d_{\mathrm{m/a}}^{3}. \qquad (1)$$

where C_m is the mass concentration (μg cm^{-3}), ρ_p the particle density (g cm^{-3}), C_n the number concentration (# cm^{-3}), and $d_{m/a}$ the mobility (SMPS/NanoID) or aerodynamic (APS) particle diameter (nm). It was assumed that the particles are spherical. First, an average particle size distribution was calculated for both the background and activity period by taking the GM particle number concentration of each size bin (C_{nDp}). In order to provide insight into the contribution of the activity, the concentration measured during the background period was subtracted from the activity period. Subsequently, the background corrected mass concentration per size bin (C_{mDp}) was calculated using the number of particles within a size bin, median diameter ($d_{m/a\ Dp}$) of the size bin, and bulk density (ρ_p) as provided by the supplier of the material. The total mass concentration was calculated by summarizing the size bins of each distribution. Finally, the background corrected mass concentration of the SMPS/NanoID and APS was summated, resulting in a GM mass concentration over a broad size range (5 nm–20 μm) and compared with the inhalation exposure estimates of the ART (see 'Statistical analyses' for more details).

Conversion from particle number to mass concentration should ideally be conducted with the particle effective density, which is not available without conducting time consuming and costly experimental tests. Since information about the bulk density of the material is most often provided by the supplier, a pragmatic choice was to use the bulk density instead (Supplementary material A is available at *Annals of Occupational Hygiene* online).

The concentrations measured with the SMPS and APS represent the total concentration of particles between the 5 nm and 20 μm present in the air, while the ART estimates the median mass of the inhalable concentration. The inhalable criterion has a 100% penetration of small particles (<1 μm), dropping to 65% for particles of 20 μm. Therefore, the concentrations measured with the APS have been corrected to correspond to the inhalable concentration as recommended by CEN, ISO, and ACGIH (Supplementary material B is available at *Annals of Occupational Hygiene* online). Particle concentrations measured by the SMPS have not been corrected since particles in the range of the SMPS (5–500 nm) have a penetration fraction of ~100%.

Statistical analysis

Correlation between the natural logarithms of the ART estimates and measured concentrations was calculated using the Pearson correlation. The experimental measurements were grouped per experiment (Experiments 1–3). Measurements conducted during Experiment 3 were subdivided into three separate groups based on the nanomaterial, i.e. measurements with (i) TiO_2, (ii) Al_2O_3, and (iii) SiO_2. The workplace data were grouped based on the potential exposure form, i.e. nanopowder (dust) and liquid aerosols containing NOAA. An overview of the defined groups is given in Table 2. To determine the accuracy of the ART to estimate GM exposure levels, relative bias was calculated using the following equation (McDonnell *et al.*, 2011):

$$\text{Relative bias} = \left(\frac{\text{bias}}{\text{measured GM}} \right) \times 100\% \qquad (2)$$

where the bias was defined as the difference between the GM of the ART estimates and the GM of the measured concentrations. A positive relative bias indicates overestimation of the model, and a negative relative bias indicates underestimation of the model.

In some cases, the background corrected values were below zero (experimental studies $n = 1$; field studies $n = 8$). Since the natural logarithm of a negative number is undefined, the negative numbers were replaced by the lowest concentration within

Table 2. Correlation between ART estimates and background corrected measured concentrations (bulk density) during experiments and field measurements

Dataset			N	# < 0 mg m^{-3}	GM$_{ART}$ mg m^{-3}	GSD$_{ART}$ mg m^{-3}	GM$_{MEA}$ mg m^{-3}	GSD$_{MEA}$ mg m^{-3}	r	P value	Relative bias %	Within 90% CI[a] %
Experimental data	Experiment 1	SiO_2 nanopowder	13	0	1.51	3.03	0.28	3.36	0.56	0.05	431	62
	Experiment 2	TiO_2 nanopowder	16	1	4.71	3.76	0.33	10.57	0.31	0.24	1310	19
	Experiment 3	All	44	0	11.79	5.5	0.76	4.02	0.35	0.02	1446	18
		TiO_2 nanopowder	16	0	16.35	3.93	0.63	2.72	0.9	<0.01	2511	0
		Al_2O_3 nanopowder	16	0	20.24	3.76	0.38	2.84	0.88	<0.01	5204	0
		SiO_2 nanopowder	12	0	3.71	8.11	2.5	2.91	0.8	<0.01	49	67
	Total experiments		73	1	6.69	5.54	0.53	5.27	0.41	<0.01	1153	26
Workplace data	All		29	8	0.89	28.61	0.02	43.34	0.67	<0.01	5115	21
	Dust		21	4	1	24.36	0.03	30.56	0.76	<0.01	3609	19
	Liquid aerosols		8	4	0.66	52.69	<0.01	118.55	0.51	0.19	12 685	25
Dust (Experiments 1–3 + workplace dust)			84	5	4.37	9.56	0.27	12.91	0.66	<0.01	1496	24
Total (all data)			102	9	3.77	11.69	0.2	18.49	0.65	<0.01	1779	25

CI, confidence interval; GM, geometric mean; GSD, geometric standard deviation; *N*, number of samples; *r*, Pearson's correlation coefficient.

[a] The 90% CI is the range derived by multiplying (upper limit) and dividing (lower limit) the estimated GM by the uncertainty factor found in the original ART calibration study (Schinkel *et al.*, 2011), i.e. a factor 4.4 (dust) or 5.8 (liquid aerosols).

the sub-dataset divided by two. All analyses were performed in R statistical software (version 3.1.2; R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Experimental studies

The evaluation of the ART estimates with a dataset of 73 measurements collected during experimental studies is summarized in Table 2. The GM (range) of the ART estimates was 6.7 mg m^{-3} (1.5–20.2 mg m^{-3}), and for the measured concentration, the GM was 0.5 mg m^{-3} (0.3–2.5 mg m^{-3}). One out of 73 background corrected concentrations was below zero. Figure 1 shows the measured concentrations plotted against the ART estimated concentrations. Detailed information about the ART estimates and measured GM concentration levels can be found in Supplementary material A, available at *Annals of Occupational Hygiene* online.

Pearson's correlation coefficient (r) between the ART estimates and measured concentrations ranged between 0.31 and 0.90 and seemed to be better for the nanomaterials individually ($r = 0.80$–0.90, $P < 0.01$) than combined ($r = 0.35$, $P = 0.02$), indicating that the ranking of the model determinants was good, but the nanomaterial specific characteristics were not well captured by the model. The correlations were better during dumping ($r = 0.90$, $P < 0.01$) than during simultaneously dumping and mixing of a (TiO_2) nanopowder ($r = 0.31$, $P = 0.24$); however, this only includes one scenario. The correlations for Experiments 1 and 4 (SiO_2 nanopowder) were $r = 0.56$ ($P = 0.05$) and $r = 0.80$ ($P < 0.01$), respectively, indicating the variance within a nanomaterial, i.e. small sample size and nanomaterial-specific characteristic.

Overall, the ART overestimates inhalable exposure to NOAA (relative bias = 49–5204%), the measured concentrations were on average a factor 12 lower than predicted by the ART. Table 2 and Fig. 1 show that the proportion of measurements within the UF defined by Schinkel *et al.* (2011) was very low, i.e. overall 74% of the GMs of the measurements were outside the UF of 4.4 (dust) or 5.8 (liquid aerosols) (Schinkel *et al.*, 2011). Exposure measurements during handling of SiO_2 nanopowders seemed to have the best fit, i.e. 62–67% of the GMs of the measurements were within the UF defined by Schinkel *et al.* (2011).

The residual plot (Fig. 2) shows a proportional bias with a negative correlation ($r = -0.50$, $P < 0.01$) between the log-transformed difference and measured concentrations. This proportional bias shows that the overestimation of the ART is highest at low concentrations and is decreasing with higher measured concentrations. The plot also shows a pattern that is associated with a discrete dependent variable illustrating that there are one or more underlying factors influencing the exposure concentration, which were not taken into account when estimating the concentration with the ART.

Workplace measurements

The dataset collected at the workplace contained 29 exposure measurements from 21 exposure situations, i.e. 8 repeated measurements. Within this dataset, the GM of the ART estimates was 1.0 mg m^{-3} (<0.01–33 mg m^{-3}) for dust scenarios and 0.7 mg m^{-3}

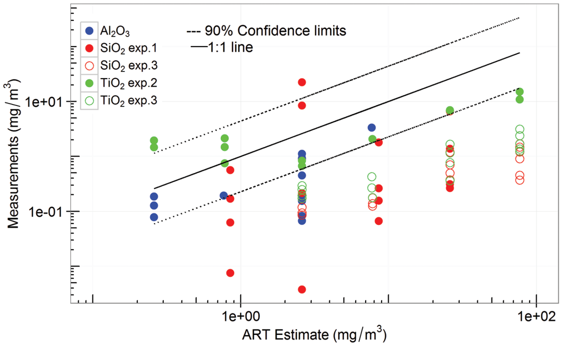

Figure 1 Art estimates versus background corrected measured concentrations (mg m^{-3}) during Experiments 1–3.

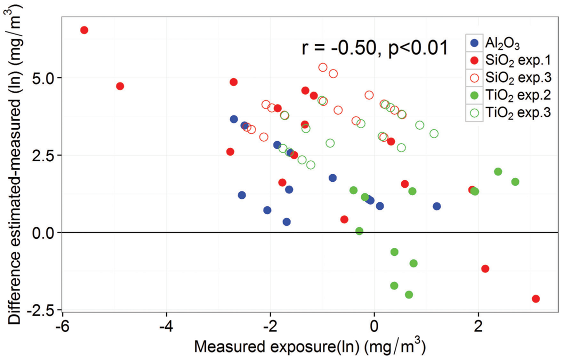

Figure 2 Residual plot of difference between measured and estimated exposure as a function of measured concentration for Experiments 1–3.

(<0.01–17 mg m^{-3}) for exposure to liquid aerosols with an overall GM of 0.9 mg m^{-3}. The GM of the measured concentrations was all lower than the ART estimates and was 0.03 mg m^{-3} (<0.01–2.59 mg m^{-3}) for dust scenarios and <0.01 mg m^{-3} (<0.01–5.64 mg m^{-3}) for liquid aerosols scenarios with an overall GM of 0.02 mg m^{-3}. Eight background corrected concentrations were below zero (Table 2). Figure 3 shows the background corrected measured concentrations plotted against the ART estimated concentrations. Detailed information about the ART estimates and measured GM concentration levels can be found in Supplementary material A, available at *Annals of Occupational Hygiene* online.

Pearson's correlation (r) between the ART estimates and measured concentration levels appeared to be good ($r = 0.67$, $P < 0.01$) and better for exposure to dust ($r = 0.76$, $P < 0.01$) than for liquid aerosols ($r = 0.51$, $P = 0.19$). The ART seemed to overestimate inhalable exposure to NOAA in all cases, with an average factor of 51. Exposure to liquid aerosols was overestimated with an average factor 127 (1.6–15 213) and dust exposure with an average factor 36 (1.3–39 663). Approximately 81% (dust) and 75% (liquid aerosols) of the GMs of the measurements were outside the UF (Table 2 and Fig. 3).

The residual plot of the workplace dataset (Fig. 4) shows a similar trend as seen in the experimental dataset, i.e. the overestimation of the measured concentration with a negative correlation (−0.56, $P < 0.01$) between the log-transformed difference and measured concentrations.

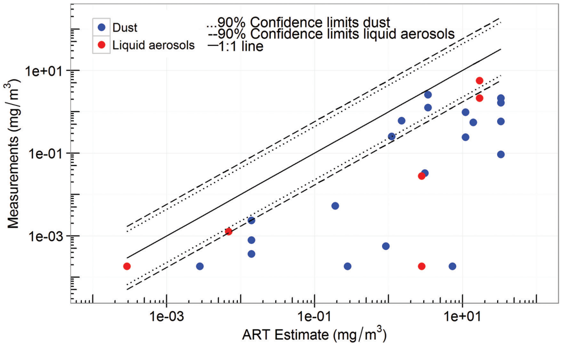

Figure 3 Art estimates versus background corrected concentrations (mg m^{-3}) during workplace measurements.

DISCUSSION

This study evaluated the validity and applicability of a generic source–receptor model (ART) for occupational exposure to NOAA using a dataset of 102 NOAA measurements collected during experimental and workplace exposure studies as currently no general quantitative nano-specific exposure models are available. This evaluation showed the capability of the model to estimate occupational exposure to NOAA and provided important insight for refinement of the model to make it more suitable for NOAA exposure assessment.

The evaluation of the model with both the experimental and workplace data showed moderate to strong correlations between the ART estimates and measured concentrations. However, the ART in most cases overestimated the measured concentrations NOAA. Overestimation was highest at low concentrations and decreased with increasing concentration. Correlations seemed to be better when looking at the nanomaterials individually compared to combined scenarios, indicating that nanomaterial-specific characteristics are not well captured within the mechanistic model of the ART. Estimates correlated better to measured concentration levels of dust (strong correlation) than liquid aerosols (moderate correlation). Overall, 23% of the measurements had an estimated GM within the UF of 4.4 (dust) or 5.8 (liquid aerosols) lower or higher than the ART estimated GM, a much smaller percentage than the 90% expected from the ART calibration study for conventional chemicals (Schinkel *et al.*, 2011).

To the authors' knowledge, there have been no other comparable validation studies of generic models

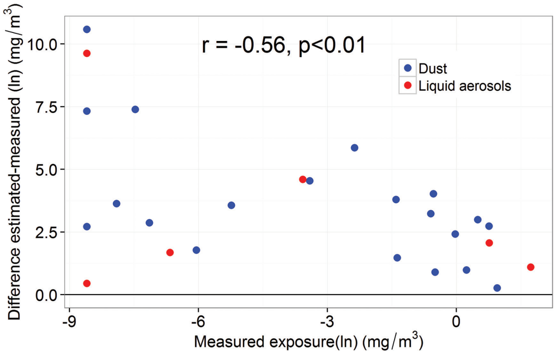

Figure 4 Residual plot of difference between measured and estimated exposure as a function of the measured exposure for workplace data.

with NOAA exposure data and it is therefore not possible to compare the results of this study with any other validation study focusing on NOAA exposure. McDonnell *et al.* (2011) validated the inhalable 'dust' algorithm of the ART using a dataset from the pharmaceutical industry with 200 task-based workplace exposure measurements of conventional chemicals. Results from this validation showed that the ART predicts exposure to dust very well with a relative bias of −32% and with 75% of the estimates within the 90% confidence interval. Our study showed that the ART estimates for exposure to NOAA dust were on average much higher (1496%) than the measured NOAA exposure concentrations. In addition, only 24% of the dust exposure estimates were within the 90% confidence interval indicating more uncertainty in the ART estimates for NOAA exposure than for conventional chemicals. These results indicate that the ART estimates are not nearly as good for predicting exposure to NOAA dust as they are for predicting exposure to conventional chemicals.

The strong correlations between the ART estimates and measured concentrations indicate that exposure to NOAA can be predicted with the use of comparable modifying factor principles as used in the ART model. However, the results indicate that nanomaterial-specific characteristics are not well captured with the ART model. Exactly, in the same experimental conditions, a higher mass concentration or airborne particles was found as a result of dumping SiO_2 nanopowder ($GM = 2.50\,mg\,m^{-3}$) compared to TiO_2 ($GM = 0.63\,mg\,m^{-3}$) and Al_2O_3 ($GM = 0.38\,mg\,m^{-3}$) nanopowder. As described in a previous study by Bekker *et al.* (2016), the SiO_2 nanopowder tested in Experiment 3 has a higher dustiness index than the other two powders. Various characteristics determine the powder's dustiness such as particle size and shape, density, moisture content, specific surface area, and surface area characteristics. Therefore, future development or refinement of NOAA exposure models should focus on investigating the effect of specific material characteristics on the dustiness of the nanopowders and consequently NOAA exposure as to enhance extrapolation across different nanopowders.

The results of this validation study are based on the largest NOAA exposure dataset to date. However, as it is shown that the exposure levels to NOAA vary considerably between and within scenarios, a more extensive NOAA exposure dataset with measurements of all relevant determinants at both source and receptor is the key for a more comprehensive validation and future development/refinement of the model to make it suitable for NOAA exposure assessment (Bekker *et al.*, 2015).

A source of uncertainty that may have influenced the measured concentration is the measurement range of the direct reading devices (10 nm–20 μm). The ART model is based on inhalable mass concentration estimates, and it is shown that NOAA are present as clusters up to 100 μm, which is above the range of the used measurement devices (Bekker *et al.*, 2015). Therefore, it may be that the used measurement devices have missed the larger particles, which contribute to the mass concentration considerably, leading to an underestimation of the measured concentration levels. Offline characterization of the inhalable dust filters (unpublished data) showed that most clusters are <30 μm with an average of 1–3 μm. However, since there is no quantitative information available about the particles >20 μm which could be different per exposure situation, the influence of these bigger particles is unclear. So future validation and calibration studies should make an effort to also include the quantification of the coarser NOAA.

The ART model estimates the total personal exposure, which is the sum of exposure resulting from the activity of interest and the background sources. However, in this study, the ART estimates were compared to the background corrected concentrations, i.e. only the particles that are present due to the activity that is being measured. A sensitivity analysis comparing the ART estimates with the non-background corrected concentrations showed comparable Pearson's correlations as the ones with the background corrected concentrations. However, the relative bias differed. For the experiments, the non-background corrected measured concentrations were on average a factor 5 lower than predicted by the ART compared to a factor 12 for the background corrected concentrations. In case of the workplace measurements, the ART even underestimated the non-background corrected concentrations with on average a factor 2, while the ART overestimated the background corrected values with on average a factor 51. During the experiments, the background concentration was kept low (<2000 particle cm^{-3}), which explains the limited effect of the background concentration on the results (Bekker *et al.*, 2016). However, since we are interested in the capability of the ART to estimate exposure to NOAA instead of the total exposure to all particles in the air, background corrected concentration should be used to adjust the ART for NOAA exposure assessment when non-specific measurement methods are used. Additional information can be found in Supplementary material C, available at *Annals of Occupational Hygiene* online.

In case of the workplace measurements, this evaluation of the ART model is based on stationary measurement results in the near field of the worker (<1 m), while ART is calibrated using personal exposure measurements. Literature shows that results may vary with distance from the source and personal exposure levels are in general found to be higher (up to factor 15, ~1 m of the worker) than exposure levels obtained with static measurement equipment (Niven *et al.*, 1992; Ogden *et al.*, 1993; Kraus *et al.*, 2002; Koponen *et al.*, 2015; Deffner *et al.*, 2016). Currently, the direct reading devices measuring the particle size distribution are relatively bulky and can therefore not be used as personal measurement devices. In order to limit the effect of distance, exposure was measured as close to the worker as possible and at breathing zone height. However, the assumption that the stationary measurements represent the personal exposure levels might have influenced the results. It is therefore expected that the differences between the ART estimates and real exposure levels is less than the results of this evaluation are suggesting.

Metric conversion introduced some uncertainties as assumptions on density, particle morphology, and size distribution were made. Since information about the particle effective density was not available, the bulk density was used for the conversion of number to mass concentration. Used measurement equipment determined the mobility (SMPS) or aerodynamic (APS) diameter, whereas the formula for metric conversion refers to the physical diameter of particles. It was assumed that particles are spherical, in order to calculate the volume and consequently mass of the NOAA measured. However, when the particles have an irregular shape the mobility diameter is always larger and the aerodynamic diameter is always smaller than the physical diameter. Additional measurements should be conducted to determine the relationship between the physical diameter and the mobility/aerodynamic diameter. Unfortunately, due to the absence of the appropriate material (equipment and powders measured), it is not feasible to conduct these additional measurements. In addition, for each size bin, the median size was assumed for all particles in that bin. Since there is no information about the effective density of the particles, physical diameter of the airborne particle or distribution of the particles within a size bin, sensitivity analyses could not be conducted and the influence of these assumptions are unclear.

The moisture content of a powder is categorized in three groups in the ART model (<5, 5–10, and >10%) with multipliers 1, 0.1, and 0.01, respectively. Based on the results of the pilot study prior to Experiment 3, the assumption was made that all silica nanopowders used during the workplace and experimental measurements had a moisture content between the 5 and 10% and all other powders <5%. When incorrect, this assumption could have led to an overestimation or underestimation of a factor 10–100.

In conclusion, this study showed that the ART in its current state is not capable to estimate occupational exposure to NOAA. The strong correlations for the individual nanomaterials indicate however that the ART and potentially other generic exposure models have the potential to be extended or adapted for exposure to NOAA. In the future, studies investigating the potential to estimate exposure to NOAA should however incorporate the effect of nanomaterial-specific characteristics in their models, as this was identified as one of the most important missing determinants in the ART.

SUPPLEMENTARY DATA

Supplementary data can be found at http://annhyg.oxfordjournals.org/.

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