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Comparing the Advanced REACH Tool's (ART) estimates with Switzerland's occupational exposure data

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Abstract

The Advanced REACH Tool (ART) is the most sophisticated tool used for evaluating exposure levels under the European Union's Registration, Evaluation, Authorisation and restriction of CHemicals (REACH) regulations. ART provides estimates at different percentiles of exposure and within different confidence intervals. However, its performance has only been tested on a limited number of exposure data. The present study compares ART's estimates with exposure measurements collected over many years in Switzerland. Measurements from 584 cases of exposure to vapours, mists, powders and abrasive dusts (wood/stone and metal) were extracted from a Swiss database. The corresponding exposures at the 50^{th} and 90^{th} percentiles were calculated in ART. To characterise the model's performance, the 90% confidence interval of the estimates was considered. ART's performance at the 50^{th} percentile was only found to be insufficiently conservative with regard to exposure to wood/stone dusts, whereas the 90^{th} percentile showed sufficient conservatism for all the types of exposure processed. However, a trend was observed with the residuals, where ART overestimated lower exposures and underestimated higher ones. The median was more precise, however, and the majority (≥ 60%) of real world measurements were within a factor of ten from ART's estimates. We provide recommendations based on the results and suggest further, more comprehensive, investigations.

INTRODUCTION

Exposure measurements are still considered the gold standard for occupational hygiene compliance testing of exposure limits. However, substance concentrations may vary between companies, workers and even the same worker over time (Kromhout *et al.,* 1993). To account for this variability, exposure assessments must be based on sufficient numbers of measurements (Kromhout, 2002). In practice, this number is seldom sufficient, due to high costs and time constraints. Alternative methods, such as exposure modelling, can screen exposure situations and target measurements more efficiently. Although modelling is the cheaper solution, the complexity of the computation grows with the number of different physicochemical determinants considered. Including the potential variability of exposure can add even further complexity (Keil, 2000). More recent statistical models, such as the Advanced REACH Tool (ART) (Fransman *et al.,* 2013), have been developed in order to estimate exposure under different working conditions, but using only 5–15 exposure determinants. Simplifications of real world phenomena, such as those in the source–receptor model described in Cherrie (1996) and Tielemans *et al.* (2008), were made to enable the statistical models to estimate exposure using a limited number of determinants. It has thus been correctly argued that models lack the accuracy of field measurements (Kromhout, 2002). However, models should aim to estimate the worst-case situation or provide exposure distribution estimates (e.g. ART) accounting for inter- and intra-worker variability.

In the European Union, these so-called generic (statistical) models are used for registration purposes under its Registration, Evaluation, Authorisation and restriction of CHemicals (REACH) legislation. This stipulates that companies manufacturing or importing high volumes of potentially dangerous chemicals (i.e. ≥ 10 metric tonnes/year) must perform a detailed chemical safety assessment and estimate potential exposure levels in numerous exposure situations. Several exposure models are currently available, based on expert judgment and/or statistical analysis of previous exposure data. Since different models often calculate different exposure estimates, leading to different conclusions about risk, the selection of the appropriate tool is crucial. To aid the selection of an appropriate model, the REACH framework advocates a tiered approach (ECHA, 2016). Tier 1 models, such as the EMKG-EXPO-TOOL (BAuA, 2016; ECHA, 2016), ECETOC TRA (ECETOC, 2009; ECETOC, 2012) are intended to provide a conservative exposure estimate and screen situations which are of some concern from those which are of no concern (Tielemans *et al.,* 2007). More sophisticated models, such as Stoffenmanager® (Marquart *et al.,* 2008; Schinkel *et al.,* 2009)—currently considered as Tier 1.5 (ECHA, 2016)– and ART (Tier 2) (Fransman *et al.,* 2013; Schinkel *et al.,* 2011), are assumed to be more refined versions of Tier 1 models. Such higher-level approaches use more exposure determinants and should thus deliver more precise exposure estimates. The model's performance (level of conservatism, accuracy and bias), however, remains unknown for a broader range of occupational conditions, due to the limited scale of data available and its restricted accessibility in the previous studies (Schinkel *et al.,* 2010; Kupczewska-Dobecka *et al.,* 2011; McDonnell *et al.,* 2011). This further inhibits straightforward model selection and, in some cases, leads to an underestimation or insufficient control of the workers exposure (Lamb *et al.,* 2015). TREXMO, a tool recently developed by Savic *et al.* (2016), may therefore prove to be a good starting point for exposure assessments since it promotes a time-efficient and coordinated use of multiple models recommended by ECHA (Guidance R.14, ECHA, 2016).

A recent study evaluating Tier 1 (including Stoffenmanager®) exposure assessment models (eteam: Lamb *et al.,* 2015) showed that the level of conservatism varied between different models and exposure types (e.g. dust, vapour). For volatile liquids, for example, ECETOC TRA v.3 showed a low level of conservatism, with ≥ 25% of exposure measurements exceeding the model's estimates; Stoffenmanager®, however, was sufficiently conservative. Previous performance assessments of ECETOC TRA v.2 (Kupczewska-Dobecka *et al.,* 2011), Stoffenmanager® (Koppisch *et al.,* 2012) revealed that these models demonstrated a satisfactory level of conservatism. For ART, a comparison with pharmaceutical data (McDonnell *et al.*, 2011) found that this model tends to underestimate the measured exposure data. Two recent studies (Landberg *et al.,* 2017; Spinazzè *et al.,* 2017) confirmed these findings for ART. However, these studies were restricted to the limited diversity of exposure situations and relatively small number of measurements per exposure situation (McDonnell *et al.,* 2011). It was often unclear whether the overall uncertainties resulted from validity or reliability issues. ART's reliability was recently investigated by comparing the exposure assessments produced by different expert groups (Schinkel *et al.,* 2014). There were substantial differences between the gold standard reference and both exposure assessors and exposure assessments. This suggested that between-user reliability could be an important contributor to overall levels of assessment uncertainty.

ART is the only inhalation Tier 2 model recommended for exposure assessment by the European Chemicals Agency (ECHA, 2016). The model was calibrated against approximately 2,000 exposure measurements from different industries and countries (Schinkel *et al.,* 2011). However, as reported in Schinkel *et al.* (2011), these measurements were insufficient to cover all the possible combinations of parameters. Since ART is proposed as a general model, its validation using external data is a vital means of investigating its weaknesses and strengths and suggesting further refinements. The present study used a set of independent field exposure measurements, collected in Switzerland over many years, to investigate ART's performance.

METHODOLOGY

Advanced REACH Tool (ART)

ART, as introduced in 2010, was developed to assess exposure to chemicals and provide more sophisticated estimates than the tools then in existence (Ogden, 2011). ART is structured as a mechanistic source–receptor model that includes exposure parameters for source emissions (e.g. vapour pressure for volatile compounds, dustiness for powders, or different activity classes), localised controls (LCs), and substance transportation or dilution in the workplace. Detailed information on its parameters is available in previous publications (Tielemans *et al.,* 2008; Marquart *et al.,* 2011; Tongeren *et al.,* 2011; Tielemans *et al.,* 2011; Fransman *et al.,* 2013). The mechanistic model calculates a dimensionless exposure score. A calibration for vapours (volatile liquids, with a vapour pressure higher than 10 Pa, as defined in ART, see Fransman *et al.,* 2013) and mists (non-volatile liquids, with a vapour pressure ≤ 10), powders (dusts) and solids (abrasive wood and stone dust) translates the score into an exposure estimate in mg/m^3 (Schinkel *et al.,* 2011). The calibration estimates also estimate exposure at different percentiles, i.e. the 50th (median), 75th, 90th, 95th and 99th (McNally *et al.,* 2014). For each of these percentiles, the model estimates different confidence intervals (CI): inter-quartile, 80%, 90% and 95%.

SUVA Database

The National Accident Insurance Fund (Schweizerische UnfallVersicherungsAnstalt, SUVA) operates under Switzerland's accident insurance law. In order to prevent occupational diseases, SUVA regularly carries out monitoring programmes and exposure measurements to ensure compliance with national Occupational Exposure Limits (OELs). These actions result in reports describing the relevant company's activities, the data measured and contextual information about the measurements (including pictures).

SUVA started collecting the reports used in the present study in 2003, but 73% of them are more recent: 2008–2012. We processed a total of 124 reports from the SUVA database. Exposure measurements were selected according to the following criteria:

- Only personal measurements were considered.
- Measurements that were not representative of an occupational activity were discarded.
- Measured concentrations above five times the appropriate short-term OEL (15-min OEL) or below 0.1 times the 8-hour OEL, although within the functional range of ART, were excluded. Values < 0.1 8-h OEL (SUVA, 2013) are not a great concern and may be considered—by definition—to be low occupational risks. Conversely, measurements > 15-min OEL (SUVA, 2013) can already be considered as occupational risks at a Tier 0 or Tier 1 level (i.e. before models like ART are applied). Less than 5% of the data was excluded due to this criterion and thus their inclusion was not expected to change the study results meaningfully.

- Reports usually included multiple measurements of the substance at different times or locations. All these measurements were used for ART's evaluation since they were considered as independent measurements.

- When several substances had been measured in the same situation and exposure period, only one substance was considered for our study (randomly selected) in order to avoid any bias due to the weighting of that situation.

- Only inhalable dust was considered for testing ART's performance with exposure to powders and solids (Marquart *et al.,* 2008; Fransman *et al.,* 2013).

- The total amount of dust was considered unless the molar fraction of a specific component was given (e.g. total welding dust and nickel content). This applied to both inert and metal dusts.

Overall, 584 relevant measurements fulfilled the inclusion criteria and were thus processed further. The exposure pollutants measured included 346 vapours, 5 mists, 115 powders, 60 wood/stone dusts and 58 metal dusts. Furthermore, task duration and non-exposed periods were considered in the conversion of measured, task-based exposures into 8-h Time-Weighted Averages (TWAs) in ART.

Data Coding in ART

Contextual data were extracted from the reports and coded into ART's corresponding exposure parameters. Both the coded parameters and measured exposure values were stored in Microsoft Office Excel 2007. R software (R development core team, 2010), version 3.3.1, was used to calculate the model's estimates based on its published scoring system (Fransman *et al.,* 2013) and the previous calibration (Schinkel *et al.,* 2011), and to analyse the data. The components of variance in McNally *et al.* (2014) were used to calculate exposure at the higher percentiles and their CIs.

Most parameters (e.g. room volume) were readily available in the reports and were directly translated into model parameters. Some parameters, such are those describing the activity carried out, however, were not explicitly noted and had to be evaluated from the pictures and textual description. Where the data were unclear, realistic conservative parameters were used. For example, when in doubt whether coarse or fine dust category is more adequate for the contaminant under concern, the latter category was selected. Substance properties (e.g. vapour pressure, boiling and melting points) were taken from TOXNET (NIH, 2016) or the ECHA database (ECHA). When vapour pressure was not readily available, it was estimated (Mackay *et al.,* 2006).

All exposure data were coded by an intern hired for the task, and the parameters were then revised by an expert. The 50th (median) and 90th percentiles, with their respective 90% confidence interval CIs, were calculated and further analysed. In addition, the median estimate and the 95th percentile, with their corresponding 95% CIs, were also analysed because they are levels recommended in Switzerland for compliance testing. The computed results are presented in the present paper’s Supplementary Material, available in the Annals of Work Exposures and Health, online. Findings for vapours and powders did not differ significantly, although different conclusions were obtained for solids.

Exposure to metals was also estimated in this study, although it is not yet applicable via the online tool. The calibration parameters for other solids (wood and stone, Schinkel *et al.,* 2011) and the scoring system published in Fransman et al. (2013) were used to calculate exposure to metals. If the results found via the calibration for wood/stone dust were determined to be robust, then they could also be used as an indication for metal dust.

Data analysis

After the contextual data had been coded into ART’s parameters, the modelled exposure was compared to SUVA’s respective measured values. Because of the variability in measured workplace exposure, single measurements generally lack representativeness and the "true" average exposure concentrations remain unknown. The fractions of measured values above or below certain thresholds were therefore considered. ART’s performance was assessed by comparing the percentage of measurements (y) below and above the 90% CI (± 1.645 standard deviations, $\hat{\sigma}$) of the 50th and 90th percentiles of the model estimate ($\hat{y}$):

$$\% = \begin{cases} \sum_i \left(\mathrm{y_i} < \ (\hat{y}_i - 1.645\hat{\sigma}_i)\right)/n \times 100 & \text{overestimation} \\ \sum_i \left(\mathrm{y_i} > \ (\hat{y}_i + 1.645\hat{\sigma}_i)\right)/n \times 100 & \text{underestimation} \end{cases} \tag{1}$$

where, y_i is the *i*th measurement out of *n* measurements for the given exposure type. If the measured data are perfectly represented by the model, the 50th and 90th percentiles will underestimate 50% and 10% of the measurements, respectively.

Regression (slope and intercept) and correlation (R-squared) coefficients were calculated to determine how well the model explained the measured exposure. The residuals were also calculated and plotted to depict systematic deviations of ART’s estimates from the measured exposure. For a measurement, the residual (*r*) is calculated as the log difference between the modelled value ($\hat{y}$) and measured value (y):

$$r = \log(\hat{y}) - \log(\mathrm{y}) \tag{2}$$

A positive residual indicates that the model overestimated the measured exposure and a negative residual indicates that the model underestimated the measured exposure. To specify whether the model overestimates or underestimates the complete set of measurements, relative bias was calculated:

$$bias = \frac{1}{n}\sum_{i=1}^{n} \log(\hat{y}) - \log(\mathrm{y}) \tag{3}$$

$$Relative\ bias = \left(e^{bias} - 1\right) \times 100\% \tag{4}$$

Precision was calculated as the percentage of ART's estimates lying within a certain factor Φ of the respective measured estimates. In this study, Φ was set to 5, 10,100 and 1,000, and thus the percentages of ART's estimates lying within these factors from the measured exposure were calculated.

Multiple linear regression

ART's dimensionless exposure score for near-field (*nf*) and far-field (*ff*), B_{nf+ff}, is given as (Fransman, Cherrie et al. 2010, McDonnell et al. 2011)

$$B_{nf+ff} = E \times H \times LC_1 \times LC_2 \times \left(D_{nf}\,(1+Su) + D_{ff} \times Seg \times Sep\right) \quad (5)$$

where: *E* is the intrinsic emission score; *H* is the handling (or activity emission) score; LC_1 and LC_2 are the primary and secondary local controls; D_{nf} *and* D_{ff} are dispersion determinants related to *nf* and *ff* exposure sources; *Seg* is segregation of the source; *Sep* is the score for the separation of worker from source; and *Su* is the score for surface contamination/fugitive emission sources.

The regression analysis was performed using the scores from ART's modifying factors and the log-transformation of each measurement from the SUVA database. ART's source emission contributes significantly to the model's estimates (Riedmann *et al.,* 2015). The source emission was therefore subdivided into its underlying factors, which were then analysed separately. For vapours, the source emission was subdivided into the scores for the three entry parameters of vapour pressure *p*, mole fraction χ, and activity coefficient γ. For powders, a similar subdivision of the activity emission potential was chosen: dustiness δ, mole fraction χ, and moisture content η. For solids, the terms *E* and *H* are not defined separately in the mechanistic model but are instead given as a combined activity emission potential *EH* (Fransman *et al.,* 2013). However, the moisture content η is available as a separate input parameter and was taken into account here as well. LC_1 and LC_2 are contracted into *LC*; the term in brackets was contracted to *D*. The regression models for measured data for vapours (y_v), powders (y_p), and solids (wood or stone and metals,y_s) are:

$$log\, y_v = \beta_0 + \beta_1\, log\, p + \beta_2\, log\, \chi + \beta_3 log\gamma + \beta_4 H + \beta_5 LC + \beta_6 D \quad (6)$$

$$log\, y_p = \beta_0 + \beta_1 \delta + \beta_2 log\chi + \beta_3 \eta + \beta_4 H + \beta_5 LC + \beta_6 D \quad (7)$$

$$log\, y_s = \beta_0 + \beta_1 EH + \beta_2 log\chi + \beta_3 LC + \beta_4 D \quad (8)$$

where, β_0 is the intercept of the model and $\beta_{i,1-6}$.are the respective regression coefficients of the exposure parameters. The logarithmic values were used for the determinants that take continuous parameters (e.g. vapour pressure), whereas the others used the scores already defined on the logarithmic scale.

RESULTS

The comparison between the modelled and measured exposures in Fig. 1 is presented separately for vapours, powders and solids (wood, stone and metal dusts). Fig. 2 shows the estimated residuals for the different exposure categories. However, mists, due to the small number of measurements (N = 5), were not shown in the figures. The percentages of under- and overestimated measurements are given in Table 1. The regression coefficients and relative biases are given in Table 2, whereas the estimated precision of the modelled estimates is given in Table 3.

Vapours. The upper limit of the 90% CI (Eq. 1) for ART's median underestimated 20% (N = 70) of measured values and overestimated 31% (N = 107) of them. For the 90th percentile, the 90% CI underestimated 7% of measurements and overestimated 44% of them. ART tends to overestimate low measured exposures and underestimate high ones (Fig. 2). Furthermore, Table 2 shows that the modelled exposure was moderately correlated with (R^2 = 0.38) and positively biased for vapour measurements.

Powders. In 30% (N = 34) of ART's median predictions and 9% (N = 10) of the 90th percentile's predictions, measured values for powders were underestimated with the corresponding upper limits of the 90% CI. The lower limit of the 90% CI (Eq. 1) for the modelled median and the 90th percentile overestimated the measured values (single data predictions) in 24% (N = 28) and 47% (N = 54) of cases, respectively. As for vapours, the residuals indicated that the model tended to overestimate lower exposures and underestimate higher ones. A weak correlation (R^2 = 0.09, Table 2) was found between the modelled and measured exposures. Unlike vapours, the modelled median was negatively biased, meaning that ART tends to underestimate the measured exposure overall.

Solids. The upper limit of the 90% CI for ART's median underestimated the measured exposure in 70% (N = 42) of the measurements for wood and stone and its lower limit overestimated 17% (N = 10) of that data. For the 90th percentile, the modelled upper limit of the 90% CI underestimated 23% (N = 14) and its lower limit overestimated 27% (N = 16) of the measurements. Measured exposure to metals was underestimated with the upper limit in 52% (N = 30) of cases and overestimated with the lower limit in 22% (N = 13). For the 90th percentile, the upper limit underestimated 3% (N = 2) and the lower limit overestimated 38% (N = 22) of the measured exposures. As above, Fig. 2 shows the same residual trend for solids, overestimating lower exposures and understimating higher ones. The regression parameters for this exposure type, as shown in Table 2, were the lowest, with R^2 within 0.02–0.04. Furthermore, negative biases were found for the modelled medians for both wood/stone and metal dust.

Precision

Depending on the exposure type, 40–74% (Table 3) of the modelled median estimates were within a factor of 5 from the measured values, 60–83% were within a factor of 10, and > 90% were within a factor of 100 or more. The results calculated for metal dusts were the most precise, whereas the least precise estimates were for wood/stone dusts. For the 90th percentile, ART's precision did not differ significantly from the results obtained for the median. The maximal deviation found between the two values was 15% (see wood/stone and metals in Table 3).

Multiple linear regression

The regression analysis of model parameters versus the (log-transformed) measured exposure for vapours, powders and solids confirmed the above findings (Tables 4–7). The models for vapours and for wood/stone and metal dusts explain 49%, 30%, 27% and 10% of the variance, respectively.

The analysis for vapours (Table 4) showed that all exposure factors, except dilution, were significant at the 5% level of significance or lower. The activity coefficient ($\beta\gamma$) showed the highest significance for vapours. More specifically, increasing γ in the model by a factor of two explained a measured exposure value eight times higher. The measured exposure was found to increase almost linearly with pressure and the mole fraction. Handling activity, localised controls and dilution showed week correlation (< 0.2) with the measured exposure. The order of significance was: $p = \chi > \gamma > LC = H > D$.

Overall, for exposure to powders, the regression analysis explained less than half (30%, Table 5) of the variance. Handling, dilution and dustiness were significant factors for powders. The order of significance was: $H > D > \delta > \eta > \chi >$ LC.

The regression analysis for wood/stone dusts explained 27% of the variability (Table 6). The only statistically significant factors were the localised exposure control and handling. The order of significance of the model parameters was: $LC > H > \eta >$ D. A substance concentration of 100% was assumed for all cases involving wood/stone dusts and thus no corresponding results were shown for the weight fraction in Table 6.

None of the exposure factors were statistically significant for metals (Table 7). The regression model was also insignificant (p value = 0.12) and only explained 10% of the variance. The order of significance for the factors was: LC > H > D. In addition, a moisture content < 5% and a substance concentration of 100% were assumed for all cases.

DISCUSSION

A set of 584 independent measurement data was used to assess the Advanced REACH Tool's performance for exposure prediction. This number might be seen as large when compared to the size of data used in ART's calibration (~2,000). 124 different exposure situations (reports), for which the measurements were taken, is also more compared to the number of exposure situations considered in two recent studies (N=14 and N=29) by Spinazzè *et al.* (2017) and Landberg *et al.* (2017). Furthermore, the occupational data used in our study reflects the work conditions in Switzerland. The chemical regulations enforced in Switzerland – the Swiss Chemical act and its ordinances - are conceptualized to be very close to REACH. The data, therefore, presents similar work conditions as that in the EU.

When using a 90% CI, ART's median prediction was insufficiently conservative for solids; it underestimated 70% of the wood/stone dust measurements and 52% of the metal dust measurements. The corresponding 90% CI for the 90th percentile was also insufficiently conservative for wood/stone dusts, with 23% of the measurements underestimated. The predictions for the 95th percentile using the 95% CI were found to be adequately conservative for all types of exposure (see Supplementary Material, available online). Unlike previous studies (McDonnell *et al.,* 2011; Landberg *et al.,* 2017; Spinazzè *et al.,* 2017), the 90% (or 95%; see Supplementary Material) CI range was accounted, which might explain the higher overestimation found.

Overall, due to the computed (relative) bias, the model's median and the 90th percentile tend to overestimate exposure to vapours. This contradicts the findings in Landberg *et al.* (2017) and in Spinazzè *et al.* (2017). The negative bias for the median estimate that was found for the other exposure types means that the central estimate rather underestimates exposure to powders, especially metal and wood/stone dusts. For powders, a similar, although more negative, bias has been already found by McDonnell *et al.* (2011). More specifically, the calculated residuals show that the model overestimates low exposure concentrations and underestimates high ones. The same observation has been reported previously for Stoffenmanager by Landberg *et al.* (2017). Furthermore, in our study, this trend is most pronounced for solid materials, especially metals – an exposure form that is not applicable in the current online version of ART. To our knowledge, there is no study comparing ART's estimates versus measured exposure to solids conducted previously.

With regard to the model's precision, the median appears to produce slightly more aligned prediction outcomes than the 90th percentile. For more than half of the cases (60–83%), ART's median prediction and the measured exposure were within the same order of magnitude, and they differed by one order of magnitude or more in less than 10% of predictions. These results are in accordance with the modelled exposure distribution in ART, as the 90% CI ranges within two orders of magnitude.

The correlation can be characterised as moderate for vapours, whereas it is weak for powders. The lowest correlations found, for metal and wood/stone dusts, mean that ART's determinants are not significant explanations of real exposure situations for this exposure type. The calculated regression coefficients (slope and intercept) appear to be arbitrary for this exposure type: they differed significantly between wood/stone dusts and those for metal dusts. This might also suggest that the calibration used for wood/stone dusts is not applicable to metal dusts.

Multiple Linear Regression

Overall, multiple linear regression explained less than 50% of the variance in the measurements. Although ART's exposure factors explained the measured values for vapours best (49%), they only explained 10% of the variance seen for metal dusts in the SUVA database. This made further interpretation of the regression coefficients found for the exposure factors in Eq. 6–8 difficult, especially for non-vapour measurements.

The slope of ~1 for vapour pressure and mole fraction indicates that both are good predictors of the exposure estimate for vapours. The activity coefficient (γ) seemed to be an even better predictor, with its slope of ~4. However, in 89% of cases, the activity coefficient was assigned a value of 1.1, slightly higher than for the pure (undisclosed) substance. The only other value chosen was $\gamma = 2$. This parameter depends strongly on the polarity and volume fractions of the substances present in the product mixture (Schwarzenbach *et al.,* 2005). The activity coefficient for an organic mixture (such as formalin, styrene or dimethyl ether, which where the substances modelled with larger activity coefficients) decreases exponentially with the increasing volume fraction of completely water miscible organic solvents (such as ethanol, a typical co-formulate). It may be possible, therefore, that this study has underestimated the activity coefficient.

LCs were also significant in the prediction of exposure to vapours. However, the database was limited (see Supplementary Material, available online) and did not cover all the LC parameters possible (see Fransman *et al.,* 2013), which might have explained their apparent limited significance. In addition, the SUVA reports only identified the primary LC.

In order to be conservative, dustiness was only modelled using the options of coarse, fine powder and extremely fine powder, since the size distribution of the particles was generally not measured. All the situations modelled for extremely fine powders overestimated exposure. Thus, it could be argued that this dustiness category's score (= 1, see Fransman *et al.,* 2013) is highly conservative. However, only eight cases (see Supplementary Material, available online) were assigned the highest dustiness category. The slope for dustiness was evaluated additionally by removing this category from the data set. The new slope was less negative (-0.1), which might mean that these eight categories were misinterpreted lower dustiness category. This may, however, explain only partly the negative slope found as there might have also been other causes.

For the cases involving powders, 83% of the measurements involved no LCs (see Supplementary Material, available online) and the data may be unbalanced. The statistical weight of the remaining 17% of cases was therefore overly significant. In addition, only a smaller number of the different LC techniques were identified for dusts. This may explain the low significance of LCs in the regression analysis. A similar situation was found for weight fractions, since only 10% of cases did not involve pure substances ($\chi = 1$).

For wood/stone dusts, the low correlation may be the result of the small number of the exposure measurements, meaning that such data was more influenced by variability (e.g. different workers, companies, etc.).

None of the exposure factors for metal dusts were statistically significant (< 5%). All the cases involved dry materials and pure substance, and therefore no results involving the moisture content or weight fraction were involved. Also, the regression model was not statistically significant because the small range of scores could not explain the variability of the measurements.

Limitations

The SUVA database covers a wide range of exposure situations and is a reflection of the working conditions in Switzerland's industry. Between-country differences could exist due to differences in working conditions or sampling strategies. The dataset used in this study could, therefore, differ from the datasets previously used to test and calibrate ART. Furthermore, the number of the different exposure situations (reports) was small to cover all the real-world exposure conditions possible. The number of measurements per exposure situation was also relatively small for an accurate representation of total exposure variability caused by between- and within-worker variabilities.

Translation of the contextual data into ART's parameters was carried out by a trained intern and later revised by an expert in the field. In most cases, this data interpretation involved a degree of uncertainty. It has been shown that ART's estimates are sensitive to this uncertainty (Riedmann *et al.,* 2015). Furthermore, an inter-user reliability study (Schinkel *et al.,* 2014) showed significant variability between multiple users' outputs when using the model.

Recommendation and Conclusion

When using ART for exposure assessments within the context of the REACH safety regulations, we recommend that investigators use the upper level of the 90% CI of the 90th percentile for predictions involving vapours and powders. However, because our study found that ART performed worst with solids, we recommend the use of the upper level of the 95% CI of the 95th percentile. Unfortunately, due to the limited number of situations corresponding to exposure to mists, we cannot provide recommendations. Also, because the exposure to metal dusts is not yet available in the tool and because of the weak performances observed, no recommendations for this exposure type can be provided.

The systematic trend observed in this study—of ART overestimating lower exposure concentrations and understimating higher ones—especially for wood/stone and metal dusts, should be further investigated and corrected. It is, however, unclear whether this trend is a drawback of the model or an artefact of the SUVA database. Further studies should also examine whether the scoring system and calibration used for wood/stone dusts can also be applied to metal dusts.

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Tables and Figures

Figure 1. SUVA measurements versus the ART model's estimates. The figures illustrate the distances of the measured exposure from the modelled 50th percentile (first row) and the 90th percentile (second row), surrounded by the corresponding 90% confidence intervals (shaded area) for vapours, powders and solids (wood/stone and metal dusts).

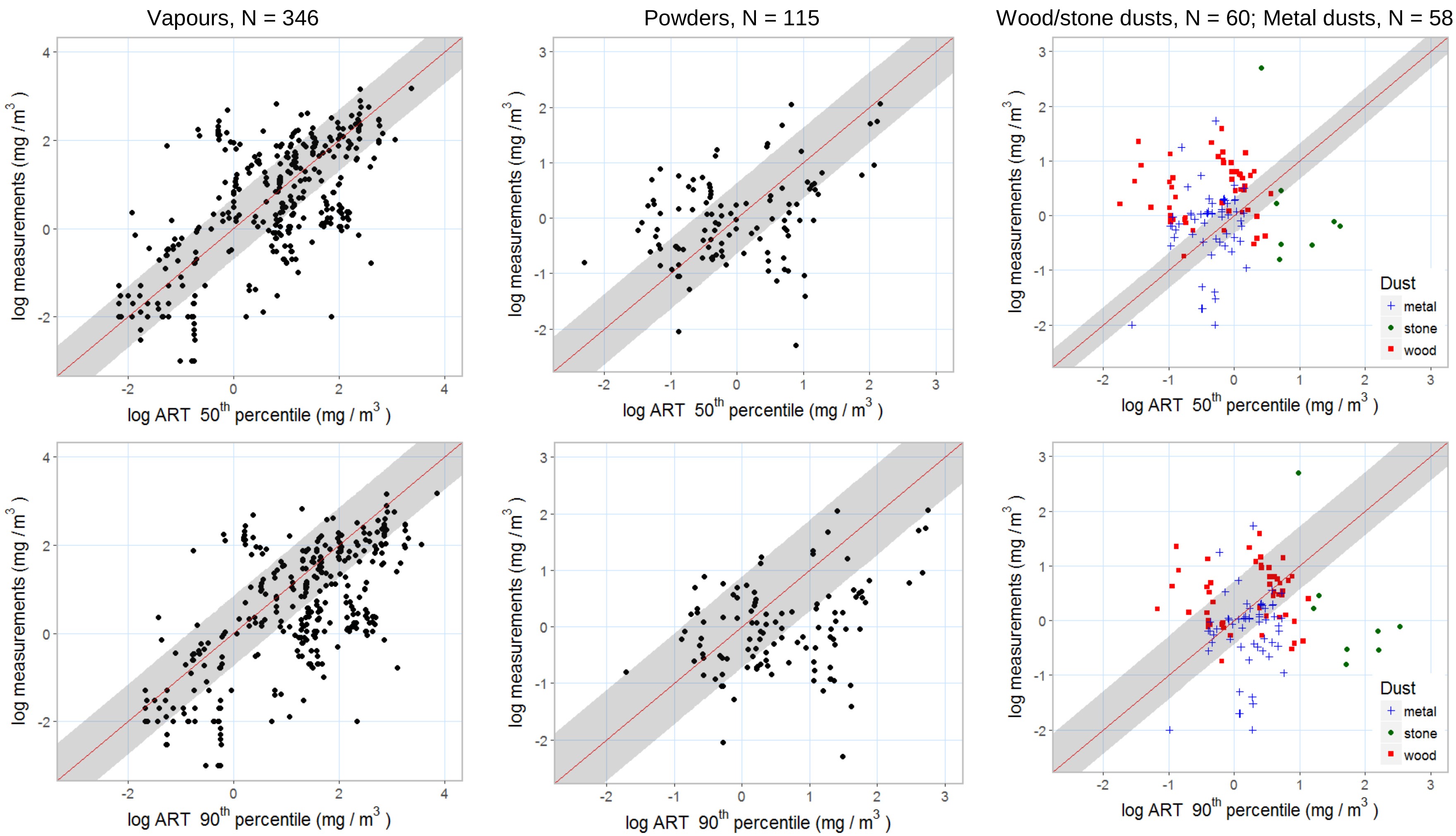

Figure 2. Residuals for vapours, powders and wood/stone and metal dusts.

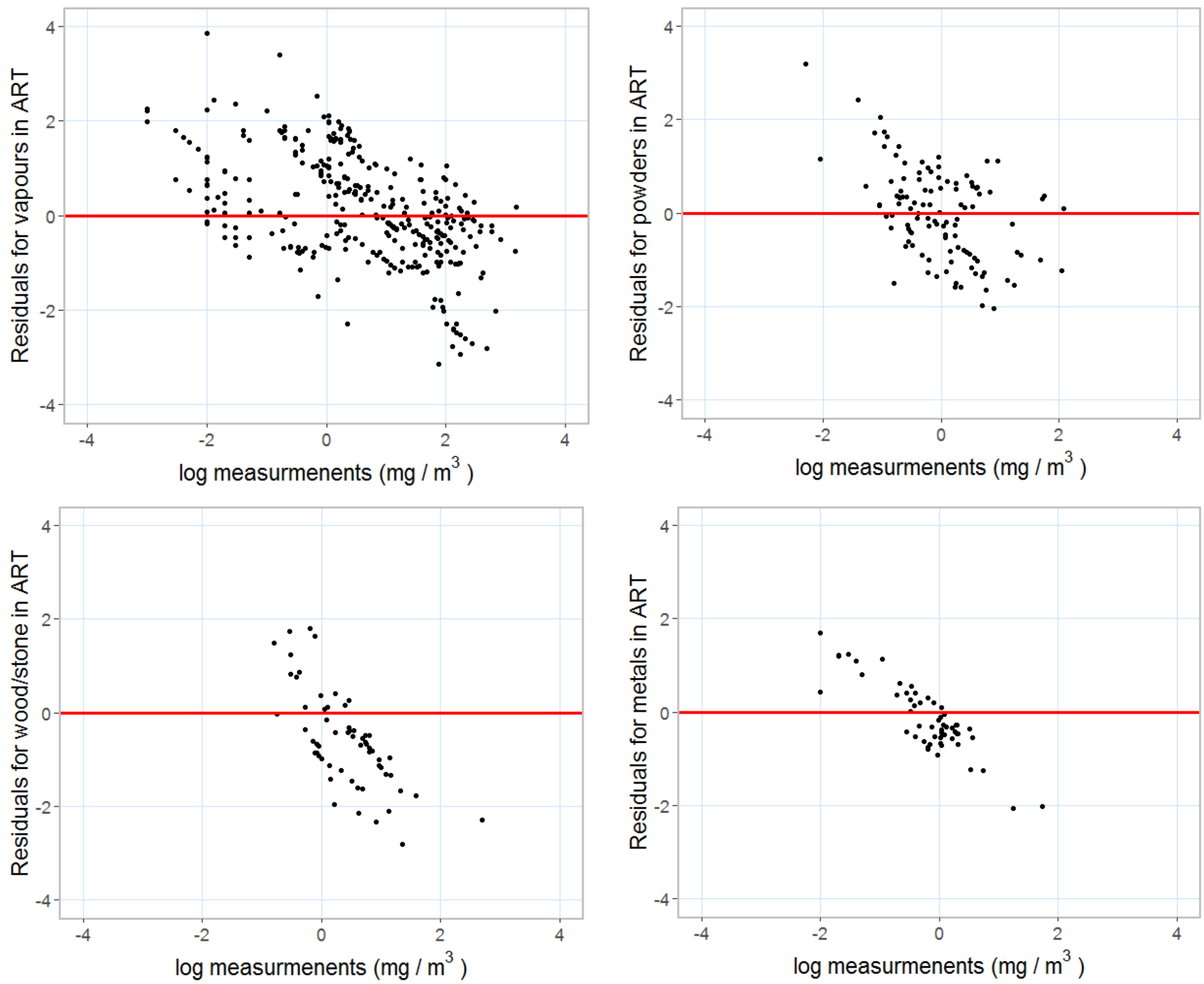

Table 1. Number of SUVA measurements used in this study, and the ART model's percentages of under- and overestimation (as calculated using Eq. 1).

Exposure type	Number (N) of measurements	90% CI for 50th percentile		90% CI for 90th percentile	
		% (N) Underestimation	% (N) Overestimation	% (N) Underestimation	% (N) Overestimation
Vapours	346	20 (70)	31 (107)	7 (24)	44 (154)
Mists*	5	N = 3	N = 0	N = 3	N = 2
Powders	115	30 (34)	24 (28)	9 (10)	47 (54)
Wood/stone dusts	60	70 (42)	17 (10)	23 (14)	27 (16)
Metal dusts	58	52 (30)	22 (13)	3 (2)	38 (22)

*Percentages were not calculated for this exposure type due to the small number of measurements available.

Table 2. Linear regression coefficients and bias for exposure measurements.

Exposure type	50th percentile				90th percentile			
	Intercept	Slope	R^2	Rel. bias, %	Intercept	Slope	R^2	Rel. bias, %
Vapours	0.10	0.65	0.38	30	-0.23	0.66	0.38	315
Powders	-0.02	0.23	0.09	-11	-0.15	0.23	0.09	249
Wood/stone dusts	0.38	-0.12	0.02	-74	0.46	-0.15	0.04	4.7
Metal dusts	-0.07	0.35	0.03	-32	-0.28	0.35	0.03	154

Table 3. Percentages of modelled point estimates lying within a factor of 5, 10, 100 or 1,000 times the measured SUVA estimates.

Factor	Percentile	Vapours	Powders	Wood/stone dusts	Metal dusts
5	50th	49	50	40	74
	90th	47	40	55	66
10	50th	63	68	60	83
	90th	57	63	70	98
10^2	50th	92	96	92	97
	90th	83	91	90	100
10^3	50th	99	98	100	100
	90th	98	97	100	100

Table 4. Coefficients of multiple linear regression for vapours.

	Estimate	**Std. error**	**Pr (> |t|)**
Intercept	-4.53	0.36	< 2.2e-16
Pressure	1.18	0.09	< 2.2e-16
Mole fraction	1.17	0.11	< 2.2e-16
Activity coefficient	4.13	0.72	2e-8
Handling	0.23	0.05	3e-5
Localised controls	0.57	0.14	3e-5
Dilution	4e-3	0.01	0.70

Multiple R^2: 0.49
p-value: < 2.2e-16

Table 5. Coefficients of multiple linear regression for powders.

	Estimate	**Std. error**	**Pr (> |t|)**
Intercept	-0.75	0.76	0.32
Dustiness	-1.07	0.39	7e-3
Weight fraction	0.35	0.29	0.23
Moisture content	0.29	0.16	0.08
Handling	0.02	3e-3	9.7e-5
Local controls	0.17	0.24	0.47
Dilution	0.41	0.14	4e-3

Multiple R^2: 0.30
p-value: 7e-7

Table 6. Coefficients of multiple linear regression for wood and stone dusts.

	Estimate	Std. error	Pr (> |t|)
Intercept	1.87	0.84	0.03
Moisture content	-1.43	0.70	0.05
Weight fraction	n.a.	n.a.	n.a.
Handling	-0.01	4e-3	0.01
Localised controls	0.72	0.23	2.3e-3
Dilution	0.24	0.26	0.36

Multiple R^2: 0.27
p-value: 2e-3

Table 7. Coefficients of multiple linear regression for metal dusts.

	Estimate	Std. error	Pr (> |t|)
Intercept	0.48	0.48	0.32
Weight fraction	n.a.	n.a.	n.a.
Moisture content	n.a.	n.a.	n.a.
Handling	-0.13	0.14	0.35
Localised controls	0.52	0.27	0.06
Dilution	3e-3	0.10	0.97

Multiple R^2: 0.10
p-value: 0.12

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