Annals of Work Exposures and Health, 2019, Vol. 63, No. 2, 218–229
doi: 10.1093/annweh/wxy091
Advance Access publication 9 December 2018
Original Article

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Evaluation of Exposure Assessment Tools under REACH: Part I—Tier 1 Tools

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Submitted 3 August 2017; revised 14 August 2018; editorial decision 26 September 2018; revised version accepted 15 October 2018.

Abstract

Tier 1 occupational exposure assessment tools recommended for use under the Registration, Evaluation, Authorization, and restriction of CHemicals (REACH) were evaluated using newly collected measurement data. Evaluated tools included the ECETOC TRAv2 and TRAv3, MEASEv1.02.01, and EMKG-EXPO-TOOL. Fifty-three exposure situations (ESs) based on tasks/chemicals were developed from National Institute for Occupational Safety and Health field surveys. During the field surveys, high quality contextual information required for evaluating the tools was also collected. For each ES, applicable tools were then used to generate exposure estimates using a consensus approach. Among 53 ESs, only those related to an exposure category of liquids with vapor pressure (VP) > 10 Pa had sufficient numbers of exposure measurements (42 ESs with n = 251 for TRAv2 and TRAv3 and

Published by Oxford University Press on behalf of The British Occupational Hygiene Society 2018.

40 ESs with n = 243 for EMKG-EXPO-TOOL) to be considered in detail. The results for other exposure categories (aqueous solutions, liquids with VP ≤ 10 Pa, metal processing, powders, and solid objects) had insufficient measurement to allow detailed analyses (results listed in the Supplementary File). Overall, EMKG-EXPO-TOOL generated more conservative results than TRAv2 and TRAv3 for liquids with high VP. This finding is at least partly due to the fact that the EMKG-EXPO-TOOL only considers pure substances and not mixtures of chemical agents. For 34 out of 40 ESs available for chemicals with VP > 10 Pa, the liquid was a mixture rather than a pure substance. TRAv3 was less conservative than TRAv2, probably due to additional refinement of some input parameters. The percentages of exposure measurement results exceeding the corresponding tool estimates for liquids with VP > 10 Pa by process category and by input parameters were always higher for TRAv3 compared to those for TRAv2. Although the conclusions of this study are limited to liquids with VP > 10 Pa and few process categories, this study utilized the most transparent contextual information compared to previous studies, reducing uncertainty from assumptions for unknown input parameters. A further validation is recommended by collecting sufficient exposure data covering other exposure categories and all process categories under REACH.

Keywords: exposure assessment tools; inhalation tools; REACH; tier tools; validation

Introduction

The Registration, Evaluation, Authorization, and restriction of CHemicals (REACH) is a regulation for chemical substances enforced from 1 June 2007 by the European Union (EU) to aim the protection of both human health and the environment. The EU European Chemicals Agency (ECHA) R14 guidance (2016) describes a tiered approach to obtain quantitative occupational exposure estimates by using Tier 1 and, if necessary, higher tier tools. Tier 1 tools, including the ECETOC TRA, MEASE, and EMKG-EXPO-TOOL, are designed to be easy to use and to provide conservative estimates of exposure. The 'higher' tier tools are developed to be used if the Tier 1 assessment suggests that the exposure may be too high. Higher tier tools include Stoffenmanager® and the Advanced REACH Tool (ART; ECHA, 2016). These are designed to more accurately estimate the exposure distribution and are more comprehensive and sophisticated, requiring more information from the user; thus, it is recommended that higher tier tools be used by experienced assessors. The background information about the scope, concept, and applicability of each tool is well described in the ECHA R14 guidance (2016). Recently, Hesse *et al.* (2015a) performed a conceptual evaluation of the ECETOC TRA (version 2 and 3), MEASE (version 1.02.01), EMKG-EXPO-TOOL, and Stoffenmanager® (version 4.5). They described strengths and weaknesses of each tool, allowing users to compare their applicability for the specific exposure situations (ESs) at hand. Note that we deliberately used a term 'exposure situation', instead of 'exposure scenario' (often used in ECHA R14 guidance), to avoid confusion; for the registration of chemical to the ECHA, it is required to attach exposure scenarios with proper risk management measures (RMMs) and operational conditions to a safety data sheet, although some workplaces that participated in this study often did not provide appropriate RMMs.

In 2015, the Institute of Occupational Medicine and Fraunhofer Institute for Toxicology and Experimental Medicine completed a project, entitled 'The Evaluation of Tier 1 Exposure Assessment Models (ETEAM) used under REACH', initiated and sponsored by the Bundesanstalt für Arbeitsschutz und Arbeitsmedizin in Germany. The project aimed to compare and evaluate the different REACH tools, including the ECETOC TRA (version 2 and 3), MEASE (version 1.02.01), EMKG-EXPO-TOOL, and Stoffenmanager® (version 4.5). The main findings of this study are published in a series of articles and reports (Hesse et al., 2015a,b; Lamb *et al.*, 2017; Tischer *et al.*, 2017; van Tongeren *et al.*, 2017). The external evaluation study was based on existing data from a range of workplaces in Europe and the USA. A total of 1702 individual measurements were used; most data were available for volatile liquids (>10 Pa at room temperature, n = 1337), followed by non-volatile liquids (≤10 Pa at room temperature, n = 210), powder handling (n = 254), metal abrasion (n = 84), and metal processing (n = 71). Overall, the evaluation showed the tools were not sufficiently conservative for a number of ESs (van Tongeren *et al.*, 2017). Medium or low levels of conservatism were reported for the ECETOC TRAv2 and TRAv3 across all of the data. The TRAv3 resulted in less conservative estimates than the TRAv2. The MEASE produced lower percentages of measurements exceeding the tool estimates (%M > T) compared to the TRAv2 and TRAv3 for the categories of metal abrasion and powder handling. For the EMKG-EXPO-TOOL, a high level of conservatism was reported for the volatile liquids and medium conservatism for the powder-handling task.

The ETEAM's external validation study comprised relatively larger data sets covering various activities compared to other previous studies listed in Supplementary Table 1 (available at *Annals of Work Exposures and Health* online) and provided valuable information (van Tongeren *et al.*, 2017). However, one limitation was the use of existing measurement data collected by different organizations for different purposes, no new exposure measurements being carried out to evaluate the tools. Assumptions about the tools' input parameters had to be made as essential contextual information required for deciding on the input parameters were missing. In addition to the study by van Tongeren *et al.* (2017), a number of other, smaller validation studies have been carried out on the tools used under REACH. Supplementary Table 1 (available at *Annals of Work Exposures and Health* online) provides a summary of external validation studies for the relevant Tier 1 tools inside and outside REACH. These previous studies were based on relatively small-scale data sets or limited operating conditions [e.g. limited process category (PROC) codes for TRA tools].

This study was conducted to evaluate the REACH tools using exposure measurements and contextual information gathered specifically for the purpose. This article describes the results of the validation of the Tier 1 tools including ECETOC TRAv2 and TRAv3, and EMKG-EXPO-TOOL. MEASE v1.02.01 (referred to as 'MEASE') was also evaluated for the applicable chemicals. However, as MEASE is not recommended for estimating exposure to organic chemicals, and as a result insufficient measurements were available to draw meaningful conclusions on the validation of MEASE, the results are presented in the Supplementary File. Results of the validation of the higher tier tools (ART and Stoffenmanager® 4.5) are presented in accompanying articles (E. G. Lee *et al.*, in preparation).

Methods

Field surveys

From 2012 through 2015, the National Institute for Occupational Safety and Health (NIOSH) conducted exposure surveys to collect personal exposure measurements at 18 workplaces in the USA. Table 1 lists the types of workplaces and number of exposure measurements grouped into six exposure categories: (i) aqueous solutions, (ii) liquids with a vapor pressure (VP) ≤10 Pa at room temperature, (iii) liquids with a VP >10 Pa at room temperature, (iv) metal processing (e.g. hot metal processes such as casting or smelting), (v) powders, and (vi) solid objects. At each workplace, the collected exposures reflected the workers' representative exposures during a typical working day (i.e. no exposure measurements made for compliance purpose or extreme cases). A total of 293 personal airborne samples were collected and analyzed for a specific contaminant of interest using the relevant NIOSH or Occupational Safety and Health Administration sampling and analytical method. At some workplaces, samples were collected and analyzed for multiple chemicals in a mixture. For these samples, only the chemical component having the highest proportion in the mixture of the product used (proportion range: 25–94% for solids

Table 1. Summary of the personal exposure measurements (by exposure category).

Exposure category	Workplaces	ES No.	*n*	Applicability of Tier 1 tools[a]
Aqueous solutions	Aircraft industry	2	4	MEASE only
Liquids with VP ≤ 10 Pa	Aircraft industry	2	5	All but MEASE and EMKG-EXPO-Tool
Liquids with VP > 10 Pa	Paint, aircraft and wind mill industries, dry-cleaning shops, hospital labs, denture lab, and print shop	42	251	All but MEASE
Metal processing	Casting and smelting industries	2	11	MEASE only
Powders	Metal powder generation and packing industry	2	11	All tools
Solid objects	Solid object packing/shipping	3	11	All tools but TRAv2 and v3
Overall		53	293	

ES No. = number of exposure situations (ESs) developed by NIOSH; *n* = number of workplace measurements.
[a]Applicability of tools was based on job tasks.

and 34–78% for liquids) was included in the analyses presented in this article. The sampling time ranged from 32 to 712 min with 88% of the measurements being longer than 240 min and 63% being longer than 360 min. Some of workplaces had a 10-h shift leading to a sampling period >600 min. The detailed information about tasks and number of samples for each task is listed in Supplementary Table 2 (available at *Annals of Work Exposures and Health* online). During the field surveys, contextual information required for each tool's input parameters were obtained. In addition, pictures and/or video clips were taken for some tasks, with the companies' permission.

Development of ES

After the field surveys, the NIOSH senior industrial hygienist who carried out the surveys developed 53 ESs based on the job tasks and chemicals, using a standard template. Along with the task descriptive information, product information including a chemical concentration, molecular weight, and VP were also included. The exposed and non-exposed times were the same for all measurements within an ES. For measurements of the same activity, but with different exposed/non-exposed times, separate ESs were developed. This was the case for the ESs based on glue application-inside tasks (ESs 46 and 47), glue application-outside tasks (ESs 48–51), and roller cleaning tasks (ESs 54–56) (Supplementary Table 2, available at *Annals of Work Exposures and Health* online).

We observed that workers frequently performed several subtasks under different control strategies. For example, the paint batch making ES (ES19) consisted of four subtasks: (i) manual addition of solid materials from the top opening of the batch (partial opening of the batch; 10% of 8-h full shift), (ii) transfer of chemical products to other containers [automatic transferring system with partial opening (<10 cm opening diameter) of the containers; 20% of full shift], (iii) manual cleaning of emptied batches with no local exhaust ventilation (LEV) present (10% of full shift), and (iv) the remaining tasks including filling, mixing, rinsing, and shipping carried out in fully enclosed systems (60% of full shift). In this example, because subtasks were conducted intermittently it was difficult to measure the exposure during each constituent subtasks separately, and hence these activities had to be treated as one single ES. The selection of task (i.e. PROC code) was based on a job task determined by company (e.g. batch maker in the batch process department for ES19). For subtasks with different exposure control methods, we used the least effective control method in the modeling to ensure the most conservative exposure estimate. In the example of ES19, we selected PROC 5 (mixing or blending in batch processes for formulation of preparations and articles) for the TRAv2 and TRAv3 and a large scale for the EMKG-EXPO-TOOL with no local ventilation but with good general ventilation for all tools. All ESs were transferred to a Microsoft Access database, identical to the one developed for the ETEAM project (van Tongeren *et al.*, 2017). The exposure measurements were separately stored and not released to the assessors until all exposure assessments with the tools were completed.

Translation of contextual information into tools' input parameters

Fifty-three ESs were divided into four batches. Each batch was sent to six assessors (E.L., J.L., N.S., B.G., J.K., and M.T.) from different organizations. All assessors were familiar with Tier 1 tools, but the familiarity with individual ESs varied depending on their experience.

Individual assessors independently used the contextual information from ESs to select the relevant input parameters for each tool. Use of respirators was ignored as the tool estimates were compared with results of exposure measurements collected from outside any respirator. Table 1 shows a summary of each tool's applicability based on the job tasks. The tools' applicability for each ES is listed in Supplementary Table 2 (available at *Annals of Work Exposures and Health* online). The assessors were blind to measurement results when deciding on the input parameters. A face-to-face meeting with all assessors was held to discuss the discrepancies between assessors and reach consensus decisions on all input parameters.

Generation of tool estimates

Exposure estimates for each tier tool were generated using the consensus set of inputs. The actual ECETOC TRAv2, TRAv3, and MEASE tools were used to obtain exposure estimates. The algorithm from the EMKG-EXPO-TOOL was incorporated into the database and used to calculate the estimates based on this tool. The estimates from 10% of the ESs were checked with results from the actual EMKG-EXPO-TOOL and no differences were observed.

Data analyses

The EMKG-EXPO-TOOL is known as a task-based tool, whereas the ECETOC TRAv2, TRAv3, and MEASE predict 8-h time-weighted average (TWA) exposure, although the estimate can be corrected if exposure is

<8 h using the conversion factor for the duration of a task. Because the exposure measurements regularly included non-exposed periods, it was necessary to adjust the exposure data accordingly. For example, for ES 29 (denture making task) a full-shift measurement was carried out, during which the worker was exposed to the chemical agent of interest for 190 min and not exposed for the remaining 290 min. In this situation, the result of the full-shift measurement cannot be directly compared to the corresponding exposure estimates obtained with the EMKG-EXPO-TOOL and the TRA tools (unless the conversion factor for the duration of a task is considered). The TWA exposure measurement results were converted to the corresponding task-based exposure estimate by multiplying the TWA estimate exposure by a factor given by the total measurement duration divided by the exposure duration. For example, if an exposure level is 50 mg m^{-3} during 120-min sample duration (during which worker was exposed for only 30 min), the corresponding task-based exposure would be 200 mg m^{-3} (50 mg m^{-3}/0.25).

For the ECETOC TRAv2, TRAv3, and MEASE, the point estimates were used. For the EMKG-EXPO-TOOL, which predicts an exposure range rather than a single estimation, the upper range value was selected for the comparison in accordance with the REACH guidance. Selection of a different value could affect the results and conclusions regarding conservatism of the tool.

The comparison between the exposure measurement data and the tool estimates was conducted by calculating the ratio of the exposure measurement result (M) to the tool estimate (T) for each pair of values, assuming that all exposure measurements were independent. We then calculated the proportion of exposure measurement results exceeding the tool estimates (%M > T), which are presented by exposure category, PROC code, and tool input parameter. Although the EMKG-EXPO-TOOL does not have the PROC code as an input parameter, the PROC codes assigned to the ESs for ECETOC TRAv2 and TRAv3 were used to stratify the comparisons of EMKG-EXPO-TOOL estimates with measurement results. Comparisons between tool estimates and measurement results were also stratified by VP [high (>10 000 Pa), medium (500 ≤ VP ≤ 10 000 Pa), and low (<500 Pa)], domain (industrial and professional), and LEV (yes and no). Pearson correlation coefficients (r_p) between the log-transformed exposure measurements and log-transformed tool estimates were also calculated. In addition, regression analyses using mixed models were conducted to determine linearity between the exposure measurement results and the corresponding tools' estimates. All data analyses were performed using the Statistical Analysis Software v. 9.4.

In addition, for the ESs for which four or more measurements were available, the 75th percentile of the measured exposure distribution was calculated and compared with the tool estimate. The percentage of ESs with the 75th percentile of the measured exposure distribution exceeding the tool estimate (%75th M > T) is presented for both TRAv2 and TRAv3 by exposure category, PROC code, and tool input parameter, providing that ≥10 ESs were available. Those are liquids with VP > 10 Pa (22 ESs), PROC 10 (11 ESs), LEV absence (16 ESs), industrial domain (10 ESs), professional domain (12 ESs), and medium VP (15 ESs).

Results

Only the results of the exposure category liquids with VP > 10 Pa are summarized because data for the other exposure categories were limited to only a few ESs (2 or 3) and had small sample sizes (≤11). The findings for the remaining exposure categories are presented in the Supplementary File (Supplementary Tables 3 and 4, and Supplementary Figure 1, available at *Annals of Work Exposures and Health* online) as these may be valuable for future research. Because MEASE is not applicable for organic substances, the data available for this tool were very limited and hence not presented here, but provided in the Supplementary File.

Description of workplace measurement data

Table 2 presents a summary of the exposure measurement results, corrected so that they reflect exposure during the relevant task, for liquids with VP > 10 Pa. Fewer exposure measurements and ESs were available for EMKG-EXPO-TOOL than for the ECETOC TRA tools because EMKG-EXPO-TOOL is not applicable to spraying processes. Fifteen or more measurements were available for the following PROCs: 5 (mixing or blending in batch processes), 10 (roller application), 13 (treatment of articles by dipping and pouring), and 15 (use as a laboratory reagent; Table 3). Most exposure measurements were available for liquids with a VP between 500 Pa and 10 000 Pa (30 ESs with n = 190 for TRAv2 and TRAv3 and 28 ESs with n = 182 for EMKG-EXPO-TOOL) and no LEV (35 ESs with n = 201 for all tools; Table 4). A wide range of measurement results was obtained (from 0.07 mg m^{-3} to 6653 mg m^{-3}) because measurements were carried out across different substances and ESs. The detailed exposure measurements

Table 2. Summary of the exposure measurement results (M), tool estimates (T), and ratio of M/T (liquids with VP > 10 Pa).

Tool	ES No.	n	Personal exposure measurement results (M)			Tool estimates (T)			Ratio (M/T)				
			AM (mg m^{-3})	GM (mg m^{-3})	Range (mg m^{-3})	AM (mg m^{-3})	GM (mg m^{-3})	Range (mg m^{-3})	GM	GSD	Range	r_p	%M > T
ECETOC TRAv2	42	251	214	24.5	0.07–6653	246	119	2.5–1210	0.21	7.05	<0.01–38.7	0.53*	22
ECETOC TRAv3	42	251	214	24.5	0.07–6653	78.1	41.3	1.75–467	0.59	6.78	<0.01–44.2	0.55*	38
EMKG-EXPO-TOOL	40	243	220	24.6	0.07–6653	744	252	0.61–3692	0.10	5.50	<0.01–13.1	0.69*	6

Note that an assumption that all individual exposure measurements were independent was applied for the data analyses. ES No. = number of exposure situations (ESs) developed by NIOSH; n = number of exposure measurements; AM = arithmetic mean exposure; GM = geometric mean exposure; GSD = geometric standard deviation; r_p = Pearson correlation coefficient; %M > T = Percentage of exposure measurement results exceeding the tool estimates.

*P-value < 0.05.

per ES are listed in Supplementary Table 2 (available at *Annals of Work Exposures and Health* online).

Comparison of task-based exposure levels with tool estimates

Exposure category

Table 2 shows a summary of the exposure measurement results (M), tool estimates (T), and ratio of M/T for volatile liquids (VP > 10 Pa). The results of other exposure categories are presented in Supplementary Table 3 (available at *Annals of Work Exposures and Health online*). For volatile liquids, the arithmetic mean (AM) and geometric mean (GM) values of the tools' estimates were greater than those of exposure measurement results, except for the AM of the TRAv3 [AM = 214 mg m^{-3} (exposure measurement) versus 78.1 mg m^{-3} (TRAv3 estimate)]. The widest range in exposure estimates for the volatile liquids was obtained for EMKG-EXPO-TOOL, followed by ECETOC TRAv2, and TRAv3. The GM values of the ratios (M/T) for the three tools were <1, indicating that the majority of the measurements were below the tool estimate. The tool estimates were moderately positively correlated with the exposure measurement data for the three tools. All tools in this study had significant linear relationships between the measurement results and tools' estimates (all P-values < 0.0001; Fig. 1). For TRAv3, there was almost 1:1 relationship (slope = 0.976) between tool estimates and measurement results. This was slightly lower for the other tools (slope = 0.837 for TRAv2 and 0.799 for EMKG-EXPO-TOOL). Plots for other exposure categories are presented in Supplementary Figure 1 (available at *Annals of Work Exposures and Health online*); due to small sample sizes, no regression line was estimated for these. The percentage of exposure measurement results exceeding the corresponding tool's estimates (%M > T) was 22% for the TRAv2, 38% for the TRAv3, and 6% for the EMKG-EXPO-TOOL. These %M > Ts were calculated based on the assumption that all exposure measurements were independent.

Table 5 compares the 75th percentile estimates of the exposure measurement results for the ESs with four or more measurements with the tool estimates. The percentage of ESs for which the TRAv2 and TRAv3 estimates were below the 75th percentile of the exposure measurement results was 32% and 59%, respectively.

By PROC code

Table 3 shows the percentage of individual exposure measurement results (modified to task-based levels)

Table 3. Percentage of the individual exposure measurement results (task based) exceeding the tool estimates (%M >T) by PROC code.

Tool		%M > T (number of exposure measurements) by PROC Code								
		3	5	7	8b	9	10	11	13	15
ECETOC TRAv2	Current study	33 (3)	0 (47)	25 (8)	0 (9)	0 (8)	39 (114)	0 (2)	0 (45)	47 (15)
	ETEAM[a]	NR	23 (60)	62 (195)	6 (249)	1 (76)	18 (245)	NR	14 (130)	NR
ECETOC TRAv3	Current study	67 (3)	9 (47)	25 (8)	0 (9)	0 (8)	64 (114)	0 (2)	4 (45)	87 (15)
	ETEAM[a]	NR	32 (60)	74 (195)	7 (249)	3 (76)	22 (245)	NR	25 (130)	NR
EMKG-EXPO-TOOL	Current study	67 (3)	0 (47)	N/A	0 (9)	0 (8)	11 (114)	0 (2)	2 (45)	0 (15)
	ETEAM[a]	NR	0 (60)	N/A	0 (73)	1 (68)	5 (244)	NR	11 (130)	NR

Note that the gray box indicates a sample size <10, and %M > T was presented to provide additional information, without any intention to draw robust conclusions. Also, an assumption that all individual exposure measurements were independent was applied for the data analyses. NR = not reported; N/A = not applicable. PROC Codes: 3 = Use in closed batch process (synthesis or formulation); 5 = mixing or blending in batch processes for formulation of preparations and articles (multistage and/or significant contact); 7 = industrial spraying; 8b = transfer of substance or preparation (charging/discharging) from/to vessels/large containers at dedicated facilities; 9 = transfer of substance or preparation into small containers (dedicated filling line, including weighing); 10 = roller application or brushing of adhesive and other coating; 11 = non-industrial spraying; 13 = treatment of articles by dipping and pouring; 15 = use as laboratory reagent.
[a]ETEAM: Study findings reported by van Tongeren *et al.* (2017).

Table 4. Percentage of exposure measurement results above the tool estimates (%M >T) by tool input parameter for liquids with VP > 10 Pa.

Tool		%M > T (number of exposure measurements)						
		Vapor pressure[b]			Domain		LEV	
		High	Medium	Low	Professional	Industrial	Yes	No
ECETOC TRAv2	Current study	35 (37)	22 (190)	0 (24)	7 (105)	32 (146)	8 (50)	25 (201)
	ETEAM[a]	37 (320)	29 (886)	18 (131)	5 (374)	40 (963)	67 (542)	5 (772)
ECETOC TRAv3	Current study	49 (37)	41 (190)	4 (24)	32 (105)	43 (146)	22 (50)	42 (201)
	ETEAM[a]	43 (320)	35 (886)	21 (131)	6 (374)	47 (963)	74 (542)	9 (772)
EMKG-EXPO-TOOL	Current study	27 (37)	2 (182)	4 (24)	1 (105)	10(138)	7 (42)	6 (201)
	ETEAM[a]	5 (191)	7 (608)	8 (106)	8 (249)	6 (656)	14 (381)	2 (514)

Note that an assumption that all individual exposure measurements were independent was applied for the data analyses.
[a]ETEAM—Study findings reported by van Tongeren *et al.* (2017).
[b]Low VP: < 500 Pa at a room temperature; medium VP: 500 ≤ VP ≤ 10 000 Pa; high VP: VP > 10 000 Pa.

exceeding the tool estimates by PROC code. Note that PROC codes having the number of exposure measurements <10 are also presented in Fig. 1 to develop a regression equation for this exposure category (i.e. not separated by PROC codes). The results of the other exposure categories are listed in Supplementary Table 4 (available at *Annals of Work Exposures and Health online*).

The highest number of measurements was available for PROC 10 (roller or brushing application, n = 114 from 14 ESs), covering a wide range of exposure measurements. Fewer measurements were available for PROC 5 (batch process for formulation of articles, n = 47 from 9 ESs), PROC 13 (treatment of articles by dipping and pouring, n = 45 from 6 ESs), and PROC 15 (use as laboratory reagent, n = 15 from 2 ESs). For all other PROCs, between 2 and 9 measurements were available. Overall, for both TRA tools, the %M > Ts calculated for PROC 5 and PROC 13 were lower than those calculated for PROC 10 and PROC 15. For PROC 10 and PROC 15, the calculated %M > Ts were considerably higher for TRAv3 than those for TRAv2.

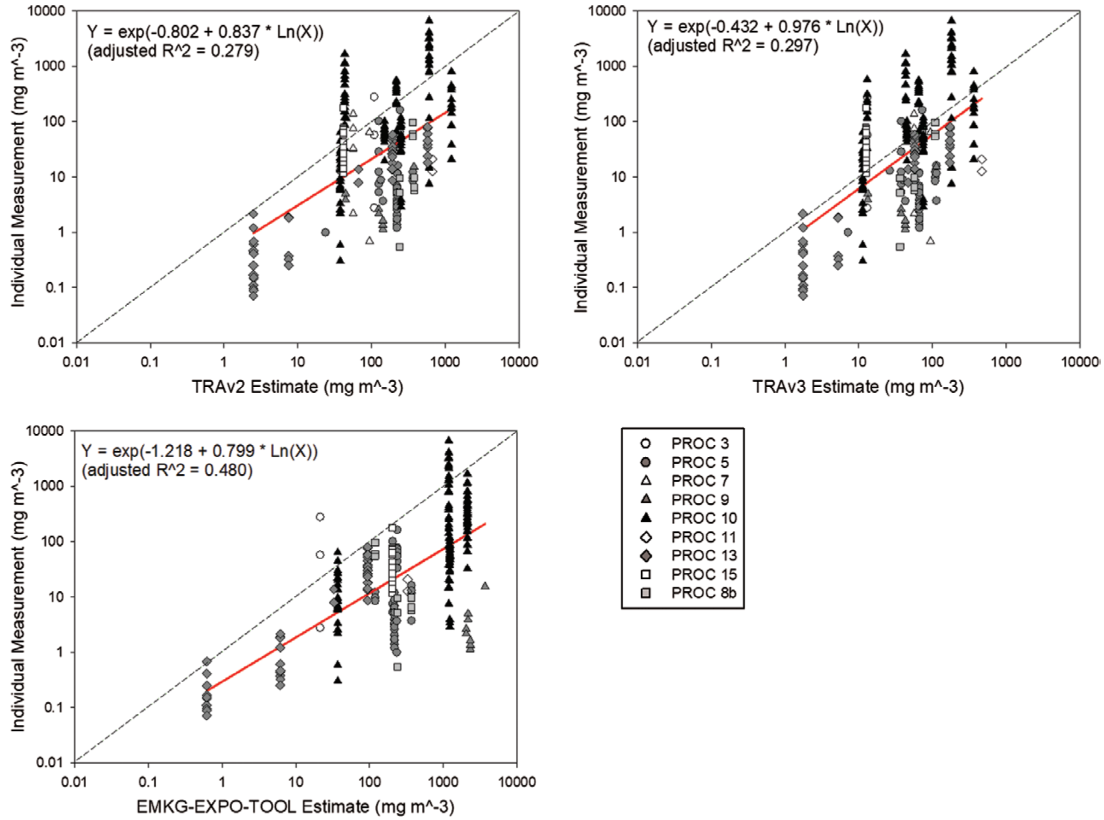

Figure 1. Comparison of exposure measurement results with tool estimates for liquids with VP > 10 Pa. The solid line indicates a regression line and the dashed line indicates 1:1 line.

Table 5. Percentage of the 75th percentile estimate from the measured exposure distribution exceeding the tool estimate (%75th M > T; for TRAv2 and TRAv3).

	Liquids with VP > 10 Pa	PROC 10	Input parameters						
			VP[a]			Domain		LEV	
			High	Medium	Low	Professional	Industrial	Yes	No
ECETOC TRAv2	32	55	N/A	40	N/A	8	75	N/A	35
ECETOC TRAv3	59	82	N/A	67	N/A	42	80	N/A	65
ES No[b]	22	11	4	15	3	12	10	5	17

Note that the %75th M > Ts reported here include those categories having the number of ESs ≥ 10. N/A = Not applicable.
[a]Low VP: < 500 Pa at a room temperature; medium VP: 500 ≤ VP ≤ 10 000 Pa; high VP: VP > 10 000 Pa.
[b]Number of exposure situations (ES) having sample sizes ≥ 4.

The EMKG-EXPO-TOOL generated less than or close to 10%M > T for PROCs 5, 10, 13, and 15. The results of %M > T for PROCs 3, 7 (TRAv2 and TRAv3 only), 8b, 9, and 11 (indicated by gray box) vary for all tools from 0 to 67%, but these are based on a limited number of measurements.

For 6 out 11 ESs for TRAv2 and 9 out of 11 ESs for TRAv3 available for PROC 10, the 75th percentiles of the measurement-based exposure distribution was greater than the tools estimates (Table 5).

By tool input parameter

Table 4 presents the results of the percentage of measurements exceeding the tool estimates by input parameter. The majority of measurements for the tools were allocated to ESs using liquids with medium

VP and ESs without LEV options; similar number of measurements were available for ESs across the domain options. The ECETOC TRAv2 and TRAv3 tools appear to be very conservative (<5% of measurements exceeding the tool estimate) for liquids with low VP (<500 Pa). However, for liquids with medium VP (500 ≤ VP ≤ 10 000 Pa) and high VP (>10 000 Pa) the TRAv2 and TRAv3 tools were less conservative (>20% of measurements exceeding the tool estimate). A smaller percentage of exposure measurement results exceeded the ECETOC TRAv2 estimates for the professional domain compared to the industrial domain and for activities with LEV present compared to those without. A similar pattern was observed for the TRAv3, but the %M > Ts were considerably higher than those for the TRAv2.

For more than 35% of the ESs (with ≥4 measurements) using liquids with medium VP, in the industrial domain or without LEV, the 75th percentile of the measured exposure distribution was greater than the tool estimate for both TRA tools (Table 5). For ESs in the professional domain, the percentage of ESs with measured 75th percentile in excess of the tool estimate was also high for the TRAv3 tool, but much lower for the TRAv2 tool.

The EMKG-EXPO-TOOL resulted in a higher proportion of measurement results exceeding the tool estimates for ESs with high VP liquids compared to ESs using low or medium VP liquids. The EMKG-EXPO-TOOL was also less conservative for ESs in the industrial domain compared to the professional domain. The EMKG-EXPO-TOOL was more or less equally conservative for ESs with and those without LEV.

Discussion

Description of workplace measurement data

Personal exposure measurements and exposure determinants were collected from 18 workplaces in the USA. Among 53 ESs, 42 ESs for TRA tools and 40 ESs for EMKG-EXPO-TOOL were used to test their performance for volatile liquids (VP > 10 Pa); the range of VP for the chemicals employed in this study was from 79 Pa to 27 500 Pa. The majority of the ESs involved situations where LEV was absent (35 out of 42 ESs for TRA tools and 35 out of 40 ESs for EMKG-EXPO-TOOL) or where chemicals were placed in the medium VP category (30 out of 42 ESs for TRA tools and 28 out of 40 ESs for EMKG-EXPO-TOOL; Table 4). In addition, the range of operating conditions was limited. For example, the number of exposure measurements assigned to PROC 10 was the highest (n = 114), whereas few measurements (n < 10) were available for PROCs 3, 7, 8b, 9, and 11. The imbalance of numbers of exposure measurements assigned to PROCs could bias overall conclusions for the performance of the tools. Initially, we aimed to collect exposure measurements covering all exposure categories and PROCs recommended by ECHA, but due to the difficulties of recruiting workplaces, this was not feasible. Further research is recommended, which should include additional workplaces covering different PROCs.

Several evaluation studies for Tier 1 exposure assessment tools used for REACH were previously conducted using pre-existing exposure data (the majority) or collected data either from field surveys or from laboratory tests. Exposure data from field surveys or laboratory tests generally include only a small number of exposure measurements. Validation studies by Schinkel *et al.* (2010), Koppisch *et al.* (2012), and van Tongeren *et al.* (2017) were carried out with a relatively large number of exposure measurements. The exposure measurements used in these studies were not specifically collected for evaluating the tools and it was necessary to assume default values for input parameters that were not recorded. A strength of the current study is the availability of high-quality contextual information (e.g. including room volume, ventilation system, LEV, chemical components in a mixture, cleanness, exposed/non-exposed time). Some information not measurable during the field surveys was obtained from the plant manager and/or occupational hygienist. For example, although we could obtain the presence of ventilation (yes or no), we had to rely on a plant manager to obtain the efficacies of LEV and/or room ventilation. Nevertheless, the contextual information for the current study was of much higher quality compared to some of the previous studies, reducing uncertainty from assumptions about unknown input parameters. On the other hand, a strength of the ETEAM study was the inclusion of a larger number of exposure measurements. Thus, it may be worthwhile to pool the exposure data of the current and ETEAM studies and perform similar analyses to evaluate Tier 1 tools.

Comparison of task-based exposure levels with tool estimates

ECETOC TRAv2

For the ECETOC TRAv2, Hofstetter *et al.* (2013) reported that the TRAv2 estimate in assessing exposure to toluene from spray paint task was 3.6 times higher than the mean exposure concentration measured in a controlled room. Ko and Yi (2013) also evaluated this tool with personal exposure data of various volatile organic chemicals and reported overestimation of the tool estimates compared with the mean exposure levels. In this study, the results are similar to the two previous studies when considering the GM values of ratios (M/T). The regression analysis showed a significant linear relationship between the exposure measurement results and tool estimates and a moderate correlation coefficient was observed. The percentage of individual measurements exceeding the tool estimates was very similar to that observed by van Tongeren *et al.* (2017) indicating that overall, the TRAv2 seemed to be conservative (i.e. %M > T less than or close to 25% and GM of ratio <1). However, 32% of the ESs with ≥4 measurements had 75th percentiles of the measured exposure distribution that was higher than the TRAv2 estimate, indicating that the tool may be less conservative.

When the comparison was made by PROC codes having sample sizes ≥15, none of the exposure measurement results exceeded the TRAv2 estimates for PROC 5 and PROC 13. However, for PROC 15 and PROC 10 the tool was much less conservative, with more than 35% of measurements exceeding the tool estimate. This was also observed when comparing the tool estimate with the 75th percentile of the measured distribution for ESs with ≥4 measurements (Table 5). Vink *et al.* (2010) validated the TRAv2 with 745 exposure measurements and reported that the tool overestimated exposures for the PROCs 11 and 13. The same results were observed in this study for the PROC 13 (even for the same PROC for the TRAv3). van Tongeren *et al.* (2017) reported considerably higher percentage of measurements exceeding the tool estimate for PROC 5 and PROC 13, but lower %M > T for PROC 10 than in this study (Table 3). PROC 15 was not included in the study by van Tongeren *et al.* Although van Tongeren *et al.* reported similar or lower level of conservatism compared to this study for the other PROCs including 7, 8b, and 9 (gray box in Table 3), no comparison can be made because of small sample sizes (n < 10) in this study.

Both current and ETEAM projects observed similar percentages of measurement results exceeding the tool estimates for the high and medium VP, industrial domain, and professional domain by assuming that all exposure measurements were independent for both studies (Table 4). In this study, we also compared the 75th percentile of the exposure distribution from ESs with 4 or more measurements with the tool estimates. On the basis of this, the TRAv2 tool appeared to be considerably less conservative, except for the %M > T for the professional domain. Noticeable differences between this and the ETEAM studies were observed for ESs with liquids with low VP, and with and without the use of LEV (Table 4). For these inputs, the ETEAM study (van Tongeren *et al.*, 2017) included a higher number of exposure measurements compared to this study, but due to the application of default values when information was not available, there are some uncertainties around the conclusion based on the ETEAM findings.

ECETOC TRAv3

The revised TRA version—ECETOC TRAv3—resulted in a higher percentage of measurement results exceeding the tool estimates than the previous version 2 for the liquids with VP > 10 Pa category (Table 2). The ETEAM validation study (van Tongeren *et al.*, 2017) found that 32% of the measurement available for volatile liquids exceeded the TRAv3 estimates, which is very similar to that which was found in this study (38%M > T). For the selected ESs where the number of exposure measurements were ≥4, the percentage of ESs with a 75th percentile of the measured exposure distribution that exceeded the tool estimate was even greater. Overall, although the GM of ratios (M/T) was <1, the findings of this study cannot conclude that the TRAv3 is sufficiently conservative for this exposure category.

For those PROCs having sample size ≥15 (PROC 5, PROC 10, and PROC 13), this study showed considerably different results of %M > T compared to those by van Tongeren *et al.* (2017; Table 3). TRAv3 resulted in the %M > Ts >25% for all input parameters in Table 4 except for the low VP allocation and LEV presence allocation. The %M > T was similar to that reported by the ETEAM study for high and medium VP and industrial domain (i.e. difference between the ETEAM study and the current study <10%). TRAv3 resulted in a higher percentage of measurement results exceeding the tool estimates compared to TRAv2 regardless of the presence of LEV in this study. Inconsistent results for the low VP, professional domain, and the LEV presence/absence were observed when compared with the ETEAM study. When the ECETOC version was updated from v2 to v3, the tool developers made a few modifications for the baseline exposure estimates for several PROCs, the domain, and the LEV presence. In particular, the ventilation option has been considerably refined by including a wider range of options (seven options including outdoors, indoors, and combinations of indoors, general ventilation, and mechanical ventilation) than the version 2 (LEV presence: yes or no). The findings of this study and the ETEAM study suggested that the refinement of ventilation might be one main factor causing the reduced level of conservatism of this tool estimates by applying higher control factors than warranted.

EMKG-EXPO-TOOL

Overall, similarly to the results from the ETEAM study, this tool was found to be highly conservative for the ESs and chemical agents studied here. The regression analysis showed a significant linear relationship between the exposure measurement results and the tool's estimates.

Both the ETEAM and current studies calculated similar percentages of measurement values exceeding estimates (e.g. either less than or close to 10%) for PROCs 5, 10, and 13 where sample size >15. In addition, the EMKG-EXPO-TOOL appeared to be highly conservative for ESs allocated to PROC 15. The tool generated highly conservative results for all options of input parameters, except for the ESs involving liquids with high VP (Table 4). Similar results were reported by the ETEAM study except for the high VP allocation and LEV presence. Kindler and Winteler (2010) found underestimation of the tool estimates for the handling of volatile liquids with the presence of LEV, but the current study did not observe similar results.

Among all Tier 1 tools in this study, the EMKG-EXPO-TOOL was the most conservative. Unlike other Tier 1 tools, the EMKG-EXPO-TOOL does not account for the proportion of a substance in a mixture but rather treats the whole mixture as a pure substance. In this study, 34 out of 40 ESs for which the tool was applicable involved a substance in a mixture, and hence the assumption with regard to mixtures could, at least partially, explain the higher level of conservatism found for this tool compared to the other Tier 1 tools. This issue was also discussed in the ETEAM validation study (van Tongeren *et al.*, 2017). Another possible explanation of the high level of conservatism is the use of the upper value of predicted exposure range as recommended for use of the tool under REACH. For further validation studies, one might consider a different validation strategy for this tool that provides an exposure measurement data range instead of one exposure value (e.g. comparing a range of exposure measurement results for a task with the predicted exposure range).

General discussion

For both TRA tools (and EMKG-EXPO-TOOL), we selected the control method that was least effective for the ESs having multiple subtasks with various control methods considering that Tier 1 tools are designed to be conservative. In this study, no LEV was assigned to 35 out of 42 ESs (~83%) for TRA tools and 35 out of 40 ESs (~88%) for EMKG-EXPO-TOOL. Among these 35 ESs for both TRA tools (and EMKG-EXPO-TOOL), 23 ESs included several subtasks (from 2 to 4 subtasks) and we assigned the least effective control method to 9 out of 23 ESs (for all tools in this study) to predict exposure estimates. This selection is likely to result in a tendency toward estimates higher than those expected when instead selecting the control method employed in the longest subtask. For validation purposes, it may be useful to select a control method generating the highest exposure level among several control methods based on the exposed time and subtask type. Ideally, this can be carried out by collecting exposure data separately for all individual subtasks. However, in practice, it would be very difficult to collect exposure measurements per subtask because most subtasks were not conducted in an order (i.e. difficult to switching a sampling media from one subtask to another). To check the influence of those 9 ESs to the overall conclusion, we redid the calculation of %M > Ts using the same data set but without exposure measurement data of 9 ESs (n = 155) for both TRA tools and EMKG-EXPO-TOOL. The calculated %M > Ts were 32% for the TRAv2, 52% for the TRAv3, and 8% for the EMKG-EXPO-TOOL (results not shown). Although these results were slightly or moderately higher than those reported in Table 4, an overall conclusion would not be changed (i.e. no influence of the results). Nevertheless, the use of the least control method may be considered a limitation of this study.

Conclusions

Overall, the results presented here are fairly consistent with the results of the ETEAM project, in that tools were shown to be conservative when used for assessing exposures to volatile agents. However, these studies suggest that the level of conservatism may not always be sufficient to fulfill the tools' required performance (i.e. 75th or 90th percentile of the exposure distribution). This study involved a limited number of activities (as expressed as PROCs) and mainly focused on activities involving volatile liquids. Stratifying the results by PROC code resulted in some contrasting results with the ETEAM project. This could be partly explained by the uncertainty in the measurement results (e.g. small sample size); to be able to validate at PROC level requires larger data sets with high quality measurement results and contextual information.

Below is a summary of areas where the performance of the tools may need to be further investigated and possibly improved in future, based on our results from ESs where a sufficient number of exposure measurements were available. For those having insufficient samples sizes, a further evaluation by collecting more exposure measurements and considering a broader range of ESs is strongly recommended.

1. 'ECETOC TRAv3': Although we presented the results of TRAv2 for the comparison with the results of

TRAv3 and previous studies, our recommendations are limited to TRAv3 because TRAv2 is no longer made available. The PROC codes recommended for consideration in future tool upgrade or development are PROC 10 (roller application) and PROC 15 (application as laboratory reagent) because of low level of conservatism. In addition, it is recommended that the algorithms for liquids with high and medium VP, profession and industrial domains, and situations without LEV are re-evaluated.

2. 'EMKG-EXPO-TOOL': Although this tool was generally highly conservative for exposures to volatile liquids with VP > 10 Pa, the tool was less conservative when applied to liquids with high VP. Although this was not observed in the ETEAM study, it is recommended that tool estimates for high volatile liquids should be re-evaluated.

Supplementary Data

Supplementary data are available at *Annals of Work Exposures and Health* online.

Funding

This project was funded internally by the National Institute for Occupational Safety and Health (Project CAN number: 939ZXEY).

Acknowledgements

The authors are sincerely thankful to Ms. Hilary Cowie (Institute of Occupational Medicine, Edinburgh, UK) and Dr. Jens Tørsløv (DHI groups, Hørsholm, Denmark) for reviewing this manuscript prior to journal submission. The authors also would like to offer special thanks to the employees who participated in our study and the employers who allowed us to access their facilities.

Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention. Mention of any company or product does not constitute endorsement by NIOSH/CDC.

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