Advances in Consumer Exposure Science: Data, Modelling and Aggregate Exposure Assessment

26th January 2016, Brussels

Workshop Report No. 31

EUROPEAN CENTRE FOR ECOTOXICOLOGY AND TOXICOLOGY OF CHEMICALS

Advances in Consumer Exposure Science: Data, Modelling and Aggregate Exposure Assessment

26th January 2016, Brussels

Workshop Report No. 31

Brussels, August 2016

ISSN-2078-7219-31 (online)

ECETOC Workshop Report No. 31

European Centre for Ecotoxicology and Toxicology of Chemicals
2 Avenue E. Van Nieuwenhuyse (Bte 8), B-1160 Brussels, Belgium.

Advances in Consumer Exposure Science: Data, Modelling and Aggregate Exposure Assessment

CONTENTS

1. SUMMARY

This workshop report summarises a workshop held in Brussels on 26th January 2016 by the ECETOC Human Exposure Data Task Force on the state of the art of consumer exposure assessment science as developed over a period of two years (2013-2015). Over forty exposure experts from industry, academia and regulatory domains came together to: (i) discuss the status of consumer exposure science; (ii) develop consensus on key gaps, and from there, (iii) identify a prioritised research agenda.

Seven presentations provided an overview of (1) The ECETOC Human Exposure Task Force; (2) Robust Exposure Assessment in Refining Risk Assessment; (3) Modelling Total Exposure to Chemicals in Multiple Sources; (4) Presentation of the Task Force's Landscaping Exercise, summarising available data, sources, models and tools; (5) The case study of phenoxyethanol in household, personal care and cosmetic products; and (6) The case study of solvent use in consumer chemical products. These topics were discussed and debated in detail in two separate discussion sessions. Finally, brainstorm sessions enabled experts to identify consensus on gaps and suggestions on how to move forward.

There was agreement that clear, harmonised guidance on aggregate consumer exposure assessment is required. To this end, delegates from the OECD, JRC, EPA and ECHA offered to discuss future cooperation on this activity within their organisations and to contribute to the Landscaping Document initiated by the ECETOC Task Force. This valuable resource brings together the currently available consumer data, sources, models and tools.

Participants decided that such guidance should include (but not be limited to) the following elements:

1. Direction on how to determine the most suitable models and data sources for specific aggregate consumer exposure assessments to include decision trees and problem formulation templates. These should have well-stated and validated (as far as is possible) applicability domains with standardised descriptors recognising the unique factors of each model that determines its fitness for purpose. This could include triggering criteria for higher tier aggregate consumer exposure assessment. It was suggested that the OECD provides a platform that could be used to harmonise these data, models, standards and tools across geographies.
2. Open access and/or commercially available databases on consumer information, including consumer use information and product composition (chemical concentration and presence probability data) across domains.
3. Direction on how the risk assessor should include a justification narrative (explaining why a particular tool and input data were chosen).
4. An agreed process to extrapolate the applicability of exposure data in different contexts as a means of 'gap filling' in data sparse situations. For example, best practice exists in the occupational setting (Money and Margary, 2002; ECHA, 2012), which could potentially be extended or adapted to consumer settings. Criteria and internationally accepted rating systems would be needed to evaluate the quality of the data and ensure confidence in such approaches.

5. Assessment of how life cycle perspectives could be applied to help determine the nature of exposures.

Finally, the following three suggestions for future research were developed, and will be discussed during future ECETOC and Cefic LRI management meetings:

1. Obtaining data on product compositions: this is essential for realistic exposure assessment, particularly when considering aggregate exposure. Without reliable composition data, exposure assessments are based on worst case assumptions giving rise to product restrictions. Questions that need to be answered include: How do we collect, store, share and maintain anonymised product composition data? How do you overcome the barriers to implementing this action across geographies and industry sector groups? Who should lead such an activity?
2. Developing an agreed process to extrapolate the applicability of exposure data in different contexts. Ideally, exposure assessments are based on actual measurements of population exposures (workers, consumers, the general population), but for many exposure scenarios, data are hard to find. In these cases, exposure must be estimated using models or by reference to data for analogous substances or situations. Currently there is paucity of advice on the circumstances where analogous data might be applied. By contrast, in hazard assessments, processes have been developed to enable data from various sources to be combined. This could be a starting point for a similar approach in exposure assessment.
3. Developing a framework for exposure assessment of exposure data-poor chemicals that includes quality and weight of evidence assessment. Questions that need answers include: Can the principles that are being developed for quality and weight of evidence of hazard assessment be applied for exposure assessment? How do you overcome the barriers to implementing this action across geographies and industry sector groups? Who should lead such an activity?

2. BACKGROUND AND AIM OF THE WORKSHOP

In the absence of additional data on product ingredients, un-validated assumptions will be used to estimate both ingredient technical function and weight fraction (concentration) information. These approaches may lead to incorrect or overly conservative exposure predictions.

Overly conservative exposure will inevitably lead to chemical restriction through legislation, including unnecessary bans on chemicals. This would result in costly reformulation efforts for industry – and potentially block new innovation. On the other hand, adequate and realistic exposure predictions may support regulatory decisions on adaptation for hazard information requirements (e.g. under REACH). In situations where human or environmental exposure is absent, or so low that additional effects information will not lead to improvement of risk management, exposure-based waiving may be considered to avoid unnecessary animal testing.

Exposure-driven risk assessment has long been included in the risk assessment of chemicals. Reliable descriptions of human external exposure and internal dose through modelling, facilitates the targeted use of emerging toxicological tools for risk assessments. Benefits of reliable exposure assessments include:

- Reduced uncertainty, enabling risk assessment to be a more representative reflection of the actual situation.
- Improved integrity of the assessment by enabling more targeted risk management decisions, based on detailed exposure assessment.
- Prevention/reduction of the need for animal testing.

Implementing refined approaches to exposure assessment requires consideration of:

- Data availability.
- Specialised tools, data sets and computational power.
- (Standard) approaches for the collection and sharing of appropriate data on consumer exposure.
- Criteria for selecting suitable exposure databases and modelling tools available.

The aims of this workshop were to:

- Present and review the current state of consumer exposure science by examining data needs, sources (including novel data sources), tools, gaps and the latest innovations.
- Develop consensus on key gaps that should be filled and identify what the major research needs are, including how to address aggregate consumer exposure.
- With the help of case studies, examine the potential for the refinement of exposure assessment using appropriate tools and techniques which are fit for purpose.

3. PLENARY LECTURES

3.1 Characterising Exposure in the 21st Century

3.1.1 Overview of the ECETOC Human Exposure Task Force

Sarah TOZER
P&G, UK

Dr Tozer introduced task force members (See Appendix D), stewards and partners involved in this ECETOC project. She explained that in many instances, exposure and toxicokinetics are more discriminating determinants of risk than is hazard. Key considerations with the progress in toxicology in the 21st century include linking consumer exposure data to *in vitro* toxicology dose response data for safety assessment. An early focus on exposure is essential as a basis to increase efficiency and reliability in risk assessment. There is a need for a structured approach for assessing and integrating human exposure data into the risk assessment. Whilst many models are available, e.g. ConsExpov.5.0[1] (Delmaar *et al*., 2005), Creme Care & Cosmetics™ (Creme Global, 2011[2]), Lifeline (The Lifeline Group[3]), and Stochastic Human Exposure and Dose Simulation or SHEDS (US EPA, 2015[4]) and others (TAGS, 2011[5]), there is a lack of guidance as to their applicability to assessing exposure in the context of the problem formulation for risk assessment.

The overall aim of the ECETOC Human Exposure Data Task Force was to provide exposure assessors with a review of exposure data sources that are available, and to provide guidance how to incorporate data inputs for high tier aggregate exposure assessment for those situations where aggregate exposure is considered relevant. The Task Force covered the following work areas:

- An overview of the current human consumer exposure landscape, which includes currently available data and tools
- Opportunities to develop exposure data sources related to specific product categories.

Aggregate exposure assessment examples (how to combine multiple sources and routes of exposure) including case study examples for phenoxyethanol, triclosan and general solvent use.

[1] Available at http://consexpo.nl/

[2] Available at http://www.cremeglobal.com/products/cosmetics/

[3] Available at http://www.thelifelinegroup.org/

[4] Available at http://www2.epa.gov/chemical-research/stochastic-human-exposure-and-dose-simulation-sheds-estimate-human-exposure

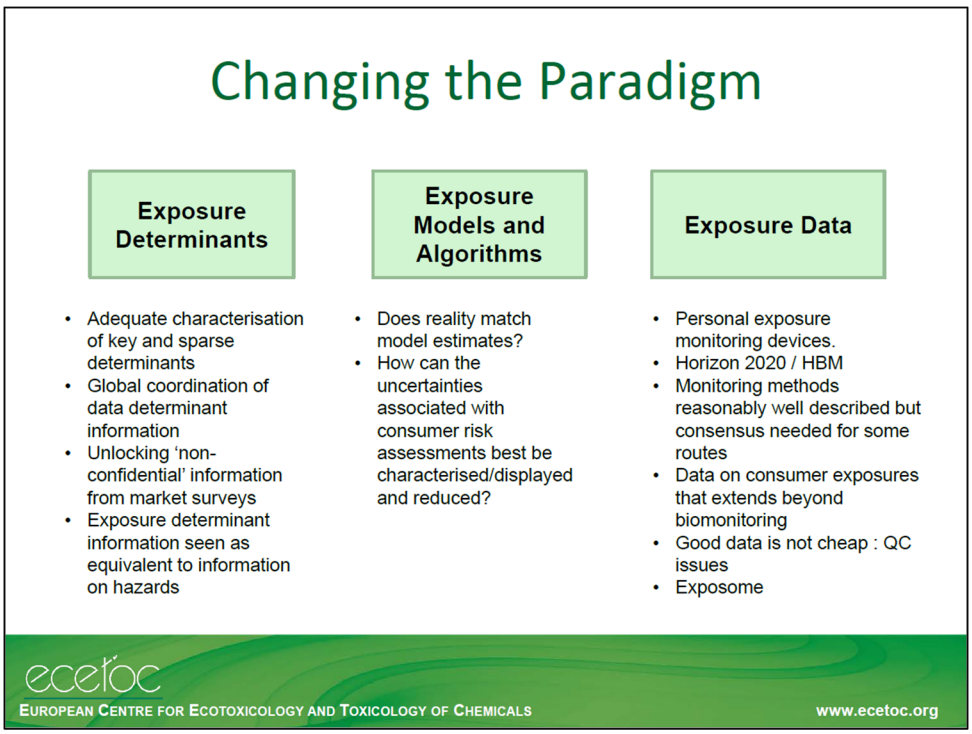
[5] Cefic Long Range Research has developed "Realistic Estimation of Exposure to Substances from Multiple Sources (TAGS)" (LRI-B5-CERTH). http://cefic-lri.org/projects/b5-certh-realistic-estimation-of-exposure-to-substances-from-multiple-sources-tags/

3.1.2 Robust Exposure Assessment in Refining Risk Assessment

Chris MONEY
Cynara Consulting, UK

Although assessments of consumer exposure are routinely undertaken, these seldom occur at a level beyond the use of simple substances in common consumer products. It is therefore appropriate to ask whether we really understand the true nature of consumer exposures (substance formulations, market penetration, regionality, habits and practices, exposure determinants) or even understand enough of consumer behaviour to make accurate predictions of consumer exposure (primary determinants of exposure for a given setting; aggregate and mixed exposures; external vs internal; population vs individual behaviours).

This presentation briefly reviewed some of the considerations behind how consumer exposure assessments are undertaken and then examined whether resources are currently deployed in an optimal manner. Key questions include: what might be the most appropriate strategies for assessing consumer exposures and what should be the considerations that inform our approaches for gap filling? How can the uncertainties associated with consumer risk assessments best be characterised and reduced and what might be some priorities for future work in the field – and suitably accounted for in risk management decision-making. Areas that need to be addressed include the perception of reality arising from the misapplication of modelled data which could result in risk management decisions that do not reflect real life exposures (e.g. cyclohexane in modelling adhesives). A key challenge is the quality and reliability of existing human and consumer exposure data. When considering strategies for improved exposure assessment, Dr Money concluded that these must be about optimising the application of existing knowledge; applying the most suitable available models and the most suitable data sources; applying techniques for improving the robustness of estimates and tiered and targeted strategies for data acquisition and application. In closing, he put forward approaches to shift the paradigm (see slide below). A key challenge is unlocking 'non



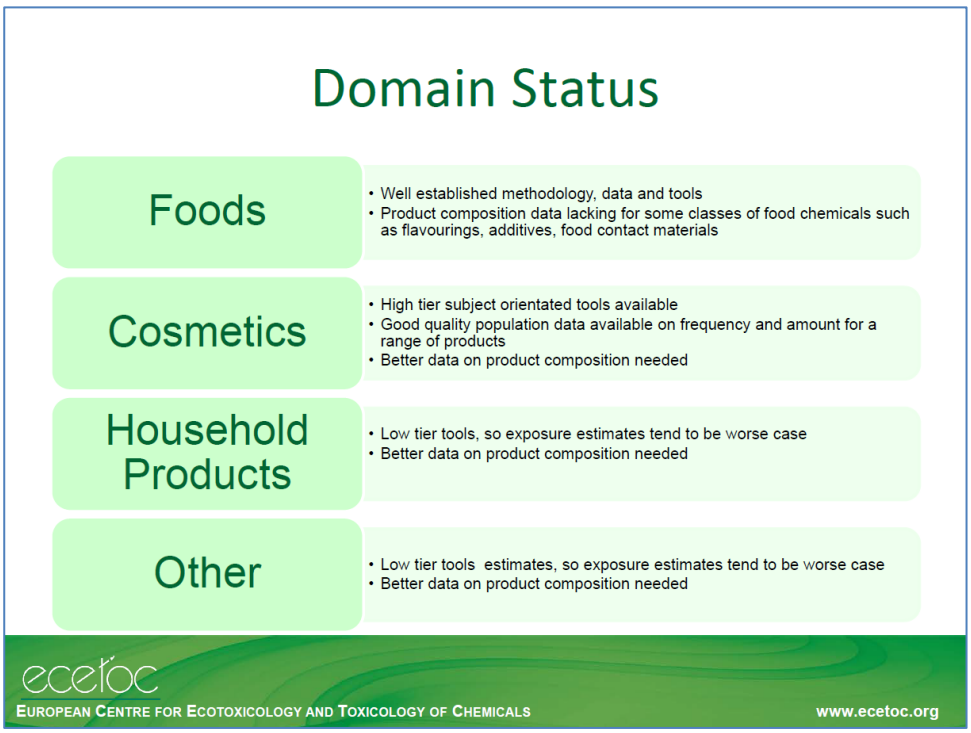
confidential' information from market surveys such as habits and practices data: this is non-product-specific information (and therefore unlikely to be viewed as confidential) and would be extremely relevant to exposure assessment.

In the audience discussion that followed, it was suggested that Read Across for exposure could be useful in certain situations, but that criteria would be needed to ensure confidence in such read across approaches. Definitions for exposure-based read across would be required. In addition, the need for concentration data and presence probability data was discussed. Obtaining such data has been tried, with some, but limited success (cosmetics, food, and most successfully – fragrances). Workshop participants recommended that learnings from these initiatives should be incorporated into other chemicals sectors. Trade associations such as the ACC and Cefic would be the logical owners for such an activity.

3.1.3 Modelling Total Exposure to Chemicals in Multiple Sources

Sarah TOZER
P&G, UK

For the purposes of the ECETOC task force work, Exposure assessment is defined as "*Exposure to a chemical from multiple sources and pathways, entering via different routes*". Aggregate exposure assessment is becoming a consideration in safety assessments in some sectors, whereas in other consumer product categories, it is less frequently considered as products may not be frequently used together. However, for chemicals that are ubiquitous, consumer exposure may even come from multiple sources (foods, consumer products) and via multiple routes. Aggregate exposure should be estimated using a tiered approach (Delmaar and van Engelen, 2006; Meek *et al.*, 2011) which begins with a conservative deterministic



estimation of exposure and evolves, as needed, to a more refined person-orientated probabilistic approach. Such high tier assessments of aggregate exposure can help to accurately represent the relative exposure sources. Dr Tozer shared examples of higher tier exposure estimates, including zinc pyrithione (a preservative) (Tozer *et al*., 2015); vitamin A, and aluminium. These examples demonstrated that, for high tier assessments across domains, there is a need for access to population input data and tools including products from multiple domains. Currently available subject-orientated tools tend to be domain specific. Probabilistic aggregate exposure modeling, conducted at the level of individuals in the population, provides realistic estimates of exposure to ingredients present in multiple products & foods. Anonymised data sharing on product composition is a clear need. Other consumer product categories need to be better explored (i.e. the frequency that products are used) in order to increase understanding on when different consumer products are used together.

In the discussion that followed, it was concluded that there is a need for confidence in the data, tools and models. It was recommended that this could be achieved through a verification mechanism of their "fit for purpose". In the occupational setting, some best practice guidance exists to ensure exposure data quality – and this could potentially be adapted and extrapolated to consumer exposure settings. An internationally recognised rating system to evaluate the quality of data would enable the evaluation of quality data. Transparency is a pre-requisite for confidence in data and mechanisms to achieve this should be established.

3.2 Overview of the Exposure Landscape – What Data, Tools, and Models Exist?

3.2.1 Presentation of the landscaping exercise; data sources; models; tools in one location

Cian O'Mahony
Creme Global, Ireland

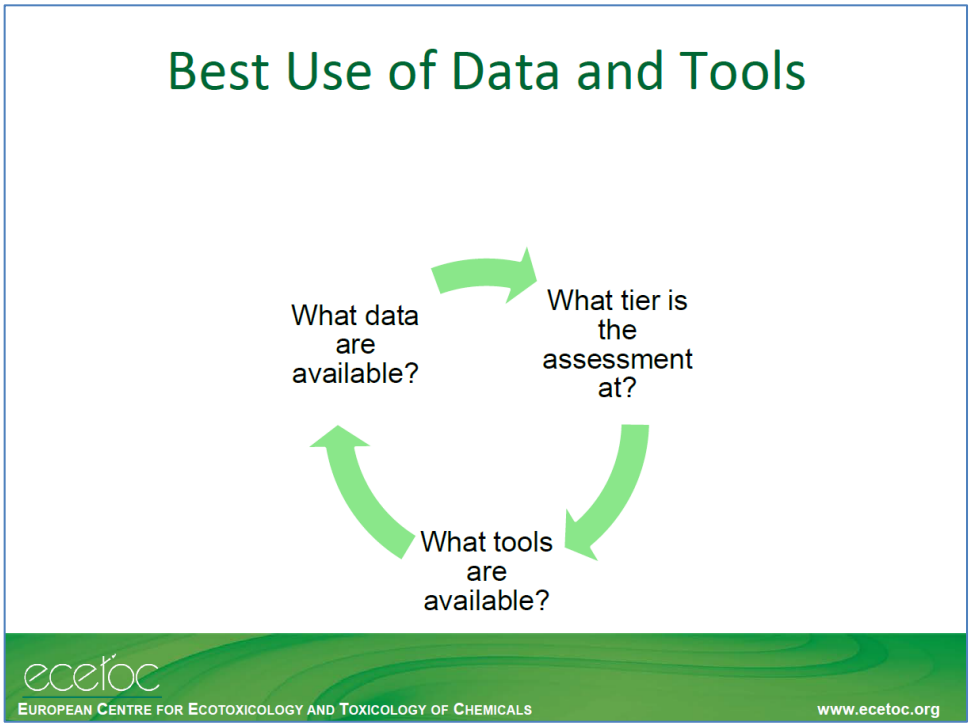
One of the key activities conducted by the task force was to develop an overview of the current human exposure science landscape, from the perspective of what data sources and tools are available for exposure assessment, with a specific focus on consumer exposure (although some occupational sources were also considered). This is with a view to providing a centralised source of information for risk assessors to avail of when carrying out an exposure assessment, to elucidate what the appropriate uses of different data and models are in different contexts, and to identify future opportunities to gather data or develop models to further the field of consumer exposure and risk assessment.

Data sources were categorised into the following categories: Exposure Algorithms, Habits and Practices Data, Co-use Data, Chemical Occurrence Data, and Presence Probability Data. The source or original reference is provided in the landscaping document, as well as some details on the nature of the data. Within the section on tools, a number of additional headings are provided: Product Category, Type of Assessment that can be Performed, Built-in Data/Data Requirements, Regions Covered, Modelling Capabilities, Routes of

Exposure Covered, Availability, Occupational or Consumer, and additional Comments. The details of each of the criteria were described and their meanings and interpretation explained.

Finally, identified opportunities for gathering new data and developing new tools, models or analyses were presented, arising out of the landscaping exercise itself. This also touched on some of the learnings from the individual case studies, and the types of data and models that can be introduced to refine exposure assessments for different purposes.

Cian O'Mahony asked participants for their thoughts on the Landscaping document: what are the gaps? What type of guidance is necessary for potential risk assessors using these tools and data? The following three questions should be kept in mind when doing an exposure assessment (see following slide).



3.2.2 Moderated Discussion (Carlos Rodriguez, P&G)

The moderated discussion centred on the following three questions:

1. **Is the Task Force report and Landscaping document a useful resource?** There was general agreement that the ECETOC Task Force work was a useful resource which could support ongoing efforts on exposure assessment within the OECD, the US EPA and the European Commission. There was an offer from representatives from these agencies to share the report and landscaping tool with interested parties within their organisations to provide comments and feedback to help ensure this work is inclusive and globally relevant. It was proposed and agreed that the work would benefit from the inclusion of a problem definition step and a decision tree describing (i) how to use the Landscaping Document and (ii) which data and tools are appropriate in context of the exposure tiers.

It was suggested the kind of decision-tree logic used in Cefic LRI TAGs (Sarigiannis, 2012), PACEM (Dudzina, 2015) and DUSTEX (Delmaar, 2015) projects might be appropriate to include in the report to inform tiered exposure assessment on current availability and limitations of input data and exposure modelling tools. The ECETOC task force will consider these suggestions when revising the task force report following this workshop.

2. **Are all the main data sources covered?** It was agreed that the OECD, US EPA, JRC and ECHA representatives at the workshop will explore how to distribute the landscaping document within their organisations to input on additional, relevant data sources. It was briefly discussed that crowd sourced exposure input (i.e. voluntarily reported) data is becoming more common on product concentrations (e.g. Codecheck) and consumer habits and practices and has potential value in estimating exposure in certain contexts. It was recognised that inherent uncertainties associated with such freely populated data sets need to be assessed and accounted for and more work is needed for establishing adequate quality control safeguards.

3. **How do we disseminate this information to make it useful for risk assessment?** One suggestion (from the JRC) was that the European Committee for Standardization (CEN) enhance the development of model documentation in the European Standards format (EN) which sets out specifications and other technical information with regard to the model's characteristics. Another suggestion was to build on the Wikipedia concept in a kind of "exposure-pedia" where stakeholders would be responsible for uploading information on benefits and limitations of the various exposure models and data. It was agreed that this concept should be investigated further – and that it would be important to build in quality control into such an initiative.

3.3 Case Studies of Exposure

3.3.1 Phenoxyethanol in household products, personal care products and cosmetics

Christiaan Delmaar
RIVM, The Netherlands

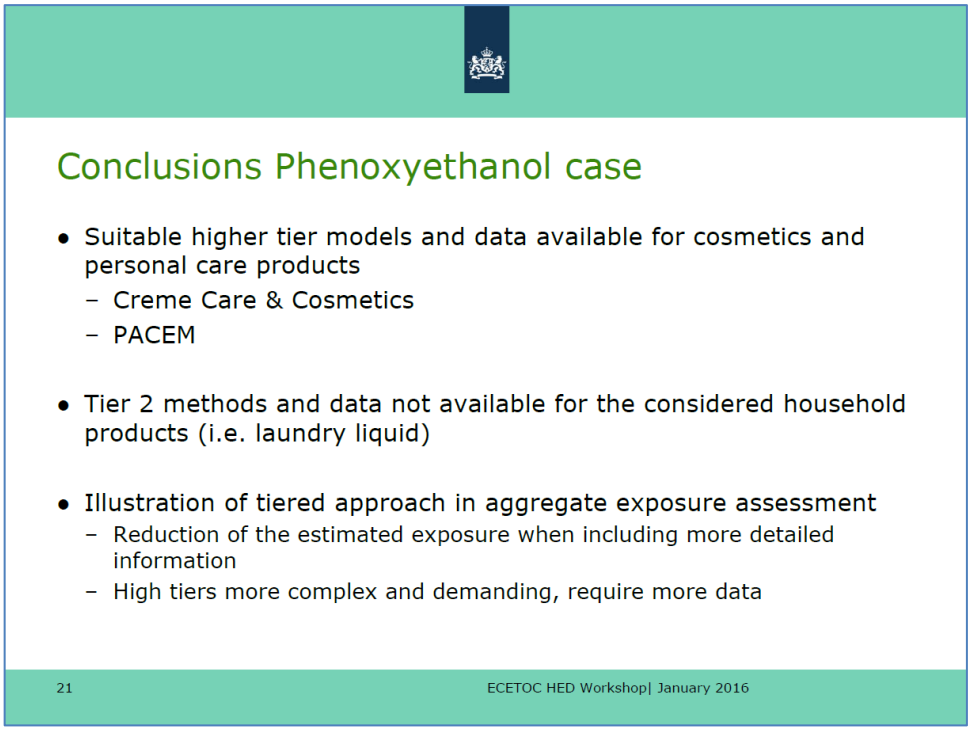
The risk assessment of a substance that is contained in multiple consumer products requires estimation of the aggregate exposure from all products combined. It is advised that the assessment of aggregate consumer exposure follows a tiered approach. Typically, such a tiered approach starts with a deterministic assessment in which single product exposure estimates are added up. If needed, the assessment is refined in higher tiers by accounting for more detailed information on exposure factors, such as co-use information and product composition information, including presence probabilities. This tiered approach to aggregate exposure assessment is illustrated in the case of phenoxyethanol in cosmetics, personal care and household products.

For phenoxyethanol in cosmetic products, as a first tier, the deterministic method to estimate aggregate exposure proposed in (SCCS, 2012) is used. Subsequently, the aggregate exposure evaluation is refined in a second tier, using two different person-oriented exposure models, the Creme Care & Cosmetics and PACEM models. In the second tier assessment, progressively more information on co-use of products and data on product composition is incorporated.

For household products, the contribution to aggregate exposure from different sources is estimated using the AISE REACT tool. As no higher tier method is currently available, the assessment was not further refined.

The case illustrates how existing tools may be used to refine aggregate exposure assessment using progressively more information. Higher tier assessments usually lead to reduced estimates of exposure, while still being protective for the population. On the other hand, higher tier assessments require more effort and data; data which is usually scarce or absent altogether. A particularly important data gap in practice, is the information on substance concentrations in consumer products.

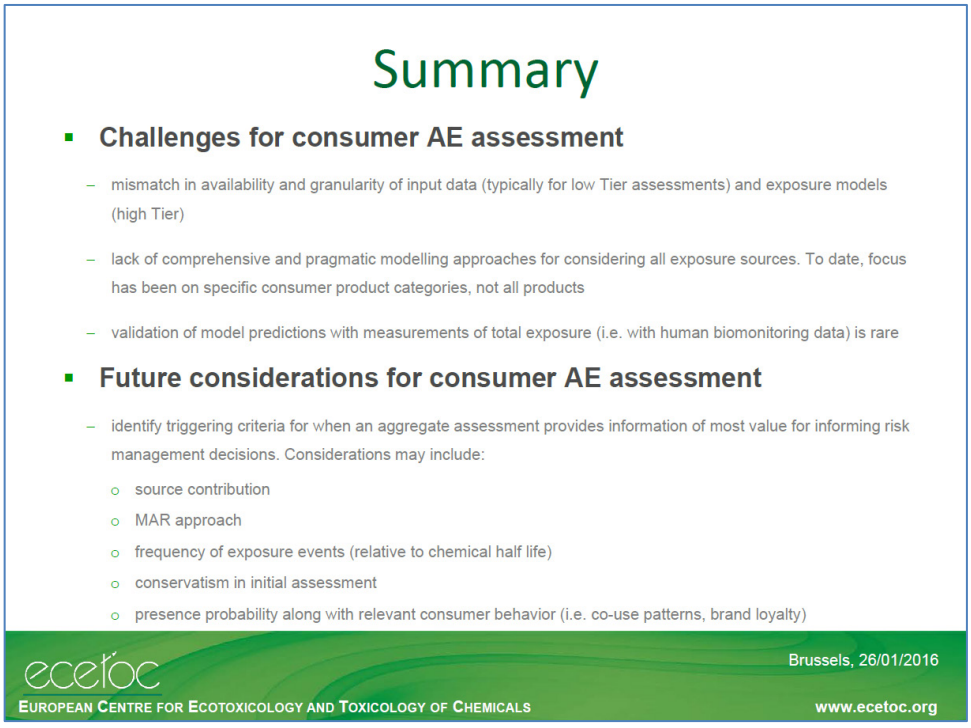
During the discussion, the need to justify choices and document the principals of why certain tools and models are used over others was highlighted. The basic premise is that it is not realistic to assume that consumers use all the products all at the same time, so adding a higher tier adds value and enables more realistic assessments.



3.3.2 Solvent use in consumer chemical products

Tatsiana Dudzina
ExxonMobil, Belgium

Solvents represent a range of chemicals finding application in various industry sectors including construction, chemical, pharmaceutical, and agriculture. They are defined as substances with the ability to dissolve, suspend or extract other materials. The range of consumer products and articles containing solvents spans cosmetics, personal care, household cleaning products, paints and coatings, adhesives and sealants, fuels and automotive care products, etc. While benefiting from a diversity of solvents and their unique properties, the general population may be exposed to them via inhalation of vapour or aerosols, dermally via direct contact or vapour absorption, and/or by incidental ingestion. Under the European Union's legislation for Registration, Evaluation and Authorisation of Chemicals (REACH), the evaluation of safe consumer use of these chemicals is normally carried out at a generic product category level using realistic worst-case scenario exposure models embedding conservative input parameters. The case study on solvent use demonstrated that, while being useful to determine safe use, the lower tier tools do not provide realistic exposure estimates that could be summed up across products to derive multi-source aggregate consumer exposure. Supplementary exposure data on product co-use, timing, duration and frequency of product application, chemical occurrence, would allow significant refinement of aggregate exposure predictions. The presentation drew upon literature case studies to also identify considerations for determining when aggregate exposure may be most informative, given the additional resources needed to support these complex assessments.



Dr Dudzina summarised the sources and typical properties of solvents (e.g. high volatility, varying water solubility, low toxicity of those introduced into consumer products) and gave a synopsis of the landscaping exercise with respect to wide range of consumer products (i.e. existing exposure models and data sources

and gaps). This demonstrated the inappropriateness of existing low tier tools to model aggregate consumer exposure. Dr Dudzina went on to review alternative approaches (i.e. grouping of product categories on their use frequency) and identify data gaps for aggregate consumer exposure assessment in application to a wide range of consumer products.

3.3.3 Key Learnings from Case Studies

Mark Pemberton
Systox, UK

Mark Pemberton summarised the key learnings from the case studies as follows:

Key learnings on Aggregate Exposure: Some tools are available (PACEM, Creme Care & Cosmetics) for cosmetics and personal care products for example. These require robust data sets (habits, practices, product co-use, chemicals composition and presence probabilities). For some domains, such as household care products, the available data are limited. Approaches are required to indicate when higher tier aggregate assessments might be a priority (information on relative contributions of different sources). Evaluations of total consumer exposure from biomonitoring studies indicate that exposure estimates from higher tier assessments are closer to reality, whereas lower tiers are overly conservative. Model verification with real-life data on a representative range of chemicals would assist to promote use/acceptance of exposure model predictions.

Opportunities for Data Acquisition: How do we determine priorities setting for data acquisition and development? How do we acquire better information on typical concentrations or ranges of a chemical in specific domains? Can we develop representative "default" exposure profiles for product types (concentration, frequency of use etc.)? Can we conduct a sensitivity analysis to determine which exposure data will contribute greatest to refining a risk assessment, in order to prioritise where data acquisition will be of most benefit?

Opportunities for Aggregate Exposure: How do we combine exposure from different domains to better reflect real life exposures i.e. establishing an exposure matrix? The following may be useful to take into account: presence probabilities (proportion of products in a category that contain the chemical); co-exposure to a given chemical from different product types with different profiles of use (consumer preferences, brand loyalty); total exposure (exposure from food, water, consumer products, environment); chemical synergies?

4. BREAKOUT GROUP SESSIONS

The workshop participants discussed specific brainstorm questions that had been communicated together with the programme prior to the workshop:

- How do we enhance utilisation of currently available tools?
- Where is there a need to develop new tools and data to improve exposure assessment?
- How can this be done? What are the practical steps that need to be taken?
- Who should drive efforts to complete the work?

1. **How do we enhance utilisation of currently available tools?** Discussions within the four breakout groups centred on the following:

   - *Guidance for Fitness of Purpose:* Well-stated and validated applicability domains with standardised descriptors recognising the unique factors of each model that determines its fitness for purpose (i.e. "pedigree") are needed. Models should be validated, and validation across models should also be conducted. Decision trees / templates would help risk assessors (i) formulate the question: what is the scope of the assessment? And, (ii) make choices for the most appropriate model, tool and data source in each set of circumstances. Case studies could be used to exemplify this guidance. Regulators should be involved in the model development and in the development of decision trees and guidance documents early on, in order to increase confidence and trust in the outcome.

   - *Transparency:* Tools, data, documentation and software should be open access. It was noted for example, that within REACH there is archived hazard information, but little in the way of archived exposure information. Transparency must also extend to explaining why the risk assessor chose to use the particular exposure tool and the particular input data (justification narrative)

   - *Maintenance and Dissemination:* Suggestions included awareness-raising through workshops, scientific events and Wikipedia-type tools (cf AOP wiki), which would require ownership at the global level (OECD).

2. **Where is there a need to develop new tools and data to improve exposure assessment**? One breakout group discussed the drivers for developing new tools and concluded that risk perception may not reflect real risk. Thus consumer perception of risk, rather than real risk, may be driving regulatory decisions. The triggers for developing new tools and data should centre on whether existing tools/data are fit for purpose:

   - *Optimise existing tools first:* Rather than develop new tools, first look at how existing tools can be better applied, and sufficiently validated, based on risk considerations: do the existing tools and data provide exposure estimates that reflect real-life exposures? Specific areas that require

focus include time integration, sensitivity analysis, accurate input parameters (e.g. retention factor); validation; definitions for read across; Life Cycle Analysis and the inclusion of indirect exposure (especially for dust and articles) vs direct exposure.

- *Build databases on consumer information:* Databases of relevant consumer information, product composition (chemical concentration and presence probability) across domains is needed more than new models (e.g. biocides used in cosmetics, preservatives, household products, etc). Companies should be encouraged to share their in-house data in an anonymised format that protects intellectual property. This could be managed at trade association level. Prioritisation of substances (e.g. as was done in the Cosmetics Ingredients Review in the US) would be a first step. Input data are needed e.g. for consumer articles and household products, and exposure data is required on sub-populations e.g. infants and children.

- *Aggregate Exposure Problem Formulation:* Although regulations increasingly call for aggregate exposure assessments, it is not widely known what approach to take in order to determine aggregate exposure and how this will be received from a regulatory perspective[6]. There is a need to get the problem formulation clear first and relate tools and data to this via templates and decision trees. Tier 1 tools are generally adequate and accepted for occupational and consumer exposure, for single product exposure. Low tier assessments should remain the first priority.

3. How can improved consumer exposure assessment data and tools be developed? What are the practical steps that need to be taken?

- *Stay within the Applicability Domain:* Use decision trees and develop validation criteria for fit for purpose.

- *Cefic LRI project on data sharing across domains*: Tools and data for aggregate exposure specific to domains and product categories exist, but there is little cross-talk across the domains. This needs to be addressed in order to achieve regulatory acceptance. A Cefic LRI project could consider chemical assessments for chemicals ubiquitous across product types that cover different categories: run case studies on these chemicals to identify what tools are available for aggregate exposure assessment, and then assess the level of exposure across these categories.

[6] Cefic Long Range Research has developed “Estimation of Realistic Consumer Exposure to Substances from Multiple Sources and Approaches to Validation of Exposure Models” (LRI-B7-ETHZ) and “Realistic Estimation of Exposure to Substances from Multiple Sources (TAGS)” (LRI-B5-CERTH). Both mentioned in the Human Exposure Data Task Force Report.

4. **Who should drive efforts to complete the work?** Regulators and policy makers are needed to identify the requirements for moving this forward and should be engaged early on in the process. Then industry, regulators, academics and others can influence discussions.

- *Public Portals to facilitate discussion and share data*: (ISES, OECD, IPCS, IP-CHEM). Templates and mechanisms for the effective and transparent sharing of data, based on specific types of use (e.g. SCEDS and sub-PCs may be models to start working from).

- *Criteria for fit for purpose and model validation*: ISES, OECD (systematic collection/archiving of useful information via IUCLID). IPCS; ECETOC, Regulators e.g. REEG. Collaboration across industry and regulators required.

- *Harmonisation of data/models/standards:* OECD presents a platform that could be used across geographies. ECHA involvement will also be important. Funding ultimately has to come from industry, taking early input and priority setting from regulators.

There was a strong recommendation for consensus on a robust science-based, fit for purpose framework/guidelines to impose discipline on the quality and adequacy of:

- Data collection/measurements

- Data analysis (tools and applications) – CEN descriptions of what an Exposure Tool/Model should "look like". Transparency to understand why certain tools are used in certain applications would be necessary. On the other hand, some participants questioned whether the introduction of such an additional layer of 'bureaucracy' in the process would be helpful.

- Application of exposure information into exposure-based risk assessment.

Exposure Science might also benefit from:

- Agreed processes to extrapolate the applicability of data in different contexts – for example could worker exposure information be applied into a different exposure domain? Is there best practice for exposure data quality (e.g. weighting criteria?) This does exist in the occupational setting: could it be extended or adapted to consumer exposure? An internationally recognised rating system would help evaluate the quality of data.

- To achieve a systematic programme/framework on "exposure quality" will require broad stakeholder involvement and agreement including OECD, ECHA and different geographies

- A life cycle analysis of exposure

The ECETOC TF report and landscaping document, and this workshop have provided a platform to begin the process of providing clear guidance on exposure assessment. As discussed, unless robust frameworks and guidance are established, variability in exposure measurements and estimates will be common place.

5. CONCLUSIONS AND RECOMMENDATIONS

The ECETOC TF Report and landscaping document, and subsequent workshop has provided a platform to begin the process of developing clear guidance on aggregate consumer exposure assessment. Unless robust frameworks and guidance are established, variability in quality of exposure assessments will be observed. Achieving a systematic programme/framework for exposure assessment to ensure "exposure quality" will require broad stakeholder involvement and agreement across EU and International institutions. There was agreement to broaden cooperation with delegates from OECD, JRC, EPA, and ECHA offering to discuss future cooperation on this activity. The following observations and recommendations were concluded from the workshop:

Workshop Observations

Data Sharing: In parts of the industry (e.g. the fragrance industry) there is good experience with collection of anonymised data on product composition for inclusion in exposure estimates, which has saved the Industry several millions of Euros, and prevented unnecessary toxicology testing. Initiatives are needed to encourage other areas of industry to collaborate in this way and make available anonymised databases for exposure assessment, while protecting intellectual property.

Optimise existing tools: Approaches should be developed (including the use of case studies) to demonstrate how existing knowledge and tools can be (more) effectively applied in aggregate consumer exposure assessments. Guidance should be developed specifically to determine what represents the most suitable available models and the most suitable data sources for specific questions. The approaches should aim to improve the robustness of estimates using tiered and targeted strategies for data acquisition and application.

Transparency: Tools, data, documentation and software should be open access.

Read Across for exposure assessment could be useful as a means of 'gap filling' in data sparse situations, but criteria need to be developed to ensure confidence in such read across approaches. Data quality (amongst other criteria) would need to be assessed in order to determine the extent to which it might be applied to other settings (Tielemans *et al*, 2002). Consensus-based definitions for exposure-based read across would be required. This could be combined with an agreed process to extrapolate the applicability of data in different contexts (Hristozov *et al*, 2014). For example best practice exists in the occupational setting (Money and Margary, 2002; ECHA, 2012): could it be extended or adapted to consumer exposure? An internationally recognised rating system would help evaluate the quality of data.

Incorporate Life Cycle Analysis? How could life cycle perspectives/analysis be applied to help determine the nature of exposures?

Workshop Recommendations

Build databases on consumer information: public portals could facilitate discussion and data-sharing. Databases of relevant consumer use information, product composition and presence probability across domains are needed. Templates and mechanisms for the effective and transparent sharing of data, based on specific types of use (e.g. SCEDS and sub-PCs). Learnings from recent sector specific initiatives to describe representative concentration and presence probability data for substances and products (fragrances, cosmetics and food) should be evaluated. Mechanisms to enable the 'non confidential' information from market surveys to be made more widely available, such as habits and practices data: this is invariably non-product-specific information and would be extremely relevant to exposure assessment. Specific mention was made of the need for concentration data and presence probability data (product composition data).

Develop Harmonised Guidance (with validation/quality weighting criteria) for Fitness of Purpose within the Applicability Domain: Develop decision trees and problem formulation templates to assist robust consumer exposure and risk assessment. Well-stated and validated applicability domains with standardised descriptors recognising the unique factors of each model that determines its fitness for purpose (i.e. "pedigree") are needed. Models should be validated, and validation across models should be conducted. Case studies could be used to exemplify this guidance. However, validation of guidance is difficult, thus a pragmatic way forward may be to build confidence in the methods by showing that the assumptions are plausible; the methods used are based on state of science approaches; and the results of the different methods of exposure assessment are compatible. The OECD provides a platform that could be used to harmonise these data/models/standards across geographies.

Establish Triggering Criteria for higher tier aggregate exposure assessment (e.g. source contribution, MAR approach, conservatism in initial assessment)

Research Proposals:

Obtaining data on product compositions: this is essential for exposure assessment, particularly aggregate exposure. Without reliable composition data, exposure assessments are based on worst case assumptions giving rise to product restrictions. Questions that need to be answered include: How do we collect, store, share and maintain anonymised product composition data? How do you overcome the barriers to implementing this action across geographies and industry sector groups? Who should lead such an activity? We should look to the example of the fragrance Industry who have achieved this while maintaining the industry's intellectual property.

Data sharing across domains: Tools and data for aggregate exposure specific to domains and product categories exist, but there is little cross-talk across the domains. A Cefic LRI project could consider chemical assessments for chemicals ubiquitous across product types that cover different categories: run case studies on these chemicals to identify what tools are available for aggregate exposure assessment, and then assess the level of exposure across these categories.

Developing an agreed process to extrapolate the applicability of exposure data in different contexts. This does not yet exist in exposure assessment, but in hazard assessments processes have been developed to

enable data from various sources to be combined. This could be a starting point for a similar approach in exposure assessment.

Developing a framework for exposure assessment of exposure data-poor chemicals. Criteria are being developed for quality and weight of evidence for hazard assessment (including read across), but not for exposure assessment. Questions that need answers include: Can the principles that are being developed for hazard assessment be applied for exposure assessment? How do you overcome the barriers to implementing this action across geographies and industry sector groups? Who should lead such an activity?

ABBREVIATIONS

ACC	American Chemistry Council
AISE	International Association for Soaps, Detergents and Maintenance Products
AOP	Adverse outcome pathway
Cefic	European Chemical Industry Council
CEN	European Committee for Standardization
ECHA	European Chemicals Agency
EN	European Standards Format
JRC	Joint Research Centre
LRI	(Cefic) Long-range Research Initiative
OECD	Organisation for Economic Co-operation and Development
PACEM	Probabilistic aggregate consumer exposure model
REACH	Registration, Evaluation nand Authorization of Chemicals
SCCS	(EC) Scientific Committee on Consumer Safety
US EPA	United States Environmental Protection Agency

BIBLIOGRAPHY

Delmaar CJ, Bokkers B, ter Burg W, Schuur G. 2015. Validation of an aggregate exposure model for substances in consumer products: a case study with diethyl phthalate in personal care products. *J Expo Sci Environ Epidemiol* 25(3):317-23.

Delmaar JE, Park MVDZ, van Engelen JGM. 2005. RIVM report 320104004/2005. ConsExpo 4.0 Consumer Exposure and Uptake Models. Program Manual.
[Available online at http://rivm.openrepository.com/rivm/bitstream/10029/7307/1/320104004.pdf]

Delmaar JE, van Engelen JGM. 2006. Aggregating Human Exposure to Chemicals and Overview of Tools and Methodologies. RIVM report 630700001/2006. RIVM, Bilthoven, The Netherlands.

Dudzina T, Delmaar CJE, Biesterbos JWH, Bakker MI, Bokkers BGH, Scheepers PTJ, van Engelen JGM, Hungerbuehler K, von Goetz N. 2015. The probabilistic aggregate consumer exposure model (PACEM): Validation and comparison to a lower-tier assessment for the cyclic siloxane D5. *Environ Int* 79:08-16.

ECHA. 2012. REACH Technical Guidance on information requirements and chemical safety assessment, Chapter R14: Occupational Exposure Estimation. European Chemicals Agency, Helsinki, Finland.

Hristozov DR, Gottardo S, Cinelli M, Isigonis P, Zabeo A Critto A, Van Tongeren M, Tran L, Marcomini A. 2014. Application of a quantitative weight of evidence approach for ranking and prioritising occupational exposure scenarios for titanium dioxide and carbon nanomaterials. *Nanotoxicology* 8(2):117-131.

Meek ME, Boobis AR, Crofton KR, Heinemeyer G, van Raaij C, Vickers C. 2011. Risk assessment of combined exposures to multiple chemicals: a WHO/IPCS framework. *Regul Toxicol Pharmacol* 60(2):S1–S7.

Money C, Margary A. 2002. Improved Use of Workplace Exposure Data in the Regulatory Risk Assessment of Chemicals within Europe. *Ann Occup Hyg* 46(3):279-285.

Sarigiannis D, Karakitsios S, Cornelis C, Van Tongeren M, De Brouwere K, Cherrie J, Torfs R, Gotti A, Karabelas AJ. 2012. A novel tiered approach to aggregate exposure assessment of chemicals in articles and the environment. Poster by the Cefic LRI B5 group presented at the 2012 Cefic LRI Annual Meeting.

SCCS. 2012. The SCCS'S Notes of Guidance for the Testing of Cosmetic Ingredients and Their Safety Evaluation, 8th revision. Scientific Committee on Consumer Safety. Opinion adopted at its 17th plenary meeting of 11 December 2012. EC Scientific Committee on Consumer Safety (SCCS) Available at:
http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_s_006.pdf (accessed 7.30.14.)

Tielemans E, Marquart H, de Cock J, Groenewold M, van Hemmen J. 2002. A Proposal for Evaluation of Exposure Data. *Ann Occup Hyg* 46(3)287-297.

Tozer SA, Kelly S, O'Mahony C, Daly EJ, Nash JF. 2015. Aggregate exposure modelling of zinc pyrithione in rinse-off personal cleansing products using a person-orientated approach with market share refinement. *Food Chem Toxicol* 83:103-110.

APPENDIX A: WORKSHOP PROGRAMME

Tuesday, 26th January 2016

09:00-09:30	*Registration and welcome coffee*	
09:30-09:40	Welcome and Review of Workshop Aims The Importance of Exposure Assessment in Risk Assessment	**Alan Poole** ECETOC

Session 1: Characterising Exposure in the 21st Century

09:40-09:50	The ECETOC Human Exposure Task Force: Overview	**Sarah Tozer** P&G
09:50-10:20	Robust Exposure Assessment in Refining Risk Assessment	**Chris Money** Cynara Consulting
10:20-10:50	Modelling Total Exposure to Chemicals in Multiple Sources	**Sarah Tozer** P&G

Session 2: Overview of the Exposure Landscape –What Data, Tools, and Models exist

10:50-11:20	Presentation of the landscaping exercise; data sources; models; tools in one location	**Cian O'Mahony** Creme Global
11:20-11:50	**Discussion**	Moderator: **Carlos Rodriguez**, P&G

Questions to motivate discussion:

- Is this a useful resource?
- Are all the main data sources covered?
- Are all the main models covered?
- How do we disseminate this information to make it useful for risk assessment?

Session 3: Case Studies of Exposure

11:50-12:00	Introduction	**Chair: Mark Pemberton** Systox
12:00-12:20	Phenoxyethanol in household products, personal care products and cosmetics	**Christiaan Delmaar** RIVM
12:20-12:40	Solvent use in consumer chemical products	**Tanya Dudzina** ExxonMobil
13:00-14:00	*Lunch*	
14:00-14:20	Key learnings from Case Studies Presentation and Audience Discussion/Feedback	**Mark Pemberton** Systox

Brainstorm Sessions: Exposure Data, Modelling and Assessment – What Gaps Exist and What Guidance is Needed?

14:20-14:30	Introduction	**Alan Poole** ECETOC
14:35-15:30	**Brainstorm Questions:** *- How do we enhance utilisation of currently available tools?* *- Where is there a need to develop new tools and data to improve exposure assessment?* *- How can this be done? What are the practical steps that need to be taken?* *- Who should drive efforts to complete the work?*	**Moderators/Rapporteurs:** **C Delmaar/M Pemberton** **C Money/C Rodriguez** **T Dudzina/C O'Mahony** **S Tozer/T Meijster**
15:30-16:00	**Plenary:** Moderators/Rapporteurs share Brainstorm results	**Madeleine Laffont** ECETOC
16:00-16:15	Wrap up and Close	**Alan Poole** ECETOC

APPENDIX B: LIST OF PARTICIPANTS

First name	Name	Affiliation	E-mail
Gerald	**Bachler**	Shell, The Netherlands	gerald.bachler@shell.com
Catherine	**Barratt**	Unilever, United Kingdom	Catherine.Barratt@unilever.com
Peter	**Boogaard**	Shell, The Netherlands	peter.boogaard@shell.com
Dagmar	**Bury**	L'Oréal, France	dbury@rd.loreal.com
Namali	**Corea**	SC Johnson, United Kingdom	ncorea@scj.com
Claire	**Davies ***	Unilever, United Kingdom	claire.davies@unilever.com
Christiaan	**Delmaar**	RIVM, The Netherlands	christiaan.delmaar@rivm.nl
Tanya	**Doktorova**	WIV-ISP Scientific Institute of Public Health, Belgium	tatyana.yordanovadoktorova@wiv-isp.be
Tatsiana	**Dudzina**	ExxonMobil, Belgium	tatsiana.dudzina@exxonmobil.com
Sandrine	**Fraize-Frontier**	ANSES, France	sandrine.fraize-frontier@anses.fr
Wouter	**Fransman**	TNO, The Netherlands	Wouter.fransman@tno.nl
Stefano	**Frattini**	ECHA, Finland	stefano.frattini@echa.europa.eu
Lars	**Hareng**	BASF, Germany	lars.hareng@basf.com
Takahiro	**Hasegawa**	OECD, France	takahiro.hasegawa@oecd.org
Astrid	**Heiland**	BfR, Germany	Astrid.Heiland@bfr.bund.de
Joke	**Herremans**	RIVM, The Netherlands	joke.herremans@rivm.nl
Bruno	**Hubesch**	Cefic-LRI, Belgium	bhu@cefic.be
Amaia	**Irizar**	IFRA, Belgium	airizar@ifraorg.org
Kristin	**Isaacs**	US EPA, USA	isaacs.kristin@epa.gov
Sylvia	**Jacobi**	Albemarle, Belgium	sylvia.jacobi@albemarle.com
Padmaja	**Kamath**	WIV-ISP Scientific Institute of Public Health, Belgium	padmaja.kamath@wiv-isp.be
Madeleine	**Laffont**	ECETOC, Belgium	madeleine.laffont@ecetoc.org
Holger	**Leidreiter**	Evonik Nutrition & Care, Germany	holger.leidreiter@evonik.com
Qiang	**Li**	Clariant, Germany	qiang.li@clariant.com
Michal	**Makuwa**	L'Oréal, France	mmakuwa@rd.loreal.com
Bette	**Meek**	University of Ottawa, Canada	Bette.Meek@uottawa.ca
Tim	**Meijster**	Shell, The Netherlands	tim.meijster@shell.com
Chris	**Money**	Cynara Consulting, United Kingdom	chrismoneyuk@gmail.com
Cian	**O'Mahony**	Creme Global, Ireland	cian.omahony@cremeglobal.com
Mark	**Pemberton**	Systox, United Kingdom	markpemberton@systox.com
Alan	**Poole**	ECETOC, Belgium	alan.poole@ecetoc.org
Trannum	**Rahim**	SC Johnson, United Kingdom	trahim@scj.com
Julian	**Roberts**	ECHA, Finland	julian.roberts@echa.europa.eu
Carlos	**Rodriguez**	P&G, Belgium	rodriguez.c.3@pg.com
Diederik	**Schowanek**	P&G, Belgium	schowanek.d@pg.com
Eleonora	**Simonini**	Solvay, Italy	eleonora.simonini@solvay.com
Sarah	**Tozer**	P&G, United Kingdom	tozer.sa@pg.com
Virpi	**Väänänen**	ECHA, Finland	virpi.vaananen@echa.europa.eu
Matthias	**Vey**	IFRA, Belgium	mvey@ifraorg.org
Alexandre	**Zenié**	EC, JRC, IHCP, Italy	alexandre.zenie@jrc.ec.europa.eu

* was unable to attend at short notice.

APPENDIX C: ORGANISING COMMITTEE

Madeleine Laffont
ECETOC, Belgium

Chris Money
Cynara Consulting, UK

Cian O'Mahony
Creme Global, Ireland

Mark Pemberton
Systox, UK

Carlos Rodriguez,
P&G, Belgium

Sarah Tozer
P&G, UK

Rosemary Zaleski
ExxonMobil Biomedical Sciences, Inc., NJ, USA

APPENDIX D : MEMBERS OF THE HUMAN EXPOSURE DATA TASK FORCE

C. O'Mahony (Co-Chair)
Creme Global, Ireland

S. Tozer (Co-Chair)
Procter & Gamble, UK

C. Davies
Unilever SEAC, UK

T. Dudzina
ExxonMobil, Belgium

R. Finking
BASF, Germany

T. Meijster
Shell Health, NL

G. Pizzella
ENI, Italy

R. Zaleski
ExxonMobil Biomedical Sciences, Inc., NJ, USA

M. Laffont
ECETOC, Belgium

A. Poole
ECETOC, Belgium

Task Force Stewards from the ECETOC Scientific Committee

M. Pemberton
Systox, UK, representing Lucite

C. Rodriguez
Procter and Gamble, Belgium

The Task Force and Workshop Organising Committee are indebted to Christiaan Delmaar of RIVM for his contributions to this initiative.

ECETOC PUBLISHED REPORTS

The full catalogue of ECETOC publications can be found on the ECETOC website:
http://www.ecetoc.org/publications

Responsible Editor:
Dr. Alan Poole
ECETOC AISBL
Av. E. Van Nieuwenhuyse 2 (bte. 8)
B-1160 Brussels, Belgium
VAT: BE 0418344469
D-2016-3001-243

Since 1978 ECETOC, an Industry-funded, scientific, not-for-profit think tank, strives to enhance the quality and reliability of science-based chemical risk assessment. Learn more at http://www.ecetoc.org/