Systematic review of published studies of ECETOC TRA Worker exposure predictions

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EUROPEAN CENTRE FOR ECOTOXICOLOGY AND TOXICOLOGY OF CHEMICALS

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SUMMARY

The ECETOC Targeted Risk Assessment (TRA) tool has been widely used by REACH registrant companies in Europe to create screening level exposure assessments for REACH dossiers of chemical substances since 2010. The module dealing with occupational exposure ('TRA Worker') provides base estimates for inhalation exposures from vapours released by liquid substances and from dust released by solid substances and for dermal exposures from all substances regardless of physical state, for a number of standardised worker activities, called Process Categories (PROCs) and coded in ECHA guidance for REACH implementation. The base estimates are subdivided across broad categories of vapour pressure and dustiness and can be adjusted for a limited set of operational conditions and risk management measures, such as ventilation in the work environment, concentration of the substance of interest in a product, shortened duration of exposure, and use of personal protective equipment. The module was derived from a previous tool used in risk assessments under the Existing Substances Regulation and issued by the UK Health and Safety Executive (HSE).

Since 2010, the performance of the TRA-Worker module has been studied by several external research groups, primarily for inhalation exposures, who have reported mixed results, thereby putting into question the validity of the TRA as a conservative screening tool. Therefore, ECETOC assembled a task force (TF) to review the published performance studies and to identify potential tool improvements. All relevant publications were identified with the help of a panel of external advisors. Published studies relied in almost all cases on exposure measurement data sets and associated descriptions of operational conditions and risk management measures in actual workplaces. In many instances it was necessary for the TF to retrieve additional information elements to examine the researchers' application of the TRA in detail, in some cases with the help of the researchers themselves. The review focussed on measurement reports with more substantive data sets as these provided more certainty about the existing exposure levels and also presented the possibility to create a high-quality, pooled database for future studies.

The TF found that, even taking all published projects together, the full scope of the TRA Worker module has still not been covered in its entirety by the published external research, hence any generic judgment on the tool's overall performance cannot be substantiated. The data and information elements used by the researchers were found to be of variable quality and completeness. In addition, a sizable part of the measurement data stemmed from workplaces with substandard exposure control practices, for example in the form of exceedances of occupational exposure limits or demonstrated poor functioning of local exhaust systems.

Although much of the material was found to be contributing useful insights into the performance of the TRA Worker, some recurring errors in the application of the TRA were identified which led researchers to draw incorrect conclusions. These errors are highlighted in this report and associated improved user guidance is in preparation.

The most prominent projects had adopted the approach of matching a TRA prediction with every single measurement. This approach led to an unbalanced basis for their conclusions in the view of the TF, because these were based on both very small and larger datasets but not accounting for the size of the datasets, whereas the TRA prediction is intended to reflect the 75th percentile of a well-characterised exposure distribution for a particular occupational use scenario.

Using only those higher quality data sets in the published materials containing 6 or more samples, representing approximately two thirds of the original material, the TF then created a curated database of data sets of six measurements or more from workplace assessments with sufficiently detailed operating conditions and risk management measures to derive a TRA estimate and for which the 75th percentile was calculated from the measurements for comparison. The detailed results of the performance assessment of the TRA-Worker module based on comparison with the curated database are reported separately in a manuscript submitted for publication in the peer-reviewed scientific literature and which will be used to develop proposals for tool updates.

The conclusion reached by the TF from the systematic review of the published studies is that these have contributed significantly to an improved understanding of the performance of parts of the TRA-Worker module, particularly when seen together. The incomplete coverage of TRA Worker's full applicability domain prevents an overall assessment of the tool's performance and identification of all necessary tool update needs. Nevertheless, since the majority of the scenarios in the reviewed publications indicated that the TRA provides conservative estimates when comparing with measurement data from occupational settings, the TRA appears to remain a suitable screening tool for occupational inhalation exposure estimation in the preparation of REACH dossiers for chemical substances.

The observed inconsistencies in the application of TRA Worker tool in the reviewed publications is being used by ECETOC to update its user guidance.

INTRODUCTION

ECETOC developed version 2 of the Targeted Risk Assessment tool (ECETOC TRA) to support companies in preparing REACH registrations dossiers, as it generates screening level estimates of human and environmental exposures to classified chemical substances. The tool has been very widely used for that purpose since 2010. Because of its relative ease of use and transparent approach, the module dealing with occupational worker estimation ('TRA Worker') is also finding application in workflows to meet regulatory obligations under worker health protection legislation around the world. Following the first round of application for the 2010 registrations, experience gained and feedback received were used to create version 3.1 of the TRA (ECETOC. 2012).

The TRA is intended as a screening tool that produces moderate overestimates of human exposure to chemicals under normal circumstances of intended use or, where conditions of use are variable across a market segment, reasonable worst-case estimates. If in such a risk assessment workflow at the screening level, the estimated exposure is judged to be not adequately controlled, then the assessor is typically expected to resort to higher, more complex exposure estimation tools or measured data sets. A number of research groups have undertaken validation studies of the tool estimates for worker exposures and reported these in the literature. Typically, these studies have utilised measured workplace exposure data along with contextual information on the tasks and workplace settings and then constructed corresponding TRA estimates for comparison. While a wide variety of results have been published, the most prominent study is the ETEAM study coordinated by the German Federal Institute for Occupational Safety and Health (BAuA), where several exposure estimations tools were compared against 2098 exposure measurements.

As the tool owner, ECETOC is committed to maintain a watching brief on such validation studies and to review these research projects periodically, particularly if such research suggests deviations from expected performance of the TRA. If found necessary, tool users will be informed, and guidance will be adjusted.

As a series of validation study projects have been reported in the period of 2010 - 2020, ECETOC assembled an expert task force (TF) to review the presented results and conclusions, and propose any adjustments to tool settings or improvements to user guidance.

Consequently, the TF reviewed the different validation studies and projects in detail in view of the quality and quantity of used data, the coverage of TRA Worker's applicability domain, and the validity of the published research. An overview of the available material of the projects as well as an indication of the adopted review and analysis approach was already published (Urbanus et al., 2020).

The present report provides the detailed assessments of the individual projects and a descriptive collective analysis of some of the main features. The materials contained in the published projects and judged by the TF as being of sufficient quality were also used to create a new database, allowing an overall picture to examine common themes emerging from the individual projects, as well as remaining data gaps. In addition, the data allow to conclude on the validity of many of the TRA v3.1 exposure estimates based on current knowledge, and any insights regarding possible further improvements of the tool or indications where use guidance needs additional clarity. Together, this results in a higher quality evidence base to support confidently the continued use of the tool in regulatory application, notably REACH dossier preparation. The results of the analysis of this

database for long-term (full-shift) occupational inhalation exposures are the subject of a separate, companion manuscript.

As for all models, the outcome of ECETOC TRA is highly dependent on the selected input parameters by the assessor based on his experience and knowledge of the tool as well his degree of information on the scenario he wants to assess. Although TRA Worker is now well established as a worker exposure model, its working principle and applicability domain are perhaps not always fully understood either by its users or all those who seek to evaluate its performance. At its simplest, TRA Worker covers 25 different conditions of workplace use (termed PROCs) of chemicals and enables exposure estimates to be obtained for a range of different types of volatile liquids and solids. In total 261 estimates describe the 25 PROCs contained in the TRA Worker for full-shift inhalation exposure. Additionally, the tool can provide estimates for peak inhalation exposure (typically 15 minutes) and dermal exposure. The model was derived from the exposure estimates as the upper end of interquartile bands originally described in the UK HSE EASE model, and hence the 75thpercentile of the exposure distribution for a use group, which consequently provides a historical link to the regulatory decisions made in previous EU chemicals regimes. The TRA Worker continues to use the 75th percentile but additionally describes the exposure experiences that might be expected to arise when workers (and their employers) follow the basic conditions of exposure control implied by EU Directives 89/391 (safety and health of workers) and 98/24 (Chemical Agents).

Since the introduction of the TRA Worker, several scientific papers have been published that seek to examine the TRA Worker's performance in one way or another. However, many of the papers only examine a limited number of exposure situations determined by PROCs and rarely extend beyond one or two different substance types compared to the 6 different types covered by the TRA Worker, together with their differentiation between industrial and professional use. Even those papers that aim to be comprehensive reviews only examine a limited percentage of the possible exposure estimate permutations contained in the TRA Worker. The objective of the TF and the approach adopted were aimed at amalgamating the findings reported in the papers after reviewing these for correctness, and building on the evidence base to enhance confidence in the application of the tool for its intended purpose.

Table 1 lists those relevant papers published since the introduction of the TRA Worker tool, primarily version 3 in 2011.

Table 1. List of publication evaluating ECETOC TRA

Year	Title	Author	Reference
2009	Evaluation of COSHH essentials: methylene chloride, isopropanol, and acetone exposures in a small printing plant	Lee EG, Harper M, Bowen RB, Slaven J	Ann Occup Hyg. 2009 Jul;53(5):463-74
2010	Use of read-across and tiered exposure assessment in risk assessment under REACH – A case study on a phase-in substance	S.R. Vink, J. Mikkers, T. Bouwman, H. Marquart, E.D. Kroese	Regul Toxicol Pharmacol. 2010 Oct;58(1):64-71

2011	Evaluation of the COSHH Essentials model with a mixture of organic chemicals at a medium-sized paint producer	Lee EG, Slaven J, Bowen RB, Harper M	Ann Occup Hyg. 2011 Jan;55(1):16-29
2011	Evaluation of the TRA ECETOC model for inhalation workplace exposure to different organic solvents for selected process categories.	Kupczewska-Dobecka M, Czerczak S, Jakubowski M	Int J Occup Med Environ Health. 2011 Jun;24(2):208-17
2015	Application of predictive models for estimation of health care workers exposure to sevoflurane	Jankowska A, Czerczak S, Kucharska M, Wesołowski W, Maciaszek P, Kupczewska-Dobecka M	Int J Occup Saf Ergon. 2015;21(4):471-9
2016	Respiratory Health - Exposure Measurements and Modelling in the Fragrance and Flavour Industry	Angelini E, Camerini G, Diop M, Roche P, Rodi T, Schippa C, Thomas T	PLoS One. 2016 Feb 10;11(2):e0148769
2017	Evaluation of Tier One Exposure Assessment Models (ETEAM): Project Overview and Methods	Tischer M, Lamb J, Hesse S, van Tongeren M.	Ann Work Expo Health. 2017 Oct 1;61(8):911-920
2017	Validation of Lower Tier Exposure Tools Used for REACH: Comparison of Tools Estimates With Available Exposure Measurements	van Tongeren M, Lamb J, Cherrie JW, MacCalman L, Basinas I, Hesse S	Ann Work Expo Health. 2017 Oct 1;61(8):921-938
2017	Comparing REACH Chemical Safety Assessment information with practice-a case-study of polymethylmethacrylate (PMMA) in floor coating in The Netherlands	Spee T, Huizer D	Int J Hyg Environ Health. 2017 Oct;220(7):1190-1194
2017	Accuracy Evaluation of Three Modelling Tools for Occupational Exposure Assessment. Ann Work Expo Health	Spinazzè A, Lunghini F, Campagnolo D, Rovelli S, Locatelli M, Cattaneo A, Cavallo DM	Ann Work Expo Health. 2017 Apr 1;61(3):284-298
2017	Evaluation of the ECETOC TRA model for workplace inhalation exposure to ethylbenzene in Japan	Ishii S, Katagiri R, Kitamura K, Shimojima M, Wada T	J Chem Health Saf. 2017 Jan; 24(1):8-20
2018	Evaluation of risk assessment approaches of occupational chemical exposures based on models in comparison with measurements	Landberg HE, Westberg H, Tinnerberg H	Safety Science. 2018;109:412-420
2019	Comparison of Quantitative Exposure Models for Occupational Exposure to Organic Solvents in Korea	Lee S, Lee K, Kim H	Ann Work Expo Health. 2019 Feb 16;63(2):197-217
2019	Evaluation of Exposure Assessment Tools under REACH: Part I-Tier 1 Tools	Lee EG, Lamb J, Savic N, Basinas I, Gasic B, Jung C, Kashon ML, Kim J, Tischer M, van Tongeren M, Vernez D, Harper M.	Ann Work Expo Health. 2019 Feb 16;63(2):218-229

METHODOLOGY OF THE SYSTEMATIC REVIEW

It is noted that no formal standard or standardized methodology exists for the validation of exposure models in the arena of regulatory occupational exposure assessment. Therefore, the TF used a systematic approach to select and review the relevant publications and to assess the published and communicated data provided by the authors. Moreover, the workflow and underlying criteria and the outcome of the assessment are documented in the present report.

Review of measurement data and TRA estimates

The key element in risk assessment and thus in this presented review approach are the underlying measurement data. All measurement data available from the validation studies were therefore verified and assessed using state-of-the-art approaches from the field of occupational hygiene for the characterisation of an exposure profile of a similar exposure group (SEG) in a particular location or situation. Consequently, reported situation/tasks covering an individual SEG with less than six individual measurements were not regarded as valid for a detailed analysis as a lower number of measurements would not reflect the existing workplace exposure with sufficient confidence. The applicability of the data was additionally verified by assessing the statistical figures from the data, e.g., geometric mean (GM), geometric standard deviation (GSD), which were calculated in cases they were not provided by the original reports. Using the GM and the GSD, 75th percentiles were calculated.

To evaluate the outcome of the different reports, the TRA Worker values in the publications and their input parameters used were evaluated and the TRA Worker values were verified by two members of the TF based on the information on substance, its properties, use and scenario settings extracted from the original survey reports to the extent possible.

Quality criteria used in study review

The systematic approach to select and review the relevant publications and to assess the published and communicated data provided by the authors was ensured by application of a quality scoring scheme (**Table 2**), which is based on the adequacy categorisation from Franken et al. (2020) resulting from the CEFIC Long-range research initiative project B-19.

Critically reviewing each study and application of a quality score also ensured, that the focus of the review by the TF was not only focusing on the measurement values and TRA estimates but also sought to extract all usable data from the publications that could support a transparent and comprehensive re-analysis of TRA performance by the TF.

Table 2. Criteria for evaluating and assigning reliability scores to exposure data.

Score	Adequacy assignment	General criteria	Examples
1	Adequate without restriction	Data of good technical and contextual adequacy is available	Completely documented measurement studies performed with validated measurement methods (published by renowned institutes) and with all information on each data point in annexes. Full and unambiguous data to select TRA input parameter settings.
2	Adequate with restrictions	Data of at least acceptable technical adequacy and information on contextual adequacy is available or can be evaluated based on the expert judgement and reasonable assumptions	Well documented measurement studies, performed with validated measurement methods (published by renowned institutes) or methods that resemble such methods closely and for which sufficient information on validity, accuracy, precision, and boundaries is available; sufficient description of context to either directly know the values for relevant factors or to make informed and justified expert judgement on a number of factors; activities may need to be categorized, based on descriptions, assumptions on scale and setting may need to be based on expert judgement, data on substance and product characteristics may need to be found in other sources or estimated.
3	Useful as supporting evidence	Data of limited technical adequacy	Measurements with undocumented sampling techniques; statistical summaries of data (vapour pressure of measured substances, concentrations of substances in products or largely different settings) that are not stratified; studies in which only the jobs of sampled workers are indicated without any indication of activities being sampled.
4	Not adequate	Data for which the technical adequacy cannot be evaluated or that are described too insufficiently to allow evaluation of several factors related to contextual adequacy	S Studies in which the sampling method is not described (e.g. no reporting of whether respirable dust, inhalable dust or total dust has been measured); the method for measuring solid/liquid aerosols is not described; studies in which no information is given on e.g. the use or no use of localized control measures, the concentration of measured substances in articles, the duration of activities within shift-based measurements, the containment of sources, etc.

FINDINGS

Coverage of the TRA Worker's applicability domain by the studies

Detailed descriptions, using a standardised template, of the reviewed materials and observations by the ECETOC Task Force are provided in **APPENDIX A**. These include any underlying original reports, retrieved by the TF, of measurement surveys in work environments that were used by the researchers in the publications.

The TRA Worker input domain contains multiple iterations of the combination based on the different parameters substance physical state (liquid or solid), volatility or dustiness (three bands), concentration in a product (four bands), exposure duration (four bands), presence of local exhaust ventilation (yes/no) and room ventilation (basic, good, enhanced), respectively. For a comprehensive assessment of the overall tool performance, many data sets covering all possible combinations are therefore needed.

In view of the possible iterations, it was expected that not all possibilities were covered by the available reports. However, surprisingly even for scenarios regarded as common activities across multiple industries, e.g., PROC 3 (closed batch operations) or 8a (transfer using non-dedicated equipment), only a limited coverage, i.e., number of data sets, by the published reports was found. Not considering further differentiation according to substance state (liquid/solid), volatility or dustiness levels, and other tool input parameters, the studies' coverage of the different PROC reviewed is shown in table 3.

Table 3. List of PROCs covered by the studies

Data set coverage	PROC
No data sets with N $\geq$ 6	1, 6, 12, 16, 17, 18, 20, 21, 22
Few data sets with N $\geq$ 6	2, 3, 4, 5, 8a, 9, 11, 13, 14, 19, 23, 24, 25
More substantive number of data sets with N $\geq$ 6	7, 8b, 10, 15

Quality and quantity of published exposure information

The key elements in the correct use of an exposure modelling tool like TRA are the availability of information on substance and use conditions and their correct translation into the available input parameters of the tool.

Unfortunately, the review of the different study reports revealed that the quality and quantity of published data used to evaluate TRA Worker varied substantially. Consequently, the published exposure estimates claimed to be calculated with TRA Worker could in some cases not be verified or even not followed how they had been generated by the study authors. The review of the studies also suggests that not all study authors have consistently used or understood TRA correctly.

While in some papers the input parameters chosen for the TRA were reported, other authors provide only a generic name of the covered scenario. The same variability was true for the reported measurement data and statistical data used for comparison with TRA values. Where in case of the ETEAM database, the original report

provided single measurement values, only the mean values with standard deviation were published in some other reports.

In addition, many instances were identified where TRA Worker estimates had been compared to individual (rather than group) exposure measurements or for different percentiles than the 75th or when exposure conditions reflect 'worst case' conditions and not those expected from the implementation of basic health and safety rules and controls. PROCs have also been incorrectly allocated or categories of volatility or dustiness incorrectly chosen.

The TF applied the four-band rating scheme during the review process to judge the reported data and to account for the variability in their quality and quantity.

Based on these ratings, 129 (93%) of the identified scenarios with data sets with N $\geq$ 6 for full-shift inhalation exposure were found to be acceptable, while 10 scenarios showed inadequate data quality (score of 4 for either the measurements or the inputs for TRA calculation) and were thus not usable for any evaluation. In all these cases, the reason of low quality was a lack of information regarding the measurement data used in the study or lack of information on the task properties or even a combination of both deficits.

Available evidence of tool performance derived from data sets with six or more measurements (N ≥ 6)

The available datasets with N ≥ 6 and sufficient data quality allowed the calculation of the P75 values to compare them with the TRA Worker values. Whilst not all PROCs and parameter combinations were covered by the available data sets, the comparison with the corresponding TRA Worker values revealed that TRA Worker calculates in general higher exposure estimates than the available measurement datasets. Full details are contained in the companion manuscript.

Frequently observed TRA coding issues

PROC assignment

The correct assignment of the PROC is fundamental for a correct exposure estimation by TRA Worker. A wrong assignment will lead to a false exposure estimation because the base estimates linked to the PROCs differ in some cases substantially due to the different tasks and associated practices and workplace settings with different exposure potential.

The review of the studies revealed that in 25% of the identified scenarios with data sets with N ≥ 6 measurements an incorrect PROC was assigned by the authors. In addition, in 7 cases (5%) the incorrect setting of use was assigned, meaning the "industrial" setting was assigned to a professional setting or vice versa.

All these findings were double-checked by two members of the TF and corrected in the further review process to allow a proper calculation of the exposure estimate with TRA.

Ventilation/local exhaust ventilation (LEV)

Ventilation is one of the fundamental technical control measures to reduce the amount of breathable substances in the workplace air. Therefore, TRA Worker includes the ability to apply good general ventilation or enhanced general ventilation and also the choice of differing levels of LEV effectiveness to the various activities described by the PROCs. **Appendix C** discusses the types of LEV that the TF considers appropriate for the various PROCs.

It has become apparent in review of the published studies, that several authors have not properly considered these underlying assumptions, thus encountered forms of ventilation that are being used in the workplace that are significantly less effective than those that the TRA Worker would anticipate might responsibly be being applied in the situation. For example, the use of movable 'elephant trunk' extraction systems when bulk weighing hazardous powders or the use of simple slot ventilation systems during material transfers, could be regarded as not appropriate as established guidance would indicate the need for much better forms of LEV in such circumstances.

It was also identified during the review of the studies, that both good general ventilation and enhanced general ventilation were frequently inappropriately applied to derive TRA Worker estimates. Often, the ventilation described in the article did not equate to that defined as being associated with the good or enhanced general ventilation standard i.e., the expectation that air exchange rate of air changes per hour can consistently be obtained (3-5 air changes per hour for good general ventilation and ≥ 5 air changes per hour for enhanced general ventilation). For example, the presence of an open window or door is unlikely to equate to good general ventilation. The same holds true for the presence of single axial fan in a wall, which is most unlikely to be sufficient to equate to enhanced general ventilation.

In addition to these incorrect assignments, for some studies the type and efficiency of ventilation and enhanced general ventilation and local exhaust ventilation could not be explicitly confirmed during the review process, leading to a lower quality score.

Duration modifier

The TRA Worker model can provide an exposure estimate as an 8-hour time-weighted average value for the activity (or PROC) selected for comparison with a reference value for human health such as a Derived No-Effect Level (DNEL). The underlying assumption is that the activity continues for the duration of the full shift. For many activities, however, their duration is significantly less than 8 hours. In such circumstances, the 'Duration' modifier needs to be applied to obtain a more realistic estimate for the full-shift exposure, because otherwise the TRA exposure estimate would be an overestimate of the true 8-hour exposure. The related factors are shown in Table 4. The 'Duration' modifier works to average out the exposure over the full workday, and it applies to activities shorter than 4 hours.

Table 4: Duration Factors applied to TRA output

Duration of activity	Exposure modifying factor
> 4 hours	1
1 - 4 hours	0.6
15 mins - 1 hour	0.2
< 15 mins	0.1

The review of the studies revealed that in some studies the duration modifier has been applied incorrectly when comparing measurement results with a TRA Worker estimate. For example, one study focused on specific activities and took measurements with a relatively short duration, typically 15 - 45 minutes, but the authors did not calculate the 8-hour time-weighted average value. At the same time, however, they included the duration factor of 0.2 in their TRA estimate. Thus, their measurements were clearly task-based but their TRA estimates represented an 8-hour period and included the assumption that the exposure task only would last 15 - 60 minutes per shift leading to a 5-fold reduction of their TRA estimate. In this case, a correct comparison between measurement results and TRA Worker estimate would have been to directly compare the task-based measurement data with the TRA Worker estimate without application of the duration modifier.

CREATION OF A CURATED DATABASE FOR FURTHER VALIDATION STUDIES

Higher quality data sets of studies with ≥ 6 measurement and sufficiently detailed operating conditions and risk management measures information were not only extracted by the TF from the published studies to examine how the validation study was conducted, but also used to create a new database for further future validation studies.

The guiding principles for creation of this new database needed to account for the validation objective, which is fundamentally different from the tool application objective in creating a chemical safety assessment. The screening tool status implies that the outputs by a calculation tool are conservative. In order to produce a conservative tool for calculation of exposure levels the coding of circumstances needs to account for obvious uncertainties like incomplete information or variable conditions, for example room ventilation, across a sector of use, by adopting scores that do not produce 'false positive' estimates. Any validation of a screening tool by means of comparison with sets of measured data, on the other hand, implies that the selected inputs are conservative to avoid 'false negative' values. As a specific example, for one scenario the indication was that the substance being assessed was present at around 5% in a product, which falls in between the two concentration bands of the TRA 1 – 5% and 5 – 25%. For risk assessment purposes, one therefore should adopt the 5 – 25% band to calculate the screening level estimate of exposure. For tool validation purposes on the other hand, one should select 1 – 5%.

Following these considerations, the TF reviewed the available information on operating conditions and risk management measures and revised them if deemed necessary and prepared a TRA Worker estimate for comparison with the 75th percentile calculated from published measurement data.

DISCUSSION

The conducted critical review of published studies on the performance of TRA Worker revealed that the full scope of the TRA Worker module has still not been covered in its entirety. Only a limited number of PROCs were used by the published studies and more importantly, only a small number of the combination of PROCs and parameter settings, i.e., LEV or task duration, were compared with TRA estimations. In many of these situations 6 or more measurement results were not available, and even in some cases only a single measurement result was used. To allow a meaningful analysis, such datasets with less than 6 individual measurements were not regarded as valid for a detailed analysis and hence were excluded by the TF. Although the ECETOC systematic review therefore set aside a considerable number of the situations included in the original published research, the part that has been taken forward for detailed review and reanalysis is considered more reliable since it included only datasets reflecting the existing workplace exposure with sufficient confidence. For example, the ETEAM original database contained 1356 individual measurement results for vapour exposure from volatile liquids, whereas the ETEAM scenarios assessed as valid and analysed in detail by the TF contained 973 individual measurement results or about 70% of the original material (see also **Table 6** in **Appendix A2**). The creation of a database by the TF was therefore necessary to allow the collection and evaluation and potential correction of TRA Worker parameters of the published study data by the members of the TF. The transparent analysis and the database can thus further be used to examine the weight-of-evidence for any quantitative tool improvements needed to address observed low conservatism and for additional future validation studies of TRA Worker.

The detailed review of the studies also revealed that most of them followed the approach of matching individual measurement results with a TRA Worker estimate despite the fact that TRA Worker is providing the 75th percentile of an exposure distribution. One of the implications of the approach used by the studies is that specific workplaces with many measurement results have more weight in the overall picture than comparable ones with few results. This simple, descriptive approach may therefore produce skewed results and not be the best suited for assessing tool performance or identifying any tool improvement needs. Additionally, such qualitative conclusions would remain relatively uninformative, as the degree of over- or underestimation, and therefore whether it mattered, would be obscured. Occupational exposure levels are well known to vary over time, e.g., from day to day and between individual workers, but can be characterized using descriptive statistical parameters such as the geometric mean and standard deviation, as they are usually lognormally distributed. Notably, the TRA Worker was never intended to predict the actual exposure level on a single day or for a single individual worker but rather to provide the typical high-end of the exposure distribution under a particular set of circumstances. Because the tool was developed from EASE which gave inter-quartile band predictions and ECETOC took the high end of those bands, as chemical risk assessment requires a point estimate for exposure, the TRA Worker predicts a value that is best interpreted as the 75th percentile of the distribution of exposure levels. From the occupational hygiene scientific literature, it is known (and now formalized in the standard EN 689:2018) that in order to define the shape of the exposure distribution for a given set of circumstances, six or more measurement results are typically needed, although there is a decreasing return in improved precision once data sets exceed 9-12 measurements. With that concept in mind the TF focused its review effort on data sets of six or more as being the most informative to assess tool performance based on calculated 75th percentile values for each data set, independent of data set size.

The review also revealed that the studies consequently quantified the percentage of measurement results above and below the TRA Worker estimate to evaluate and rate the performance of TRA Worker. For example, the ETEAM set a cut-off of not more than 10% of underestimations as an indication of 'high conservatism' of the tool; between 11 and 25% indicating 'medium conservatism'; and more than 25% underestimations indicating 'low conservatism'. While there is general consensus that conservatism is an important requirement for a screening level tool such as the TRA Worker which has its place in an efficient workflow for the creation of exposure scenarios in a REACH dossier, there are no agreed standards for the interpretation of what might constitute low, medium or high conservatism.

In summary, the detailed analysis of the peer-reviewed scientific literature on the validation of TRA Worker revealed that there is an incomplete coverage by the studies of TRA Worker's overall applicability domain which prevents an overall assessment of the tool's performance an identification of the needs for a comprehensive tool update. However, for the majority of the valid scenarios studied the TRA appears to be conservative and hence suitable as a screening tool. In order to address some of the more prominent application errors, additional guidance is provided in **APPENDIX B** (on the distinction of industrial and professional workers) and in **APPENDIX C** (which discusses local exhaust ventilation configuration in relation to PROCs).

The curated database created by the TF during the project allows to follow the data analysis performed as well as the conclusion on the validity of data and its reasoning. The database therefore is a useful data source to examine the weight-of-evidence for any quantitative tool improvements needed to address observed low conservatism and for further future validation studies of TRA.

APPENDIX A: DETAILED REVIEW OF VALIDATION STUDIES AND THEIR DATA SOURCES

A1 Vink

CRITERIA	REVIEW
Paper/Report reference	Use of read-across and tiered exposure assessment in risk assessment under REACH – A case study on a phase-in substance S.R. Vink, J. Mikkers, T. Bouwman, H. Marquart, E.D. Kroese. Regul. Tox. & Pharmacol., vol 58 (2010) 64-71
Scope of the study	
• Short description of objective of the study and study design	A read-across as non-testing strategy was combined with a tiered exposure assessment for the risk characterisation of 1-methoxypropan-2-ol (PGME). Read-across from the selected source substances provided data which were comparable with experimental data available for target substance PGME.
• Type of study	This case study investigates the use of read across and tiered exposure assessment for risk assessment under REACH. It is not a validation study on the ECETOC TRA tool (or other tools).
• PROC coverage	PROC 8a, 11 and 13
• Relevant information for evaluation and improvement of TRA tool?	No. No direct comparison is made between exposure estimates of the TRA Worker and available measurement data. The TRA Worker estimates for scenarios on paint spraying (with 15 and 30 % of PGME in the product and with and without LEV) are compared with the 90th percentile of 745 inhalation exposure measurements (with and without LEV combined) of PGME during spraying with various techniques from the MEGA database (BAUA). All data were converted to 8hr averages. Secondly, the TRA Worker version 2 tool was used.
Conclusions	
• Conclusion on suitability of paper for TRA evaluation	Not suitable, as no direct comparison is made between distinct exposure scenario for which measured data are available and TRA Worker estimates.
• Any other remarks	The paper is not an evaluation study. In the paper no direct comparison is made between measurements and TRA Worker estimates.

A2 ETEAM

The project popularly known as ETEAM was initiated by the German Federal Agency for Occupational Health and Safety (BAuA) in 2012 (Tischer et al., 2017). The project aimed to compare measured exposure data against

the modelled estimates from the commonly encountered REACH Tier 1 worker models (TRA Worker, MEASE, Stoffenmanager® and EMKG). ECETOC participated in the Advisory Board to the project. Although the project is the largest of its type, it has been hampered by the difficulties to identify large numbers of representative exposure measurements for the range of situations demanded by REACH.

To achieve its aims, the researchers set out to create a database of measured data against which the predictions of the various models being evaluated could be compared. Data were submitted by 11 major institutions, including those from the US. Several thousand sets of measured data were offered by these institutions to the ETEAM researchers. In order to ensure that only data of a high quality were included in the database, the researchers developed quality criteria which the data were required to meet (and which relate both to the integrity of the measurements as well as supporting contextual data that enable such data to be interpreted). However, the consequence of applying the criteria to the data were that only a small fraction of the data submitted were deemed acceptable for inclusion in the database.

Table 5 below is taken from the ETEAM sub-study Report on the External Validation Exercise (Lamb et al., 2015) and summarises the distribution of the data that were accepted into the database.

Table 5: Individual measurement data by allocated PROC code

	PROC codes																		
Exposure category	3	4	5	7	8a	8b	9	10	11	13	14	15	19	21	22	23	24	25	Total
Non-volatile liquids[1)]	0	0	0	7	1	0	0	26	262	10	2	4	4	0	0	0	0	0	316
Volatile liquids[2)]	4	59	60	195	70	250	76	245	41	130	178	1	47	0	0	0	0	0	1356
Metal abrasion	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	87	0	87
Metal processing	0	0	0	0	0	0	0	0	0	0	0	0	0	0	16	14	0	41	71
Powder handling	0	1	63	8	74	54	30	0	0	0	24	0	0	0	0	0	0	0	254
Wood processing	0	0	0	0	0	0	0	0	0	0	0	0	0	14	0	0	0	0	14
Total	4	60	123	210	145	304	106	271	303	140	204	5	51	14	16	14	87	41	2098

[1)] non-volatile liquids are defined as liquids with a vapour pressure (at room temperature) ≤10 Pa.
[2)] volatile liquids are defined as liquids with a vapour pressure (at room temperature) >10 Pa.

The expectations for any exposure model are that its predictions are reliable across a full range of substance types (i.e. different physico-chemical forms such as dusts, gases and vapours), as well as the routes and forms of exposure that the use of such substances can be expected to result in (for example, inhalation and dermal exposures and exposures to dusts, aerosols and vapours/gases). A further expectation is that the models might reasonably be expected to account for the commonly encountered OCs and RMMs, as well as whether the substance is encountered in the pure form or as part of a mixture. Table 5, however, clearly shows that not only are several of the key PROCs not represented in the database, but that the database is dominated by measurements of volatile liquids and that for many PROCs no or few data exist against which any comparison might be made.

Because complex analyses require a lot of data (for example, covering the range of volatilities and use characteristics covered by exposure models), the ETEAM researchers chose to assume data homogeneity from across the 11 contributing institutions and to pool exposure measurements for common PROCs in order to calculate statistics for the grouped data. No prior testing of goodness of fit was undertaken. Unfortunately, this has resulted in high GSDs being associated with many of the analyses and these factors serve to limit the extent to which any reliable conclusion can be drawn from the analyses.

In 2016, upon request, an ad-hoc TF of ECETOC obtained access to the ETEAM database and conducted a first, partial re-analysis with focus on those PROCs where the ETEAM results suggested underestimation of exposure by the TRA Worker.
In all, the ETEAM database contained 548 entries coded by an ESID number with individual measurement data, of which 454 related to inhalation exposure, with the remaining 94 relating to dermal exposures. The 548 entries contained a total of 2543 samples. The database also contained 80 aggregate data sets.
The 2016 ECETOC TF selected 337 ESID entries (all inhalation data) by removing scenarios outside of the TRA domain, i.e., plant protection and biocide products (chlorpyrifos, glyphosate), solids-in-liquids (e.g., cuprous oxide in anti-fouling paint), wood dust and a series of metals data.

The partial re-analysis was presented at the 2016 conference of ISES and was included in Appendix 2 of ECETOC TR 131. In the present project this re-analysis has been progressed further, in particular by including data contained in the ETEAM database that was not originally included in the original ETEAM analyses and through a complete and closer scrutiny of the underlying source data (an undocumented randomised quality assurance being applied in the ETEAM study). In order to avoid the issues arising from data pooling, ECETOC identified 65 datasets within the ETEAM database that contained 6 or more samples from a single workplace and from which reliable statistical descriptors could be calculated (in particular the 75th percentile, as the TRA Worker predicts this value for the working group). A summary of the ETEAM data used in this re-analysis is shown in the following table 6.

Table 6: ETEAM data used in the ECETOC re-analysis

ETEAM data source	Number of entries in original database	Number of samples in original database	Min and max number of data points per entry	Number of entries with N > 6 measured data for a Similar Exposure Group	Number of samples for entries with N > 6 measured data
ART	33	555	4 - 88	28	515
BAuA	109	110	1 – 2	1	14*
NIOSH	53	645	1 – 146	26	576
SECO (SUVA)	124	326	1 - 17	10	100
UK HSE/HSL	8	20	1 - 5	0	0
Lund University	7	17	1 - 4	0	0
TOTAL		1673		65	1205

* Measurement data for ethanol from a number of optician's workshops were combined into one SEG data set.

A2.1 ART

In the ETEAM database 33 datasets were identified that originate from the database used by IOM/TNO/HSL Consortium for the validation of ART (Advanced REACH Tool), a CEFIC LRI funded project. For 25 of these

datasets the ETEAM calculated an ECETOC TRA v3 estimate. 15 datasets (8h- TWA measurements) were identified with N ≥ 6 samples (11 datasets for liquids and 4 datasets for solids). 4 datasets contained less than 6 samples, 6 datasets contained short-term measurements. Several of these datasets had been provided to the Consortium by companies represented in the TF. For around half of these datasets, additional information on activity and operational conditions could be retrieved. The datasets cover a variety of industrial and professional working situations: graffiti removal, glassware cleaning, brooming, draining activities (car recycling), paint spraying, lamination of articles, tabletting/weighing (pharmaceutical industry), unloading of solids and a number of operations in a gasoline plant (loading of tank-trucks, filling of drums, refuelling, routine plant inspections). The table below describes the ETEAM dataset originating from the ART project and how these was used for the ETEAM project.

CRITERIA	**REVIEW**
Paper/Report reference	Validation of Lower Tier Exposure Tools Used for REACH: Comparison of Tools Estimates with Available Exposure Measurements (https://academic.oup.com/annweh/article/61/8/921/3978978). Van Tongeren M, Lamb J, Cherrie JW, MacCalman L, Basinas I, Hesse S. Ann Work Exp Health 2017; 61(8): 921-938 Ann Work Exp Health 2017; 61(8): 921-938
Scope of the study	
• Short description of objective of the study and study design	The ART data are included in the database of the ETEAM study (refer to A2).
• Type of study	Retrospective review of measured data compared to constructed TRA Worker values for individual data points for multiple PROCs
• PROC coverage	ART-datasets assigned to: PROC 2, 8a, 8b, 9, 10, 11, 13, 14, 19
• Relevant information for evaluation and improvement of TRA tool?	In the ETEAM study single measurements were compared to TRA Worker estimates. The TRA Worker provides a P75 exposure estimation. It is more relevant to compare a dataset with a number of results for the same activity (PROC) and the measured P75 with the TRA Worker predicted exposure (P75).
Scenario description	
• Sufficient contextual information to assign PROC, setting, volatility?	In the ETEAM paper no reference is made to the original surveys in which the data are collected. However, as around half of these datasets originate from companies represented in the TF, for these datasets additional information on activity and operational conditions could be retrieved. Furthermore, the information in the database itself in general is of sufficient quality to assign PROC, setting and volatility.
• Sufficient contextual information for selection of exposure modifier settings?	See answer above.

• Is contextual information available to reconstruct the assignments made by the researchers?	See answer above.
ECETOC TRA domain	
• Are scenarios within the TRA domain?	For 25 of the 33 datasets in the ETEAM database, the ETEAM calculated an ECETOC TRA v3 estimate. All these 25 scenarios are within the TRA Worker domain.
Assignment of PROCs and OC/RMMs	
• Has a team approach and a process for assignment been followed?	The original paper was based on experienced exposure scientists reviewing the data and agreeing on the parameters to be used for creating the exposure model.
• Has the assignment of PROCs been done correctly?	For 11 of the 15 TWA-8hr datasets the TF agreed with the assignment by the ETEAM. In general, the PROC assignment by the ETEAM was done correctly.
• Has the assignment of ind./prof. setting been done correctly?	The assignment of the setting by ETEAM and ECETOC team was identical in 14 out of the 15 datasets.
• Is the selected volatility band correct?	Yes. The vapour pressure for benzene is at the border between medium and high volatility. For tool validation purposes, the ECETOC team agreed with the ETEAM selection of medium fugacity.
• Has the assignment of exposure modifying factors been done correct?	Only for one dataset the TF assigned another exposure modifying factor than the ETEAM (e.g. LEV yes instead of no). In this situation a vapour recovery system was present during loading activities outdoors. As TRA Worker does not allow the combination LEV + outdoors, theoretically the assignment by the ETEAM of no LEV is correct. For conservative reasons the TF deviated from this rule.
Exposure measurements	
• Sampling & analytical methods according to accepted standards?	Yes. Most of these datasets originate from companies represented in the TF. Sufficient information on sampling and analytical methods is available to state that this has been done to accepted standards.
• Have personal measurements in breathing zone been taken?	Yes.
• If not, is sufficient explanation provided on representativity of measurements?	N/A

• 8hr TWA exposure: have full shift samples been taken?	For all 15 TWA-8hr datasets, the samples taken are intended to be representative of a full shift. Note that the database also contained 6 datasets with short-term measurements.
• If not, is sufficient explanation provided on representativity of measurements?	N/A
• Short term exposure: have 15-minute samples been taken?	As stated above, the database also contained 6 datasets with short-term measurements. These have not yet been analysed.
• If not, is sufficient explanation provided on representativity of measurements?	N/A
Comparison of estimated with measured exposure	
• Is the measured exposure based on newly collected data, data from old surveys or simulated data?	All ART data come from old surveys.
• For data from old surveys or simulated data, has sufficient justification been provided whether these measurements are representative for the scenario under investigation?	No. However, based on the information that is available, it is reasonable to assume that the data are representative for the scenarios under investigation.
• How many measurements have been carried out per scenario?	PROC 2: 19 PROC 8a: 7 Proc 8b: 29, 8, 24, 23, 88, 23, 36 PROC 9: 7 PROC 10: 9 PROC 11: 21 PROC 13: 7 PROC 14: 11 PROC 19: 8
• For datasets representative for a unique exposure	Not in the original paper. The authors used single measurements for direct comparison with the TRA Worker predicted exposure (representing the P75).

scenario, has the P75 been calculated and compared with the TRA estimate?	The TRA worker TF used data that had 6 or more measurements. The P75 was calculated and compared with the TRA Worker predicted exposure (representing the P75).
• Is sufficient information available or can this be obtained to reconstruct the data-analysis?	Yes, based in the information in the database plus additional information from the companies that provided the data to the database.
Conclusions	
• Conclusion on suitability of paper for TRA evaluation	The original paper, addressing the ART datasets next to many other datasets is suitable for TRA Worker evaluation.
• Any other remarks	N/A

A2.2 BAuA

The German Federal Agency for Occupational Health and Safety (BAuA) provided exposure measurements to the ETEAM study contributing 109 datasets in its database from a series of field surveys conducted in German workplaces by occupational hygiene agencies. Many of them originated from campaigns that had targeted a particular sector, such as the furniture manufacturing industry where solvent exposures in coating applications were measured. Other sectors included among others screen printing, textile and plastic recycling. In order to address confidentiality restrictions imposed by the data owners, the ETEAM database listed the data in anonymised format and all but one consisting of a single measurement, hence making it impossible to understand which data originated from the same workplace. Based on the descriptions provided it was possible to group some of the data for a specific activity from similar workplaces, in particular a set from opticians' workshops and for which the survey report (F1660) was shared with ECETOC by BAuA.

A2.3 NIOSH

The US National Institute for Occupational Safety and Health (NIOSH) contributed 53 datasets in the ETEAM database of individual measurements with the number of measurements per entry varying from 1 to 146. Of these, 26 datasets were found to have N $\geq$ 6. Their principal source were Health Hazard Evaluation reports, an activity where industrial hygienists of NIOSH investigate exposure levels in specific plants in the US. These reports are publicly available and often contain a good level of detail on the conditions of use, including improvement recommendations by the industrial hygienists and hence pointing at observed deficiencies in the investigated workplaces.

CRITERIA	REVIEW
Paper/Report reference	Validation of Lower tier Exposure Tools Used for REACH: comparison of Tools Estimates With Available Exposure Measurements

	Van Tongeren M, Lamb J, Cherrie JW, MacCalman L, Basinas I, Hesse S. Ann Work Exp Health 2017; 61(8): 921-938
Scope of the study	
• Short description of objective of the study and study design	Collection of measurement data from various institutions, creation of a database. Comparison of the measurement results with lower tier exposure models to determine if the exposure models are sufficiently conservative in exposure predictions
• Type of study	Retrospective review of measured data compared to constructed TRA Worker values for individual data points for multiple PROCS
• Note	The article does not provide information to the original source data. The authors have constructed a ratio of the measured concentration / constructed TRA Worker values for individual measurements. No consideration for the data from SEGs was considered. Particularly, NIOSH reports can address situations of workplaces in poor control (request for intervention) and correspondingly the measurement results may not align with the TRA Worker construction.
• Summary of original data sources	NIOSH reports: A review of the original datasets was possible when searching the NIOSH Health Hazard Evaluation site https://www.cdc.gov/niosh/hhe/default.html References 1 and 2 are original papers in the Annals of Work Exposure and Health (previously Annals of Occupational Hygiene). *(1) Evaluation of COSHH essentials model with a mixture of organic chemicals at a medium sized paint producer Lee, Slaven, Bowen and Harper Annal 30 November 2010 (published 2011)* The Control of Substances Hazardous to Health (COSHH) Essentials model was evaluated using full-shift exposure measurements of five chemical components in a mixture [acetone, ethylbenzene, methyl ethyl ketone, toluene, and xylenes] at a medium-sized plant producing paint materials. Two tasks, batch-making and bucket-washing, were examined. *(2) Evaluation of COSHH essentials: Methylene chloride, Isopropanol and acetone exposures in a small printing plant Lee, Harper, Bowen, Slaven Annal 12 May 2009* This study evaluated the Control of Substances Hazardous to Health (COSHH) Essentials model for short-term task-based exposures and full-shift exposures using measured concentrations of three volatile organic chemicals at a small printing plant *(3) HETA 96-0145-2684 Especially for you Coloma Wisconsin Kevin Hanly, Gregory Kinnes* A Health Hazard Evaluation (HHE) was conducted on April 14–16, 1997, by the National Institute for Occupational Safety and Health (NIOSH) at Especially for You, Limited, located in Coloma, Wisconsin. This HHE was conducted following a confidential employee request regarding styrene vapor and sanding dust exposure in the Resin and Finishing department. The company manufactures a variety of home decorative

	items including plastic articles by curing polyester resin in preformed molds. *(4) HETA 95-0209-2515 Parson Footwear, Parsons, West Virginia July 1995. Steve Berardinelli, Brad Husberg* On April 7, 1995, the National Institute for Occupational Safety and Health (NIOSH) received a confidential employee request for a health hazard evaluation (HHE) at the Parsons Footwear plant in Parsons, West Virginia. The request stated that employees in the packing department were experiencing sinus problems, headaches, sore throats, hoarseness, dizziness, nausea, lightheadedness, and stomach problems. Employees began experiencing these symptoms in December 1994, after a new formulation of socklining glue was introduced in the packing department. *(5) Health Hazard Evaluation Report 94-0220-2526 Exxon Company USA Houston Texas September 1995 Calvin Cook Ronald Kovein* During November 30 through December 2, 1994, the National Institute for Occupational Safety and Health (NIOSH) conducted a health hazard evaluation (HHE) at two Exxon service stations located in the greater Newark, New Jersey area. NIOSH investigators performed environmental monitoring to assess service station attendants' exposures to oxygenated gasoline that contained methyl tert–butyl ether (MtBE), which is an oxygenating compound blended with unleaded gasoline to help reduce vehicle emissions. Environmental measurements were made using two methods: (1) conventional air sampling (NIOSH Method 1615) and (2) video exposure monitoring with the use of real–time instrumentation. *(6) HETA 99-0163-2771 Superior Drywall Millsboro Delaware Joshua Harney, Elena Page, John McKernan* The National Institute for Occupational Safety and Health (NIOSH) received a confidential Health Hazard Evaluation (HHE) request in March 1999, from employees of Superior Drywall, Millsboro, Deleware. The request named drywall hanging as a job of concern for possible exposure to vapors from drywall adhesive. On May 19-20, 1999, NIOSH investigators conducted a site visit at Superior Drywall operations. Environmental monitoring was conducted at different work sites for organic vapors evolving from drywall adhesive. The NIOSH physician interviewed drywall hangers and reviewed the Occupational Safety and Health Administration (OSHA) Log and Summary of Occupational Injuries and Illnesses (Form 200) for the years 1997 and 1998. *(7) HETA 2004-0372-3054 Entek International, Lebanon, Oregon Angela Bauman, Elena Page, Charles Mueller, Greg Burr, Edward Hitchcock* On August 24, 2004, NIOSH received a technical assistance request from the Oregon Department of Human Services concerning dementia and neurologic dysfunction among workers exposed to TCE at Entek International in Lebanon, Oregon. In an initial NIOSH site visit in November 2004, NIOSH investigators found GA air concentrations of TCE ranging from 20 to 40 ppm in production areas. A medical questionnaire revealed that 48% of Entek International workers

	reported feeling high or lightheaded while at work in the last 30 days, compared to 19% of non-TCEexposed workers at an adjacent facility, Entek Manufacturing. *(8) HETA 2000-0410-2891 STN Cushion Company, Thomasville, North Carolina Josh Harney, Jeffrey Hess, Doug Trout* On August 28, 2000, the National Institute for Occupational Safety and Health (NIOSH) received a confidential request for a health hazard evaluation (HHE) at STN Cushion Company (STN) in Thomasville, North Carolina. The request was submitted by employees concerned about health effects potentially associated with 1-bromopropane (1-BP, also called n-propyl bromide) and 2-bromopropane (2-BP, also called isopropyl bromide) exposures during the spray application of an adhesive. The employees' concerns centered around neuropathy (abnormal nerve function), weakness and numbness in the lower extremities, dizziness, and headaches *(9) HETA 98-0153-2883 Custom Products Morresvile, NC Chrisopher Reh, Vince Mortimer, Jeffrey Nemhhauser, Doug Trout* On March 17, 1998, the National Institute for Occupational Safety and Health (NIOSH) received a request for a health hazard evaluation (HHE) at Custom Products, Inc. in Mooresville, North Carolina. The request was submitted by the North Carolina Department of Labor, and centered on workers' exposure to 1-bromopropane (1- BP) during the spray application of solvent-based adhesives. In response to this request, NIOSH investigators conducted two surveys at the facility *(10) HETA 2003-0203-2952 Wallace Computer Services, Clinton, Illinois Melissa Finley, Elena Page* Investigators from the National Institute for Occupational Safety and Health (NIOSH) responded to a confidential request for a health hazard evaluation (HHE) from printing press operators at Wallace Computer Services, Clinton, Illinois. These employees had symptoms perceived to be caused by exposure to inks and solvents on the job. NIOSH investigators visited the facility to characterize workers' exposures, evaluate symptoms, and provide recommendations to reduce potential health effects. *(11) HETA 2002-0379-2901 Superior Label Systems, Mason Ohio Gregory Burr, Mark Methner, Elena Page* In 2001, NIOSH performed a health hazard evaluation (HHE) at Superior Label Systems, Inc., (SLS) because some employees were having blurry vision at work. NIOSH investigators took air samples, had workers complete questionnaires, and performed eye examinations. We found that employees had work-related vision problems which were associated with two chemicals S dimethylisopropanolamine (DMIPA) and dimethylaminoethanol (DMAE). The company stopped using DMIPA and employee complaints decreased. A follow-up survey was conducted in August 2002 to determine how DMIPA and DMAE levels in the air had changed and whether employees no longer had blurry vision.

(12) HETA 2000-0374-2998 Engineered Fabrics Corporation, Rockmart, Georgia Lren Tapp, Dino Mattorano, Chales Mueleer, Angela Weber, Chris Reh

On July 26, 2000, the National Institute for Occupational Safety and Health (NIOSH) received a confidential request for a health hazard evaluation (HHE) from employees of Engineered Fabrics Corporation (EFC) in Rockmart, Georgia. EFC manufactures aircraft fuel cells. The employees reported headache; dizziness; fatigue; memory loss; and respiratory, nasal, and skin problems believed to be related to solvent exposures (toluene, acetone, and methyl ethyl ketone [MEK]) used in the Large Spray (LS) and Small Spray (SS) fuel cell departments

ESID Ref	Scenario description	Assigned PROC	Substance	# of Samples	Reference
9585 9591	Paint production	4 19	Ethyl Benzene Butan-2-one	24 18	(1)
9570 9573	Small Printing plant	10 10	Acetone Propan-2-ol	30 73	(2)
9830	Manufacture of decorative items	14	Styrene	7	HETA 96-0145-2684
9879	Manufacture of shoes	10	Heptane	7	HETA 95-0209-2515
9885	Service station attendant	8b	MTBE	10	(HETA 1994-0220-2526
9899	Drywall hanging using adhesives	10	n-hexane	6	HETA 99-0163-2771
10113 10117	Production of microporous polyethylene	14	Trichloroethylene	137	HETA 2004-0372-3054
10209	Manufacture of cushions with spray adhesive	7	1-Bromopropane	43	HETA 2000-0410-2891
10368	Printing press operation	8a	Trichloroethylene	18	HETA 2003-0203-2952
10380 10385	Flexographic printing	8a	dimethylaminoethanol (DMAE)	19 13	HETA 2002-0379-2901
10386 10392 10400 10401 10403	Manufacture of cushions with spray adhesive	7	1-Bromopropane	7 11 20 15 21	HETA 98-0153-2883
10411	Manufacture of aircraft fuel tanks	10	Acetone	29	HETA 2000-0374-2998

• PROC coverage	PROC 2, 3,4,5,7,8a,8b,9,10,11,13,14,15,19,24,25
• Relevant information for evaluation and improvement of TRA tool?	Yes, for most studies. Report HETA 2003-0203-2952 had insufficient details to construct a TRA Worker exposure estimate.
Scenario description	
• Sufficient contextual information to assign PROC, setting, volatility?	The setting and PROC could be mostly determined from the original paper. The providers of the data initially provided a suggested PROC, related to the activity being measured. There was sufficient information to determine the setting (IND/PROF) and from the chemical substance being monitored the VP and MW could be obtained. In some instances, it was necessary to go back to the original data (if the reference was provided e.g NIOSH HETA report) to understand the situation and activity to confirm setting and PROC. The setting (IND/PROF) was, in the opinion of the TF, incorrectly assigned in 5 of 65 cases.
• Sufficient contextual information for selection of exposure modifier settings?	Information was provided in the initial data collection phase to identify the exposure modifier settings. In several instances it was required to review the original paper or report to determine if the exposure modifiers reported were reported as being effective e.g LEV or mechanical ventilation. For several of the NIOSH HETA reports it was clear that although there was LEV it was not functioning effectively and in other cases mechanical ventilation was in place but again reported to not be functioning correctly
• Is contextual information available to reconstruct the assignments made by the researchers?	The researchers who constructed the ETEAM database did not look at the original data or question the data provided. Many of the submitted measurements were taken on request due to concerns of worker health and welfare, when the workplace was possibly not in a situation of providing adequate exposure control. In these instances, the modelled exposure based on the information to the researchers was not correct and the modelled exposure should be higher due to the exposure modifiers being less effective. It was possible to fully reconstruct the NIOSH data sets from the original HETA reports, with one exception.
ECETOC TRA domain	
• Are scenarios within the TRA domain?	The scenarios used for the TF fit into the TRA Worker Domain.
Assignment of PROCs and OC/RMMs	
• Has a team approach and a process for assignment been followed?	The original paper was based on experienced exposure scientists reviewing the data and agreeing on the parameters to be used for creating the exposure model. The process did not include filtering for datasets with samples less than 6 or to review the source data to correctly identify exposure modifiers.
• Has the assignment of PROCs been done correctly?	PROC assignment from the ETEAM was correct in a majority of cases. There are several instances in which, according to the TF, the PROC was incorrectly assigned (21 of 65).

• Has the assignment of ind./prof. setting been done correctly?	The setting was, in the opinion of the TF, incorrectly assigned in 5 of 65 cases.
• Is the selected volatility band correct?	In 2 instances the TF disagreed with the fugacity assignment. Substances considered from the ETEAM database by the TF: Acetone Benzene Ethyl Benzene Isoamyl acetate Trichloroethylene 1 bromo propane Butan -2 one Glutaraldehyde Heptane Toluene N methyl Pyrillidone Styrene Ethanol Propan 2 ol Methyl tert butyl ether Hexane Di methyl amino ethanol Pentane Copper oxide Calcium carbonate Magnesium stearate Inhalable dust Amoxicillin Lactose Aluminium oxide Copper Aluminium Iron oxide Chromium Formaldehyde N butyl acetate
• Has the assignment of exposure modifying factors been done correct?	Information was provided in the initial data collection phase to identify the exposure modifier settings. In several instances it was required to review the original paper or report to determine if the exposure modifiers reported were reported as being effective e.g., LEV or mechanical ventilation. For several of the NIOSH HETA reports it was clear although there was LEV it was not functioning effectively and in other cases mechanical ventilation was in place but again reported to not be functioning correctly. In the opinion of the TF, there were 9 instances of mechanical ventilation being incorrectly assigned, 9 instances of LEV being incorrectly assigned and 1 instance with a disagreement on whether the activity was indoor or outdoor
Exposure measurements	

• Sampling & analytical methods according to accepted standards?	With the large number of datasets and the wide variety of source data it was not possible to verify the validity of the source measurements, although NIOSH, ART and SUVA have reputations on the quality of the data generated and it must be accepted the data is credible.
• Have personal measurements in breathing zone been taken?	Only measurements related directly to personal air measurements in the breathing zone were included. This was possible with referring to the source data and the original measurements
• If not, is sufficient explanation provided on representativity of measurements?	N/A
• 8hr TWA exposure: have full shift samples been taken?	The samples taken are intended to be representative of a full shift, when referring to the original source data
• If not, is sufficient explanation provided on representativity of measurements?	N/A
• Short term exposure: have 15-minute samples been taken?	Yes, but not included in this reanalysis.
• If not, is sufficient explanation provided on representativity of measurements?	N/A
Comparison of estimated with measured exposure	
• Is the measured exposure based on newly collected data, data from old surveys or simulated data?	The ETEAM data is "old" data provided to the authors in order to generate a database. Some of the NIOSH surveys went back to the mid-1990s.
• For data from old surveys or simulated data, has sufficient justification been provided whether these measurements are representative for the scenario under investigation? •	No. The researchers who constructed the ETEAM database did not look at the original data or question the data provided. Many of the submitted measurements were taken on request due concerns of worker health and welfare, when the workplace was not in a situation of providing adequate exposure control. In these instances, the modelled exposure based on the information to the researchers was not correct and the modelled exposure should be higher due to the exposure modifiers being less effective.
• How many measurements have been carried out per scenario?	PROC 2: 19 PROC 3: 6 PROC 4: 24 PROC 5: 6 PROC 7: 9,34,7,11,20,15,21,7,8,6 PROC 8a: 16,19,13,7 Proc 8b: 29,8,24,23,88,23,36,10,6 PROC 9: 7,7 PROC 10: 9,30,73,7,6,29,8

	PROC 11: 11,21 PROC 13: 7,6 PROC 14: 137,137,7,11 PROC 15: 7,7,11,6,13,21,6 PROC 19: 14,18,12,6,8 PROC 24: 12,15,15,6 PROC 25: 6
• For datasets representative for a unique exposure scenario, has the P75 been calculated and compared with the TRA estimate?	Not in the original paper. The authors used single measurements for direct comparison with a P75 exposure model. The TF used data that had 6 or more measurements to calculate the P75 and compare directly to an exposure model prediction P75
• Is sufficient information available or can this be obtained to reconstruct the data-analysis?	Yes, using the original source data above and beyond what is in the original database
Conclusions	
• Conclusion on suitability of paper for TRA evaluation	The original paper must be included for TRA Worker evaluation as this paper forms the basis of a challenge to validity and fitness for purpose of the TRA Worker as a tier 1 tool
• Any other remarks	All of the data in the ETEAM report are retrospective with a number of measurements taken from workplaces which were in a poor state of exposure control.

A2.4 SECO/SUVA

The exposure measurement reports from the Swiss "Unfallversicherungsanstalt" (SUVA) contributed 124 datasets in the ETEAM database of individual measurements with the number of measurements per entry varying from 1 to 17. Of these, 10 datasets were found to have a total number of measurement points with N $\geq$6. Additionally, several entries could be combined as they were reporting exposure measurements for the same substance at the same workplaces, taken on different occasions during the same measuring campaign. The total number of SUVA studies with N $\geq$6 measurement points was thus 13, of which 12 were considered suitable for inclusion in the analysis. The exposure measurement data had been generated in the years between 2003 and 2012 during campaigns of occupational exposure measurements performed by industrial hygienists of SUVA, who investigated exposure levels at specific professional or industrial workplaces in Switzerland. The original SUVA reports were not published, but SUVA made the reports available to the Unisanté group at the University of Lausanne for the purpose of systematic analysis and use in the "ETEAM study". The data points for each single measurement and the accompanying information on the conditions of use and circumstances of exposure measurements were summarised in an Excel worksheet that was shared with the ECETOC TRA Worker TF by SUVA. The one data set judged not usable concerned heptane exposures in polyester casting operations where it was unclear how the chemical was used in the process, and hence no PROC could be assigned, noting also that the PROC code (24 - High (mechanical) energy work-up of substances bound in materials and/or articles) assigned initially by the ETEAM does not provide estimates for vapour exposure in the TRA.

CRITERIA	REVIEW
Paper/Report reference	Validation of Lower tier Exposure Tools Used for REACH: comparison of Tools Estimates with Available Exposure Measurements Van Tongeren M, Lamb J, Cherrie JW, MacCalman L, Basinas I, Hesse S. Ann Work Expo Health. 2017 Oct 1;61(8):921-938.
Scope of the study	
• Short description of objective of the study and study design	Collection of measurement data from various institutions, for the purposed of creation of a database. Comparison of the measurement results with lower tier exposure models to determine if the exposure models are sufficiently conservative in exposure predictions.
• Type of study	Retrospective review of measured data compared to constructed TRA Worker values for individual data points for multiple PROCs
• Note	The article does not provide information on the original source data. The authors have constructed a ratio of the measured concentration / constructed TRA Worker values for individual measurements. Several of the SUVA studies were performed to investigate workplaces in poor control of occupational exposure (request for intervention).
• Summary of original data sources	**SUVA reports:** A review of the original datasets was not possible. According to an expert at SUVA, the original report are not available as electronic files and the original paper files have likely been destroyed. An evaluation of the data was carried out by the Unisanté group at the University of Lausanne as part of the ETEAM project, and a summarising Excel file was made available to the ECETOC TRA Worker TF by SUVA in 2020.
• PROC coverage	PROC 3, 5, 7, 8b, 10, 24
• Relevant information for evaluation and improvement of TRA tool?	Yes.
Scenario description	
• Sufficient contextual information to assign PROC, setting, volatility?	The setting and PROC for the twelve SUVA scenarios were determined from the Excel file summarising the original reports. Sufficient contextual information was provided to assign a PROC. There was sufficient information to determine the setting (professional or industrial). An industrial setting had been assigned to all exposure scenarios, and no change of the setting was done.

	Sufficient information was provided in the data file on the chemical substances being monitored and the dustiness, VP and MW (as appropriate) could be obtained.
• Sufficient contextual information for selection of exposure modifier settings?	Limited information was provided in the data evaluation on the selection of exposure modifiers. In some of the SUVA studies, it seemed that LEV was present, but it was not functioning effectively and in other cases mechanical ventilation was in place but again appeared to not be functioning correctly (which could explain why SUVA conducted measurements at a workplace).
• Is contextual information available to reconstruct the assignments made by the researchers?	Yes for 12 data sets of 6 measurements or more. It was possible to obtain SUVA data from the originators (UniSanté) of the ETEAM submissions, but the original field survey reports and measurement data were not available.
ECETOC TRA domain	
• Are scenarios within the TRA domain?	The scenarios used for the analysis fit into the TRA Worker Domain.
Assignment of PROCs and OC/RMMs	
• Has a team approach and a process for assignment been followed?	The original paper was based on reviews by experienced exposure scientists analysing the data and agreeing on the parameters to be used for creating the exposure model. The process did not include filtering for datasets with samples less than 6. No review of the source data was performed to correctly identify exposure modifiers.
• Has the assignment of PROCs been done correctly?	PROC assignment from the ETEAM was correct in a majority of cases. The suggested PROC was changed for three SUVA scenarios on the basis of the contextual information given in the data file summarising the original reports.
• Has the assignment of ind./prof. setting been done correctly?	The setting for the SUVA scenarios was correctly assigned in all twelve cases.
• Is the selected volatility band correct?	The assigned fugacity was not changed for the SUVA scenarios considered in the analysis.
• Has the assignment of exposure modifying factors been done correctly?	There is limited information available on the exposure modifying factors, as the original SUVA reports are not accessible. It cannot be estimated whether the assignment was done correctly.
Exposure measurements	
• Sampling & analytical methods according to accepted standards?	With the large number of datasets and the wide variety of source data it was not possible to verify the validity of the source measurements, although NIOSH, ART and SUVA have reputations on the quality of the data generated and it must be accepted the data is credible.
• Have personal measurements in	Yes. Only measurements related directly to personal air measurements in the breathing zone were included in the analysis This was possible with referring to the summarised source data.

breathing zone been taken?	
• If not, is sufficient explanation provided on representativity of measurements?	N/A
• 8hr TWA exposure: have full shift samples been taken?	The samples taken were intended to be representative of a full shift, when referring to the original source data. Exact sampling durations are included in the SUVA data.
• If not, is sufficient explanation provided on representativity of measurements?	N/A
• Short term exposure: have 15-minute samples been taken?	Yes
• If not, is sufficient explanation provided on representativity of measurements?	N/A
Comparison of estimated with measured exposure	
• Is the measured exposure based on newly collected data, data from old surveys or simulated data?	The ETEAM data including the SUVA measurement data are “old” data provided to the authors in order to generate a database
• For data from old surveys or simulated data, has sufficient justification been provided whether these measurements are representative for the scenario under investigation?	No. The researchers who constructed the ETEAM database did not look at the original data or question the data provided. Many of the submitted measurements were taken on request due concerns of worker health and welfare, when the workplace was not in a situation of providing adequate exposure control. In these instances, the modelled exposure based on the information given to the researchers was not correct and the modelled exposure should be higher due to the exposure modifiers being less effective.
• How many measurements have been carried out per scenario?	PROC 3: 6 PROC 5: 6 PROC 7: 6 PROC 8b: 6 PROC 10: 8 PROC 15: 26, 12, 17, 9 PROC 24: 6
• For datasets representative for a	Not in the original paper. The authors used single measurements for direct comparison with a P75 exposure model.

unique exposure scenario, has the P75 been calculated and compared with the TRA estimate?	The TF used data that had 6 or more measurements. The P75 over all measurement points in a dataset was calculated and compared directly to the TRA Worker exposure model prediction
• Is sufficient information available or can this be obtained to reconstruct the data-analysis?	Yes, if all available information is analysed above and beyond what is in the Access database. This includes the summary of the original SUVA source data.
Conclusions	
• Conclusion on suitability of paper for TRA evaluation	The original paper must be included for TRA Worker evaluation as this paper forms the basis of a challenge to validity and fitness for purpose of the TRA as a tier 1 tool
• Any other remarks	All of the data in the ETEAM report are retrospective with a number of measurements taken from workplaces which are in a poor state of exposure control. This should be considered when TF discusses the representativeness of the data included in the comparison.

A2.5 HSE/HSL

The ETEAM database lists 11 datasets which originated from the UK Health and Safety Executive (HSE) and Laboratory (HSL), covering 8 situations where exposures to volatile liquids occurred and 3 where exposure was to solids. Although the datasets contain supporting information on the circumstances of sampling and for key exposure determinants, none of the datasets contained 6 or more samples. They have therefore not been taken forward for use within this TRA Worker reanalysis.

A2.6 Lund University

The ETEAM database contained 7 datasets which originated from the University of Lund. Since all of them had only less than 6 datasets, they have not been taken forward for reanalysis.

A3 Landberg

CRITERIA	REVIEW
Paper/Report reference	Evaluation of risk assessment approaches of occupational chemical exposures based on models in comparison with measurements; Hanna E. Landberg, Håkan Westberg, Håkan Tinnerberg

	Safety Science 109 (2018) 412–420
Scope of the study	
• Short description of objective of the study and study design	"The aim of this study was to investigate approaches to risk assessment of chemicals based on exposure assessment models relative to occupational exposure limits values (OELs) and derived no-effect levels (DNELs) and in comparison, with measurements relative to OELs. A second aim was to evaluate the modelled recommended outcome and compare it with measurements of exposure."
• Note	The article's results cannot be directly re-constructed from the paper and the Supplementary data cited in this article and published in similar other publications by the authors. Furthermore, it is not possible to identify the exposure determinants used to develop the TRA Worker estimates. The overall number of ESs for which significant representative sample data are available (n>6) is limited. The information on the measurements is limited, i.e. no information on validity or measurement time.
• List of supplementary materials referred to	– Landberg, H.E., Axmon, A., Westberg, H., Tinnerberg, H., 2017. A study of the validity of two exposure assessment tools: Stoffenmanager and the advanced REACH tool. Ann.Work Expo Health 61, 575–588. – Landberg, H.E., Berg, P., Andersson, L., Bergendorf, U., Karlsson, J.-E., Westberg, H., Tinnerberg, H., 2015. Comparison and evaluation of multiple users' usage of the exposure and risk tool: Stoffenmanager 5.1. Ann. Occup. Hyg. 59, 821–835.
• Type of study	Evaluation based on comparison with measurement data and comparison with other modelling tool results
• PROC coverage	7, 8b are identified as being addressed by the article.
• Relevant information for evaluation and improvement of TRA tool?	No, as only limited information is available, although the authors concluded that "ECETOC TRA was the least conservative model, with 31% of measured exposure above the modelled exposure. ECETOC TRA is less conservative than Stoffenmanager®, ART"
Scenario description	
• Sufficient contextual information to assign PROC, setting, volatility?	Name of substance, and short description of type of industry, situation and activity given with link to previous publications. No PROC assignment by the authors
• Sufficient contextual information for selection of exposure modifier settings?	Not published, but partly available in referenced publications.

• Is contextual information available to reconstruct the assignments made by the researchers?	Not published and contacting the authors twice did not result in any supporting feedback.
ECETOC TRA domain	
• Are scenarios within the TRA domain?	Yes, judged on limited information
Assignment of PROCs and OC/RMMs	
• Has a team approach and a process for assignment been followed?	"The exposure assessments made with models were done by at least two occupational hygienists at a time to reduce some of the variations between users. All situations were transferred from the templates into the models by the same individual."
• Has the assignment of PROCs been done correctly?	Not published, thus evaluation not possible
• Has the assignment of ind./prof. setting been done correctly?	Not published, thus evaluation not possible
• Is the selected volatility band correct?	Not published, thus evaluation not possible
• Has the assignment of exposure modifying factors been done correct?	Not published, thus evaluation not possible
Exposure measurements	
• Sampling & analytical methods according to accepted standards?	Partly yes, based on information in referenced publications. However, limited information, e.g., LoD or sampling time
• Have personal measurements in breathing zone been taken?	Yes
• If not, is sufficient explanation provided on representativity of measurements?	No
• 8hr TWA exposure: have full shift samples been taken?	No detailed information for scenarios given, but only general statement: "The tasks were often performed during whole working days but if they were only performed on short time periods but multiple times a day, the total time for the task was calculated."
• If not, is sufficient explanation provided on representativity of measurements?	No
• Short term exposure: have 15 minute samples been taken?	No
• If not, is sufficient explanation provided on representativity of measurements?	No

Comparison of estimated with measured exposure	
• Is the measured exposure based on newly collected data, data from old surveys or simulated data?	Data already published in referenced publications by Landberg et al. 2015 and 2017
• For data from old surveys or simulated data, has sufficient justification been provided whether these measurements are representative for the scenario under investigation?	Yes
• How many measurements have been carried out per scenario?	2 to 15
• For datasets representative for a unique exposure scenario, has the P75 been calculated and compared with the TRA estimate?	No, AM and GM (95% CI) were calculated.
• Is sufficient information available or can this be obtained to reconstruct the data-analysis?	No. When contacted with a request for further details of the surveyed workplaces in order to construct TRA estimates, the researchers indicated that they had no longer access to their field notes.
Conclusions	
• Conclusion on suitability of paper for TRA evaluation	Not suitable
• Any other remarks	Observations down the supply chain for a particular scenario in the workplace which is being compared with modelled data from the registrant who should have had correct info from the Downstream User to ensure all OC and RMM are in place to ensure RCR< 1.

A4 Angelini

CRITERIA	**REVIEW**
Paper/Report reference	Respiratory Health – Exposure Measurements and Modelling in the Fragrance and Flavour Industry Eric Angelini, Gerard Camerini, Malick Diop, Patriche Roche, Thomas Rodi, Christine Schippa, Thierry Thomas; PLoS ONE 2016
Scope of the study	

CRITERIA	REVIEW
• Short description of objective of the study and study design	Objective: "better estimate the real level of hazardous respiratory exposure of workers". Design: A set of 430 personal exposure measurements was obtained, covering 27 volatile organic compounds. For each measurement, exposure modelling was performed with ECETOC TRA and a comparison was made between estimated and measured exposure. Based on measurement results, adjustments were made to the TRA tool to avoid underestimation; in this way a company-specific TRA version was created.
• Type of study	Evaluation based on a comparison with measurement data.
• PROC coverage	Fragrance and flavour industry - Industrial environment Activities covered: • Weighing-mixing; • Packaging; • Reconditioning-transferring The article does not specify which PROC codes have been assigned to these activities. The authors confirmed they have applied PROC8b for all activities.
• Relevant information for evaluation and improvement of TRA tool?	Yes. Note that the authors state they applied TRA v3; in reality their estimates were derived with v2! (with different base estimate (PROC8b) as well as different LEV efficiency). The authors conclude: For 37% of the measurements, the estimated exposure was higher than the measured value. For the modified TRA: for 98% of the measurements, the exposure as estimated with the modified model was higher than the measured value.
Scenario description	
• Sufficient contextual information to assign PROC, setting, volatility?	Yes, as authors have provided additional information (e-mail; telecons).
• Sufficient contextual information for selection of exposure modifier settings?	Yes, as authors have provided additional information (e-mail; telecons). Note that information on duration, concentration, ventilation (and use of RPE) is not described in the paper.

CRITERIA	REVIEW
• Is contextual information available to reconstruct the assignments made by the researchers?	Yes, see above.
ECETOC TRA domain	
• Are scenarios within the TRA domain?	Yes.
Assignment of PROCs and OC/RMMs	
• Has a team approach and a process for assignment been followed?	The paper does not contain these details.
• Has the assignment of PROCs been done correctly?	Yes, PROC8b is considered adequate. PROC9 could have been an alternative and would lead to higher base estimates.
• Has the assignment of ind./prof. setting been done correctly?	Yes, industrial use has been applied.
• Is the selected volatility band correct?	Not in all cases. An incorrect band was selected for 3 out of 24 substances. (The authors have provided additional information; the paper does not contain the information to confirm correct selection of volatility band.)

CRITERIA	REVIEW
• Has the assignment of exposure modifying factors been done correctly?	No. Issues exist for assignment of duration and concentration factors, as well as the LEV. The authors applied the duration factor (0.1 or 0.2), while the measurement was related to 5-60 minutes typically. As the measurement is not relating to a full shift, the TRA Worker estimate does not require adjustment for duration. In addition, the peak exposure factor was not applied for short-term measurements. Furthermore, the authors applied in some cases a concentration factor for the diluted product for the activity of weighing, while this was performed with the pure substance. The authors applied LEV as RMM (effectiveness 95% in TRA v3); however, based on own measurements with and without LEV, the authors assessed the LEV efficiency in the plant to be around 70% in practice (type: 'elephant trunk', movable capture hood; for this type an effectiveness of 95% cannot be expected, see for example Controlling airborne contaminants at work: A guide to local exhaust ventilation (LEV) HSG258 (hse.gov.uk)). The combination of the factors above means that the re-analysis by TF yields significantly different estimates than those from the authors. The MANE estimates became very low because of the application of LEV (95% reduction) and duration factor (80-90% reduction). (The authors have provided additional information; the paper does not contain the information to confirm correct selection of exposure modifying factors.)
Exposure measurements	
• Sampling & analytical methods according to accepted standards?	The 27 compounds were covered by five different measurement methods. These methods were all developed and validated in-house. Four methods included adsorption on Tenax, thermal desorption and GC-MS. One method included adsorption on Silica, liquid desorption and GC-MS. Validation details for one method are described in the Supporting information. The measurements were task-based and according to the method descriptions, measurement duration ranges from < 15 mins to < 45 mins.

CRITERIA	REVIEW
	Compounds included: Acetaldehyde Acetyl Methyl Carbinol Acetyl Propionyl Benzaldehyde Benzene Benzyl Alcohol Butyl Acetate Butyl Alcohol Cinnamic Aldehyde Diacetyl Dimethyl Sulfide Ethanol Ethyl Acetate Ethyl Formiate Ethyl Lactate Ethyl Methyl Butyl Ketone Furfural Furfuryl Alcohol Hexane Isoamyl Acetate Isoamyl Alcohol Isobutyl Alcohol Isopropyl Alcohol Isovaleric Aldehyde Methanol Propionic Aldehyde Propyl Alcohol
• Have personal measurements in breathing zone been taken?	Yes, according to information from authors. Breathing zone was not specified in the article. “Measurement carried out on an operator” according to Table S4 (Supplementary Information)
• If not, is sufficient explanation provided on representativity of measurements?	N/A
• 8hr TWA exposure: have full shift samples been taken?	No. Measurement results relate to relatively short periods of time, typically 5-60 mins (additional info from authors). Paper and supplementary documentation do not describe duration of the measurements.
• If not, is sufficient explanation provided on representativity of measurements?	The paper performs a direct comparison between the task exposure measurements and the TRA Worker estimates.
• Short term exposure: have 15 minutes samples been taken?	See above.

CRITERIA	REVIEW
• If not, is sufficient explanation provided on representativity of measurements?	See above.
Comparison of estimated with measured exposure	
• Is the measured exposure based on newly collected data, data from old surveys or simulated data?	Newly collected data in company facility.
• For data from old surveys or simulated data, has sufficient justification been provided whether these measurements are representative for the scenario under investigation?	N/A
• How many measurements have been carried out per scenario?	A total of 430 measurements have been collected, for: • 27 different compounds • 3 different activities. Note that some samples have been analysed for multiple substances and therefore these results can not be regarded as independent. The analysis done in the paper is limited to a direct comparison at individual measurement level between measured and estimated exposure. The measurements focused on 3 activities: Weighing-mixing; Packaging; Reconditioning-transferring. However, the comparison between estimate and measurement was performed at the individual measurement level, not at the worker contributing scenario (or activity) level.
• For datasets representative for a unique exposure scenario, has the P75 been calculated and compared with the TRA estimate?	Re-analysis of the data by TF. The authors had limited the analysis of estimated versus measured data to a 1:1 comparison per measurement. Would have expected analyses of aggregated data, e.g. stratified by PROC and Volatility Class; and then comparing 75-percentile of measured data with TRA Worker estimate.
• Is sufficient information available or can this be obtained to reconstruct the data-analysis?	Yes, with the additional information provided by the authors.
Conclusions	
• Conclusion on suitability of paper for TRA evaluation	Suitable (with additional information from authors).

CRITERIA	REVIEW
• Any other remarks	A re-analysis of the data has been performed: the authors have shared the underlying data used for the TRA Worker modelling, including at the individual measurement level: • PROC • Duration • Concentration • Ventilation/LEV • RPE use in addition to the data provided in the supporting information: The re-analysis highlighted that the authors have incorrectly applied some TRA Worker parameters, especially duration and LEV. There is a need for additional instructions to better inform TRA Worker users on the use of these parameters. LEV should only be selected as RMM if the LEV equipment is fit for purpose and there is evidence it delivers the effectiveness as applied in the TRA Worker model.

A5 Spee

CRITERIA	REVIEW
Paper/Report reference	Comparing REACH Chemical Safety Assessment information with practice – a case study of polymethylmethacrylate (PMMA) in floor coatings in the Netherlands Ton Spee, Daan Huizer Int Journal of Hyg & Env Health (2017) 220, p 1190-1194
Scope of the study	
• Short description of objective of the study and study design	Comparison of ECETOC TRA worker v3 exposure estimates in the CSR of the manufacturer with real life measured exposures of methylmethacrylate (MMA) during PMMA flooring in practice.
• Type of study	Personal exposure to MMA was measured at 4 construction sites. 14 full shift and 14 task-based samples were collected. The task-based results were compared with the data in the CSR of the manufacturer.
• PROC coverage	PROC10 and PROC19

• Relevant information for evaluation and improvement of TRA tool?	Yes. Part of the data and situations described can be used for evaluation of the TRA Worker.
Scenario description	
• Sufficient contextual information to assign PROC, setting, volatility?	Yes, sufficient contextual information has been provided to assign PROC, setting, volatility; all exposure data are described in the paper.
• Sufficient contextual information for selection of exposure modifier settings?	Yes, as above.
• Is contextual information available to reconstruct the assignments made by the researchers?	Yes, as above.
ECETOC TRA domain	
• Are scenarios within the TRA domain?	Yes.
Assignment of PROCs and OC/RMMs	
• Has a team approach and a process for assignment been followed?	Not applicable. The paper addresses a relatively limited comparison of data. Secondly, a comparison is made with the (assignments in the) CSR. Researchers are well experienced in exposure assessment and use of modelling tools.
• Has the assignment of PROCs been done correctly?	Yes.
• Has the assignment of ind./prof. setting been done correctly?	Yes.
• Is the selected volatility band correct?	Basically yes. However, if the process temperature is > 40 °C, the high volatility band instead of the moderate volatility band should be selected.
• Has the assignment of exposure modifying factors been done correctly?	In the CSR LEV has been assumed. This is not realistic for this type of activities in construction sites. Therefore, LEV has not been selected.
Exposure measurements	

• Sampling & analytical methods according to accepted standards?	Sampling and analytical methods are described to some detail. Analysis has been performed by a well-known accredited laboratory according to MDHS no 96.
• Have personal measurements in breathing zone been taken?	Yes.
• If not, is sufficient explanation provided on representativity of measurements?	Not applicable.
• 8hr TWA exposure: have full shift samples been taken?	Yes (6.5 to 8 hrs), and task-based samples (sampling time not provided in paper).
• If not, is sufficient explanation provided on representativity of measurements?	Not applicable.
• Short term exposure: have 15 minutes samples been taken?	No.
• If not, is sufficient explanation provided on representativity of measurements?	Not applicable.
Comparison of estimated with measured exposure	
• Is the measured exposure based on newly collected data, data from old surveys or simulated data?	The comparison with the CSR is based on newly collected data.
• For data from old surveys or simulated data, has sufficient justification been provided whether these measurements are representative for the scenario under investigation?	Not applicable.
• How many measurements have been carried out per scenario?	Task based: PROC10, indoors, no ventilation: n=1 PROC10, indoors, ventilation: n=4 PROC10, outdoors: n=4 PROC19, indoors, no ventilation: 4 PROC19, outdoors: n=1 Full shift: PROC10, indoors: n=14

	Of the full shift data one of the datasets could be used for the TRA v3 evaluation (n=6; personal full shift; PROC10; floor laying indoors, bakery)
• For datasets representative for a unique exposure scenario, has the P75 been calculated and compared with the TRA estimate?	No, however the P75 can be calculated from the available data.
• Is sufficient information available or can this be obtained to reconstruct the data-analysis?	Yes. Data-analysis has been reconstructed. Changes: LEV set to no instead of yes.
Conclusions	
• Conclusion on suitability of paper for TRA evaluation	Suitable with restrictions. This is not a full study on evaluation of the TRA Worker, however some of the data can be used for TRA Worker evaluation.
• Any other remarks	The paper is not a full evaluation study. In the paper the comparison is made between measurements and TRA Worker estimates in the CSR for the substance MMA.

A6 Spinazzè

CRITERIA	REVIEW
Paper/Report reference	Accuracy evaluation of three modelling tools for occupational exposure assessment. Andrea Spinazzè, Filippo Lunghini, Davide Campagnolo, Sabrina Rovelli, Monica Locatelli, Andrea Cattaneo, Domenico Cavallo. Annals of Work Exposures and Health, 2017, Vol. 61, No. 3, 284–298.

CRITERIA	REVIEW
• Note	Publications cited in this research were retrieved and examined by ECETOC: - Bello et al. Determinants of Exposure to 2-Butoxyethanol from Cleaning Tasks: a Quasi-experimental Study. Ann. Occup. Hyg., Vol. 57, pp. 125-135, 2013 - Moolla et al. Assessment of occupational exposure to BTEX compounds at a bus diesel-refueling bay. A case study in Johannesburg, South Africa. Science of the Total Environment 537, pp. 51–57, 2015 - Hollins et al. Airborne benzene exposures from cleaning metal surfaces with small volumes of petroleum solvents. International Journal of Hygiene and Environmental Health 216 (2013) 324–332 - Hammond et al. Occupational exposure to styrene vapor in a manufacturing plant for fiber-reinforced composite in wind turbine blades. Ann. Occup. Hyg., Vol. 55, pp 591-600, 2011 - Hashimoto et al. Evaluation of the Control-Banding Method – Comparison with Measurement-based comprehensive risk assessment. J. Occup. Health, 2007; 49: 482-492 - Plisko MJ and Spencer JW. Evaluation of a mathematical model for estimating solvent exposure in the workplace. Journal of Chemical Health & Safety, May/June 2008 - Carlo et al. In-depth study: an occupational exposure assessment of styrene and noise in the fiber-reinforced plastic boat manufacturing industry. NIOSH report EPHB 306-16a, 2007 - Koontz et al. Modelling aggregate exposures to glycol ethers from use of commercial floor products. International Journal of Toxicology, 25:95–107, 2006

CRITERIA	REVIEW
• Short description of objective of the study and study design	Objective: "Evaluate the accuracy and robustness of three exposure modelling tools (Stoffenmanager, TRA v3.1, ART), by comparing available measured data for exposure to organic solvents and pesticides in occupational exposure scenarios". Design: Data sets of personal exposure measurements were extracted from eight published papers and exposure survey reports available on-line. The described conditions of use were converted into TRA Worker estimates by Spinazzè et al. The reported measurement data were used to calculate descriptive statistics which were then merged to develop overall tool performance indicators for accuracy and robustness, separately for solvents and pesticides.
• Type of study	Evaluation based on a comparison with measurement data published by other researchers (except the publication by Koontz et al which used a modelling tool to quantify exposure levels).
• PROC coverage	Industrial and professional work environments, activities covered: • Public bathroom cleaning with product containing 6% 2-butoxy-ethanol (PROC 10) • Bus refuelling with diesel (PROC 8a) • Surface cleaning (PROC 10) • Gel coating by hand-spray (PROC 7) and hand lay-up (PROC 10) • Vacuum-assisted moulding operation (PROC 2) • Petroleum factory operations (pipeline disconnection, drum filling, sludge shoveling, washing of sample bottles and test engine parts, road tanker top loading) (PROCs 8b and 10) • Part cleaning in a mechanical workshop (PROC 10) • Floor stripping (PROC 10)
• Relevant information for evaluation and improvement of TRA tool?	Yes, for the solvent scenarios (TRA Worker not considered to be applicable to active ingredients of pesticide products), in some cases with changes of PROC-selection and correction of modifying factors.
Scenario description	
• Sufficient contextual information to assign PROC, setting, volatility?	Yes.

CRITERIA	REVIEW
• Sufficient contextual information for selection of exposure modifier settings?	Yes mostly, although not in all cases: - Content of BTEX in diesel fuel is not known
• Is contextual information available to reconstruct the assignments made by the researchers?	Yes, this is well documented in detailed tables in the on-line supplemental material.
ECETOC TRA domain	
• Are scenarios within the TRA domain?	Yes for the solvent studies with the exception of one scenario in the Hammond study where workers entered a confined space (the inside of the wind turbine blade under construction) without forced ventilation. No for the pesticide scenarios.
Assignment of PROCs and OC/RMMs	
• Has a team approach and a process for assignment been followed?	The paper does not contain these details.
• Has the assignment of PROCs been done correctly?	Yes, in general; exceptions: - Moolla study, PROC 8a for refuelling, Concawe use map indicates PROC 8b; - PROC3 instead of PROC2 in the Hammond study for the vacuum-assisted moulding operation; idem for the infusion scenario of the Carlo study (both are batch-type operations, hence PROC3, not continuous (PROC2)
• Has the assignment of ind./prof. setting been done correctly?	Yes
• Is the selected volatility band correct?	Yes

CRITERIA	REVIEW
• Has the assignment of exposure modifying factors been done correctly?	Not in all cases: - Bello study: assigned good general ventilation (-30%) whereas description indicates basic ventilation (no reduction) - Moolla study: assumed 1-5% benzene and toluene in diesel, and 5-25% xylene, whereas there are no such data in the original publication and Concawe data suggest benzene and toluene are nearly absent and xylenes is <0.2% for diesel fuel; also assumed inappropriate exposure duration (15 min – 1 hour) for full-shift exposure - Hammond study: assigned enhanced general ventilation (-70%) whereas description indicates good general ventilation (-30%); adjusted incorrectly for duration of <1 hour (no correction needed for direct comparison with measurements) - Hashimoto study: assumed enhanced general ventilation (-70%) although this information is not provided in the original publication. Should have picked outdoor (-30%), except for laboratory tasks (sample bottle and test engine parts washing) where enhanced ventilation is reasonable - Carlo study: assigned enhanced general ventilation (-70%) whereas description indicates basic ventilation (no reduction)
Exposure measurements	
• Sampling & analytical methods according to accepted standards?	This information is mostly limited, but not raising concerns.
• Have personal measurements in breathing zone been taken?	Yes, according to information from authors, except Moolla who utilised data from a static continuous monitoring system.
• If not, is sufficient explanation provided on representativity of measurements?	N/A
• 8hr TWA exposure: have full shift samples been taken?	In some cases yes (Hammond, Hashimoto), but many measurements related to relatively short periods of time – some shorter than 15 min, raising the possibility to assess these with the peak exposure prediction facility of the TRA.
• If not, is sufficient explanation provided on representativity of measurements?	Not explicitly in most cases, as the authors utilised other researchers' data. The justification could come from using a large number of data and situations.
• Short term exposure: have 15 minutes samples been taken?	Yes.

CRITERIA	REVIEW
• If not, is sufficient explanation provided on representativity of measurements?	N/A
Comparison of estimated with measured exposure	
• Is the measured exposure based on newly collected data, data from old surveys or simulated data?	Data from old surveys of workplaces to which the researchers did not have direct access.
• For data from old surveys or simulated data, has sufficient justification been provided whether these measurements are representative for the scenario under investigation?	See above
• How many measurements have been carried out per scenario?	This was variable. Five data sets of 6 or more (8-19) were extracted from the Hammond and Carlo studies for inclusion in the ECETOC curated database.
• For datasets representative for a unique exposure scenario, has the P75 been calculated and compared with the TRA estimate?	Where possible, the researchers calculated the P75 from the available data. In some cases, only average exposure data per scenario were provided (Hashimoto).
• Is sufficient information available or can this be obtained to reconstruct the data-analysis?	Yes, based on the information in the on-line supplemental data.
Conclusions	
• Conclusion on suitability of paper for TRA evaluation	Parts are suitable
• Any other remarks	The authors concluded that the TRA Worker for solvents presented overall acceptable results and no cases of strong underestimation. The other models assessed in the study were seen as more robust and TRA Worker use should be limited to cases in which a strong conservative and worst-case evaluation is necessary. Their evidence base included however several erroneous calculations, and hence the conclusion may not be valid.

A7 Jankowska

CRITERIA	REVIEW
Paper/Report reference	Application of predictive models for estimation of health care workers exposure to sevoflurane. Jankowska A., Czerczak S., Kucharska M., Wesołowski W., Maciaszek P., Kupczewska-Dobecka M. Int J Occup Saf Ergon. 2015;21(4):471-9.
Scope of the study	
• Short description of objective of the study and study design	Objective: to determine if ECETOC TRA version 3 and Stoffenmanager version 5.5, the knowledge-based artificial intelligence programs, could accurately choose specific sevoflurane concentration ranges that correspond to the professional exposure of medical personnel during administration of anaesthetics by comparing model-estimated exposure levels with the measurement data obtained in the workplace. Design: Measurements included determinations of sevoflurane in the workplace air of 117 operating rooms of 31 hospitals in one Polish region. Measurements were carried out at the time of various surgical procedures during administration of anaesthetics by endotracheal intubation. The measurement results were compared with the values estimated using two models: ECETOC TRA and Stoffenmanager.
• Type of study	Evaluation based on comparison with measurement data
• PROC coverage	Professional work environments, activities covered: • PROC8a (transferring Sevoflurane from the anaesthetic apparatus to the lungs through the respiratory tube belonging to the anaesthetic system and the endotracheal tube) • PROC2 (operating rooms provided with air conditioning system)
• Relevant information for evaluation and improvement of TRA tool?	Yes, valuable for specific working environment
Scenario description	
• Sufficient contextual information to assign PROC, setting, volatility?	Yes, information regarding condition of use is available to re-perform the ECETOC TRA Worker analysis

CRITERIA	REVIEW
• Sufficient contextual information for selection of exposure modifier settings?	Yes, general information available
• Is contextual information available to reconstruct the assignments made by the researchers?	No detailed information for all cases
ECETOC TRA domain	
• Are scenarios within the TRA domain?	Yes
Assignment of PROCs and OC/RMMs	
• Has a team approach and a process for assignment been followed?	No
• Has the assignment of PROCs been done correctly?	No, PROC8a refers to the exposures associated with the bulk transfer of substances in general, and therefore the assignment of PROC8a is questionable
• Has the assignment of ind./prof. setting been done correctly?	Yes, prof.
• Is the selected volatility band correct?	Yes
• Has the assignment of exposure modifying factors been done correctly?	Yes, in general
Exposure measurements	
• Sampling & analytical methods according to accepted standards?	No
• Have personal measurements in breathing zone been taken?	Yes
• If not, is sufficient explanation provided on representativity of measurements?	NA
• 8hr TWA exposure: have full shift samples been taken?	No
• If not, is sufficient explanation provided on representativity of measurements?	At least 6h

CRITERIA	REVIEW
• Short term exposure: have 15 minutes samples been taken?	No
• If not, is sufficient explanation provided on representativity of measurements?	No
Comparison of estimated with measured exposure	
• Is the measured exposure based on newly collected data, data from old surveys or simulated data?	Measured data from 2016 to 2010, relatively new
• For data from old surveys or simulated data, has sufficient justification been provided whether these measurements are representative for the scenario under investigation?	NA
• How many measurements have been carried out per scenario?	No information
• For datasets representative for a unique exposure scenario, has the P75 been calculated and compared with the TRA estimate?	No. The concentration from TRA Worker estimation was misused as 90th percentile and compared with 90th percentile of the measured data.
• Is sufficient information available or can this be obtained to reconstruct the data-analysis?	No, original measured data is missing
Conclusions	
• Conclusion on suitability of paper for TRA evaluation	Suitable after recalculation (Not suitable due to the misused exposure estimation percentile of TRA Worker; however, it is suitable for TRA Worker evaluation after recalculation of 75th percentiles)
• Any other remarks	The concentration from TRA Worker estimation was misused as 90th percentile and compared with 90th percentile of the measured data. However, TRA Worker is intended to reflect the 75th percentile value of the 8-hour value.

CRITERIA	REVIEW
• ECETOC summary statement for ENES 3.2 review – updated December 2020	The article indicated that the TRA Worker underestimated the assessed concentration. However, in this case study, the concentration from TRA Worker estimation was assumed to be a 90th percentile and compared with the 90th percentile of the measured data. Considering the fact that the TRA Worker is intended to reflect the 75th percentile value of the 8-hour value, the comparison of TRA Worker value with measured value is not valid.

A8 Kupczewska

CRITERIA	REVIEW
Paper/Report reference	Evaluation of the TRA ECETOC model for inhalation workplace exposure to different organic solvents for selected process categories M. Kupczewska-Dobecka, S. Scerczak & M. Jakubowski International Journal of Occupational Medicine and Environmental Health 2011;24(2):208-217
Scope of the study	
• Short description of objective of the study and study design	"To describe the operation principle of the TRA ECETOC model … and the utilisation of that model for assessment of inhalation exposures to different organic solvents for … a given application" Exposure estimates were retrospectively assigned for 14 scenarios (from 3 different plants: paint & lacquers factory, a shoe factory and a refinery) that had existing measurement data of exposure to organic solvents (toluene, ethyl acetate, acetone)
• Type of study	Evaluation based on a comparison with measurement data from 3 different plants. The working conditions and activities in these 3 settings were translated in inputs for the TRA worker v2 tool.
• PROC coverage	The authors selected PROCs 1, 2 and 10. Paint & lacquers factory, synthesis section: PROC2 Shoe factory: PROC10 Refinery: PROC1 (Note that these may not have been the best choice!)
• Relevant information for evaluation and improvement of TRA tool?	In principle yes, the data and situations described can be used for evaluation of the TRA Worker,but note: • TRA v2 was applied. • Limited contextual information was available on the scenarios/measurements.
Scenario description	

• Sufficient contextual information to assign PROC, setting, volatility?	Limited, but in general sufficient contextual information present. However, based on the information, one might select different PROCs and setting: 1. Paints and lacquers factory, synthesis section: measurement results for toluene, ethylacetate, acetone and xylene. PROC 2 has been assigned. However, one would expect a batch process to be in place, so PROC 3 or 4 could be more appropriate. Exposure estimates would become higher in that case. 2. Shoe factory: measurement results for toluene, ethyl acetate and acetone, relating to 3 different activities: sole manipulation, sewing section, shoe assembly. PROC 10 has been assigned to all 3 activities (roller/brush application of glues) but the authors comment "the documentation of the testing of workplaces at which measurements had been performed does not contain information whether the exposure was only to vapours, or to vapours and aerosols of the applied glue." It is unclear whether glue spraying was applied or not. The authors indicate PROC 7 could be used in that case. Note that depending on the work setup PROC 11 (non-industrial spraying) could then be deemed appropriate as well. 3. Refinery: Toluene measurements. PROC 1 has been selected. However, the article has no details on operator activities, nor on the toluene concentration in the process streams. Most likely, for most of the described functions (supervisor, process, controller, operator, mechanician) and assuming a continuous process, some exposure will occur. Therefore a PROC2 seems more appropriate.
• Sufficient contextual information for selection of exposure modifier settings?	Limited, see above.
• Is contextual information available to reconstruct the assignments made by the researchers?	Partially, see above.
ECETOC TRA domain	
• Are scenarios within the TRA domain?	Yes
Assignment of PROCs and OC/RMMs	

• Has a team approach and a process for assignment been followed?	Not described in the article.
• Has the assignment of PROCs been done correctly?	Partially, see above.
• Has the assignment of ind./prof. setting been done correctly?	Not clear, not described in the article. However, based on the information provided, one can deduct that industrial setting has been used for the 3 plants. For the shoe factory, this seems not appropriate, the type of activities and conditions are better reflected by professional setting.
• Is the selected volatility band correct?	Volatility bands not described in article. The following band would apply: • Toluene – Medium • Ethyl acetate – High • Acetone – High • Xylene – Medium. Based on the information in table 4, one can deduct that the correct volatility band has been chosen for each situation.
• Has the assignment of exposure modifying factors been done correctly?	Concentration information is available for the paints and lacquers factory and the shoe factory. When reconstructing the TRA Worker modelling outcomes, it turns out that the authors apparently have applied a 90% LEV reduction for the Paints and Lacquers factory. This is insufficiently described/clarified in the article (refer to "Workplace atmosphere measurements info", first bullet: "with ventilation"). E.g.: Toluene – Paints & Lacquers factory – PROC2 – 1-5% Authors present 0.2 ppm estimate. Based on TR107, PROC2 estimate for medium volatility is 10 ppm, with 80% reduction for 1-5% gives 2 ppm → factor 10 higher. The exposure estimates for shoe factory and refinery are consistent with the inputs described in the article. Note that the authors write that "full information on the workplace ventilation efficiency was not accessible"; therefore use of "good basic ventilation" (providing 30% reduction instead of 90%) seems more appropriate.
Exposure measurements	

• Sampling & analytical methods according to accepted standards?	Not described in the article. Only this information is provided: “Air sampling was by individual dosimeters”.
• Have personal measurements in breathing zone been taken?	Personal measurements: yes Breathing zone: not described.
• If not, is sufficient explanation provided on representativity of measurements?	Not described in the article.
• 8hr TWA exposure: have full shift samples been taken?	Yes “Air sampling was by individual dosimeters, 7.5 h during 8-h shift.”
• If not, is sufficient explanation provided on representativity of measurements?	N/A
• Short term exposure: have 15 minutes samples been taken?	No
• If not, is sufficient explanation provided on representativity of measurements?	N/A
Comparison of estimated with measured exposure	
• Is the measured exposure based on newly collected data, data from old surveys or simulated data?	Not clearly described in the article. It could be both data from existing surveys or newly collected data.
• For data from old surveys or simulated data, has sufficient justification been provided whether these measurements are representative for the scenario under investigation?	Not described in the article.

• How many measurements have been carried out per scenario?	Table 3 contains an overview of all individual measurement results per scenario. There are fourteen scenarios (combinations of substance/activity). Number of measurements per scenario ranges from 5 to 23. Only the datasets with N ≥ 6 samples have been used for the evaluation of the TRA Worker v3.
• For datasets representative for a unique exposure scenario, has the P75 been calculated and compared with the TRA estimate?	No. For each scenario, the authors compare the TRA Worker estimate with the median value. However, the P75 can be calculated from the available data.
• Is sufficient information available or can this be obtained to reconstruct the data-analysis?	Yes. Data-analysis has been reconstructed. Changes: Use of TRA v3 estimates instead of v2 estimates. Paints & lacquers: Use of PROC4 instead of PROC2, leading to a higher TRA estimate; industrial setting was kept, as well as LEV (90 %), although it may be more realistic to use good ventilation (30 %); note that in that case the TRA estimates would again be higher. Shoe factory: although professional instead of industrial setting is more appropriate, Industrial setting was kept for conservative reasons; secondly, good basic ventilation (30 %) was used instead of LEV (90 %), which again is much more realistic. Refinery: use of PROC2 instead of PROC1, as there will be some opportunity for exposure and a continuous process is assumed; alternatively, PROC4 could be selected, leading to higher TRA Worker exposure estimates; furthermore, outdoors has been selected instead of indoors (typical outdoor activity) and therefore LEV (90 %) is set to no.
Conclusions	
• Conclusion on suitability of paper for TRA evaluation	Suitable with restrictions.
• Any other remarks	As the individual measurement results are provided, it is possible to calculate the P75 for comparison with TRA Worker estimate. However, that does not take away other shortcomings: • Unclarity about the quality of measurement data • Unclarity on activities and correct assignment of PROCs • Unclarity on actual presence of LEV in paints/lacquers factory and shoe factory.

A9 Hofstetter

CRITERIA	REVIEW
Paper/Report reference	Modelling Tools and Near-Field, Far-Field Model in Assessing Occupational Exposure to Toluene from Spray Paint. Hofstetter E., Spencer J.W., Hiteshew K., et al. Annals of Occupational Hygiene, Vol 57, No 2, pp 210-220, 2013
Scope of the study	
• Short description of objective of the study and study design	Evaluation of 3 exposure assessment models: **Ecetoc TRA v2.0**, ART, NF-FF model (Spencer and Plisko, 2007) for one exposure scenario: toluene from spray painting in a controlled exposure chamber
• Type of study	Experimental study
• PROC coverage	PROC 11: Non-industrial spraying Note: assignment of *PROC 7: Industrial spraying* is probably more appropriate
• Relevant information for evaluation and improvement of TRA tool?	Yes, it contains well documented high-quality measurements of paint spraying in controlled situation (exposure chamber)
Scenario description	
• Sufficient contextual information to assign PROC, setting, volatility?	Yes
• Sufficient contextual information for selection of exposure modifier settings?	Yes
• Is contextual information available to reconstruct the assignments made by the researchers?	Yes
ECETOC TRA domain	
• Are scenarios within the TRA domain?	Yes
Assignment of PROCs and OC/RMMs	

• Has a team approach and a process for assignment been followed?	Yes (based on "authors' professional judgement")
• Has the assignment of PROCs been done correctly?	Probably not. *PROC 07: Industrial spraying* is probably more appropriate. Note: authors assign *PROC 11: Non-industrial spraying* to a scenario of spraying that occurs in a highly controlled exposure chamber: defined and controlled ACH, standardised process (e.g.: pre-defined duration, volume of spray paint, cleaning of the chamber after each experiment), involvement of trained and well-instructed painters
• Has the assignment of ind./prof. setting been done correctly?	Probably not. *PROC 07: Industrial spraying* is probably more appropriate. Note: authors assign *PROC 11: Non-industrial spraying* to a scenario of spraying that occurs in a highly controlled exposure chamber: defined and controlled ACH, standardised process (e.g.: pre-defined duration, volume of spray paint, cleaning of the chamber after each experiment), involvement of trained and instructed painters.
• Is the selected volatility band correct?	Yes (Toluene 3637 Pa => medium fugacity)
• Has the assignment of exposure modifying factors been done correctly?	Yes (but for TRA Worker V 2.0 only)
Exposure measurements	
• Sampling & analytical methods according to accepted standards?	Yes (NIOSH 1501)
• Have personal measurements in breathing zone been taken? •	Yes (240 minutes samples: n=11 and 15 minutes samples: n=22)
• If not, is sufficient explanation provided on representativity of measurements?	Not applicable
• 8hr TWA exposure: have full shift samples been taken?	No, 240-minute TWA samples (Scenario: 4 minutes spraying + 11 minutes NF exposure + 225 minutes FF exposure)

• If not, is sufficient explanation provided on representativity of measurements?	Yes
• Short term exposure: have 15 minutes samples been taken?	Yes (Scenario: 4 minutes spraying + 11 minutes NF exposure)
• If not, is sufficient explanation provided on representativity of measurements?	yes
Comparison of estimated with measured exposure	
• Is the measured exposure based on newly collected data, data from old surveys or simulated data?	Newly collected measurement data
• For data from old surveys or simulated data, has sufficient justification been provided whether these measurements are representative for the scenario under investigation?	Not applicable
• How many measurements have been carried out per scenario?	11 personal samples ('long term': 240 minutes) 22 personal samples ('short term': 15 minutes)
• For datasets representative for a unique exposure scenario, has the P75 been calculated and compared with the TRA estimate?	No. Authors compare de mean value (probably AM) of 4 hr TWA measurements with TRA Worker v 2.0 8-hr TWA output.
• Is sufficient information available or can this be obtained to reconstruct the data-analysis?	Yes. Note: authors report "*mean*, *standard deviation* and *95% confidence interval*"
Conclusions	
• Conclusion on suitability of paper for TRA evaluation	Paper is suitable for TRA Worker evaluation, because of good quality measurement data of paint spraying in controlled exposure chamber
• Any other remarks	Only 1 scenario: spraying paint (toluene)

A10 Lee, S.

CRITERIA	REVIEW
Paper/Report reference	Comparison of quantitative exposure models tor occupational exposure to organic solvents in Korea Lee S, Lee K, Kim H. Annals of Work Exposures and Health, 2019, vol. 63, no. 2, 197-217.
Scope of the study	
• Short description of objective of the study and study design	Evaluation of the accuracy, precision and conservatism of three models, including ECETOC TRA v3.1.
• Type of study	Comparison of model predictions and repeated exposure measurements from 10 survey reports in Korea (390 exposure measurements, 10 solvents, cleaning tasks in 51 situations at 33 companies in 15 industries).
• PROC coverage	PROC7, PROC10, PROC13, PROC15
• Relevant information for evaluation and improvement of TRA tool?	In principle, the study contains relevant information for evaluation and improvement of the tool, provided the original information from the reports used is available for review. The 10 reports were a selection of 126 exposure surveys made in 2005 and 2006. These surveys covered 450 task-based situations at several hundred different companies in Korea (6000 repeated exposure measurements for various type of substances, e.g. solid, liquids, dust). No clarification is provided why these 10 reports for volatile liquids have been selected. According to the authors, the contextual information included detailed task descriptions, frequency and duration of task, working conditions, engineering controls, RPE and ventilation systems. Pictures during performing the tasks were provided. However, no examples of such contextual information were provided. Before doing the modelling, the researchers visited 12 companies, producing small electrical appliances, flat panel displays, personal mobile devices and other products in 2016, with the objective to observe, identify and determine the principal factors, input parameters and related characteristics for entering in the models. Whether the same (or same type of) companies with similar exposure situations were visited is not mentioned. They conclude that the cleaning tasks, the solvents used, the quantities used and the working conditions have not considerably changed since 2005/2006 (despite the fact that the products were manufactured using upgrade process tools with more efficient ventilation systems and engineering technologies!). It is not clear how these visits have impacted the exposure modelling based on the original data.
Scenario description	

• Sufficient contextual information to assign PROC, setting, volatility?	No, not in the paper as such, possibly in the original reports. With respect to the selection of PROCs, it is not clear why for the trichloroethylene (TCE) scenarios only PROC10 and 13 have been selected, while in the description in table 1 also spraying activities are mentioned (where a PROC7 or, in case of professional setting PROC11, is more applicable. This also applies to the allyl alcohol (AA) and acetone (ACE) scenarios, where all activities are listed as spraying, while PROC7 or PROC11 is not selected. For the glutaraldehyde (GTA) scenarios (detergent manufacturing) the task description lists "spraying in a container", however not PROC7 or 11 was selected but PROC15. For the acetonitrile (ATN) and toluene (TOL) scenarios again PROC10 was selected, while the activity is clearly described as spraying. In conclusion for most of the scenarios the selection of the PROC is not in line with the description of the activity. With respect to the setting, based on the information provided on the type of companies and activities the selection of industrial setting for all exposure situations might not be sufficiently conservative.
• Sufficient contextual information for selection of exposure modifier settings?	The original reports most likely contain sufficient information for selection of exposure modifier settings, but this cannot be evaluated.
• Is contextual information available to reconstruct the assignments made by the researchers?	Based on the information provided in the paper the assignments can be reconstructed, however on some of the PROC and exposure modifier settings there is considerable uncertainty.
ECETOC TRA domain	
• Are scenarios within the TRA domain?	Yes, except for the scenarios on HCFC (no 46 to 51). HCFC is a gas. This is not covered by TRA Worker. These datasets have been excluded from the evaluation of the TRA Worker v3.
Assignment of PROCs and OC/RMMs	
• Has a team approach and a process for assignment been followed?	The authors claim that each of the assessors had sufficient experience to apply the modelling tools (although the choice of PROCs for application of the TRA Worker is questionable). In the process of assigning parameter settings, it seems that in case of disagreement the two main authors took the final decision on assignment (e.g. not excluding situations when there was disagreement).
• Has the assignment of PROCs been done correctly?	There is uncertainty on the PROC assignment, see above.
• Has the assignment of ind./prof. setting been done correctly?	Based on the information provided on the type of companies and activities the selection of industrial setting for all exposure situations is most likely not sufficiently conservative.
• Is the selected volatility band correct?	Yes.

• Has the assignment of exposure modifying factors been done correctly?	See above.
Exposure measurements	
• Sampling & analytical methods according to accepted standards?	Limited information is provided. The authors state the use of "certified analytical methods (mostly NIOSH methods).
• Have personal measurements in breathing zone been taken?	Yes, although breathing zone is not specifically mentioned.
• If not, is sufficient explanation provided on representativity of measurements?	Not relevant.
• 8hr TWA exposure: have full shift samples been taken?	Yes, sample duration was in general between 360-480 minutes; in some cases: 240 minutes.
• If not, is sufficient explanation provided on representativity of measurements?	Not applicable.
• Short term exposure: have 15 minutes samples been taken?	Yes. Sample time was between 15 to 30 minutes. The datasets with short term measurements have not been taken into account (included in a separate database with short term measurements).
• If not, is sufficient explanation provided on representativity of measurements?	Not applicable.
Comparison of estimated with measured exposure	
• Is the measured exposure based on newly collected data, data from old surveys or simulated data?	Data from old surveys from 2005-2006.
• For data from old surveys or simulated data, has sufficient justification been provided whether these measurements are representative for the scenario under investigation?	Refer to scope of the study: Relevant information for evaluation and improvement of TRA Worker.
• How many measurements have been carried out per scenario?	Depends on the scenarios. In a few cases as low as 2 measurements are available. However, there are also scenarios with 10 or more measurements. Only the scenarios with N $\geq$ 6 measurements have been included in the database for evaluation of the TRA Worker v3.

• For datasets representative for a unique exposure scenario, has the P75 been calculated and compared with the TRA estimate?	Yes.
• Is sufficient information available or can this be obtained to reconstruct the data-analysis?	As stated above, on some of the PROC and exposure modifier settings there is considerable uncertainty. Most likely the information in the original reports is sufficient to construct the TRA Worker estimates, however the original reports are not available in English.
Conclusions	
• Quality score (B19 scheme)	Data quality exposure survey: 1 Data quality for TRA Worker application: 3
• Conclusion on suitability of paper for TRA evaluation	If the original studies could be obtained in English, the paper would be suitable for TRA Worker evaluation. However, the original studies are only available in Korean. However, based on the available information, including the information in the supplementing tables, an attempt was made to construct the TRA Worker v3 estimates.
• Any other remarks	• The outcome of the comparison between measured and estimated exposure is strongly impacted by the selection of the PROC and the industrial or professional setting, as done by the authors. In most of the scenarios the selection of the PROC is questionable and presumably not sufficiently conservative. • Secondly, in this study in all cases an industrial setting is assumed, which is not very likely. • In the construction of TRA Worker estimates by the TF the PROC selection has been changed for some of the datasets, based on contextual information in the paper and the supplementing materials (datasets TCE-2-twa, PCE-2-twa, PCE-5-twa perchloroethylene): PROC10 changed to PROC7; dataset AA-1-twa: PROC13 changed to PROC15). • For all datasets where the use of RPE was set to YES, this has been changed to NO (as there is no indication that measurements have been performed inside the masks).

A11 Lee, E.

CRITERIA	REVIEW
Paper/Report reference	Evaluation of Exposure Assessment Tools under REACH: Part I - Tier 1 Tools.

	E. G. Lee, J. Lamb, N. Savic, I. Basinas, B. Gasic, C. Jung, M. L. Kashon, J. Kim, M. Tischer, M. van Tongeren, D. Vernez, M. Harper Ann Work Expo Health. 2019 Feb 16;63(2):218-229.
Scope of the study	
• Short description of objective of the study and study design	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 EMKGEXPO-TOOL. MEASE v1.02.01 (referred to as 'MEASE') was also evaluated for the applicable chemicals. 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, 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.
• Note	The article's results cannot be directly re-constructed from the paper and the Supplementary data available for the article. Furthermore, it is not possible to identify the exposure determinants used to develop the TRA Worker estimates. The overall number of ESs (n=14) for which significant representative sample data are available (n>6) is limited. In addition, the method of analysis applied in the original article (which assumes data homogeneity from samples pooled from across ESs with similar PROCs) is flawed as evidenced by the large ES GSDs.
• List of supplementary materials referred to	Emily Lee at NIOSH has kindly made available to ECETOC the ES descriptions and data used in the 2019 publication. These, together with other relevant publications from NIOSH, have enabled reliable TRA Worker predictions to be made for the scenarios where 6 or more exposure measurements are available (12 for volatile liquids and 2 for dusty solids): 1. Evaluation of Styrene and Dust Exposures and Health Effects during Fiberglass-Reinforced Wind Turbine Blade Manufacturing, Joshua M. Harney, Anna-Binney McCague, Kristin J. Cummings, Jean Cox-Ganser, HHE Report No. 2013-0056-3256, August 2016, 2. Lee E, Slaven J, Bowen R, Harper M (2011) Evaluation of the COSHH Essentials model with a mixture of organic chemicals at a medium-sized paint producer, Ann. Occup. Hyg. , vol. 55, no. 1, pp. 16-29. 3. Lee E, Harper M, Bowen R, Slaven J. (2009) Evaluation of COSHH Essentials: Methylene Chloride, Isopropanol, and Acetone

	Exposures in a Small Printing Plant, Ann. Occup. Hyg., vol. 53, no. 5, pp. 463-474. 4. Eun Gyung Lee,[1] Braxton Lewis,[1] Dru A. Burns,[1] Michael L. Kashon,[2] Seung Won Kim,[1] and Martin Harper[1]Assessing Exposures to 1-chloro-4-(trifluoromethyl) Benzene (PCBTF) in U.S. Workplaces, J Occup Environ Hyg. 2015; 12(7): D123–D130. 5. Duane Hammond, Alberto Garcia, H. Amy Feng, Occupational Exposures to Styrene Vapor in a Manufacturing Plant for Fiber-Reinforced Composite Wind Turbine Blades, Annals of Occupational Hygiene, Volume 55, Issue 6, July 2011, Pages 591–600
• Type of study	Evaluation based on comparison of TRA Worker estimates for a PROC with measurement data
• PROC coverage	PROCs 3,5,7,8b,9,10,11,13,15 and 23 are identified as being addressed by the article. However, for liquids, only PROCs 5, 10 and 15 are supported by significant sample numbers (n≥6), all of these relate to moderate volatility liquids and the distribution across PROCs is not uniform. Solids exposures are limited to PROCs 8b and 23.
• Relevant information for evaluation and improvement of TRA tool?	Yes, when use is also made of the underpinning data sources then the article yields high quality information required for revaluating exposure tools, but limited to liquids with VP>10 Pa
Scenario description	
• Sufficient contextual information to assign PROC, setting, volatility?	Yes, when use is also made of the underpinning data sources then iinformation on exposure determinants and volatility is available. Limited information for solids and high/low volatility liquids.
• Sufficient contextual information for selection of exposure modifier settings?	Yes: “During the field surveys, contextual information required for each tool’s input parameters were obtained”. However, no detailed information is provided in the paper (but can be obtained from the relevant supporting data sources)
• Is contextual information available to reconstruct the assignments made by the researchers?	Not published but subsequent correspondence with the authors has enabled assignment of TRA Worker estimates to be identified and reliable reconstructions made
ECETOC TRA domain	
• Are scenarios within the TRA domain?	Mostly. Some ESs are not covered by the TRA Worker (e.g. those addressing “solids-in-liquids”). Similarly, ‘glue application’ refers to GRP in turbine blade manufacture and potential for confined space work.
Assignment of PROCs and OC/RMMs	

• Has a team approach and a process for assignment been followed?	Yes. Six assessors from different organisations (although no information provided on extent of between user variability etc)
• Has the assignment of PROCs been done correctly?	Partly. No detailed information provided in article but based on subsequent provision of supporting information then basis for assigning some PROCs questionable (e.g., see Table S2 – path lab assigned PROC 13 whereas PROC15 would appear to be more appropriate.
• Has the assignment of ind./prof. setting been done correctly?	Mostly. No detailed information contained within the article but supporting data sources enable reliable assignment
• Is the selected volatility band correct?	Yes. Most are liquids with Vp>10 Pa
• Has the assignment of exposure modifying factors been done correctly?	No detailed information in article. Basis for relationship between TWA measurements and task average exposure estimates can be extracted from supporting data sources and, in some cases, these are not correct
Exposure measurements	
• Sampling & analytical methods according to accepted standards?	The samples obtained have applied the relevant NIOSH or Occupational Safety and Health Administration sampling and analytical methods for personal monitoring
• Have personal measurements in breathing zone been taken?	Yes. No detailed information in the article although supporting Data sources indicate personal monitoring was undertaken.
• If not, is sufficient explanation provided on representativity of measurements?	N/A
• 8hr TWA exposure: have full shift samples been taken?	Yes, either full shift samples taken or alternative sampling periods intended to reflect TWA of task duration. Any TWA modifications consistent with occupational hygiene practices.
• If not, is sufficient explanation provided on representativity of measurements?	This can be inferred from examination of the data sources but is not possible from the information presented in the article

• Short term exposure: have 15-minute samples been taken?	No
• If not, is sufficient explanation provided on representativity of measurements?	N/A
Comparison of estimated with measured exposure	
• Is the measured exposure based on newly collected data, data from old surveys or simulated data?	Newly collected data
• For data from old surveys or simulated data, has sufficient justification been provided whether these measurements are representative for the scenario under investigation?	N/A
• How many measurements have been carried out per scenario?	Total of 293 measurements obtained across 53 scenarios. However, only datasets for PROC 5, 10 and 15 contain more than 6 samples and these only examine moderate volatility liquids (n=162).
• For datasets representative for a unique exposure scenario, has the P75 been calculated and compared with the TRA estimate?	Yes. In the article, the 75th percentile of the measured exposure distribution was calculated and compared with the TRA Worker estimate. However, the P75 was calculated for all the pooled data within a PROC without any prior test of data homogeneity. The data sources suggest this is likely an inappropriate assumption based on scenario GSDs.
• Is sufficient information available or can this be obtained to reconstruct the data-analysis?	The article and Supplementary tables contain insufficient information for reliable re-construction. However, when the article is read in the context of the supporting data sources then sufficient information is available to develop reliable TRA estimates for certain (but not all) ESs.
Conclusions	

• Conclusion on suitability of paper for TRA evaluation	This paper requires careful interpretation for the reasons outlined. Only a limited number of scenarios (PROCs) contain sufficient measurement data from a representative range of different settings to allow meaningful conclusions to be drawn. Furthermore, analysis of the data sources of how TRA determinants were assigned reveals incorrect choice of PROC 13 (when quantities in use reflect PROC15) and occasional errors for choice of substance concentration, task duration and use of LEV
• Any other remarks	In the article, no test of goodness of fit was undertaken prior to statistical analysis of (pooled) datasets (covering more than one scenario). Rather, the authors assume data independence and homogeneity (when examination of the relevant data sources indicates that many are clearly heterogeneous).

A12 Ishii

CRITERIA	REVIEW
Paper/Report reference	Evaluation of the ECETOC TRA model for workplace inhalation exposure to ethylbenzene in Japan. Satako Ishii, Ritsuko Katagiri, Kimiyoshi Kitamura, Masaaki Shimojima, Takeharu Wada Journal of Chemical Health and Safety Volume 24, Issue 1, January–February 2017, Pages 8-20
Scope of the study	
• Short description of objective of the study and study design	To determine whether TRA Worker could be used in the Japanese workplace when Japanese companies perform voluntary risk management for occupational exposure.
• Type of study	Retrospective review of measured data compared to constructed TRA Worker values for individual data points for multiple PROCS
• PROC coverage	PROC2, 3,4,5,8a,8b, 13,14,15 manufacturing of styrene monomer; PROC 7 & 10 painting of ships with solvent-based paints
• Relevant information for evaluation and improvement of TRA tool?	The data collected in 2009 & 2010 comprising of 119 tasks were noted to be before the implementation of suitable risk management measures. The data from 2014-2015 were

	generated after such risk management measures had been considered. The data from manufacturing PROCs indicate that 94% of TRA Worker estimates exceed the measured values. None of the manufacturing PROC measurements exceeded the TLV of 20 ppm. PROC 7 & 10 related to the painting activity indicated that 32% of cases the measured value exceeded the TRA Worker values, specifically for PROC 10 this rises to 58%. In 91% of cases for PROC 10 the TLV was exceeded and 40% for PROC 7. The paper makes comparison for individual data points with no consideration of grouping with the same modifying factors.
Scenario description	
• Sufficient contextual information to assign PROC, setting, volatility?	Yes: Appendix contains the following information. PROC, state, VP, LEV, setting (ind/prof), indoor/outdoor, duration, RPE, concentration, measured value (ppm), estimated value (TRA Worker: ppm) and ratio (TRA Worker values/measured value). There is no quantitative indication of mechanical ventilation (it can be calculated in most instances from TRA Worker and other MFs)
• Sufficient contextual information for selection of exposure modifier settings?	Yes, detailed as above
• Is contextual information available to reconstruct the assignments made by the researchers?	Yes, in the most part, relying on the TF to calculate mechanical ventilation rate, or to suggest the type of mechanical ventilation
ECETOC TRA domain	
• Are scenarios within the TRA domain?	Yes
Assignment of PROCs and OC/RMMs	
• Has a team approach and a process for assignment been followed?	Unclear if team approach was used for PROC assignment
• Has the assignment of PROCs been done correctly?	Yes, manufacturing PROCS assigned correctly and painting PROCS assigned correctly

• Has the assignment of ind./prof. setting been done correctly?	Yes
• Is the selected volatility band correct?	Yes, in the appendix with full details some VP values are not consistent, but still within the volatility banding fugacity
• Has the assignment of exposure modifying factors been done correctly?	Yes
Exposure measurements	
• Sampling & analytical methods according to accepted standards?	2009 and 2010 used methodology developed by sub-committee. 2014-2015 survey: Sampling in breathing zone at 100ml/min Analytical methodology used a modified NIOSH 5515 for Poly aromatic hydrocarbons using mass selective detector. Data points related to PROC 7 with LEV and duration >4 hours have identical results for both concentration >25% and 5-25%;
• Have personal measurements in breathing zone been taken?	Yes
• If not, is sufficient explanation provided on representativity of measurements?	NA
• 8hr TWA exposure: have full shift samples been taken?	Unclear on duration of monitoring. Duration of task as a modifying factor defined in Table A1. The measurement results, as defined by the authors in the text, are 8hr TWA results.
• If not, is sufficient explanation provided on representativity of measurements?	NA
• Short term exposure: have 15 minutes samples been taken?	No
• If not, is sufficient explanation provided on representativity of measurements?	Not defined
Comparison of estimated with measured exposure	
• Is the measured exposure based on newly collected data,	Retrospective data, prior to an intervention 2009 & 2010 and post intervention 2014-2015

data from old surveys or simulated data?	
• For data from old surveys or simulated data, has sufficient justification been provided whether these measurements are representative for the scenario under investigation?	Yes. The data is from retrospective studies and has, in the case of painting, exceedances of exposure above the TLV
• How many measurements have been carried out per scenario?	PROC 2: 2 PROC 3: 2 PROC 4: 1 PROC 5: 5 PROC 8a: 16 Proc 8b: 7 PROC 9: 11 PROC 13: 4 PROC 14: 1 PROC 15: 3 Painting PROC 7: 47 PROC 10: 38 Above relate to tasks, no indication of number of measurements per task
• For datasets representative for a unique exposure scenario, has the P75 been calculated and compared with the TRA estimate?	No. Calculation of the TRA Worker estimates in the paper is inconsistent, calculated TRA Worker values for the comparison based on indoors having good ventilation with MF = 0.7
• Is sufficient information available or can this be obtained to reconstruct the data-analysis?	With access to the original data yes, from the paper as is No
Conclusions	
• Conclusion on suitability of paper for TRA evaluation	Suitable for evaluation, but limited data points on many PROCS. The evaluation is based on individual measurements and does not group similar data. By extracting the information from the appendix there are a number of data sets with n≥6 but only for PROC 7 and 10 for painting activities.
• Any other remarks	Medium volatility substance in an industrial setting in non-EU workplaces.

• ECETOC summary statement for ENES 3.2 review	Paper and data are suitable but limited to PROCs 7 & 10 with sufficient number of tasks evaluated, noting that there is significant exceedance above TLV for painting PROCs.

A13 CONCAWE

CONCAWE commissioned a team of researchers from Fraunhofer ITEM and IOM to compare the exposure estimates in its REACH dossiers for petroleum substances with measured exposure data. CONCAWE had used the TRA v2 in 2010 to create chemical safety assessments, including several sector-specific adaptations as documented in report 11/12 (Concawe, 2012). The ITEM/IOM review was published in CONCAWE report 13/18 and its Supplement (Concawe, 2018). Some of the data sources used by the ITEM/IOM team were the same as used in the ETEAM project, e.g., from BAuA field studies (Auffarth et al., 2002) and NIOSH. Additionally, the project reviewed and included a large number of exposure measurement records contained in CONCAWE reports for gasoline (reports 9/02 (Concawe, 2002) and 5/09 (Concawe, 2009)), kerosine (report 6/07 (Concawe, 2007)) and gas oils (report 1/06 (Concawe, 2006)), and some data from literature sources (e.g., Periago and Prado, 2005).

Because of the sector-specific adaptations used by CONCAWE and the resulting customised exposure estimates for some classes of petroleum substances, the findings of the ITEM/IOM team have limited direct relevance to the performance evaluation of the standard TRA Worker by ECETOC. However, many of the included data sets were found to be of sufficient quality for the comparison with standard TRA Worker v3 calculated exposure estimates and are hence included in the newly created ECETOC curated database.

APPENDIX B: DISTINCTION BETWEEN INDUSTRIAL AND PROFESSIONAL USES

Industrial and professional use in the context of ECETOC TRA

(Based on the text related to the topic in ECETOC Reports TR 107 and TR 131 and the ECHA Guidance document R12 and the ECHA Guidance for Downstream Users)

The TRA tool for workers originally made no distinction between the industrial and professional uses of a substance. However, following the RIP 'REACH Implementation Project' 3.2-2 activity, it was felt that there was a need to distinguish between professional and industrial uses as part of the process for developing a substance's 'life cycle tree' (the introduction of the Process Category to define tasks or process types from a worker perspective). Accordingly, in the update of the exposure predictions in TRA Worker v2 the capability was introduced to differentiate the exposure estimates of the two types of use as well as the efficiency in operation of certain risk management systems, e.g. (local extract) ventilation systems. Industrial experience demonstrates that the nature of handling and the lower level of control in non-industrial (professional) settings often gives rise to elevated exposures, due to a lower availability of suitable and dedicated equipment and a lower level of factors as operating procedures, training and supervision.

For industrial uses, the TRA Worker assumes a higher level of equipment provision, supervision and training than that which might be typically encountered in professional uses e.g., permanent exposure controls that are subject to systems of routine inspection and maintenance; codification of methods of safe work in procedures and OH&S management systems. In general, this type of conditions only (but not necessarily) applies to industrial production sites, large construction sites and/or large maintenance/repair and service sites with a relatively high amount of processed chemicals per site.

Professional uses represent the base case of the TRA Worker and equate to use under practices following the basic education and training expected to be provided to employees consistent with the provisions of EU H&S Regulations (notably 89/391/EC and 98/24/EC) and often promoted by sector organisations in seminars, publications and vocational schemes. Typical examples of professional use are small maintenance and cleaning services, small building and construction enterprises, craftsmen, hairdressers, painters, etc.

Experiences with life-cycle building and reviews of studies in which the TRA tool for workers has been applied and a distinction has been made between industrial and professional use indicate that this distinction is not always simple and requires some understanding of how different industry sectors are likely to be operated. The typical conditions of use leading to emissions and exposures in a given situation may not fully align with the broad definitions described above. Secondly, the scenario description alone may not always be sufficient to be able to reliably assign a relevant PROC and use domain. For example, it is also necessary to know how a substance is being used (e.g., for a coating, is it via processes that are primarily using spraying, rolling, brushing or dipping). Therefore, when in doubt about the actual conditions or when there is no clear confirmation that a process can be considered as industrial use both on industrial nature of process/activity and level of control, it is recommended to assume that processes or activities are professional and not industrial. Secondly, it should also be noted that where 'industrial' activities are identified, then the registrant should clearly indicate

that these are supported by some form of 'established' Occupational Health and safety (OH&S) management system, which could be considered as an Operational condition (OC) that is communicated as part of relevant Exposure Scenarios (ES).

For more detailed information, refer to: ECETOC Technical Report 107 and 131, ECHA Guidance on Information Requirements and Chemical Safety Assessment Chapter R12: use description, ECHA Guidance for Downstream Users

APPENDIX C: PROCESS CATEGORIES ('PROCS') AND LOCAL EXHAUST VENTILATION EFFICIENCY

General Ventilation and Local Exhaust Ventilation in the context of ECETOC TRA

When the TRA Worker is used 'prospectively', such as in the case of developing REACH EAs/CSRs, then the risk assessor using the TRA Worker will assign an efficiency to the chosen general ventilation (GV) class ('good' or 'enhanced') based on the informed user choices (such as information supplied via Use Maps). The supporting ES should then communicate the need for this type of GV via appropriate standard phrases (such as those of ESCom). It is then for the downstream user to ensure that the local system of GV is such (e.g. location of task relative to ventilation sources, direction of airflow, training and supervision of employees, etc.) that it provides exposure reduction equivalent to the scenario described in the ext-SDS.

For the development of the ECETOC curated database, the vast majority of the data reviewed had TRA Worker parameters assigned retrospectively based on contextual information in the published papers or regulatory agency reports e.g. NISOH HHE. The type and efficiency of GV and local exhaust ventilation (LEV) for the papers and reports could not be explicitly confirmed and in those cases the ventilation modifying factors (MFs) were based on reasonable practicality in the described workplace. In the case where LEV was present and functioning, the default efficiency from the TRA Worker was used unless there was contextual information to apply a reduction in the modifying factor.

Local extraction ventilation (LEV)

The TRA Worker assigns differing levels of LEV effectiveness to the various activities described by the PROCs. The effectiveness values were chosen to represent what might reasonably be achieved for that use when suitable LEV (for the activity/task) is properly installed, sited, used and maintained e.g. HSG 258. In the case of industrial uses, a value of 90% generally applies apart from PROCs 7 (Industrial spraying) and 8b (Transfer of chemicals at dedicated facilities), where a value of 95% is applied to reflect the likelihood that more efficient forms of extraction will be encountered. However, for PROC 24 (High energy work-up of substances bound in materials), a lesser value of 80% applies as extraction efficiencies of 90% are not routinely associated with this activity. For professional uses, a general value of 80% is applied that reflects the lower levels of worker training and supervision that are frequently encountered in many professional settings. The professional LEV efficiencies for PROCs 8b are 90% for volatile substances and 80% for solids. Professional spraying activities (PROC 11) are assumed to have an 80% extraction efficiency.

It has become apparent in the TF's review of the published studies, however, that several authors have not properly taken into account these underlying assumptions. For example, some studies have encountered forms of ventilation that are being used in the workplace that are significantly less effective than those that the TRA Worker would anticipate might responsibly be being applied in the situation. For example, the use of

mobile 'elephants trunk' extraction systems when bulk weighing hazardous powders or the use of simple slot ventilation systems during material transfers, when established guidance would indicate the need for much better forms of LEV in such circumstances. Similarly, some authors have used as a comparator the monitoring data from studies where it has been demonstrated that the LEV in place in the workplace was inadequate (in design and installation, use and/or from insufficient maintenance). In these cases, it is inappropriate to apply the TRA Worker LEV default values to derive the TRA Worker estimate. Rather, an assumed effectiveness towards 0% would have been more appropriate.

These distinctions are important. The TRA Worker is intended to help identify the nature of RMMs/controls that should be applied to ensure that exposures to a substance do not constitute a health risk. This means that should the TRA Worker assume 90% LEV efficiency for a PROC, the supplier is expected to communicate RMM advice consistent with that assumption and the user consequently needs to take steps (correct design, installation, use, etc.) to ensure the advice is correctly implemented. In this respect, the EsCom standard phrases for use in the communication of RMMs in ext-SDSs allow for such a linkage. Doing otherwise not only represents an incorrect use of the TRA Worker but is also likely to place workers at an elevated risk of exposure to hazardous substances.

Similarly, when making comparisons of TRA Worker estimates with 'real-life' values, then it is necessary to examine the true nature of the exposure determinants associated with any scenario/use for which a TRA Worker estimate is being developed and to ensure these are properly accounted for in process for how the estimate is determined. With the TRA Worker, estimates are easy to generate. But representative and reliable estimates require prior analysis of the situation by a knowledgeable person e.g. experienced and competent occupational hygienist.

Table 7: Example types of LEV for PROCs that constitute good practice and will provide adequate control

PROC/description	LEV Effectiveness (PW/IND)	Indicative LEV Type
5/mixing blending	80% / 90%	Walk in booth / capture hood
7 Industrial spraying	n/a/95%	Walk in booth/ Downflow booth
8a/Transfer (non dedicated)	80% / 90%	Slot extraction at transfer point
8b/ Transfer dedicated	90%/95%	Total enclosure
9/ transfer into small containers	80% / 90%	Capturing hood/receiving hood
10/roller application or brushing	80% / 90%	Capturing hood/receiving hood
11/non industrial spraying	80%/n/a	Small enclosure
13/ dipping and pouring	80% / 90%	Partial enclosure
14/ tabletting, compression, extrusion	80% / 90%	Capturing hood
15/ laboratory	80% / 90%	(Fume cupboard) partial enclosure

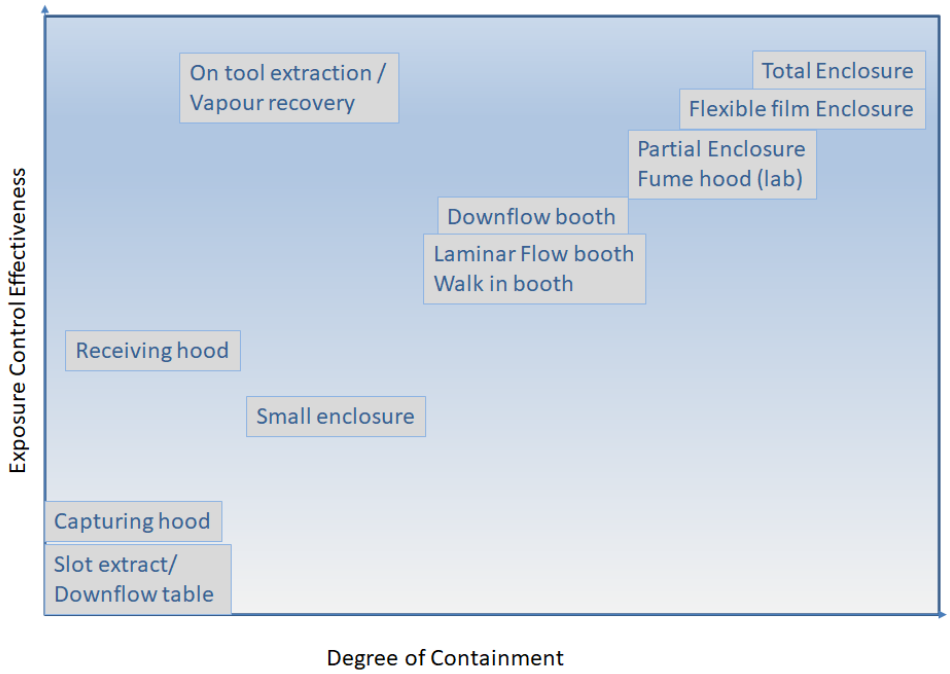

Figure 1: Efficiency and containment of LEV systems

Incorrect application of LEV was identified by Hebisch et al. where it was noted that for LEV the following deficits were noted:

- Incorrect positioning of the LEV
- No repositioning of the LEV
- Air velocities of the LEV too small
- Leakage in the transfer duct or damaged capture hood.

General Ventilation

The TRA Worker includes the ability to apply two levels of general ventilation: good GV (GV) and enhanced (EGV), offering a 30% and 70% exposure reduction to the base estimate, respectively, as the Modifying Factor (MF), and indicating the number air changes per hour (ACH) required to achieve these.

The conditions relating to what constitute GV and EGV and when each might be applied are described below (Table 8) in accordance with section 2.2.3 of TR114.

Table 8: Conditions of GV and EGV

Type of general ventilation	Application	Ventilation effectiveness
Basic general ventilation	Corresponds to: Basic natural ventilation Typically, 1-3 ACH	0% MF=1.0
Good general ventilation	Corresponds to: Good natural (e.g, doors and windows open and or non-engineered mechanical ventilation Typically, 3-5 ACH	30% MF = 0.7
Enhanced general ventilation	Corresponds to: Engineered mechanical ventilation At least 5-10 ACH	70% MF=0.3
Outdoor	Corresponds to “use outdoors”	30% MF=0.7

It was identified during the current review of the studies, that both good GV and enhanced GV were frequently inappropriately applied to derive TRA Worker estimates. Two commonly encountered failures were noted:

1. The ventilation described in the article did not equate to the definition as being associated with the good GV standard i.e. the expectation that an air exchange rate of 1-3 air changes per hour can consistently be obtained. Often the GV described in the article was unlikely to be effective to any great extent. For example, the presence of an open window or door is unlikely to equate to good GV. The same holds true for a simple axial flow fan in the wall, especially when it is remote from the activity.

2. The ventilation described in publications did not equate to the definition as being associated with the good EGV standard i.e. the expectation that a minimum air exchange rate of 5 (but preferably at least 10) air changes per hour can consistently be obtained. For example, the presence of single axial fan in a wall is most unlikely to be sufficient to equate to enhanced GV. The same can also be said of a recirculating HVAC system or a roller shutter door in an industrial unit.

In the course of the review the TF have used GV, EGV and LEV as stated in the published papers unless there was good evidence to apply a different level of control. Where any differences have been applied by the TF this has been referenced in the comments field of the database.

ABBREVIATIONS

ART	Advanced Reach Tool
BAuA	Bundesanstalt für Arbeitsschutz und Arbeitsmedizin
Cefic	European Chemical Industry Council
CSR	Chemical Safety Report
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemicals
ECHA	European Chemicals Agency
DNEL	Derived No-Effect Level
GM	Geometric Mean
GSD	Geometric Standard Deviation
LEV	Local Exhaust ventilation
NIOSH	The National Institute for Occupational Safety and Health
NOEC	No-observed-effect concentration
OC	Operating Conditions
PROC	Process Category
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
RMM	Risk Management Measures
RPE	Respiratory Protective Equipment
SEG	Similar Exposure Group
TF	Task Force
TLV	Threshold Limit Value
TWA	Time-Weighted Average

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