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Stoffenmanager exposure model: development of a quantitative algorithm

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Summary

In the Netherlands, the web-based tool called "Stoffenmanager" was initially developed to assist SMEs to prioritize and control risks of handling chemical products in their workplaces. The rationale of the underlying exposure algorithm is based on work of Cherrie and colleagues but is adapted in several ways. The aim of the present study was to explore the accuracy of the Stoffenmanager exposure algorithm. This was done by comparing its semi quantitative exposure rankings for specific substances with exposure measurements collected from several occupational settings to arrive at a quantitative exposure algorithm. Exposure data were collected using two strategies. First, we conducted 7 surveys specifically for validation of the Stoffenmanager. Second, existing occupational exposure data sets were collected from various sources. This resulted in 392 and 320 measurements for solid and liquid scenario's, respectively. The Spearman correlation coefficients between Stoffenmanager scores and measurements appeared to be good for handling solids (r_S = 0.82; N = 392; P < 0.0001) and liquid scenarios (r_S = 0.83; N = 320; P < 0.0001). However, the correlation for liquid scenarios appeared to be somewhat lower when calculated separately for sets of volatile substances with a vapour pressure > 10 Pa (r_S = 0.56; N=104; P < 0.0001) and non-volatile substances with a vapour pressure ≤ 10 Pa (r_S = 0.58; N = 216; P < 0.0001). The mixed effect regression models with Stoffenmanager as independent parameter explained a substantial part of the total exposure variability (53% for solid scenarios and 75% for liquid scenarios). Hence, this performance increases our confidence in the use of the Stoffenmanager as a generic tool for risk assessment. The mixed effect regression models presented in this paper may be used for assessment of so called reasonable worst case (RWC) exposures. This evaluation is considered as an ongoing process and when more good quality data become available the analyses described in this paper will be expanded.

Contents

1 Introduction

Important drivers of the development of generic and user friendly approaches for assessment of workplace health risks are the introduction of the Chemical Agents Directive (European Commission, 1998) and, more recently, the REACH legislation in Europe. As exposure is a complex process and varies enormously between workers and over time (Kromhout et al., 1993), the assessment of chemical risks requires a logical strategy or tool to focus resources on those situations with the greatest potential for adverse health effects (Mulhausen and Damiano, 1998). Currently, there exists a vast range of screening tools that are intended to systematically address workplace chemical risks (Money, 2003). The COSHH Essentials system (Russel et al., 1998; Maidment et al., 1998; Garrod and Rajan, 2003) and the ECETOC TRA (ECETOC, 2004) are among the most prominent and accepted examples for chemical exposure. Comparable tools are also available for pharmaceutical active ingredients (Naumann et al., 1996). Available screening models for chemical exposure have recently been reviewed in the context of guidance setting for REACH (http://ecb.jrc.it/home.php?contenu=/document/reach/rip-find-reports/rip-3.2-1-CSA-CSR).

The core requirements of any screening tool should be that it is simple, readily understood, and with an appropriate level of conservatism (Tielemans et al., 2007). In general, one of the main weaknesses of the available screening tools is that only few have been properly validated. This prohibits a comprehensive evaluation and weighing of the available tools. Tools that are, at least to some extent, validated are COSHH Essentials (Tischer et al., 2003; Jones and Nicas, 2006a, b; Money et al., 2006), ECETOC TRA (ECETOC, 2004), and EASE (Bredendiek-Kämper, 2001; Cherrie and Hughson, 2005; Hughson and Cherrie, 2005; Creely et al., 2005; Johnston et al., 2005). In the near future, insight into accuracy of models should substantially grow in order to make transparent decisions concerning the selection of sound screening tools. This may also result in the selection of several complementary tools, each with a distinct validity domain.

In the Netherlands, the web-based tool called “Stoffenmanager” was initially developed to assist SMEs to prioritize and control risks of handling chemical products in their workplaces. The background and underlying assumptions of the Stoffenmanager are described by Marquart et al. (2007). The rationale of the underlying exposure algorithm is based on work of Cherrie et al. (1996; 1999) but is adapted in several ways. The model uses process information, physicochemical characteristics, and mass balances to give a relative ranking of exposure situations. The aim of the present study was to explore the accuracy of the Stoffenmanager exposure algorithm. This was done by comparing its semi quantitative exposure rankings for specific substances with exposure measurements collected from several occupational settings to arrive at a quantitative exposure algorithm.

2 Materials and methods

2.1 Outline of Stoffenmanager exposure algorithm

The Stoffenmanager exposure algorithm has been described elsewhere by Marquart et al. (2007). For description of specific parameters and classes within parameters we refer to that paper. The exposure algorithm is based on a source-receptor approach and incorporates modifying factors related to source emission and dispersion of contaminants. Each parameter is divided into classes with scores on a logarithmic scale, i.e. ranging from 0 through 0.03, 0.1, 0.3, 1, 3 to 10. The total personal exposure level (C_t) is the sum of exposure levels due to near field (NF) sources (C_{nf}), far field (FF) sources (C_{ff}), and diffusive sources (C_{ds}), adjusted for possible use of control measures at the worker such as a control room (η_{imm}):

$$C_t = (C_{nf} + C_{ff} + C_{ds}) \cdot \eta_{imm} \qquad (1)$$

Exposure due to NF sources (C_{nf}) is a multiplicative function of handling (H), intrinsic emission (E), local control measures (η_{lc}), and general ventilation in combination with room size (η_{gv_nf}):

$$C_{nf} = E \cdot H \cdot \eta_{lc} \cdot \eta_{gv\_nf} \qquad (2)$$

Exposure due to FF sources (C_{ff}) is described according to a similar multiplicative function:

$$C_{ff} = E \cdot H \cdot \eta_{lc} \cdot \eta_{gv\_ff} \qquad (3)$$

Note that for the FF source the same intrinsic emission, handling and local control measures are assumed as for the NF source.

The diffusive source (C_{ds}) representing background concentration is expressed as follows:

$$C_{ds} = E \cdot a \qquad (4)$$

In this expression *a* represents a relative multiplier for potential of background sources, depending on the regularity of inspections of machines and on the cleaning procedure in the work area.

The intrinsic emission for dusts is derived from a table with weighing factors for dustiness, based on descriptions of observed dustiness. The intrinsic emission for liquids is based on vapour pressure and is expressed as follows:

$$E = (P / 30.000) \cdot F \qquad (5)$$

With *P* representing vapour pressure (Pascal) and *F* a factor equal to the fraction of a substance in a mixture. In order to predict total volatile organic compound exposure (i.e. the sum of *n* solvents) we used:

$$E = \sum_{i=1}^{n} (P_i / 30000) \cdot F_i \qquad (6)$$

2.2 Collation of exposure data

Exposure data were collected using two strategies. First, we conducted 7 surveys specifically for validation of the Stoffenmanager. For scenario's describing the handling of solids, we conducted inhalable dust measurements in the animal feed industry, construction industry, textile industry, and bakeries and flour handling industry. Personal air samples were obtained from a random sample of potentially exposed workers in the companies. The dust samples were collected using a portable pump with a flow rate of 2 l/min and a Teflon filter mounted in a PAS6 sampling head. Sampling was performed in the breathing zone of the worker for approximately 4 hours. For scenario's describing the handling of liquids, task-based measurements to solvents were conducted in auto body repair shops, printing industry, and metal industry. Inhalation exposure to solvents during a specific task was assessed by personal air sampling using an air sampling pump (flow rate of 250 ml/min) and charcoal adsorption tubes. Samples were transported to an external laboratory (RPS). After extraction with CS_2 the samples were analyzed on a broad range of organic solvents (approximately 250), using GC-FID.

Occupational hygienists conducted all surveys using a checklist to collect information in a structured way. This checklist allowed the hygienist to record frequency and duration of tasks conducted and the relevant Stoffenmanager parameters for each task. Information on substances and its concentrations in a mixture were retrieved from SDS available at the workplace. In those cases that the concentration was given in ranges the midpoint of the range was used in the analyses.

Secondly, occupational exposure data sets were collected from archives of TNO. These data originated from research projects funded by the Dutch Government in the past years. In addition a network of industry and occupational health services participating in the Dutch "VASt program" was used to collect more exposure data. The VASt program is established by the Dutch Ministry of Social Affairs and Employment to assist SMEs in reinforcing the working condition policy on hazardous substances (http://vast.szw.nl). In the context of this program a large number of research and consultancy projects was conducted and funded (partly) by the Dutch Government. We used this momentum to collate exposure data. The data collection process was facilitated by a request for data on the "VASt" website. In addition, a specific newsletter concerning the evaluation study was sent to contact persons of various sectors and companies. Both task-based and shift-based exposure measurements were collected.

Guidelines for data quality were applied to rank data into one of 3 categories: good, moderate or poor. Only good quality data were eventually used in the analyses. Exposure data were labelled to be of good quality if required core information was documented (Rajan et al., 1997; Tielemans et al., 2002) and if all Stoffenmanager parameters could be retrieved. The latter criterion was stringent and we rejected any data sets not meeting this criterion. Often an occupational hygienist had to make further enquiries with the original researchers to retrieve additional details with respect to Stoffenmanager parameters and help clarify any ambiguities.

2.3 Data processing and statistical analyses

Both the measured exposure data and contextual information to derive Stoffenmanager scores were collected in a relational database in Microsoft Access 2003. To safeguard confidentiality data were entered anonymously into the database. Based on the contextual information assignment of Stoffenmanager scores was carried out blind by one occupational hygienist. Subsequently, these scores were reviewed by another occupational hygienist and in case of inconsistencies the assessment was discussed until consensus was reached. Both occupational hygienists were involved in the development of the Stoffenmanager exposure algorithm. When multiple tasks were conducted during a measurement, Stoffenmanager scores were calculated for each task and then combined together as a time-weighted summation for the tasks making up the measurement period.

The data were analyzed using SAS statistical Software (version 9.1.3; SAS Institute, Cary, NC). Visual inspection of the measured concentrations for solid and liquid scenarios showed a log-normal rather than a normal distribution, so descriptive statistics are presented both as arithmetic and geometric mean levels with geometric standard deviation and range. In situations where measured values were below the limit of detection (LOD), 0.5 times the LOD was substituted for measured values (Hornung and Reed, 1990).

Spearman correlation coefficients were calculated to study the relation between Stoffenmanager scores and measured exposure concentrations. Mixed-effect regression models were used to further explore this relation by using log-transformed exposure data as dependent variable and log-transformed Stoffenmanger scores as independent variable, with random between (σ^2_{bc}) - and within-company (σ^2_{wc}) components of variance. A compound symmetry covariance structure was used to model the data. The mixed-effect regression models can be used to predict geometric mean exposure levels for a given Stoffenmanager score. The variation around the prediction is given by the components of variance. Hence, the random components of variance in conjunction with relevant *z* values of the standard normal distribution can be used to predict a more conservative cutpoint for a given Stoffenmanager score. To arrive at a 90 percentile the prediction of the geometric mean should be multiplied using the following factor (*M*):

$$M = e^{1.28\cdot\sqrt{\sigma_{bc}^2+\sigma_{wc}^2}} \qquad (7)$$

Graphical analyses of residuals were performed to evaluate assumptions of homoscedasticity. Statistical analyses were conducted separately for scenario's covering the handling of solids and liquids. For liquids, more detailed analyses were performed for volatile and non-volatile substances.

3 Results

The results presented in Table 1 show the wide range of 14 different industries with in total 392 measured exposure data ranging from 0.0001 to 420 mg/m^3 for inhalable dust scenarios collected in several companies per industry (Table 1). The highest geometric mean dust exposure levels were found among task-based measurements in the paint industry (GM = 31.9 mg/m^3; GSD = 4.26), the construction industry (GM = 13.4 mg/m^3; GSD = 3.15) and the rubber/plastic industry (GM = 12.2 mg/m^3; GSD = 3.05). Similar information is presented in Table 2 for the liquid scenarios (measuring solvents, pesticides/biocides or isocyanates) with in total 320 measured exposure data in eight different industries ranging from 0.0002 to 1,762 mg/m^3 (Table 2). The highest geometric mean solvent exposure levels were found in the orthopaedic shoe manufacturing (GM = 128 mg/m^3; GSD = 3.50) and the metal industry (GM = 56.7 mg/m^3; GSD = 5.89).

Table 1. Descriptive statistics of available measured exposure data for inhalable dust scenarios.

Type of industry/study	N	K	Median sampling time (min)	AM (mg/m^3)	GM (mg/m^3)	GSD	Range (mg/m^3)
Overall	392	86	210	19.1	1.79	13.4	0.0001 - 420
Pharmacies	78	7	14	0.17	0.05	5.81	0.0001 - 2.63
Bakeries	56	17	382	2.75	1.31	3.18	0.05 - 48.0
Construction industry	88	27	218	25.7	13.4	3.15	0.80 - 310
Experimental study	36	1	15	84.3	36.2	4.01	5.22 - 313
Woodworking industry	23	5	250	2.53	1.74	2.63	0.20 - 7.20
Fertilizer industry	6	1	465	1.76	1.16	2.70	0.42 - 5.12
Dairy products	3	1	391	1.00	0.73	2.85	0.24 - 1.92
Animalfeed industry	40	4	248	4.53	1.62	4.10	0.18 - 54.5
Metal industry	4	3	199	32.3	7.99	10.0	0.74 - 94.6
Transhipment industry	5	2	301	11.3	7.97	3.11	1.20 - 21.3
Rubber/plastic production	4	1	147	19.4	12.2	3.05	3.50 - 51.8
Textile industry	28	6	232	0.50	0.25	3.04	0.06 - 4.82
Printing	1	1	447	0.53	0.53	-	-
Paint industry	20	10	53	74.3	31.9	4.26	1.90 - 420

N = Number of samples; K = Number of companies; AM = Arithmetic mean; GM = Geometric mean; GSD = Geometric standard deviation

Table 2. Descriptive statistics of available measured exposure data for liquid scenarios.

Type of industry/study	Substance	N	K	Median sampling time (min)	AM (mg/m^3)	GM (mg/m^3)	GSD	Range (mg/m^3)
Overall		320	97	39	54.8	0.36	58.6	0.0002 - 1,762
Shipbuilding industry	Biocides	31	8	70	1.32	0.38	6.29	0.007 - 9.03
Car repair industry	Solvents	15	8	10	59.3	4.66	9.98	0.36 - 563
Pest and weed control	Biocides	36	26	56	0.007	0.004	3.62	0.0002 - 0.03
Car repair industry	Isocyanates	90	17	9	0.58	0.08	13.6	0.0006 - 4.52
Metal industry	Solvents	56	14	24	175	56.7	5.89	1.06 - 1,572
Orthopaedic shoe manufacturing	Solvents	26	10	510	257	128	3.50	10.4 - 1,762
Horticulture	Pesticides	59	12	62	0.05	0.02	5.19	0.0003 - 0.42
Silkscreen printing industry	Solvents	7	2	293	8.84	4.72	5.00	0.23 - 17.2

N = Number of samples; K = Number of companies; AM = Arithmetic mean; GM = Geometric mean; GSD = Geometric standard deviation

Tables 3 and 4 describe the occurrence of key parameters for calculating the Stoffenmanager score for both the solid (Table 3) and liquid scenarios (Table 4). These tables allow for the fact that multiple tasks may have been performed during one (shift) measurement. This resulted in a total of 799 tasks for the dust scenarios (Table 3) and 444 tasks for the liquid scenarios (Table 4).

Table 3. Descriptive statistics for solid scenario's (392 measurements).

Parameter	N	%
Number of tasks*	799	100
Ventilation		
General ventilation present	626	78.3%
General ventilation absent	173	21.7%
Room size		
< 100 m^3	222	27.8%
100 – 1000 m^3	353	44.2%
> 1000 m^3	202	25.3%
Outside	22	2.8%
Intrinsic emission score**		
0.1	0	0.0%
0.3	20	2.5%
1.0	151	18.9%
3.0	593	74.2%
10	35	4.4%
Handling score**		
0	73	9.1%
0.1	132	16.5%
0.3	126	15.8%
1.0	68	8.5%
3.0	300	37.5%
10	100	12.5%
Local controls		
None (score = 1)	639	80.0%
LEV (score = 0.3)	146	18.3%
Enclosure (score = 0.3)	1	0.1%
LEV and enclosure (score = 0.03)	5	0.6%
Wetting (score = 0.3)	8	1.0%
Near Field exposure source		
Present	739	92.5%
Absent	60	7.5%
Far Field exposure source		
Present	306	38.3%
Absent	493	61.7%

* Total number of tasks conducted in the 392 measurements.

** Scores indicate the exposure potential of a product or handling: 0.1 (low) to 10 (high) (see Marquart et al., 2007)

Table 4. Descriptive statistics for liquid scenario's (320 measurements).

Parameter	N	%
Number of tasks*	444	100%
Ventilation		
General ventilation present	243	54.7%
General ventilation absent	142	32.0%
Spray cabin	59	13.3%
Room size		
< 100 m^3	111	25.0%
100 – 1000 m^3	140	31.5%
> 1000 m^3	154	34.7%
Outside	39	8.8%
Handling score**		
0	5	1.1%
0.1	17	3.8%
0.3	19	4.3%
1.0	172	38.7%
3.0	43	9.7%
10	188	42.3%
Local controls		
None (score = 1)	319	71.8%
LEV (score = 0.3)	90	20.3%
Enclosure (score = 0.3)	4	0.9%
LEV and enclosure (score = 0.03)	31	7.0%
Near Field exposure source		
Present	423	95.3%
Absent	21	4.7%
Far Field exposure source		
Present	197	44.4%
Absent	247	55.6%

* Total number of tasks conducted in the 320 measurements.

** Scores indicate the exposure potential of a handling: 0.1 (low) to 10 (high) (see Marquart et al., 2007)

The Spearman correlation coefficients appeared to be good for handling solids (r_S = 0.82; N = 392; P < 0.0001) and liquid scenarios (r_S = 0.83; N = 320; P < 0.0001) (Table 5). However, the correlation for liquid scenarios appeared to be somewhat lower when calculated separately for sets of volatile substances with a vapour pressure > 10 Pa (r_S = 0.56; N=104; P < 0.0001) and non-volatile substances with a vapour pressure ≤ 10 Pa (r_S = 0.58; N = 216; P < 0.0001) (Table 5).

Table 5. Spearman correlation between Stoffenmanager scores and measured exposure concentrations (in mg/m^3).

Scenario	N	r_s	P-value
Handling of solids	392	0.82	<0.0001
Handling of liquids	320	0.83	<0.0001
Volatile substances*	104	0.56	<0.0001
Non-volatile substances**	216	0.58	<0.0001

N = Number of measurements; r_s = Spearman correlation coefficient

* Including all substances with vapour pressure > 10 Pa (organic solvents)

** Including all substances with vapour pressure ≤ 10 Pa (isocyanates, biocides, pesticides)

The further exploration of the data by using mixed effects models with a random company effect resulted in the models presented in Table 6 and graphically illustrated for inhalable dust (Figure 1) and liquid scenarios (Figure 2). Both models had an intercept (dust: $\beta_0 = 1.74$; standard error = 0.15 / liquids: $\beta_0 = 6.07$; standard error = 0.37), but the slope of the regression line appeared to show a positive linear relation between Stoffenmanager scores and measured inhalable dust concentrations ($\beta_1 = 0.72$; standard error = 0.05) and liquid concentrations ($\beta_1 = 0.88$; standard error = 0.04) (Figure 1; Figure 2; Table 6). These two regression equations enable the prediction of geometric mean exposures (*GM*) for a given Stoffenmanager score (C_t):

$$GM_{solid} = e^{1.74+0.72\cdot\ln(C_t)}$$

$$GM_{liquid} = e^{6.07+0.88\cdot\ln(C_t)}$$

Total variance appeared to be somewhat higher for the liquid scenarios ($\sigma^2_{total} = 4.51$) compared with the solid scenarios ($\sigma^2_{total} = 2.45$). Based on these variance components the difference between the predictions of the GM and the reasonable worst case (90th percentile) was estimated to be a factor 7.4 ($e^{(1.28 * \sqrt{(2.45)})}$) for solid scenarios and a factor 15.2 ($e^{(1.28 * \sqrt{(4.51)})}$) for liquid scenarios.

Table 6. Mixed-effects regression models with Stoffenmanager scores as fixed effect and random between- and within-company components of variance.

	Handling solids		Handling liquids	
	Estimate	SE	Estimate	SE
Intercept (β_0)	1.74	0.15	6.07	0.37
Stoffenmanager score (β_1)	0.72	0.05	0.88	0.04
Components of variance:				
Between-company (σ^2_{bc})	1.31	0.26	1.56	0.43
Within-company (σ^2_{wc})	1.15	0.09	2.96	0.28
Explained variance	53%		75%	

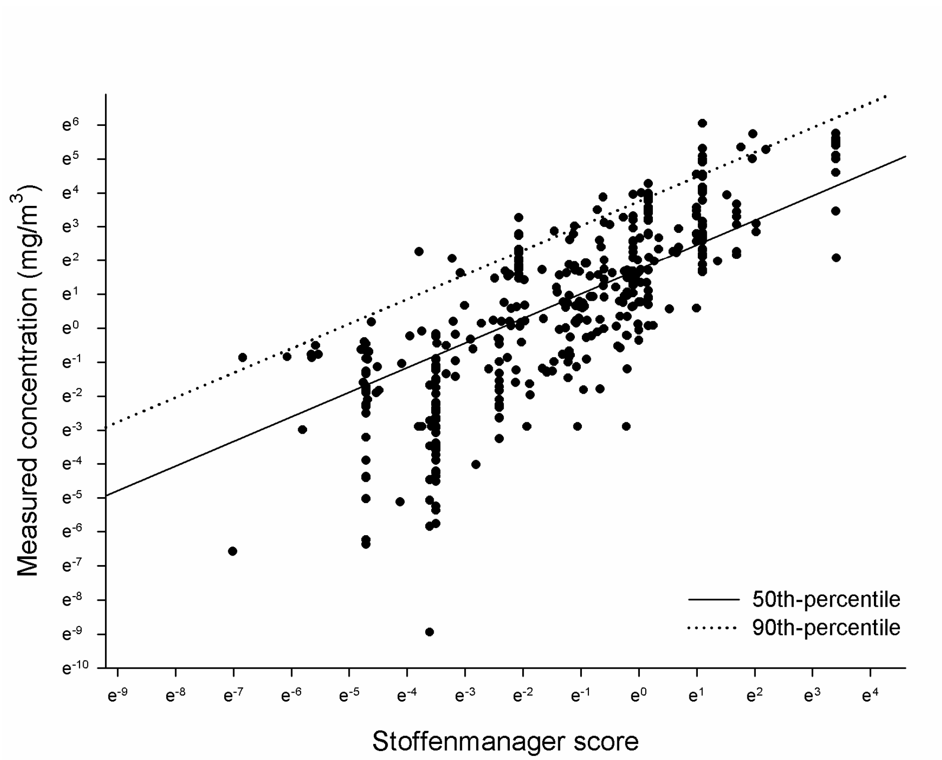

Figure 1 Association between Stoffenmanager scores and measured inhalable exposure concentrations (mg/m³) for handling of solids

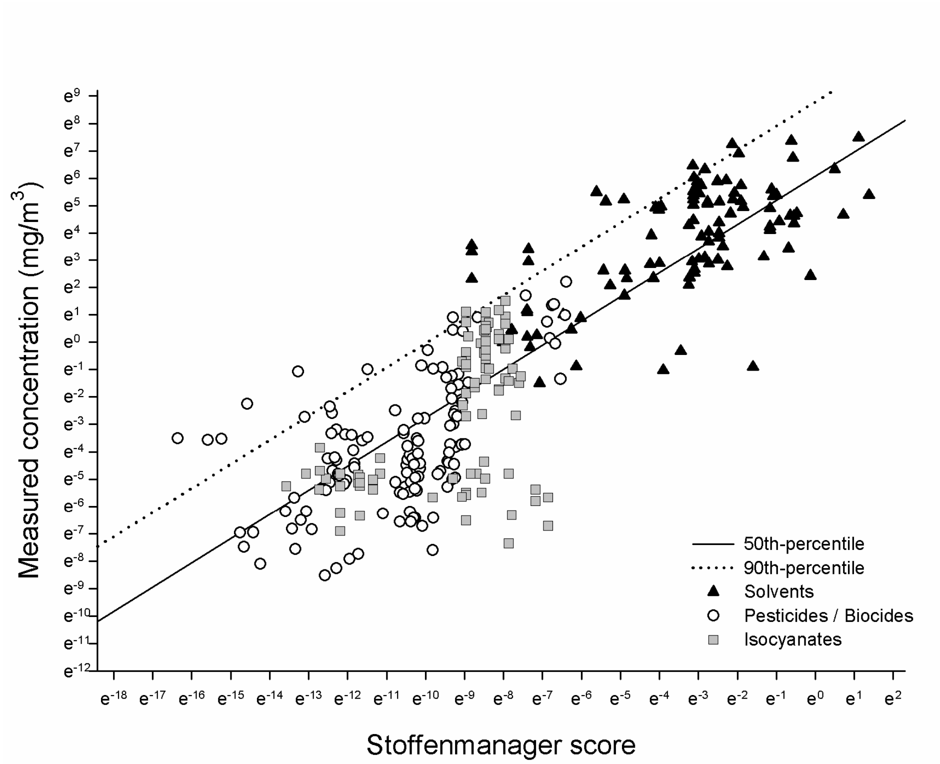

Figure 2. Association between Stoffenmanager scores and measured exposure concentrations (mg/m^3) for liquid scenarios

4 Discussion

Although the concept of validation has been recognized as an indispensable part of model development (Armstrong et al., 1992; Schneider and Holst, 1996), only few validations of exposure models for risk assessment are described in the literature (Tischer et al., 2003; Jones and Nicas, 2006; ECETOC, 2004; Cherrie and Hughson, 2005; Hughson and Cherrie, 2005; Money et al., 2006; Bredendiek-Kämper, 2001; Johnston et al., 2005). The present study indicated that there is good agreement between Stoffenmanager scores and exposure measurements for both solid and liquid scenarios. The mixed effect regression models with Stoffenmanager as independent parameter explained a substantial part of the total exposure variability (53% for solid scenarios and 75% for liquid scenarios). This proportion of explained variance is well in accordance with other, more specific exposure studies focusing on a particular industrial setting (Burstyn and Teschke, 1999). Hence, this performance increases our confidence in the use of the Stoffenmanager as a generic tool for risk assessment. Yet, a cross validation has to be conducted in order to evaluate the accuracy of the mixed effect models (Hornung, 1991). This cross validation using a small set of good quality exposure data will be conducted in a subsequent step (Schinkel et al., 2007).

Notwithstanding the good correlation the data show substantial variability in exposure measurements given a certain Stoffenmanager score. It is likely that various sources of uncertainty are responsible for this observed variability. First, there is uncertainty in the information describing the input parameters. Some parameters were most likely estimated with substantial error. For instance, the fraction of a substance in a mixture is often indicated in very broad ranges (e.g. 25-50%) in the available SDS. Likewise, other factors at the workplace may be assessed with varying degrees of error. Although we applied rigid quality control criteria for inclusion of data this source of uncertainty undoubtedly resulted in discrepancies between model estimates and measurements.

Secondly, there is the usual degree of sampling and analytical error inherent in the measurement data (Tielemans et al., 2002). Hence, measurements do not reflect true exposure and are itself an ‘alloyed gold standard’ (Wacholder et al., 1993). We consider this to be a relatively unimportant source of uncertainty, as measurement error is generally believed to be minor as compared to true exposure variability (Nicas et al., 1991).

A third, more fundamental reason for discrepancies between Stoffenmanager estimates and exposure measurements is model uncertainty. The conceptual model underlying the Stoffenmanager may be incomplete or contain errors. As exposure is influenced by so many aspects only the most dominant processes can be accounted for (Morgan and Henrion, 1990). The Stoffenmanager exposure algorithm is to a large extent based on a well described model of Cherrie et al. (1996; 1999) with some modifications, i.e., the definition of intrinsic emission for liquid scenarios, assumptions with respect to the strength of FF sources (similar tasks and local controls are assumed as for NF sources), and the definition of background exposure due to diffusive sources. It is generally felt that the underlying concepts incorporate the critical determinants of exposure (Creely et al., 2005). Yet, there is further scope for improvement by the provision of high-quality guidance information, a further description of how workers become exposed (conceptual model), and more validated information on the parameter values (Goede et al., 2007).

An important issue related to model uncertainty is that the Stoffenmanager inherently assumes that exposure is linearly dependent on the concentration of a substance in a mixture. However, the evaporation of a substance is also dependent on the specific composition of the mixture and on the activity coefficient of each component reflecting molecular interactions (Nielsen and Olsen, 1995; Fehrenbacher and Hummel, 1996). In addition, one should ideally use the mole fraction of a substance in a mixture instead of a mass fraction to predict partial vapour pressure. In practice, however, there is only limited information on characteristics of the mixture available so that we had to rely on less adequate, but accessible information.

The model of Cherrie and colleagues has previously also been evaluated (Cherrie and Schneider, 1999; Semple et al., 2001). The correlation coefficients found in their evaluation study are in accordance with or somewhat higher than the results presented in this paper. The main differences between study results is that the Stoffenmanager is evaluated over a broad range of exposure levels (up to 7 or 8 orders of magnitude) and that we found more scattering of exposure levels within a given Stoffenmanager score (i.e., “noise”). This discrepancy may well be explained by the fact that the methodology of Cherrie and colleagues was used in a flexible manner with specific guidance material tailored to the particular assessment scenarios. This also included range-finding exposure data to calibrate the assessor. This is likely to help improve the accuracy and reliability of estimates, as is also shown by Hawkins and Evans (1989) and Post et al. (1991). In contrast, the Stoffenmanager algorithm was applied in a much more rigid manner with closed definitions for each parameter. A more flexible approach with additional guidance for each specific situation is impossible for the generic version of the Stoffenmanager. However, when used to estimate exposures in branch-specific scenarios for a limited set of substances, the specific Stoffenmanager model (calibrated to a subset of specific substances data) will most likely be more accurate and reliable than the generic version.

The mixed effect regression models presented in this paper may be used for assessment of so called reasonable worst case (RWC) exposures. The assessment can be based upon an appropriate percentile from the log-normal distribution described by the regression model in terms of the random components of variance. The TGD for risk assessment of new and existing substances currently recommends the 50^{th} percentile for typical exposure and the 90^{th} percentile for RWC exposure (ECB, 2003). However, these recommendations are not necessarily relevant for use of the Stoffenmanager. The TGD recommendations relate to measured data sets in rather broad exposure scenarios (e.g. “spray painting with solvent based paints”). Stoffenmanager scenarios can be defined much more specifically. Therefore, if conservative Stoffenmanager inputs are used to describe a scenario, we recommend using the 75th percentile as the estimator of the reasonable worst case exposure level. If more average Stoffenmanager inputs are used for parameters that vary within a broad scenario, such as room size and local controls, the 90th percentile would be preferred as estimator of the reasonable worst case.

As the scatter of exposure measurements for a given Stoffenmanager score is rather large, the differences between 50th and 90th percentile is a factor up to 7.4 for solid and 15.2 for liquid scenario's, respectively. These factors can be considered "safety factors" to incorporate model uncertainty and inherent exposure variability in the risk assessment process. Clearly, alternative safety factors based on the random components of variance can easily be calculated if another RWC exposure definition is considered more appropriate. However, more exposure data are needed in the future to properly investigate whether components of variance are relatively stable across the whole range of Stoffenmanager scores. Some heteroscedasticity of residual variability by exposure group was observed (i.e. more variability for isocyanates) but should be explored further when more data become available.

The observed scattering might be reduced by further optimization of the conceptual model in the future. Yet, an additional strategy will be to combine the model estimates with available measurements relevant for the particular assessment scenario. Such an alternative strategy using Bayesian techniques to update model results with exposure data is proposed by Creely et al. (2005) and elaborated on by Tielemans et al. (2007). A few applications of a Bayesian approach to exposure assessment have already been described (Ramachandran et al, 1999, 2003; Hewett et al., 2006). As random between-company exposure variability in the mixed-effect models is large there is potential for substantial improvement of Stoffenmanager estimates using site-specific data, even if only few measurements are available. We are currently exploring the possibilities of Bayesian techniques to update Stoffenmanager predictions.

This study did not look at the reliability of the algorithm: i.e., do different users produce the same results for the same exposure scenarios (Armstrong et al., 1992)? The Stoffenmanager scores were derived by one assessor and these results were reviewed by another assessor. Some subjective assessment methods have been evaluated and show good inter-rater agreement (Semple et al., 2001; van Wendel de Joode et al., 2005). Most parameters in the Stoffenmanager algorithm are not prone to subjective interpretation and simply require an objective description of the situation (e.g., LEV is present or not; a subjective assessment of efficacy of LEV is not required). However, two parameters provide to some degree the opportunity for subjective judgement: i.e., handling parameter and intrinsic emission for solids (dustiness). This potential for multiple interpretation of the same situation was reduced as much as possible by providing transparent descriptions and by giving various examples for each parameter class. Nevertheless, a reliability study focusing on these aspects should be conducted in the near future.

This study had also other limitations. Although the collated exposure data cover a wide range of Stoffenmanager parameters, there is still lack of appropriate data and not all Stoffenmanager parameter combinations are included in the validation data set. For solid scenarios, not all intrinsic emission scores are well represented; substances with very low and high dustiness potential are not covered by the data. In addition, a very limited number of measurements in the dataset was conducted outside. Hence, the performance of the model for these situations is not properly described by the data in this study. Occupational activities such as processing of melted or burning materials (e.g., hot moulding, calandering) or hot work techniques (e.g. welding, soldering) are lacking in the data set. Hence, these types of activities are outside the validity domain of the Stoffenmanager algorithm and should be dealt with in a later stage.

We could have included more exposure data with limited contextual information to increase the coverage of this study. Yet, as a validation heavily depends on the quality of data this would have reduced the confidence in the results. It was our goal to derive mixed-effects regression models with only limited residual error. Currently, a web-based database containing all relevant contextual information is under development (STEAMbase: SToffenmanager Exposure And Modelling database). The systematic collation of exposure measurements with all relevant Stoffenmanager parameters ensures a growing evidence base. Therefore, this evaluation is considered as an ongoing process and when more good quality data become available the analyses described in this paper will be expanded. In general, we believe it is important to regularly update validation and calibration of exposure models as workplace scenario's, exposure levels, and relations between determinants and exposure will change over time (Kromhout and Vermeulen, 2000).

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6 Signature

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