Approaching cross-sector aggregate substance exposure assessment for consumers

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European Centre for Ecotoxicology and Toxicology of Chemicals
Rue Belliard 40, B-1040 Brussels, Belgium

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SUMMARY

There is increasing public awareness and regulatory interest regarding potential health risks posed by aggregate exposure to consumers, i.e., exposure to a substance from multiple sources and routes managed across different regulatory frameworks. For example, in the EU, the Scientific Committee for Consumer Safety (SCCS) recommends in its 10th revision of the 'Notes of Guidance for the Testing of Cosmetics and their Safety Evaluation' (SCCS, 2022) that aggregate exposure "needs to be calculated in the case where several product categories contribute". Also, in the European Cosmetics Regulation (EC) 1223/2009, substances classed as carcinogenic, mutagenic or toxic to reproduction (CMR) class 1A/1B should be assessed for total (aggregate) exposure, considering their simultaneous presence in cosmetics, foods, medicines, and in products covered by the REACH (Registration, Evaluation and Authorisation of Chemicals) legislation (Regulation (EC) No 1272/2008). This report considers available methodologies for assessment of aggregate exposure assessment for consumers that are less precautionary than screening methods whilst being less labour-intensive than higher tier, in-depth studies.

The first step in any cross-sector assessment would be to ascertain whether one or more of the consumer exposures are close to being at the safe limit for one or more of the application areas. In such a case, additional exposures could be important. Simple summation of worst-case exposure estimates might be sufficient should the exposure not exceed the safety limit, in which case more detailed work would not be needed. Refined further work would be needed when simple exposure summation exceeds the defined safe limit.

Cross-sector assessments for a single substance need to establish the amount of substance in use. This can start by considering standard Tier 1 exposure estimates[1] at the point of consumer exposure, or estimates of the exposure derived from tonnage data for the applications, or some combination of the two.

Detailed habits and practices studies can be used to produce reliable exposure estimates at the cross-sector level. However, generation of such studies can be resource intensive.

Working from the total tonnage could provide a simplified approach for estimating exposure. However, tonnage estimates for each use are rarely publicly available, and data also need to be available on the number of people exposed to estimate individual exposure. Even if these data were available, the results are likely to be indicative, order-of-magnitude estimates of consumer exposure. Lack of tonnage data can result in conservative estimates of consumer exposure.

Similarly, the conclusions expressed in 2016 by the ECETOC Task Force on Effective Use of Human Exposure Data in Risk Assessment of Chemicals (Technical Report (TR) No. 126; ECETOC, 2016) suggested that refined and realistic aggregate consumer exposure assessment relies on detailed exposure input data. The present report investigates whether there are any useful developments since 2016 that can be applied to estimate

[1] As specified in Section 1.2, Tier 1 is used in this report to refer to a refined (but not in depth) Tier 0 (i.e. simple outputs from screening tools) exposure assessment.

aggregate exposure more simply in cases where there may be data gaps, and puts forward some proposals about how progress could be made without detailed input data.

The limited developments described in this report show that published methodology has not changed dramatically since the 2016 study, although some new and useful exposure tools and exposure data are emerging in some sectors. If total tonnage data used in the EU for all relevant applications were available, and an indication of the number of users could be obtained, then a reasonable ranking of the relative exposures could be generated, which could help to set risk assessment priorities.

It is evident that not all consumer exposures can be estimated to the same level of confidence because for many sectors there is a lack of good exposure input data, such as habits and practices data and estimates of concentrations of substances in products. So, exposure comparison across sectors is uncertain, because in some sectors there is good availability of data and existing tools, whereas in other sectors data are very scarce. The case studies in the present work do suggest that consumer exposure via the environment is generally low compared to direct use, and so it is suggested that estimation of this indirect exposure is in most cases a lower priority.

The cosmetics industry has spent much effort generating exposure data for the SCCS over the last two decades and this information, which is published in the SCCS Notes of Guidance for cosmetic testing (SCCS, 2022), provides exposure estimates for a range of individual products and for a set of total products that can be used for estimating aggregate exposure. In 2022, RIVM (National Institute for Public Health and the Environment) released an online version of their probabilistic aggregate consumer exposure model (PACEM)[2], which can assess aggregate exposure to cosmetics and some household care products. For sectors outside cosmetics and household care, some tools such as ConsExpo[3] (also RIVM) have useful default models for assessing exposure to individual products, but tools for assessing aggregate exposure are not available, neither is any definitive cross-sector guidance available, and this is in part due to a lack of exposure input data for many uses. The Nordic SPIN[4] (Substances in Products in the Nordic countries) database has some information about registered uses for some applications in the terms of tonnage information, and the availability of such data might enhance cross-sector assessments if it were combined with estimates of the populations who are exposed to these different uses.

In the work reported here, a series of case studies (plasticisers, solvents, preservatives) were undertaken to investigate the adequacy of tools and data available to assess aggregate exposure. The main finding was that progress is hard to make without published information about use patterns. The case studies have suggested that information about tonnage in use for an application would be useful for cross-sector assessment. Limited evidence has been gathered to show that a reasonable estimate of cross-sector exposure can be done, without needing a higher tier (in-depth) study, when relevant use information exists.

[2] https://www.rivm.nl/en/consumer-exposure-to-chemical-substances/exposure-models/PACEM
[3] https://www.rivm.nl/en/consexpo
[4] http://spin2000.net/

This work has shown that the concepts of regional and local scale tonnage, that is used in environmental exposure assessment for REACH, can also be relevant to human exposure when seeking an understanding of detailed exposure patterns. This could be a route to develop better understanding of cross-sector exposures.

The Conclusions and Recommendations set out some specific areas of action should cross-sector aggregate exposure assessment methods need to be developed by any stakeholders.

1. INTRODUCTION

The basic structure of the document is as follows: this Introduction deals at some length with why cross-sector aggregate exposure assessment for consumers is an important but difficult topic; there is discussion of prior art in Section 2, and relevant models in Section 3 that are already available; case studies set out in Section 4 indicate the kind of approaches that could be useful in cross-sector work; Section 5 proposes a general method for cross-sector aggregate exposure assessment and Section 6 defines conclusions and recommendations from this project.

1.1 Background

There is increasing stakeholder interest regarding potential health risks posed by aggregate exposure to consumers, i.e., exposure to a substance from multiple sources via multiple routes. The key points to consider are:

- Whether and when aggregate exposure assessment would be warranted for substances and how comprehensive such assessments should be in different situations.
- Whether considering one source at a time can be sufficiently accurate to identify (or potentially miss) significant risks to the environment and human health.
- Aggregate exposure assessment would very frequently be cross-sector (which is the term used in this report), but regulation usually only has a single area of jurisdiction, and different regulations sometimes have very different objectives[5].
- How many substances will require a cross-sector aggregate assessment.

The focus of this report is solely on consumer exposure for substances which are regulated under several regulatory regimes. For the most part, if only one regulation applies then aggregate exposure is often considered, at least in part. For example, in principle within REACH, multiple sources of consumer exposure should be addressed in a Chemical Safety Report (CSR). Other frameworks in the EU, but also outside the EU, also have requirements for aggregate exposure assessment. However, guidance is missing for most of these frameworks. Usually, cross-sector assessments are so far not foreseen in the relevant European regulatory regimes.

Teeguarden *et al*. (2016), have been involved in the development of the concept of aggregate exposure pathway (to parallel the thinking about adverse outcome pathways). They show a useful overview of the technical context of exposure assessment, from releases through to internal concentrations in humans

[5] In this report, 'sector' is taken to mean an area of regulation or a topic wherein exposure assessment is needed, e.g., as part of research and development.

(**Error! Reference source not found.**). It is evident from the wide range of sciences involved, that compromise between complete understanding and practicality must be made.

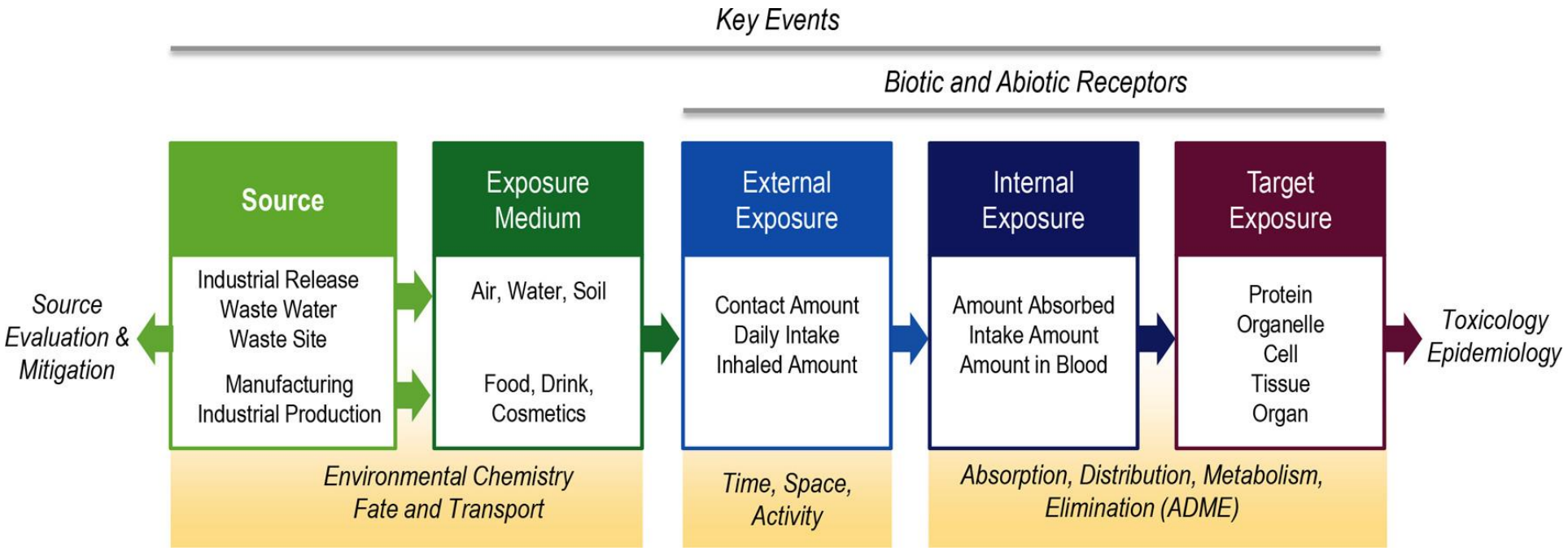

***Figure** 1. Reprinted with permission from "Teeguarden JG, Tan YM, Edwards SW, et al. 2016. Completing the Link between Exposure Science and Toxicology for Improved Environmental Health Decision Making: The Aggregate Exposure Pathway Framework. Environ Sci Technol. 50(9):4579-4586". Copyright © 2016, American Chemical Society.*

Original figure description: The principal components of an Aggregate Exposure Pathway (AEP) cover all necessary levels of ecological, biological and physical organization from sources to target tissue. Each box represents a key event which is a measurable change in a chemical state and concentration that is essential, but not necessarily sufficient, for the movement of a chemical from a source to the target site exposure. Each arrow represents a key event relationship which links a pair of key events. AEP's can be used to accumulate information for source mitigation, or use in epidemiology and toxicology. (Teeguarden et al. 2016)

1.2 Objectives of this project

An ECETOC Task Force entitled 'Mid-tier approach to aggregated exposure assessment' was established and aimed to further develop the thinking reported in ECETOC TR No. 126 (ECETOC, 2016; key conclusions summarised in Section 2.1 of this report). The Task Force examined whether cross-sector assessments can be easily performed considering the tools and data that are readily available, and aimed to identify the limits on what can be achieved.

It is anticipated that those performing aggregate exposure assessments will wish to address many substances without needing to generate extensive datasets, either to fulfil a regulatory need or to aid setting of priorities for higher tier work.

The key objective has been to develop a framework for aggregate exposure assessment that is not based on Tier 1 (screening)[6] precautionary approaches and where a Tier 2 (high level) assessment cannot be simply done due to lack of readily available data and/or tools. A high-level in-depth assessment requires research and collaboration in the entire supply chain, and usually takes several years.

The main barriers to achievement of the objectives are:

- Manufacturing and import volumes for chemicals (as a proxy for consumer use) not being available.
- Lack of data on exposure determinants governing aggregate exposure (e.g. concentration data, product use frequency/amount/location, confidential formulation composition recipes, habits and practices/consumption data, detailed data on exposure timing and duration).
- Uncertainty related to quality and relevance of exposure input data (which applies to single-jurisdiction, i.e. non-cross-sector, exposure estimates also).

Bruinen de Bruin *et al*. (2022) emphasise the need for exposure scenario frameworks to be developed. In this paper they state:

> *"Identified key areas of actions are to develop a common scientific exposure assessment framework, supported by baseline acceptance criteria and a shared knowledge base enhancing exchangeability and acceptability of exposure knowledge within and across EU chemicals-related policies. Furthermore, such framework will improve communication and management across EU chemical safety, security and sustainability policies comprising sourcing, manufacturing and global trade of goods and waste management. In support of building such*

[6] This is taken to be refinement on Tier 0, but not in depth. It is assumed that Tier 0 data, i.e. simple outputs from screening tools, will have already been subject to reasonable refinement before attempting cross-sector assessment.

> *a common framework and its effective use in policy and industry, exposure science innovation needs to be better embedded along the whole policymaking cycle, and be integrated into companies' safety and sustainability management systems. This will help to systemically improve regulatory risk management practices."*

Furthermore, Bruinen de Bruin *et al*. (2022) state:

> *"Over the last 4 years, the 'Europe Regional Chapter of the International Society of Exposure Science' (ISES Europe) mobilised experts from different disciplines, policy domains and stakeholder groups to jointly prepare the foundation for a European Strategy on Exposure Science 2020–2030."* (see Fantke *et al*., 2020).

In a context where exposure science as a discipline is still developing, the topic of cross-sector aggregate exposure assessment should and must be seen as part of those developments.

1.3 Challenges and scope

The structures of regulatory regimes vary across legislation and indeed between geographical regions. There is consequently no consistent guidance for assessment of aggregate exposure available. The main challenge is to be able to evaluate exposures across various uses, and to devise an effective risk mitigation strategy covering all key exposure sources and informing risk management options under different regulatory regimes.

At present, the scope and robustness of human aggregate exposure assessments differ across chemical end-use sectors. Where aggregate exposure assessments are done, they generally follow a tiered approach, starting with a very conservative assessment (screening) and refining if necessary and only if the exposure data exist to allow such refinement. The work undertaken in 2016 by the ECETOC Task Force on Effective Use of Human Exposure Data (TR No. 126; ECETOC, 2016) showed that realistic aggregate consumer exposure assessments use high tier approaches that rely on detailed data about consumer habits and practices, and chemical concentration data in consumer products. When using lower tier exposure tools with conservative assumptions prompted by lack or paucity of such data, simple summation of the worst-case exposure(s) from multiple sources usually results in high aggregate exposure estimates, potentially artifactually exceeding the hazard-based reference value. The background to aggregate consumer exposure is described at some length in TR No. 126, which discusses cosmetics and personal care products, foods and packaging, household products, home maintenance, automotive products, articles, garden chemicals, and biocides, among others.

Many substances are present in different consumer products that are covered by a variety of regulations. However, the present Task Force has found only a few cross-sector exposure studies. While Tier 1 aggregate assessments may be fit for many purposes such as screening level assessments, for some substances their use will be limited because the conservative estimation of aggregate

exposure could exceed the reference dose/safe limit of the substance under assessment, suggesting a human health risk when in fact the exposure might be much lower and there is no safety risk. With a lack of robust data on how consumers are exposed to substances through uses of these consumer products it is currently not possible to refine these Tier 1 estimates.

The screening level of exposure assessment is termed herein Tier 1 and is often based upon worst case assumptions or extrapolation from surrogate data. For 'higher tier' assessments for consumer aggregate exposure, more detailed data on exposure patterns is required, such as data on consumer use patterns and compositional data for the products containing the substance in question. To conduct higher tier studies for many substances would be very resource intensive because these exposure input data are currently not publicly available, so this would need to be obtained before embarking on the assessment. It should be noted that findings from high tier exposure studies could help the development of other cross-sector assessments where there is a paucity of exposure input data.

While in the cosmetics and personal care products sector, robust exposure data and tools are available to enable sound high tier aggregate exposure assessments, for many other sectors, the exposure input data (habits and practices, product use, substance concentration data, etc) are unavailable or scattered over various frameworks, where the data may not be easily available or compatible with aggregation. Therefore, the exposure modelling to include these sources is often not possible without first running detailed surveys to collect the data. This involves considerable time and the collaboration of many stakeholders across different sectors. That may need to be the way forward in some instances, but the purpose of the work is to explore whether simpler approaches are available.

While Tier 1 assessments of different uses may be aggregated, and can be fit-for-purpose in some cases, there are the following important uncertainties:

1. Whether to examine the distribution of the substance within the indoor environment, which may be relevant to some substances.
2. Whether and how to assess the probability of co-use, i.e. some proportion of the population could be users of, or exposed to, the substance for only a few or for all the exposure scenarios, during a specified time frame.
3. How to limit conservatism by multiplying high percentiles from available data or other risk assessment inputs.
4. When exposures occur at different times, is the persistence of a substance in the body an important factor that could be relevant for aggregate exposure?

This project looks at the progression of aggregate exposure assessments from Tier 1 to a higher tier and explores potential methodologies that can be used as a mid-tier assessment. The term mid-tier is used in some places in the report as a convenient description of the progression. An ideal high tier study will succeed in understanding items 1 to 4 listed above and give a clear understanding of exposure and risk. A mid-tier assessment study will describe some of the exposures but with less uncertainty than screening (Tier 1). For general regulatory compliance, it will most likely not replace a screening level of risk characterisation performed one scenario at a time. Only high tier studies are likely to give fully robust exposure estimates, but this refinement may not always be needed.

Eichler *et al*. (2021) have set out an ambitious framework for the assessment of semi-volatile organic compounds, which covers sources and fate in the consumer environment. This is considered as a high-level overview.

Although EU regulators have set out some generally expressed thoughts about "one substance one assessment" (OSOA), no details have emerged so far. This Task Force considers that cross-sector methodology should help priority setting when considering issues such as:

- Which substances or uses are of greatest concern?
- Which exposure routes are the most important?
- Where will exposure data generation have the greatest impact in improving exposure modelling?

Another application area of aggregate exposure knowledge is targeted mixture risk assessment. The quality of combined exposure assessment to multiple substances is a function of robustness of aggregate exposure estimates for individual substances. This phenomenon has been demonstrated by Kennedy *et al*. (2019), who showed that the number and composition of pesticide mixtures prioritised for risk assessment differed depending on whether non-dietary exposure sources were included or not. In that respect, an incorrect understanding of aggregate exposure to substances in question may misinform the scope of mixture risk assessment or render it incomplete.

Regarding OSOA, The European Chemical Industry Council (CEFIC) has set out some useful points in its May 2021 position paper, which states that exposure assessment tools and methodology could be centralised on a common platform, and indeed that has been discussed in ECETOC Workshop Report No. 35 (ECETOC, 2017) and by ISES Europe in particular (International Society of Exposure Science, Europe Chapter, at https://ises-europe.org/group/exposure-models (ISES Europe, 2022)), and Schlüter *et al*. (2022).

This project was initiated to explore the data and exposure assessment methods already available that may be useful for a cross-sector assessment. The main features/benefits of these approaches are that they would allow assessments to:

- Maximise use of existing exposure data.
- Help identify key exposure sources for a substance of interest.
- Inform the need and scope of a more detailed high-tier aggregate assessment.

Cross-sector methods should enable (semi-quantitative) evaluation of complexities and uncertainties stemming from combination of different exposure assessment methods when deriving an aggregate exposure estimate, multiple pieces of evidence and independent sources of information.

The project deliverables are thought to be most useful and instructive for aggregation of exposures in combination from REACH evaluations and/or restriction proposals, US Environmental Protection Agency (EPA) risk evaluations, Life Cycle Impact Assessments, alternatives assessments, safety assessments of cosmetic ingredients, biocidal and plant protection product constituents, food additives and food contact materials. Cross-sector approaches should ideally facilitate rapid yet realistic[7] aggregate exposure evaluation, without the need to recourse to the worst-case assumptions in low tier assessments, and would enable industry to confirm safety of existing and new-to-the-market substances in an efficient manner. Experts from each sector could form working groups that kick off activities to avoid overlapping areas that may double-count potential exposure.

This project is focused on consumer exposure, with the hope that data and methods identified herein may also be suitable for estimation of worker aggregate exposure, particularly for professional users, who may be comparable to consumers in knowledge/training, duration, frequency and methods of use. Specialised professional users (with sufficient training) and industrial users are probably not covered by these data and methods. Those consumers who are also workers in the chemical industry, or who are professional users of chemical products, are not addressed explicitly. In the nature of consumer exposure, significant acute or short-term exposure from one source may occur, which is the proper subject of the assessment of single uses. High exposure from two acute/short-term sources whilst possibly unlikely for a consumer should be considered in the assessment steps, because for some toxicological effects this may be important[8]. However, long-term exposure (usually on a comparable low exposure level) from multiple sources is the primary focus here.

Elements of exposure assessment fitting into scope of this project are summarised below in Table 1.

[7] In this report 'realistic' is taken to mean information about reasonably-likely exposures; it is understood that modelling methods are not aimed usually at providing certainty about exposure levels.

[8] The derivation of safe levels from toxicological data also introduces a degree of conservatism, but that is not discussed further in this report.

Table 1. Project elements in scope

Note: Not every one of the elements listed below has been addressed specifically in this report.

Focus area	Exposure aspect/element
Chemicals management system	REACH (incl. formulated products and articles, Man via Environment) Biocides Regulation, Plant Protection Products Regulation Food contact plastics materials Reg Toys Directive Cosmetics Directive Medical Devices Directive
Exposure pathways	Near-field direct (use) Near-field indirect (residential) Far-field (environmental, background) Dietary (for food additives, FCM) Dietary (for natural ingredients in food)
Substances	Hazardous/classified for human health hazard*
Data streams	Substances in products (use, presence, concentration) Products co-use Substances in exposure media (indirect exposure) (Sub)population characteristics
ADME	Route-specific absorption rates Elimination $t_{1/2}$ **
Aggregation strategies/approaches	Low-tier summation of (worst-case or refined) use/product specific exposures Ranking of exposure sources according to their individual contribution to aggregate exposure Grouping of exposure sources, e.g. by use frequency, activity type, co-use knowledge (available or derived).

* Substances with local and systemic hazards may require different strategies for aggregated exposure assessment
** Critical to know for different aggregation timeframes

The following elements were assessed to be out of scope of this project:

- Worker aggregate exposure in industrial settings or for specialised professional users (from different tasks/processes).
- Combined exposure to (groups of) multiple substances with the same or similar mode of action.
- An in-depth discussion of all the possible toxicological endpoints and the way these interact with exposure assessment.
- Detailed evaluation of the various tools and models which exist.

1.4 Principal methods of this project

The project workflow was built to encompass a range of possible examples/cases where aggregate consumer exposure assessment may be warranted, along with various data requirements and availability. Those were then investigated in case studies for three types of substance:

1) Plasticisers,

2) Solvents[9],

3) Preservatives.

The case studies specifically investigated different approaches to exposure aggregation strategies, both within and across end-use product sectors. Also, comparative analysis of aggregate exposure estimates obtained with methods such as biomonitoring compared to those from low-tier and higher tier assessments was conducted to "calibrate" identified cross-sector approaches and to identify their application boundaries. A simple spreadsheet was developed by the Task Force to facilitate this, to illustrate how cross-sector assessment can be facilitated.

Findings from the case studies inform the proposal of a stepwise approach to aggregate exposure assessment set out in Section 5, with identified methods and exposure input data-streams constituting its main elements.

[9] i.e., substances used primarily and specifically for their solvation properties (all substances have some such properties)

2. PRIOR ART AND CURRENT REGULATORY CONTEXT

2.1 ECETOC and other reviews (including regulatory safety assessments)

The key conclusions of the ECETOC Technical Report 126 "Guidance for Effective Use of Human Exposure Data in Risk Assessment of Chemicals" (ECETOC, 2016) are summarised as follows:

- Exposure assessments should involve an iterative process, and should be conducted using a tiered strategy. The lowest tier involves a semi-quantitative assessment of all the sources, pathways and routes contributing to aggregate exposure to a substance. The mid-tier tends to be a deterministic estimate with conservative assumptions, while the higher tier is a more realistic estimation of population exposure with increased use of measured data using probabilistic methods. At the highest tier, exposure is modelled with a person-orientated approach using raw data sets.

- Many tools and databases exist to support consumer exposure assessment, as demonstrated in the landscaping effort. Users can select the data and tools that best fit their specific situation and level of assessment.

- Most consumer exposures tools are designed to evaluate single substance, single use assessments.

- Higher tier exposure assessments require more realistic and representative data to the situation being assessed and additional understanding of data correlations.

- Subject-oriented aggregate tools (PACEM[10], Creme Care[11]) are available that allow aggregate exposure assessment within some consumer product domains. For example, in cosmetics and personal care products, the availability of robust tools and data sets (habits and practices data with product co-use, and the use of presence probabilities) allow refined estimates of aggregate exposure.

- A major challenge in estimating aggregate exposure in many product categories is obtaining representative information on exposure factors (habits and practices data, co-use data, substance concentration data and substance occurrence data), as well as potential

[10] https://www.rivm.nl/en/consumer-exposure-to-chemical-substances/exposure-models/PACEM

[11] https://www.cremeglobal.com/creme-care/

correlations between these factors. For some domains, such as household care products, the available data are limited.

- Guidance should be developed to indicate when higher tier aggregate assessments could be a priority. Considerations include relative contributions of different sources, level of conservatism in a screening single source assessment (for example, the case study indicates a higher tier aggregate assessment may produce a lower exposure estimate than the maximum screening exposure predicted for single uses), and total exposure levels from representative biomonitoring studies.

- Model verification with real-life data (e.g. biomonitoring) on a representative range of substances would assist to promote use/acceptance of exposure model predictions. Wider engagement of industry, the public and regulators into the generation, harmonisation and management of input data related to consumer exposure will foster the advances in aggregate exposure modelling, especially in domains where currently little data are available. Although it may be possible to find case-studies in the published literature for a limited number of substances.

It is not necessary in the present report to expand on these concepts nor to reproduce the work already reported. However, some simple examples of the need for cross-sector aggregate exposure assessment reiterate why the work of TR No. 126 needs development:

- Some screening tools show inhalation exposures at or near the saturated vapour pressure of a substance. As a physicochemical reality, more than one use of that substance cannot give rise to exposure above that concentration.

- Exposures from service life of articles, ingestion of food, etc. can be background level exposures which are often not well described in screening.

- Exposure to a personal care product may be dealt with well by cosmetics guidance, but the same substance could be in a cleaning product and assessed at different levels of detail. The problem is that detailed results from one use type could be combined with more crude data from a different use, and misleading conclusions can be reached.

2.2 Regulatory context

In the EU, no common methodology for aggregate consumer exposure assessment between regulatory systems exists, and there is no agreed methodology within the REACH Regulation or other frameworks. The need to understand the numbers of consumers exposed, distribution and exposure routes is stated in REACH guidance, but no specific methods are described. However, most of the EU regulatory frameworks ask for aggregate exposure assessments. The level of uncertainty in risk characterisation or assessment is not the same for all regulatory systems. Discussion of various regulatory frameworks is provided in Annex 1.

In the important case of REACH, the guidance documents give examples of the current challenges with cross-sector aggregate exposure assessment. These are described in Table 2 below.

Table 2. Comment on REACH guidance relevant to mid-tier aggregate exposure assessment

Extract from the R.15 Guidance (ECHA, 2016)	**Task Force comment**
Summing up the RCRs resulting from Tier 1 tool estimates leads to a conservative outcome.	This is one reason why the present work has been undertaken.
In most cases more sophisticated (e.g. probabilistic) methods and corresponding comprehensive datasets will be needed, in order to properly reflect the co-use pattern of products across consumers.	The problem with this statement is that this implies that high tier in-depth study is the only way forward. The need is for some tools which are more accessible and appropriate to the need.
Such methods [probabilistic] are available for certain product groups. Exposure to the substance via different products may also be relevant when adjusting assessments for short duration over the day, or when characterising the risk related to infrequent exposure.	This implies, correctly, that the realistic pattern of use by consumers should be considered. Consumers will not be exposed from all possible sources continuously. The magnitude of the relative source contributions is also relevant. So, if a source has a relatively low contribution, it may not be worth the effort to characterise the magnitude of exposure because its significance is negligible to the aggregate exposure.
In addition to direct exposure resulting from the use of products, the general population may be exposed to the substance via the environment (ambient air, drinking water and food).	This is clearly understood within this report.
In order to produce a meaningful risk characterisation, it is important for the assessor to understand and take into account the uncertainties associated with the information/data that is provided (related to both hazard assessment and exposure assessment).	An important principle, which at this stage can be considered quantitatively in respect of likely ranges of properties and exposure. Qualitative evaluation can also be helpful.

These principles were kept in mind in the case studies set out in this report.

3. RELEVANT MODELS, SOFTWARE AND TOOLS

The Task Force has not been able to identify any off-the-shelf software suitable for cross-sector analysis in the case studies. Some relevant existing models such as PACEM and Creme Care are considered useful for tiers above screening, although they currently only include data from cosmetic and personal care and household sectors.

To meet the objectives of the case studies several tools were employed, including but not limited to:

1. A new spreadsheet tool which has been set up by the Task Force for basic cross-sector aggregate exposure calculation, which takes use pattern data and estimates reasonable worst case use levels from tonnage on the market (see Annex 2).
2. For individual uses with a cross-sector study, models such as ConsExpo[12] were employed, which have been shown to be useful for the refinement of screening assessments for each exposure.
3. RAIDAR-ICE[13] (Risk Assessment IDentification And Ranking – Indoor and Consumer Exposure) is considered useful once release rates are known, because it refines domestic exposure according to distribution between air and surfaces.
4. The Indoor model[14] can give distribution information (as in RAIDAR-ICE) and can also give very useful insights into time-dependent inhalation exposures in the home.
5. EUSES[15] (European Union System for the Evaluation of Substances), EQC[16] (EQuilibrium Criterion) model, RAIDAR[17] (Risk Assessment IDentification And Ranking) or other similar models can help provide estimates of human exposure via the environment.

In the case studies, recognised exposure inputs and factors like those in the SCCS guidance (SCCS, 2022) have been used to help set up the parameters used in the models.

[12] https://www.rivm.nl/en/consexpo

[13] https://arnotresearch.com/raidar-ice/

[14] https://www.trentu.ca/cemc/resources-and-models/indoor-model

[15] https://echa.europa.eu/support/dossier-submission-tools/euses

[16] https://www.trentu.ca/cemc/resources-and-models/eqc-equilibrium-criterion-model

[17] https://arnotresearch.com/raidar/

Models that may be of use in cross-sector aggregate exposure assessment are listed in more detail in Annex 3.

4. CASE STUDIES

4.1 Introduction

Case studies have been used to explore different approaches to cross-sector consumer aggregate exposure assessment, and to identify limitations. Even though higher-tier source data are used to develop the case studies, the amount of information needed at a minimum to conduct a cross-sector assessment can be identified. For substances where no higher-tier prior art exists, it is not easy to perform a cross-sector assessment due to lack of readily available information. Therefore, the case studies are not necessarily ideal for the purpose of this work, i.e. to explore potential methodologies for mid-tier assessment (between Tier 1 screening and higher tier), but do demonstrate the principles and the challenges.

The case studies should be considered as a starting point for the examination of possible approaches (they are not definitive pieces of exposure or risk assessment work). Complex issues about effects are not addressed, although the case studies have been developed for data-rich substances in respect of human health effects. The learning points from the case studies will be drawn from evaluation against the criteria set out in the earlier sections of this report. The spreadsheet tool developed by the Task Force for basic level aggregate exposure calculation (Annex 2) has been used as part the case studies. The spreadsheet tool takes use pattern data and estimates reasonable worst case use levels from tonnage on the market. The total per use is then split to the regional and local scales.

4.2 Plasticisers

4.2.1 Sectors of importance

The service life of plasticisers has been an important topic for regulators for many years; for example it is included in the Plastics Additives OECD exposure scenario document (OECD, 2014) regarding environmental exposure to plastics additives. No defined methodology exists for assessing consumer exposure, although there have been many studies in which indoor concentrations of plastics additives including plasticisers have been reported.

Main/common uses of plasticisers (in no particular order) include:

- Food contact materials and food additives.
- Cosmetics (e.g., nail polishes).
- Coatings and adhesives, sealants.
- Polishes and waxes.

- Plastic articles, incl. construction materials, interiors (flooring, furniture), electronics, toys.
- Treated textiles, footwear.

Data on use patterns of articles are not widely available. Therefore, plasticisers are relevant to the present work.

4.2.2 EFSA and ECHA joint work

It is of interest to note that the European Food Safety Authority (EFSA) has drawn attention to joint work with the European Chemicals Agency (ECHA) on phthalate plasticisers in response to European Commission requests to re-evaluate their presence in food contact materials. As a pilot for the 'One-Substance, One-Assessment" approach (under the EC's Chemicals Strategy for Sustainability[18]), the following two public consultations were conducted in 2021:

1) Draft opinion aimed at identifying the prioritisation of phthalate and structurally similar substances for re-evaluation.

2) Draft protocol for the approach to one-substance-one [risk and hazard] assessment.

In November 2022, the final versions of the above opinion and protocol were published, identifying transparently the prioritisation for the risk assessments and how this will apply to both the hazard and risk assessment protocols, separately. In much the same way this report aims to do, the EFSA protocol (ESFA, 2022) describes an approach for selecting relevant data based on appraising the relevant and available evidence and its potential to be integrated for use in exposure assessments (in the context of any uncertainties that may need to be addressed). For the exposure risk assessment (ESFA, 2022), the approach is broadly broken down into three questions:

1) What is the overall chronic and/or acute dietary exposure to the prioritised substances in different population groups and age classes in the EU?

2) How much of the chronic and/or acute dietary exposure to the prioritised substances originates from Food Contact Materials (FCMs) in the different population groups and age classes in the EU?

3) How does dietary exposure due to FCMs compare with the overall (dietary and non-dietary) exposure of EU consumers?

[18] https://environment.ec.europa.eu/strategy/chemicals-strategy_en

These are worked through using a range of sub-questions applicable to each main question, that must be answered in terms of:

- Which evidence requirements are necessary ("evidence needs") to answer the sub-question?
- Which methods are available ("methods") for answering the sub-question?
- An assessment on their suitability, including an evaluation on the uncertainties ("uncertainty analyses") when methods (both for answering the specific sub-question and for integrating evidence across the sub-questions) are applied to the main question.

Whilst logical in terms of methodology, laid out in a well-structured and comprehensive approach, the published protocol highlights several challenges experienced in this ECETOC Task Force: primarily the current lack of representative exposure data sources. Whilst some comprehensive EFSA consumption databases exist, with aspects that help answer the three main questions on the use of phthalates as plasticisers in FCMs, many of the reviews on approaches described as methods rely on future recommendations in the form of:

- Continued/further/deeper exploration of available databases to select relevant data specific to the sub questions.
- Literature reviews, with a prescribed protocol for their performance.
- Data call-ins, market surveys and surveillance studies (including, where appropriate, biomonitoring data).
- National legislative restrictions or cut off values, to be inferred as a reasonable worst case.

Many of these method limitations end up stated under the uncertainty analyses, related to "incomplete information".

Specifically related to the work of this ECETOC Task Force, sub-questions 3.1 and 3.2 of the EFSA protocol detail potential non-dietary routes of exposure of phthalates to consumers. The "evidence needs" are much the same as have been discussed across the case studies included in this report: identifying product categories where case studied substances are utilised cross-sector to better inform usage and exposure (both amounts and potential routes of human exposure). Indeed, a similar approach is identified for phthalate exposure by EFSA as has been applied in the Task Force case studies, using tonnage bands as a potential proxy for consumer exposure. RIVM factsheets[19] were also identified as a useful source of information. However, challenges were noted for phthalates in respect

[19] RIVM (Dutch National Institute for Public Health and the Environment) fact sheets are available online: https://www.rivm.nl/en/consexpo/fact-sheets

of the variable quality of the information provided in REACH dossiers, lack of available data on conditions of use, and overestimation of exposure when employing Tier 1/screening tools. In conclusion, the protocol details a theoretical structure for an approach to conducting exposure assessment of phthalate plasticisers (and structurally similar substances) but does not go so far as to perform an example case study, due to the lack of currently available and relevant information for all three main questions EFSA seeks to answer.

4.2.3 Other relevant information

ECHA has also been looking at plastics additives (see https://echa.europa.eu/plastic-additives-initiative). The Task Force has not examined the models for additive movement from plastic to air that ECHA has been developing, since that is a particular detailed technical matter.

It should also be noted that ConsExpo does examine service life, but it has not been applied in this case study. See also the RIVM report "Emission of chemical substances from solid matrices A method for consumer exposure assessment", Report 320104011/2010, Delmaar (2010). (https://www.rivm.nl/bibliotheek/rapporten/320104011.pdf). This is a relatively complex tool so we have not applied it here.

4.2.4 Approach in this case study

A comprehensive literature search was not performed[20], but a publication (Little *et al*., 2012) concerning DEHP (di-2-ethylhexyl phthalate) provides useful information for the development of a limited case study. The paper by Little *et al*. (2012) is a useful general review and also includes some examples. One of note is the use of DEHP as a plasticiser in flooring. The data relate to times prior to regulatory controls of its use coming into force.

The data concerning DEHP in flooring were interpreted by the Task Force using the spreadsheet tool to obtain the maximum release to air. That result was then modified using RAIDAR-ICE to estimate the actual vapour concentration.

The only application discussed here[21] is use in flooring, without using complex physical models. However, models for loss of substance from plastics are available and could be applied to other uses. The general approach could then be applied in a cross-sector way by inclusion of other applications of DEHP.

[20] That is because this report is not a comprehensive examination of DEHP.

[21] The amount of information about DEHP is so wide-ranging that a limited study only was made.

Some information about the use of DEHP in flooring is presented by Little *et al*. (2012) and is set out in Table 3 below.

Table 3. DEHP use in flooring information adapted from Little et al. (2012)

Tonnage in the EU for this use	30200 t
Service life	Considered in the paper to be 20 years
DEHP content in flooring as made	20%
Flooring use rate	2.9 kg/m^2
Per capita use level	0.58 kg DEHP as an average across the population.
Total amount of flooring per person	52 m^2, averaged over population of 500 million in EU.
Typical measured gas phase concentration of DEHP in the home (No information about range)	0.02 µg/m^3

It is considered that the direct exposure of skin from contact with flooring can be ignored, but exposure is via air. There is loss to wastewater (and then to the environment) after cleaning and washing processes in the home.

For comparison, the aggregate exposure from DEHP use in flooring has been estimated using the spreadsheet tool using the assumptions detailed in Table 4.

Table 4. DEHP use in flooring assumptions for use in case study

EU tonnage	30000 **tonnes per annum (tpa)**
Regional tonnage (default)	3000 tpa
Local scale total amount per year coming into new product[22]	1500 kg (3000 t x 0.005 – default factor for local use)
Number of houses in the local scale (our estimate)	3000 households for 10000 people
Flooring change rate (our estimate)	Once in 5 years in some part of the house, i.e . 600 households in the local area in any one year;
At time of installation, the mass of DEHP	2.5 kg (1500 / 600); this is a realistic use level for one house.
Fraction to air in first year	Assume 10% lost during first year (in line with model estimates for a 20-year service life (rate declines with time).
Amount per day volatilised	i.e. 0.25 kg/365 = 0.69 g per day in the first year
Concentration in air before any removal processes, for a house volume of 100 m^3 and air exchange dilution factor of 5 /d (our estimates)	Before air exchange: 6.9 mg/m^3 With air exchange 1.4 mg/m^3
Some simple estimate of actual volatilisation is needed. For DEHP, RAIDAR-ICE shows 0.01% left in air after adsorption and washing processes.	Giving worst case amount in air as 0.14 $\mu g/m^3$ The value of 0.01% appears to be a limit value; it is likely much less due to the strength of adsorption.

The predicted exposure is higher than that measured but shows that a reasonable worst case value can be obtained quickly.

4.2.5 Findings

A value of the reasonable worst-case exposure of a consumer over one year through air to a plasticiser (DEHP in flooring) was estimated using the Task Force spreadsheet tool (Annex 2), although the RAIDAR-ICE estimates of volatilisation (used to modify the spreadsheet output of maximum release to air to estimate the actual vapour concentration) may be conservative. The allocation of the amount on the market being spread over all households made sense in terms of the use pattern. The estimated value aligned reasonably with some reported measurements.

This simple approach could be useful as part of cross-sector assessment of any plastics additive.

[22] One year's production is considered on the assumption that the largest release is in the first year.

4.3 Solvents

4.3.1 Approach

This section describes initial proposals of simplified cross-sector aggregate consumer exposure assessments of N-methyl pyrrolidone (NMP) and hexamethyldisiloxane (HMDS). The case studies are based, however, on prior higher-tier studies which help to calibrate cross-sector methods.

Even in these cases, information on EU use pattern is not readily available from public sources.

4.3.2 NMP

The US EPA 2020 risk evaluation of N-methyl pyrrolidone (NMP) was the primary source for this case study (US EPA, 2020). This includes a description of consumer uses. It also gives estimates and measurements relating to daily levels of consumer products use. Exposure parameters such as daily use amounts and indoor air concentrations for the applications as a cleaner, adhesive, paint, paint remover and specialist inks are given. The report also gives tonnages in the US going into these applications, but without splitting industrial and consumer uses; a total of around 6000 t, based on work largely concluded in 2018. The picture in the US is relevant to a historic (pre-2013) EU use pattern, and in that way is applied in the present work.

The Nordic SPIN database has been accessed, for comparison with the US EPA data. In 2018 the total for SE, NO, DK and FI for preparations to be used by consumers was around 450 tpa. The amount in preceding years was similar; experience of Task Force members shows Nordic use to be around 10% of EU use, which suggests broad equivalence in the EU to the US tonnage.

However, the EU Restriction on NMP means that these uses will largely have ceased, although products containing up to 0.3% NMP are legal. The 2013 EU Restriction Annex XV dossier for NMP gives similar uses but with only around 150 tpa total in the EU. It is not easy to rationalise the SPIN data with the CLP limits or the Restriction. This illustrates an intrinsic difficulty of obtaining reliable tonnage data.

The HBM4EU project[23] is one relevant reference for non-occupational exposure based on published data of NMP biomonitoring. This study used urine samples from 60 students per year, so the concentrations are most likely relevant only to background rather than consumer use, given that students are not usually typical consumers, although that is uncertain here. Only one study in relation

[23] https://www.hbm4eu.eu/

to the general population and its sub-groups has been identified (Ulrich *et al*., 2018). NMP and NEP (N-ethylpyrrolidone) metabolite concentrations were determined in 540 24-h urine samples of the German Environmental Specimen Bank collected from 1991 to 2014. NMP metabolites 5-hydroxy-*N*-methyl-2-pyrrolidone (5-HNMP) and 2-hydroxy-*N*-methylsuccinimide (2-HMSI) as well as NEP metabolites 5-hydroxy-*N*-ethyl-2-pyrrolidone (5-HNEP) and 2-hydroxy-*N*-ethylsuccinimide (2-HESI) were determined by stable isotope dilution analysis using solid phase extraction followed by derivatisation (silylation) and GC–EI–MS/MS. The respective metabolites were identified: 5-HNMP in 98.0 % and 2-HMSI in 99.6% of the samples; 5-HNEP in 34.8 % and 2-HESI in 75.7% of the samples. Calculated median daily intakes in 2014 were 2.7 µg/kg bw/day for NMP and 1.1 µg/kg bw/day for NEP (Ulrich *et al*, 2018).

The use of the exposure model in this case study attempts to model the US risk evaluation exposure data within the spreadsheet tool.

4.3.2.1 Key data from US EPA

Consumer uses are listed on pages 39 to 46 of the USEPA risk evaluation of NMP (US EPA, 2020), as shown in Table 5.

Table 5. Uses of NMP in the United States (Based on "US EPA Report", 2020, p. 39-46) Adapted from: *https://www.epa.gov/sites/default/files/2020-12/documents/1_risk_evaluation_for_n-methylpyrrolidone_nmp_casrn_872-50-4.pdf#page=39*

Category	Sub-category
Paints and coatings	Paint and coating removers Adhesive removers Lacquers, stains, varnishes, primers, floor finishes.
Paint additives and coating additives not described by other codes	Paints and arts and crafts paints.
Adhesives and sealants	Glues and adhesives, including lubricant adhesives.
Other uses	Automotive care products Cleaning and furniture care products, including wood cleaners, gasket removers Lubricant and lubricant additives including hydrophilic coatings.

The numbers of products and the weight fraction of NMP are on page 192 of the US EPA report (US EPA, 2020). These are modelled in respect of the dermal and inhalation exposure routes (*ibid* page 57). The conditions of use are shown in Table 6 overleaf.

Table 6. Consumer Conditions of Use and Modeling Input Parameters (Reprinted from "US EPA Report", 2020, p. 192) Retrieved from: https://www.epa.gov/sites/default/files/2020-12/documents/1_risk_evaluation_for_n-methylpyrrolidone_nmp_casrn_872-50-4.pdf#page=192

Original Table Header: Table 2-78. Consumer Conditions of Use and Modeling Input Parameters

Consumer Conditions of Use	**Form**	**Selected U.S. EPA (1987) Survey Scenario [a]**	**Room of Use [b]**	**Duration of Use (min) [c,d]**			**Mass of Product Used (g, [oz]) [e]**		
				$_{10}$th	**$_{50}$th**	**$_{95}$th**	**$_{10}$th**	**$_{50}$th**	**$_{95}$th**
Adhesives and Sealants	Liquid	Contact Cement, Super Glues, and Spray Adhesives	Bathroom/ Utility Room/ Outdoors	0,33	4,25	60	0.92 [0.03]	7.69 [0.25]	132.87 [4.32]
Adhesives Remover	Liquid	Adhesive Removers	Utility Room	3	60	480	17.85 [0.67]	213.17 [8]	1705.33 [64]
Auto Interior Cleaner	Liquid	Solvent-type Cleaning Fluids or Degreasers	Automobile	2	15	120	16.56 [0.56]	96.11 [3.25]	946.35 [32]
Auto Interior Spray Cleaner	Aerosol	Solvent-type Cleaning Fluids or Degreasers	Automobile	2	15	120	16.60 [0.56]	96.34 [3.25]	946.53 [32]
Cleaners/ Degreasers	Liquid	Solvent-type Cleaning Fluids or Degreasers	Utility Room	2	15	120	16.23 [0.56]	94.19 [3.25]	927.43 [32]
Engine Cleaner/ Degreaser	Liquid	Engine Cleaners/ Degreasers	Garage	5	15	120	73.15 [2.91]	291.60 [11.60]	1206.60 [48]
Paint	Liquid	Latex Paint	Garage	30	180	810	349.63 [10.67]	4194.24 [128]	23068.31 [704]
Paint and Coating Removers	Liquid	Paint Remover survey data from ABT (1992)	Bathroom/ Utility	--	90	396	--	540	1.944
Spray Lubricant (Mold release)	Aerosol	Other Lubricants (Non-Automotive)	Utility Room	0,08	2	30	3.40 [0.10]	18.71 [0.55]	170.05 [5.00]

Original Table Header: Table 2-78. Consumer Conditions of Use and Modeling Input Parameters

Consumer Conditions of Use	**Form**	**Selected U.S. EPA (1987) Survey Scenario [a]**	**Room of Use [b]**	**Duration of Use (min) [c,d]**			**Mass of Product Used (g, [oz]) [e]**		
				$_{10}$th	**$_{50}$th**	**$_{95}$th**	**$_{10}$th**	**$_{50}$th**	**$_{95}$th**
Stains, Varnishes	Liquid	Stains, Varnishes, and Finishes	Living Room	10	60	360	61.07 [2.00]	366.42 [12.00]	3908.44 [128.00]
Arts and Crafts	Liquid	Latex Paint	Utility Room	30	180	810	5.44 [0.17]	65.27 [2.00]	358.98 [11.00]

[a] The U.S. EPA 1987 Survey was used to inform values used for duration of use and mass of product used. Where exact matches for conditions of use were not available, scenario selection was based on product categories that best met the description and usage patterns of the identified consumer conditions of use.
[b] The room of use was a selection within the Consumer Exposure Model to model the most likely location of the consumer product use and exposure.
[c] Duration of use is time of use per event and assumes only one use per day.
[d] Low-end durations of use reported by U.S.EPA 1987 that are less than 0.5 minutes are modeled as being equal to 0.5 minutes due to that being the minimum timestep available within the model.
[e] Mass of product used within U.S.EPA 1987 for given scenarios is reported in ounces but were converted to grams using reported densities in the product SDSs or MSDSs.

Estimated air concentrations (8 h time weighted average (TWA)) from the consumer uses are modelled by US EPA (*ibid* pages 195 to 205, set out in Table 7). Methods are reported (not herein). The US EPA report also estimates internal concentrations in the user.

For all the uses, variations studied include intensity of use, high or low weight fraction in product. The tonnage in the US was also given.

Table 7. US EPA modelled exposures to NMP (Based on "US EPA Report", 2020, p. 195-205) Adapted from: *https://www.epa.gov/sites/default/files/2020-12/documents/1_risk_evaluation_for_n-methylpyrrolidone_nmp_casrn_872-50-4.pdf#page=195*

Use (in the order of the US EPA report)	Range of modelled concentration in air	Typical fraction in product	Tonnage in US
Adhesives and sealants	0.18 to 1.74 mg/m³	85%	Very low
Adhesive removers	1.4 to 21.7 mg/m³	60%	Very low
Cleaners used in motor vehicles	2.9 to 54 mg/m³ (interiors) 18.5 to 281 mg/m³ (engines).	5% 40%	250
Art paint and hobby use	0.014 to 18.3 mg/m³.	1%	300
Stains, inks, varnishes and coatings	0.68 to 12.5 mg/m³.	10%	100
Paint and coating removers	6.2 to 232 mg/m³.	60%	5000

Consumer exposures to NMP from the US EPA model were identified and then summed in the Task Force aggregate exposure spreadsheet.

4.3.2.2 Findings

The key parts of the spreadsheet tool applied to NMP are shown in Table 8. Annex 2 provides further explanation about the sheet.

Table 8. Spreadsheet tool inputs and results for NMP

Note: hd = head = a person

			NMP	NMP	NMP	NMP		Man via Environment total from EUSES	Overall exposure total
			1	2	3	4			
	Parameter	Unit	Cleaning solvent	Hobbies	Paint	Paint remover	Consumer uses total		Use + MVE
Tonnes in EU for use		t/y	250	300	100	5000	**5650**		
Regional tonnage fraction	0.1	t/y	25	30	10	500			
Local amount fraction	0.002	kg/y	50	60	20	1000			
Overall mass per year average per person	10000	g/hd/y	5	6	2	100			
Fraction of population who are users			0.01	0.1	0.01	0.1			
Frequency per day of use		/d	0.1	0.1	0.1	0.1			
Fraction of substance in formulation			0.4	0.01	0.1	0.6			
mass per user person per year		g/hd/y	500.00	60	200	1000			
mass per user per event on a day		g/hd	1.37E+01	1.64E+00	5.48E+00	2.74E+01			
amount of formulated product		g	34.25	164.38	54.79	45.66			
mass per person per day average	365	g/hd/d	1.370	0.164	0.548	2.740			
Fraction to air during application			0.8	0.8	0.8	0.8			

			NMP	NMP	NMP	NMP		Man via Environment total from EUSES	Overall exposure total
			1	2	3	4			
	Parameter	Unit	Cleaning solvent	Hobbies	Paint	Paint remover	Consumer uses total		Use + MVE
Fraction to waste water averaged over time			0.1	0.1	0.1	0.1			
worst case fraction to skin corrected for volatility			0.1	0.1	0.1	0.1			
external exposure of skin	60 kg/hd	mg/kg/d	2.3E+00	2.7E-01	9.1E-01	4.6E+00	**8.04E+00**		
fraction absorbed from skin			0.1	0.1	0.1	0.1			
internal average		mg/kg/d	2.3E-01	2.7E-02	9.1E-02	4.6E-01	**8.04E-01**	5.08E-04	**8.04E-01**
Sum of fractions			1.000	1.000	1.000	1.000			
indoor air mass/event		mg/d	1.10E+03	1.32E+02	4.38E+02	2.19E+04			
air exchange per day	24	/d							
room volume	24	m^3							
indoor air concentration during event		mg/m^3	1.90E+01	2.28E+00	7.61E+00	3.81E+02	**4.09E+02**	2.34E-06	**4.09E+02**
Internal exposure via air	2.88E-01	mg/kg/d	5.48E+00	6.58E-01	2.19E+00	1.10E+02	**1.18E+02**	6.74E-07	**1.18E+02**
									1.18E+02
fraction to waste water			0.100	0.100	0.100	0.100			
to regional release to air		kg/d	62	74	25	1233		1.39E+03	
to regional release to waste water		kg/d	7	8	3	137		1.55E+02	
to continental release to air								1.25E+04	
to continental release to waste water								1.39E+03	

Points of note from this case study are:

- The spreadsheet tool can give results for these kinds of consumer uses as reported by US EPA, by setting up a simplified simulation of major findings of the higher tier study. The modelling was targeted at the low end of the ranges reported by US EPA because use levels in the EU were lower. Therefore, the spreadsheet gives an indication of how a total tonnage can be broken down.

- For the four identified uses, the user factors (frequency and fraction of population) are low, although higher for paint remover due to the higher tonnage.

- For three of the uses, the use occurs less than once per day.

- The modelled tonnage is from the US EPA tonnage and an EU tonnage based on SPIN, but those are much higher than reported in the Annex XV dossier.

- The biomonitoring data (Ulrich *et al*, 2018) gave a mean daily intake of 2.7 µg/kg bw/day. The spreadsheet gives 804 µg/kg bw/day; the metabolic elimination of NMP is not included in the spreadsheet, which is one factor that could relate to this difference.

The case study provides information on the use pattern of a non-aqueous solvent being used in a consumer setting. Without information about tonnage and exposure from an in-depth study, it is difficult to develop a reliable estimate of exposure.

4.3.3 Hexamethyldisiloxane

4.3.3.1 Summary

Hexamethyldisiloxane (HMDS) has been studied widely, as reported in public sources, although no higher tier study of any type was found. This case study includes personal care and sealant examples.

Information sources about HMDS that have been used are:

- The OECD Screening Initial Assessment Profile (SIAP) from 2017[24] (based on much older research) which gives information about tonnages on the market and the consumer applications.

[24] https://one.oecd.org/document/ENV/JM/MONO(2016)39/en/pdf

- An Australian government review (NICNAS, 2019); this is the most up-to-date review of the toxicology, but there is no exposure information.
- A Canadian government review (Environment Canada, 2019), which gives useful exposure data.
- Nordic SPIN database, which shows approx. 70 tpa largely in personal care.

Therefore, the HMDS example is useful given that it shows how difficult cross-sector assessments can be when use information is limited.

The spreadsheet tool has been used to model the Canadian human exposure data but with EU tonnages.

4.3.3.2 Key data

The OECD SIAP referred to above shows 1000 tpa in the EU for personal care formulation. There are also potential consumer uses of sealants.

The Health Canada report referred to above gives indoor measured concentrations as 0.02 to 0.67 µg/m^3. Uses in the Health Canada report include several product types. Estimated potential exposures to HMDS (page 16 of the Health Canada report) are shown in Table 9:

Table 9. Exposure information for HMDS from Health Canada. (Based on "Environment Canada", 2019) Adapted from: https://www.canada.ca/en/environment-climate-change/services/evaluating-existing-substances/draft-screening-assessment-siloxanes-group.html **Product scenario**	**Maximum concentration**	**Dermal per event systemic exposure (mg/kg bw)**	**Inhalation mean event concentration (mg/m³)**	**Dermal daily systemic exposure (mg/kg/d)**
Body lotion	3%	0.00019		0.00019
Aerosol bandage adhesive	67%	0.0016	0.73	
Facial makeup	45%	0.00069		0.00085
Hair styling product	100%	0.00054		
Nail polish drying drops	100%		13.3	

4.3.3.3 Spreadsheet tool applied to HMDS

An in-depth study of the cyclic siloxane decamethylcyclopentasiloxane (D5) has been carried out (Dudzina *et al*., 2015). That study was used to calibrate the spreadsheet tool for D5 in respect of daily

use levels of product and exposures (dermal and inhalation of indoor air), then the same approach was applied to HMDS. The D5 work is not reported here.
The spreadsheet for HMDS covers 11 of the personal care uses that are standard in the SCCS guidance (SCCS, 2022) and aims to give daily use of the formulated product in alignment with SCCS, but taking into account the tonnage on the market. It has, however, not been possible to rationalise the information from Health Canada.

The personal care uses could have been modelled using either PACEM or the Creme Care model for example, but the purpose here was to show a simple method (even though less detailed). The presence of HMDS in sealants is set up in the spreadsheet to give a realistic daily exposure. Little is known about the miscellaneous consumer uses that would be covered by REACH. The information entered is shown in Table 10.

Table 10. Spreadsheet tool inputs and results for HMDS

		PC applications											Impurity in sealant	Misc consumer uses		MVE total from EUSES	Overall exposure total
		1	2	3	4	5	6	7	8	9	10	11	12	13			
	Unit	Shower gel	Shampoo	Hair styling	Body lotion	Face cream	Hand cream	Foundation	Face	Deodorant stick	Deodorant spray	Hair conditioner			Consumer uses total		Use + MVE
Tonnes in EU for use	t/y	70	70	100	100	20	20	5	5	5	5	10	1	500	**911**		
Regional tonnage fraction	t/y	7	7	10	10	2	2	0.5	0.5	0.5	0.5	1	0.1	50			
Local amount fraction	kg/y	14	14	20	20	4	4	1	1	1	1	2	0.2	100			
Overall mass per year average per person	g/hd/y	1.4	1.4	2	2	0.4	0.4	0.1	0.1	0.1	0.1	0.2	0.02	10			
Fraction of population who are users		0.02	0.005	0.005	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.02	0.5			
Frequency per day of use	/d	1.43	1	1.14	2.28	2.14	2	1	2	2	2	1	0.1	1			
Fraction of substance in formulation		0.01	0.15	0.5	0.9	0.9	0.9	0.4	0.5	0.5	0.2	0.2					
mass per user person per year	g/hd/y	70.00	280.00	400.00	2000.00	400.00	400.00	100.00	100.00	100.00	100.00	200.00	1.00	20.00			
mass per user per event on a day	g/hd	1.34E-01	7.67E-01	9.61E-01	2.40E+00	5.12E-01	5.48E-01	2.74E-01	1.37E-01	1.37E-01	1.37E-01	5.48E-01	2.74E-02	5.48E-02			
amount of formulated product per event per day	g	13.41	5.11	1.92	2.67	0.57	0.61	0.68	0.27	0.27	0.68	2.74					
mass per person per day average	g/hd/d	0.192	0.767	1.096	5.479	1.096	1.096	0.274	0.274	0.274	0.274	0.548	0.003	0.055			
Fraction to air during application		0.01	0.01	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.8			
Fraction to waste water		0.95	0.95	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05			

		PC applications											Impurity in sealant	Misc consumer uses		MVE total from EUSES	Overall exposure total
		1	2	3	4	5	6	7	8	9	10	11	12	13			
	Unit	Shower gel	Sham poo	Hair styling	Body lotion	Face cream	Hand cream	Foundation	Face	Deodorant stick	Deodorant spray	Hair conditioner			Consumer uses total		Use + MVE
averaged over time																	
worst case fraction to skin corrected for volatility		0.04	0.04	0.35	0.35	0.35	0.35	0.35	0.35	0.35	0.35	0.35	0.35	0.15			
external exposure of skin	mg/kg/d	1.3E-01	5.1E-01	6.4E+00	3.2E+01	6.4E+00	6.4E+00	1.6E+00	1.6E+00	1.6E+00	1.6E+00	3.2E+00	1.6E-02	1.4E-01	6.15E+01		
fraction absorbed from skin		0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01			
internal average	mg/kg/d	1.3E-03	5.1E-03	6.4E-02	3.2E-01	6.4E-02	6.4E-02	1.6E-02	1.6E-02	1.6E-02	1.6E-02	3.2E-02	1.6E-04	1.4E-03	6.15E-01	1.98E-03	**6.17E-01**
Sum of fractions		1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000			
indoor air mass/event	mg/d	1.92E+00	7.67E+00	6.58E+02	3.29E+03	6.58E+02	6.58E+02	1.64E+02	1.64E+02	1.64E+02	1.64E+02	3.29E+02	1.64E+00	4.38E+01			
air exchange per day	/d																
room volume	m^3																
indoor air concentration during event	mg/m^3	2.33E-03	1.33E-02	1.00E+00	2.50E+00	5.33E-01	5.71E-01	2.85E-01	1.43E-01	1.43E-01	1.43E-01	5.71E-01	2.85E-02	7.61E-02	**6.01E+00**	2.66E-06	**6.01E+00**
Internal exposure via air	mg/kg/d	6.71E-04	3.84E-03	2.88E-01	7.21E-01	1.54E-01	1.64E-01	8.22E-02	4.11E-02	4.11E-02	4.11E-02	1.64E-01	8.22E-03	2.19E-02	**1.73E+00**	7.66E-07	**1.73E+00**
																	2.35E+00
fraction to waste water		0.950	0.950	0.050	0.050	0.050	0.050	0.050	0.050	0.050	0.050	0.050	0.050	0.050			
to regional release to air	kg/d	1	1	26	26	5	5	1	1	1	1	3	0	130	2.03E+02		
to regional release to waste water	kg/d	18	18	1	1	0	0	0	0	0	0	0	0	7	4.70E+01		
to continental release to air	kg/d														1.82E+03		

		PC applications											Impurity in sealant	Misc consumer uses		MVE total from EUSES	Overall exposure total
		1	2	3	4	5	6	7	8	9	10	11	12	13			
	Unit	Shower gel	Shampoo	Hair styling	Body lotion	Face cream	Hand cream	Foundation	Face	Deodorant stick	Deodorant spray	Hair conditioner			Consumer uses total		Use + MVE
to continental release to waste water	kg/d														4.23E+02		

4.3.3.4 Findings

Points of note from this case study are:

- To achieve a daily use level consistent with SCCS norms for personal care (PC) uses, the user factor (frequency and fraction of population) is low (typically 0.005). This low value arises because the products are specialised, not widely used.
- The total modelled tonnage is 1001 tpa, but that cannot be corroborated against actual values.
- For the use of sealant, a frequency of 0.1 implies use every 10 days; this is high but could apply to a hobbyist.

4.3.3.5 Useful learning points

The SCCS guidance (SCCS, 2022) provides authoritative insights into the pattern of use of consumer personal care products.

The spreadsheet tool was useful in bringing together a variety of exposure routes including cross-sector.

It is clear that an expert tool such as PACEM or the Creme Care model would be more useful than the simple spreadsheet for the cosmetics uses, but the spreadsheet approach easily allows other applications to be included.

4.4 Preservatives

This section examines two higher tier studies to find informative methods for consumer aggregate exposure assessment that could apply to a cross-sector study.

The term “preservatives” refers to the functional name for a wide variety of compounds that help to slow down or prevent the growth of microorganisms, such as bacteria, yeasts and fungi, in a wide range of products including foods, medicines, and personal care products. Also, products like paints, glues, household cleaning products and toys can contain preservatives, especially water-based products. As these preservatives limit the growth of microorganisms, they help to prevent microbial contaminations that may cause irritation or infections. In addition, antioxidant preservatives can help in keeping personal care products from spoiling by suppressing reactions that can occur when ingredients in them react with oxygen. As such, preservatives play an important role in many products that are used daily by prolonging the shelf life of the products.

4.4.1 Methylisothiazolinone

This is a longer discussion than the other case studies due to the amount of information in the primary source. The following sections from 4.4.1.1 to 4.4.1.3 describe a higher tier study that is already available in the literature, comments on this approach can be found in section 4.4.1.4, while a simpler mid-tier approach is attempted in 4.4.1.5 and its conclusion can be found in 4.4.1.6.

4.4.1.1 Approach

This section describes how to perform a cross-sector human aggregate exposure for preservatives with methylisothiazolinone (MI) as an example preservative. MI is frequently used in personal care products like sunscreen and shampoo, as well as cleaning products, paint and aqueous toys like clay and toy slime. They ensure that a product does not spoil and that its shelf-life is prolonged.

The main source considered in this case study is the recent RIVM report (Affourtit *et al*., 2022).

Extensive work to determine the aggregate exposure of isothiazolinones (IT) used as preservatives and analysis of cross-sector aggregate exposure of IT including MI are described in the RIVM report. This investigation by RIVM was carried out by estimation of the extent to which various product groups contributed to the total exposure, as people can be exposed to IT via various different products every day. The total exposure in both adults and children was investigated for three widely used substances: methylisothiazolinone, chloromethylisothiazolinone (CMI) and benzisothiazolinone (BIT). The results of this investigation indicated that, in some cases, the total exposure could be higher than the safe amount. More research is needed to know whether this is really the case. For example, for many products the exact amount of IT they contain is unknown. In addition, it is not always possible to know how many people use such products and how often.

The Netherlands Food and Consumer Product Safety Authority (NVWA) has measured the amount of IT in hundreds of different products (further details are in the next section). RIVM used these measurements to calculate the exposure using the PACEM (the Probabilistic Aggregate Consumer Exposure Model, developed at RIVM) and ConsExpo computer models. ConsExpo can provide a first estimation of the exposure that occurs when a person uses a single product. With PACEM, exposure to multiple products can be calculated. Furthermore, PACEM gives a more realistic estimation of the exposure, because it uses concrete data about the frequency of use. PACEM is a person-oriented model in which the exposure distribution of a large population is simulated based on product use surveys; aggregate exposure can be calculated by application of realistic use data of products. In addition, the model calculates with distributions instead of one (worst-case) value for the amount of product used, thus accounting for variations in product use by a person. Addition of the different exposures in this way, to obtain an aggregate exposure distribution in the population, gives a more realistic picture than the worst-case assumption that the entire population uses all products every day. Moreover, this method can be used to determine the relative contributions of individual product groups to the aggregate exposure of a specific substance in a population.

As IT and MI are often used in various products, estimated consumer exposure to IT from single products is very likely to be an underestimation of the actual exposure. To determine whether there is a health risk from exposure to IT in various consumer products, an aggregate exposure is needed, i.e. the summed exposure from all IT-containing products. The aim of the research by RIVM (Affourtit *et al*., 2022) was to get more insight in the aggregate dermal exposure of consumers to IT, and the contribution of the distinct products to this exposure, specifically personal care products (PCP), household cleaning products (HCP), (wall) paint, toys and glue.

Consumer exposure has been typically calculated by RIVM per single product using ConsExpo. ConsExpo also allows the aggregation of exposure to a single substance present in multiple products. However, this aggregation can only be performed in a conservative manner without taking differences in use patterns within a population into account. PACEM was used by RIVM to estimate aggregate consumer exposure to IT in personal care products (PCP) and home care products (HCP) in an adult population. Cosmetics and REACH regulations and Toy Safety Directive 2009/48/EC would be the regulatory context. However, for several product groups, sub-populations (children) and exposure scenarios, product use surveys are not available or not implemented in PACEM. For these cases, ConsExpo was used to estimate the exposure to IT. These cases included exposure to paint (adults) and laundry products (adults). Also, exposure of children to IT in PCP was estimated with ConsExpo. Children are exposed to IT from washed fabrics and cleaned floors. This post-application exposure scenario was calculated with ConsExpo. For the estimation of exposure, measurement data from the Netherlands Food and Consumer Product Safety Authority (NVWA) of IT in various consumer products were used. These data were complemented with relevant data from available reports and literature on IT in consumer products. To investigate the contribution of various sources to the IT exposure, comparison of the dermal load associated with each source needs to be performed. However, the results of PACEM and ConsExpo differ in their level of conservatism and may not be directly comparable. Also, comparison of exposure estimates with ConsExpo should be performed with some caution due to different levels of uncertainty in each exposure scenario. Several factors within the exposure estimation affect the dermal exposure estimation, including assumptions regarding the use frequency of products and the amount of product applied, the assumed concentration of IT in products, the occurrence of IT being present in products of a particular product group, and the estimation of the fraction of product that remains on the skin after application. Keeping these considerations in mind, the aggregate exposure of adults to IT, expressed as MI-equivalents, seems to be primarily driven by either PCP or HCP. Regarding single products, the estimated dermal loads demonstrate that glues and wall paints may be major contributors to the IT exposure for adults. The IT exposure in children via shampoo was approximately two orders of magnitude higher than that via shower gel/foam/scrub, and comparable to that via putty and toy slime. The estimated post-application exposures from laundry product and floor cleaner are multiple orders of magnitude lower than the exposure to shampoo, putty and toy slime.

RIVM recommended to further investigate the exposure to IT, since the aggregate dermal loads were frequently in the same order of magnitude as the corresponding Acceptable Exposure Levels (AEL). AEL is calculated from the No Expected Sensitisation Induction Level (NESIL) and the applied Sensitisation assessment factors SAFs (i.e. AEL = NESIL/Total SAFs) (Api *et al*., 2020). AEL is determined by dividing the Weight of Evidence (WoE) NESIL by product Sensitisation Assessment Factors (SAF)

(Api *et al*., 2008). AEL is expressed in terms of dose/unit area/day. The definition of this AEL allows identification of exposures to ingredients that are acceptable (below the AEL or unacceptable above the AEL).

4.4.1.2 Selection of relevant products by RIVM (Affourtit *et al*.) for Aggregate exposure assessment of IT containing products including MI

Information on IT concentrations in consumer products was obtained from measurements and published literature. Product data obtained through the below mentioned sources were only included in the aggregate exposure analyses if data were available on the concentration of at least one of the three IT (MI, CMI or BIT). In addition, PCP concentration data were only included in the analyses if the measurements took place after January 1st 2018. This is because a new restrictive measure on MI and CMI concentrations was enforced at that time. Since then, the use of MI in PCP is further limited to a maximum of 15 ppm in rinse-off products and is banned from leave-on PCP. Finally, due to differences in regulations between continents, concentration data for PCP, HCP and toys were only included if the measured product was produced in Europe.

Specifically, the following data sources were screened:

Measurement data (NVWA, Personal communication, 2021 – as reported in Affourtit *et al*., 2022):

- PCP, HCP, paints and toys (n=808)
- Slime and putty (n=58)
- PCP (n=414)
- PCP (n=65)

Data from literature:

- HCP (n=34) (Marrero-Alemán *et al*., 2020)
- HCP (n=72) (Garcia-Hidalgo *et al*., 2017)
- HCP (n=7) (Ezendam *et al*., 2018)
- Paint (n=61) (Thomsen *et al*., 2018)
- Paint (n=35) (Schwensen *et al*., 2015)
- Paint (n=63) (Goodier *et al*., 2018)
- Glue (n=37) (Goodier *et al*., 2019)

Since the main goal of the RIVM research was to determine the relative contributions of individual product groups to the aggregate exposure to IT using PACEM, products were categorised into groups according to the product types supported by PACEM.

4.4.1.3 Conclusions relating to exposure extracted from the RIVM report

- The estimated dermal loads associated with exposure to PCP and HCP were similar[25].
- Glues, wall paints and laundry detergent are potentially relevant contributors to the total IT exposure of adults, both when dose addition of different IT applies, and when treating exposure to each IT separately.
- Aqueous toys, i.e. toy-slime and putty, cannot be overlooked as contributors to the dermal load of IT in children, as the dermal load associated with exposure to aqueous toys was similar to that of shampoo.
- In general, the dermal load associated with exposure to CMI is lower than those associated with exposures to MI and BIT.

4.4.1.4 Recommendations from the RIVM report relevant to this report

Based on the results and uncertainties identified by RIVM and the conclusions formulated in the previous section, the following recommendations were made:

- To reduce the uncertainties regarding the estimated dermal loads, additional, representative data needs to be acquired concerning both IT concentrations and product use patterns of consumer products. As glue and wall paints have been identified as potentially relevant contributors to the IT exposure of adults, IT concentrations measurement in various types of glue and wall paints would help to further refine the calculations for adults. Moreover, acquiring and incorporating product use patterns of glue and wall paint in PACEM would enable to include these product groups in the aggregate exposure estimations. This would give a more complete view on the total exposure of adults to IT.
- The results presented in the RIVM report demonstrate that aqueous children's toys may be relevant contributors to the dermal load of IT in children. It was therefore recommended to verify the quality of the IT concentration data in putty and slime and to further refine the exposure scenarios regarding the use of children's toys. In addition, it is recommended to conduct surveys to provide a better insight into the use patterns of children's toys. If the

[25] The dermal load was estimated: *exposure estimations for adults (including non-consumers) expressed as dermal load (µg/cm^2) via various sources; product groups in case calculated with PACEM and single products in case calculated with ConsExpo. The dermal load derived with PACEM is based on survey information of use amount, use frequency and body weight, and a lognormal distribution for weight fraction. For other inputs (e.g. retention factors) point values are applied. The dermal load derived with PACEM represents the dermal load of the general population including non-consumers.*

estimated dermal loads remain high after refinement of the exposure scenarios and elaboration of the concentration data in these toy products, risk management measures such as IT restrictions in putty and toy slime may need to be considered. Another option would be to reconsider the classification limits of the three categories of toy materials (Toy Safety Directive 2009/48/EC).

- In the RIVM research, aggregation of IT exposure was performed over a timeframe of 24 hours. However, there is no evidence that this period is the most appropriate for skin sensitisation after exposure to various consumer products. Further research on the aggregation time period relevant to skin sensitisation is needed in order to further reduce the uncertainty of the estimated dermal loads used in the quantitative risk assessment.

- Since the estimated dermal loads aggregated over PCP and HCP were in the same order of magnitude as the corresponding AELs for all three IT, further research may be necessary to verify the results. In particular, since HCP likely contributes more to the skin sensitisation effect, it is recommended to focus on further refining and improving the exposure estimates for HCP. In addition, one could subsequently investigate the impact of potential IT restrictions on the dermal load by simulating the dermal loads for various HCP in which IT concentrations above a certain limit are excluded. Another option to investigate true correlation would be to overlay usage with epidemiology reports of skin sensitisation (or other health effects) in the general public.

- The RIVM research estimated the aggregate dermal loads for IT following exposure to various product groups. Product groups were included in case measured IT concentration data were available. However, due to the lack of IT concentration data, various product groups had to be excluded. Additional IT concentration data are necessary for products groups that may potentially contain IT. Such products groups are, for instance, medicines (e.g. ointments and creams) and animal care products (e.g. shampoos, perfumes, detanglers and grooming wipes). Similarly, product use patterns of these product groups should be investigated to allow incorporation of additional product groups in the aggregate exposure estimates performed in PACEM. In the interpretation of the comparison between dermal load values and AELs for the different IT, specific attention should be given to the applied safety assessment factors (SAF). Particularly, the matrix SAF is important in the current research. This SAF is (amongst others) used to account for the presence of irritating substances in the product that may increase the sensitising potency of IT in the product. Although in the RIVM research, not all product groups are expected to contain irritating substances, a matrix SAF of 3 was used for all product groups. A possible way of refining this matrix SAF would be to define and apply a matrix SAF per product group. For example, Ezendam *et al*. (2018) defined a matrix SAF of 3 for HCP, and a matrix SAF of 1 for PCP.

Therefore, even a very detailed study was not able to address all matters definitively. The RIVM study certainly helps to set out the issues that need to be addressed in other cross-sector studies and could make understanding of other preservatives easier to achieve.

4.4.1.5 Findings using a simplified spreadsheet method

An attempt was made first by the Task Force to calculate the aggregate exposure of MI from different products using PACEM. However, in the absence of realistic exposure scenarios and values, a conservative estimate based on the limits of MI in personal care and home care products was used.

The purpose here is to identify whether very simple modelling has value. This approach starts from a tonnage on the market. The Task Force evaluated the literature available for MI and exposure models aggregate exposure to check if adequate exposure data are available to determine the mid-tier aggregate exposure from all the products ranging from personal care, home care, paints, glues, biocides, etc. The TF also examined the availability of tonnage data; however, it was found that tonnage data are not available for MI in the EU.

Tonnage data available from the SPIN database were considered in the home cleaning air freshener category (which was not named specifically in the RIVM report (Affourtit *et al*., 2022). Since detailed tonnage data in SPIN are not available for other categories and cosmetics, full assessment could not be done using the spreadsheet tool.

The calculation by the spreadsheet method is described below for the use where tonnage data are available, i.e., home cleaning air freshener (see Table 11). Average MI tonnage per year in the Nordic region is 1.8 tonnes (estimated 18 tonnes in the EU – not proven). Ideally SPIN would have contained cross-sector applications, but these could not be identified.

Table 11. Spreadsheet tool inputs and results for MI as an air freshener

					Air freshener (SPIN)		**MVE total from EUSES**	**Overall exposure total**	**Internal concentration total**
			Parameter	**Unit**		**Consumer uses total**		**Use + MVE**	
Dermal		Tonnes in EU for use		t/y	18	18			
	default	Regional tonnage fraction	0.1	t/y	1.8				
	default	Local amount fraction	0.002	kg/y	3.6				
	number in region	Overall mass per year average per person	10000	g/hd/y	0.36				
		Fraction of population who are users			1				
		Frequency per day of use		/d	1				
		Fraction of substance in formulation			0.0035				
		mass per user person per year		g/hd/y	0.36				
		mass per user per event on a day		g/hd	9.86E-04				
		amount of formulated product		g	0.28				
	days per year	mass per person per day average	365	g/hd/d	0.001				
		Fraction to air during application			0.001				
		Fraction to waste water averaged over time			0.583				

					Air freshener (SPIN)		MVE total from EUSES	Overall exposure total	Internal concentration total
			Parameter	Unit		Consumer uses total		Use + MVE	
		worst case fraction to skin corrected for volatility			0.999				
	Body weight	external exposure of skin	60 kg/hd	mg/kg/d	1.6E-02	1.64E-02			
		fraction absorbed from skin			0.416				
		internal average		mg/kg/d	6.8E-03	6.83E-03	3.02E-06	6.83E-03	(regional total daily intake + near field dermal uptake)
		Sum of fractions			1.000				
Inhalation		indoor air mass/event		mg/d	9.86E-04				
		air exchange per day	24	/d					
		room volume	24	m^3					
		indoor air concentration during event		mg/m^3	1.71E-06	1.71E-06	8.64E-09	1.72E-06	(regional PECair + near field))
	Factor	Internal exposure via air	2.88E-01	mg/kg/d	4.93E-07	4.93E-07	2.49E-09	4.96E-07	(inhalation MVE + near field inhalation uptake)
Total								6.84E-03	all routes
For MVE		fraction to waste water			0.583				
	Contributions	to regional release to air		kg/d	2	2.06E+00			
		to regional release to waste water		kg/d	3	2.88E+00			
		to continental release to air				1.85E+01			
		to continental release to waste water				2.59E+01			

The spreadsheet shows dermal exposure to be higher than inhalation exposure. However, no realistic comparison with the other work is possible.

4.4.1.6 Useful learning points

Based on the overall analysis, literature review and scientific analysis, the Task Force concluded that more information is needed to determine the exposure of MI in different products including the concentration, frequency of application, uncertainty factors, etc., in order to determine cross-sector aggregate exposure, even at a screening level.

Even a detailed study of preservatives based on many products (Affourtit *et al*., 2022) could not reach definitive conclusions, which illustrates that assessment of aggregate exposure is a complex challenge.

4.4.2 Parabens

4.4.2.1 Introduction

This case study moves from annual tonnage to daily personal exposure to the preservative methyl paraben using the spreadsheet tool.

The paraben substances have antibacterial and antioxidant properties, typically used in pharmaceutical and personal care products. The regulatory status of the various substances is not discussed here.

4.4.2.2 Sources

This case study uses three references: two main sources for information, and a third source for review purposes. These were:

1. Danish Ministry of the Environment. 2013. Survey of parabens. Part of the LOUS-review. Environmental Project No. 1474, Copenhagen K, Denmark.
2. Cowan-Ellsberry CE and Robison SH. 2009. Refining Aggregate Exposure: Example using Parabens. *Regul. Toxicol. Pharmacol.* 55(3):321-329.
3. Csiszar SA, Ernstoff AS, Fantke P and Jolliet O. 2016. Stochastic modeling of near-field exposure to parabens in personal care products. *J Expo Sci Environ Epidemiol*. 27(2):152-159.

Aylward *et al*. (2020) made an in-depth study of the parabens in respect of high tier comparison of exposure using SCCS methods, ConsExpo, RAIDAR-ICE, SHEDS (Stochastic Human Exposure and Dose Simulation Model) and Creme Care. It is suggested therein that high tier methods and multiple models may be needed for an in-depth understanding.

4.4.2.3 Overview of the method

Source 1 was used to gain an approximate idea of the tonnage on the market for methyl and propyl paraben, although only the methyl substance is discussed here; other parabens are used at much lower levels. Source 1 also gives an indication of use pattern which is consistent with that from source 2. Source 2 provides information from a survey conducted in the US[26]. The steps used in source 2 were the identification of:

1. Products on the market
2. Amounts of methyl paraben (MP) in products
3. Fraction of those surveyed using particular product types.
4. Prediction of exposures derived from survey data.
5. Dermal penetration amount applied.
6. How predictions compare to biomonitoring data.
7. Calculated product use levels derived from the above.

The spreadsheet calculations performed in this case study have a similar scope but follow these steps:

1. Estimate tonnage in the EU and split between uses, if possible.
2. Estimate fraction of the population using products containing MP.
3. Calculate internal loading from dermal and inhalation routes.

Source 2 derives daily use predictions from a survey, whereas the spreadsheet tool calculates those from a sufficiently realistic understanding of use pattern based on expert knowledge. Clearly source 2 represents a higher tier method to aggregate exposure, and the spreadsheet tool is a Tier 1 screening exercise.

It is not the purpose of this report to describe the results in source 2 in detail, but rather to explain how the spreadsheet tool was applied to obtain results. There are uncertainties in the various adjustable parameters.

[26] Around 3300 female employees of P&G provided detailed information about their use of personal care products.

4.4.2.4 Input data

Source 1 indicates a total tonnage of around 60 tpa in the Nordic countries in the years up to the date of the report (2013); these data are from the SPIN database. However, 30 tpa were assigned to biocides, even though such applications are not authorised under the Biocidal Products Regulation. Source 1 also shows around 4 tpa being used in household cleaning products. Source 2 does not describe such uses. Source 1 also indicates that uses in food are now minimal, which is consistent with source 2. Previous use in pharmaceutical products is also discounted. Therefore, it is estimated by the Task Force from source 1 that the tonnage of MP in the EU was around 300 tpa for cosmetics and 40 tpa in cleaning products. Other uses mentioned in source 1 are not considered further. The significance of the uncertainties in the methods is discussed later in this report.

Source 2 indicates the main personal care use areas of MP to be:

1. Oral hygiene
2. Eye products, such as mascara
3. Leave-on lotions and creams
4. Rinse-off products, such as shampoos and conditioners.

There is no external validation of the use patterns available other than the survey reported in detail in source 2. For the spreadsheet tool, the options considered were to simply have one use only, in leave-on cosmetics, or give an estimated breakdown of tonnage to fit with the source 2 results. For purposes of illustration, the second approach is more helpful and therefore was used.

Other input parameters are described in the next section.

4.4.2.5 Model and results

The inputs to, and outputs from, the spreadsheet are shown in Table 12 below, with comments.

Table 12. Spreadsheet tool inputs and results for methyl paraben

		Leave on cosmetics	Wash off cosmetics	Oral hygiene	Eye products	Cleaning products	Comment
Tonnes in EU for use	t/y	230	10	50	10	40	The split of the total are estimates based on the proportions of use described in source 2
Regional tonnage	t/y	23	1	5	1	4	Default
Local amount	kg/y	46	2	10	2	8	Default
Overall mass per year average	g/hd/y	4.6	0.2	1	0.2	0.8	Amount if all of the population is exposed equally
User factor		0.25	0.25	0.25	0.25	0.1	Fraction of the population actually exposed: estimate based on source 2
Frequency	/d	1	1	2	1	0.1	Assumption
Fraction in formulation		0.0035	0.002	0.002	0.003	0.002	From source 2
mass per user person per year	g/hd/y	18.40	0.8	4	0.8	8	
mass per person per event	g/hd	5.04E-02	2.19E-03	5.48E-03	2.19E-03	2.19E-01	
amount of product	g	14.40	1.10	2.74	0.73	109.59	The amount of formulated product is a useful check with actual practice and agrees satisfactorily with source 2 for the cosmetics uses.
mass per person per day average	g/hd/d	0.050	0.002	0.011	0.002	0.022	
Fraction to air during application		0.01	0	0	0.01	0	Assumed to be relatively involatile.
Fraction to waste water during application		0	0.9	0.9	0	0.95	Assumptions
fraction to skin corrected for volatility and amount to water		0.99	0.1	0.1	1	0.05	
external exposure of skin	mg/kg /d	8.3E-01	3.7E-03	1.8E-02	3.7E-02	1.8E-02	For uses 1-4 these results are in good agreement with source 2.
fraction absorbed from skin		0.8	0.8	0.8	0.8	0.8	From source 2
internal average	mg/kg /d	6.7E-01	2.9E-03	1.5E-02	2.9E-02	1.5E-02	

The total aggregated exposure is 0.92 mg/kg/d external and 0.73 mg/kg/d internal. Source 2 reports a total aggregated exposure 'of 1.03 mg/kg/d external. Whilst this appears to be very satisfactory as a fitting exercise, there are assumptions and also the EU use pattern could be different to that found amongst US P&G employees. In reality, agreement within an order of magnitude is all that could be realistically expected.

It is interesting to note that source 2 indicates that over 95% of those surveyed used a product containing MP. From the model assumptions above as 'non-users' we have 0.75 x 0.75 x 0.75 x 0.75 = 32%, suggesting that there is scope for refinement.

Source 2 does not compare the derived amount of product per day with the SCCS guidance, but they appear to be very consistent with each other.

The exposures calculated by the spreadsheet tool (top down) and Source 2 (bottom up) represent reasonable maximum intakes far below the exposures that would come from screening methods. However, source 3 usefully shows (using probabilistic methods) that while the total of around 1 mg/kg/d is reasonable, the median is below that because a substantial proportion of the population do not use all product types. Source 3 is a higher tier study.

4.4.2.6 Uncertainties and their significance

In the table below the key inputs used in the spreadsheet tool are discussed.

Table 13. Spreadsheet tool inputs for methyl paraben, and comments on uncertainties and their significance

	Key value	Unit	Comment
Tonnes in EU for use	340	t/y	The total tonnage is estimated as a factor on the SPIN tonnage and could be +/- a factor of 2
Regional tonnage	Regional fraction 0.1		These are EU defaults from REACH guidance which is found to be reliable for substances with widespread use; taken together, for a specific case could be +/- a factor of 2
Local amount	Local fraction 0.002		
User factor			These factors may not be applicable to EU; uncertainty cannot be easily estimated.
Frequency		/d	Frequency of use by an individual who has purchased a product are unlikely to be significant assumptions.
Fraction in formulation			These factors may not be applicable to EU; uncertainty cannot be easily estimated.
Fraction to air during application			The values used are subject to unknown uncertainty but could be estimated by use of models if time permitted.

4.4.2.7 Conclusions

The spreadsheet tool moves from total tonnage per use down to an exposure per day of the users. The values have been in part derived from parameters described in source 2 so it is expected that there should be some consistency with it.

The spreadsheet tool may be useful for other substances in preservative applications, since the methyl paraben case study gives a good insight into use patterns, user factors, etc.

The spreadsheet is seen to be a useful screening tool, although it is reliant on tonnage on the market per application, and the assumptions could be important.

Even for a well-studied substance such as MI, the information available to estimate consumer exposure from total tonnage is not ideal, although results were obtained. However, the estimates derived are relatively efficient in comparison to a more comprehensive, higher-tier study.

4.5 General conclusions from the case studies

Although not reported in detail, the Task Force case studies all showed that exposure of humans via the environment was far lower than from direct exposures.

4.5.1 Concerns about research into uses and potential for exposure

The brief case studies set out in Section 4 demonstrate the same problem encountered by many risk assessors in the absence of representative exposure measurement reports, which is the lack of readily available information about uses of substances and the quantities on the market, at a level appropriate to cross-sector assessment. There are some data available, but the work has shown that these are often incomplete and out of date. Rather than describing those issues for each case study each time, the following general findings are reported here.

Total tonnage on the market is important for several reasons. Firstly, it is necessary to assess the potential for human exposure via the environment realistically, so that the far-field (i.e. environmental background) and near-field (i.e. direct and indirect use) exposures can be compared and aggregated if necessary. It is relatively easy to establish whether far-field exposure is important by considering roughly the relative magnitude of the far-field exposures compared to the near-field exposures. Also, total tonnage combined with per capita use rate gives a crude indication of the number of people who could be exposed. However, it does not consider the variability of exposure across a population or where the use rate may be concentrated in an industry or population.

Only stakeholders with robust use data could perform cross-sector assessments without major uncertainties. Regulators are part of the target audience for this work, but even regulatory submissions do not always give much information, depending on the regulation being adhered to. One necessary advance in the future would

be to share anonymised information across industry for use in exposure assessment. This is already occurring in the cosmetic and personal care sector and in the fragrance industry among groups including Cosmetics Europe and the Research Institute of Fragrance Materials (RIFM). Such work involves a well-co-ordinated, collaborative effort.

It should be noted that several well-researched sources give indications of single product exposures. These include:

1. OECD exposure scenario documents.[27]
2. AISE REACT tool.
3. ECETOC TRA.
4. SCCS guidance.
5. The RIVM ConsExpo software and factsheets.[28]
6. RIVM PACEM software.
7. Creme Global software.
8. Previous national, European and international substance reviews.[29]

Different regulatory regimes require a variety of tonnage data. In the REACH Regulation as it stands, it is not possible even for regulators to know the amounts going into each use unless all registrants have submitted a combined exposure assessment.

The Nordic SPIN database gives useful information about the tonnages of substances which have consumer applications (pure or formulated) in Sweden, Norway, Denmark, and Finland. These countries tend to reflect at around 10% of the EU levels, based on experience of the authors of this report from previous work, and can be extrapolated to EU levels to some extent. Its reliability is uncertain.

Therefore, stakeholders with an interest in cross-sector assessments will encounter the same problem. One solution would be for industry to confidentially share tonnage data. In the absence of this, the case studies have explored what other options are available.

The difficulty of access to tonnage, and also habits and practices, data certainly makes reliable cross-sector aggregate assessment very challenging.

[27] Although these focus on the environment they do give very useful information about use pattern.

[28] ConsExpo and its associated factsheets contains more information than simpler screening tools.

[29] These can provide a calibration of methodologies.

4.5.2 Limitations

Originally, a wide spectrum of consumer exposure sources was considered for investigation of exposure refinement potential (per source/product) and review of advanced aggregation strategies across exposure sources (e.g. food contact material, household and DIY products, biocidal products). However, as the project progressed, it became evident that for some end-uses and product types, no or very few exposure data were available, hampering reliable analysis and solid conclusions. It is clear that availability of data about use levels, exposure and numbers of consumers exposed is very much lacking for some consumer exposures.

4.5.3 Positive outcomes

Prior art from relevant higher tier work can provide a template for a cross-sector assessment. It is possible to emulate the results of higher tier studies using an intermediate approach that is not reliant on screening.

Several of the studies show that the tonnage produced is only compatible with typical daily use levels if the users of the substance represent only a fraction of the whole population: if the tonnage was spread over the whole population then the use levels per person would be too low relative to known norms.

The intermediate level between screening and higher tier assessments cannot easily be defined because the level of information available about use rates varies for the different applications; however, experienced risk assessors may be able to establish conclusions at a level appropriate to the substance and its use pattern.

5. GENERAL METHOD FOR CROSS-SECTOR AGGREGATE EXPOSURE ASSESSMENT

This section sets out basic advice and the principles to adopt in cross-sector aggregate exposure assessment for consumers. As shown by the case studies (Section 4), there is no definitive systematic methodology as yet due to the lack of availability of exposure data (e.g. tonnage, use patterns, substance concentration data, etc.) for many uses and the absence of specific regulatory imperatives in many sectors, which has led to a lack of published cross-sector assessments. That is not to say that data cannot be generated or shared, and defined methods cannot be developed; it is simply that they have not emerged during the research for this report. However, section 5.1 summarises the preparatory work that is necessary, and section 5.2 gives some ideas to apply.

The approaches needed are applicable to many types of substance and exposures. Because use patterns are individual to consumer products/exposure sources, it cannot presently be envisaged that relevant stakeholders could perform cross-sector assessments for many substances at once in an automated way. This might be possible once data are generated on exposure inputs, such as consumer habits and practices together with information on substance concentration and occurrence.

5.1 Planning and information needs

This report has dealt with hypothetical cases where summed screening level exposures would give over-estimated exposures and simple refinements are hard to achieve[30]. The case studies have shown that a high priority must be given to obtaining data on the amount of substance (and the amount of formulated product) in use for each application. This was envisaged even in REACH guidance; it is an essential link between simply listing uses and the estimation of the true exposure estimates. It is needed because otherwise the only option is an in-depth higher tier study.

All reasonable public sources should be utilised but for many sectors significant data gaps exist. Therefore, some sufficient purpose of the assessment must be set so that producers and importers can be asked for amounts on the market and the pattern of use in the value chain.[31]

The identification of a few high tier case studies in the scientific literature which contain relevant information is very helpful as a guide to the approaches needed. In addition, it is imperative that assessors (e.g., exposure

[30] Given that cross-sector assessment is not likely to be a routine activity then it is reasonable to assume that assessors will have first examined ways to model the individual contributions with models that are more like Tier 1 than simple Tier 0 screening.

[31] It is recognised that competition law is an issue here, and, in common with many areas of regulatory-related work, facilitation by neutral bodies will be needed.

scientists) have sufficient knowledge of the application areas of the substance to develop reasonable understanding of the use levels.

5.2 Reaching useful conclusions in an aggregate exposure assessment

5.2.1 What could 'useful' be?

Outputs would ideally include:

- The most significant contribution to enable realistic cross-sector aggregate exposure assessment would be to collect data: this should include tonnage, habits and practices and product/source composition (concentration and occurrence). Efforts could be targeted at collecting data for the exposure sources that contribute the most to the aggregate assessment, which could be identified in the Tier 1 study.

- The most significant contributions to consumer exposure can be identified. As an example, it is relatively easy to show that contribution of exposure via the environment is small compared to direct use sources;[32] this would be particularly important if the amounts on the market are uncertain, and a sensitivity analysis was called for.

- Identification of where further research is needed, for the specific substance but also for the application itself.

5.2.2 Stepwise methodology

Only if there is a likelihood that exposure by different uses and/or routes exceeds the safe limit should an aggregate exposure assessment be warranted. Table 14 below sets out suggestions for principles to follow. In a first step, assessors should make a justified decision about the need of an aggregate exposure assessment based on whether there is more than one exposure source that contributes and whether the combined exposure assessment is likely to be near to or to exceed the defined safety limit.

[32] an exception to this would be very persistent and very bioaccumulative substances, but these should have been identified by PBT/vPvB assessment long before cross-sector assessment would be suggested.

Table 14. Suggested stepwise approach to cross-sector assessment

Step		Outcomes	Notes and observations
	This scheme makes two starting assumptions (steps 1 and 2):		This step implies that the substance possesses some relevant toxicological hazard(s).
1	*An aggregate cross-sector study is needed by a stakeholder, and there is no prior work such as an in-depth risk assessment on the substance.*	Proceed to step 2	*A sufficient human biomonitoring study of the general population would be included within the scope of "in-depth".*
2	*Summed long-term risk characterisation ratios from standard Tier 0/1 methods gives a result suggesting that aggregate exposure is > acceptable exposure limits.*	Proceed to Step 3	*Tier 0/1 here means reasonable use of ECETOC TRA, ConsExpo, ART, etc*
3	Consider prior art including the case studies in this report for examples of the thinking needed for a cross-sector assessment	Proceed to Step 4	The prior art can give ideas of principles that may be helpful for other cases.
4	Assess possible range of tonnage on the market which could give rise to consumer exposures.	Proceed to Step 5	At this stage availability of tonnage information in Europe is very limited. REACH dossiers, SPIN and other databases may help, in addition to published sources. Research into market size can also be undertaken, although one substance will rarely dominate the market.
5	Consider whether there can be significant indirect consumer exposure due to service life of articles	Proceed to Step 6	This will be taken into the aggregate exposure calculation although for the most part it can easily be shown to be lower than near-field exposures (see case studies).
6	Consider releases to the environment and hence human exposure via the environment from all life cycle stages including consumer use. This may only need to be a qualitative assessment since it is likely to be a small contribution to human exposure.	Proceed to Step 7	This will be taken into the aggregate exposure calculation. EUSES or other models (RAIDAR, UseTox) can be used for calculation of exposure via the environment.
7	Review any human biomonitoring, physicochemical and toxicokinetic data that is available for the substance.	Proceed to Step 8	This may be taken into the aggregate exposure calculation. The rate of elimination from the body is relevant to judging the significance of multiple exposures.
8	List the consumer exposure routes from near-field uses, and set the daily exposures based on available published/accepted values such as SCCS guidance, ConsExpo, prior high-tier studies, etc	Proceed to Step 9	

Step		Outcomes	Notes and observations
9	Sum the consumer exposures from the uses, service life and via the environment. There will be a range of reasonable outcomes in the absence of definitive tonnage information.	If the sum of the risks is now < acceptable exposure limits, then STOP. Otherwise proceed to Step 10	It is possible that the sum of the risks is reduced compared to step 2, because daily use levels will have been reconsidered. The assessor needs to have a picture of the use pattern that is a reasonable account of how the substance is formulated and used. It does not, however, look at loss processes.
10	Use a model[33] to examine what fraction of the potential exposure of consumers to the substance can result in uptake by the consumer; this could reduce the exposure estimate.	If the sum of the risks is now < acceptable exposure limits, then STOP. Otherwise proceed to Step 11	Processes such as reaction, adsorption to surfaces could reduce human exposure. This is likely to be beneficial for all substances, in the judgement of the Task Force members.
11	For some exposures the durations may be small and infrequent, so aggregate exposure on the same day is unlikely. Therefore, consider setting the aggregate exposure simply to the largest exposure plus service life and via the environment.	If the sum of the risks is now "< acceptable exposure limits, then STOP. Otherwise proceed to Step 12	Toxicokinetic data could be relevant here.
12	Obtain accurate information about the detail of the use pattern but judge whether high tier research can be avoided.	Proceed to Step 13	This will require research, with some authority enforcing the response from the supply chain. I
13	How many people are exposed to the substance and is it likely for an individual to be exposed to all the uses? Reconsider whether aggregate exposure is likely. Therefore, consider setting the aggregate exposure simply to the largest exposure plus service life and via the environment if important.	If the sum of the risks is now < acceptable exposure limits, then STOP. Otherwise proceed to Step 14	Will require expert judgement.
14	A higher tier assessment will probably be needed.		

[33] Such as RAIDAR-ICE, Indoor or UseTOX.

6. CONCLUSIONS AND RECOMMENDATIONS

6.1 Summary of the project processes

In the future, cross-sector aggregate exposure assessment will very likely be necessary and important for a variety of stakeholders.

The objectives of the project identified three barriers to the achievement of cross-sector assessment:

- Manufacturing and import volumes not being available.
- Lack of data on exposure determinants governing aggregate exposure.
- Uncertainty related to quality and relevance of exposure input data.

The project work, including case studies, confirms that these barriers are real. However, a set of useful information requirements for cross-sector assessment has been identified, as follows:

1. Possible range of tonnage on the market which could give rise to consumer exposures.
2. Information about service life of articles.
3. Potential for human exposure via the environment.
4. Consumer exposure routes from direct product uses, and set the daily exposures based on available published/accepted values.
5. The fraction of the potential exposure of consumers to the substance which can result in uptake by the consumer.
6. Insight into the durations of exposures that may be small and infrequent.
7. Information about tonnage on the market broken down into a realistic number of different applications: how many people are exposed to the substance and is it likely for an individual to be exposed to all the uses?

6.2 Conclusions

- Although there are high tier assessments for single substances, which can be learned from and utilised, there are still too few to cover all possible consumer exposures thoroughly.
- Cross-sector assessment is difficult due to a lack of exposure input data (habits and practices and product/source composition) for many sources.

- Cross-sector assessment at an intermediate level of detail can reproduce broad conclusions of higher tier studies at far lower levels of resource requirements, but more case studies are needed; the reliability will be lower, however.

- Useful cross-sector assessments have the potential to provide valuable insights for both regulatory decision-making and stakeholders, including in the prioritisation for chemical assessments.

- Information about use patterns, including tonnage on the market, is essential, but is not readily available for most applications. Guidance such as that from SCCS which includes information about typical patterns of use of formulated products is very helpful in the assessment process.

- Tools are available to help develop a cross-sector assessment: ConsExpo, PACEM, and Creme Care but are limited only to certain domains.

Bringing together exposure sources from different regulatory frameworks can be achieved at a mid-tier level by use of an integrated platform, such as the spreadsheet tool described in the report.

6.3 Recommendations

6.3.1 Infrastructure

- It is probable that high-level cross-sector regulatory developments would need to set parameters before any guidance could be developed. The number of consumers exposed, and the frequency of exposure, need careful consideration.
- Regulators and the regulated need to consider ways to make realistic use tonnages and daily use patterns more readily available when there is real need for aggregate exposure assessment.
- Where aggregate exposure assessment is needed, realistic parameters for cross-sector assessment would be needed in respect of frequency of use, probability of aggregate exposure occurring, protection goals.
- Models are available, as is training in them, but in-depth evaluation by all stakeholders of their application to cross-sector aggregate assessment is needed.
- The concepts of regional and local scale tonnage that is used in environmental exposure assessment for REACH can be useful for consumer exposure assessment.

6.3.2 Tools, methods, and experiences

- Basic steps of cross-sector assessment have been set out in Section 5.

- The spreadsheet tool, and other models, employed herein could, after development and evaluation, be brought together into one platform, which would facilitate greatly the cross-sector assessment process for consumers.
- Evaluators will require a sufficient understanding of the substance and exposure to recognise input versus output in modelling and its context within real-world exposure.
- It is suggested that a workshop or follow-up Task Force could be based around this report, as a way to increase the sharing of experiences across different stakeholders, and implement the refinements available from different sectors. The follow-up could further develop the spreadsheet tool.

ABBREVIATIONS

2-HESI	2-hydroxy-N-ethylsuccinimide
2-HMSI	2-hydroxy-N-methylsuccinimide
5-HNEP	5-hydroxy-N-ethyl-2-pyrrolidone
5-HNMP	5-hydroxy-N-methyl-2-pyrrolidone
ADME	Absorption, Distribution, Metabolism, and Elimination
AEL	Acceptable Exposure Levels
BIT	Benzisothiazolinone
CEM	Consumer Exposure Model
CLP	Classification, Labelling and Packaging
CMI	Chloromethylisothiazolinone
CMR	Carcinogenic, Mutagenic or toxic to Reproduction substances
CSR	Chemical Safety Report
D5	Cyclic siloxane decamethylcyclopentasiloxane
DEHP	di-2-ethylhexyl phthalate
EFSA	European Food Safety Authority
EQC	Equilibrium Criterion Model
EUSES	European Union System for the Evaluation of Substances
FCM	Food Contact Materials
FFDCA	Federal Food, Drug, and Cosmetic Act
HBM4EU	European Human Biomonitoring Initiative
HCP	Household cleaning products
HMDS	Hexamethyldisiloxane
IMAP	Inventory Multi-tiered Assessment and Prioritisation

ISES	The International Society of Exposure Science
IT	Isothiazolinones
MCCEM	Multi-Chamber Concentration and Exposure Model
MI/MIT	Methylisothiazolinone
MP	Methyl paraben
NEP	N-ethylpyrrolidone
NESIL	No Expected Sensitisation Induction Level
NICNAS	National Industrial Chemicals Notification and Assessment Scheme
NoG	Notes of Guidance
NMP	N-methyl pyrrolidone
NVWA	The Netherlands Food and Consumer Product Safety Authority
OSOA	One Substance One Assessment
PACEM	Probabilistic Aggregate Consumer Exposure Model
PBT	Persistent, Bioaccumulative and Toxic
PC	Personal care
PCP	Personal care products
PPP	Plant Protection Product
RAIDAR	Risk Assessment IDentification And Ranking
RAIDAR-ICE	Risk Assessment IDentification And Ranking – Indoor and Consumer Exposure
RCR	Risk Characterisation Ratio
REACH	Registration, Evaluation and Authorisation of Chemicals
RIFM	Research Institute of Fragrance Materials
RIVM	National Institute for Public Health and the Environment
RMM	RIsk Management Measures
SAF	Sensitisation Assessment Factors

SCCS	Scientific Committee on Consumer Safety
SDS	Safety Data Sheet
SHEDS	The Stochastic Human Exposure and Dose Simulation Model
SIAP	Screening Initial Assessment Profile
SPIN	Substances in Products in the Nordic Countries
TWA	Time weighted average
US EPA	US Environmental Protection Agency
vPvB	very Persistent and very Bioaccumulative
WoE	Weight of Evidence

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Note: All websites were accessed in January 2023

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7. ANNEX 1: REGULATORY REQUIREMENTS AND GUIDANCE

7.1 REACH

The context here is consumer exposure.

The REACH guidance document R.15 (Version 3.0, July 2016) contains some key principles. In section **R.15.6 Risk Characterisation.** The text is reproduced here (with minor edits for clarity):

> *According to REACH Annex I, the registrant should consider risks from combined/(aggregated) exposure across different uses (products) relevant for his substance. He is, however, not obliged to carry out a risk characterisation related to uses of the substance not covered in his own registration." In the context of this guidance, the addition of routes will be referred to as "combination" while the addition of sources will be referred to as "aggregation". Risks resulting from exposure to the substance via simultaneous use of different products may be taken into account (where relevant) through summing up of risk characterisation ratios for systemic effects across exposure scenarios. This could be relevant for instance when products are used routinely together (e.g. cleaning products) and the risk characterisation for the single product use is close to 1. However please note that simply summing up the RCRs resulting from Tier 1 tool estimates leads to a rather conservative outcome. In most cases more sophisticated (e.g. probabilistic) methods and corresponding datasets will be needed, in order to properly reflect the co-use pattern of products across consumers. Such methods are under development for certain product groups. Exposure to the substance via different products may also be relevant when adjusting assessments for short duration over the day, or when characterising the risk related to infrequent exposure. In addition to direct exposure resulting from the use of products, the general population may be exposed to the substance via the environment (ambient air, drinking water and food). In the environmental assessment these routes are considered by default and the resulting risk characterisation for long-term systemic effects may need to be taken into account when assessing the overall exposure to a substance. The outcome of the risk characterisation is used to decide whether safe use can be demonstrated or if further iterations are needed. Once the final iteration has shown sufficient control of risks for consumers the assessment can be finalised. This is the case if i) the exposure estimates are below the DNEL and ii) the likelihood of effects due to irritation, corrosion and sensitisation or other non-threshold effects is negligible. The RMMs and operational conditions ensuring control of risk for consumers (i.e. mainly the characteristics of a safe consumer product and the underlying assumption on habits and practices) should be documented in final exposure scenarios. If certain consumer uses are not supported or are advised against due to health risks, this should be recorded in the CSR and communicated via the extended Safety Data Sheet (extended SDS). In order to produce a meaningful risk characterisation, it is important for the assessor to understand and take into account the uncertainties associated with the information/data that is provided (related to both hazard assessment and exposure*

assessment). The registrant is expected to include a reflection on the most significant uncertainties in his assessment.

Furthermore, the text includes a footnote:

Please note, that the REACH terminology is not fully aligned with the one used at OECD and WHO level with regard to the use "combined exposure or risk". Under REACH this always refers to one substance and not to combination of different substances. The WHO/IPCS Framework on Combined Exposure defines the terms aggregated and cumulative exposure as:

Aggregate exposure: The demographic, spatial and temporal characteristics of exposure to a single chemical through all relevant pathways (e.g. food, water, residential uses, occupational) and routes (e.g. oral, dermal, inhalation). Aggregate risk is the risk associated with multiple pathways/routes of exposure to a single chemical. Cumulative exposure: Defines the aggregate exposure (see above) to multiple chemicals. Cumulative risk is the combined risk from aggregate exposure to multiple chemicals (and may be restricted to chemicals that have a common mechanism of toxicity).

The absence of any further guidance on how to perform aggregate exposure (at whatever tier) provides clear justification in respect of REACH for the current project to have been undertaken.

7.2 Pesticidal products

7.2.1 Regulatory requirements and Guidance

Plant protection products (PPPs) are regulated in accordance with Regulation (EC) No 1107/2009, where active substances must undergo risk assessments under the guidance of the European Food Safety Authority (EFSA) for all scenarios of exposure (including, relevant to the consumer, non-dietary exposure from amateur use, proximity to spray events on crops I.e., resident/bystanders and dietary exposure from consumption of food commodities). Over recent years, the Commission has been working to account for cumulative effects of pesticides as a key part of the 2020 Chemicals Strategy for Sustainability. Key actions related to this ambition include "account[ing] for the cocktail effect of chemicals when assessing risks from chemicals" and "establishing a simpler "*one substance one assessment*" process for the risk and hazard assessment of chemicals". However, to date this has focused on PPPs and pesticide residues and in the context of the REFIT exercise, it was concluded that

the work on developing the method for Cumulative Risk Assessment[34] was more complex than initially expected. In 2021, this led to a noted action plan for the work to be accelerated (SANTE/10178/2021).

However, co-formulants that constitute the majority of a Plant Protection Product (by mass or volume) are authorised according to the specifications of Regulations (EU) 284/2013 (part A, section 1.4.1.) and are regulated under the jurisdiction of the European Chemicals Agency (ECHA) as general chemicals, following REACH regulation and risk assessment methodologies (see section 7.1).

Whilst consumption data from EU populations and regional diets is relatively accessible and, indeed, is utilised in EFSA risk assessment at the PPP level, exposure is primarily from residues of active substance. Other PPP exposure scenarios lack sufficient data (e.g., incidental resident/bystander exposure or amateur use from home gardening) to enable mid-tier assessment with any meaning, but are speculated to account for little cumulative chronic exposure in the same way non-occupational DIY or hobby enthusiasts have only occasional use patterns.

7.3 Biocides

7.3.1 Regulatory requirements and Guidance

ECHA Guidance on the Biocidal Products Regulation (Volume III Human Health - Assessment & Evaluation (Parts B+C)) provides comprehensive instruction on how to perform human risk assessment to meet the Biocidal Products Regulation (BPR, Regulation (EU) 528/2012) that governs the authorisation for the active substance for us in biocidal products registered in the EU. The latter contains the following text under Annex IV, related to cumulative risk assessment:

“15. In carrying out the assessment, the possibility of cumulative or synergistic effects shall also be taken into account. The Agency [ECHA] shall, in collaboration with the Commission [EC], Member States and interested parties, develop and provide further guidance on the scientific definitions and methodologies for the assessment of cumulative and synergistic effects”

However, in the same way as similar guidance for PPPs, different regulation is applied to the active substance separately from co-formulants, with the latter treated as general chemicals that follow REACH regulation and risk assessment methodologies as previously outlined (see section 7.1).

[34] https://www.efsa.europa.eu/en/news/cumulative-risk-assessment-pesticides-faq describes the issues around exposure to different active substances

Typically, active substances utilised for PPP or biocides are not produced in large quantities and have specific applications that are not likely to contribute to cumulative exposure in the same way as general chemicals. However, there are instances of cross-over between active substances utilised in ag-chem and home or consumer biocides, particularly insecticides, that may warrant inclusion as case studies as mid-tier methodology improves. But for co-formulants, risk assessment methodologies and application of mid-tier approaches have been difficult to apply in both biocidal and PPP sectors, due to commercial sensitivity around formulation and constituent chemical compositions as well as limited exposure data in Tier-1 models (that rely on conservatism to demonstrate acceptable exposure and highly likely to significantly over-estimate real world exposure).

7.4 Cosmetics

7.4.1 Regulatory requirements

Since July 2013, Regulation (EC) No 1223/2009 harmonises the safety of cosmetics within the Member States, simplifies procedures and streamlines terminology.

In Europe, a cosmetic product (also known as personal care product) means any substance or mixture intended to be placed in contact with the external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance, protecting them, keeping them in good condition or correcting body odours.

For cosmetic and personal care product exposures, the SCCS recommend a tiered approach to assessing aggregate exposures to ingredients. In the first stage (low tier), exposure is coarsely estimated based on generic exposure scenarios with conservative point values as model parameters (screening level). In the SCCS Notes of Guidance for Cosmetic Testing and their Safety Evaluation (SCCS 2022), it is recommended at this low tier to calculate the exposures to a list of standard product types (17 products) assuming maximal concentrations in all product categories and then to add all of these exposures together to give an aggregate total exposure estimate to the ingredients, which can then be used in a screening level risk assessment. If the risk assessment shows sufficient margin of safety, then there is no need to further characterise the exposure. This is a very conservative method as it assumes that a consumer uses all the products at a high percentile (approximately 90-95th) use level every day and that each cosmetic contains the maximal concentration of the ingredient in question. It is not realistic but serves the purpose of a simple, screening level assessment.

If a refinement is necessary, a probabilistic approach can be followed by the use of appropriate models and/or tools. However, this needs to be clearly justified. For regulatory purposes, the SCCS require that the probabilistic approach is conservative but realistic and transparent.

In particular, for probabilistic assessments the SCCS recommends the following:

- Habits and practices (product use frequency data) in a population may be treated probabilistically, under the assumption that they will not change rapidly over time.

- The target protection goal will be the 95th percentile of the European population, and this value should be used for deriving the margin of safety.

While the SCCS accepts the use of distributions of frequency of product use and co-use in the aggregate exposure assessment, the ingredient concentrations in product categories should normally cover the worst case, i.e. for ingredients with restrictions on concentrations and applicability domains (Annex III of the EU Cosmetic Regulation), also in the probabilistic assessment the maximal allowed concentrations should be used, and for other ingredients the maximal concentrations that are realistically foreseeable in a specific product category. This means, that although the assessment is probabilistic, it is still quite conservative as it assumes that every product that is used by a consumer in the European population contains the ingredient at a maximal level. This is not reflective of the reality where ingredients are only present in a proportion of products and the concentration of the ingredient, if present, will vary from product to product. It would be possible to factor this ingredient occurrence data into the probabilistic assessment to make it more refined/realistic, but this approach has not been accepted by the SCCS. The SCCS cite the reason for not accepting occurrence data in probabilistic assessments as being because product formulations may be highly variable over time, so that an assessment of ingredient concentrations at a specific point in time may not cover the use of the ingredient in the future. However, it is possible to account for this by looking at the trend of occurrence data over time and factoring this into the assessment, by using a conservative estimate of occurrence that allows for market fluctuation of ingredient occurrence over time.

The SCCS also state that for reasons of transparency, the model equations and the input parameters need to be provided together with the exposure estimates in the exposure report. This is so that the exposure calculation is reproducible. If this is not possible, because a specific tool has been used, the original input file containing used distributions and all settings, and the original output file should be provided in the exposure assessment. The output file needs to contain the date of the assessment, the relevant model settings and parameters for this assessment and the associated results, ideally not only in tabular form by giving relevant percentiles of the exposure distribution, but also by graphical visualisation.

There is a need for better consistency and transparency for exposure reporting and it is recommended that guidance is developed to facilitate consistent information on exposure assessment to aid this.

7.4.2 Guidance

In Europe, the Scientific Committee for Consumer Safety (SCCS) outlines how to assess consumer exposure as a basis of a cosmetic safety evaluation(in their '11th Notes of Guidance (NoG) for the Testing of Cosmetic Ingredients and their Safety Evaluation' (SCCS, 2022). The SCCS states in the 11th NoG:

"To save time and resources, a tiered approach is normally followed [to exposure assessment] that first investigates exposure based on generic exposure scenarios with conservative point values as model parameters (screening level)."

"For the safety evaluation of cosmetics, such a screening level approach is the calculation of aggregate exposure according to the NoG. The parameter values presented there can be used as the basis for an additive deterministic first-tier assessment. If a refinement is necessary, a probabilistic approach can be followed by the use of appropriate models and/or tools. However, this needs to be clearly justified. For regulatory purposes, the probabilistic approach needs to be conservative but realistic and transparent."

A tiered approach to exposure assessment has been followed, starting at the screening level using a deterministic evaluation as per the SCCS NoG (2022).

7.5 Food additives and food contact materials

7.5.1 Regulatory context

7.5.1.1 Food contact materials

The following text is derived from:

https://ec.europa.eu/food/safety/chemical-safety/food-contact-materials_en

Food comes into contact with many materials and articles during its production, processing, storage, preparation and serving, before its eventual consumption. Such materials and articles are called Food Contact Materials (FCMs). Food contact materials are either intended to be brought into contact with food, are already in contact with food, or can reasonably be brought into contact with food or transfer their constituents to the food under normal or foreseeable use. This includes direct or indirect contact. Examples include:

- containers for transporting food
- machinery to process food
- packaging materials
- kitchenware and tableware.

FCMs should be sufficiently inert so that their constituents neither adversely affect consumer health nor influence the quality of the food. To ensure the safety of FCMs, and to facilitate the free movement of goods, EU law provides for binding rules that business operators must comply with.

The EU Rules on food contact materials can be of general scope, i.e. apply to all FCMs or apply to specific materials only. EU law may be complemented with Member States national legislation if specific EU rules do not exist.

The safety of FCM is evaluated by the European Food Safety Authority (EFSA).

The safety of Food Contact Materials is tested by the business operators placing them on the market, and by the competent authorities of the Member States during official controls.

7.5.1.2 Food additives

The following text is derived from:

https://ec.europa.eu/food/safety/food-improvement-agents/additives/eu-rules_en

All additives in the EU must be authorised and listed with conditions of use in the EU's positive list based on:

- A safety assessment.
- The technological need.
- Ensuring that use of the additive will not mislead consumers.

Regulation EC 1333/2008 sets the rules on food additives: definitions, conditions of use, labelling and procedures. It contains:

- Annex I: Technological functions of food additives
- Annex II: Union list of food additives approved for use in food additives and conditions of use
- Annex III: Union list of food additives approved for use in food additives, food enzymes and food flavourings, and their conditions of use
- Annex IV: Traditional foods for which certain EU countries may continue to prohibit the use of certain categories of food additives
- Annex V: Additives labelling information for certain food colours

Other pieces of EU legislation relevant to food additives are the following:

Regulation (EC) No 178/2002 lays down the general principles and requirements of food law. There are various amendments.

7.5.2 Relevance of food to this study

When the goal of a mid-tier assessment is to examine all possible sources of exposure to a consumer, then clearly food additives and food contact materials should be considered. However, there is no case study in this report which covers those sources in a very direct way. The case studies on plasticisers and preservatives have some relevance in terms of methodology.

7.6 EPA

This section is included as a comparison to EU regulations.

7.6.1 Regulatory requirements

According to TSCA, conditions of use are defined as the circumstances, as determined by the Administrator, under which an industrial chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of (US EPA 2023a). Consumer use is defined as the use of a chemical or a mixture containing a chemical (including as part of an article) when sold to or made available to consumers for their use (US EPA 2021). EPA relies on the CDR, publications, industry (public meetings and meetings with companies), industry groups, chemical users and other stakeholders to aid in identifying and verifying the consumer conditions of use for a chemical in the US (US EPA 2020).

Regarding deriving exposure estimates during the chemical risk evaluation phase, EPA relies on modelling software including Multi-Chamber Concentration and Exposure Model (MCCEM) and Consumer Exposure Model (CEM) (US EPA 2020). MCCEM is utilised to estimate consumer indoor air concentrations of chemicals released from products or materials in residential scenarios (e.g., houses, apartments, townhouses) over time (US EPA 2023b). CEM estimates indoor air/dust concentrations, dermal exposure, and mouthing exposure for various consumer products and materials. Subsequently, PBPK software is utilised to estimate internal dose.

MCCEM and CEM rely on the EPA's Exposure Factors Handbook, which provides information on generic exposure factors such as body weights, body part surface areas, house volumes and house ventilation rates (US EPA 2011).

EPA defines aggregate exposure as the combined exposure to an individual from a single chemical substance across multiple routes and multiple pathways (US EPA 2003). TSCA requires that a risk evaluation describe whether aggregate exposures are considered in the exposure assessment and the basis for that consideration (US EPA 2017). If insufficient information is available, aggregate exposure assessments may not be included in risk assessments (US EPA 2020).

7.6.2 Guidance

In support of pesticides, EPA has previously issued a guidance on aggregate exposure assessment (US EPA 2001) in response to Congress amending the Federal Food, Drug, and Cosmetic Act (FFDCA) in 1996.

8. ANNEX 2: TASK FORCE SPREADSHEET TOOL

8.1 A spreadsheet which combines cross-sector exposures to a substance deterministically

The ECHA R.15 guidance for human exposure assessment jumps from screening techniques to advanced higher tier concepts; some methods could be beneficial for cross-sector assessments.

As part of this project and to help with the case studies, a simple spreadsheet has been developed which could be used to combine exposures from sources across different sectors. It aims to give reasonable aggregate exposure estimates for an individual. It is something of a "thought-starter" rather than being a proposal for a definitive tool.

The main purpose of the spreadsheet is to bring together all the identified consumer exposures for a substance, and its main features are:

- It generates reasonable worst-case inhalation and dermal exposures; users can estimate the amount of volatilisation based on knowledge or other models (the sheet does not do this automatically)
- Allows for exposure via air or diet from background sources via the environment, though these must be calculated externally
- Results from more sophisticated methods can be factored in
- It allows for any number of consumer exposures at a daily exposure level
- Gives an indication of an approach to establish the frequency of near-field exposures and the number of consumers exposed.

There should always be some discussion of the inherent uncertainties of the assessment, and indeed they may be high. The sensitivity of any result to uncertainty is a key part of the scientific method. The spreadsheet method cannot possibly replace existing uncertainties but will place them into as broad a context as possible.

8.2. The basic concept and how it was developed

The sheet can only provide a reasonable estimate if it is first calibrated by reference to previous detailed studies of other related substances. This point is addressed as part of the case studies.

The sheet builds on some of the longstanding concepts in REACH guidance (and its predecessors) in respect of the tonnage distribution of substances used widely across the population. The REACH guidance R.16 explains the concepts. The *per capita* use of a substance then needs to align with

realistic use levels based on sources such as the SCCS guidance for personal care, ConsExpo fact sheets, or more detailed studies already published, including biomonitoring.

The estimate of amount of substance used by a person starts from the tonnage on the market and the known uses and the size of the population. Where information is available, the user frequency can be edited from a default of 1. Next, a calculated use per day is derived, considering that some users will be exposed far more than others. This is herein termed 'user factor'; for example, a factor of 0.01 means that 1 person in 100 is exposed via the stated use. At this stage the value is found by trial and error or expert knowledge to arrive at a realistic daily use rate, which may be subject to uncertainty for uses where no information is available.

Similarly, the frequency per day or average number of exposures per year is also derived from expert knowledge or reasonable expectation. Useful expert knowledge can be found in the guidance published by SCCS for cosmetic products or in higher tier studies of similar substances.

Amounts of formulated product used per day can be found in SCCS guidance, ConsExpo, etc, for many uses.

The personal care and household use exposures are then summed deterministically, but this implies that one individual could be subject to all the possible exposures. Where any of the user factor values is low then that is unlikely. No proposals are made herein about how to assess the reasonableness of the summation.

Human exposure via the environment is calculated externally from the spreadsheet using EUSES or an equivalent model. The inputs to EUSES from consumer uses are derived within the sheet, but other environmental sources (such as industrial uses) would ideally be included in EUSES for this purpose.

Dermal exposure is estimated based on the use pattern as described. For personal care products some of the SCCS norms are applied. Internal concentration following the external exposure is estimated in a very simple way.

Indoor air concentration is calculated based on an estimate of the amount of volatilisation. Internal concentration following the external inhalation exposure is estimated.[35]

Human exposure via the environment (mass per day) value can be added to the dermal and inhalation exposures.

[35] The method used was to apply the factor given in REACH R.15 guidance to convert air concentration to internal body concentration.

The user enters the number of days per year that the substance is used. It is then a matter of judgement about whether overlap on the same day is likely or not.

The benefits of the sheet are:

- It allows many sources of exposure to be brought together
- Addresses number of users and frequency of use
- Prompts the user to think carefully about the sources.

These are key parts of aggregate exposure assessment.

The case studies include an exploration of the value of the spreadsheet and show some examples. It might be considered that the model should be made more sophisticated. However, it is not intended to be a substitute for standard exposure modelling methods for which assumptions about the amount of substance at the point of use are made. It is intended to be a framework for assessment based on tonnage on the market and amounts in use applied to Tier 1 data. The application within the case studies shows that there can be considerable uncertainty about use pattern, whatever tool is used to perform calculations.

8.3. Specific content of the spreadsheet

The relevant row headings from the spreadsheet are shown, with comments, overleaf. There is a column for each use and then capacity to sum exposures from all uses if required. Default fractions can be over-written.

Table 15. Parameters included in the Task Force spreadsheet for summing exposures

		Topic Blue = fixed Red = calculated	Parameter	Unit	Comments where necessary
Dermal		Tonnes in EU for use		t/y	Total for each use
	default	Regional tonnage fraction	0.1	t/y	Default fraction of the use in an EU Region
	default	Local amount fraction	0.002	kg/y	Fraction of the regional amount at Local scale
	number in region	Overall mass per year average per person	10000	g/hd/y	10000 people at Local scale
		Fraction of population who are users			User entered
		Frequency per day of use		/d	From guidance or judgement
		Fraction of substance in formulation			From knowledge of the sector
		mass per user person per year		g/hd/y	
		mass per user per event on a day		g/hd	
		amount of formulated product		g	
	days per year	mass per person per day average	365	g/hd/d	
		Fraction to air during application			Guidance or expert judgement/modelling
		Fraction to waste water averaged over time			Guidance or expert judgement/modelling
		worst case fraction to skin corrected for volatility			Guidance or expert judgement/modelling
	Body weight	external exposure of skin	60 kg/hd	mg/kg/d	
		fraction absorbed from skin			Not a fixed value, but can be modelled

		Topic Blue = fixed Red = calculated	Parameter	Unit	Comments where necessary
		internal average		mg/kg/d	
		Sum of fractions			
Inhalation		indoor air mass/event		mg/d	
		air exchange per day		/d	Use entered
		room volume		m^3	Use entered
		indoor air concentration during event		mg/m^3	
	Factor	Internal exposure via air	2.88E-01	mg/kg/d	
For MVE, then modelled externally for consumer intake		fraction to waste water			Guidance or expert judgement/modelling
	Contributions	to regional release to air		kg/d	
		to regional release to waste water		kg/d	
		to continental release to air		kg/d	Total less regional amount
		to continental release to waste water		kg/d	Total less regional amount
Total					This includes all internal loads

Green shaded cells are user entered.

8.4. Potential improvements

Uptake from skin and from indoor air should be modelled in whatever way those with expert knowledge of the substance consider to be optimal, but at this stage RAIDAR-ICE is proving to be useful. An uptake factor can be included in the sheet. Inbuilt regional and continental scale exposure via the environment would be highly beneficial.

The Task Force considers that the sheet demonstrates some principles about cross-sector methods, and shows that progress can be made without very complicated tools.

9. ANNEX 3: MODELS

This section includes models that have been considered, rather than being the result of a comprehensive review of their features or method of use.

9.1 Methods for near-field exposure

See Table overleaf.

Table 16. Near-field models describing their purpose and usefulness in modelling human exposure in a way suitable for mid-tier assessment

Acronym	Model name	Description	Source
ConsExpo		ConsExpo can be used to calculate quickly and reliably the exposure of the consumer to substances in all consumer products.	https://www.rivm.nl/en/consexpo
Creme	Creme Care	Software tool for consumer analysis and safety assessment of personal care and cosmetic products.	https://www.cremeglobal.com/creme-care/
PACEM	Probabilistic Aggregate Consumer Exposure Model	Potentially useful for human exposure but publications cover only the cosmetics sector applications.	https://www.rivm.nl/en/consumer-exposure-to-chemical-substances/exposure-models/PACEM
SHEDS	The Stochastic Human Exposure and Dose Simulation Model: High-Throughput	These US EPA models cover all exposure routes, are complex and comprehensive, but not readily accessible.	https://www.epa.gov/chemical-research/stochastic-human-exposure-and-dose-simulation-sheds-estimate-human-exposure
RAIDAR-ICE	Risk Assessment IDentification And Ranking - Indoor and Consumer Exposure	The spreadsheet model brings together information on chemical partitioning, degradation, fate and transport, exposure, toxicokinetics, hazard and risk estimation for organic chemicals in indoor environments at a screening-level. Continuous release is assumed. RAIDAR-ICE is currently parameterised to a representative residence under North American conditions and for a representative adult male.	https://arnotresearch.com/ Li *et al*, 2018 and 2019.
USEtox	UNEP/SETAC scientific consensus model for characterising human toxicological and ecotoxicological impacts of chemical emissions in life cycle assessment	USEtox is a scientific consensus model endorsed by UNEP's Life Cycle Initiative for characterising human and ecotoxicological impacts of chemicals.	https://usetox.org/
Indoor		Similar in scope to RAIDAR-ICE, but not in a spreadsheet. It allows for releases in the home which are non-continuous, and provides an output of amount or concentration of substance vs time.	https://www.trentu.ca/cemc/resources-and-models/indoor-model

9.2 Far-field exposure

See table overleaf.

Table 17. Regional scale models considered in the project, describing their purpose and usefulness in modelling human exposure via the environment

Acronym	Model name	Description	Source
EUSES	European Union System for the Evaluation of Substances		https://echa.europa.eu/support/dossier-submission-tools/euses
TAGS		In principle comprehensive and useable but this came from a CEFIC LRI project which was not completed or maintained.	http://cefic-lri.org/projects/b5-certh-realistic-estimation-of-exposure-to-substances-from-multiple-sources-tags/
SHEDS	The Stochastic Human Exposure and Dose Simulation Model: High-Throughput	These US EPA models cover all exposure routes, are complex and comprehensive, but not easy to use for non-experts.	https://www.epa.gov/chemical-research/stochastic-human-exposure-and-dose-simulation-sheds-estimate-human-exposure
EQC and related	EQuilibrium Criterion Model	Simple environmental models from Trent University, but without a human exposure model. Gives more information than EUSES for the environment but lacks the human exposure part. EQC was investigated in some detail and was set up with an environment very similar to that used in EUSES. It was necessary to include water movement out of soil to get a simulation similar to EUSES. EQC is simpler to use than EUSES and provides clear pictures of the transport and reaction processes relevant to environmental distribution. It does not suggest that the concentrations generated by EUSES and EQC are very different to one another, other than that EQC specifically shows movement out of soil as a mass flow, which EUSES does not.	https://www.trentu.ca/cemc/resources-and-models/eqc-equilibrium-criterion-model
USEtox	UNEP/SETAC scientific consensus model for characterising human toxicological and ecotoxicological impacts of chemical emissions in life cycle assessment	The team working on this includes experts who developed EUSES. The outputs are environmental concentrations but the authors state that the main application is life cycle assessment for comparison of different substances. It is not easy to use. However, there are frequent training events.	https://usetox.org/
RAIDAR	Risk Assessment IDentification And Ranking	The model brings together information on chemical partitioning, degradation, fate and transport, bioaccumulation, exposure, toxicity and risk for the prioritisation and screening-level assessment of organic chemicals. The evaluative regional-scale environment includes representative ecological and agricultural receptors and far-field exposures for an adult human.	https://arnotresearch.com/

MEMBERS OF THE TASK FORCE

Wade Barranco	LyondellBasell, US
Mark Best	Syngenta, UK
Peter Fisk (TF Chair after first year)	Green Chemical Design Ltd, UK
Tushar Mahale	Lubrizol, IN
Carlos Rodriguez (TF Steward)	P&G, BE
Urs Schlueter	BAuA, DE
Sarah Tozer	P&G, UK
Ben van Ravenzwaay (TF Steward)	Wageningen University, NL
Wouter ter Burg (external advisor)	RIVM, NL

Former members:

Gerald Bachler	Dupont, NL
Tatiana Dudzina (TF Chair for first year)	Exxonmobil, BE
Peter Fantke	DTU, DK
Lauren Jones	ex-SC Johnson, UK
Chris Money	Consultant, UK

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Responsible Editor:
Blanca Serrano Ramon
ECETOC AISBL
Rue Belliard 40
B-1040 Brussels, Belgium
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