EVALUATION OF THE SAFETY OF RECYCLATES IN COSMETIC AND DETERGENT PACKAGING

— Scientific Dossier —

Summary

The dossier outlines experimental results and their interpretation, substantiating the safety evaluation methodology for recycled polyolefin materials (LDPE, HDPE, PP) intended for cosmetic and detergent applications. This methodology aims to be straightforward, scalable, and applicable across all sector applications. Central to this approach is pellet testing, which does not depend on transforming these pellets into finished products (bottles, sachets, etc.).

The evaluation is based on detecting and identifying substances using non-targeted analysis on migrates in ethanol 95% and 50%, proposed as simulants for aqueous and lipophilic products. The challenge of detecting substances present in low concentrations is addressed by employing a test with a simulant-to-pellets volume ratio close to 1:1. The conditions of 10 days at 60°C ensure results that are time-independent and determined solely by the concentration in the granule, the partition coefficient with the simulant, and the mass dilution ratio of simulant to granules. The results are demonstrated to align with those obtained using extraction protocols that utilize dichloromethane as a solvent and with tests performed on finished products.

The conversion of test concentrations to exposure concentrations is proposed based on conservative assumptions, validated for hundreds of substances regarding partition coefficients between polyolefins and simulants. Estimators utilizing two tests (an extraction and migration test) only apply to identified substances that can be matched between tests and are not recommended. More conservatively constructed estimators requiring a single migration test are preferred. They allow for evaluating all detected substances, even if they are neither identified nor previously evaluated toxicologically.

The 31 samples of recycled material studied showed that up to half of the substances might not be identified due to their lack of correspondence in mass spectroscopy databases and retention index databases. TTC thresholds and structural alerts are employed to define exposure thresholds for all substances without precluding the use of more specific existing thresholds for identified substances. The entire approach was applied to the 31 samples for three potential applications: shampoo and lotion for adults and shower gel for children. The approach is comprehensive enough to be generalized for evaluating the quality of recyclates at the start of the value chain to finished products at the other end.

Highlights

- **Extensive Safety Studies**: CosPaTox has undertaken comprehensive safety studies on post-consumer recycled (PCR) plastics, particularly PE and PP, for their suitability as packaging materials in cosmetics, detergents, and home care products. The project's work encompassed analytical testing and toxicological assessment phases, including developing use case scenarios.
- **Analytical Testing Insights**: A large-scale interlaboratory comparison revealed the presence of diverse chemical substances in PCR plastics, some unrelated to their intended packaging application. This underscores the importance of thorough safety assessments before using recycled plastics.
- **Non-targeted Screening Requirement**: Detecting a wide array of substances in PCR materials highlights the necessity for non-targeted screening alongside targeted analyses to ensure comprehensive safety evaluations.
- **Migration Testing Results**: Testing on recycled plastic pellets suggested a significant overestimation of potential substance migration compared to actual finished packaging products. This finding stresses the importance of tailored testing approaches for accurate risk assessment.
- **Toxicological Assessment Findings**: Factors such as packaging design, product type, and consumer usage significantly influence the level of exposure to substances migrated from PCR packaging. Model safety assessments have successfully applied toxicological principles to establish maximum acceptable consumer exposure (MACE) values.
- **Risk vs. Hazard**: The studies emphasize that a chemical's hazard profile does not equate to consumer risk if exposure is maintained below established MACE values.
- **Guidance for Industry Implementation**: CosPaTox offers detailed testing procedures, use case examples, and a comprehensive list of detected substances with toxicological data to help the industry effectively apply these safety principles.
- **Quality Categorization for Recyclers**: Recyclers are encouraged to adopt the proposed testing procedures to categorize PCR materials into defined quality levels. This will aid converters and brand owners in conducting safety assessments and risk management.
- **Enhancing Safety and Adoption of Recycled Plastics**: By providing actionable recommendations for the safe use of recycled plastics in packaging, CosPaTox aims to foster the wider adoption of sustainable materials in the cosmetic and home care product sectors.
- **Industry-wide Benefits**: The guidelines set forth by CosPaTox are designed to benefit the entire value chain from recycled plastic suppliers to the end-users by establishing standard safety evaluations and quality definitions for recycled materials, ensuring a robust risk assessment framework.

Preamble

The documents produced by the CosPaTox project—namely, the dossier and guidelines—serve distinct but complementary purposes. The dossier is designed for individuals seeking scientific insights into the risks associated with the mass transfer of substances from post-consumer recycled materials to cosmetic and homecare products. In contrast, the guidelines distill crucial principles and procedural steps for conducting safety assessments, extending beyond the remit of the CosPaTox project to facilitate broader applicability.

This dossier synthesizes and critically examines the experimental outcomes realized throughout the CosPaTox project. Its composition was entrusted to scientists outside the experimental phase to ensure impartiality. These scientists were granted comprehensive access to both raw data and methodologies, enabling an objective appraisal from the vantage points of mass transfer dynamics and risk assessment. The consortium's decision to adopt this approach underscores a commitment to maintaining neutrality when interpreting the findings.

Deemed significantly novel, the dossier's content merits dissemination through scientific peer-reviewed journals. While the consortium aspires to such publications, the actual submissions were not finalized at the time of this dossier's completion. The dossier has undergone factual verification and received the endorsement of the consortium members, ensuring that its conclusions and recommendations accurately reflect the gathered evidence. Meanwhile, the guidelines broaden the scope to include practical considerations such as quality management procedures, which were deliberated and ratified by the consortium members, thereby enriching the foundation for the safe and informed application of recycled materials in sensitive product categories.

The CosPaTox Consortium

CosPaTox originates from the #ForumRezyklat initiative launched by dm-Drogeriemarkt in 2018, which focuses on strategies to increase circular economy awareness, with a specific objective to sort recyclable materials by type. Over time, this approach will raise the recycling rate and the proportion of recycled materials used in packaging. In addition, the Forum is committed to reducing overall packaging amounts and ensuring new packaging is designed with recyclability in mind, so that it becomes a resource within a circular economy.
CosPaTox, a Consortium focused on the intersection of Cosmetics, Packaging, and Toxicology, is committed to formulating so-far missing specific safety assessment guidance for high-quality Post-Consumer Plastic Recyclates (PCRs) to be used in cosmetic product and detergent packaging. CosPaTox' goals also include the establishment of testing methodologies.
CosPaTox members represent the entire value chain for the packaging types in focus: brand owners, packaging producers, fillers, retailers, waste management companies, and recyclers. They have also assembled a team of external scientific experts specializing in toxicology and post-consumer packaging waste recycling.

Project management: Consortia Management GmbH

Chairman of the Consortium: Dr. Michael O.E. Scriba

To deliver this dossier, CosPaTox partnered with:

- Fraunhofer Institute for Process Engineering and Packaging IVV
- FH Campus Wien – University of Applied Sciences Vienna
- FABES Forschungs-GmbH
- Prof. Dr. Olivier Vitrac, AgroParisTech and INRAE, founding members of the University of Paris-Saclay
- Dr. Dennis Bankmann, Independent scientific consultant

CosPaTox Members:

Alpla Werke Lehner GmbH & Co. KG
Amcor Group GmbH
APK AG
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Avient S. a. r. l.
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Procter & Gamble Service GmbH
REMONDIS Recycling GmbH & Co.KG
Sauer GmbH & Co. KG
Siegwerk Group Holding AG & Co. KG
Valorplast S.A.
Veolia Environnement SA
Weleda AG
Werner & Mertz GmbH

Correspondences between the dossier and the guideline document

The correspondence between sections of the dossier and the guidelines helps the reader navigate through the different documents and sections.

	Scientific dossier (this document)	Guideline document (companion document)	Comment for the reader
Principles of safety and risk assessment	Sections 5.1 and 5.2	Sections C.5, E.4	A similar background is provided in both documents. It is an important prerequisite for the reader.
Principles of mass transfer	Appendices 1 - 2	-	Their reading is not required.
Description of tested samples	Section 2.1 and Appendix 4	Section D.1	Refer to these sections for the samples used for validation.
Experimental protocol for migration testing and substance detection, identification, and quantification	Sections 2.2 and 3	Sections D.1, D.2, and D.3	The dossier describes extensively the protocols.
Extrapolation rules from tests to actual exposure concentrations	Section 4	-	The dossier reviews the different scenarios for evaluating exposure concentrations from tests.
Detailed showcases of risk assessment	Section 5.3 and Appendices 7-9	Section D.5	Prefer the dossier for detailed showcases
Discussion on limitations, conservatism	Section 6	-	Refer to the scientific discussion for a critical review of choices.
Recommendations	Section 7	Section C.4 and C.5	Prefer the guideline documents for practical procedures.

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1. Introduction

The CosPaTox project assesses the suitability of recycled polyolefin plastic materials (low-density polyethylene, high-density polyethylene, and isotactic polypropylene) for direct contact with cosmetic products in line with the European Regulation (EC) No 1223/2009 on cosmetic products and in line with the advisory document of the Association Cosmetics Europe (2019). Because the use of recycled materials is not specifically regulated, the dossier represents a voluntary industry effort to reduce the environmental impact of such packaging while ensuring a safe use for the intended use. The recycled material is evaluated without considering its origin or the nature of the recycling process. It is assessed in pellet form for potential use in cosmetic and homecare products, which may have varying requirements depending on the final use, packaging, and end-user (adult, child)[1].

The evaluation does not cover the packaging's functionality (technical and physical properties) but its safety for cosmetic or detergent contact. The recyclates may be contaminated with substances from prior products in contact, mixtures containing additives, and residues [1][2]. The dossier details the principles of an evaluation that can apply to any material without requiring prior knowledge of the origin, the level of decontamination applied, and residual concentrations. The only requirement is that the tested recyclate does not present any significant odor or visual discoloring in contact with ethanol or oil, which disqualifies them for cosmetic and detergent applications. The project specifically developed test protocols to i) routinely characterize the post-consumer contaminants of the recycled material in terms of substance identity and quantities, ii) evaluate a priori the possible migration of these substances from polyolefins toward the targeted product, and iii) estimate a maximum exposure for the targeted application. A review of applicable regulations and toxicological databases has been conducted to establish a database of potentially acceptable substance thresholds according to the expected exposure pathways of cosmetic products. The guideline refers to these thresholds as maximum acceptable consumer exposure (MACE). The entire methodology has been tested against knowledge and samples available on the market when preparing this dossier.

This dossier compiles the essential elements of our methodology and its findings. Our approach is designed as an upstream assessment tool for recycled materials, not as a direct substitute for evaluating finished products or their packaging. Our choice underscores the complexities introduced by material recycling in a circular economy, prompting a shift from the traditional substance-by-substance assessment prevalent in OECD countries to a more holistic material evaluation, including unknown and non-evaluated substances. This new approach contemplates evaluating materials containing dozens of substances, many of which are unidentifiable, unquantifiable, or beyond current assessment capabilities.

The dossier is organized into six distinct sections; the dossier unfolds as follows:

The initial section describes the experimental methodology and its efficacy in detecting substances within recycled materials and routinely quantifying their transfer risks. Our analytical work utilizes untargeted gas chromatography-mass spectrometry (GC-MS), which is optimal for analyzing organic volatile and semi-volatile compounds.

The third section presents the empirical basis for our chosen evaluation framework, detailing results as test concentrations C_{test} for both identified and unidentified substances. A default scenario presumes the presence of substances present in the recyclate but not detected at the chosen simulant's detection limit, acknowledging the possibility of substances present but not detected.

[1] See section C.1.2 of the guideline.
[2] See section C.5.2 of the guideline.

In the fourth section, we delve into the meticulous conversion of C_{test} to an exposure concentration (C_F), factoring in product characteristics and packaging. This critical step in safety assessment reflects the complexity of estimating exposure from recyclates.

The fifth section illustrates the material safety assessment through exposure scenarios encompassing identified substances, those only detected, and potentially undetected ones. Highlighting the dependency of safety on specific applications and products, several case studies demonstrate how conclusions can vary for the same pellet sample.

A general discussion follows in the sixth section. It describes the main features of the approach followed while discussing its application in decision-making and its preidentified limitations

The final section concludes the dossier with recommendations for routinely implementing our methodology. These guidelines aim to facilitate the standardization of recycled material qualification processes, enable their integration into quality procedures, and enable the downstream industry to utilize generated data post-initial assessment.

2. Materials and Methods

This section details the materials and methodologies employed in CosPaTox study. The concepts of mass transfer that support the testing protocol are detailed in **Appendices 1 and 2**. Though the experiments have been carried out for different contact times, diffusion modelling was not necessary. Considerations about extrapolation at different times and temperatures are only given in the **Appendix 3** and not discussed in the dossier.

2.1. Materials

2.1.1. *Post-consumer recycled plastics*

The study focused on thirty-one samples of post-consumer recycled (PCR) polyolefins, including low-density polyethylene (LDPE), high-density polyethylene (HDPE), and isotactic polypropylene (PP). These samples were sourced from seven recycling facilities throughout 2022 and provided in pellet form. The collection encompasses a diverse mix of materials, ranging from those with clear food-grade compliance to others of indeterminate origin, all subject to varying degrees of pre-laboratory processing such as sorting and washing (both cold and hot treatments). The standard sample size for analysis was set at 2 kg. However, for certain pellet batches, up to 50 kg was collected to facilitate the production of finished goods such as jars, bottles, and films for further testing. Detailed information on each sample, including its origin and processing, is provided in **Table 1**.

***Table 1**. Summary of Post-Consumer Recycled Polyolefins Analyzed in the CosPaTox Project. A detailed description of samples is given in **Appendix 4**.*

PCR Polymer	Sample codes	Number of Samples	Origin of Recyclates
LDPE	rLDPE1 … rLDPE5	5 pellets 5 films made of pellets	Mostly unknown, except for LDPE4 and LDPE5†
HDPE	rHDPE1 …. rHDPE15	15 pellets 10 bottles made of pellets	To be determined (TBD)
PP	rPP1… rPP11	11 pellets 8 jars made of pellets	TBD

†LDPE 4 is identified as a low-standard technical sample originating from a basic mechanical recycling process applied to post-consumer waste. It offers insight into potential contaminants introduced from such waste streams. The cleaning procedure for this sample involved multiple stages: shredding, dry cleaning, cold washing, drying, and finally extrusion.

This diverse collection of PCR materials provides a comprehensive basis for assessing the safety and suitability of recycled plastics in various applications, particularly in contact with cosmeticand homecare products. The geometry characteristics of the pellets are listed in **Table 2**.

***Table 2**. Pellets Characteristics Measured by Computed Xray Tomography*

PCR Polymer	Mass of pellets Min < Average < Max (mg)	Specific surface area 5^{th} Percentile < Average < 95^{th} percentile (mm^2/g)
LDPE	13 < **35** < 42	1723 < **2101** < 2918
HDPE	6 < **27** < 48	1695 < **1938** < 2279
PP	33 < **20** < 60	1647 < **1898** < 2134

Two hundred mL bottles were processed from each pellet to compare the migration from pellets and real recipients. The internal surface area of the bottles was about 23,970 ± 70 mm^2 with a weight varying from 18.7 g to 19.4 g (average value: 19.1 g).

2.1.2. *Considered substances*

Due to the limitations of current technological capabilities, it is impractical for either routine or specialized laboratories to screen for every substance contained within a material comprehensively. The CosPaTox project has adopted a non-targeted gas chromatography-mass spectrometry (GC/MS) screening approach to navigate this challenge. This method leverages a high-temperature program designed to detect high molecular weight compounds without compromising the integrity of the chromatographic column—a precaution essential to avoid false-positive results.

In polyolefin materials such as those studied here, linear or branched non-aromatic aliphatic compounds are prevalent. These substances are dominant in recycled materials and virgin polyolefins, suggesting their inherent presence in the polymer matrix. A large number of these compounds could potentially signal premature matrix degradation. Consequently, they are considered in our risk analysis individually rather than in aggregate, diverging from the common practice of utilizing the overall migration limit concept, which we do not employ here.

Our analysis emphasizes aromatic and unsaturated aliphatic compounds, terpenes, and esters resulting from the degradation of antioxidants and stabilizers, as well as those introduced through contamination from prior contact with other products. Notably, some compounds, such as phthalates, are subject to restrictions under the REACH regulation due to their potential health impacts.

Substance identification reliability in our analysis depends on several factors, including the sophistication of the analytical equipment, the proficiency of laboratory personnel, the availability of appropriate internal standards, and the comprehensiveness of the mass spectral databases employed for chemical identification.
Moreover, for families of substances associated with significant health concerns—such as Polycyclic Aromatic Hydrocarbons (PAHs), Primary Aromatic Amines (PAA), Polychlorinated Biphenyls (PCB), and metals, which pose carcinogenic risks or allergenic potential—targeted analyses are indispensable. We provide a concise summary of the methodologies applicable to these substances, including metals, PAHs, PAA, etc., as detailed in our guideline [2]. This dual approach, combining non-targeted screening with targeted analyses, ensures a thorough and nuanced understanding of the chemical landscape within recycled polyolefins, setting the groundwork for a comprehensive safety assessment

2.1.3. *Typical cosmetic and homecare packaging for risk assessment*

Cosmetic and homecare packaging, characterized by its higher specific surface area exposure, demands distinct materials, design, and functionality considerations, diverging significantly from food packaging. These distinctions are crucial for conducting a comprehensive risk assessment, particularly when employing recycled materials (recyclates) in packaging applications.

This report examines three scenarios, with a baseline scenario emerging from a worst-case analysis: packaging 2 g of product within a sachet measuring 40 mm × 70 mm. The scenarios detailed in **Table 3** revolve around a 200 mL bottle weighing 19.1 g, showcasing variations in Specific Exposure Daily Dose (SED) ranging from 0.8 to 65 mg of cosmetic product per kg body weight (BW) daily. These variations account for whether the cosmetic product is rinse-off or leave-on and whether it is intended for adult or infant use. A constant weight dilution factor (product-to-packaging ratio) of 8.3 is applied across all scenarios, regardless of the simulant used for aqueous or oily cosmetic products. This factor, deemed conservative for both Ethanol 50% and Ethanol 95% simulants, supports the relevance of these scenarios for generic risk assessments across diverse container types prevalent in the cosmetic and homecare sectors.

The outlined scenarios offer a structured approach to risk assessment for recyclates in cosmetic packaging. By accommodating various product types and consumer demographics, the study ensures broad applicability to the safety evaluations required for the diverse range of products within the cosmetic and homecare industry. An overview of cosmetic packaging geometries including actual dilution factors for risk assessment is shown in **Appendix 5**.

***Table 3**. Typical Cosmetic Packaging and Scenarios to be Used for Risk Assessment*

Target / Characteristics	**worst-case (for reference)**	**Shampoo**	**Shower Gel**	**Body Lotion**
Scenario	Worst-case†	CosPaTox	CosPaTox	CosPaTox
Cosmetic Product Type	any	Rinse-off	Rinse-off	Leave-on
Consumer	**Adult**	**Adult**	**Infant**	**Adult**
Application per day	17.4 g	10.46 g	18.67 g	7.82 g
Retention factor	1	0.01	0.01	1
Resorption	1	0.5	1	0.5
$Body\ Weight\ (BW)$	$60\ kg$	$60\ kg$	$5\ kg$	$60\ kg$
Specific Exposure Daily Dose of cosmetic product (SED)	290 mg/kg$_{BW}$/day	0.8 mg/kg$_{BW}$/day	37 mg/kg$_{BW}$/day	65 mg/kg$_{BW}$/day
Container	**(based on sachets 40 mm x 70 mm)**	**bottle**	**bottle**	**bottle**
Product Volume (V_F)	1 L	200 mL	200 mL	200 mL
Container Weight (W)	-	19.1 g	19.1 g	19.1 g
Contact Surface Area (A)	280 dm²	240 cm²	240 cm²	240 cm^2
Polyolefin Density (ρ_P)	1000 kg·m^{-3}	920 kg·m^{-3} (LDPE) 950 kg·m^{-3} (HDPE) 900 kg·m^{-3} (PP)	920 kg·m^{-3} (LDPE) 950 kg·m^{-3} (HDPE) 900 kg·m^{-3} (PP)	920 kg·m^{-3} (LDPE) 950 kg·m^{-3} (HDPE) 900 kg·m^{-3} (PP)
Simulant	**Ethanol 95% (ETH95)**	**Ethanol 50% (ETH50)**	**ETH50**	**ETH95**
Simulant Density at Room Temperature (ρ_F)	782 kg·m^{-3}	877 kg·m^{-3}	877 kg·m^{-3}	782 kg·m^{-3}
Weight Dilution Factor: $L_{actual} = \frac{\rho_F V_F}{W}$	-	9.1	9.1	8.1-8.3
Weight Dilution Factor (approximation used): L_{actual}	-	8.3	8.3	8.3

†SCCS Notes of Guidance for testing of cosmetic substances and their safety evaluation, 8th Revision 2012, SCCS/1501/12 [3].

2.2. Methods

The CosPaTox project opts for working with pellets rather than finished products. This choice facilitates early evaluation before the recycled material's use is determined. This approach does not necessarily replace the finished product assessment, which likely encompasses a broader mix of sources and compound degradation during subsequent transformations. To develop a routine application, the pellets were tested in laboratory conditions under extractive conditions and accelerated transfer conditions at 60°C. The choice of comparable solvent/simulant and pellet mass aims not to replicate usage for cosmetic products but rather to limit the dilution affecting substance detectability. This approach avoids the need for a concentration step through evaporation or sublimation, which could result in the significant loss of substances. Tests were repeated across laboratories to validate the protocol under various contact time conditions. The goal was to establish conditions where the number of detected substances and their concentrations no longer depended on the duration of the test.

2.2.1. *Extraction and migration protocols*

Extraction and migration were carried out directly on recycled pellets in closed 3, 5, or 10 mL vials, chosen to minimize the volume of the headspace. A computer tomography study on recycled pellets was carried out to characterize the dimensionality of the pellets. Approximately 20 to 160 standard recycled pellets were present in one gram, each having a mass of around 27 mg (see **Table 2**). These cylindrical pellets typically measure 3 mm in diameter and 4 mm in length, yielding a surface ranging from 26 to 82 mm^2. These geometric attributes are essential for understanding mass transfer processes in testing conditions.
Extraction and migration conditions are summarized in **Table** 4. Extraction was carried out at the boiling point (40°C) of dichloromethane, facilitating the sorption and swelling of pellets. Migration conditions were conducted in accelerated conditions at 60°C. Variable durations were used to determine the best contact conditions and to verify whether a thermodynamic equilibrium was reached between the pellets and the liquid in contact. At thermodynamical equilibrium and without chemical reactions, the number of substances and their concentrations become independent of time.

***Table 4**. Experimental Designs to Analyze Contaminants in PCR during the CosPaTox Project*

Evaluation category	Conditions	Codes
Extraction protocol	• Total immersion in dichloromethane at 40°C with $L \approx 1$ (*e.g.* 1 g of pellets in 1 mL of solvent; 2 g + 3 mL, 3 g + 3 mL, etc.). • Duration from 1h to 14 days All experiments are duplicated or triplicated	Equivalent to P1 (on pellets)
Migration protocol	• Total immersion in simulants (ethanol 95% and ethanol 50%) at 60°C with $L \approx 1$ (3 g pellets in 3 mL of simulants) • Duration from 1 to 21 days All experiments are duplicated or triplicated	Equivalent to P2, P3 and P4 (on pellets)
	• Same conditions as above with ethanol 95%, $L \gg 1$ (the quantity of pellet represents the same surface area as inside a 200 ml bottle, *e.g.* 12.81 g of rHDPE pellets) • Enrichment by evaporation for factor 10	Equivalent to P5 (on pellets)
	• Same conditions as above with ethanol 95% and $L \gg 1$ (the weight of the real 200 mL rHDPE bottle ~ 25.6 g in contact with 200 mL of simulants) • Enrichment by evaporation for factor 10	Equivalent to B1 (on bottles)

2.2.2. *Untargeted analyses of substances*

Volatile and semi-volatile compounds were separated in gas chromatography (GC) using a high-temperature program with a column that minimized bleeding. The protocol is detailed in **Table** 5. A quadrupole mass detector was used as a universal detector. Semi-quantification was conducted by assuming a linear response of the quadrupole detector.
The limit of detection (DL) was evaluated at 0.128 mg/L, referred to as 4,4'-difluoro biphenyl. A substance was considered identified (i.e., associated with a detected peak) only if its retention index and mass spectrum were identified with confidence above 50%. Peaks above DL without matches were tagged as unidentified compounds.

***Table 5**. Program of GS-MS analyses*

Column	Rxi-5Sil MS (Restek, USA) (30 m x 0.25 mm Id x 0.50 µm df)
Carrier gas	Helium
Split	10 mL/min
Injection Volume	1 µL
Injector Temperature	10°C →280°C
Temperature Program	100 °C @ 5 °C/min → 150 °C @ 7 °C/min → 280 °C @ 10 °C/min, 12 min → 320 °C @ 80 °C/min, 15 min
Temperature of Transfer Line	270°C
Scan Range	35 - 550 g/mol
Source Temperature	230°C
Detector	Quadrupole
Detector Temperature	150°C
Peak identification	identified on TIC signal (total ion detector). Limit of detection defined as 1% internal standard
Substance identification	double matches as retention index (RI) and mass spectrum with a minimum confidence of 50%
Substance quantification	via area referring to area of internal standard (see **Table 16**)
Mass Spectra Database	Internal "in-house" database containing more than 600 substances built by CosPaTox partner under the same conditions. NIST Standard Reference Database 1A (version NIST23, National Institute of Standards and Technology, Gaithersburg, MD, USA) including 394,054 Spectra for 347,100 chemical compounds.
Retention Index Database	Kovatz index or retention index of substance i was calculated from its retention time t_i and retention of trailing (t_n) and heading (t_{n+1}) *n*-alkanes as $100\left[1+\frac{t_i-t_n}{t_{n+1}-t_n}\right]$. The NIST 23 GC method/Retention Index Database including the retention indices of 180,618 compounds.

The detector response for unknown samples was calibrated against four internal standards, which are enumerated in **Table 6**. Semi-quantification utilizing a linear response model for the quadrupole detector allows for an approximate but reasonably accurate estimate of the concentrations of various substances. It must be noted that this assumption of linearity is contingent on the calibration range and operating conditions, thus contributing to some degree of uncertainty in the final concentration estimates. The concentration determined at the

***Table 6**. Internal standards utilized for semi-quantification*

Chemical Name	CAS	M (g/mol)	Concentration Range (mg/L)
Tridecane	629-50-5	184.36	11 ± 1
4,4'-Difluorobiphenyl	398-23-2	190.19	13 ± 1
3-tert-Butyl-4-hydroxyanisole	121-00-6	180.24	10 ± 1
Bis(2-Ethylhexyl) Phthalate-d4*	93951-87-2	394.6	10 ± 1

**this internal standard is no longer considered at the end of the project due to a non-sufficient separation of the deuterated and non-deuterated phthalate under the chosen GC conditions*

The concentration determined at the end of this procedure is called C_{test}. It applies to all detected molecules identified by selecting the standard with the closest structural proximity or by selecting the standard that maximizes the response for unidentified substances.

2.2.3. *Safety Assessment Approach*

The suitability evaluation of a material is conditioned by the fact that no identified substance or merely detected substance, or any substance potentially present at the detection limit or below in the product, leads to an exposure exceeding the acceptable exposure.

For any identified substance, the acceptable threshold is determined from its Cramer classification [4] and the detection of any alert structures that could suggest a genotoxic nature of the substance. The classification was carried out with the help of the open-source software ToxTree [5, 6] in its version 3.1 based on the predicted SMILES structures [7]. This classification allows defining a default Threshold of Toxicological Concern (TTC). The approach has been initially proposed by Ref. [8] and has subsequently been endorsed by the European Food Safety Authority (EFSA) [9]. As a golden rule, the TTC approach should not be used for substances for which EU food/feed legislation requires the submission of toxicity data, or when sufficient data are available for a risk assessment, or if the substance under consideration falls into one of the exclusion categories. Based on the substances listed by the Cosmetic regulation or found in recyclates, the CosPaTox consortium compiled an extensive list of substances with their MACE values based on TTC or NOAEL or DNEL when available. The TTC approach is associated with five default MACE values reported in **Table 7**.

***Table 7**. MACE (Maximum Acceptable Consumer Exposure) values associated with the TTC approach (default approach).*

Classification	**MACE in µg/kg body weight per day**	**Recommendation for cosmetics and detergents**
With structural alter for genotoxicity	0.0025	Applicable
Organophosphates and carbamates	0.3	Not relevant for cosmetics and detergents[†]
Cramer class III	1.5	Applicable
Cramer class II	9.0	Apply Cramer class III instead[‡]
Cramer class I	30	Applicable

[†]*SCCS (European Scientific Committee on Consumer Safety) discusses applicable thresholds for pesticides with and without carbamates and organophosphates in Table A.13 of Ref. [10].*
[‡]*As SCCS acknowledged, substances belonging to class I must be treated as class III since available databases do not well support class II [11].*

The overall approach for evaluating the exposure associated with each substance is presented in **Table 8** for each detected substance, only identified or suspected in the recyclate. Any unidentified substance is a priori qualified as potentially genotoxic and must, therefore, be compared to the most conservative MACE value. The conversion of the test concentration C_{test} to the exposure concentration $C_{exposure}$ is described in Section 4. Its expression depends on the applied test strategy.

***Table 8**. Principle of Safety Assessment Applied to Each Category of Substance Integrated in the Non-targeted Analysis*

Type of substance	Identified substance	Detected but not identified substance	Substance not detected
Test concentration (mg/kg simulant)	C_{test}	C_{test}	Detection limit (DL) : 0.1 or 0.3 mg/kg
Exposure concentration (mg/kg product)	$C_F = f(C_{test}, application)$†		$C_F = f(DL, application)$†
Consumer Exposure (mg of substance/kg body weight/day)	$CE = C_F \times SED$ with SED the specific exposure daily dose to the considered product (mg of product/kg body weight / day)		
Classification	**Table 7** for the TTC approach or other classification based on NOEL‡ or DNEL‡	Potentially genotoxic	
Maximum acceptable Consumer Exposure (mg/kg body weight/day)	$MACE$ from **Table 7** or from other approaches (regulation, NOEL‡, DNEL‡)	$MACE$=0.0025	
Criterion of safety	$CE < MACE$		

†The equation model converting the test concentration C_{test} into the exposure concentration C_F is discused and presented in section 4. It depends on the test(s) applied and the application (type of product, product-to-packaging ratio).
‡NOEL = No Observed Effect Level; DNEL = Derived No-Effect Level

3. Results and Discussion

This section presents the pivotal outcomes of the CosPaTox project, centering on the untargeted analysis of pellets made from recycled materials, namely rLDPE, rHDPE, and rPP. Our primary aim is to meticulously evaluate and refine a methodology that efficiently detects, identifies, and quantifies substances, streamlining the analysis process. To this end, we focus on simple maceration protocols at low dilution ratios (L), targeting a reduction in the complexity and number of analytical steps. The effectiveness of various methodologies is scrutinized based on their capacity to encompass a broad spectrum of compounds and their precision in inferring structural identities through retention times and mass spectra. A critical aspect of this research is its practical application to 31 distinct recyclate samples drawn from real-world scenarios. This methodological approach is instrumental in navigating the complex task of determining the safety of materials sourced from recycled products, offering a pragmatic and efficient framework for comprehensive safety assessments.

3.1. Typical extraction and detection performances of compounds from untargeted analyses

The analytical evaluation of compounds in recyclates, such as rHDPE, employing an untargeted methodology applicable to both volatile and semi-volatile compounds, involves a broad range of uncertainties. These span the initial detection and identification of substances to the quantification of their concentrations under various extraction conditions or the assessment of their potential migration levels. **Figure 1** presents the number of compounds detected (eluted) from a typical rHDPE recyclate sample. The validity of these results depends on their consistency across repeated measurements and their accordance with the anticipated dynamics of interaction between the tested pellets and the contacting liquid, which may be a solvent or an extraction medium. Ideally, after a set period, the number of leachable chemicals, i.e., detected or identified substances, should stabilize, indicating that additional contact time does not significantly change the detectable compound count. The proportion of identified to detected compounds should also remain constant over time.

Compounds are identified from the total ion chromatogram (TIC). They are considered to be derived from the sample if they can be distinguished from those in a control column run, signifying their absence in the blank. The significant challenge presented by unidentified compounds and oligomers requires meticulous attention. Identification involves a two-step process. Initially, the Kovats retention index (RI) linked to the TIC peak is matched with RI databases. The success of this step solely depends on the comprehensiveness of the RI database. The subsequent step utilizes ion chromatogram (IC) signals to approximate the likely low-resolution mass spectrum of the substance, proposing a potential chemical structure from a mass spectra database. The accuracy of spectrum reconstruction heavily relies on the intensity of fragmented ions and the ability to differentiate them from background noise, particularly at low resolution. Consequently, not all detected compounds can be reliably identified. With low-resolution mass spectra, identified compounds correspond to the best database matches, posing a considerable risk of misidentification for intermediate matches.
Oligomers, due to their broad molecular distribution, may deviate from this extraction/migration-identification scheme, releasing over extended periods under highly extractive conditions beyond the duration of experiments. Given that the true prevalence of substances in recyclates is, by definition, independent of the testing condition (whether extraction at 40°C in dichloromethane or migration measurements at 60°C with EtOH 95% and 50%), a robust testing method for hazard identification should yield a substance count that approximates what is expected under short-term extractive conditions before the release of high molecular weight oligomers.

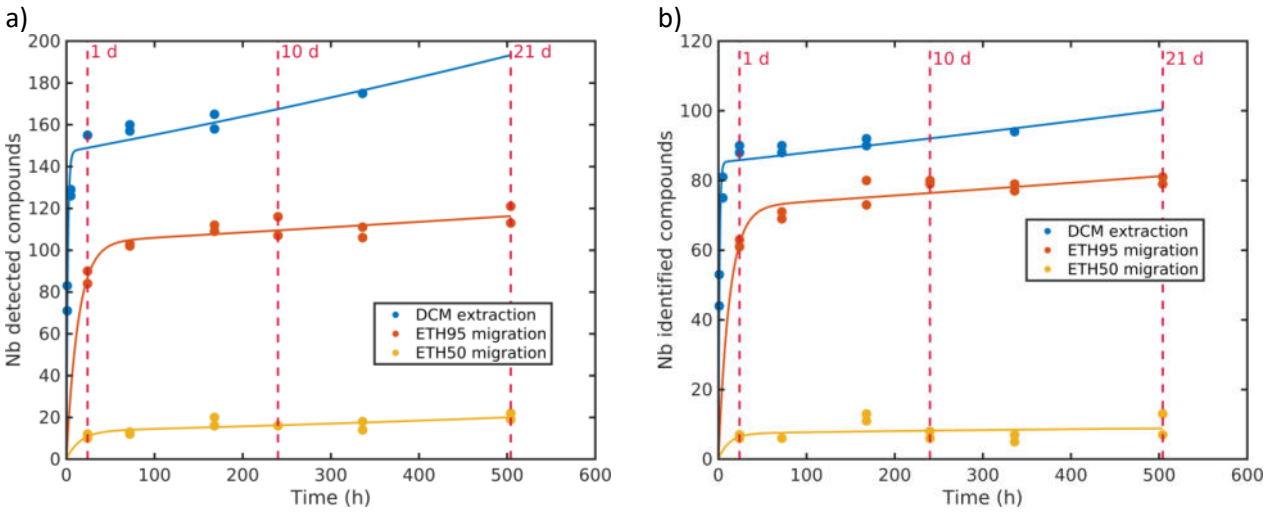


***Figure 1**. Evolution of the total number of detected substances (a) and the number of identified substances (b) in rHDPE sample as a function of contact time and contacting liquid. The continuous curves represent fitted kinetics as the sum of two saturating exponential models.*

Detailing **Figure 1**a, we observe a substantial count of substances detected in rHDPE, nearing two hundred. The data suggest a combination of two distinct first-order kinetic processes: a rapid phase and a slower one. The slower kinetic phase, particularly pronounced in extractive conditions with dichloromethane, extends beyond 20 days, eventually accounting for 40% of all released substances. As this kinetic trend is absent in migration conditions (EtOH 95% and 50%), these substances are deemed irrelevant for hazard analysis. This inference is corroborated by the trends in **Figure 1**b, where the excess of detected substances in extractive conditions is primarily attributed to linear compounds, likely intact or oxidized HDPE oligomers with slow extractability kinetics.

The enumeration of detected and identified compounds is provided in **Table 9**. One to two days of extraction in dichloromethane are sufficient to collect all compounds detected in migration conditions on longer contact, typically 10 days. A day's migration in ethanol 95% at 60°C isolates 75% of these compounds, with an identifiability rate between 60% to 70%. Conversely, detection and identification rates significantly drop in ethanol 50%, where merely 10% to 15% of substances are detectable, and less than half of these are conclusively identifiable. This is likely due to the limited chemical affinity between the predominantly hydrophobic compounds and the more polar ethanol 50% simulant. The detection limits for both ethanol 95% and ethanol 50% are comparably established between 0.1 and 0.3 $mg \cdot kg^{-1}$, indicating a systematic challenge in substance detection and identification of hydrophobic migrants in ethanol 50%.

***Table 9**. Comparison of the number of identified vs. total substances over time in rHDPE sample. The reported values rely on the continuous approximation models shown in **Figure 1** .*

Contact Time (h)	Dichloromethane (Identified)	Ethanol 95% (Identified)	Ethanol 50% (Identified)	Dichloromethane (Total)	Ethanol 95% (Total)	Ethanol 50% (Total)
24 (1 day)	85	61	6	148	86	10
240 (10 days)	92	76	8	167	109	16
504 (21 days)	100	81	8	193	116	20

Highlights: Hazard identification requires a step capable of recognizing substances transferred to the extraction or migration medium above the detection threshold. Substances close to this limit may be identifiable but are usually unidentifiable. Substances present below this threshold are, by definition, undetectable and unidentifiable. For those migrating above the limit, 30 to 50% remain unidentified, constrained by limited database resources. Overall, a day-long extraction optimally extracts, detects, and identifies substances, while 10-day tests in EtOH95 at 60°C enable the identification of 75% of substances found in DCM, excluding the oligomer fraction, which complicates mass spectra collection. Detection for hazard identification in ethanol 50% is less reliable due to lower concentrations in this simulant but the test alone may be sufficient to evaluate the risk of mass transfer for identified substances. Across all methods, the prevalence of substances is identified with an error margin of 10 to 20%, and not all substances are consistently detected or identified in repetitions, especially for those bordering the detection limit, underscoring inherent experimental variability.

3.2. Typical profiles of identified compounds in recyclates

A representative rHDPE sample analysis reveals that about 26% (92 out of 348) of the total identified substances across multiple analyzed recyclates were present in this single sample after just a day's maceration in dichloromethane (DCM). This pattern of pollutant occurrence is not random, substantiating the predictability of contamination. It lays a strong foundation for deriving comprehensive conclusions and specific recommendations. Such insights underline the necessity for a systematic risk assessment approach or a more refined strategy that categorizes substances based on their chemical structure, concentration levels, and hazard potential.

Statistical analysis of recurring contaminants relied on developing an expansive database of substances. The primary identifier used is the retention index. which allows the recognition of the substance across multiple samples, whether or not it is identifiable. The only condition is that the substance is not coeluted with other substances. Among 348 unique substances (same retention index and similar ions) detected across LDPE (5 samples), HDPE (15 samples), and PP (11 samples) recyclates, half (180 substances) were identifiable (with a likely chemical structure), and 89% of these were found uniformly in rLDPE, rHDPE, and rPP. This indicates that only a portion is likely related to oligomers and their degradation products. The 180 identified substances are classified according to their probable primary sources as outlined below (with further details in Table 2 of the guideline [12]):

- PE/PP Packaging (including oxidized and breakdown products from oligomers and additives)
- Food Residues
- Residues from Other Consumer Products
- Exogenous Contaminants and Intentional Additives
- Ambiguous or Variable Predominant Origin

This categorization provides clues on the possible origins and chemical classes of migrants from recycled polyolefins. **Figure 2** displays the toxicological classification, as per the Cramer Classification, of the 180 identified substances. A third of these substances are categorized under the most severe toxicological classes, either potentially genotoxic or belonging to Cramer Class III. Assuming this distribution is representative for all samples and substances, it implies that 55 out of 168 unidentified substances might necessitate similar categorization.

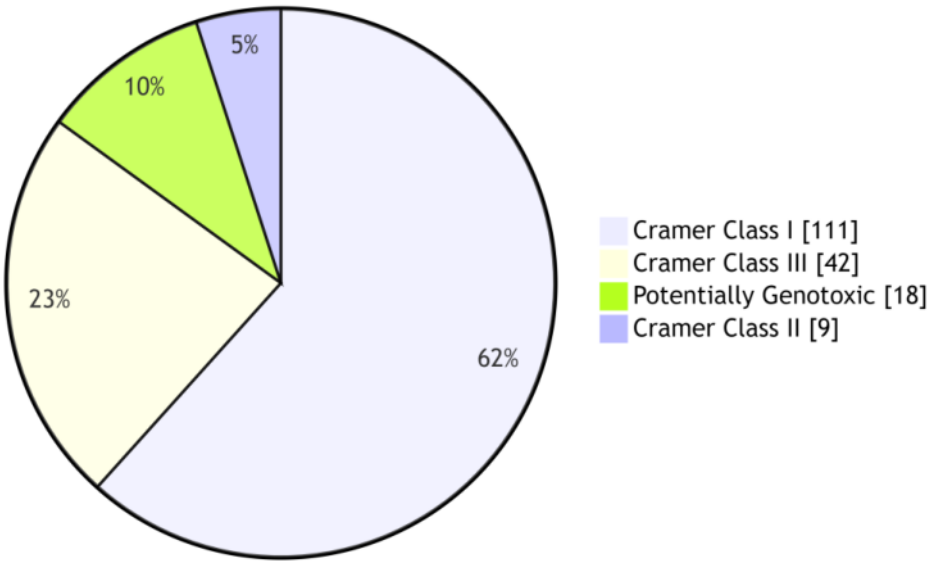


***Figure 2**. Distribution of toxicological classes for the 180 substances detected and identified in polyolefin recyclates (31 samples, 348 unique substances), ordered by decreasing prevalence.*

Highlights: Substance categorization, particularly as potentially genotoxic, relies heavily on expert judgment and the identification of alerts. This process is limited to successfully identified substances.
A comprehensive aggregation of all substances suggests that their presence and detectability can be regarded as independent random events. From this analysis, we estimate that approximately 10% of the substances have the potential to be genotoxic.
This preliminary estimate of genotoxicity should extend to the unidentified fraction of chemicals. For instance, if a sample contains more than ten unidentified substances, it is prudent to assume that at least one could be genotoxic, existing at a concentration at or above the detection limit in the analyzed medium.
This conclusion holds regardless of the choice of extraction or migration medium, as the detection limits for dichloromethane and hydroalcoholic solutions are similar. The implications for risk assessment are significant, suggesting a conservative approach should be adopted for unidentified substances, considering the potential health risks associated with genotoxic compounds.

3.3. Concentration ranges of substances in recyclates

This section delves into the semi-quantitative determination of concentration ranges for detected substances in recyclates. The focus is on substances whose concentrations exceed the detection limit of 0.1-0.3 $mg \cdot kg^{-1}$. Accurate identification is pivotal, and the closest matching internal standard is used for semi-quantification, especially for substances within the same chemical class.

3.3.1. *Variability in concentration ranges*

The concentration ranges of substances are subject to significant variability, influenced by the testing medium used. **Figure 3** illustrates these concentration ranges based on the 50th and 95th percentiles for the same rHDPE sample analyzed earlier (**Figure 1**). This analysis aggregates data from all detected chemicals, given that the individual substance release kinetics in each medium (dichloromethane, ethanol 95%, and 50%) were too irregular for clear trends. Concentration estimates often carried errors exceeding 50%, primarily for values near the detection limit. Aggregation helped discern a more consistent kinetic behavior for extraction/migration, except in ethanol 50%, where results remained largely inconsistent due to concentrations hovering around detection limits. For ethanol 95%, median concentrations stabilized below 2 mg·kg^{-1}, with a 95th percentile upper limit under 20 mg·kg^{-1}. These figures doubled in dichloromethane for identical substances.

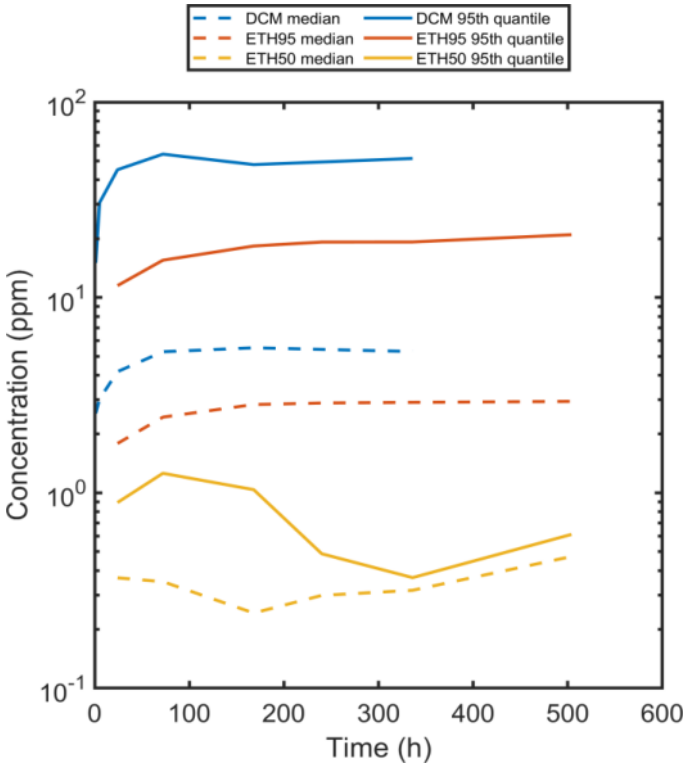


***Figure 3**. Evolution of the 50th and 95th percentiles of concentration distribution with contact time for the rHDPE sample shown in **Figure 1**. The statistical interpretation is derived from six extraction or migration tests.*

All values of concentrations over time of substances in rHDPE, obtained with dichloromethane and hydroalcoholic solutions are reported in **Appendix 6**.

3.3.2. *Comparative analysis on a substance basis*

Table 10 presents a detailed comparative analysis of concentration ranges for twelve selected substances, identified based on their common presence in recyclate samples across various chemical families and molecular sizes. This comprehensive evaluation spans all examined samples and types of polymers, facilitating a direct comparison of how substance prevalences vary across different methods. Concentration ranges appeared to be consistently matched between 10 days of exposure in ethanol 95% and 3 days in dichloromethane, although the presence of oligomers occasionally complicates this comparison.

The findings illustrate that, despite the inherent inaccuracies, non-targeted analysis can yield reproducible results across both extraction and migration conditions in ethanol 95%. The capability to detect and identify substances using methods P1-P4 is assessed here by estimating their prevalence across various batches. This assessment is subject to significant uncertainty, especially for substances with lower prevalence. Concentration levels for the most frequently encountered substances (those with the highest prevalence) significantly exceed the detection limit in both extraction and migration conditions in ethanol 95%, with values ranging from the order of mg/kg to tens of mg/kg. This demonstrates the non-targeted analysis's effectiveness in identifying substances across various conditions, albeit with varying degrees of certainty depending on the substance's prevalence.

Highlights. The chosen medium notably influences concentration ranges in tests. Dichloromethane consistently yielded the highest values, with ethanol 95% showing about half these levels. In ethanol 50%, reliability was compromised due to proximity to detection limits.
A lack of substance detection in ethanol 50% should not be misconstrued as an absence in the recyclate or non-migration; it could result from concentrations near detection limits.
A meta-analysis revealed that certain chemical families, such as ethers, salicylates, phthalate esters, and fragrances, exhibit higher prevalence than others.
A multimodal approach combining dichloromethane extraction with ethanol 95% migration testing proves to be particularly effective, with each method complementing the other's limitations. This combined approach enhances reliability in both prevalence and concentration range assessments.
There is a notable correlation between identification and quantification errors, underscoring the critical role of detection limits. In dichloromethane and ethanol 95%, most substances were detected at concentrations significantly above the detection limit, lending credibility to the robustness of identification and quantification methods employed.

***Table 10**. Comparative concentrations measured using protocols P1-P4 for twelve common substances in recycled polyolefins.*

Chemical Name ranked in the ascending order of Mw	CAS	Category 9 cat.†	M (g/mol)	P1: DCM 3d@40°C	P2: ET95 3d@60°C	P3: ET95 10d@60°C	P4: ET50 3d@60°C
				conc. in mg/kg as measured (%prevalence)			
pentanal	110-62-3	ALD	86.13	**rLDPE**: n.d. (0%) **rHDPE**: 0.243 (20%) **rPP**: n.d. (0%)	**rLDPE**: n.d. (0%) **rHDPE**: 0.342 (20%) **rPP**: n.d. (0%)	**rLDPE**: 0.401 (40%) **rHDPE**: n.d. (0%) **rPP**: 0.273 (9.1%)	**rLDPE**: n.d. (0%) **rHDPE**: n.d. (27%) **rPP**: n.d. (0%)
beta-pinene	127-91-3	TER	136.23	**rLDPE**: 0.267 (20%) **rHDPE**: 3.26 (33%) **rPP**: 0.518 (10%)	**rLDPE**: n.d. (0%) **rHDPE**: 1.2 (33%) **rPP**: 0.335 (27%)	**rLDPE**: n.d. (0%) **rHDPE**: 1.75 (33%) **rPP**: 0.509 (9.1%)	**rLDPE**: n.d. (0%) **rHDPE**: n.d. (0%) **rPP**: n.d. (0%)
benzophenone	119-61-9	UV	182.22	**rLDPE**: n.d. (0%) **rHDPE**: 4.25 (6.7%) **rPP**: n.d. (0%)	**rLDPE**: 0.998 (80%) **rHDPE**: 1.71 (20%) **rPP**: n.d. (27%)	**rLDPE**: 2.73 (40%) **rHDPE**: 2.32 (13%) **rPP**: 2.65 (36%)	**rLDPE**: n.d. (0%) **rHDPE**: 0.63 (87%) **rPP**: n.d. (30%)
amyl salicylate	2050-08-0	SAL	208.25	**rLDPE**: 0.694 (60%) **rHDPE**: 6.64 (80%) **rPP**: 4.79 (90%)	**rLDPE**: n.d. (20%) **rHDPE**: 3.89 (80%) **rPP**: 0.752 (100%)	**rLDPE**: 0.178 (60%) **rHDPE**: 4.2 (80%) **rPP**: 1.01 (91%)	**rLDPE**: n.d. (0%) **rHDPE**: 0.312 (33%) **rPP**: n.d. (0%)
2-phenyldecane	4537-13-7	AB	218.38	**rLDPE**: n.d. (0%) **rHDPE**: 6.28 (93%) **rPP**: 2.16 (90%)	**rLDPE**: n.d. (0%) **rHDPE**: 3.83 (93%) **rPP**: 0.476 (82%)	**rLDPE**: 0.184 (20%) **rHDPE**: 3.64 (87%) **rPP**: 0.579 (82%)	**rLDPE**: n.d. (0%) **rHDPE**: n.d. (0%) **rPP**: n.d. (0%)
diethyl phthalate	84-66-2	PHTH	222.24	**rLDPE**: n.d. (0%) **rHDPE**: n.d. (0%) **rPP**: 3.85 (40%)	**rLDPE**: n.d. (40%) **rHDPE**: 2.58 (13%) **rPP**: n.d. (45%)	**rLDPE**: 7.63 (60%) **rHDPE**: n.d. (0%) **rPP**: n.d. (0%)	**rLDPE**: 0.337 (20%) **rHDPE**: 0.612 (80%) **rPP**: 0.486 (80%)
3,5-di-tert-butyl-4-hydroxybenzaldehyde	1620-98-0	ALD	234.33	**rLDPE**: n.d. (0%) **rHDPE**: 0.262 (6.7%) **rPP**: 1.32 (20%)	**rLDPE**: n.d. (0%) **rHDPE**: n.d. (6.7%) **rPP**: n.d. (0%)	**rLDPE**: 2.59 (20%) **rHDPE**: n.d. (0%) **rPP**: n.d. (0%)	**rLDPE**: n.d. (0%) **rHDPE**: n.d. (20%) **rPP**: n.d. (20%)
1-(2,3,8,8-tetramethyl-1,2,3,5,6,7,8,8a-octahydronaphthalen-2-yl)ethanone	68155-66-8	FRA	234.38	**rLDPE**: 1.52 (20%) **rHDPE**: 5.36 (6.7%) **rPP**: 5.16 (90%)	**rLDPE**: 1.68 (20%) **rHDPE**: 1.95 (6.7%) **rPP**: 0.824 (91%)	**rLDPE**: 2.71 (20%) **rHDPE**: 3.03 (6.7%) **rPP**: 2.31 (100%)	**rLDPE**: n.d. (0%) **rHDPE**: n.d. (0%) **rPP**: n.d. (20%)
dioctyl ether	629-82-3	ETH	242.44	**rLDPE**: 4.48 (20%) **rHDPE**: 49 (100%) **rPP**: 5.85 (80%)	**rLDPE**: 2.89 (60%) **rHDPE**: 30 (100%) **rPP**: 2.02 (100%)	**rLDPE**: 3.21 (60%) **rHDPE**: 34.7 (100%) **rPP**: 2.85 (91%)	**rLDPE**: n.d. (0%) **rHDPE**: n.d. (0%) **rPP**: n.d. (0%)
2-ethylhexyl salicylate	118-60-5	SAL	250.33	**rLDPE**: 4.95 (20%) **rHDPE**: 22.6 (47%) **rPP**: 4.3 (50%)	**rLDPE**: 3.71 (20%) **rHDPE**: 9.45 (60%) **rPP**: n.d. (36%)	**rLDPE**: 3.89 (20%) **rHDPE**: 14.2 (53%) **rPP**: n.d. (45%)	**rLDPE**: n.d. (0%) **rHDPE**: 0.125 (27%) **rPP**: n.d. (0%)
hexadecanamide	629-54-9	AMID	255.44	**rLDPE**: 15.6 (20%) **rHDPE**: n.d. (0%) **rPP**: n.d. (0%)	**rLDPE**: 19.1 (20%) **rHDPE**: n.d. (0%) **rPP**: n.d. (0%)	**rLDPE**: 12.8 (40%) **rHDPE**: n.d. (0%) **rPP**: 2.43 (18%)	**rLDPE**: 3.62 (40%) **rHDPE**: 0.122 (20%) **rPP**: 0.304 (90%)
octocrylene	6197-30-4	UV	361.5	**rLDPE**: 16.6 (20%) **rHDPE**: 10.2 (67%) **rPP**: n.d. (0%)	**rLDPE**: 14 (20%) **rHDPE**: n.d. (13%) **rPP**: n.d. (0%)	**rLDPE**: 14.9 (20%) **rHDPE**: 4.42 (40%) **rPP**: 2.16 (36%)	**rLDPE**: n.d. (0%) **rHDPE**: n.d. (0%) **rPP**: n.d. (0%)

†Substance categories: AB: alkyl-substituted aromatic, ALD: aldehydes, AMID: fatty acid amides, ETH: ethers (symmetric or not), FRA: fragrances, PHTH: phthalate esters, SAL: salicylate esters, TER: terpenes, UV: photo-initiators.

3.4. Discussion

3.4.1. *Interpretation of the test concentration C_{test}*

Understanding the distinction between test concentrations (in mg/kg of media in contact), C_{test}, and exposure concentrations or concentration in media in contact, C_F, is crucial in the context of safety assessments for recycled materials. Experimental results demonstrated that C_{test} quickly becomes independent of time under both extraction and accelerated migration conditions. The diffusion rate for molecules up to 400 g/mol does not limit the transfer. The value of the test concentration depends solely on the thermodynamic equilibrium established between the recycled material and the contact medium. It is assumed that the liquid is sufficiently mixed so that C_{test} effectively represents the concentration in the medium

For ethanol 95% and 50%, the material balance between the start and end of the test leads to the following equilibrium:

$$C_{test} = \frac{C_P^0}{K + L_{test}}$$

Eq. 1

where C_P^0 the initial concentration of the substance in the pellet (units in mg/kg of pellets); L_{test} is the simulant-to-pellet weight ratio: 0.78 and 0.88 (close to unity) for ethanol 95% and ethanol 50%, respectively. K is the partition coefficient of the substance between the pellets and the simulant (*i.e.*, the ratio of their residual concentrations). This is the same K value that controls the thermodynamic equilibrium between the container made from these pellets and the product, assuming that the latter can be conservatively replaced by the same simulant for estimating the exposure concentration C_F.

Denoting K^{95} and K^{50} as the partition coefficients with ethanol 95% and ethanol 50%, we can derive a relative representation of partition coefficients based on the ratio of their test concentrations $x = \frac{C_{test}^{95}}{C_{test}^{50}}$ and Eq. 1:

$$K^{50} = xK^{95} + (x-1)L_{test} \approx x(K^{95} + 1) - 1$$

Eq. 2

Taking $x = 10$ as a rough but representative estimate of the ratio between simulants and $K^{95} \approx 1$ leads to K^{50} values 19 times larger. The difference in chemical affinity between ethanol 95% and ethanol 50% explains the differences in test concentrations observed on the same samples.

A similar rationale applies to tests performed in dichloromethane, but the partition coefficient involved is set between an insoluble polymer and a dispersive solvent. The value of K^{DCM} is expected to be close to zero, making Eq. 1 becomes:

$$C_{test}^{DCM} = \frac{C_P^0}{K^{DCM} + L_{test}^{DCM}} \approx \frac{C_P^0}{L_{test}^{DCM}} \approx C_P^0$$

Eq. 3

with $L_{test}^{DCM} = 1.32$ based on the density of dichloromethane (close to unity).

The lower K value in dichloromethane would explain the generally higher test concentrations than in simulants. Using dichloromethane offers a more robust estimate of the residual concentration in the pellets (C_P^0) regardless of the substance's polarity.

Highlights.
The value of the test concentration C_{test} is determined by two quantities that may not be known: the partition coefficient K_{test} and the initial concentration in the pellets C_P^0. The difference in partition coefficients in ethanol 95% and ethanol 50% explains the significant concentration variations observed between the two simulants.
Only the dichloromethane test could yield results independent of K_{test} for all substances since $K^{DCM} < 1$. As it leads to values close to total mass transfer (full extraction), it provides the most accurate estimator of C_P^0.

3.4.2. *Distribution of substance prevalence across samples and polymers*

The distribution of prevalence for both detected and identified substances provides critical insights. Assuming that each method ideally has similar efficacy in detecting substances, the prevalence rates should align across methods. Substances commonly present in different samples should exhibit a prevalence greater than 50%. These dynamics are depicted in **Figure 4**.

For substances with a prevalence over 50%, extraction conditions under P1 (using DCM) demonstrated superior detection effectiveness. Conversely, the P3 method appears more effective for substances with lower prevalence, especially under migration conditions in ethanol 95%. The P4 method, involving migration in ET50, shows the least efficiency, with a notable detection gap ranging between 35% and 47%. A comparative analysis between P1 and P3 suggests an uncertainty range of 5 to 30 substances, emphasizing the need for combining results from both P1 and P3 to minimize this uncertainty.

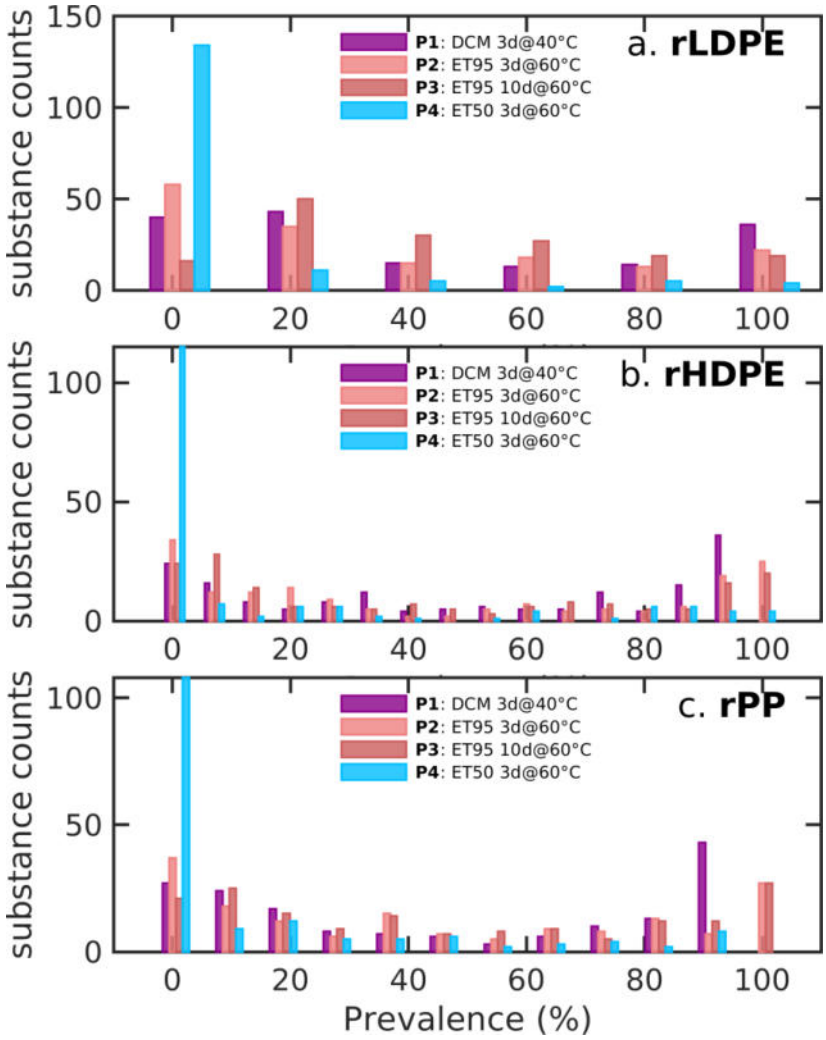


***Figure 4**. Prevalence of detected substances across samples (a: 5 samples of rLDPE, b: 15 samples of rHDPE, c: 11 samples of rPP) as determined by test methodologies (P1-P4).*

3.4.3. *Prevalence benchmarks for each toxicological class*

The ability of each test method to identify hazardous substances is further scrutinized in **Figure 5**. This figure benchmarks the performance of each method against P1, assessing the average prevalence ratios for different toxicological classes. It becomes evident that methods P2 and P4 are less reliable for identifying hazardous substances, particularly those suspected of being genotoxic or classified under Cramer Class III. In comparison, P1 and P3 methods yield relatively consistent results, with an uncertainty margin of about 20% for all identified substances, attributable to issues like column bleeding and the presence of oligomers.

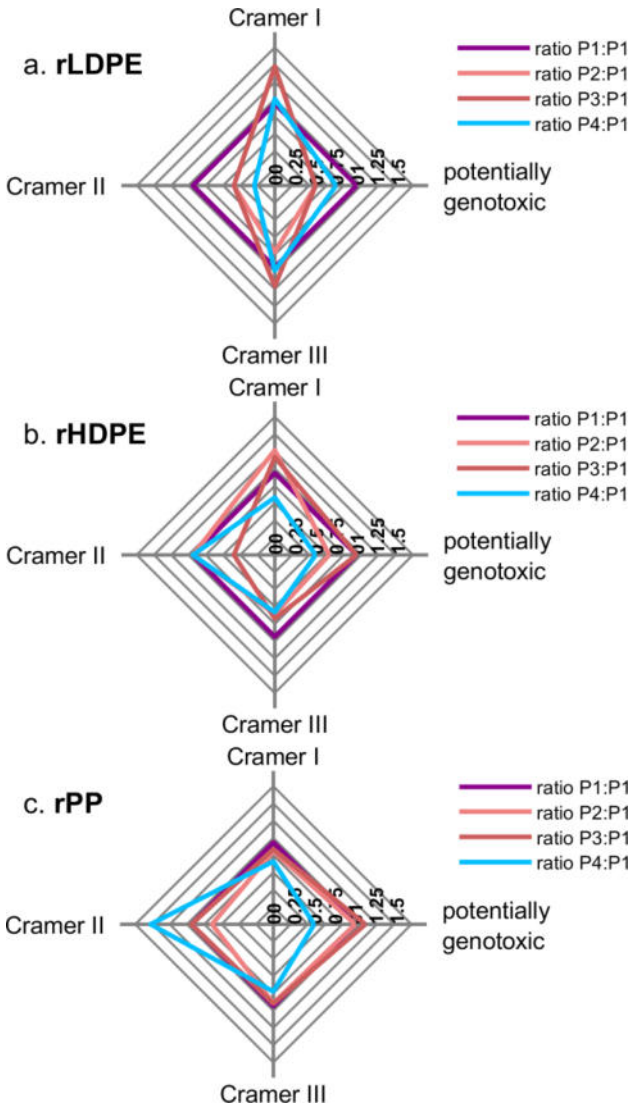


***Figure 5**. ratio of average substance prevalence relative to the P1 method for different toxicological classes. A ratio below one indicates a shortfall in the method's detection capabilities.*

3.4.4. *Influence of detection limits and testing protocols on substance identification and quantification*

The interplay between analytical detection limits and specific test protocols (P1-P4) significantly impacts our ability to identify and quantify hazardous substances. Substances with concentrations near the detection limit are more likely to evade detection, potentially leading to an underestimation of their prevalence. The potential interrelation between the prevalence of substances and their concentrations, as revealed in tests P1-P4, is systematically examined in **Figure 6**.

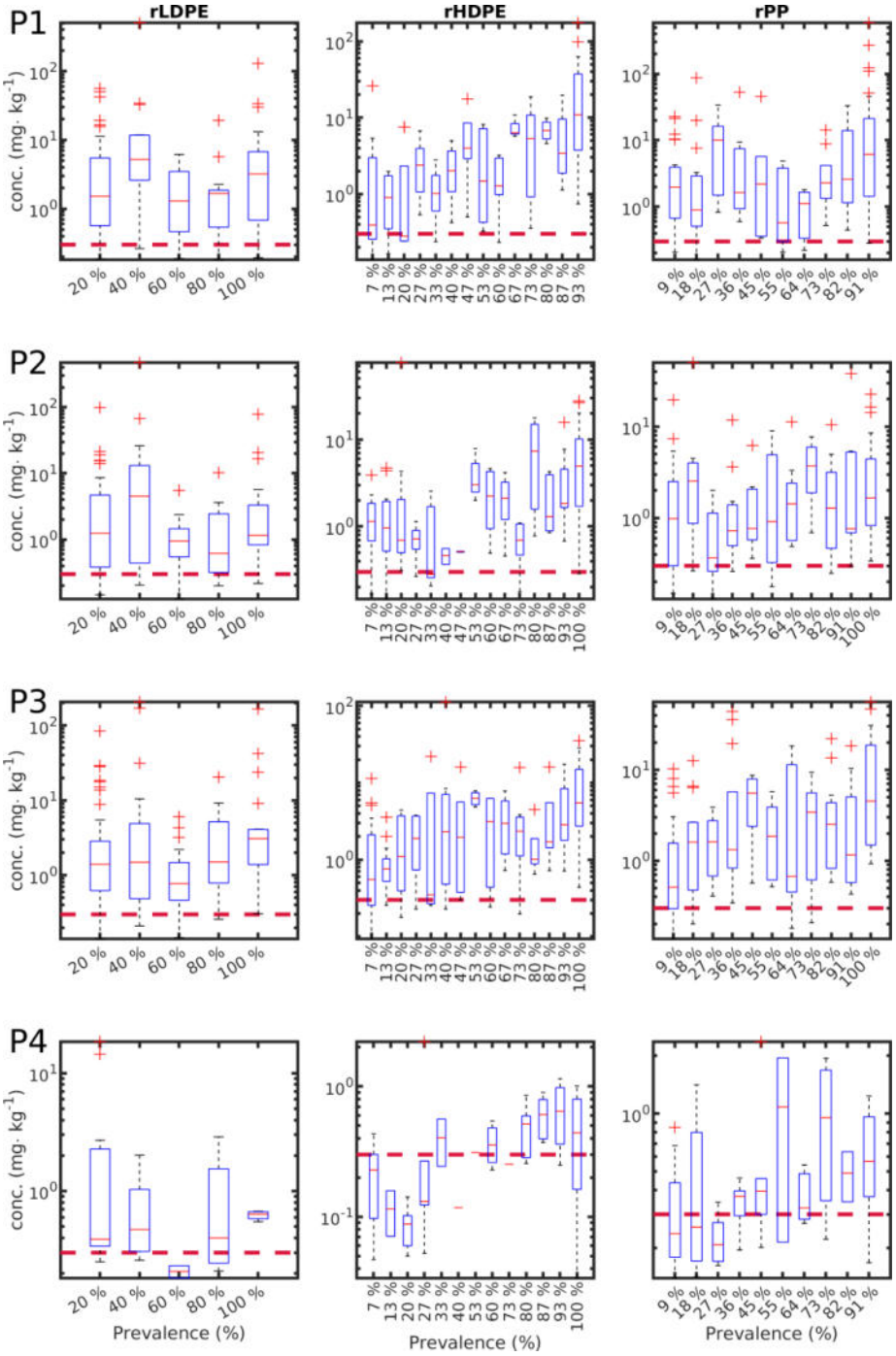


Figure 6*. Correlation between measured concentrations (logarithmic scale) and the prevalence of substances. Concentration data are visualized using box-and-whisker plots, where the central box delineates the interquartile range (25th to 75th percentile) with the median concentration highlighted by a red line. Whiskers extend from the box to denote the 5th and 95th percentiles, while outliers are indicated by red crosses. A thick red dash line marks the quantification limit, set at* $0.3\ mg \cdot kg^{-1}$*, serving as reference for reliable concentration levels.*

A correlation between concentration and prevalence implies a bias in the detection method, suggesting that substances with higher concentrations are more prevalently detected. This bias is observable across all polymers and is particularly pronounced in the P4 test with HDPE, where the larger sample size enhances statistical significance. The P4 method often records concentrations close to detection limits, thus underestimating the real prevalence of substances.

These analyses highlight the critical need for robust testing protocols to reliably detect a wide range of substances, particularly those posing potential hazards. The choice of testing method and understanding its limitations and biases are crucial in accurately assessing the safety of recycled polymers.

Highlights.
Key findings emerged when evaluating the detection methods for chemicals in recycled polymers. The P1 extraction method in dichloromethane (DCM) showed superior detection capabilities for substances with over 50% prevalence, while the P3 method excelled for substances with lower prevalence. The P4 method, using ET50, however, was less effective, revealing a notable shortfall in detecting a wide spectrum of substances.

Comparative analysis indicated that methods P2 and P4 were less reliable in identifying hazardous substances, particularly those suspected to be genotoxic or classified under Cramer Class III. In contrast, P1 and P3 yielded more consistent results, with an estimated 20% uncertainty mainly due to column bleeding and the presence of oligomers.

The interplay between detection limits and testing protocols significantly influenced substance identification. Near the detection limit, hazardous substances are more likely to be missed, potentially leading to underestimation. This was especially evident in the P4 test with HDPE, where concentrations close to detection limits masked the true prevalence of substances.

These insights highlight the importance of selecting robust testing protocols for recycled polymers. Understanding these methods' limitations and biases is crucial for accurate and reliable safety assessments. This approach ensures that assessments reflect real-world contamination scenarios, guiding effective strategies for material safety in recycling.

3.4.5. *Cosmetic/homecare product categories and the choice of simulants*

In the CosPaTox project, ethanol 95% v/v and ethanol 50% v/v served as key simulants for assessing the migration of substances from post-consumer recycled (PCR) plastics into cosmetic products. These simulants were strategically selected to overestimate potential material-simulant interactions and exposure levels, while also facilitating analytical processes. The choice was not primarily driven by their resemblance to actual cosmetic formulations but more by their efficacy in representing a wide range of product characteristics.
For a comprehensive safety assessment of recyclates in cosmetic packaging, ethanol 95% (or dichloromethane as an alternate) emerges as the preferred simulant for hazard identification and risk characterization. This preference is underpinned by multiple independent studies that validate its effectiveness in safely estimating the concentration of hazardous chemicals within hydrophobic cosmetic formulations [13-15]. Conversely, ethanol 50% is more apt for evaluating the migration in hydrophilic (polar) cosmetic products, as well as in detergents and home care products, where its properties align better with the product nature.

Highlights. Ethanol 95% emerges as the optimal simulant for evaluating the safety of post-consumer recycled (PCR) polyolefins in contact with cosmetics, detergents, and home care products. It effectively aids in substance detection and accurate toxicological classification. In ethanol, 95% concentration assessments are reliable for extrapolating exposure concentrations in hydrophobic products. Ethanol 50%, while not ideal for hazard identification, is apt for assessing migration into hydrophilic cosmetic formulations and various home care products.

4. Estimation of the Exposure Concentration C_F

For risk assessment, mass transfer needs to be evaluated via the concept of exposure concentration C_F, which is the expected concentration in the product. For other interpretations of mass transfer in particular as amounts instead of concentrations, refer to Appendices 2,3 and 7.

4.1. Principles of the extrapolation from test to exposure concentration

The concentration determined in tests, particularly when using a dilution factor L_{test} close to unity (see experimental protocols in **Table** 4), is not representative of the exposure concentration C_F consumers might encounter, assuming that accelerated conditions may represent the state of mass transfer at the end of product shelf-life. This discrepancy necessitates careful consideration when interpreting test results for real-world exposure scenarios.
To bridge this gap, a conservative method for extrapolating the test concentration, C_{test} from the test dilution factor L_{test} to the actual product usage dilution factor, L_{actual}, is employed. The formula to estimate exposure concentration is adapted as follows:

$$C_F = \frac{C_P^0}{K + L_{actual}}$$

Eq. 4

where C_P^0 represents the initial concentration of the substance in the pellet and K, the partition coefficient between the recyclate and the simulant partition coefficient, are the variables to be determined.

Integrating Eq. 1 (or its alternative, Eq. 3), we can reframe Eq. 4 to eliminate dependency on C_P^0:

$$C_F = \frac{K_{test} + L_{test}}{K + L_{actual}} C_{test}$$

Eq. 5

In this equation, K_{test} equals K when employing ethanol-based simulants (either 50% or 95%).

Given the practical scenario where K significantly exceeds L_{actual}, a series of pragmatic approximations can be applied to streamline the estimation process. **Appendix 4** shows that L_{actual} exceeds unity, often reaching values as high as 50, where 3 is a lower bound (see typical cosmetic packaging details **Table 20 and Table 21** and **Appendix 5**).

Highlights: This conservative extrapolation strategy aims to align test concentrations closer to real-life exposure concentrations by accounting for the difference in dilution factors between test conditions and actual product use. By adjusting for the partition coefficient and devising a method that circumvents the direct need to determine the initial concentration, C_P^0, Eq. 5 offers a more tailored and theoretically grounded approach to predicting consumer exposure levels from PCR materials.

4.2. Estimating Partition Coefficients between Recyclates and Ethanol-based Simulants

Utilizing dicholoromethane test to approximate the initial concentration in the pellets $C_P^0 \approx L_{test}^{DCM} C_{test}^{DCM}$ (referencing Eq. 4), we can apply Eq. 1 to calculate the partition coefficients between recyclates in relation to both ethanol-based simulants:

$$K^{95} \approx \frac{L_{test}^{DCM} C_{test}^{DCM}}{C_{test}^{95}} - L_{test}^{95}$$

$$K^{50} \approx \frac{L_{test}^{DCM} C_{test}^{DCM}}{C_{test}^{50}} - L_{test}^{50}$$

Eq. 6

Here, the superscripts 95 and 50 denote the ethanol content of the simulant, either 95 or 50 %, respectively. The calculated partition coefficients across all substances identified in dichloromethane and simulant tests are depicted in **Figure 7**. For ethanol 95%, partition values predominantly cluster around unity, indicating a balanced distribution. Conversely, for ethanol 50%, values are more varied, ranging up to 1000, aligning with the lower concentrations observed in ethanol 50% tests. The median values for ethanol 50% lie between 10 and 35, which are similar to L_{actual} values. Notably, values near or below unity are recorded for higher polarity substances.

Highlights:
The differentiation in partitioning between ethanol 95% and 50% underscores the hydrophobic nature of substances within recyclates.
With ethanol 95%, partition coefficients (K^{95}) are reasonably assumed to hover around unity, suggesting a near-equal distribution between the simulant and recyclate.
The spread of partition coefficients with ethanol 50% reflects a broad spectrum of substance behaviors, making it challenging to pinpoint a singular value for all. Median values align with or exceed L_{actual}, though lower coefficients are possible for polar substances.

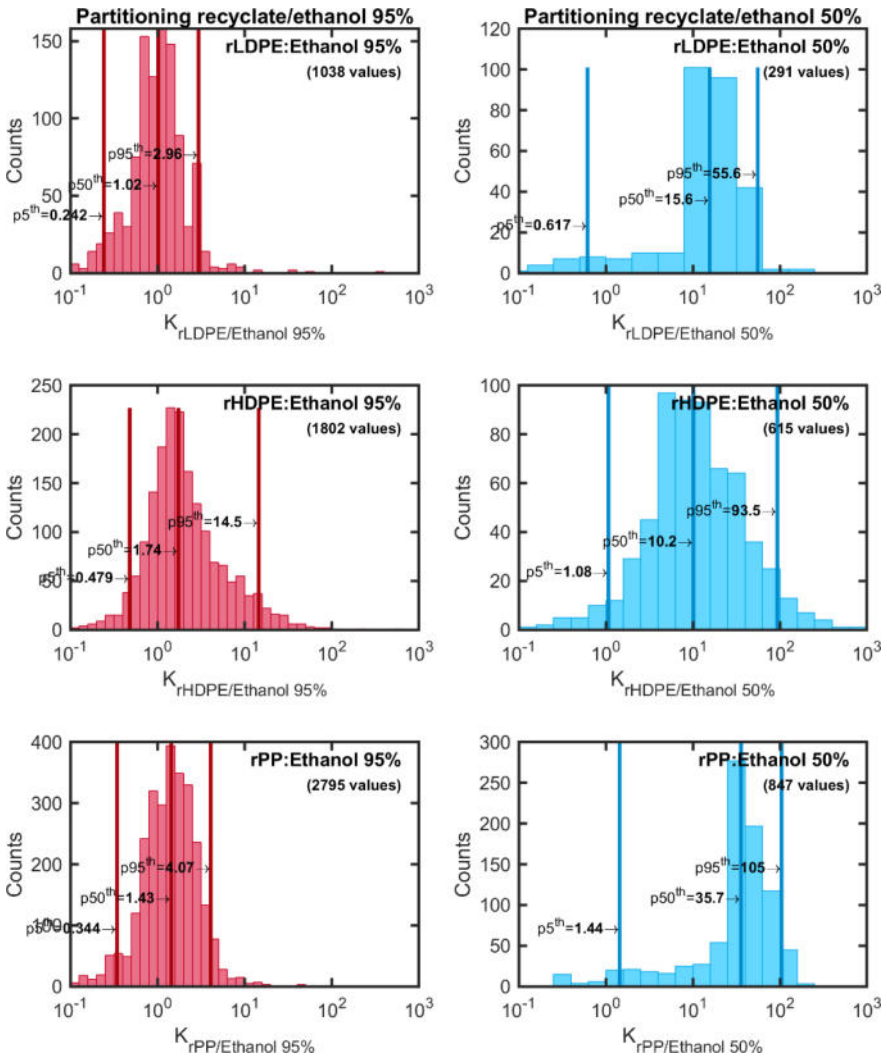


***Figure 7**. Displays the distribution of partition coefficients for substances across the three recyclate families when interacting with ethanol-based simulants. The vertical bars represent the 5th , 50th and 95th percentile values, as p5th, p50th and p95th, respectively.*

4.3. Practical Rules to Estimate Conservatively Consumer Exposure

Two strategies can be applied to evaluate the exposure concentration C_F. The first involves combining an extraction test in dichloromethane, which assesses the concentration in the recycled material C_P^0, with a test in the simulant recommended for the intended application. This approach requires no approximations and yields coherent results as long as $C_{\text{test}}^{\text{DCM}} \geq C_{\text{test}}^{95}$ or $C_{\text{test}}^{\text{DCM}} \geq C_{\text{test}}^{50}$. The second strategy uses a single test and employs an approximation for the denominator $K + L_{\text{actual}}$ in Eq. 5. Table 1 summarizes the different possibilities and the rationale behind the proposed choices to always overestimate the exposure concentration, regardless of the source of uncertainty.

This approach ensures that the estimated consumer exposure is calculated conservatively, considering all potential variables and uncertainties involved in the process. By adhering to these practical guidelines, risk assessors can ensure a higher level of safety in evaluating consumer exposure to substances from recycled materials.

The estimators have no uniqueness because they depend on the testing strategy. Even with the extraction test in dichloromethane, there is an assumption about the partition coefficient with the solvent and therefore about the reality of total extraction. All the estimators produced are constructed to be conservative in all cases. In the case of the test in ethanol 95%, a dilution effect of the migration is considered. On the other hand, in the case of ethanol 50%, the dilution effect is not introduced because it is considered that the recycled material is far from being depleted of hydrophobic substances under test conditions. The more polar substances would be depleted, but since the dilution effect is not applied, the estimator also remains conservative in this situation.

Definition

In our assessment framework, an 'estimator' is defined as a mathematical model or formula tailored to conservatively estimate exposure levels to substances within recycled materials. This conservative estimation is crucial in situations where direct measurement is unfeasible, for instance, when evaluations are performed on pellets rather than the finished product. By design, an estimator conservatively extrapolates and inherently overestimates exposure concentrations from test outcomes. It incorporates considerations of uncertain partition coefficients and actual dilution factors, affecting test results and real-world mass transfer dynamics. This method ensures a cautious approach, prioritizing safety particularly when one single test is applied.

Important notice

The application of dual tests (specifically, a combination of extraction and migration tests) for exposure estimation is limited strictly to substances that have been confidently identified in both tests. This methodology does not apply to substances identified in only one test or remain unidentified. The exposure estimation must rely on a single-test estimator for these latter categories. Consequently, even with the preference to utilize a dual-test estimator for identified substances, it becomes necessary to also employ a single-test estimator for unidentified substances or those detected at the limit of quantification. This approach ensures comprehensive coverage, acknowledging that such substances, by their nature, cannot be consistently paired across both extraction and migration tests.

Highlights. Given the complexity of establishing a unified estimator based on the chosen test strategy, it is crucial to understand that even with dichloromethane extraction tests, assumptions about the partition coefficient with the solvent, and thereby on the completeness of extraction, are made.

All the estimators devised are structured to ensure conservatism under all circumstances. Specifically, in ethanol 95% tests, a dilution effect of migration is considered. However, in ethanol 50% tests, this dilution effect isn’t applied since it is presumed that the recycled material isn't fully depleted of hydrophobic substances under test conditions. While polar substances might be exhausted, the absence of applied dilution effect ensures the estimator remains conservative even in this scenario.

Table 11. Practical relations to estimate exposure concentrations conservatively from test concentrations. The equations assumed that L_{test} is close to unity.

Number of tests performed (target)	Type of test	Robust estimators overestimating exposure	Justification/Rationale
Dual-test (lipophilic product)	Dichloromethane (^{DCM}) AND Ethanol 95% (^{95})	$C_P^0 \approx L_{test}^{DCM} C_{test}^{DCM} \approx C_{test}^{DCM}$ $K \approx \frac{C_P^0}{C_{test}^{95}} - L_{test}^{DCM} \approx \frac{C_{test}^{DCM}}{C_{test}^{95}} - 1$ $C_{exposure} = \frac{C_P^0}{K + L_{actual}}$ *Eq. 7*	No approximation beyond $K_{test}^{DCM} \approx 0$. If due to experimental errors $C_{exposure} < 0$, use $C_P^0 \approx (1 + L_{test}^{DCM}) C_{test}^{DCM} \approx 2$. In this alternative scenario, $K_{test}^{DCM} \approx 1$.
Dual-test (aqueous product)	Dichloromethane (^{DCM}) AND Ethanol 95% (^{95})	$C_P^0 \approx L_{test}^{DCM} C_{test}^{DCM} \approx C_{test}^{DCM}$ $K \approx \frac{C_P^0}{C_{test}^{50}} - L_{test}^{DCM} \approx \frac{C_{test}^{DCM}}{C_{test}^{50}} - 1$ $C_{exposure} = \frac{C_P^0}{K + L_{actual}}$ *Eq. 8*	
One single-test (lipophilic product)	Dichloromethane (^{DCM})	$C_{exposure} = \frac{K_{test}^{DCM} + L_{test}}{K^{95} + L_{actual}} C_{test}^{DCM} \approx \frac{C_{test}^{DCM}}{1 + L_{actual}} \approx \frac{C_{test}^{DCM}}{L_{actual}}$ *Eq. 9*	$K_{test}^{DCM} \approx 0$ $K^{95} \approx 1$ $L_{actual} > 1$
One single-test (lipophilic product)	Ethanol 95% (^{95})	$C_{exposure} = \frac{K^{95} + L_{test}}{K^{95} + L_{actual}} C_{test}^{95} \approx \frac{2}{1 + L_{actual}} C_{test}^{95} \approx 2 \frac{C_{test}^{95}}{L_{actual}}$ *Eq. 10*	$K^{95} \approx 1$ $L_{actual} > 1$
One single-test (aqueous product)	Ethanol 50% (^{50})	$C_{exposure} = \frac{K^{50} + L_{test}}{K^{50} + L_{actual}} C_{test}^{50} \approx \frac{K^{50}}{K^{50} + L_{actual}} C_{test}^{50} \approx C_{test}^{50}$ *Eq. 11*	$K^{50} > L_{actual}$ $L_{actual} > L_{test}$

4.4. Concentration Exposure for Substances Present at the Detection Limit or Below

Exposure concentration values for substances at or below the detection limit (DL) are deduced solely from single-test estimators (see **Table 11**). The corresponding values, C_F^{DL}, based on DLs of 0.3 mg/kg and 0.1 mg/kg, are presented in **Table 12** for the typical 200 mL bottle scenario investigated in this study ($L_{actual} = 8.3$, refer to **Table 3**). A significant implication of presuming unidentified substances might be present at the DL is their estimated exposure in ethanol 50%, being 4.2 times greater than in ethanol 95%. This discrepancy arises from the non-application of dilution effects in the ethanol 50% results, coupled with the uniform detection limits across both simulants.

***Table 12**. Exposure concentrations for substances at the detection limit (DL) when $L_{actual} = 8.3$.*

Type of test(code): Target	**Practical Relation (from**	$\boldsymbol{DL}$**=0.1 mg/kg**	$\boldsymbol{DL}$**=0.3 mg/kg**
Dichloromethane (DCM): lipophilic product	$C_{exposure} \approx \frac{DL}{L_{actual}}$	$C_{exposure}$≤0.012 mg/kg product	$C_{exposure}$≤0.036 mg/kg product
Ethanol 95% (95): lipophilic product	$C_{exposure} \approx 2\frac{DL}{L_{actual}}$	$C_{exposure}$≤0.024 mg/kg product	$C_{exposure}$≤0.072 mg/kg product
Ethanol 50% (50): aqueous product	$C_{exposure} = DL$	$C_{exposure}$≤0.1 mg/kg product	$C_{exposure}$≤0.3 mg/kg product

Highlights:
Exposure estimates for substances at or below detection limits significantly vary depending on the simulant used, highlighting a more conservative approach in ethanol 50% due to the non-application of dilution effects, unlike in ethanol 95%.

The factor 2 applied to ethanol 95% (assumption of equal distribution between pellets and simulant) does not hold for dichloromethane (assumption of complete extraction). Exposure concentrations derived from measurements at or below detection limits are consequently twice lower.

For a detection limit of 0.1 mg/kg, the lowest exposure concentration C_F applicable for the highest L_{actual} value of 50 is 0.004 mg/kg and 0.1 mg/kg in ethanol 95% and ethanol 50%, respectively.

4.5. Discussion

Table 13 illustrates that the test concentration (C_{test}) significantly overestimates the actual exposure concentration (C_F). This discrepancy arises from employing a mass dilution ratio (L_{test}) in testing scenarios that is considerably lower than what is observed in real container applications ($L_{test} \ll L_{actual}$). A comparison of concentrations from test P3 (1:1 contact in ethanol 95%) and bottle B1 reveals that employing C_{test}^{95} as an approximation for C_F results in a median overestimation factor of 12.6, aligning closely with the actual dilution ratio (L_{actual}) of 8.3. It is noteworthy that only 0.2% of the test values yielded underestimations compared to the concentrations found in bottles, with some instances of overestimation reaching up to a factor of 100. Given the impracticality of these overestimation factors in reflecting true consumer exposure, it is advised to apply Eq. 10 and incorporate L_{actual} in the C_F estimation process. The rationale for maintaining a degree of conservatism in this approach is further substantiated in subsequent discussions for both identified substances and those non-identified yet detected.

4.5.1. *Robustness of the estimation of exposure concentration C_F from test concentration C_{test}: application to ethanol 95% tests*

The reliability of the estimator outlined in **Table 11** for calculating exposure concentration C_F from test concentration C_{test} for a broad range of substances was assessed in ethanol 95% using an assumption of one single test (*i.e.*, Eq. 10). This evaluation involved a comparison between estimated C_F values derived from pellets subjected to a 10-day maceration in ethanol 95% at 60°C and direct migration measurements from bottles B1 after undergoing a 10-fold reconcentration. The comparative analysis, illustrated in **Figure 8**, encompasses 1043 paired comparisons. The findings indicate a median overestimation of migration by Eq. 10 by a factor of 3, deemed conservative and thus suitable for safety assessment purposes. The likelihood of underestimating migration stands at 8.3%. Employing a unit partition coefficient $K = 1$ introduces greater conservatism compared to $K = 0$, the latter implies complete migration into ethanol 95%, especially when applying a minimal test dilution factor. Opting for $K = 0$ would have increased the underestimation risk to 25.7%, with actual migration rates being 0.42 times lower or less than the estimated value for 5% of the samples, demonstrating a cautious approach to estimating exposure concentrations.

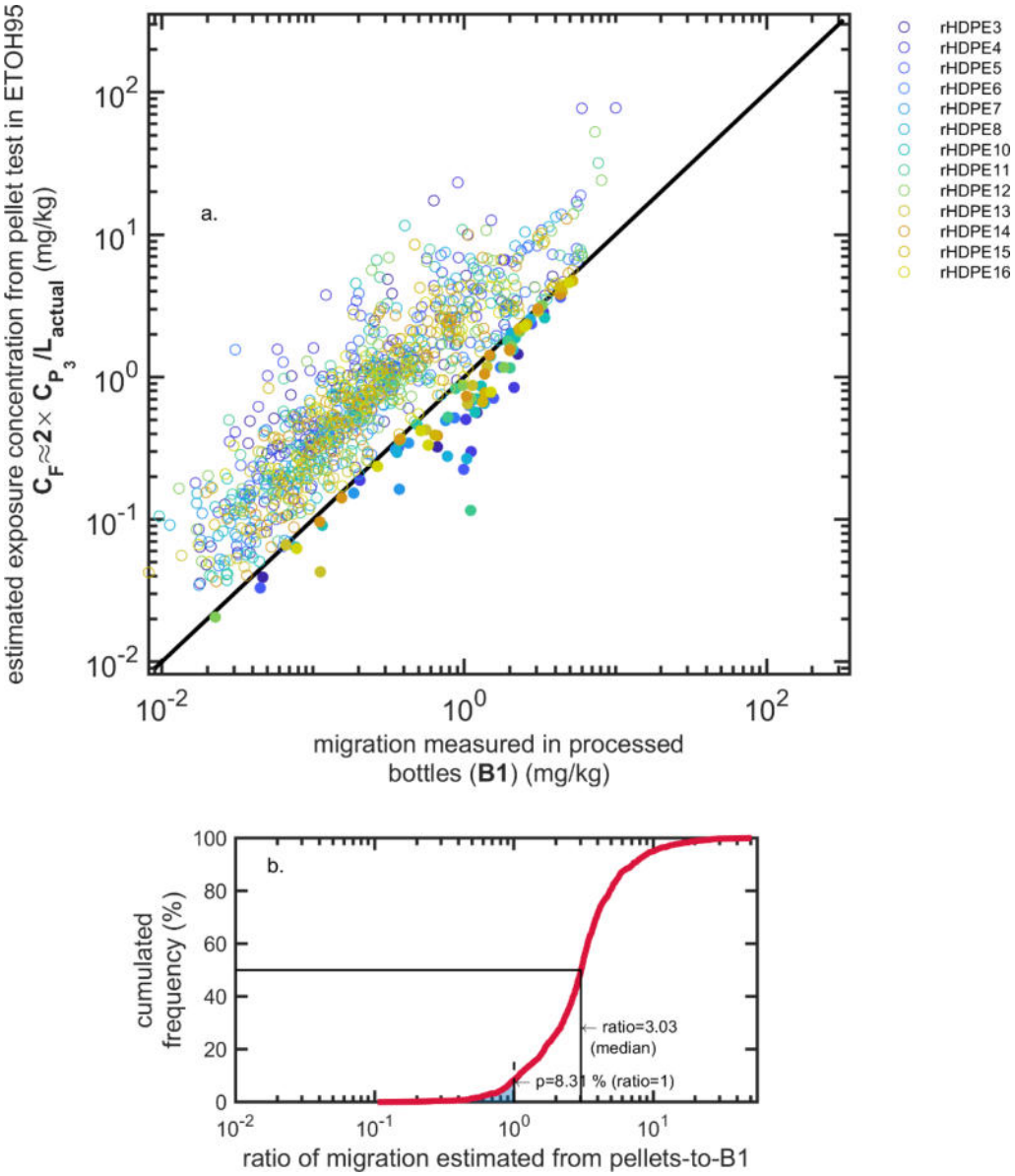


***Figure 8**. Comparative analysis of estimated exposure concentrations (single-test estimator for ethanol 95%) and direct migration measurements. (a) This graph compares exposure concentrations estimated using Eq. 1 based on pellet tests and the actual migration concentrations obtained from bottles manufactured from the same HDPE recycled pellets. The analysis encompasses 1043 paired comparisons, focusing on substances concurrently identified in both pellet and bottle tests across thirteen HDPE recycled pellet samples. The underestimated values appear with filled symbols. The solid line represents the equation y=x. (b) Distribution of the ratio C_F-to-actual migration ratio in bottles B1.*

Highlights.
Equation 10 is a reliable method for extrapolating exposure levels in ethanol 95% based on pellet tests, adaptable to specific container geometries.
The methodology demonstrates a controlled risk of underestimation at approximately 8% while typically overestimating exposure by a factor of 3, ensuring a conservative safety margin.
Central to this extrapolation method is the dilution ratio, defined as the ratio of product weight to container weight, providing a crucial factor in estimating exposure concentrations.

4.5.2. *Distribution of C_F Values from Single-test Extrapolations*

Single-test extrapolations are indispensable for estimating actual exposure concentrations for substances, whether they are identified, unidentified, detected, or not. When employing ethanol 95% tests for extrapolation, both the actual dilution factor and a factor of two are considered, accounting for both partitioning and the dilution effect during the test. Conversely, with ethanol 50% tests, the recycled material is hypothesized to act as an infinite reservoir, resulting in an actual exposure concentration that remains unaffected by the liquid volume in contact. This premise aligns with the expectation of minimal fraction transfer in aqueous simulants. **Figure 9** depicts the extrapolated actual exposure concentrations for shampoo (aqueous product) and body lotion (lipophilic product) scenarios, assuming storage in 200 mL bottles crafted from tested rLDPE, rHDPE, and rPP pellets. The displayed distributions compile all recorded values from both identified and unidentified substances across all samples of each polymer type.

Distinct distributions emerge between identified and unidentified substances, the latter often linked with lower test concentrations. The exposure concentration values determined for the detection limits (0.1 and 0.3 mg/kg) are critical for risk assessments concerning non-detected substances at or below these limits. Notably, in ethanol 50%, up to half of the unidentified substances fall below the detection threshold, compared to less than a quarter for identified substances. This discrepancy underscores the conservative nature of extrapolating from ethanol 50% test results. In ethanol 95%, the exposure from detected substances markedly differs from potential exposure due to undetected substances.

Assuming the tested samples and substances accurately represent market-available streams, the maximum exposure concentration for a 200 mL bottle could ascend to 100 mg/kg in a lipophilic product, with a median value just under 1 mg/kg. For aqueous products, the peak concentration would not exceed 10 mg/kg, with median values ranging between 0.1-0.4 mg/kg—lower for unidentified substances and higher for identified ones.

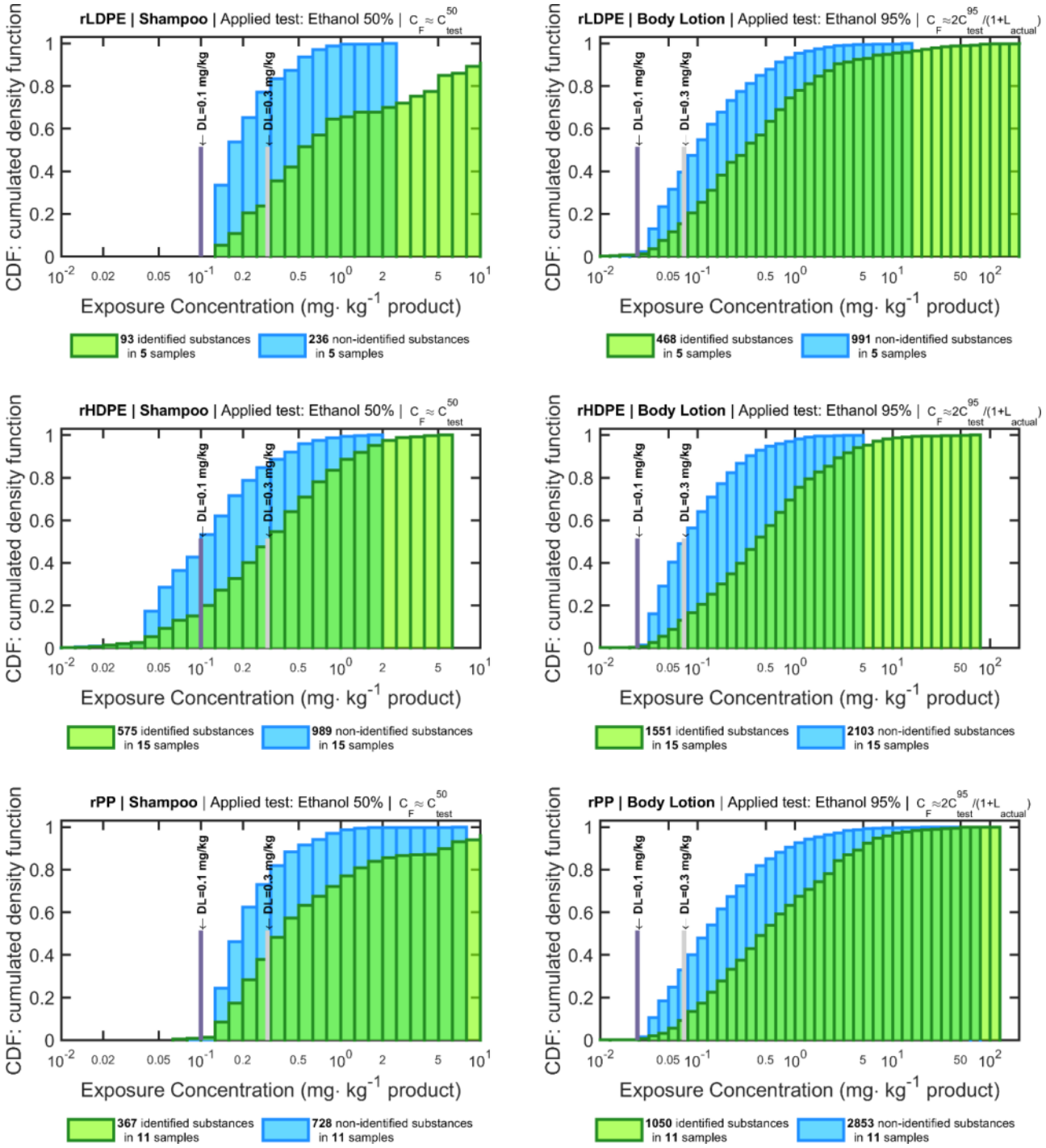


***Figure 9**. Cumulative Distribution Function (CDF) of actual exposure concentrations (mg/kg in simulant) extrapolated from pellet tests to shampoo (aqueous) and body lotion (lipophilic) stored in 200 mL bottles for all substances detected in all tested samples of rLDPE, HDPE, and rPP. Distinct distributions for identified and non-identified substances are presented. Vertical bars indicate exposure concentrations for non-identified substances, posited to be at two detection limits: 0.1 and 0.3 mg/kg in the test.*

Highlights:

Employing a single-test approach is contingent upon multiple assumptions ensuring the conservative nature of expected exposure concentration estimators. Factoring in an assumption of substance exposure at detection limits is crucial, given many substances, especially unidentified ones, are near these limits.

The feasibility of identifying substances through non-targeted analysis cannot be deemed independent of concentration, with identification becoming increasingly challenging at lower concentrations.

Exposure concentration values are reasonably presumed dependent on polymer concentration but independent of polyolefin type, allowing uniform extrapolation rules for LDPE, HDPE, and rPP. The predominance of transferable hydrophobic substances in recycled polyolefins does not rule out a reservoir effect of the material in tests, coupled with high partition coefficients leading to low test or exposure conditions concentrations, which are dilution-independent.

For substances that can be identified, uncertainty in their assessment can be addressed by performing an extraction test with dichloromethane or by comparing results from a migration test using ethanol 95%. Nevertheless, this strategy does not have universal applicability. Insights from the CosPaTox project reveal that employing dichloromethane to enhance detection or identification proves to be marginally beneficial; it showed improvement for fewer than 25% of substances that were either undetected or unidentified in the ethanol 95% tests

5. Safety Evaluation Framework for Recyclates in Cosmetic and Detergent Applications

This section delineates the comprehensive safety assessment protocols applied to substances potentially present in materials, whether they are completely detected and identified or not. The employed methodologies are grounded in quantitative risk assessment standards, recognized and endorsed by international regulatory authorities. These protocols are designed to protect human health against a spectrum of exposures, encompassing environmental pollutants to food-related hazards and substances absorbed after skin contact [16].

5.1. Overview

The safety evaluation scheme for post-consumer recycled (PCR) materials intended for cosmetic and detergent uses is a rigorous and structured process that involves several critical stages to ensure consumer protection. This multifaceted assessment aligns with regulatory requirements, including those outlined by the Cosmetic Regulation and REACH. It is further reinforced by established risk assessment frameworks, such as those elaborated by the US Environmental Protection Agency (EPA) [17].
The process is summarized in **Figure 10**. It commences with planning and scoping to delineate the risk assessment's scope and determine the appropriate methodology for the evaluation. A problem formulation stage follows, establishing the major factors relevant to the specific assessment and developing a conceptual model that outlines the relationship between stressors and human health effects. This forms the basis for the risk assessment, which is divided into exposure and effects assessments—evaluating both the potential for exposure to the consumer and the possible adverse health effects due to that exposure.

An essential aspect of the evaluation of PCR materials is the exposure-based risk assessment (EBRA), which emphasizes that risk is not solely predicated on the presence of a chemical but also on the level and context of consumer exposure. Risk characterization integrates both exposure and effects assessments to provide a cohesive set of conclusions about the risk, adhering to the principles of transparency, clarity, consistency, and reasonableness.
Safety data for known plastic additives and their common degradation products are well-documented and readily accessible. However, non-intentionally added substances (NIAS) present a unique challenge, often necessitating additional safety evaluations. Techniques like Structure-Activity Relationship (SAR), the Threshold of Toxicological Concern (TTC), and Physiologically Based Pharmacokinetic (PBPK) modeling are invaluable in these scenarios, providing means to address data gaps and refine risk assessment assumptions.
The effects assessment considers the full spectrum of potential toxicological impacts, from systemic toxicity to localized effects like skin sensitization. While traditional animal toxicity studies have been the mainstay of hazard data, contemporary approaches now incorporate in vitro, in-silico methods, and epidemiological studies, contributing a wealth of nuanced data to the hazard identification phase.

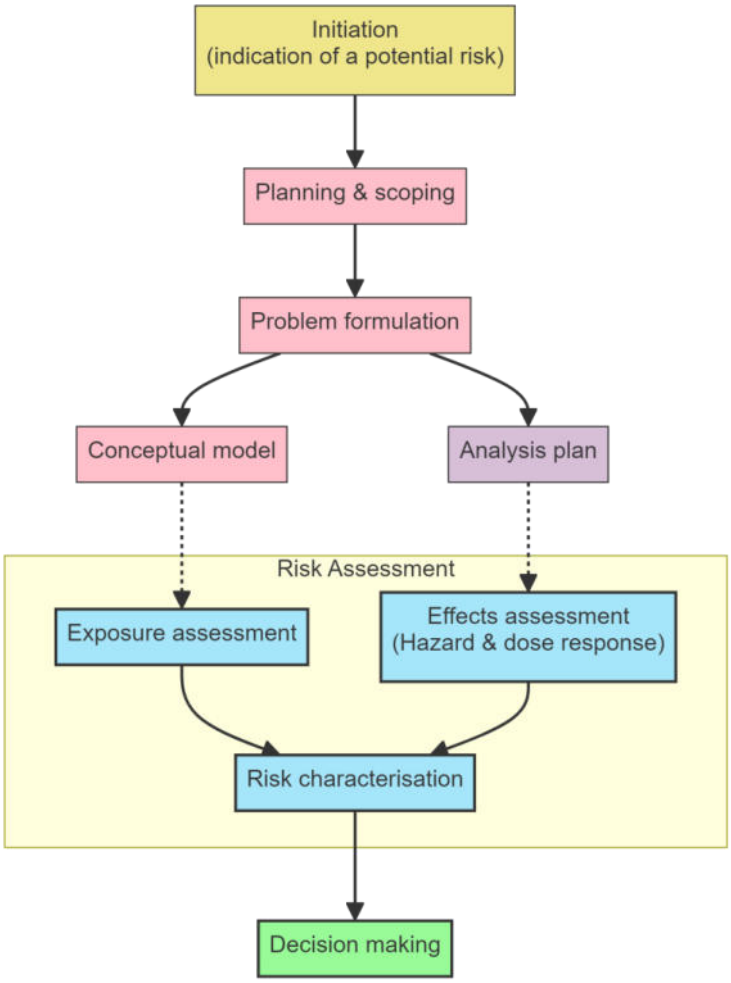


***Figure 10**: Visualization of the* risk assessment *approach, based on [17].*

The final determination of safe exposure levels takes into account the entirety of available toxicological data, including acute, chronic, carcinogenic, mutagenic, and reproductive toxicity effects. Toxicologists and safety assessors are tasked with reconciling conflicting data and deriving a unified threshold for safe exposure, employing a weight-of-evidence approach. An overview of available approaches for PCR materials is summarized in **Table 13**.

Due to the large spectrum of substances in PCR materials with many of them having incomplete toxicological profiles, read-across strategies and in silico predictions supplement the data landscape, guided by frameworks such as those from the European Chemicals Agency (ECHA) and tools like ToxTree[7] and the OECD QSAR toolbox [18]. These predictions and classifications hinge on a thorough understanding of the substance's chemical structure, necessitating expert oversight in their application.

For substances with minimal exposure to chemicals of unknown toxicological profile, the TTC approach is pivotal in scenarios, providing a threshold below which there is no significant risk to human health. This is particularly applicable in the context of recycled materials for packaging, where the TTC model offers a pragmatic and conservative method for ensuring safety.

Table 13. Approaches to Defining Safe Levels of Substances in Post-Consumer Recycled Materials

Data Availability	Methodology or Approach	Description
Comprehensive Data Set	Direct Threshold Values	Utilize established safe levels such as TDI, RfD, DNEL, specific to exposure routes (oral, inhalation, dermal) derived from extensive toxicological studies.
Limited or No Toxicological Data but the Chemical Structure is Known	Read-Across Approach	Apply toxicological profiles of similar substances to infer safe levels, guided by frameworks from authoritative bodies like ECHA.
Only the Chemical Structure is Known	In Silico Prediction including TTC Approach	Computational models, such as ToxTree or the OECD QSAR toolbox, can predict toxicological properties and assign risk levels based on chemical structure. The Threshold of Toxicological Concern (TTC) methodology assigns default safety thresholds based on Cramer classes for substances without specific toxicity data.
No Structure Information	Genotoxic TTC	Without structural information, only the genotoxic TTC default value could be used as a precautionary approach.
Specific Skin Sensitization Concerns	DST Approach	Apply the Dermal Sensitization Threshold (DST) for substances when skin sensitization is possible and exposure is low.

Finally, for evaluating skin sensitization potential, the Dermal Sensitization Threshold (DST) approach provides a framework for assessing substances with unknown or unproven non-sensitizing properties. However, CosPaTox's approach has refrained from conducting in vitro skin sensitization tests on substances unlikely to transfer from recycled materials in quantities large enough to surpass the DST threshold.

Highlight.

Overall, the safety evaluation scheme presented herein reflects a holistic and conservative strategy for assessing the safety of PCR materials in cosmetics and detergents, incorporating various tools and methodologies to ensure a comprehensive protection of consumer health.

5.2. Key-step Review of Applicable Approaches

5.2.1. *Key steps*

The key steps for risk assessment and management are listed in **Table 14** in connection with data sources and applicable methodology. The principles and rationale attached to each methodology are summarized hereafter.

***Table 14**. Essential key steps of safety assessment and applicable approaches*

Step	Process	Description	Data Sources	Methodology
Risk Assessment Initiation	Planning & Scoping	Define process and general scope for conducting risk assessment to serve its intended purpose.	Any internal document, this dossier	Multi-disciplinary team involvement
Problem Formulation	Conceptual Model & Analysis Plan	Identify major factors for assessment, create a model describing linkages between stressors and effects, and develop an analysis plan.	As above	Analytical approach, identification of exposed populations and endpoints
Exposure & Effects Assessment	Hazard Identification & Dose-Response	Assess potential for exposure and effects, including hazard identification and dose-response assessment.	Animal studies, in vitro/in silico models, epidemiology	Use of SAR, TTC, PBPK modeling
Risk Characterization	Integration & Estimation	Integrate exposure and effects assessments to provide synthesized conclusions about risk.	As above	Adherence to TCCR principles: transparency, clarity, consistency, reasonableness
Decision Making	Informing Options	Provide comprehensive assessment for risk management options, explaining how the risk assessment informed the decision.	As above	Decision documentation, reflecting risk assessment context

5.2.2. *Risk assessment*

During an initial assessment, conservative default assumptions are commonly used. An initial risk characterization may conclude that there is sufficient data to evaluate the chemical (even using conservative, default assumptions) or that additional data are needed to refine the assessment. Otherwise, the use of the constituent at the intended level cannot be supported, and it is warranted that either the level of the chemical under evaluation or reformulation with a different material be recommended. If it is necessary to obtain additional data, the risk characterization step is repeated

once those data become available. The entire risk assessment process is repeated until sufficient data exist or until it is determined that the chemical under evaluation cannot be supported.

5.2.3. *Effects assessment*

The major toxicological endpoints to consider relevant in this context include but are not limited to systemic toxicity (acute, subchronic, or chronic toxicity, reproductive and developmental toxicity, genetic toxicology, carcinogenicity) and local effects (skin sensitization). The safety data evaluated during the hazard identification phase can come from various sources. Historically, studies within the published scientific literature have been the primary and most reliable source of hazard data for animal toxicity. However, nowadays, other sources such as in vitro and in-silico models, probabilistic pharmacokinetics, and epidemiology studies are adding valuable additional information about the potential hazard of a material. Today, alternative tools such as Structure-Activity Relationship (SAR), Threshold of Toxicological Concern (TTC), and Physiologically Based Pharmacokinetic (PBPK) modeling enable a mechanism to fill toxicity data gaps and/or refine assumptions used throughout the risk assessment process. All available hazard data are reviewed, and the most relevant critical effect is determined; hazard data also provides critical contextual information specific to the mode of action, species differences in response, and characteristics of the dose-response relationship.

A result of the effects (hazard) assessment is the limit at which daily and lifelong exposure can occur without adverse health effects. This limit is defined in several variants, for example, Tolerable Daily Intake (TDI), Reference Dose (RfD), Derived No-Effect Level (DNEL), among others The limits are specific for the exposure route by ingestion, inhalation, or dermal absorption, which needs to be considered when assessing a specific route of exposure, *e.g.*, dermal exposure to a cosmetic product. Unfortunately, dermal limits are not always available for many trace chemicals. In these cases, a limit specific to the oral exposure route can be considered, thus resulting in an even more conservative risk value in most cases. If no data exist for the chemical, alternative methodologies such as SAR and TTC can be considered.

Use of toxicological data

It is generally recommended to focus on the types of studies and the *toxicological endpoints* most relevant to a product category. For the risk assessment of the exposure to small amounts of chemical substances, as is potentially the case for contaminants from packaging materials, information from studies on *chronic effects* and information on *carcinogenicity, mutagenicity, and reproductive toxicity* are generally more relevant than data from *acute toxicity* studies.
Data from toxicological studies and the derived safe exposure thresholds for specific substances can be conflicting, as the design and quality of the studies and the approach to translating the study results into a safe exposure threshold may vary. A trained toxicologist or safety assessor can convert between different types of thresholds, apply a weight-of-evidence approach between different or conflicting threshold values, and derive a single value for risk assessment [19].

Use of a read-across approach

In practice, many substances' toxicological profile is incomplete. In such cases, a trained toxicologist may apply a *read-across* approach. A detailed description of the ECHA read-across framework for assessing chemicals under REACH can be found in Ref. [20]. ECHA also guides applying QSAR principles for grouping chemicals of comparable toxicological profile [21].

Use of in silico prediction of toxicological properties

Where no information about a substance's toxicity, including genotoxicity [22], is available from studies, the use of *prediction models* can be considered. This approach is applied to food contact materials and articles [9]. Prediction models classify chemical substances by defining a set of rules that are applied to their chemical structure. The classification may be in the form of assigning the substance to a defined level of risk or producing "*structural alerts*" that the substance may exhibit certain

toxicological properties. Based on a substance's chemical structure, prediction models cannot be applied to substances whose structure is unknown.
Where such models are computer-based, they are called *in silico* prediction. Software for performing in silico prediction is available both in the public domain and as commercial products, with, for example, ToxTree [7] and the OECD QSAR toolbox [18] being well-known, publicly available tools.
Due to different possible choices for the ruleset and its variants, a detailed assessment of the prediction quality, for example, by combining multiple tools and documentation of the parameters used for an in-silico prediction, is essential. In silico prediction requires supervision and should involve a toxicologist or subject matter expert who can adequately assess the process's inputs and outputs. Detailed guidance can be found in [21].

Use of the toxicological threshold of concern (TTC) approach

A common ruleset for classifying chemicals for which no toxicological data is available has been proposed in Ref. [23], defining the so-called Cramer classes. For cosmetic applications, the following classes are recommended by the European Scientific Committee on Consumer Safety (SCCS) [11]:

- Class I: substances with a simple chemical structure and for which efficient modes of metabolism exist, suggesting a low order of oral toxicity
- Class III: substances with chemical structures that permit no strong initial presumption of safety or may even suggest significant toxicity or have reactive functional groups

The Cramer class system has been developed over the years and adopted widely, including in the *toxicological threshold of concern* (TTC) approach used in the safety assessment of food contact materials in the EU [24][3] and has been reviewed by the SCCS [4]. This approach assigns a TTC to groups of substances, including each Cramer class.[4]
The TTC concept is an approach to evaluating risks that acknowledges the view that a threshold of exposure to chemicals exists below which there is no significant risk from systemic toxicity to human health [26]. It is, therefore, a helpful approach where a low exposure to substances of unknown toxicological profile occurs.

The TTC concept is widely applied for the safety evaluation of packaging materials [27] and the evaluation of post-consumer recycled plastics used in packaging materials [28] in contact with food. In addition, TTC has been incorporated into the evaluation of flavoring substances [8] and the evaluation of cosmetic ingredients [29]. Based on the work of Munro, Renwick and Danielewska-Nikiel [8], EFSA promotes a more conservative TTC approach with regard to potentially DNA-reactive mutagens and/or carcinogens with a threshold of 0.15 µg/person/day for substances found in food [30, 31], an approach also found in the SCCS Notes for Guidance.
Over time, the evaluation of the TTC concept has demonstrated that, for the substance classes to which it can be applied, none of the evaluated specific non-cancer endpoints (e.g., reproductive and developmental toxicity) were more sensitive than the cancer endpoint. Therefore, using the TTC value of 0.15 µg/person/day provides an adequate *margin of safety* for all toxicological endpoints, meaning that at exposures below this value, the exact chemical identity of a substance is not required to be known.

[3] In the evaluation by EFSA, it was noted that TTC should not be used when actual toxicological data is available, and that it does not cover certain classes of substances. A trained toxicologist may exercise their own judgement on how to approach the assessment of such substances.
[4] See for example Table 2 in Ref. [25] Su Q-Z, Vera P, Nerín C, Lin Q-B, Zhong H-N. Safety concerns of recycling postconsumer polyolefins for food contact uses: Regarding (semi-)volatile migrants untargetedly screened. *Resources, Conservation and Recycling*. 2021;**167**:105365..

Use of the dermal sensitization threshold approach

Information and data generated from investigating *systemic toxicity* do not allow for the evaluation of skin sensitization. While information about skin-sensitizing properties/potency may be available for some substances migrating from packaging and may inform a (quantitative) risk assessment, it is expected that such information will be missing for a significant number of migrating substances.
Similar to the TTC concept for toxicity, the Dermal Sensitization Threshold (DST) [27] approach can be used in the risk assessment for skin-sensitizing substances in cases of low human exposure.
The authors of the DST approach derived a safe threshold of 64 µg/cm² to which safety factors are applied according to the QRA II approach developed by the International Fragrance Association (IFRA) [32]. These safety factors are application-specific and suggested to be set to 100 or 300 by IFRA, resulting in a threshold-of-safety of 0.64 µg/cm² and 0.21 µg/cm², respectively, for skin sensitizing substances and for substances for which absence of sensitization is not proven.

Use of in vitro test methods for toxicological properties

Practical testing may be conducted where existing toxicological data, prediction models, or the TTC concept are insufficient to complete a risk assessment. Such testing will generally be performed *in vitro*, on artificial samples rather than animals or humans.

Bacterial reverse mutation test

The bacterial reverse mutation test or 'Ames' test [33] is used across industries to identify DNA-reactive *mutagens* as a first step within testing strategies for *genotoxicity* (*e.g.,* as part of REACH and CLP regulations) [34]. Mutations are measured as a reversion to amino acid dependency for bacterial growth. The results of six different strains in total, identifying different types of mutations, are recommended in OECD TG 471 [33] to conclude on the mutagenic potential of a chemical substance.

In vitro skin sensitization test methods

Several in vitro skin sensitization assays have gained regulatory acceptance in recent years.
However, considering the difference in magnitude between skin sensitization thresholds derived from the DST model and the toxicological thresholds derived from the TTC model, CosPaTox has decided not to conduct *in vitro* skin sensitization tests. Substances were not expected to transfer from recycled materials into the product, which exhibits an unknown skin sensitization potential but for which enough toxicological data is available to derive a maximum acceptable consumer exposure (MACE) above the threshold resulting from the DST model.

5.2.4. *Exposure assessment*

The exposure assessment for probabilistic exposure analysis is designed to evaluate the potential dose of a compound or mixture to which a population may be exposed. The primary method for recyclates is deterministic exposure assessment, also known as screening level assessment. This approach utilizes specific point values and straightforward models to generate a point estimate of exposure, representing either a high-end or average exposure scenario. The advantage of deterministic assessments lies in their simplicity, leveraging available data (measured or estimated concentrations) and employing basic exposure scenarios, such as product use at the end of its shelf life when the concentration in the product is at its maximum, to yield easily interpretable results.

These deterministic methods are versatile, suitable for initial screenings and more detailed evaluations, and can be integrated into broader assessments involving multiple stressors and pathways. They cover exposure routes, magnitude, duration, and frequency comprehensively. Exposure estimation can be conducted through direct measurements or calculated exposure models. The process is structured into tiers, reflecting the depth of detail involved. Tier 1 relies on default, conservative assumptions, while Tier 2 introduces more specific data related to the recyclate and its usage, moving away from conservative assumptions towards more refined scenarios.

Typically, external exposure is calculated by multiplying the concentration or fraction of a substance in a source by the quantity of the source interacting with or reaching a specific site/target in the human body. A tiered approach is usually adopted to optimize time and resources, starting with generic exposure scenarios and conservative model parameters for an initial screening. These preliminary conservative exposure estimates are further refined through probabilistic methods or other refinements in a subsequent tier when necessary.

Tiered Assessment Overview:

- **Tier 1:** To estimate a worst-case exposure scenario, this method utilizes conservative default assumptions, such as assuming 100% dermal or mucosal membrane penetration or direct skin contact with the chemical constituent.

- **Tier 2:** This tier incorporates more detailed chemical and product-specific information, like construction or usage characteristics, to refine the exposure assessment. Outcomes from Tier 2 may indicate the need for further refinement and detailed assessments, possibly involving additional migration data or dermal absorption studies.

Subsequent tiers may be introduced for even more detailed and refined exposure assessments, allowing for a comprehensive and iterative approach to assessing the risk of substances in PCR materials.

5.2.5. *Risk characterization*

Justification for the Approach Used

Risk characterization represents the culmination of the risk assessment process, synthesizing findings from exposure assessment, hazard identification, and dose-response analysis to inform risk management and decision-making. This complex integration can yield outcomes presented via two main methodologies. Predominantly in food contact material assessments, this involves translating the maximum permissible exposure into a maximum allowable concentration in the material or intended product. This approach has been recommended for assessing recycled PET in food contact scenarios [28, 35], calculating safety margins in food packaging design [12], and establishing specific migration limits for positively listed substances. This leads to clear benchmarks for acceptable material safety levels.
However, applying this food-contact methodology to cosmetics presents challenges due to the varied exposure conditions that cannot be succinctly encapsulated in a simple scenario akin to daily consumption from food packaging. As a result, the risk characterization for cosmetics and detergents shifts focus to deriving maximum exposure concentrations tailored to specific product applications. The risk is then assessed using established concepts such as the Margin-of-Exposure (MOE) and the Margin-of-Safety (MOS).

Margin-of-Exposure (MOE):

The MOE method involves comparing the estimated human exposure to a benchmark dose, like the No Observed Adverse Effect Level (NOAEL), without accounting for potential uncertainties or data extrapolations. This straightforward comparison helps to gauge the proximity of real-world exposures to levels known to be safe from experimental studies.

Margin-of-Safety (MOS):

In contrast, the MOS approach compares estimated human exposure to a risk threshold deemed to carry a minimal risk of adverse effects, such as a Reference Dose (RfD), Acceptable Daily Intake (ADI), or other risk metrics that incorporate considerations for data uncertainties and extrapolation. Regulatory bodies and risk assessors generally consider an MOS value greater than 1 to signify a safety margin unlikely to result in harm, thereby ensuring human safety.

By leveraging these two analytical constructs (MOE and MOS), the risk characterization process for cosmetics and detergents provides a nuanced and adaptable framework for the diverse conditions under which consumers may interact with these products. This methodological adaptation underscores the complexity and necessity of tailoring risk assessment strategies to each product characteristics and associated exposure scenarios.

Principles

While substances with hazardous properties can pose risks at even low concentration levels, exposure limits that mitigate unacceptable risks and ensure consumer safety can be established. This approach focuses on assessing potential effects—a factor that cannot be altered—to determine a manageable level of exposure at which the risk is deemed acceptable. Thus, a Maximum Acceptable Consumer Exposure (MACE) value is derived.
The MACE value can then be transformed into a Maximum Acceptable Concentration (MAC) of a substance in a product, taking into account consumer usage patterns and resulting exposure scenarios. Furthermore, the MACE can be adapted to determine a maximum acceptable concentration of a substance in packaging materials and, by extension, in recycled plastic materials. The conversion process is illustrated in **Figure 11**. The values of MACE and MAC in a product are related. They can be

compared with the outcomes of extraction or migration tests performed on pellets after conversion in exposure concentration. Detailed instances of these conversions are discussed in subsequent sections The MACE can be further converted into a *maximum acceptable concentration* of a substance in a product by considering how consumers use the product and what exposure results from this use (*exposure scenario*)[5]. This conversion is visualized in Error! Reference source not found.. The following s ections provide practical examples.

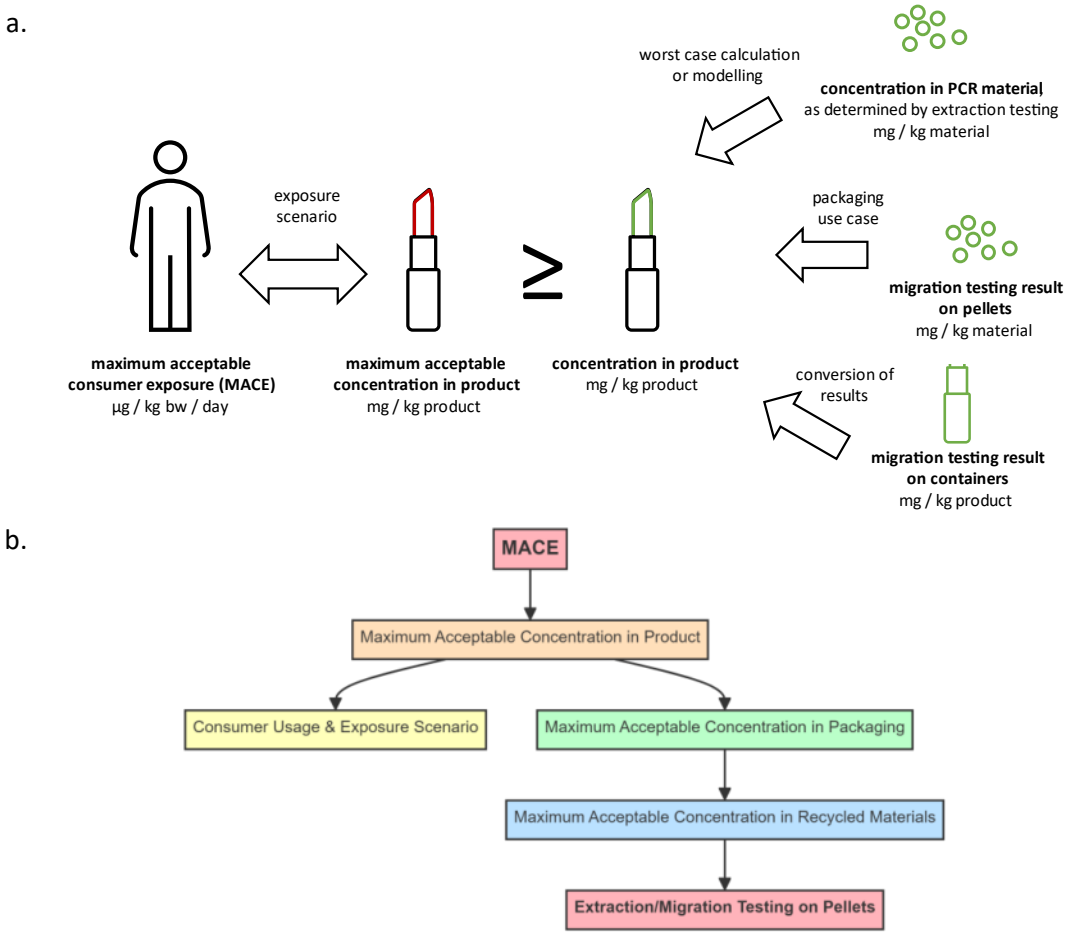


***Figure 11**. Relationship between the Maximum Acceptable Consumer Exposure MACE, Maximum Acceptable Concentration in a product (MAC), and the results of extraction or migration testing on pellets. (a) Criterion of acceptation knowing MACE value. (b) Relationship between MACE, MAC and test results.*

[5] This differentiation considers that packaging does not necessarily contain only recycled plastic but may also contain a share of virgin material. Furthermore, packaging may contain multiple types of recycled plastic, including of different purity.

5.3. Case Studies: Safety Assessment for Cosmetic Applications Using rHDPE4

5.3.1. *Data Overview for HDPE-04 Material*

The CosPaTox project has analyzed pellets from various post-consumer recycled (PCR) materials, including HDPE-04, to demonstrate the risk assessment process for cosmetic applications. Specifically, three distinct scenarios were considered:

(1) an adult's shampoo use (aqueous product),

(2) a infant's washing gel use (aqueous product),

(3) an adult's body lotion use (lipophilic product).

The datasets for HDPE-04 encompass results from several extraction and migration experiments, detailed below (refer to Annex 9 for comprehensive data).

- **P1 Experiment**: extraction of pellets in dichloromethane (DCM) at a 1:1 ratio for 3 days at 40°C.
- **P2 Experiment**: migration of pellets in ethanol 95% at a 1:1 ratio for 3 days at 60°C.
- **P3 Experiment**: migration of pellets in ethanol 95% at a 1:1 ratio for 10 days at 60°C.
- **P4 Experiment**: migration of pellets in ethanol 50% at a 1:1 ratio for 10 days at 60°C.
- **P5 Experiment**: Interaction of pellets with ethanol 95% at a 1:7 ratio for 10 days at 60°C.
- **B1 Experiment**: Interaction of a bottle with ethanol 95% at a 1:8.3 ratio for 10 days at 60°C.

The risk assessment methodology adopted by CosPaTox utilizes the outcomes of 1:1 migration experiments involving the pellets of the material in a selected simulant, with subsequent extrapolation to the actual product container. This extrapolation is essential for evaluating the release risk of both identified and non-identified substances. **Table 15** summarizes the applicable validation strategy. For the ethanol 95% test (P3), the risk assessment can be directly validated with the one derived from the containers manufactured from the same tested pellets.

***Table 15**. Review of tests used for safety evaluation and validation. The validation is indirect when it does not correspond to similar conditions.*

Product	Test used for safety evaluation in 200 mL HDPE bottle	Validation test
Adult's shampoo	P4	P1, P3 (indirect)
Infant's washing gel	P4	P1, P3 (indirect)
Adult's body lotion	P3	P5, B1 (direct)

This structured approach ensures a detailed evaluation by integrating direct analytical findings with practical applications, from the initial pellet material to the final product's container. It highlights the necessity for rigorous material-level testing and the critical role of robust extrapolation techniques in affirmatively determining consumer safety

Since evaluating one single recyclate may involve assessing the risk of dozens of substances, the exposure concentrations calculated for the three targeted applications are summarized as distributions in **Figure 12**. The calculation details are detailed in the following sections.

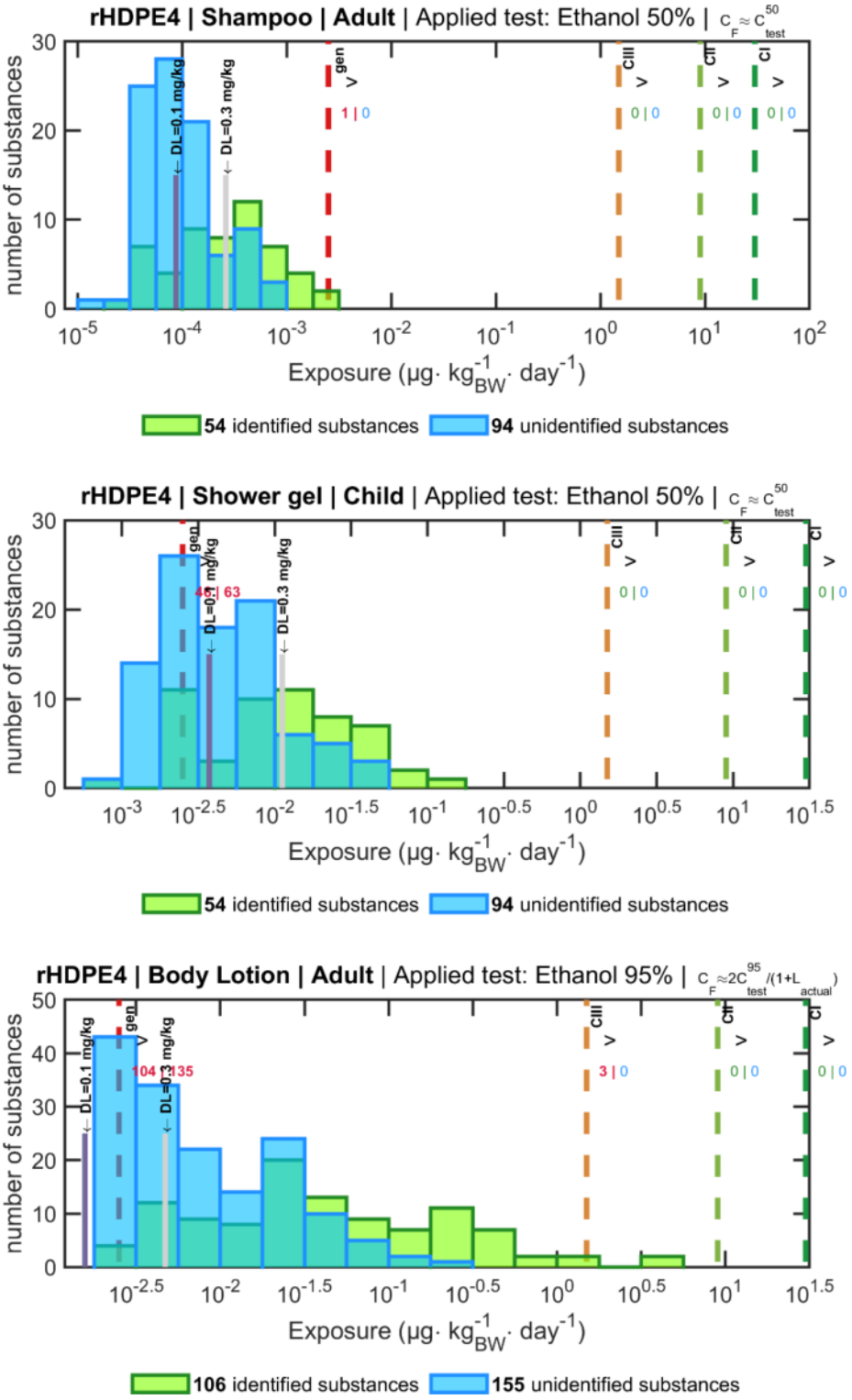


***Figure 12**. Distribution of exposure calculated for the three applications of rHDPE4 pellets (adult shampoo, child's shower gel, and adult body lotion) intended to be processed in 200 mL bottles. Continuous vertical lines represent the exposure associated with exposure concentrations equal to detection limits (DL) of 0.1 and 0.3 mg/kg. Dashed vertical lines show maximal exposure values for Cramer class III (CIII), II (CII), and I (CI) substances. The number of substances exceeding each threshold is shown as number of "identified|unidentified" substances regardless of their classification.*

5.3.2. *Use case 1: Shampoo application, adult*

This section evaluates the risk assessment process using HDPE-04 for manufacturing 200ml shampoo bottles. The P4 experiment, which examines pellet interaction with ethanol 50% for 10 days at 60 °C, is considered most relevant due to shampoo's typical composition. The detection limit (DL) for migration is set at 0.1 mg/kg. As per the section 4.3, we infer that the estimated concentration from migration (C_F) aligns with the concentration observed in the P4 experiment (C_{test}) :

$$C_F \approx C_{test}$$

Eq. 12

Accordingly, 1 mg/kg detected in the experiment equals the same concentration in the shampoo. The exposure assessment follows SCCS Notes of Guidance guidelines [36], assuming that the daily shampoo used by consumers is 10.46 g. Considering it a rinse-off product, only a fraction of 1% remains on the skin. For an adult weighing 60 kg, a 50% skin absorption rate is assumed according to SCCS recommendations. As a result, the systemic exposure dose (SED) is calculated as:

$$\text{SED}_{\text{shampoo}} = \frac{10.46\,\text{g} \times 1\% \times 50\%}{60\,\text{kg}} = 0.00087\,\text{g shampoo/kg body weight/day}$$

The substance-specific exposure reads:

$$\text{SED}_{\text{substance}} = \text{C}_\text{F} \times \text{SED}_{\text{product}}$$

Eq. 13

It is worth noticing that $\text{SED}_{\text{product}}$ has convenient units in g product/kg body weight/day. Exposure concentrations with units in mg substance/kg product are equivalent to µg substance/g product.

Assessment of Genotoxic Compounds

Firstly, we assess whether substances migrating below the detection limit, potentially with genotoxic properties, exceed the TTC for genotoxic substances (0.0025 µg/kg bw/day). With a detection limit considered at 0.1 mg/kg, a substance detected at this level is presumed to be also present at a concentration C_F of 0.1 mg/kg in the shampoo. The consumer exposure to such a substance is calculated as:

$$\text{SED}_{\text{genotoxic}} = 0.1\ \mu\text{g/g} \times 0.00087\ \text{g/kg bodyweight/day}$$

$$\text{SED}_{\text{genotoxic}} = 0.000087\ \mu\text{g/kg/day}$$

Eq. 14

The calculated value is far below the TTC for genotoxic substances (0.0025 µg/kg body weight/day), indicating that substances migrating below the detection limit pose no significant risk.

Assessment of Unidentified Substances

For detected but unidentified substances, their potential hazard at the first tier is considerably overestimated by assuming they all could be potentially genotoxic. Based on the highest detected

concentration in the simulant (0.985 mg/kg), the maximum consumer exposure to unidentified substances

$$\text{SED}_{\substack{\max \\ unidentified}} = 0.985\ \mu g/g \times 0.00087\ g/kg\ \text{bodyweight/day}$$

$$\text{SED}_{\substack{\max \\ unidentified}} = 0.00086\ \mu g/kg/day$$

Eq. 15

The maximum exposure to unidentified substances is still below the TTC for genotoxic substances.

Assessment of Identified Substances

For identified substances, a search for substance-specific study data is required to assign a specific safe threshold (MACE). If the assignment is not possible, a Cramer classification and a TTC threshold can be used alternatively. Since TTC thresholds are assumed to be very conservative, the process can be reversed to prioritize the substances that exceed TTC.

The current case study identified substances with concentrations ranging from 0.024 to 3.089 mg/kg. Only one substance, 7,9-di-tert-butyl-1-oxaspiro(4,5)deca-6,9-diene-2,8-dione, a degradation product of BHT type antioxidant (butylated hydroxytoluene), exceeds the concentration threshold related to the TTC for potentially genotoxic substances ($\frac{0.0025\ \mu g/kg\ body\ weight/day}{0.00087\ g/kg\ bodyweight/day}$ =2.87 mg/kg) with a concentration of 3.089 mg/kg. This substance necessitates a detailed hazard evaluation. The second highest concentration, 2.317 mg/kg, is indeed met for p-octyl acetophenone and lower than the genotoxic threshold.

No information is available on the potential genotoxicity of the BHT by-product. Without genotoxic structure alerts, it is classified under Cramer Class III. Its exposure at the measured concentration ($3.089\ \mu g/g \times 0.00087\ g/kg\ bodyweight/day = 0.0027\ \mu g/kg/day$) is below the TTC threshold for Cramer Class III substances (1.5 µg/kg body weight/day). This outcome underscores the significance of classifying substances that exceed specific thresholds. Evaluating all substances collectively, as illustrated in **Figure 12**, allows focusing on the most critical ones but does not eliminate the need for precise analysis as soon as a threshold is surpassed. The procedure should start with the lowest thresholds.

Conclusion on the suitability of HDPE04 pellets for producing shampoo bottles

The assessments of non-detected, unidentified, and identified semi-volatile residues showed that HDPE-04 is suitable for manufacturing 200-mL shampoo bottles intended for adult use.

5.3.3. *Use Case 2: Washing Gel Application for a Child*

This scenario explores the application of a washing gel designed for small children, packaged in a 200ml bottle made from HDPE-04. Like the shampoo case, the P4 experiment (ethanol 50% simulant) reflects potential migration levels into the product. Notably, this case utilizes a higher limit of detection (DL) of 0.3 mg/kg.

The SCCS Notes of Guidance suggests an 18.67g daily usage of washing gel for adults, applied analogously for children. Given it's a rinse-off product, a 1% retention factor after rinsing is presumed.

A 100% skin absorption rate is assumed as a precautionary measure for children. The systemic exposure dose (SED) for a child weighing 5 kg is calculated as follows:

$$\text{SED}_{\text{Gel}} = \frac{18.67\text{g} \times 1\% \times 100\%}{5\text{kg}} = 0.03734\text{g washing gel/kg bodyweight/day}$$

Eq. 16

Assessment of Unidentified Substances

Initially, the analysis ensures that the limit of detection (DL) of 0.3 mg/kg is stringent enough to prevent undetected genotoxic substances from exceeding the TTC for genotoxicity. This concentration correlates to an exposure of 0.0112 µg/kg bw/day, surpassing the TTC of 0.0025 µg/kg bw/day, indicating a potential risk from undetected genotoxic substances.

$$\text{SED}_{\text{substance}} = 0.3\ \mu\text{g/g} \times 0.03734\ \text{g/kg bodyweight/day}$$

$$\text{SED}_{\text{substance}} = 00112\ \mu\text{g/kg bodyweight/day}$$

Eq. 17

The requirement for a more sensitive DL (0.06 mg/kg Solvent) underlines the necessity for stringent detection thresholds in PCR material qualification. Unidentified substances exceeding this revised LD and numerous identifiable substances within this experiment potentially breach the TTC for genotoxic substances.

Prioritizing Substances Surpassing the Genotoxic TTC

Addressing identified substances surpassing the genotoxic TTC involves directly assigning a Cramer Class/TTC value or identifying an appropriate MACE through additional analysis. For instance, benzyl salicylate (CAS 118-58-1) observed at 0.544 mg/kg, corresponds to an exposure of 0.0203 µg/kg bw/day. Given a Derived No Effect Level (DNEL) of 790 µg/kg bw/day from its REACH dossier, this concentration is not considered risky to consumers.

Conclusion of the Evaluation

Challenges arise with undetected or unidentified substances, as their potential risk cannot be directly assessed. Emphasis should be on substances detected but not identified, with further analysis potentially required for qualification. Strategies for qualification include blending with virgin material to dilute potential risks or enhancing analytical efforts to improve substance identification.

For HDPE-04, blending (<7% with virgin material) or identifying numerous unidentified substances seems impractical. However, combining results from ethanol 50% migration experiments with those from dichloromethane or ethanol 95% could offer insights into the hazards of non-detected or non-identified substances, potentially validating HDPE-04 for this application if genotoxic substances are absent. This combined approach might facilitate a more accurate estimation of individual substance partition coefficients, although it necessitates further exploration and data collection.

Possible Directions of Refinement

Evaluating the unidentified substances and those below the detection limit presents a significant challenge. For perspective, while the limit of detection (DL) constrains the exposure assessment to above 0.0112 µg/kg bw/day, the maximum exposure for an unidentified substance in this analysis is calculated at 0.0368 µg/kg bw/day. Initially, priority should be given to detected yet unidentified substances in the migration experiment. Depending on the chosen risk management strategy, substances migrating below the detection threshold might already be accounted for.

Several strategies for further material qualification include:

1. **Blending with Virgin Material**: The material could be deemed acceptable if blended with virgin material such that the expected migration does not pose a consumer risk, as detailed in chapter 5.6.

2. **Identification Efforts**: If the number of unidentified substances that exceed the Threshold of Toxicological Concern (TTC) for potentially genotoxic substances is low, additional efforts could be made to identify these substances accurately. This may involve utilizing more advanced analytical methods. Successfully identified substances can then be evaluated similarly to those identified in the initial experiment.

3. **Additional Experimental Data**: Utilizing data from additional experiments conducted with dichloromethane or ethanol 95% can aid in the hazard analysis of unidentified or undetected substances.

4. **Genotoxicity Testing**: Chemical analysis could be complemented with genotoxicity testing, such as an Ames test, to identify DNA-reactive mutagens.

In the context of HDPE-04, options (1) and (2) seem impractical due to the low percentage of HDPE-04 that can be blended with virgin material and the high number of unidentified substances, making dedicated analytical identification challenging.

Options (3) and (4) are viable alternatives. Although not part of the initial CosPaTox objectives, validating the absence of genotoxic substances through suitable testing can support considering non-identified and non-detected substances as Cramer Class III by default, ensuring consumer exposure does not exceed 1.5 µg/kg bw/day. This rationale, given that the exposures for non-detected and non-identified substances do not surpass 0.0112 µg/kg bw/day and 0.0368 µg/kg bw/day, respectively, could justify the acceptance of HDPE-04 for certain applications.

Extending risk-assessment by including the test results from more severe migration conditions

An additional approach involves correlating the findings from the ethanol 50% migration experiment with those from experiments using dichloromethane or ethanol 95%. Assuming the latter identifies all potentially migratable substances, this comparison could provide valuable insights into the hazards of substances not detected or unidentified in the ethanol 50% experiment. If no genotoxic substances are identified in DCM or ethanol 95% experiments, assuming the same for substances not detected or unidentified in the ethanol 50% experiment may be reasonable. This method, through routine data collection, could also enhance the estimation of partition coefficients for individual substances.

In the examination of HDPE-04, an additional 76 substances were detected in the migration experiments using ethanol 95%, as detailed in **Appendix 8**. This brought the total count of identified substances, when combined with those identified in the ethanol 50% migration experiment, to 130. Many of these substances appear on the CosPaTox compiled list, yet only a subset has been assigned

specific MACE values. Those substances lacking a MACE assignment are either noted as posing no identified hazard or lacking available data.

A deeper dive into substances flagged with no identified hazard often reveals ample study data within their respective REACH dossiers to assess their hazard potential, albeit without a derived DNEL value. Examples include bumetrizole (CAS 3896-11-5) and ethyl caprate (CAS 110-38-3), for which sufficient data exist, but the registrants have not established specific DNEL (derived no-effect level) values.

For substances listed as lacking data, further investigation sometimes uncovers additional information. For instance, amberone (CAS 68155-66-8) is registered under REACH not by its CAS number but under its EC number, leading to a MACE of 17.2 mg/kg bw/day noted in its REACH dossier. Some substances are also evaluated by institutions such as EFSA, like ethyl oleate (CAS 111-62-6), in the context of food/feed applications. In such cases, assigning a Cramer Class based on structural information is a practical interim approach. All substances identified without current data on the list can be classified into Cramer Classes I or III.

Additionally, certain substances not covered in the CosPaTox list, particularly cyclosiloxanes, were identified. Schmitt *et al.* [37] evaluated the applicability of the TTC approach to organosilicon compounds and suggested that Cramer Class III offers a sufficient protective classification for their chemical class.

The comprehensive hazard analysis of substances identified in the ethanol 95% migration experiment suggests that they do not have genotoxic properties. This finding, considered within a weight-of-evidence framework, supports the safety evaluation of HDPE-04 and reinforces the material's suitability for cosmetic packaging applications.

5.3.4. *Use Case 3: Body Lotion Application for Adults*

This scenario examines the suitability of HDPE-04 for a body lotion packaged in a 200 mL bottle, targeting adult users. Considering body lotions' lipophilic nature, data from either DCM or ethanol 95% experiments after 10 days can be utilized for risk assessment. Here, the ethanol 95% experiment is chosen.

Exposure concentration

As detailed in section 4.5.2, to estimate migrating substances' expected concentration in the 200 mL bottle (C_F), a factor of 2 is applied to the concentration measured in the test (C_{test}), accounting for the partitioning of substances in 1:1 migration tests. Using a simplification, this use case adopts an 8.3 dilution factor (L_{actual}), derived for ethanol 95% as a simulant in a 200 mL bottle weighing 19.1 g. Hence, the bottle's concentration can be approximated from the measured data as:

$$C_F = 2\frac{C_{\text{test}}}{L_{actual}} = 2\frac{C_{\text{test}}}{8.3}$$

Eq. 18

Assessment of Unidentified Substances

Following the SCCS Notes of Guidance [36], consumers' average daily body lotion application is 7.82 g. As a leave-on product, it's assumed to fully remain on the skin, implying a 100% retention factor. Skin absorption is estimated at 50%. Therefore, for an adult weighing 60kg, the Systemic Exposure Dose (SED) is:

$$SED_{\text{lotion}} = \frac{7.82g \times 100\% \times 50\%}{60\ kg} = 0.065\ g/kg/day$$

Eq. 19

Assuming a detection limit (DL) of 0.1 mg/kg in the simulant, the minimal concentration in the product calculates to:

$$C_F = \frac{2 \times 0.1\ mg/kg}{8.3} = 0.024\ mg/kg$$

Eq. 20

This corresponds to a consumer exposure of 0.00156 µg/kg bw/day, below the TTC for genotoxic substances (0.0025 µg/kg bw/day). Thus, non-detected substances likely do not present an unacceptable risk in this context. The absence of risk is also visible in **Figure 12** (bottom subplot), where the exposure mark associated with DL=0.1 mg/kg is on the left of the TTC-based MACE value for genotoxic substances.

Assessment of identified Substances

The analysis for both identified and non-identified substances estimates consumer exposures ranging from 0.002 µg/kg bw/day to 5.1 µg/kg bw/day for identified substances and from 0.002 µg/kg bw/day to 0.27 µg/kg bw/day for non-identified ones. This implies that several substances exceed the TTC for potentially genotoxic substances. Notably, excluding the factor of 2 for estimating exposure concentration would still exceed the TTC for genotoxic substances, highlighting the importance of considering conservative estimates in the risk assessment process.

Possible Directions of Refinement

The potential refinements for this use case align with those detailed in section 5.3.3 and are not elaborated on further here.

The data under consideration facilitates a nuanced comparison between results derived from pellet experiments and those from migration experiments conducted with actual bottles (referenced in section 4.5). In the migration experiment involving pellets, a total of 261 substances were detected, of which 106 were successfully identified. Conversely, the bottle experiment yielded a marginally lower tally of 178 substances, with 99 being identified. Among these, 77 substances were consistently detected in both pellets and bottles. The analysis generally indicated higher consumer exposure estimates based on pellet results, except for five higher alkene/alkanes (1-tetracosene, nonadecane, docosane, hexacosane, tetracosane), where exposure based on bottle results was found to be 1.1 – 3.7 times higher. Substances identified exclusively in the bottle experiment included specific alkenes and alkanes, along with BHT and certain fragrance materials, with the highest exposure for bottle-exclusive substances calculated at 0.1293 µg/kg bw/day and an average exposure of 0.0231 µg/kg bw/day.

A notable observation is the significantly higher count of unidentified substances in the pellet experiment compared to the bottle experiment. For the unidentified substance with the highest

concentration detected in each experiment, consumer exposure was estimated at 0.2738 µg/kg bw/day for the pellet experiment and 0.0856 µg/kg bw/day for the bottle experiment. This indicates a threefold higher exposure to a potentially genotoxic substance in the pellet experiment, underscoring the conservative nature of this testing approach. Notably, the exposure level of 0.2738 µg/kg bw/day from the pellet experiment also surpasses the highest exposure calculated for substances found only in the bottle experiment. This analysis suggests that, at least for HDPE-04, pellet testing provides a sufficiently conservative basis for assessing the bottle's safety, reinforcing the method's utility in preemptively gauging potential consumer exposure risks.

5.3.5. *Comprehensive Summary of Risk Assessment Across All Tested Materials*

Appendix 9 presents a detailed comparative analysis of the risk assessment outcomes for all materials evaluated within the scope of this study, extending beyond the specific examination of HDPE-04. This comprehensive overview facilitates a broader understanding of how various post-consumer recycled (PCR) materials might perform across various cosmetic application scenarios. The risk assessment for each material against each use case scenario, as previously delineated, is visually summarized through individual graphical representations. These graphs distinctly mark the number of identified substances (represented in green) and non-identified substances (depicted in blue), correlating to their respective consumer exposure levels within specific product applications.

For enhanced clarity and to guide interpretation, the graphs incorporate several key indicators:

- Consumer exposure levels are anchored to either a limit of detection (DL) threshold of 0.1 mg/kg solvent or 0.3 mg/kg simulant as they define the minimum exposure to any substance. This demarcation is strictly tied to exposure factors and remains constant across different use case scenarios, but it does not fluctuate with variations in the materials tested.
- Additionally, the figures embed Threshold of Toxicological Concern (TTC) benchmarks for potentially genotoxic substances alongside thresholds for distinct Cramer Classes. These TTC values are consistent across all materials, facilitating a standardized comparison framework.

The graphical analysis enables multifaceted insights:

- It allows for assessing whether, within a given experimental setup, the TTC for potentially genotoxic substances is surpassed and whether this breach is attributed to identified substances, unidentified substances, or a combination thereof. This differentiation has significant implications for the material's risk assessment profile.
- The graphical data also opens avenues for conjecture on a material's acceptability for cosmetic applications, contingent upon the availability of study data negating the migrating substances' genotoxic properties. In such instances, the risk assessment may pivot primarily on the TTC benchmark for Cramer Class III substances, suggesting a pathway for material approval based on a conservative safety margin.

This section aims to distill the critical findings from the comprehensive risk assessments, offering a synthesized view that underscores the potential application feasibility of various PCR materials in cosmetic product manufacturing, grounded in rigorous safety and exposure analysis.

For the 15 HDPE samples detailed in **Appendix 9**, under the shampoo application scenario, all unidentified substances remained below the Threshold of Toxicological Concern (TTC) for potentially

genotoxic substances. However, in 5 of these materials (Nos. 4, 8, 11, 12, and 15), one identified substance exceeded the TTC for potentially genotoxic substances. In HDPE-5, three identified substances were found to exceed this threshold. Since identified substances can typically undergo a more detailed risk assessment, all these materials are deemed suitable for shampoo applications.

In scenarios involving washing gel for infants and body lotion for adults, both unidentified and identified substances surpassed the TTC for potentially genotoxic substances. Yet, all substances stayed beneath the threshold for Cramer Class III substances for the washing gel application. For this scenario, a refined assessment to rule out genotoxic properties is necessary for all materials to qualify. The situation is similar for body lotion applications; however, the gap between the highest observed exposure dose of substances and the Cramer Class III threshold is narrower. In materials HDPE-4, -11, and -12, the TTC for Cramer Class III is exceeded by 2-3 identified substances, necessitating a specific risk assessment for these substances for material qualification.

For LDPE materials, the general findings echo those of the HDPE samples, with a notable exception: in the shampoo application context, it's estimated that 4-9 identified substances exceed the TTC for genotoxic substances. Since identified substances can undergo specialized assessments, all LDPE materials are expected to be suitable for shampoo applications. LDPE-4 stands out because 9 identified substances exceed the genotoxic TTC, and the thresholds for Cramer Classes III (and II) are surpassed by 8 and 1 identified substances, respectively. Although LDPE-4 may apply the same risk mitigation strategies as other LDPE materials, it warrants closer scrutiny, suggesting that other materials might be preferable for cosmetic applications.

PP materials, on average, present the highest count of substances, both identified and unidentified, exceeding the TTC for genotoxic substances. In the shampoo scenario, about 4-6 identified substances (but no unidentified ones) surpass the TTC for potentially genotoxic substances. Similar outcomes are observed in the washing gel application, where both unidentified and identified substances exceed the genotoxic TTC yet fall below the Cramer Class III threshold. This also applies to some PP materials in the body lotion scenario, while others have identified substances breaching the Cramer Class III limit.

Two PP materials exhibit notable exceptions. PP-10 is unique for having a non-identified substance exceeding the TTC for potentially genotoxic substances in the shampoo scenario, requiring additional validation to confirm the absence of genotoxic activity for final qualification. Meanwhile, PP-5 has two unidentified substances crossing the Cramer Class III threshold, rendering it unsuitable for body lotion applications, even if genotoxic properties can be disproved.

5.3.6. *General remarks on the risk assessment approach*

The risk assessment methodology outlined in the preceding chapter hinges significantly on the presence and concentration of unidentified substances. Refinements in the assessment aim to enhance the understanding of the hazards posed by these substances. As previously mentioned, classifying all unidentified substances as potentially genotoxic represents a conservative stance, diverging substantially from reality. The analysis of identified substances suggests that merely about 10% of unidentified substances could potentially possess genotoxic properties. This perspective introduces several considerations, given the variable nature of substance migration from recycled materials and the unlikely scenario of continuous exposure to the same substances at unchanging concentrations over a lifetime. This assumption underpins the Threshold of Toxicological Concern (TTC) approach. It is reasonable to infer that only one out of every ten analyzed materials might exhibit the most concentrated unidentified substance genotoxic characteristics. This understanding adds an additional layer of safety to the risk assessment process.

For instance, enhancing the evaluation of a material—where unidentified substances surpass the TTC threshold for genotoxic substances—by incorporating targeted genotoxicity testing seems a

sufficiently conservative strategy. This approach also compensates for variables difficult to control, such as methodological discrepancies in analytical techniques, material variability, and the generation of new contaminants while manufacturing final packaging from the analyzed pellets.

While creating high-quality Post-Consumer Recycled (PCR) pellets is beyond the scope of the CosPaTox project, the effectiveness of the analytical methods plays a critical role in the risk assessment outcome. Improving the detection limit and increasing the proportion of identifiable substances enhances the likelihood of a material's suitability for specific cosmetic or detergent applications.

Recognizing that the risk assessment result offers an estimated risk level associated with using a tested material is crucial. The decision-making process, or risk management, then involves determining whether such a risk is acceptable for consumer use or whether additional risk mitigation measures are warranted.

5.3.7. *Discussion on Exposure to Potentially Concerning Individual Substances*

The untargeted approach facilitates constructing an exposure profile tailored to the intended application. The worst-case profile of the top 12 substances leading to an estimated exposure exceeding half of the TTC value value is depicted in **Figure 13** for the adult body lotion scenario as revealed by testing the 31 recyclates considered in the project. The ranking of substances varies depending on the simulant used. While substances leading to intermediate exposures are common across samples, the most hazardous substances appear randomly, corroborating the hypothesis of incidental contamination. Coincidently, the potential exposures to most substances in tested samples remain below their TTC values.

A meta-analysis of the average exposures across all samples and polymers was conducted. **Table 16** summarizes the maximum exposure expected for the most frequently encountered substances. The analysis highlights the overrepresentation of certain classes of contaminants in recycled polyolefins, including phthalic esters and biocidal substances. These results underscore the necessity of targeting specific classes of substances such as phthalates, aromatic amines, pesticides, and polycyclic aromatic compounds using more focused methods.

Table 16. Worst-case exposure to the most prevalent hazardous substances for the adult body lotion scenario, as evaluated from a meta-analysis that included all samples and polymers.

Substance	**Highest exposure expressed as TTC fractions**
Bis(2-ethylhexyl)phthalate (DEHP)	367 × TTC
Dibutyl phthalate	19 × TTC
Diisobutylphthalate	8.7 × TTC
2-Ethoxyethanol	7.2 × TTC
Decamethyl cyclopentasiloxane	5.4 × TTC
Benzenepropanoic acid, 3,5-bis(1,1- dimethylethyl)-4-hydroxy-, methyl ester	4.4 × TTC
unidentified	3.1 × TTC
Ethylene brassylate	2.7 × TTC
Caryophyllene	1.9 × TTC
p-t-Bucinal	1.8 × TTC
4-tert-Butylphenol	1.5 × TTC
Cyclotetrasiloxane, octamethyl- (D4)	1.5 × TTC
Benzylbenzoate	1.4 × TTC
Dodecamethylcyclohexasiloxane	0.6 × TTC

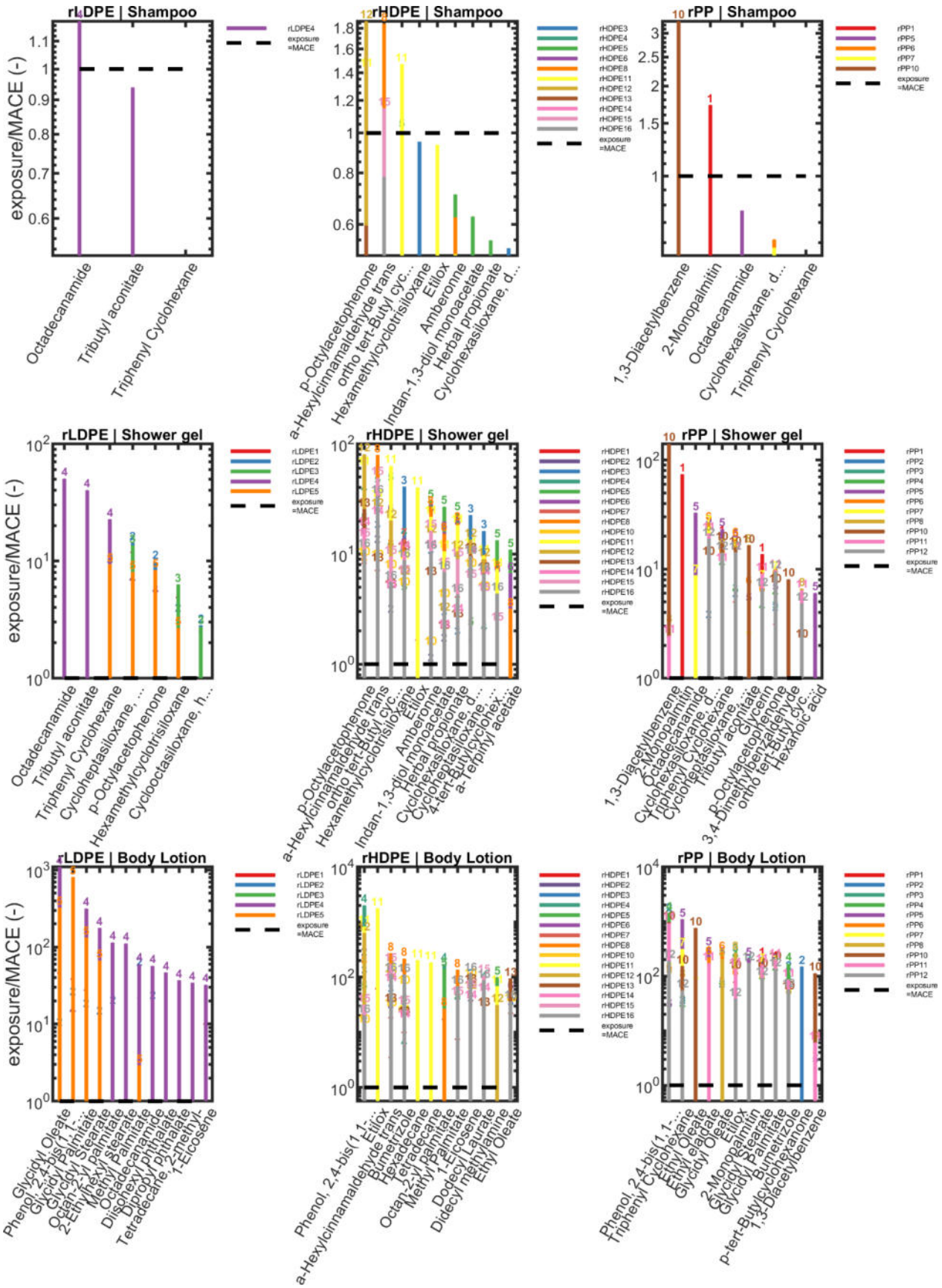


***Figure 13**. Classification of hazardous substances in all samples leading to an exposure exceeding half of the TTC value, where TTC is used here as MACE value. The digits represents the polymer code.*

6. General Discussion

6.1. Summary of Main Aspects: a Unified Methodology for Semi-volatile Compounds

The CosPaTox project did not aim to cover all possible cases but to gather enough results to recommend an approach for directing recycled polyolefin material streams toward detergent and cosmetic applications. This report relies exclusively on results obtained from untargeted analysis, which is considered the cornerstone of any rational approach to evaluating the safety of recyclates. This does not preclude more targeted analyses or the search for inorganic contaminants in polyolefins.

In the CosPaTox approach, each detected peak must be evaluated and decided upon, including substances that could be present below the detection limit, making the approach holistic. This comprehensiveness makes evaluations significantly more complex than what is generally practiced for food contact. Since not all peaks can be confidently associated with a substance, it is not feasible to systematically match results from different tests, such as those from a dichloromethane extraction and a migration test. Thus, CosPaTox explored simple tests that minimize experimental complexity and can be robustly used individually to assess potential exposure to each substance, whether identified or not.

CosPaTox did not seek to minimize difficulty. For each substance, a test result provides a value dependent on several well-established but unknown factors: concentration in the recycled material, the substance's diffusion coefficient, and the partition coefficient with the considered simulant. The first quantity can only be securely determined in a solvent (e.g., dichloromethane), but that does not represent cosmetic products. The last two properties are difficult to establish and cannot be tabulated if the substance is unknown. These challenges led to the exclusion of migration modeling approaches used for food contact materials, as they were, at best, only applicable to identified molecules. They also increased the evaluation burden for systematic application to dozens or hundreds of substances. These difficulties were circumvented by constructing overestimates of exposure concentrations for cosmetic products. The approach was validated by determining the partition coefficient distribution for the two studied simulants (ethanol 50% and 95%) and demonstrating that thermodynamic equilibrium was reached in accelerated tests at 60°C after about ten days.

The central tool of the developed approach is the pellet test, which eliminates the need for available formed articles. The test, involving a small volume of simulant, is not only eco-friendly (low waste) but can be systematized on a large scale with vial trays or racks, allowing thousands of samples to be placed in an oven under acceptable safety conditions without the risk of fire or explosion due to rational use of simulant volume. It is important to remember that migration cells used for food contact are much larger, and a test typically requires at least 100 mL of simulant and a concentration step. Here, only 3 mL of simulant is required and used without a concentration step that would necessitate rotary evaporators or sublimation systems.

The interpretation workload is reduced by using exposure concentration assumptions that do not require detailed characterization of the packaging material geometry. Only the mass ratio of the cosmetic product to its packaging is required. A database of nearly 800 substances has been assembled to help users find acceptable thresholds for substances listed in various European regulations. For non-evaluated substances and even unidentified substances, TTC thresholds are applied. The open-source ToxTree software allows for quick substance classification based on its structure. This report provides all the bases and justifications to train a future operator in risk assessment. More general elements are also available in the guidelines.

6.2. Demonstrating Suitability for Cosmetic Product Contact

The framework presented in this dossier facilitates demonstrating the suitability of post-consumer recycled (PCR) materials for contact with cosmetic, detergent, and homecare products using specified criteria, concepts, and methodologies as outlined in the previous sections. However, it is crucial to acknowledge that this approach does not enable the formal demonstration of a material's non-suitability for a given application. The non-suitability for contact with cosmetic products can only be conclusively established through direct testing involving the specific cosmetic product and its intended packaging. This delineation stems from the inherently conservative safety approach adopted at various stages of the material evaluation process.

One expected consequence of the approach's important conservatism is that it is easier to demonstrate suitability for detergents and homecare products than for leave-on cosmetic products, presenting higher risks of exposure. Without precluding refined testing for specific cosmetic products, the proposed approach will enable recyclers to robustly analyze their PCR material and understand whether it suits generic categories of applications: leave-on, rinse-off cosmetics, and detergent/homecare applications.

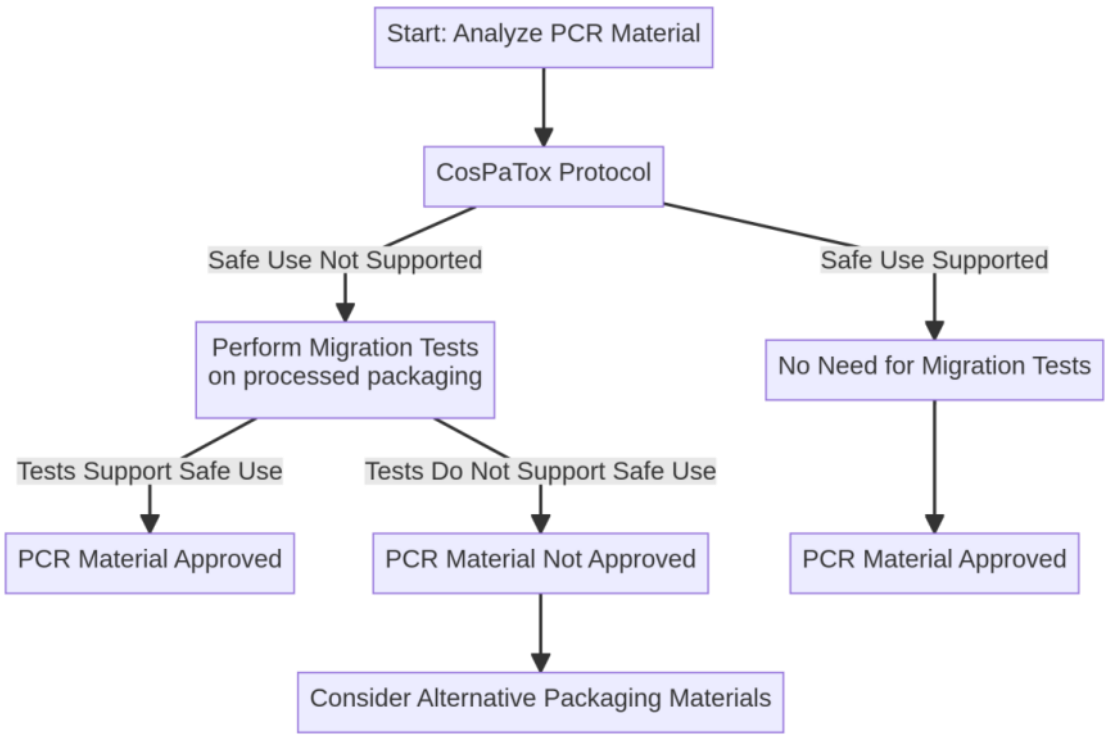


***Figure 14**. The decision-making process for evaluating the suitability of PCR materials in cosmetic packaging outlines a structured approach based on the CosPaTox Protocol, from initial screening to final determination.*

Figure 14 outlines the evaluation process for determining the compatibility of Post-Consumer Recycled (PCR) materials with cosmetic and detergent/homecare packaging applications. Following the CosPaTox Protocol, this workflow supports decisions informed by the results of migration tests, including approving or disapproving PCR materials for specific uses. The diagram underscores the complexity of the assessment process, spotlighting the need for specialized analytical methods and tailored criteria that consider a range of factors impacting the safety of the final product. This decision-making process varies between recyclers, packaging manufacturers, and brand owners, each looking

at things from their perspective within the supply chain. Recyclers seek the broad applicability of their materials, while brand owners may require additional analyses based on the specific end-use of their packaging. Crucially, the exchange of information, particularly concerning identified substances and their maximum concentrations found in tests through untargeted analyses, is vital.

Traceability from the finished packaging back to the tested pellets can secure the demonstration from both ends of the supply chain despite the production volumes involved and the necessary blending of materials from different sources. Sharing this information helps prevent duplicative efforts and is a key aspect of risk communication throughout the supply chain.

6.3. The Sources of Conservatism in the CosPaTox Protocol

The CosPaTox protocol introduces several overestimation factors into the exposure calculation, which are essential for the approach's robustness. Due to thermodynamic control, cosmetic or detergent products are assumed to be contaminated at their maximum achievable contamination, and the amounts of product used, remaining on the skin, and being absorbed by the skin barrier are maximized. Therefore oral and dermal risk values are applied to conservative account for systemic and local endpoints.

The CosPaTox project compared worst-case exposure concentrations assessed with bottles and pellets. The median overestimation for ethanol 95% reaches a factor of three, with a risk of underestimation lower than 10%. In most cases, this overestimation is by design and ensures conservative consumer safety. The threshold of 10% is below the threshold of analytical errors, and it would be futile to seek a lower risk when errors on measured concentrations are at least double. Removing the factor of 2 in the concentration exposure rule in ethanol 95% cut by half the median overestimation of 3/2=1.5 but at the expense of underestimation in 25% of cases. If experimental errors on concentrations were significantly over 25%, the factor of 2 could be disregarded.

The assumption of non-detected substances present at a concentration equal to the detection limit in the test brings additional conservatism. Indeed, a non-detected substance may not be present. Assuming a fifty-fifty chance it is present, the theoretical exposure would be halved. This assumption is generally accepted in chronic exposure studies. However, it can be contested in the case of recyclates since the CosPaTox project unambiguously shows that several or even dozens of substances are present at concentrations below the detection limit. In the case of an almost certain presence of a substance below the detection limit, the choice is no longer between 0 and the detection limit. Hence, it is recommended to maintain exposure at the detection limit without a moderating factor.

It should also be noted that the CosPaTox project does not account for the reduction in product volume during use. The assumption of thermodynamic equilibrium is applied here and is assumed to be reached before the consumer uses the product. This assumption is generally conservative in terms of consumer exposure.

6.4. The Risk Management of Unindentied Substances

The ability to identify and quantify substances is contingent upon the analytical methodology, the comprehensiveness of the database utilized, and the availability of reference standards. Acceptability criteria, therefore, must embrace a level of compromise, acknowledging that absolute safety evaluation is unattainable. This limitation stems from several factors: the assessments are conducted on pellets rather than finished products; they do not account for certain substances like additives,

colorants, or technological aids added in subsequent stages, nor do they consider degradation products resulting from further processing.

The extrapolation rules are still inherently conservative and estimate the migration from pellets to specific cosmetic product categories. They tend to overestimate the quantities transferred. Moreover, the most cautious toxicological classification is attributed to unknown substances. Essentially, the provisions made for unidentified substances aim to facilitate the utilization of recycled material in cosmetic and detergent/homecare packaging production rather than to inhibit it. It especially directs the cleanest material streams towards the most sensitive applications. Packaging end-users must verify the ultimate safety based on their packaging's geometry, product characteristics, and the intended conditions of use.

Substances detected but unidentified pose a significant challenge for risk assessment due to the uncertainty surrounding their chemical structures and, by extension, their toxicological profiles. Considering that only 10% of identified substances are classified under the conservative "potentially genotoxic" category, labeling all unidentified substances as genotoxic appears overly prudent, particularly when the likelihood suggests only one such substance may be present among ten.

To address this challenge, a comparative analysis with virgin materials, evaluated using the CosPaTox protocol, was conducted. The findings, depicted in **Figure 17**, reveal that the cumulative count of substances in branched polymers such as LDPE and PP exceeds 300. Conversely, the total for linear HDPE is approximately a third of that figure. These results underscore, if necessary, that the dilemma of unidentified substances is also present in virgin materials, even if they do not present safety concerns.

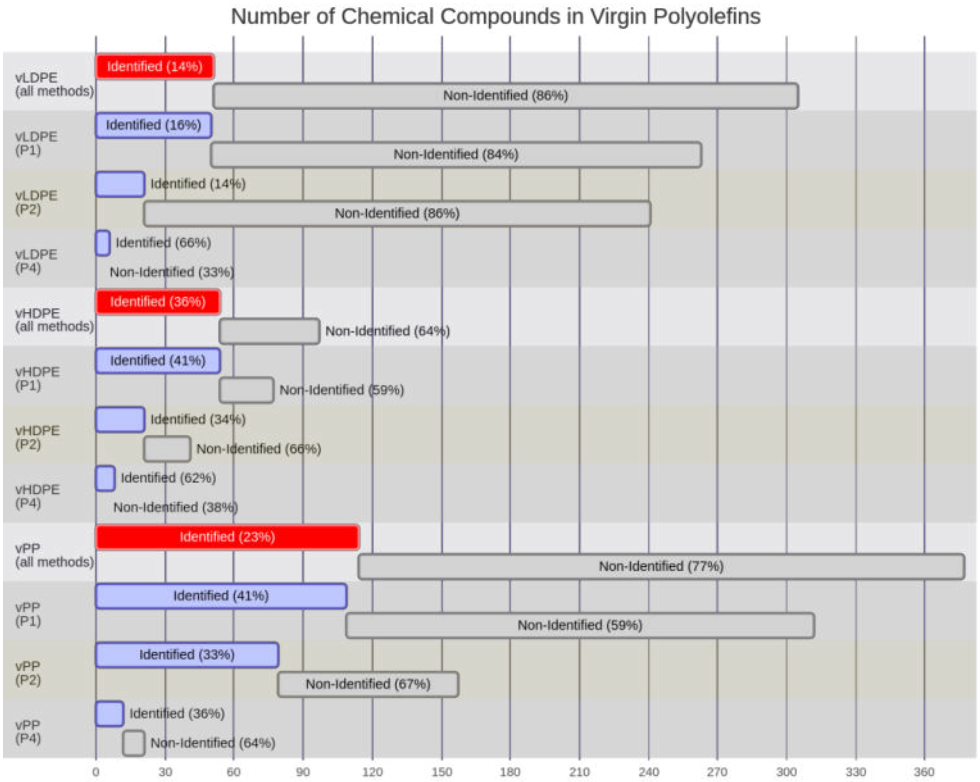


***Figure 15**. Prevalence of unidentified compounds in virgin polyolefins: three samples each of LDPE, HDPE, and PP.*

6.5. Are Two Batches Suitable for Contact Also Suitable When Mixed?

As discussed in section 5, blending PCR batches can help to mitigate risks for batches not qualified for either rinse-off or leave-on applications due to a too high risk of exposure for one or several substances. Assessing the suitability of mixed batches obtained by blending with either virgin or cleaner polymer involves nuanced consideration of the mixing process, including whether the granules are physically mixed without regranulation or undergo regranulation after melting. Typically, the assessment methodology employed is sufficiently conservative, allowing for the presumption that combining two or more batches deemed acceptable individually should also result in an acceptable mixture. This approach does not account for potential interactions and the formation of new compounds resulting from the mixture.

The rationale for encouraging blends is summarized in three cases;

- When contaminants from batch A are diluted with virgin material from batch B, the substances present in batch A are diluted in the AB mixture by default. Therefore, conducting a separate evaluation of the AB mixture is unnecessary and may yield less reliable results than evaluating batches A and B independently.

- For recycled pellets A and B, which statistically contain the same compounds, mixing these batches would likely result in a more uniform detection of compounds (reducing randomness in presence) without significantly altering the concentration levels within the samples.

- The only instance where the assessment of a mixed batch AB might diverge from the assessments of its constituent batches A and B is when they exhibit significantly different concentration levels of contaminants. In practical industrial applications, melting and mixing batches A and B should homogenize the intrinsic variabilities found in each, leading to a more uniform distribution of substances within the mixture.

As a rule of thumb, mixed/blended recycled materials should be considered to contain more substances than their initial counterparts before mixing/blending. Their concentrations tend to be smoothed out, reducing the risk of high exposure to fortuitous hazardous contaminants. This smoothing effect contributes to the overall safety assessment of the mixed material, suggesting that a well-blended mix might even enhance the predictability and uniformity of exposure to potential contaminants. Finally, blending with virgin polyolefins is always a safe solution to improve the safety profile of a non-qualified batch.

7. Conclusions and Prospects

The CosPaTox project, while not aiming to resolve every aspect of recycled material evaluation—spanning a vast array of concerns beyond the scope of this scientific dossier—provides a comprehensive view of methodologies and approaches within its guidelines, drafted concurrently with this report. Central to experimental efforts within CosPaTox has been the scientific risk assessment of the transfer of semi-volatile organic substances from articles made entirely or partially from recycled polyolefin materials (LDPE, HDPE, PP) to cosmetics or detergents, thereby evaluating the consumer exposure risk from circular economy materials.

Addressing the myriad complications posed by the almost infinite diversity of possible contaminants—often at very low concentrations due to the incidental nature of contamination or the mixing of recycled materials during collection or recycling—was circumvented by developing an original method. This method pivots on evaluating pellets rather than finished articles. This choice, initially intuitive, is justified upstream by the need to direct recycled material flows towards safe applications, ensuring the availability of sufficient quantities by combining sources with equivalent safety profiles. The conclusions of the CosPaTox project retrospectively affirm the relevance of this approach.

Given the volumes of recycled material to be tested and the frequency of tests, far exceeding the needs for virgin material—which requires evaluation only when processes and formulations change—the standard test relies on accelerated migration tests (10 days at 60°C) with a 1:1 simulant-to-pellets ratio, typically 3g in 3mL of ethanol 95% for lipophilic/fatty products and ethanol 50% for aqueous products. These conditions obviate the need for a concentration step and limit the use of large solvent volumes. Ethanol 95% provides a very realistic worst-case scenario compared to results obtained by extraction at 40°C in dichloromethane under similar test conditions. The number of detected substances, the number of identifiable substances, and their transferred quantities are similar.

Utilizing high-temperature elution programs, non-targeted chromatographic analysis in GC-MS is the only feasible generic technique. It separates dozens, if not hundreds, of substances in migrates or extracts. Identification of substances requires mass spectrum databases as well as retention time databases. They must be combined with in-house databases consolidated by the recurrence of certain risk substances for better routine identification. Only semi-quantification is possible based on internal standards with structural homology with the molecules sought. Identification and quantification are constrained by the inherent limits of the methodology, which, however, are part of the current state of the art for non-targeted substance search.

The dossier proposes several strategies for extrapolating test results on pellets to expected concentrations in actual containers. All extrapolations are built on conservative assumptions regarding partition coefficients and initial quantities. The comparison of results with bottles produced from the same pellets confirms that concentrations are overestimated, with a risk of overestimation well below the sources of uncertainty. This has made it possible to propose a very conservative estimator based on a single test or a more realistic estimator based on a migration and extraction test. A single test is preferred because it does not require the pairing of peaks obtained from different tests, thus allowing the application of any detected substance, even if it is not identified.

The protocol allows for consideration of many substances whose number is one to two orders of magnitude larger than that considered for virgin materials, which nonetheless present a similarly large count of transferable substances. This choice justifies the systemic nature of the evaluation of non-

targeted searched substances. Non-identified substances in recycled polyolefins can account for up to half of the substances detected in migrates. The proposed risk evaluation and management approach considers them potentially genotoxic, assuming chronic consumer exposure to them at maximized skin retention and absorption levels for the uses. All these precautions ensure the extremely conservative nature of the approaches considered. The possibility of exposure to potentially genotoxic substances at concentrations below the detection limit is also considered. This choice justifies that the results of a test are not necessarily corroborated by a more severe test that could have highlighted the transfer of other substances. The analytical detection limit is indeed the same for extractions, migrations, and regardless of the hydroalcoholic simulant used (ethanol 50% or ethanol 95%). The comprehensiveness of the situations considered reasonably covers situations where false negatives (non-identified or misidentified substances) are present due to unavoidable analytical errors.

The conclusions of this study can be used in two ways: either to produce quality/safety indicators for recycled material based on maximum concentrations that must not be exceeded or to produce evaluations of potential exposure for the envisaged application and consumer. This second possibility is preferred in the scientific report to demonstrate the effect of the product and target on the acceptance criterion, while both are described in the guidelines. The report describes other levels of sophistication that can go as far as considering time and temperature effects for more specific applications.

Although the evaluation of recycled material presents a level of complexity significantly higher than that required for virgin material, a demonstration of tailoring the approach for both test execution and interpretation is proposed. The establishment of databases (analytical, toxicological) can be broadly shared across samples. Information obtained at one value chain stage can be directly utilized at another if entities agree to share test results. Non-targeted tests and analyses do not preempt the need for evaluations required for specific classes of substances (bisphenols, nonylphenols, aromatic amines, polycyclic aromatic hydrocarbons, phthalates, etc.) and heavy metals. This holistic approach facilitates a nuanced understanding and application of recycled materials in a way that ensures safety while promoting the circular economy's goals.

8. References

[1] Cecon VS, Da Silva PF, Curtzwiler GW, Vorst KL. The challenges in recycling post-consumer polyolefins for food contact applications: A review. *Resources, Conservation and Recycling*. 2021;**167**:105422.

[2] Palkopoulou S, Joly C, Feigenbaum A, Papaspyrides CD, Dole P. Critical review on challenge tests to demonstrate decontamination of polyolefins intended for food contact applications. *Trends in Food Science & Technology*. 2016;**49**:110-20.

[3] SCCS. Scientific Committee on Consumer Safety: The SCCS notes of guidance for the testing of cosmetics ingredients and their safety evaluation. *SCCS/1647/22*. 2012;**8th revision**.

[4] Cramer GM, Ford RA, Hall RL. Estimation of toxic hazard—A decision tree approach. *Food and Cosmetics Toxicology*. 1976;**16**:255-76.

[5] Patlewicz G, Jeliazkova N, Safford RJ, Worth AP, Aleksiev B. An evaluation of the implementation of the Cramer classification scheme in the Toxtree software. *SAR and QSAR in Environmental Research*. 2008;**19**:495-524.

[6] Lapenna S, Worth A. Analysis of the Cramer classification scheme for oral systemic toxicity - implications for its implementation in Toxtree. JRC Report JRC66022. Luxembourg (Luxembourg): Publications Office of the European Union; 2011.

[7] Toxtree Project. *Toxtree - Toxic Hazard Estimation by decision tree approach*. 2024 [cited 2024 March 7th, 2024]; Available from: https://toxtree.sourceforge.net/index.html.

[8] Munro IC, Renwick AG, Danielewska-Nikiel B. The Threshold of Toxicological Concern (TTC) in risk assessment. *Toxicology Letters*. 2008;**180**:151-6.

[9] EFSA Scientific Committee, More SJ, Bampidis V, Benford D, Bragard C, Halldorsson TI, Hernández-Jerez AF, Hougaard Bennekou S, Koutsoumanis KP, Machera K, Naegeli H, Nielsen SS, Schlatter JR, Schrenk D, Silano V, Turck D, Younes M, Gundert-Remy U, Kass GEN, Kleiner J, Rossi AM, Serafimova R, Reilly L, Wallace HM. Guidance on the use of the Threshold of Toxicological Concern approach in food safety assessment. *EFSA Journal*. 2019;**17**:e05708.

[10] SCCS. Scientific Committee on Consumer Safety: The SCCS notes of guidance for the testing of cosmetics ingredients and their safety evaluation. *SCCS/1628/21*. 2021;**11th revision**.

[11] SCCS. Scientific Committee on Consumer Safety: The SCCS notes of guidance for the testing of cosmetics ingredients and their safety evaluation. *SCCS/1647/22*. 2023;**12th revision**.

[12] Nguyen P-M, Goujon A, Sauvegrain P, Vitrac O. A computer-aided methodology to design safe food packaging and related systems. *AIChE Journal*. 2013;**59**:1183-212.

[13] Hoekstra E, Brandsch R, Dequatre C, Mercea P, Milana MR, Stoermer A, Trier X, Vitrac O, Schaefer A, Simoneau C. Practical guidance document on the implementation of diffusion modelling for the estimation of specific migration in support of Regulation (EU) No 10/2011. *https://eceuropaeu/jrc/en/publication/practical-guidelines-application-migration-modelling-estimation-specific-migration*. 2015.

[14] Cospatox Project. Voluntary industry guideline for the risk assessment of recycled plastics for the use in cosmetic products and detergent packaging: Guidance for recycled PE and PP 2023.

[15] Baner A, Bieber W, Figge K, Franz R, Piringer O. Alternative fatty food simulants for migration testing of polymeric food contact materials. *Food Additives & Contaminants*. 1992;**9**:137-48.

[16] Cooper I, Goodson A, O'Brien A. Specific migration testing with alternative fatty food simulants. *Food Additives & Contaminants*. 1998;**15**:72-8.

[17] EPA. Framework for Human Health Risk Assessment to Inform Decision Making. Report 100/R-14/001. U.S. Environmental Protection Agency Office of the Science Advisor Risk Assessment Forum 2014. p. 63.

[18] OECD. *The OECD QSAR Toolbox*. 2024 [cited 2024 March 8, 2023]; Available from: https://www.oecd.org/chemicalsafety/risk-assessment/oecd-qsar-toolbox.htm.

[19] ECHA. Guidance on information requirements and chemical safety assessment R.8: Characterisation of dose [concentration] - response for human health - Draft Version 3.0. EFSA; 2018. p. 19.
[20] ECHA. Read-Across Assessment Framework (RAAF). European Chemicals Agency; 2017. p. 59.
[21] ECHA. Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of chemicals.: ECHA; 2008. p. 134.
[22] WHO. Section 4.5 Genotoxicity - Second Edition. *Environmental Health Criteria 240 - Principles and methods for the risk assessment of chemicals in food*. Stuttgart, Germany: World Health Organization; 2020. p. 4-1 - 4-121.
[23] Lickly TD, Bell CD, Lehr KM. The migration of Irganox 1010 antioxidant from high-density polyethylene and polypropylene into a series of potential fatty-food simulants. *Food Additives & Contaminants*. 1990;**7**:805-14.
[24] National Research Council. Risk Assessment in the Federal Government: Managing the Process. Washington, DC: The National Academies Press; 1983. 205p.
[25] Su Q-Z, Vera P, Nerín C, Lin Q-B, Zhong H-N. Safety concerns of recycling postconsumer polyolefins for food contact uses: Regarding (semi-)volatile migrants untargetedly screened. *Resources, Conservation and Recycling*. 2021;**167**:105365.
[26] EFSA, More SJ, Bampidis V, Benford D, Bragard C, Halldorsson TI, Hernández-Jerez AF, Hougaard Bennekou S, Koutsoumanis KP, Machera K, Naegeli H, Nielsen SS, Schlatter JR, Schrenk D, Silano V, Turck D, Younes M, Gundert-Remy U, Kass GEN, Kleiner J, Rossi AM, Serafimova R, Reilly L, Wallace HM. Guidance on the use of the Threshold of Toxicological Concern approach in food safety assessment. *EFSA Journal*. 2019;**17**:e05708.
[27] EFSA. Scientific Opinion on Exploring options for providing advice about possible human health risks based on the concept of Threshold of Toxicological Concern (TTC). *EFSA Journal*. 2012;**10**:2750.
[28] Barthélémy E, Spyropoulos D, Milana MR, Pfaff K, Gontard N, Lampi E, Castle L. Safety evaluation of mechanical recycling processes used to produce polyethylene terephthalate (PET) intended for food contact applications. *Food Additives & Contaminants: Part A*. 2014;**31**:490-7.
[29] Kroes R, Renwick AG, Feron V, Galli CL, Gibney M, Greim H, Guy RH, Lhuguenot JC, van de Sandt JJM. Application of the threshold of toxicological concern (TTC) to the safety evaluation of cosmetic ingredients. *Food and Chemical Toxicology*. 2007;**45**:2533-62.
[30] EFSA. Scientific Opinion on the criteria to be used for safety evaluation of a mechanical recycling process to produce recycled PET intended to be used for manufacture of materials and articles in contact with food. *EFSA Journal*. 2011;**9**:2184.
[31] Kroes R, Renwick AG, Cheeseman M, Kleiner J, Mangelsdorf I, Piersma A, Schilter B, Schlatter J, van Schothorst F, Vos JG, Würtzen G. Structure-based thresholds of toxicological concern (TTC): guidance for application to substances present at low levels in the diet. *Food and Chemical Toxicology*. 2004;**42**:65-83.
[32] Kienzler A, Bopp SK, van der Linden S, Berggren E, Worth A. Regulatory assessment of chemical mixtures: Requirements, current approaches and future perspectives. *Regulatory Toxicology and Pharmacology*. 2016;**80**:321-34.
[33] OECD. Test No. 471: Bacterial Reverse Mutation Test2020.
[34] ECHA. Guidance on Information Requirements and Chemical Safety Assessment Chapter R.7a: Endpoint specific guidance. Version 6.0. European Chemicals Agency; 2017. p. 609.
[35] EFSA Panel on food contact materials e, flavourings, aids p. Scientific Opinion on the criteria to be used for safety evaluation of a mechanical recycling process to produce recycled PET intended to be used for manufacture of materials and articles in contact with food. *EFSA Journal*. 2011;**9**:2184.
[36] SCCS. Scientific Committee on Consumer Safety: The SCCS notes of guidance for the testing of cosmetics ingredients and their safety evaluation. *SCCS/1602/18*. 2018;**10th revision**.
[37] Schmitt BG, Jensen E, Laufersweiler MC, Rose JL. Threshold of Toxicological Concern: Extending the chemical space by inclusion of a highly curated dataset for organosilicon compounds. *Regulatory Toxicology and Pharmacology*. 2021;**127**:105074.

[38] Safford RJ. The Dermal Sensitisation Threshold—A TTC approach for allergic contact dermatitis. *Regulatory Toxicology and Pharmacology*. 2008;**51**:195-200.

Appendix 1. Definitions of some mass transfer concepts

In the framework of the **CosPaTox** project, a deep understanding of mass transfer phenomena is crucial for accurately modeling and analyzing the safety of materials in contact with cosmetic or detergent products. As such, **Table 17** provides precise definitions of key mass transfer terms and concepts. These are integral to the methodologies employed in our investigations and serve as the foundational lexicon for designing experiments, interpreting results and drawing scientifically robust conclusions.

***Table 17**. List of terms and concepts used in the project CosPaTox*

Terms	Description
Desorption	Desorption refers to the comprehensive process that controls both the diffusion of substances within a polymer matrix and their dissolution into a contacting medium, such as a cosmetic product or its liquid simulant.
Diffusion or Molecular Diffusion	Diffusion is the fundamental transport phenomenon responsible for the dispersion of substances within a polymer or liquid medium due to thermal motion. Observable net flux and concentration gradients emerge when two media, containing differing concentrations of the substance, come into contact. In the absence of external forces and interactions, the net flux is inversely proportional to the concentration gradient, with the proportionality constant known as the diffusion coefficient. Its SI unit is m^2/s.
Extraction or Solvent Extraction	Extraction involves using a solvent to swell the polymer, thereby accelerating desorption into a liquid simulant. Halogenated solvents like dichloromethane and chloroform are particularly effective for polyolefins. Solvents with high dipolar moments further facilitate dissolution, making it easier to determine polymer concentrations post-maceration
Extraction Testing (analogy with food contact materials	According to Commission Directive (EC) 97/48 related to food contact materials, "*Other tests [i.e., not related to migration testing], which use media having a very strong extraction power under very severe test conditions, may be used if it is generally recognized, on the basis of scientific evidence, that the results obtained using these tests ("extraction tests") are equal to or higher than those obtained in the test with simulant D*".
Liquid Simulant	A liquid simulant serves as a stand-in for a real product (e.g., cosmetic or detergent) to simplify the chemical analysis originating from the material.
Maceration	Maceration is the process of soaking a material in a liquid, either a solvent or a liquid simulant, for an extended period to facilitate mass transfer
Mass Action Law	The mass action law posits that net mass fluxes are proportional to the concentrations or amounts of substances present in the system.
Migration	In regulatory contexts concerning food contact materials and cosmetics, migration describes the desorption of substances from packaging and their subsequent accumulation in the contacting product. The term encompasses both diffusion and substance partitioning between the packaging and the product.
Migration Testing (analogy with food contact materials)	According to Commission Directive (EC) 97/48 related to food contact materials, "**In application of the general criteria that the determination of migration should be restricted to the test conditions which, in the specific case under examination, are recognized to be the most severe on the basis of scientific evidence*,…".

	Regulation (EU) 10/2011 precises "*The sample shall be placed in contact with the food simulant in a manner representing the worst of the foreseeable conditions of use as regard contact time in Table 1 and as regard contact temperature in Table 2*". (Annex 5, Chapter 2) "*…the specific migration values shall be expressed in mg/kg applying the real surface to volume ratio in actual or foreseen use*." (Article 17 - **Expression of migration test results**)
Partition Coefficient or Distribution Coefficient	This coefficient represents the equilibrium concentration ratio of a substance between the material and the contacting liquid or product. At low concentrations in the polymer, this ratio is generally volume-ratio independent and can be considered an intrinsic property of the substance for the specified material-liquid pairing.
Potential Release	Potential Release quantifies the fraction of a substance present in the material that can transfer to the product or liquid simulant in contact. Factors influencing this include the liquid's volume, contact time, and the substance's partition coefficient.
Sorption	Sorption is the converse of desorption and pertains to the mass transfer of substances from a liquid medium into the material through dissolution and diffusion within the material.
Solvent	A solvent is a liquid that facilitates the dissolution of substances, aiding in the mass transfer processes.
Thermodynamic Equilibrium	In the context of mass transfer, thermodynamic equilibrium is reached when a substance's chemical potential equalizes between two contacting compartments, resulting in zero net flux. While molecular exchange continues, an observer would note time-invariant concentrations; any substance entering one compartment is matched by an equivalent amount exiting it.

Appendix 2. Mass transfer balance and thermodynamic considerations

The mass transfer of pollutants from recyclates (subscript P meaning "*polymer*") to liquid cosmetic or detergent products (subscript F meaning "*fluid*") obeys basic principles, including mass balance between before (subscript 0) and after some time of contact t at temperature T, mass diffusion in the polymer and partition or distribution of the substance between P and F according to their relative chemical affinity.
The concentrations C_X with $X = P, F$ are expressed in mass concentrations with typical units in mg/kg.

Mass balance

The mass balance equation between the polymer (P) and the fluid (F) reads as:

$$\begin{aligned} m^0 &= \rho_P V_P C_P^0 \\ &= \rho_P V_P C_P^{(t,T)} + m^{(t,T)} \\ &= \rho_P V_P C_P^{(t,T)} + \rho_F V_F C_F^{(t,T)} \\ &= (\rho_P V_P K + \rho_F V_F) C_F^{(t,T)} \end{aligned}$$

Eq. 21

Variables:

- $\rho_P V_P$: mass of the polymer defined as the product of polymer density (ρ_P) and polymer volume (V_P).
- $\rho_F V_F$: mass of the fluid defined as the product of product density (ρ_F) and product volume (V_F).

According to the context (testing, exposure estimation, modeling), mass transfer can be characterized by concentrations, absolute transferred amounts $m^{(t,T)}$ or relative transferred amounts so-called "*Potential Release*" (PR). This last concept provides a robust framework for mass balance calculations amidst numerous uncertainties. Not intrinsic to either the polymer or the substances in question, the potential release and concentration in tested conditions require proper extrapolation techniques to be applicable for real-world exposure scenarios ("*actual exposure*"). This appendix elucidates the definitions and relationships among various quantities, including more general formulations than the ones adopted in the dossier in the sake of simplicity.

Definition of the Potential Release PR

The potential release PR of substances from the Post-Consumer Recyclate (PCR) material is framed within the previous mass balance principles. The formula for the effective potential release of a substance (PR) is given as:

$$PR = \frac{m^{(t,T)}}{m^0} = \frac{\rho_F V_F C_F^{(t,T)}}{\rho_P V_P C_P^0} = L \frac{C_F^{(t,T)}}{C_P^0} = \frac{L}{K+L} \times PR_T^{(t,T)} = PR_E^{(L,T)} \times PR_T^{(t,T)}$$

Eq. 22

Where:

- m^0: Maximum amount of substance that can be transferred, present in the PCR.

- $m^{(t,T)}$: Amount of substance transferred at time t and temperature T.
- C_P^0 and $C_P^{(t,T)}$: Initial and time- and temperature-dependent concentrations of the substance in the polymer, respectively.
- $C_F^{(t,T)}$: Concentration of the substance in the liquid simulant or cosmetic product.
- K: Partition coefficient (polymer-to-simulant).

$L = \frac{\rho_F}{\rho_P}\frac{V_F}{Al_P}$ is the simulant-to-recyclate mass ratio or dilution factor.

The effective potential release can be dissected into thermodynamic and kinetic components:

$$PR = PR_E \times PR_T$$

Eq. 23

Where:

- $0 \leq PR_E = \frac{L}{K+L} \leq 1$ is the thermodynamically controlled potential release, dependent on the dilution ratio L and the simulant used (either ethanol 50% or 95%).
- $0 \leq PR_T \leq 1$ is the kinetically controlled potential release, largely independent of L for sufficiently large values of L.

Relationship between exposure (PR_E) and test (PR_E^{test}) potential release

The relationship between the potential-release coefficients under real-world exposure (PR_E) — *associated with the dilution ratio* L — and accelerated test conditions on pellets (PR_E^{test}) — *associated with the dilution* L^{test} — can be succinctly described by the following equations:

$$\begin{aligned} PR_E &= \frac{L}{K+L} \\ &= \frac{1}{\frac{L^{test}}{L}\left(\frac{1}{PR_E^{test}} - 1\right) + 1} \\ &= \frac{1}{\Gamma\left(\frac{1}{PR_E^{test}} - 1\right) + 1} \end{aligned}$$

Eq. 24

These formulations are underpinned by the assumption that the partition coefficient K exhibits concentration-independence and adheres to linear, reversible sorption/desorption isotherms. According to the considered substance, its value is expected to range between 0.05 and 10,000. K influences the potential release of the substance as soon as K is commensurable or larger than L. Additionally, **the values of PR_E^{test} remain invariant to concentration changes, given that the substance in question is effectively quantified in the simulant**.

NOTE 1

The coefficient $\Gamma = \frac{L^{test}}{L}$ serves as a scaling factor that mediates the divergence between the partition-release coefficients obtained from real-world exposure assessments and accelerated tests. **Reporting**

Γ is mandatory in all safety evaluation to quantify this divergence. For example, a PR_E^{test} value of 0.1 would lead to a "real" potential release of $\frac{1}{9\Gamma+1}$. That is for $\Gamma \approx 0.1$, one gets $\frac{PR_E}{PR_E^{test}} \approx 5.3$. The value of PR_E^{test} and PR_E are commensurable only when they approach unity.

NOTE 2
It is important to note that while PR_E excludes temperature-induced effects (captured instead by PR_T), such exclusion is justifiable. This is due to the generally low impact of factors like free-volume effects and isosteric heat of sorption on the partition coefficient K. Additionally, similar temperature-dependent behaviors are often observed in both the polymer and the liquid in contact, resulting in a canceling effect on K.

NOTE 3
Lastly, discrepancies that may arise between the accelerated test conditions and actual exposure scenarios are addressed by incorporating safety factors into the PR_E^{test} values. These safety factors buffer against unforeseen variables or uncertainties, thereby enhancing the safety assessment's robustness.

Relationship between potential release and simple extraction by maceration
The foundational mass balance equations discussed earlier are valid provided no concurrent chemical reactions or volatile emissions would alter the mass balances. In the context of extraction conditions, the partition coefficient K is generally expected to be close to or less than 1. Specifically, dichloromethane (DCM) induces swelling in polyolefins, rendering a K value close to 1 as a worst-case scenario for arbitrary substances. This, in turn, leads to a worst-case potential release value of 2 when a dilution ratio $L_{DCM}^{extraction}$ of 1 is employed.
When the same mass of sample and solvent/liquid is used for both extraction and testing the potential release, the relationship can be expressed as:

$$\begin{aligned} PR_E^{test} &\approx \min\left(1{,}2\frac{\rho_F V_F^{test} C_F^{test}}{\rho_{DCM} V_{DCM} C_{DCM}^{extraction}}\right) \\ &\approx \min\left(1{,}2\frac{C_F^{test}}{C_{DCM}^{extraction}}\right) \end{aligned}$$

Eq. 25

Here, the test conditions could be in either ethanol 95% (ET95) or ethanol 50% (ET50). The factor 2 arises due to the condition $L_{DCM}^{extraction} = 1$, wherein half of the measured amount is conservatively assumed to still be present in the recyclate.
The safety factor 2 can be mitigated through successive extractions, confirming the recyclate depletion. Underestimating the concentration in the recyclate will cause an underestimation of the exposure concentration.

Relationship Between PR and Exposure Concentration C_F
Understanding the relationship between the exposure concentration C_F and the initial concentration in the recyclate $C_{P,0}$ is critical for assessing potential health implications. Following existing literature and specifically as elucidated by Zhu et al. (2019), the exposure concentration $C_F^{(t,T)}$ post a designated contact duration t and temperature T between the liquid simulant (F) and the recyclate (P) can be framed as:

$$
\begin{aligned}
C_F^{(t,T)} &= \frac{PR_T^{(t,T)}}{K+L} \times C_{P,0} \\
&= \frac{PR_T^{(t,T)}}{K + \frac{\rho_F}{\rho_P}\frac{V_F}{A\ell_P}} \times C_{P,0} \\
&= PR_E^{(T)} \times PR_T^{(t,T)} \times \frac{C_{P,0}}{L} \\
&= PR^{(t,T)} \times \frac{C_{P,0}}{L}
\end{aligned}
$$

Eq. 26

The pivotal role of "potential release" concepts can be well appreciated when considering different operational scenarios—accelerated test conditions aiming at thermodynamic equilibrium, actual exposure conditions, and the worst-case scenarios that stipulate the upper bounds of acceptable contaminant concentrations (C_F^{max}). The formulae representing these scenarios are summarized as:

$$
\begin{aligned}
\text{Accelerated Test (Equilibrium):} \quad & C_F^{test} = \frac{PR_E^{test}}{L^{test}} \times C_{P,0} \\
\text{Actual Exposure:} \quad & C_F = \frac{PR_E \times PR_T}{L} \times C_{P,0} \\
\text{Worst-Case Scenario:} \quad & C_F^{max} = \frac{1}{L} \times C_{P,0}^{max}
\end{aligned}
$$

Eq. 27

Appendix 3. Extended Evaluation Using a Diffusion Model

Main goal

In accelerated conditions, thermodynamic equilibrium is reached within days or weeks. Therefore, diffusion modeling is unnecessary in most cases and PR_T can be assumed to be equal to unity. This appendix describes a simplified diffusion model that can be streamlined to evaluate PR_T in more general cases when the effects of time t and temperature T effects need to be considered in the estimation of the actual exposure concentration C_F. It is based on the assumption that high molecular weight in polyolefins needs a significant amount of time to reach the packaging surface in contact with the cosmetic or detergent product. This time is controlled by the mass diffusion of the substance in the polymer. Existing analytical solutions of mass diffusion problems with uniform diffusion coefficients and initial concentrations are used to derive a closed form of PR_T.

Diffusion Model

For monolayer materials and when substances are identified, the kinetic control can be evaluated through a conservative analytical expression of the diffusion problem. The potential release PR_T is then estimated from Eq. 4.18 in Crank's book [26] as:

$$PR_T(t,T,M) = \min\left[\frac{2\sqrt{Fo}}{\sqrt{\pi}}, 1 - \frac{2}{\pi^2}\exp\left(-\frac{\pi^2}{4}Fo\right)\right]$$

Eq. 28

where t and T refer to contact time and temperature, respectively. The Fourier number (Fo) is given by:

$$Fo = \frac{D_P(M,T)t}{l_P^2} = D_P(M,T)\frac{A^2}{V_P^2}t$$

Eq. 29

The real diffusivity for polyolefins can be conservatively estimated using the Piringer equation [38]:

$$D(M,T) = e^{A'_P - 0.1351M^{2/3} + 0.003M - \frac{\tau+10454}{T+273.15}}$$

where M represents the molecular mass in $g \cdot mol^{-1}$, and T is the temperature in °C. The constants A'_P and τ are specified in **Table 18**.

***Table 18**. Parameters of the Piringer model for polyolefins (applicable for $30 \leq M \leq 2000\ g \cdot mol^{-1}$ and $T \leq 90°C$).*

	HDPE	PP (homo and random)	PP (block copolymer)
A'_P	14.5	13.1	11.5
τ (K)	1577	1577	0

Appendix 4. Tested Post-consumer Materials (pellets)

Recycled materials considered within the CosPaTox project are listed in **Table 19**. The data and sourcing are anonymized. The description and information combine observations and declarative statements from suppliers.

***Table 19**. Identification of samples and sourcing. The dossier refers indifferently to samples with and without the prefix r indicating a postconsumer/recycled origin (e.g., LDPE or rLDPE).*

Sample Code	Recycled/PCR material code	Supplier	Description	Information
LDPE 1	rLDPE 1	M	rLDPE granules for flexible packaging	PCR, commercial waste (Austria)
LDPE 2	rLDPE 2	B	standard quality cold-washed	no information
LDPE 3	rLDPE 3	B	standard quality cold-washed	no information
LDPE 4	rLDPE 4	C	LDPE from conventional mechanical recycling	LDPE from conventional mechanical recycling
LDPE 5	rLDPE 5	C	LDPE from solvent-based process	LDPE from solvent-based process
HDPE 1	rHDPE 1	B	for extrusion blow molding	(100%), hot washed, deodorized (state of the art
HDPE 2	rHDPE 2	B	(granules) for extrusion blow molding	(100%), hot washed, deodorized (state-of-the-art
HDPE 3	rHDPE 3	E	HDPE natural	hot washed, post-treated
HDPE 4	rHDPE 4	E	HDPE grey/white	hot washed, post-treated
HDPE 5	rHDPE 5	F	HDPE pellets (EU country 1)	mix body and home care, warm washed
HDPE 6	rHDPE 6	F	HDPE pellets (EU country 1)	mix body and home care, warm washed, post-treated
HDPE 7	rHDPE 7	F	HDPE pellets (EU country 2)	Hot-washed or steam-washed material
HDPE 8	rHDPE 8	F	HDPE pellets (EU country 2)	detergents, shampoo, hot washed

HDPE 10	rHDPE 10	F	HDPE pellets (EU country 3)	household, warm-washed, post-treated (deodorization)
HDPE 11	rHDPE 11	G	HDPE pellets	hot washed
HDPE 12	rHDPE 12	G	HDPE pellets (improved color)	hot washed, post-treated (deodorization)
HDPE 13	rHDPE 13	K	HDPE Colored I	presorted plastic
HDPE 14	rHDPE 14	K	HDPE Colored II	presorted plastic
HDPE 15	rHDPE 15	A	HDPE pellets	no information
HDPE 16	rHDPE 16	A	HDPE pellets	no information
PP 1	rPP 1	B	PP granules for injection molding	cold washed, 100% PCR
PP 2	rPP 2	B	PP granules for injection molding	State-of-the-art sorting/recycling
PP 3	rPP 3	B	White r-PP (granules) for injection molding	(100%), hot washed, deodorized (state of the art
PP 4	rPP 4	B	(granules) for injection molding	(100%), hot washed, deodorized (state of the art
PP 5	rPP 5	E	PP colored	cold-washed, post-treated
PP 6	rPP 6	E	PP colored	cold-washed, post-treated with a special process
PP 7	rPP 7	E	PP colored	cold-washed, special degassed and post-treated
PP 8	rPP 8	E	PP colored	cold-washed
PP10	rPP10	F	PP pellets (EU country 4)	(mainly FG), Cold-washed, post treated (deodorization)
PP 11	rPP 11	G	PP pellets	hot washed
PP 12	rPP 12	K	PP colored	presorted plastic

Appendix 5. Actual Dilution Factors for Cosmetic Packaging

Table 20 and Table 21 detail the geometrical parameters commonly encountered respectively in cosmetic packaging and in packaging for laundry and home care products, providing insights into their typical usage patterns. These parameters are crucial for estimating partition coefficients and exposure concentrations in risk assessments. It serves to clarify how these packaging attributes may influence key factors in the safety assessment of these product categories.
Generally, the dilution factors, denoted as L, exhibit lower values for cosmetic, laundry, and home care products compared to food applications, with values above 50 or more. The Pareto chart in **Figure 16** shows that the likely value is ranged from 10 to 15. Due to these lower dilution factors, the partition coefficient K assumes a more pronounced role in influencing the exposure concentration C_F. Utilizing conservative estimates for K—for instance, setting $K = 0.1$ or any value less than unity—may result in a significant overestimation of C_F.

***Table 20**. Geometrical characteristics and typical usage of cosmetic packaging.*

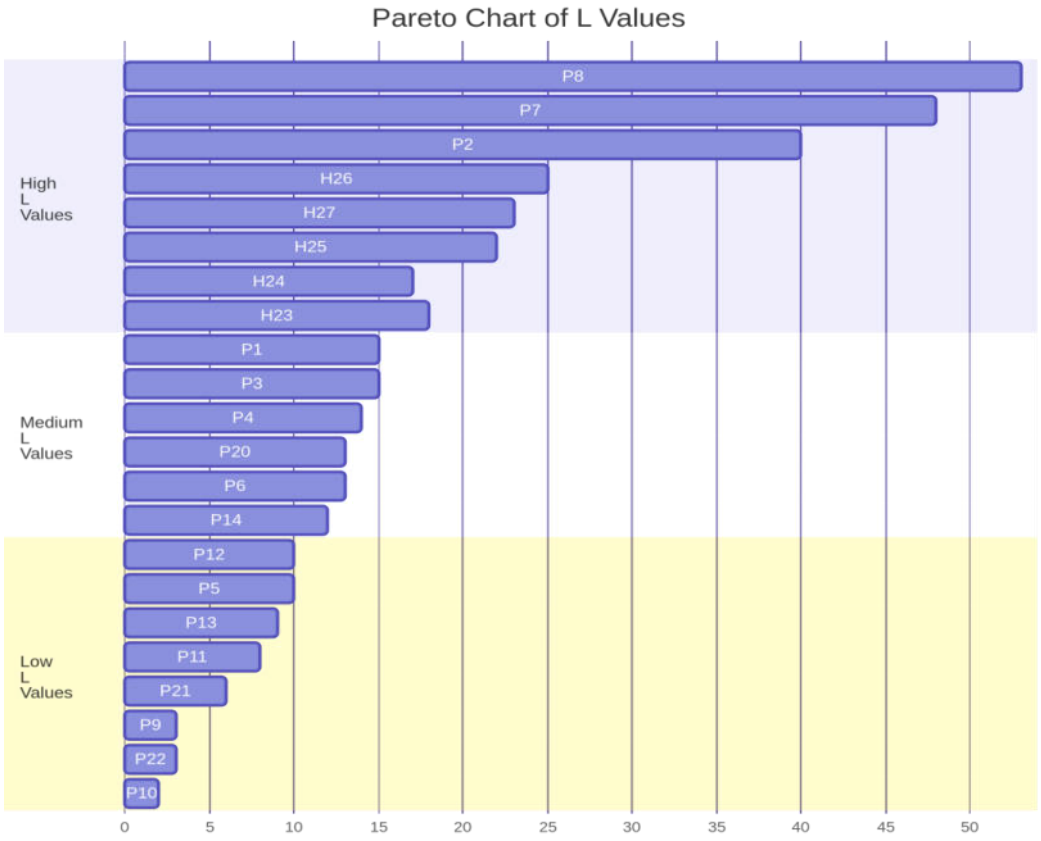
Code	Packaging Type	Polymer	Product Content	V_F	Packaging weight: $\rho_P V_P$	Packaging thickness ℓ_P	Surface area in contact A	Dilution factor L	Shelf life
units	**[g]**	**[µm]**	**(typical)**	**[mL]**	**[g]**	**[µm]**	**[cm²]**	**(-)**	**[years]**
P1	tube	HDPE	shampoo	250	17.0	500	238	15	3
P2	closure	PP	shampoo	250	6.2	480	0.6	40	3
P3	bottle	HDPE	shampoo	300	20	n.d.	325	15	2.5
P4	bottle	HDPE	shampoo	500	36.0	450	373	14	3
P5	bottle	HDPE	shampoo	250	25.8	400	240	10	3
P6	bottle	HDPE	shampoo	300	23.0	300	249	13	3
P7	pouch	PE	shampoo /shower gel	500	10.5	175	480	48	3
P8	pouch	PE	shampoo /shower gel	1000	18.7	205	725	53	3
P9	pouch	PE	cosmetic	15	5	n.d.	n.d.	3	3
P10	sachet	PE	cosmetic	2	1.1	120	70	2	3
P11	spray	HDPE	deodorant	100	13.0	391	141	8	3
P12	spray	HDPE	deodorant	150	15.0	437	205	10	3
P13	spray	HDPE	deodorant	200	22.0	452	197	9	3
P14	tube	HDPE	creme	75	6.5	n.d.	90	12	2.5
P15	film	LDPE/PP	wet wipes	56 pieces	n.d.	80	858	n.d.	2.5
P16	film	LDPE/PP	wet wipes	80 pieces	n.d.	80	999	n.d.	2.5
P17	film	LDPE/PP	wet wipes	48 pieces	n.d.	80	708	n.d.	2.5
P18	film	LDPE/PP	wet wipes	56 pieces	n.d.	95	858	n.d.	2.5
P19	film	PE/PP	wet wipes	80 pieces	n.d.	95	999	n.d.	2.5
P20	bottle	PET	mouth wash	400	30	n.d.	450	13	2.5
P21	tube	PP	cosmetic	30	4.78	n.d.	500	6	3
P22	bottle	PP	mascara	20	7.3	400	n.d.	3	3

***Table 21**. Geometrical characteristics and typical usage of laundry and home care packaging*

Code	Packaging Type	Polymer	Product Content	V_F	Packaging weight: $\rho_P V_P$	ℓ_P	L
units	**[g]**	**[µm]**	**(typical)**	**[mL]**	**[g]**	**[µm]**	**(-)**
H23	bottle	PET	hand dish wash	450	24.7	200	18

H24	bottle	PET	automatic dish wash	1080	62	400	17
H25	bottle	PET	special detergent	1000	46	400	22
H26	bottle	HDPE	special detergent	3000	120	400 to 700	25
H27	bottle	PP	heavy duty detergent	3000	130	500 to 1000	23

a)



b)

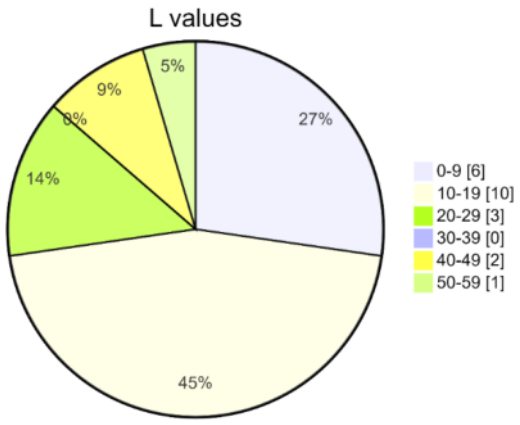


***Figure 16**. Pareto chart (a) and distribution (b) of L values for cosmetic and homecare products.*

Appendix 6. Concentration distributions of substances in rHDPE

The concentration distributions are presented in the **Figure 17** for the same concentration classes. All values (number of substances and corresponding concentration ranges) are detailed in **Table 22**.

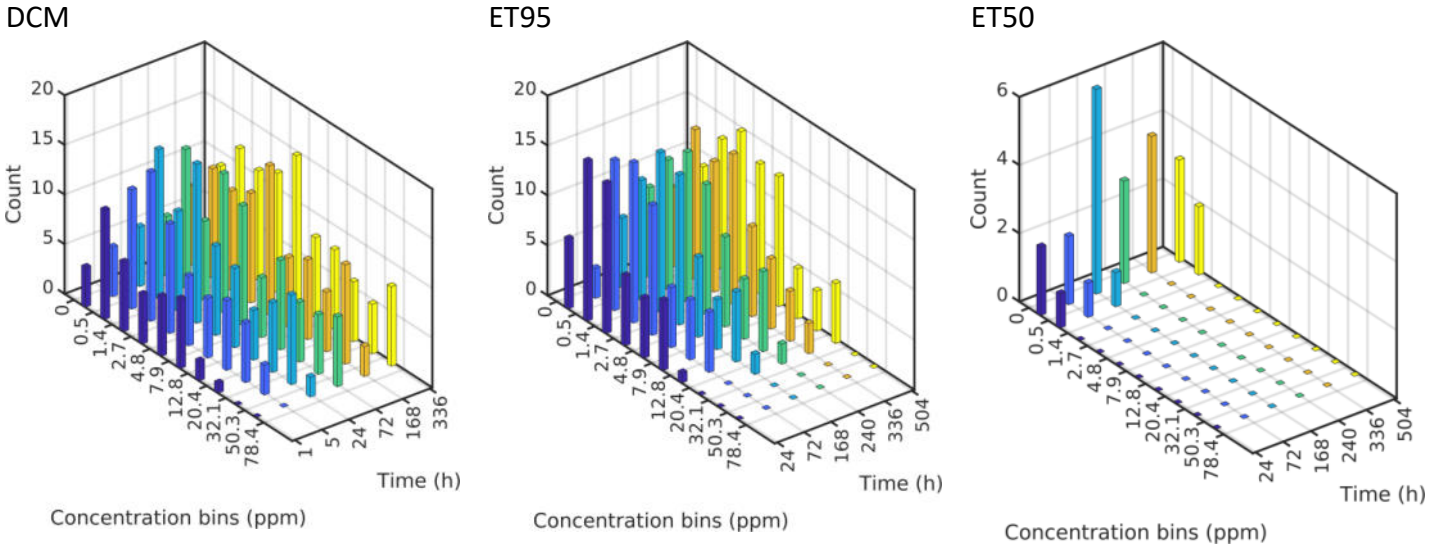


***Figure 17**. Evolution of the concentration distribution of identified substances as a function of contact medium (DCM, EtOH95 and EtOH 50) and contact time in rHDPE. Experiments were repeated 6 times.*

***Table 22**. Number of substances within each concentration range as determined by DCM extraction, ethanol 95%, and ethanol 50% mass transfer (3 values per cell) in rHDPE sample.*

Conc. range (ppm) / Time (h)	0-0.55	0.55-1.40	1.40-2.71	2.71-4.75	4.75-7.91	7.91-12.80	12.80-20.38	20.38-32.11	32.11-50.29	50.29-78.43
1	4, -, -	11, -, -	7, -, -	5, -, -	6, -, -	7, -, -	2, -, -	1, -, -	0, -, -	-, -, -
5	5, -, -	12, -, -	15, -, -	11, -, -	7, -, -	6, -, -	7, -, -	6, -, -	3, -, -	-, -, -
24	6, 7, 2	15, 16, 1	10, 15, 0	16, 7, 0	9, 6, 0	8, 7, 0	5, 1, 0	7, 0, 0	9, 0, 0	-, 0, 0
72	6, 3, 2	14, 15, 1	8, 16, 0	14, 13, 0	12, 6, 0	6, 6, 0	9, 6, 0	6, 0, 0	6, 0, 0	-, 0, 0
168	8, 7, 6	11, 12, 1	10, 16, 0	11, 15, 0	15, 8, 0	7, 5, 0	8, 7, 0	6, 2, 0	10, 0, 0	-, 0, 0
240	-, 9, 3	-, 13, 0	-, 15, 0	-, 13, 0	-, 9, 0	-, 6, 0	-, 8, 0	-, 2, 0	-, 0, 0	-, 0, 0
336	-, 8, 4	-, 15, 0	-, 13, 0	-, 15, 0	-, 9, 0	-, 7, 0	-, 5, 0	-, 3, 0	-, 0, 0	-, 0, 0
504	-, 9, 3	-, 13, 2	-, 15, 0	-, 13, 0	-, 13, 0	-, 5				

Appendix 7. Temporal Dynamics of Potential Release PR_E^{test}

The temporal evolution of the potential release, PR_E^{test}, was investigated through time-resolved sampling of concentrations in dichloromethane (DCM), using the measurements at one day as a baseline. These analyses are visualized in **Figure 18**.

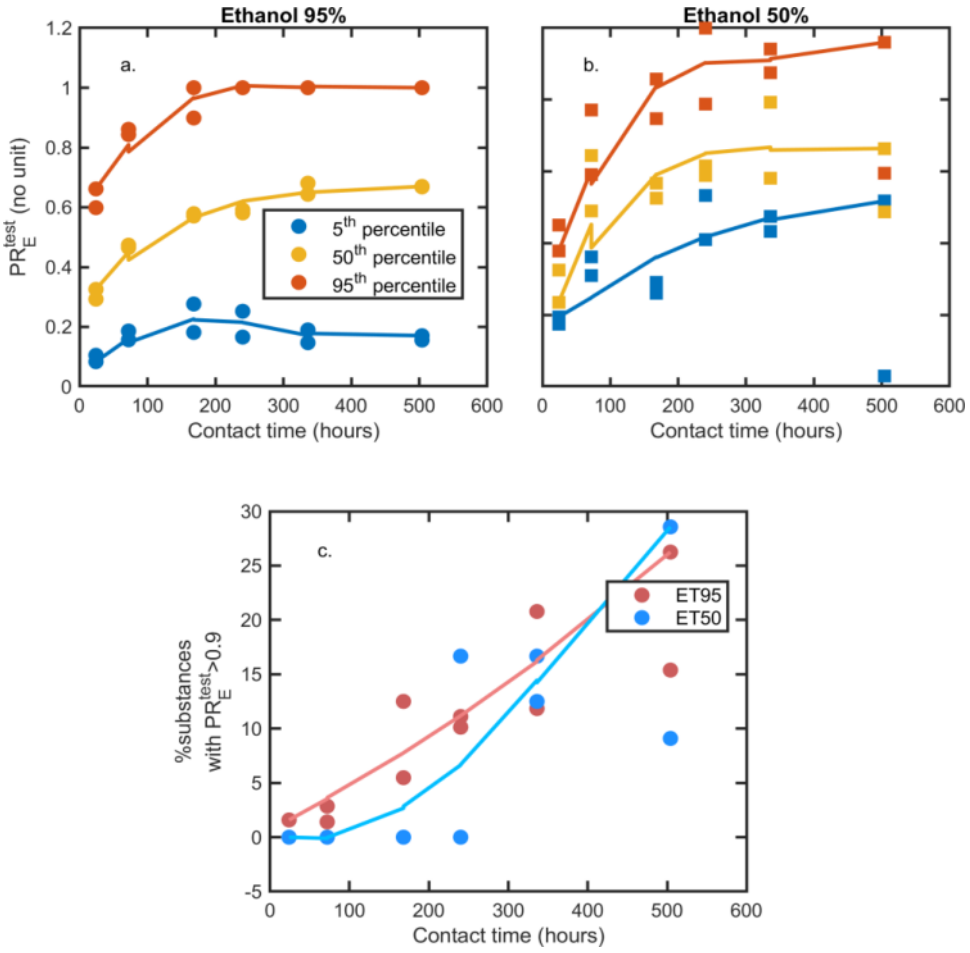


Figure 18. *Time-dependent evolution of PR_E^{test} in recycled high-density polyethylene (rHDPE) samples across different solvents: a. ET95, b. ET50, and c. Fraction of substances with PR_E approaching or equalling unity. The smooth curves represent data filtered via a moving local polynomial approximation.*

Key Observations:

1. **Stability:** The potential release of tested substances reached a stable distribution after approximately 10 days of interaction with food simulants.

2. **Sample Population:** The statistical analysis was restricted to substances that yielded quantifiable concentrations. This subset was significantly larger for ethanol 95% (ET95) as compared to ethanol 50% (ET50).

3. **Convergence:** Interestingly, despite initial disparities, the potential release coefficients converged for both ET95 and ET50 over an extended period. For example, approximately 10% of substances in ET95 and 5% in ET50 necessitated the use of $PR_E^{test} = 1$ after 10 days.

4. **Lack of Correlation:** Upon verification, it was found that $PR_E^{test,ET95}$ and $PR_E^{test,ET50}$ were not correlated, revealing the intricacies of the release dynamics.

Methodological Caveats:

It is crucial to note the limitations in estimating PR_E^{test} when concentrations in DCM are approaching detection limits. Under such circumstances, the protocol's reliability for potential release estimation is compromised.

Statistical Rigor:

The findings underscore the importance of adopting a tiered analytical framework to accommodate the heterogeneity in potential release behaviors. However, it is essential to reiterate that the presented results are based solely on a single rHDPE sample, and the statistical robustness, particularly for ET50, remains insufficient. Thus, the extension and validation of these findings across additional samples is an imperative next step.

Appendix 8. Raw data from the Safety Evaluation of the Sample LDPE04

This Appendix is available as an independent Microsoft Excel worksheet.

Appendix 8 (April 09, 2024)
to the CosPaTox Dossier "Evaluation of the Safety of Recyclates in Cosmetic and Detergent Packaging"

This appendix contains the substance-specific results for the use cases as described in chapter 5.3 of the Dossier:

Use case 1 (chapter 5.3.2):	Assessment of a 200 ml shampoo bottle for adult use based on the analytical results P4 (pellets, 50% EtOH) for rHDPE-04
Use case 2 (chapter 5.3.3):	Assessment of a 200 ml washing gel bottle for infant use based on the analytical results P4 (pellets, 50% EtOH) for rHDPE-04
Use case 3 (chapter 5.3.4):	Assessment of a 200 ml body lotion bottle for adult use based on the analytical results P3 (pellets, 95% EtOH) and B1 (200 ml bottle, 95% EtOH) for rHDPE-04

"Hazard identification" relates to the discussion in chapter 5.3.3 "Extending risk-assessment by including the test results from more severe migration conditions";
at the time of preparing this table, the substance list has not been in ist final status.

The following results are given in the different tables:

C(Test)	the concentration measured in the simulant of the specific test
C(F)	the concentration calculated to be present in the product based on C(Test) (only if different from C(Test))
SED	Systemic exposure dose; the dose to which consumers are exposed to under the use conditions of the respective product, based on C(Test) or C(F)

This appendix was provided by CosPaTox as a supplement to help exemplifying the extrapolation rules and consequences for risk assessment as discussed in the Dossier; the data have not been reviewed in detail by the main author of the Dossier, but taken as is for detailing the use cases. Any errors or inaccuracies in the data provided with this appendix, that may impact the conclusions made in the Dossier, are attributed to the members of CosPaTox .

For more details, please see the detailed explanations of the use cases in the Dossier

Compound	CAS	Pellet (rHDPE4); 50% EtOH C(Test) mg/kg	Adult's shampoo SED (µg/kg bw/d)	Infant's washing gel SED (µg/kg bw/d)
	Limit of detection	*0.1*	0.0000872	0.0037340
	Limit of detection	*0.3*	0.0002615	0.0112020
Diphenyl Ether	101-84-8	0.186	0.0001621	0.0069452
4-tert-Butylcyclohexyl acetate cis	10411-92-4	0.052	0.0000453	0.0019417
Peach lactone_?-Undecalactone	104-67-6	0.048	0.0000418	0.0017923
p-Octylacetophenone	10541-56-7	2.317	0.0020197	0.0865168
Ethylene brassylate	105-95-3	0.228	0.0001987	0.0085135
Dibutyl adipate	105-99-7	0.051	0.0000445	0.0019043
Dihydrocitronellol	106-21-8	0.229	0.0001996	0.0085509
Tetradecamethylcycloheptasiloxane	107-50-6	0.142	0.0001238	0.0053023
Cycloheptasiloxane, tetradecamethyl	107-50-6	0.128	0.0001116	0.0047795
1,3-Propanediamine	109-76-2	0.067	0.0000584	0.0025018
Pentanal	110-62-3	0.171	0.0001491	0.0063851
1-Dodecanol	112-53-8	0.418	0.0003644	0.0156081
Benzyl salicylate	118-58-1	0.544	0.0004742	0.0203130
Benzophenone	119-61-9	0.372	0.0003243	0.0138905
Benzyl benzoate	120-51-4	0.526	0.0004585	0.0196408
Galaxolide	1222-05-5	0.199	0.0001735	0.0074307
Phenoxyethanol	122-99-6	0.05	0.0000436	0.0018670
Isobornyl Acetate	125-12-2	0.909	0.0007923	0.0339421
Dimethylacetamide	127-19-5	0.144	0.0001255	0.0053770
BHT	128-37-0	0.024	0.0000209	0.0008962
a-Hexylcinnamaldehyde trans	1331-92-6	1.487	0.0012962	0.0555246
Ethyl acetoacetate	141-97-9	0.257	0.0002240	0.0095964
Dodecanoic acid	143-07-7	0.476	0.0004149	0.0177738
3,5-di-tert-Butyl-4-hydroxybenzaldeh	1620-98-0	0.072	0.0000628	0.0026885
t-BME	1634-04-4	0.161	0.0001403	0.0060117
Cyclopentane, ethyl-	1640-89-7	0.432	0.0003766	0.0161309
Herbal propionate	17511-60-3	0.577	0.0005030	0.0215452
Methyl (3-oxo-2-pentylcyclopentyl)ac	24851-98-7	0.761	0.0006633	0.0284157
Etilox	36294-24-3	1.755	0.0015298	0.0655317
1-Hexadecanol	36653-82-4	0.771	0.0006721	0.0287891
Anethol	4180-23-8	0.079	0.0000689	0.0029499
Ethylene glycol monododecyl ether	4536-30-5	1.07	0.0009327	0.0399538
Eucalyptol	470-82-6	0.297	0.0002589	0.0110900
Carvacrol	499-75-2	0.049	0.0000427	0.0018297
Cyclohexasiloxane, dodecamethyl-	540-97-6	0.432	0.0003766	0.0161309
Cyclopentasiloxane, decamethyl-	541-02-6	0.188	0.0001639	0.0070199
Hexamethylcyclotrisiloxane	541-05-9	0.931	0.0008115	0.0347635
Cyclotetrasiloxane, octamethyl-	556-67-2	0.345	0.0003007	0.0128823
Cyclooctasiloxane, hexadecamethyl-	556-68-3	0.06	0.0000523	0.0022404
Octadecamethylcyclononasiloxane	556-71-8	0.054	0.0000471	0.0020164
n-Hexadecanoic acid	57-10-3	1.188	0.0010355	0.0443599
Stearic acid	57-11-4	0.168	0.0001464	0.0062731
Limonene	5989-27-5	0.073	0.0000636	0.0027258
n-Hexyl salicylate	6259-76-3	0.591	0.0005152	0.0220679

Consumer exposure > TTC for potentially genotoxic substances

Consumer exposure < TTC for potentially genotoxic substances

TTC for potentailly genotoxic substances = 0.0025 µg/kg bw/d

Metilox	6386-38-5	0.437	0.0003809	0.0163176
Amberonne	68155-66-8	0.964	0.0008403	0.0359958
Didecyl methylamine	7396-58-9	0.359	0.0003129	0.0134051
7,9-Di-tert-butyl-1-oxaspiro(4,5)deca-	82304-66-3	3.089	0.0026926	0.1153433
Diethyl Phthalate	84-66-2	0.276	0.0002406	0.0103058
Diisobutyl phthalate	84-69-5	0.233	0.0002031	0.0087002
Dibutyl phthalate	84-74-2	0.474	0.0004132	0.0176992
ortho tert-Butyl cyclohexyl acetate	88-41-5	0.736	0.0006415	0.0274822
2,4-Di-tert-Butylphenol	96-76-4	1.449	0.0012630	0.0541057
Indan-1,3-diol monoacetate	XXX-01-1	0.486	0.0004236	0.0181472

Unidentified substances	0.985	0.0008586	0.0367799
	0.933	0.0008133	0.0348382
	0.894	0.0007793	0.0333820
	0.606	0.0005282	0.0226280
	0.576	0.0005021	0.0215078
	0.575	0.0005012	0.0214705
	0.553	0.0004820	0.0206490
	0.507	0.0004419	0.0189314
	0.458	0.0003992	0.0171017
	0.454	0.0003957	0.0169524
	0.437	0.0003809	0.0163176
	0.381	0.0003321	0.0142265
	0.287	0.0002502	0.0107166
	0.278	0.0002423	0.0103805
	0.247	0.0002153	0.0092230
	0.225	0.0001961	0.0084015
	0.215	0.0001874	0.0080281
	0.209	0.0001822	0.0078041
	0.201	0.0001752	0.0075053
	0.199	0.0001735	0.0074307
	0.198	0.0001726	0.0073933
	0.197	0.0001717	0.0073560
	0.194	0.0001691	0.0072440
	0.193	0.0001682	0.0072066
	0.188	0.0001639	0.0070199
	0.186	0.0001621	0.0069452
	0.184	0.0001604	0.0068706
	0.174	0.0001517	0.0064972
	0.172	0.0001499	0.0064225
	0.172	0.0001499	0.0064225
	0.16	0.0001395	0.0059744
	0.157	0.0001369	0.0058624
	0.155	0.0001351	0.0057877
	0.152	0.0001325	0.0056757
	0.151	0.0001316	0.0056383
	0.145	0.0001264	0.0054143
	0.143	0.0001246	0.0053396

0.14	0.0001220	0.0052276
0.117	0.0001020	0.0043688
0.114	0.0000994	0.0042568
0.111	0.0000968	0.0041447
0.11	0.0000959	0.0041074
0.109	0.0000950	0.0040701
0.109	0.0000950	0.0040701
0.107	0.0000933	0.0039954
0.107	0.0000933	0.0039954
0.106	0.0000924	0.0039580
0.104	0.0000907	0.0038834
0.102	0.0000889	0.0038087
0.099	0.0000863	0.0036967
0.099	0.0000863	0.0036967
0.093	0.0000811	0.0034726
0.088	0.0000767	0.0032859
0.084	0.0000732	0.0031366
0.079	0.0000689	0.0029499
0.079	0.0000689	0.0029499
0.076	0.0000662	0.0028378
0.073	0.0000636	0.0027258
0.072	0.0000628	0.0026885
0.071	0.0000619	0.0026511
0.07	0.0000610	0.0026138
0.07	0.0000610	0.0026138
0.07	0.0000610	0.0026138
0.066	0.0000575	0.0024644
0.065	0.0000567	0.0024271
0.065	0.0000567	0.0024271
0.065	0.0000567	0.0024271
0.064	0.0000558	0.0023898
0.064	0.0000558	0.0023898
0.063	0.0000549	0.0023524
0.062	0.0000540	0.0023151
0.061	0.0000532	0.0022777
0.061	0.0000532	0.0022777
0.054	0.0000471	0.0020164
0.053	0.0000462	0.0019790
0.052	0.0000453	0.0019417
0.051	0.0000445	0.0019043
0.051	0.0000445	0.0019043
0.05	0.0000436	0.0018670
0.047	0.0000410	0.0017550
0.046	0.0000401	0.0017176
0.046	0.0000401	0.0017176
0.045	0.0000392	0.0016803
0.045	0.0000392	0.0016803
0.044	0.0000384	0.0016430
0.044	0.0000384	0.0016430
0.044	0.0000384	0.0016430

0.043	0.0000375	0.0016056
0.043	0.0000375	0.0016056
0.043	0.0000375	0.0016056
0.043	0.0000375	0.0016056
0.043	0.0000375	0.0016056
0.034	0.0000296	0.0012696
0.016	0.0000139	0.0005974

Compound	CAS	Pellet, 95% EtOH			Bottle, 200 ml, 95% EtOH			Substances identified in both pellets and bottle
		C(Test) [mg/kg]	C(F) [mg/kg]	SED [µg/kg bw/d]	C(Test) [mg/kg]	C(F) [mg/kg]	SED [µg/kg bw/d]	
	Limit of detection	*0.1*	*0.024*					
	Limit of detection	*0.3*	*0.072*					
1-Eicosene					19.84	1.98	0.1293	
Bumetrizole		0.80	0.193	0.0126	0.44	0.04	0.0028	x
2,2,4,4,6,8,8-Heptamethylnonane		0.75	0.180	0.0118	0.17	0.02	0.0011	x
5-Phenyldecane		0.27	0.064	0.0042				
4-Phenyldecane		0.44	0.107	0.0070				
Diphenyl Ether	101-84-8	0.71	0.172	0.0112	0.67	0.07	0.0044	x
1-Tetracosene	10192-32-2	1.24	0.300	0.0195	11.10	1.11	0.0723	x
Hexanedioic acid, bis(2-ethylhexyl) es	103-23-1	1.45	0.349	0.0227				
4-tert-Butylcyclohexyl acetate cis	10411-92-4	0.62	0.151	0.0098	0.36	0.04	0.0023	x
Peach lactone_?-Undecalactone	104-67-6	0.31	0.076	0.0049				
2-Ethylhexanol	104-76-7	0.29	0.069	0.0045	0.38	0.04	0.0025	x
p-Octylacetophenone	10541-56-7	6.64	1.599	0.1042	1.01	0.10	0.0066	x
Ethylene brassylate	105-95-3	2.06	0.497	0.0324				
Ethyl octanoate	106-32-1	0.83	0.200	0.0130				
Ethyl Laurate	106-33-2	28.33	6.827	0.4449	5.65	0.57	0.0368	x
Cycloheptasiloxane, tetradecamethyl-	107-50-6	0.27	0.066	0.0043				
Cyclohexanone	108-94-1			0.0000	0.25	0.03	0.0017	
1,3-Propanediamine	109-76-2			0.0000		0.00	0.0000	
Isopropyl myristate	110-27-0	27.60	6.651	0.4334	18.55	1.85	0.1209	x
Ethyl caprate	110-38-3	1.60	0.384	0.0251				
Squalene	111-02-4	2.20	0.531	0.0346				
Ethyl stearate	111-61-5	41.55	10.012	0.6524	10.51	1.05	0.0685	x
Ethyl Oleate	111-62-6	22.51	5.423	0.3534	7.13	0.71	0.0465	x
Methyl laurate	111-82-0	0.31	0.075	0.0049				
Undecane	1120-21-4			0.0000	0.23	0.02	0.0015	
1-Tetradecene	1120-36-1			0.0000	0.90	0.09	0.0058	
Decanal	112-31-2	0.32	0.078	0.0051				
Methyl Palmitate	112-39-0	5.18	1.249	0.0814	3.23	0.32	0.0211	x
Dodecane	112-40-3	1.56	0.377	0.0245	0.99	0.10	0.0065	x
1-Dodecanol	112-53-8	1.28	0.308	0.0200	0.54	0.05	0.0035	x
1-Tetradecanol	112-72-1	2.00	0.483	0.0315				
1-Octadecene	112-88-9	11.05	2.663	0.1736	12.03	1.20	0.0784	x
1-Octadecanol	112-92-5	28.64	6.902	0.4498	9.16	0.92	0.0597	x
Benzyl salicylate	118-58-1	4.91	1.182	0.0771	1.91	0.19	0.0124	x
Ethylhexyl Salicylate	118-60-5	5.55	1.336	0.0871	1.88	0.19	0.0122	x
Benzyl benzoate	120-51-4			0.0000	1.38	0.14	0.0090	
Galaxolide	1222-05-5	4.34	1.045	0.0681	1.85	0.19	0.0121	x
Phenoxyethanol	122-99-6	0.17	0.041	0.0027				
Ethyl Myristate	124-06-1			0.0000	1.04	0.10	0.0068	
Isobornyl Acetate	125-12-2			0.0000	0.56	0.06	0.0037	
a-Isomethyl ionone	127-51-5	0.60	0.145	0.0094				
BHT	128-37-0			0.0000	1.21	0.12	0.0079	
a-Hexylcinnamaldehyde trans	1331-92-6	12.87	3.101	0.2021	5.23	0.52	0.0341	x
2,2,4,6,6-Pentamethylheptane	13475-82-6	0.17	0.040	0.0026				
Dodecyl Laurate	13945-76-1	12.77	3.076	0.2005	11.94	1.19	0.0778	x
Ethyl acetoacetate	141-97-9			0.0000				
Isopropyl palmitate	142-91-6	70.61	17.014	1.1087	55.37	5.54	0.3608	x
Dodecanoic acid	143-07-7	1.46	0.352	0.0230	0.28	0.03	0.0018	x
a,a-Dimethylphenethyl acetate	151-05-3	0.15	0.036	0.0023				
Eicosane, 2-methyl-	1560-84-5			0.0000	0.33	0.03	0.0022	
Dodecane, 2-methyl-	1560-97-0			0.0000	0.22	0.02	0.0014	
1-Docosene	1599-67-3			0.0000	19.66	1.97	0.1281	
Herbal propionate	17511-60-3	1.85	0.446	0.0291	0.88	0.09	0.0057	x
1-Hexacosene	18835-33-1			0.0000	5.40	0.54	0.0352	
1-Octacosene	18835-34-2			0.0000	2.64	0.26	0.0172	
4-tert-Butylcyclohexyl acetate trans	1900-69-2	0.25	0.061	0.0040				
Amyl salicylate	2050-08-0	0.67	0.161	0.0105	0.38	0.04	0.0025	x

Consumer exposure > TTC for potentially genotoxic substances

Consumer exposure < TTC for potentially genotoxic substances

TTC for potentailly genotoxic substances = 0.0025 µg/kg bw/d

Irganox 1076	2082-79-3	11.21	2.702	0.1761	2.07	0.21	0.0135	x
Tonalid	21145-77-7			0.0000	1.71	0.17	0.0112	
2-Ethylhexyl stearate	22047-49-0	17.25	4.155	0.2708	11.54	1.15	0.0752	x
3-Phenyldodecane	2400-00-2	3.44	0.828	0.0540	1.43	0.14	0.0093	x
2-Hexyl-1-decanol	2425-77-6	0.38	0.091	0.0059	0.50	0.05	0.0032	x
Methyl (3-oxo-2-pentylcyclopentyl)ac	24851-98-7	1.71	0.411	0.0268	0.31	0.03	0.0020	x
2-Phenyldodecane	2719-61-1			0.0000	2.85	0.28	0.0185	
6-Phenyldodecane	2719-62-2	2.21	0.532	0.0346	0.76	0.08	0.0049	x
5-Phenyldodecane	2719-63-3	1.89	0.456	0.0297	0.96	0.10	0.0063	x
4-Phenyldodecane	2719-64-4	1.52	0.367	0.0239	1.08	0.11	0.0071	x
Triphenyl Cyclohexane	28336-57-4			0.0000	1.96	0.20	0.0128	
Benzoic acid, dodecyl ester	2915-72-2	3.43	0.826	0.0538	2.99	0.30	0.0195	x
Benzoic acid, tridecyl ester	29376-83-8	5.51	1.329	0.0866	4.67	0.47	0.0304	x
Phenol, 2,4-bis(1,1-dimethylethyl)-, p	31570-04-4	320.15	77.145	5.0273	59.95	5.99	0.3907	x
Etilox	36294-24-3	322.29	77.661	5.0609	100.46	10.05	0.6547	x
1-Hexadecanol	36653-82-4	18.15	4.373	0.2850	6.31	0.63	0.0411	x
Anethol	4180-23-8			0.0000	0.33	0.03	0.0021	
6-Phenyltridecane	4534-49-0	1.89	0.455	0.0297	1.01	0.10	0.0066	x
5-Phenyltridecane	4534-50-3	1.21	0.293	0.0191	0.65	0.07	0.0043	x
4-Phenyltridecane	4534-51-4	1.39	0.334	0.0218	0.82	0.08	0.0053	x
3-Phenyltridecane	4534-52-5	1.19	0.287	0.0187	0.95	0.09	0.0062	x
2-Phenyltridecane	4534-53-6			0.0000	2.35	0.23	0.0153	
Ethylene glycol monododecyl ether	4536-30-5	4.61	1.110	0.0723	0.96	0.10	0.0062	x
4-Phenylundecane	4536-86-1	2.29	0.551	0.0359	0.96	0.10	0.0062	x
Benzene, (1-ethylnonyl)-	4536-87-2	2.05	0.494	0.0322	1.13	0.11	0.0074	x
2-Phenylundecane	4536-88-3	1.54	0.372	0.0242	1.47	0.15	0.0096	x
2-Phenyldecane	4537-13-7	1.54	0.372	0.0243	0.98	0.10	0.0064	x
6-Phenylundecane	4537-14-8	0.47	0.112	0.0073	0.24	0.02	0.0015	x
5-Phenylundecane	4537-15-9	2.01	0.484	0.0316	0.70	0.07	0.0046	x
3-Phenyldecane	4621-36-7	0.35	0.085	0.0056	0.18	0.02	0.0011	x
Eucalyptol	470-82-6	0.43	0.104	0.0068				
Cyclopentasiloxane, decamethyl-	541-02-6	0.31	0.076	0.0049				
Ethyl Linoleate	544-35-4	14.25	3.434	0.2238	1.94	0.19	0.0126	x
Hexadecane	544-76-3	13.33	3.212	0.2093	19.22	1.92	0.1253	x
Octan-2-yl palmitate	55194-81-5	27.55	6.639	0.4326	18.18	1.82	0.1185	x
Cyclotetrasiloxane, octamethyl-	556-67-2	0.15	0.036	0.0023				
n-Hexadecanoic acid	57-10-3	15.63	3.766	0.2454	1.22	0.12	0.0079	x
Octadecane	593-45-3	19.38	4.671	0.3044	45.16	4.52	0.2943	x
Limonene	5989-27-5	0.65	0.156	0.0102				
Ethyl elaidate	6114-18-7	22.00	5.301	0.3454				
n-Hexyl salicylate	6259-76-3	12.96	3.123	0.2035	6.49	0.65	0.0423	x
Ethyl Palmitate	628-97-7	52.38	12.623	0.8226	15.09	1.51	0.0984	x
Tetradecane	629-59-4	6.15	1.483	0.0966	6.35	0.64	0.0414	x
Pentadecane	629-62-9	1.64	0.395	0.0257	1.83	0.18	0.0119	x
Hexadecene	629-73-2			0.0000	4.67	0.47	0.0304	
Heptadecane	629-78-7	2.51	0.604	0.0393	4.27	0.43	0.0278	x
Di-n-Octylether	629-82-3	18.23	4.392	0.2862	11.08	1.11	0.0722	x
Nonadecane	629-92-5	0.78	0.189	0.0123	2.04	0.20	0.0133	x
Docosane	629-97-0	11.85	2.856	0.1861	33.40	3.34	0.2177	x
Hexacosane	630-01-3	2.09	0.504	0.0329	10.25	1.03	0.0668	x
Octacosane	630-02-4			0.0000	3.29	0.33	0.0214	
Diethyl terephthalate	636-09-9	1.90	0.458	0.0298				
Phytan	638-36-8	0.35	0.085	0.0055	0.39	0.04	0.0025	x
Metilox	6386-38-5	2.57	0.620	0.0404	0.44	0.04	0.0028	x
Tricosane	638-67-5			0.0000	3.78	0.38	0.0247	
Plastic additive 27	6422-86-2	3.51	0.846	0.0551				
Tetracosane	646-31-1	3.51	0.845	0.0550	21.36	2.14	0.1392	x
Benzoic acid	65-85-0	0.40	0.097	0.0063				
Amberonne	68155-66-8	6.96	1.676	0.1092	1.55	0.15	0.0101	x
Benzoic acid, pentadecyl ester	68411-27-8	2.69	0.648	0.0422	2.30	0.23	0.0150	x
Benzoic acid, tetradecyl ester	70682-72-3	4.89	1.177	0.0767	3.47	0.35	0.0226	x
Didecyl methylamine	7396-58-9	26.80	6.457	0.4208	20.76	2.08	0.1353	x

Lilial	80-54-6	0.43	0.103	0.0067				
7,9-Di-tert-butyl-1-oxaspiro(4,5)deca-	82304-66-3	8.54	2.058	0.1341				
1-Propylpentyl laurate	84713-06-4	10.87	2.620	0.1707	8.70	0.87	0.0567	x
Isoamyl Salicylate	87-20-7	0.37	0.088	0.0057				
ortho tert-Butyl cyclohexyl acetate	88-41-5	4.23	1.019	0.0664	0.50	0.05	0.0033	x
Menthol	89-78-1	0.22	0.053	0.0035				
2-Methoxy naphthalene	93-04-9	0.34	0.082	0.0054	0.49	0.05	0.0032	x
Tris(2,4-di-tert-butylphenyl) phosphat	95906-11-9	96.47	23.246	1.5149	9.07	0.91	0.0591	x
2,4-Di-tert-Butylphenol	96-76-4	6.50	1.566	0.1020	0.58	0.06	0.0038	x
Indan-1,3-diol monoacetate	XXX-01-1	0.98	0.235	0.0153	0.45	0.05	0.0030	x
Unidentifed substances		17.37	4.186	0.2728	13.13	1.31	0.0856	
		10.62	2.560	0.1668	4.22	0.42	0.0275	
		7.56	1.821	0.1187	3.91	0.39	0.0255	
		6.34	1.528	0.0996	3.80	0.38	0.0247	
		5.68	1.370	0.0893	3.04	0.30	0.0198	
		5.61	1.351	0.0881	2.84	0.28	0.0185	
		4.61	1.111	0.0724	2.37	0.24	0.0154	
		4.42	1.065	0.0694	2.14	0.21	0.0139	
		3.48	0.838	0.0546	2.05	0.21	0.0134	
		3.47	0.836	0.0545	1.98	0.20	0.0129	
		3.33	0.803	0.0523	1.81	0.18	0.0118	
		3.28	0.790	0.0515	1.70	0.17	0.0111	
		3.22	0.777	0.0506	1.68	0.17	0.0110	
		3.05	0.734	0.0478	1.63	0.16	0.0106	
		2.96	0.713	0.0465	1.55	0.15	0.0101	
		2.29	0.553	0.0360	1.41	0.14	0.0092	
		2.20	0.531	0.0346	1.29	0.13	0.0084	
		2.13	0.513	0.0334	1.25	0.13	0.0082	
		2.01	0.485	0.0316	1.19	0.12	0.0078	
		1.90	0.458	0.0299	1.19	0.12	0.0077	
		1.90	0.457	0.0298	1.16	0.12	0.0076	
		1.88	0.452	0.0295	1.11	0.11	0.0073	
		1.86	0.447	0.0291	1.04	0.10	0.0068	
		1.85	0.446	0.0291	0.92			
		1.84	0.443	0.0289	0.92			
		1.72	0.414	0.0270	0.91			
		1.72	0.413	0.0269	0.88			
		1.71	0.411	0.0268	0.81			
		1.69	0.407	0.0265	0.79			
		1.64	0.395	0.0257	0.77			
		1.63	0.393	0.0256	0.75			
		1.63	0.392	0.0255	0.75			
		1.60	0.385	0.0251	0.74			
		1.48	0.355	0.0232	0.73			
		1.45	0.350	0.0228	0.72			
		1.43	0.345	0.0225	0.69			
		1.34	0.324	0.0211	0.69			
		1.33	0.320	0.0209	0.68			
		1.28	0.309	0.0201	0.65			
		1.28	0.308	0.0201	0.64			
		1.21	0.292	0.0190	0.63			
		1.14	0.276	0.0180	0.62			
		1.10	0.264	0.0172	0.62			
		0.99	0.238	0.0155	0.61			
		0.98	0.235	0.0153	0.60			
		0.89	0.213	0.0139	0.59			
		0.87	0.211	0.0137	0.57			
		0.85	0.205	0.0134	0.53			
		0.81	0.195	0.0127	0.50			

0.75	0.181	0.0118	0.49
0.73	0.175	0.0114	0.48
0.72	0.174	0.0113	0.46
0.72	0.173	0.0113	0.45
0.66	0.158	0.0103	0.43
0.65	0.157	0.0102	0.41
0.64	0.155	0.0101	0.40
0.63	0.151	0.0098	0.40
0.61	0.147	0.0096	0.40
0.61	0.147	0.0096	0.39
0.60	0.145	0.0094	0.38
0.60	0.144	0.0094	0.36
0.57	0.138	0.0090	0.36
0.55	0.133	0.0086	0.34
0.55	0.133	0.0086	0.32
0.54	0.131	0.0085	0.32
0.49	0.119	0.0077	0.32
0.47	0.112	0.0073	0.31
0.46	0.112	0.0073	0.31
0.46	0.111	0.0073	0.30
0.46	0.111	0.0073	0.30
0.45	0.109	0.0071	0.29
0.44	0.106	0.0069	0.29
0.42	0.102	0.0066	0.29
0.42	0.101	0.0066	0.28
0.40	0.097	0.0063	0.28
0.38	0.092	0.0060	0.27
0.37	0.089	0.0058	0.27
0.36	0.087	0.0057	0.27
0.36	0.086	0.0056	0.26
0.35	0.085	0.0055	0.26
0.35	0.084	0.0055	
0.35	0.084	0.0054	
0.34	0.081	0.0053	
0.33	0.080	0.0052	
0.33	0.080	0.0052	
0.33	0.079	0.0051	
0.33	0.078	0.0051	
0.32	0.077	0.0050	
0.31	0.075	0.0049	
0.31	0.074	0.0048	
0.30	0.073	0.0048	
0.30	0.073	0.0047	
0.29	0.070	0.0046	
0.28	0.068	0.0044	
0.28	0.067	0.0044	
0.27	0.065	0.0042	
0.27	0.065	0.0042	
0.27	0.064	0.0042	
0.26	0.062	0.0040	
0.25	0.060	0.0039	
0.25	0.059	0.0039	
0.24	0.057	0.0037	
0.24	0.057	0.0037	
0.23	0.056	0.0036	
0.23	0.055	0.0036	
0.23	0.054	0.0035	
0.22	0.054	0.0035	
0.22	0.053	0.0035	
0.22	0.053	0.0034	
0.22	0.053	0.0034	
0.21	0.051	0.0033	

0.20	0.049	0.0032
0.20	0.047	0.0031
0.19	0.047	0.0031
0.19	0.047	0.0030
0.19	0.047	0.0030
0.19	0.046	0.0030
0.19	0.046	0.0030
0.19	0.045	0.0030
0.19	0.045	0.0029
0.18	0.044	0.0029
0.18	0.044	0.0029
0.18	0.043	0.0028
0.18	0.043	0.0028
0.18	0.043	0.0028
0.18	0.043	0.0028
0.18	0.042	0.0028
0.17	0.041	0.0027
0.17	0.041	0.0027
0.17	0.041	0.0027
0.17	0.040	0.0026
0.17	0.040	0.0026
0.16	0.039	0.0026
0.16	0.039	0.0025
0.16	0.039	0.0025
0.16	0.038	0.0025
0.16	0.038	0.0025
0.16	0.038	0.0025
0.16	0.038	0.0025
0.16	0.037	0.0024
0.15	0.037	0.0024
0.15	0.037	0.0024
0.15	0.036	0.0023
0.15	0.035	0.0023
0.14	0.034	0.0022
0.14	0.034	0.0022
0.14	0.034	0.0022
0.14	0.034	0.0022
0.14	0.034	0.0022
0.14	0.033	0.0022
0.14	0.033	0.0022
0.14	0.033	0.0022
0.13	0.032	0.0021
0.13	0.032	0.0021
0.13	0.030	0.0020

			pellet (rHDPE-04), 95%EtOH	pellet (rHDPE-04), 50%EtOH	CosPaTox SOI list		
Compound	CAS	Class	mg/kg solvent	mg/kg solvent	Found on list	Value	Dose descriptor
7,9-Di-tert-butyl-1-oxaspiro(4,5)deca-6,9-diene-2,	82304-66-3	3	8.54	3.089	x	1.5	µg/kg bw/day
p-Octylacetophenone	10541-56-7	3	6.64	2.317	x	no data available	
Etilox	36294-24-3	3	322.29	1.755	x	no data available	
a-Hexylcinnamaldehyde trans	1331-92-6	3	12.87	1.487	x	no data available	
2,4-Di-tert-Butylphenol	96-76-4	3	6.50	1.449	x	3.75	mg/kg bw/day
n-Hexadecanoic acid	57-10-3	2	15.63	1.188	x	2.5	mg/kg bw/day
Ethylene glycol monododecyl ether	4536-30-5	3	4.61	1.07	x	0.5	mg/kg bw/day
Amberonne	68155-66-8	3	6.96	0.964	x	no data available	
Hexamethylcyclotrisiloxane	541-05-9	4		0.931			
Isobornyl Acetate	125-12-2	3		0.909	x	75	µg/kg bw/day
1-Hexadecanol	36653-82-4	2	18.15	0.771	x	55	mg/kg bw/day
Methyl (3-oxo-2-pentylcyclopentyl)acetate isome	24851-98-7	3	1.71	0.761	x	2.5	mg/kg bw/day
ortho tert-Butyl cyclohexyl acetate	88-41-5	3	4.23	0.736	x	30	µg/kg bw/day
n-Hexyl salicylate	6259-76-3	3	12.96	0.591	x	300	µg/kg bw/day
Herbal propionate	17511-60-3	3	1.85	0.577	x	no data available	
Benzyl salicylate	118-58-1	3	4.91	0.544	x	790	µg/kg bw/day
Benzyl benzoate	120-51-4	3		0.526	x	1.42	mg/kg bw/day
Indan-1,3-diol monoacetate	XXX-01-1	3	0.98	0.486	x	no data available	
Dodecanoic acid	143-07-7	2	1.46	0.476	x	2.5	mg/kg bw/day
Dibutyl phthalate	84-74-2	3		0.474	x	7	µg/kg bw/day
Metilox	6386-38-5	3	2.57	0.437	x	no data available	
Cyclopentane, ethyl-	1640-89-7	1		0.432	x	no data available	
Cyclohexasiloxane, dodecamethyl-	540-97-6	4		0.432	x	no hazard identified	
1-Dodecanol	112-53-8	2	1.28	0.418	x	44.5	mg/kg bw/day
Benzophenone	119-61-9	3		0.372	x	50	µg/kg bw/day
Didecyl methylamine	7396-58-9	3	26.80	0.359	x	no data available	
Cyclotetrasiloxane, octamethyl-	556-67-2	4	0.15	0.345	x	3.7	mg/kg bw/day
Eucalyptol	470-82-6	3	0.43	0.297	x	600	mg/kg/day
Diethyl Phthalate	84-66-2	3		0.276	x	750	µg/kg bw/day
Ethyl acetoacetate	141-97-9	3		0.257	x	4167	mg/kg bw/day
Diisobutyl phthalate	84-69-5	3		0.233	x	210	µg/kg bw/day
Dihydrocitronellol	106-21-8	3		0.229	x	0.75	mg/kg bw/day
Ethylene brassylate	105-95-3	3	2.06	0.228	x	no hazard identified	
Galaxolide	1222-05-5	3	4.34	0.199	x	2.3	mg/kg bw/day
Cyclopentasiloxane, decamethyl-	541-02-6	4	0.31	0.188	x	5	mg/kg bw/day

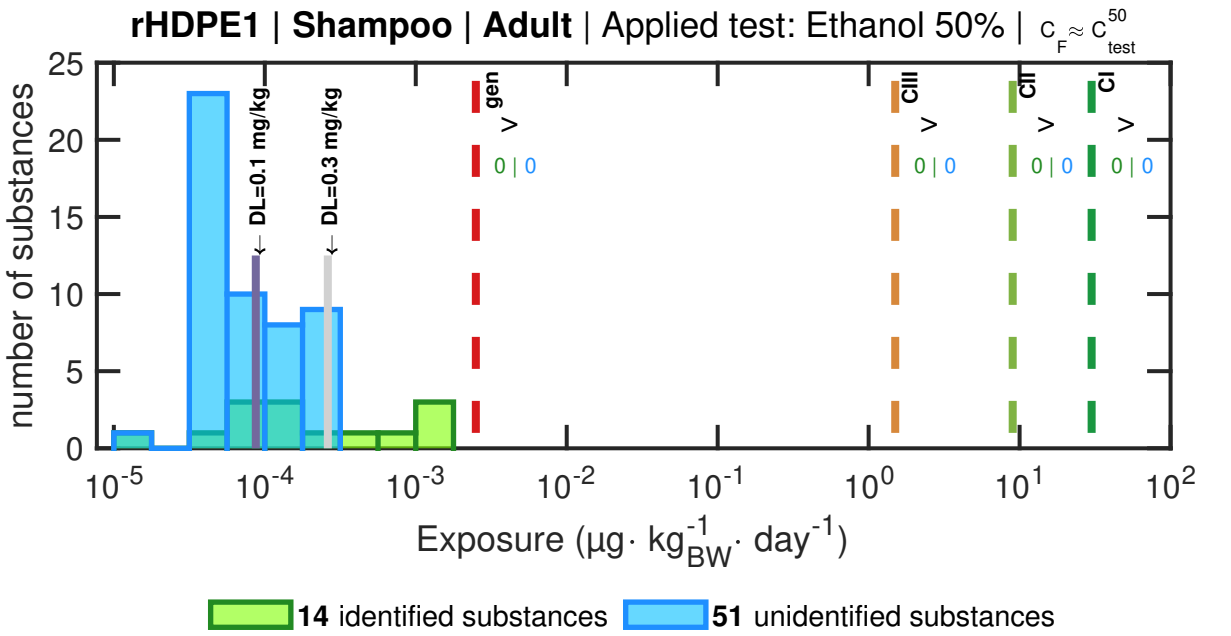
Diphenyl Ether	101-84-8	3	0.71	0.186	x		301	mg/kg/day
Pentanal	110-62-3	3		0.171	x	no data available		
Stearic acid	57-11-4	2		0.168	x		2.5	mg/kg bw/day
t-BME	1634-04-4	3		0.161	x		7.1	mg/kg bw/day
Dimethylacetamide	127-19-5	3		0.144	x		2	mg/kg bw/day
Tetradecamethylcycloheptasiloxane	107-50-6	4		0.142				
Cycloheptasiloxane, tetradecamethyl-	107-50-6	4	0.27	0.128				
Anethol	4180-23-8	3		0.079	x	no hazard identified		
Limonene	5989-27-5	3	0.65	0.073	x		4.8	mg/kg/day
3,5-di-tert-Butyl-4-hydroxybenzaldehyde	1620-98-0	3		0.072	x	no data available		
1,3-Propanediamine	109-76-2	3		0.067				
Cyclooctasiloxane, hexadecamethyl-	556-68-3	4		0.06				
Octadecamethylcyclononasiloxane	556-71-8	4		0.054				
4-tert-Butylcyclohexyl acetate cis	10411-92-4	3	0.62	0.052	x	no hazard identified		
Dibutyl adipate	105-99-7	2		0.051	x	no hazard identified		
Phenoxyethanol	122-99-6	3	0.17	0.05	x		9.23	mg/kg bw/day
Carvacrol	499-75-2	3		0.049	x		44.4	µg/kg bw/day
Peach lactone_?-Undecalactone	104-67-6	3	0.31	0.048	x		2.7	mg/kg bw/day
BHT	128-37-0	3		0.024	x		250	µg/kg bw/day
Bumetrizole	3896-11-5	3	0.80		x	no hazard identified		
2,2,4,4,6,8,8-Heptamethylnonane	4390-04-9	1	0.75		x	no hazard identified		
5-Phenyldecane	4537-11-5	3	0.27		x	no data available		
4-Phenyldecane	4537-12-6	3	0.44					
1-Tetracosene	10192-32-2	1	1.24		x	no data available		
Hexanedioic acid, bis(2-ethylhexyl) ester	103-23-1	2	1.45		x		1.7	mg/kg/day
2-Ethylhexanol	104-76-7	2	0.29		x		1.1	mg/kg bw/day
Ethyl octanoate	106-32-1	2	0.83		x	no hazard identified		
Ethyl Laurate	106-33-2	2	28.33		x		30	µg/kg bw/day
Isopropyl myristate	110-27-0	2	27.60		x		1.6	mg/kg/day
Ethyl caprate	110-38-3	2	1.60		x	Low hazard		
Squalene	111-02-4	3	2.20		x		1.94	mg/kg bw/day
Ethyl stearate	111-61-5	2	41.55		x		31	mg/kg/day
Ethyl Oleate	111-62-6	2	22.51		x	no data available		
Methyl laurate	111-82-0	2	0.31		x	no hazard identified		
Decanal	112-31-2	3	0.32		x		3.52	mg/kg bw/day
Methyl Palmitate	112-39-0	2	5.18		x	no hazard identified		
Dodecane	112-40-3	1	1.56		x	no hazard identified		
1-Tetradecanol	112-72-1	2	2.00		x		44.4	mg/kg bw/day

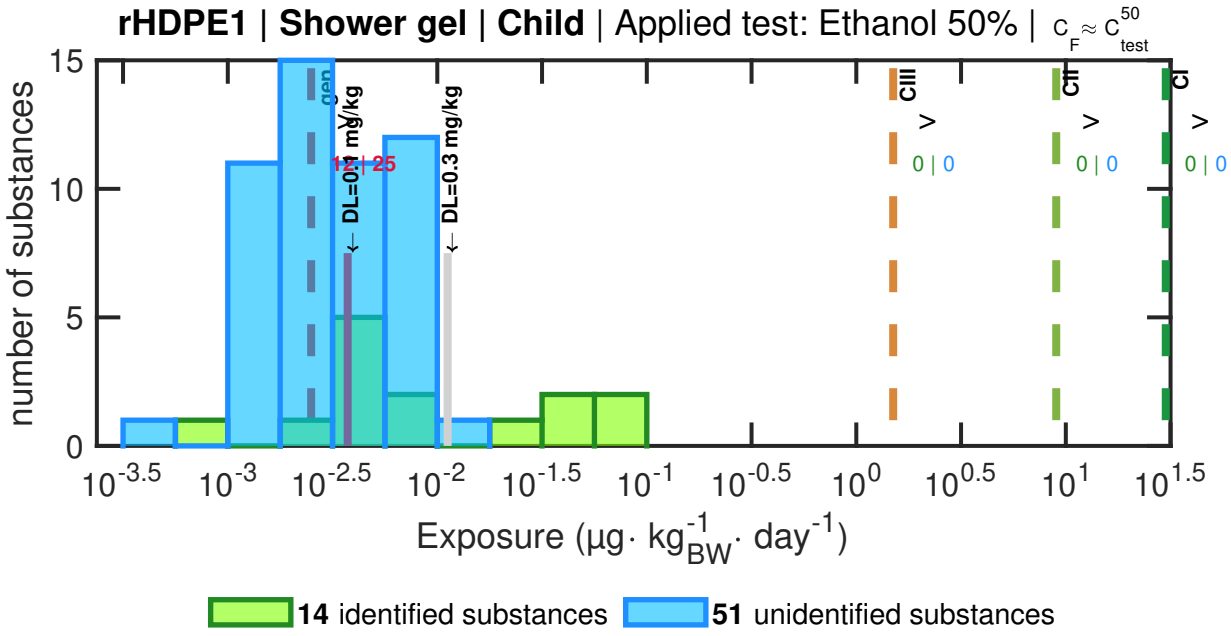
1-Octadecene	112-88-9	1	11.05			x	no hazard identified		
1-Octadecanol	112-92-5	2	28.64			x		55	mg/kg bw/day
Ethylhexyl Salicylate	118-60-5	3	5.55			x		2.4	mg/kg/day
a-Isomethyl ionone	127-51-5	3	0.60			x		35.5	µg/kg bw/day
2,2,4,6,6-Pentamethylheptane	13475-82-6	1	0.17			x	no hazard identified		
Dodecyl Laurate	13945-76-1	2	12.77			x	no hazard identified		
Isopropyl palmitate	142-91-6	2	70.61			x		1.83	mg/kg bw/day
a,a-Dimethylphenethyl acetate	151-05-3	3	0.15			x		1.8	mg/kg bw/day
4-tert-Butylcyclohexyl acetate trans	1900-69-2	3	0.25			x	no data available		class 3
Amyl salicylate	2050-08-0	3	0.67			x		0.45	mg/kg bw/day
Irganox 1076	2082-79-3	3	11.21			x		0.64	mg/kg bw/day
2-Ethylhexyl stearate	22047-49-0	2	17.25			x	no hazard identified		
3-Phenyldodecane	2400-00-2	3	3.44			x	no data available		
2-Hexyl-1-decanol	2425-77-6	2	0.38			x	no hazard identified		
6-Phenyldodecane	2719-62-2	3	2.21			x	no data available		
5-Phenyldodecane	2719-63-3	3	1.89			x	no data available		
4-Phenyldodecane	2719-64-4	3	1.52			x	no data available		
Benzoic acid, dodecyl ester	2915-72-2	3	3.43			x	no data available		
Benzoic acid, tridecyl ester	29376-83-8	3	5.51			x	no data available		
Phenol, 2,4-bis(1,1-dimethylethyl)-, phosphite (3:	31570-04-4	3	320.15			x	no hazard identified		
6-Phenyltridecane	4534-49-0	3	1.89			x	no data available		
5-Phenyltridecane	4534-50-3	3	1.21			x	no data available		
4-Phenyltridecane	4534-51-4	3	1.39			x		9	µg/kg bw/day
3-Phenyltridecane	4534-52-5	3	1.19			x		9	µg/kg bw/day
4-Phenylundecane	4536-86-1	3	2.29			x	no data available		
Benzene, (1-ethylnonyl)-	4536-87-2	3	2.05			x		9	µg/kg bw/day
2-Phenylundecane	4536-88-3	3	1.54			x	no data available		
2-Phenyldecane	4537-13-7	3	1.54			x	no data available		
6-Phenylundecane	4537-14-8	3	0.47			x	no data available		
5-Phenylundecane	4537-15-9	3	2.01			x		9	µg/kg bw/day
3-Phenyldecane	4621-36-7	3	0.35			x	no data available		
Ethyl Linoleate	544-35-4	2	14.25			x		30	µg/kg bw/day
Hexadecane	544-76-3	1	13.33			x	no hazard identified		
Octan-2-yl palmitate	55194-81-5	2	27.55			x	no data available		
Octadecane	593-45-3	1	19.38			x	no hazard identified		
Ethyl elaidate	6114-18-7	2	22.00			x	no data available		
Ethyl Palmitate	628-97-7	2	52.38			x		30	µg/kg bw/day
Tetradecane	629-59-4	1	6.15			x	no hazard identified		

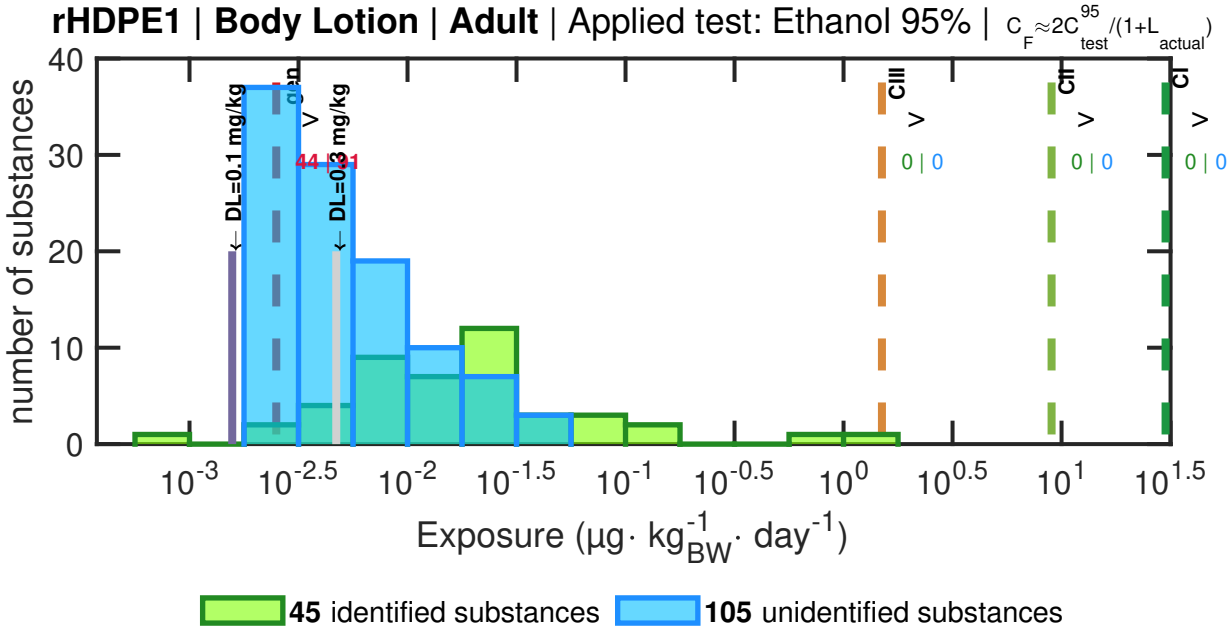
Pentadecane	629-62-9	1	1.64			x	no hazard identified		
Heptadecane	629-78-7	1	2.51			x	no hazard identified		
Di-n-Octylether	629-82-3	3	18.23			x		25	mg/kg bw/day
Nonadecane	629-92-5	1	0.78			x	no data available		
Docosane	629-97-0	1	11.85			x	no hazard identified		
Hexacosane	630-01-3	1	2.09			x	no data available		
Diethyl terephthalate	636-09-9	3	1.90			x		30	µg/kg bw/day
Phytan	638-36-8	1	0.35			x	no data available		
Plastic additive 27	6422-86-2	3	3.51			x		3.95	mg/kg bw/day
Tetracosane	646-31-1	1	3.51			x	no data available		
Benzoic acid	65-85-0	3	0.40			x		16.6	mg/kg bw/day
Benzoic acid, pentadecyl ester	68411-27-8	3	2.69			x	no hazard identified		
Benzoic acid, tetradecyl ester	70682-72-3	3	4.89			x	no data available		
Lilial	80-54-6	3	0.43			x		62.5	µg/kg bw/day
1-Propylpentyl laurate	84713-06-4	2	10.87			x	no data available		
Isoamyl Salicylate	87-20-7	3	0.37			x		30	µg/kg bw/day
Menthol	89-78-1	3	0.22			x		4.7	mg/kg bw/day
2-Methoxy naphthalene	93-04-9	3	0.34			x		625	µg/kg bw/day
Tris(2,4-di-tert-butylphenyl) phosphate	95906-11-9	3	96.47			x		1.5	µg/kg bw/day

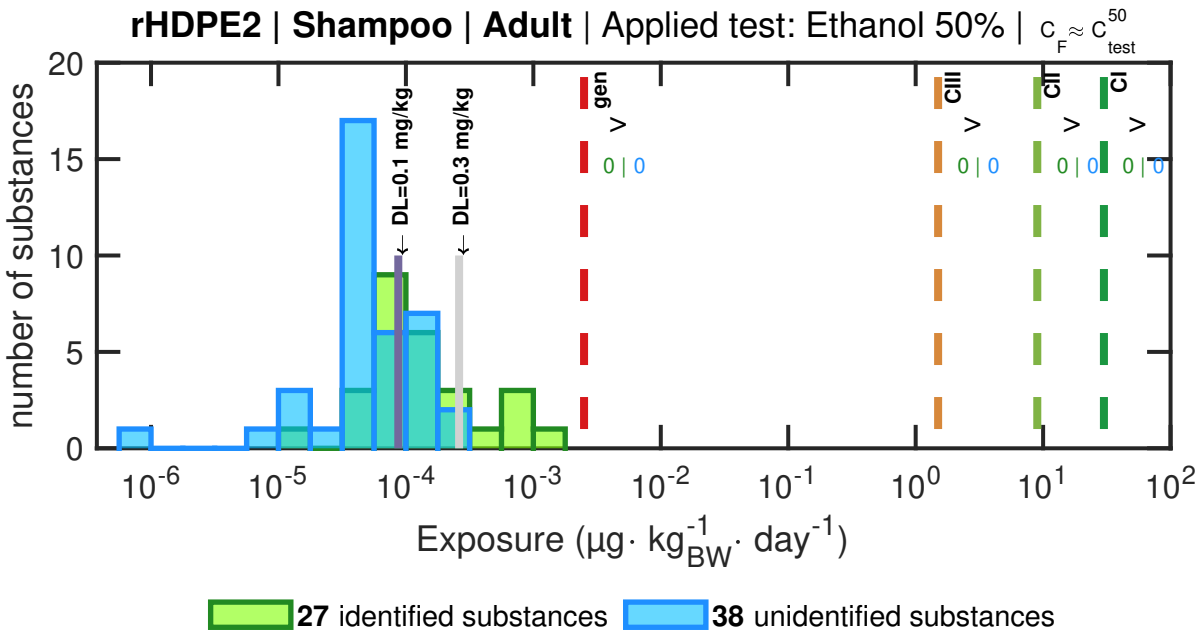
Appendix 9. Safety evaluation of the 31 materials tested in the project CosPaTox

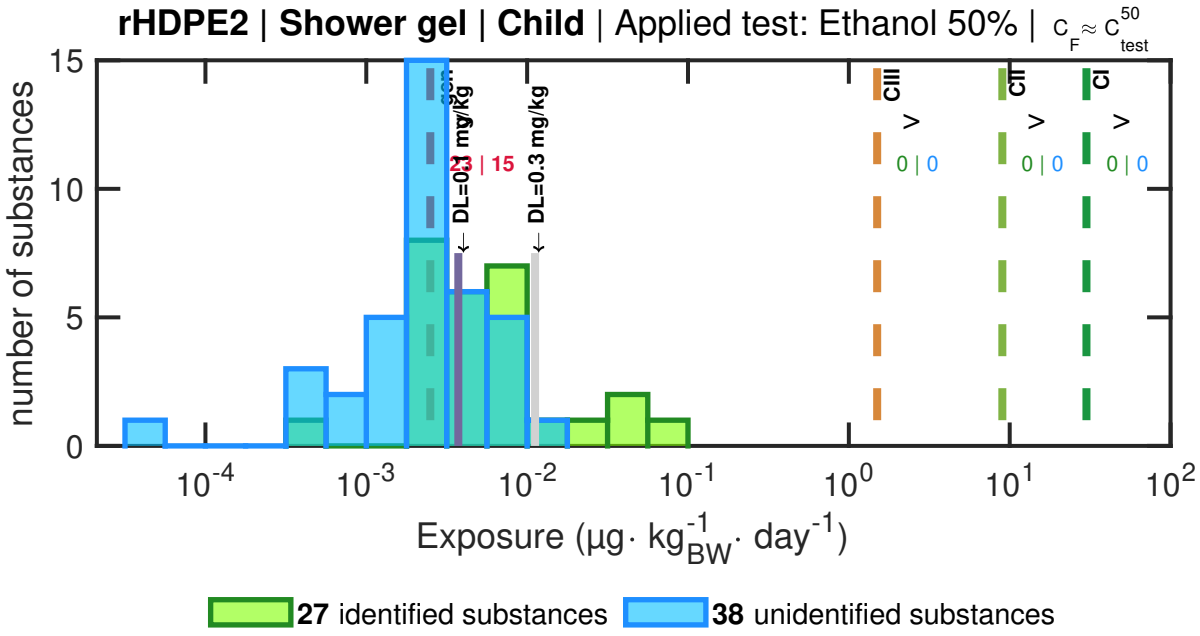
The 31 materials were tested according to scenarios described in **Table 3** with a methodology explained in section 5.3.

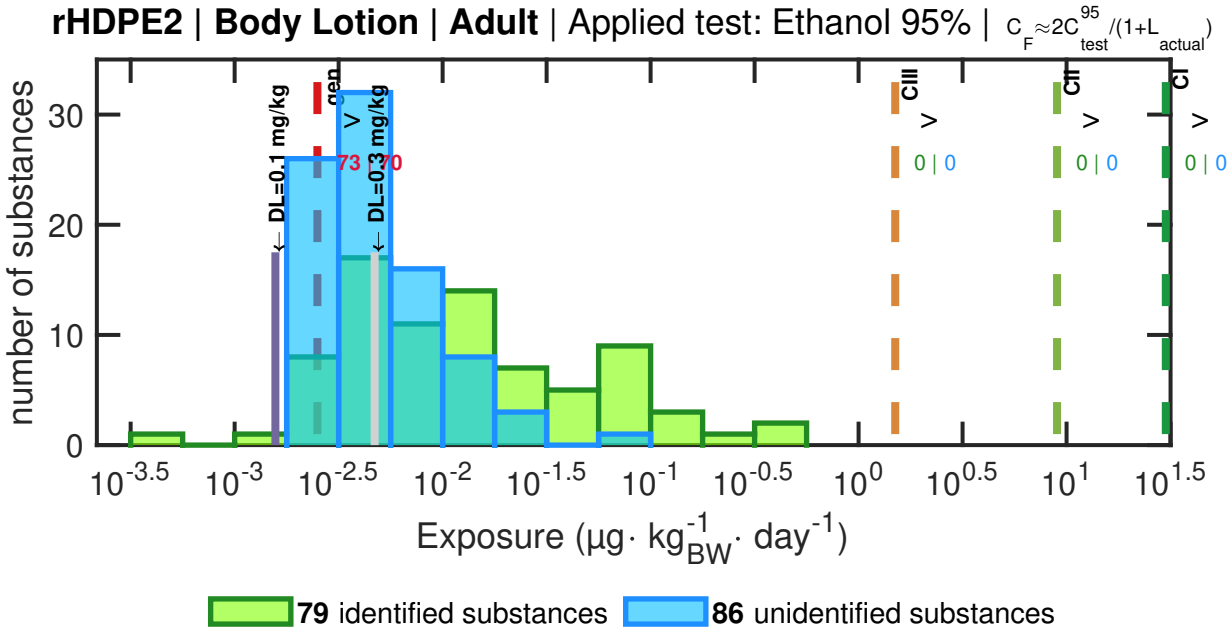

rHDPE1 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
0 | 0
Exposure (µg· kg^{-1}_{BW}· day^{-1})
14 identified substances
51 unidentified substances

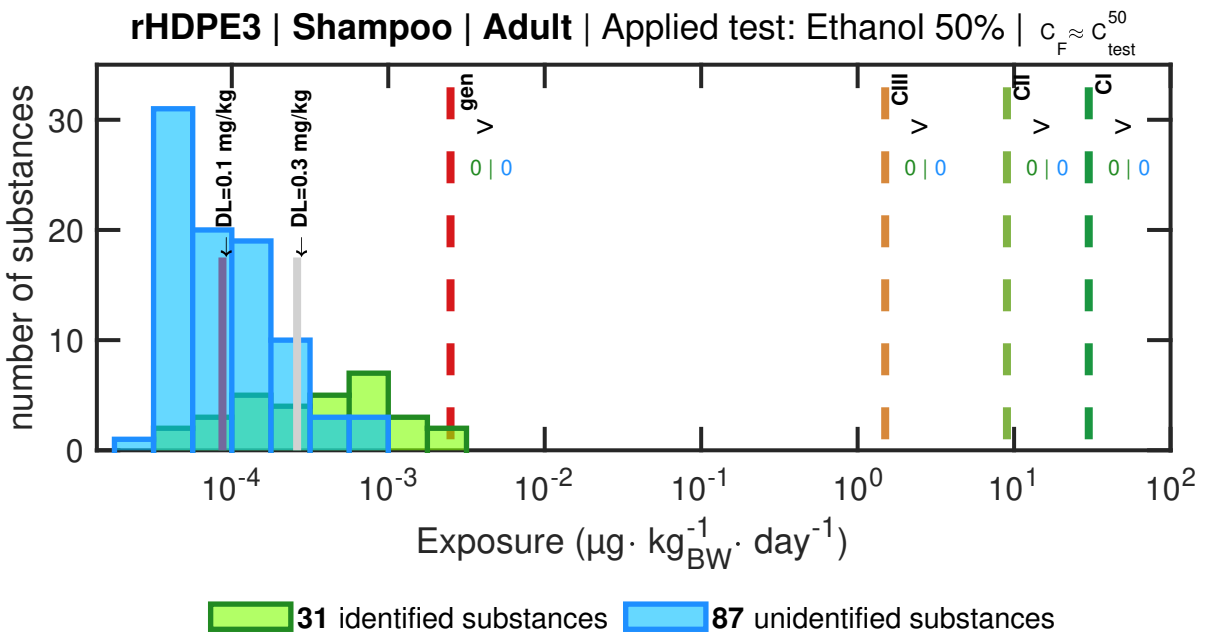

rHDPE1 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
11 | 25
CIII
CII
CI
0 | 0
Exposure (µg· kg^{-1}_{BW}· day^{-1})
14 identified substances
51 unidentified substances

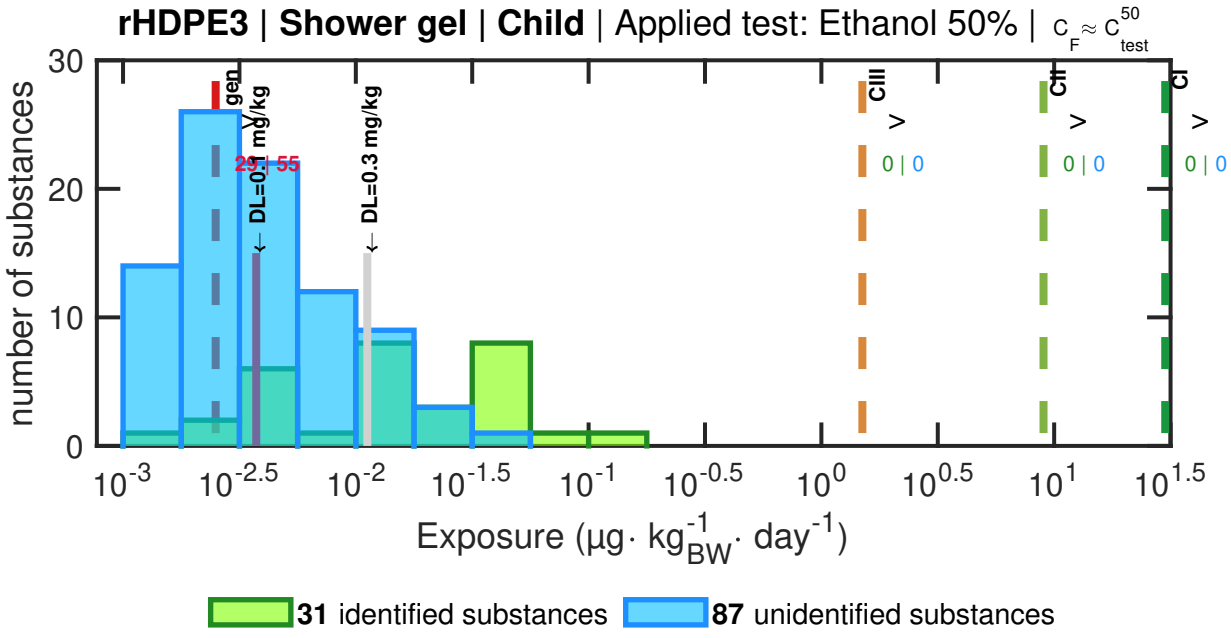

rHDPE1 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
44 | 91
CIII
CII
CI
0 | 0
Exposure (µg· kg^{-1}_{BW}· day^{-1})
45 identified substances
105 unidentified substances

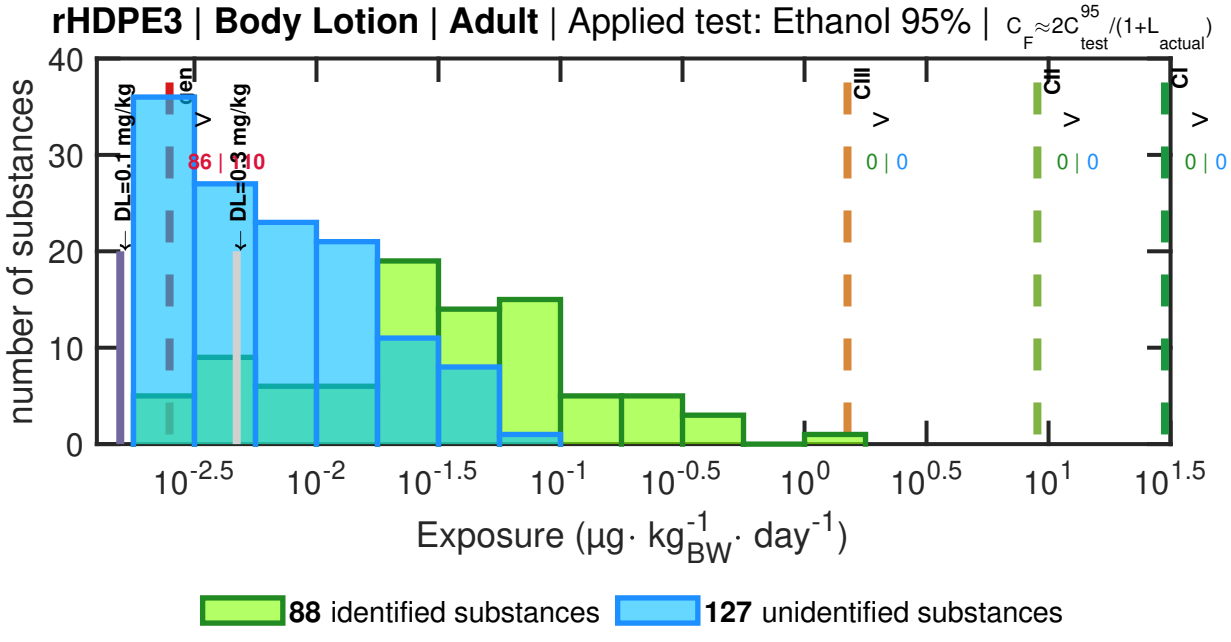

rHDPE2 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
0 | 0
27 identified substances
38 unidentified substances

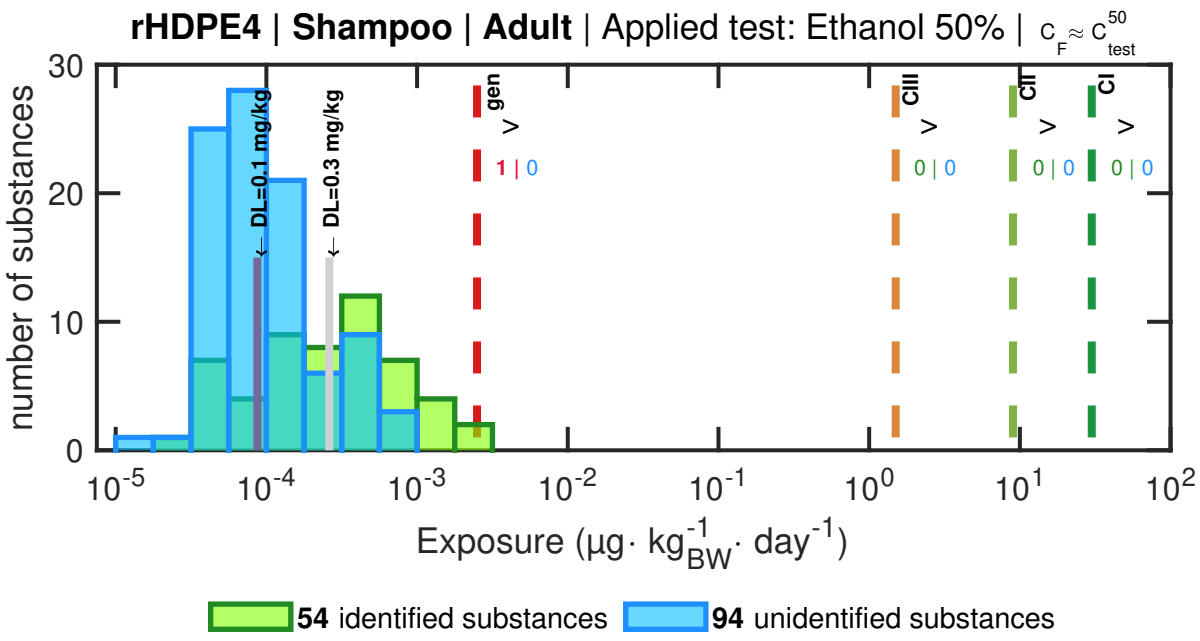

rHDPE2 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.3 mg/kg
23 | 15
CIII
CII
CI
0 | 0
27 identified substances
38 unidentified substances

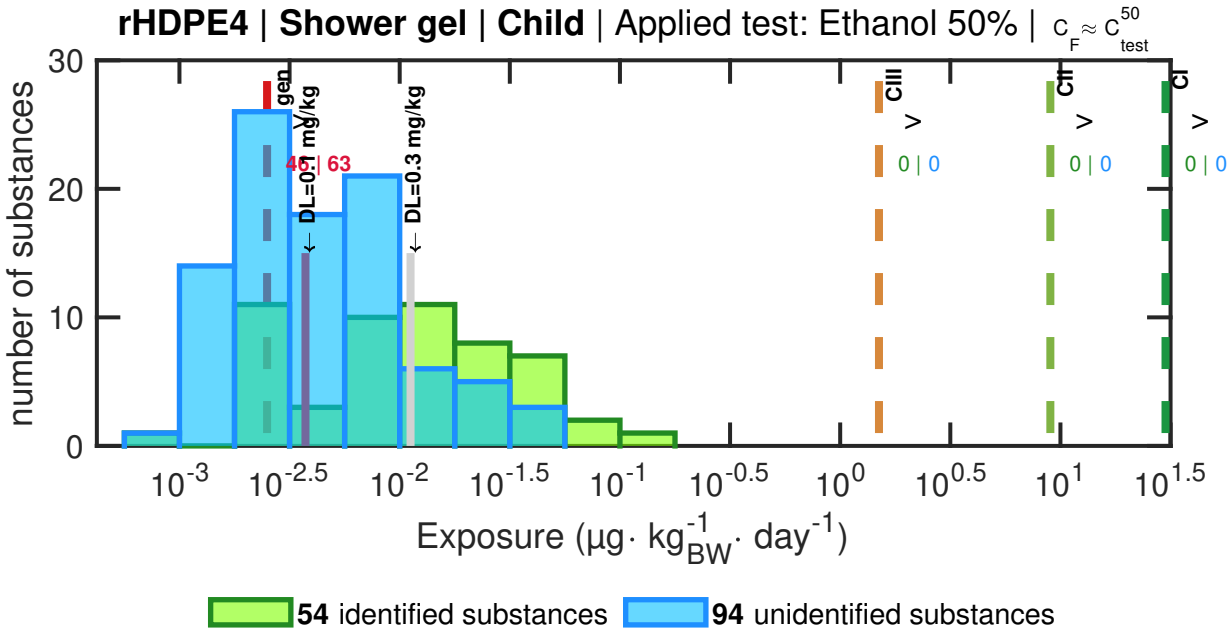

rHDPE2 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
73 | 70
CIII
CII
CI
0 | 0
79 identified substances
86 unidentified substances

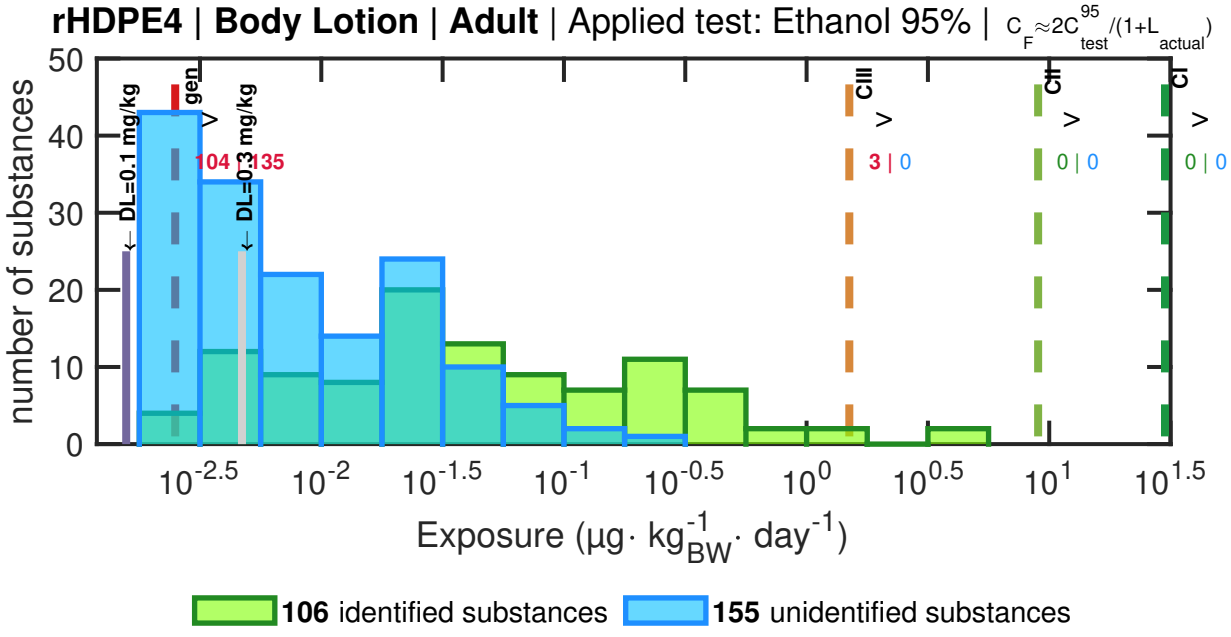

rHDPE3 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
0 | 0
Exposure (µg· kg$^{-1}_{BW}$· day^{-1})
31 identified substances
87 unidentified substances

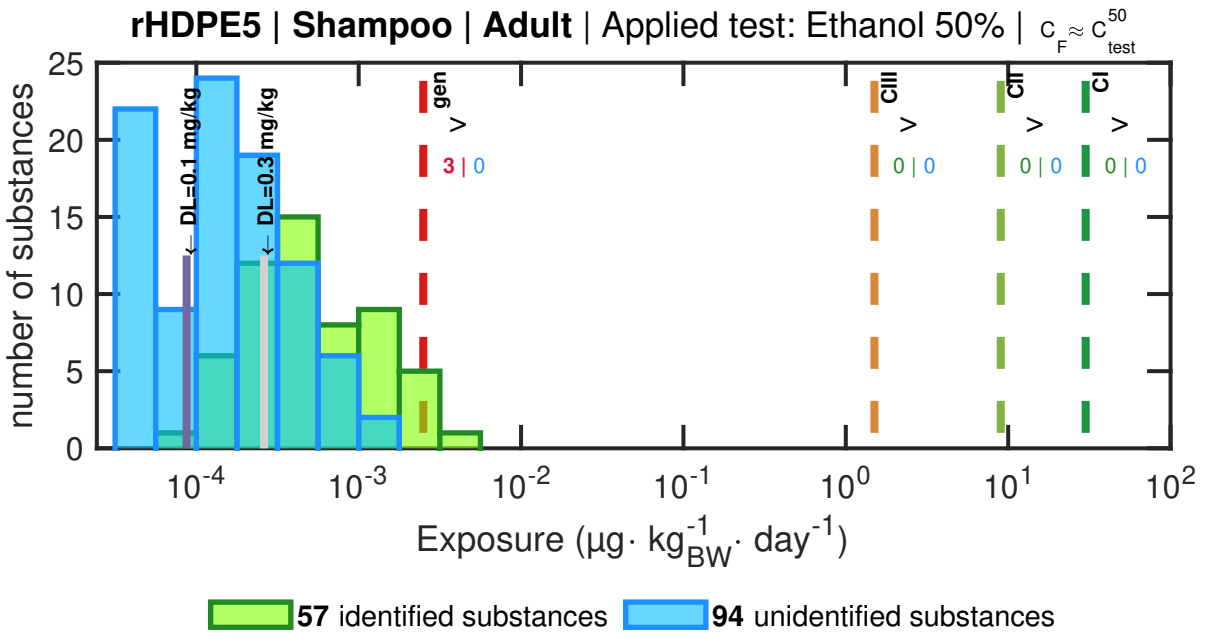

rHDPE3 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
gen
DL=0.3 mg/kg
CIII
CII
CI
0 | 0
Exposure (µg· kg$^{-1}_{BW}$· day^{-1})
31 identified substances
87 unidentified substances

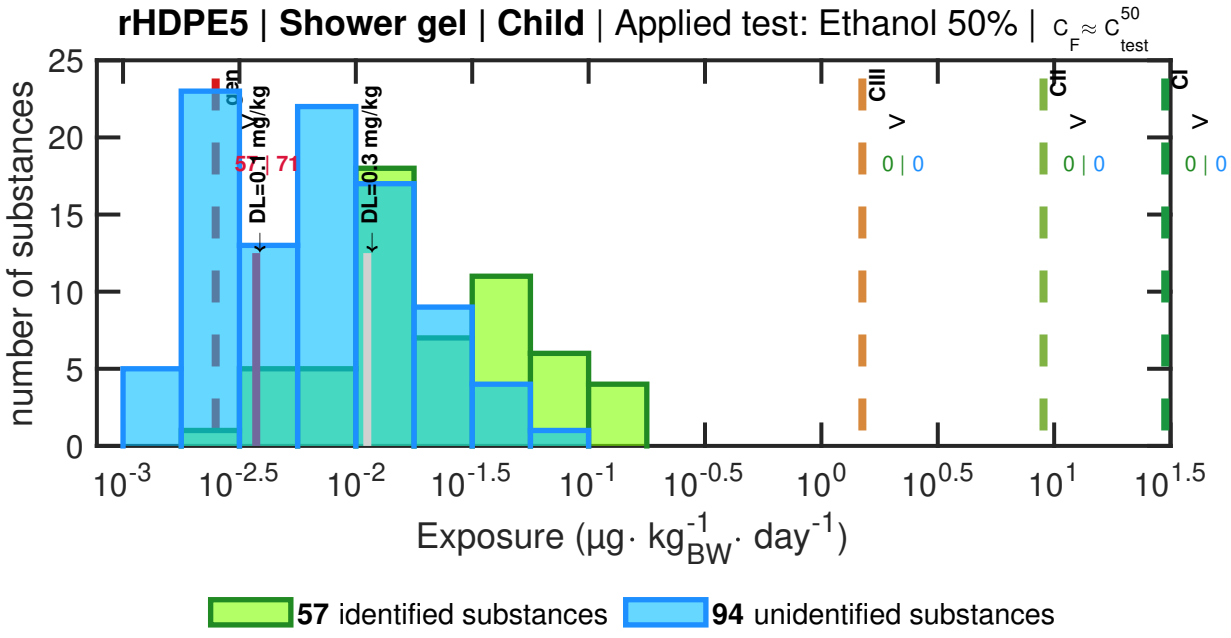

rHDPE3 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
DL=0.1 mg/kg
gen
DL=0.3 mg/kg
CIII
CII
CI
0 | 0
Exposure (µg· kg$^{-1}_{BW}$· day^{-1})
88 identified substances
127 unidentified substances

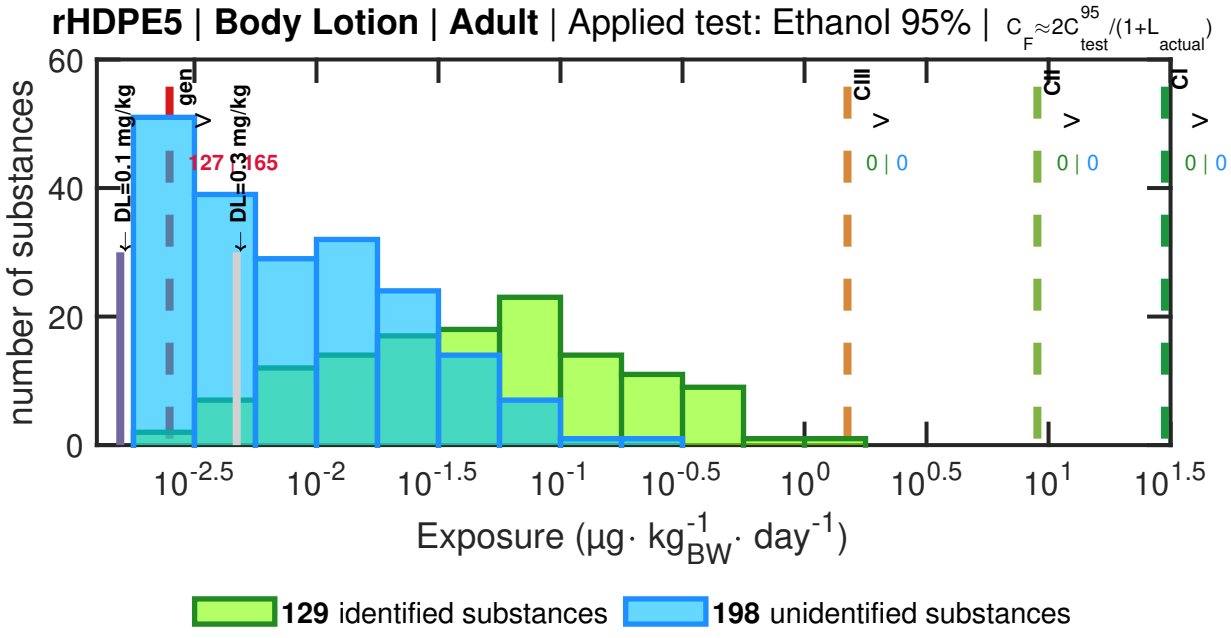

rHDPE4 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
1 | 0
0 | 0
0 | 0
0 | 0
54 identified substances
94 unidentified substances

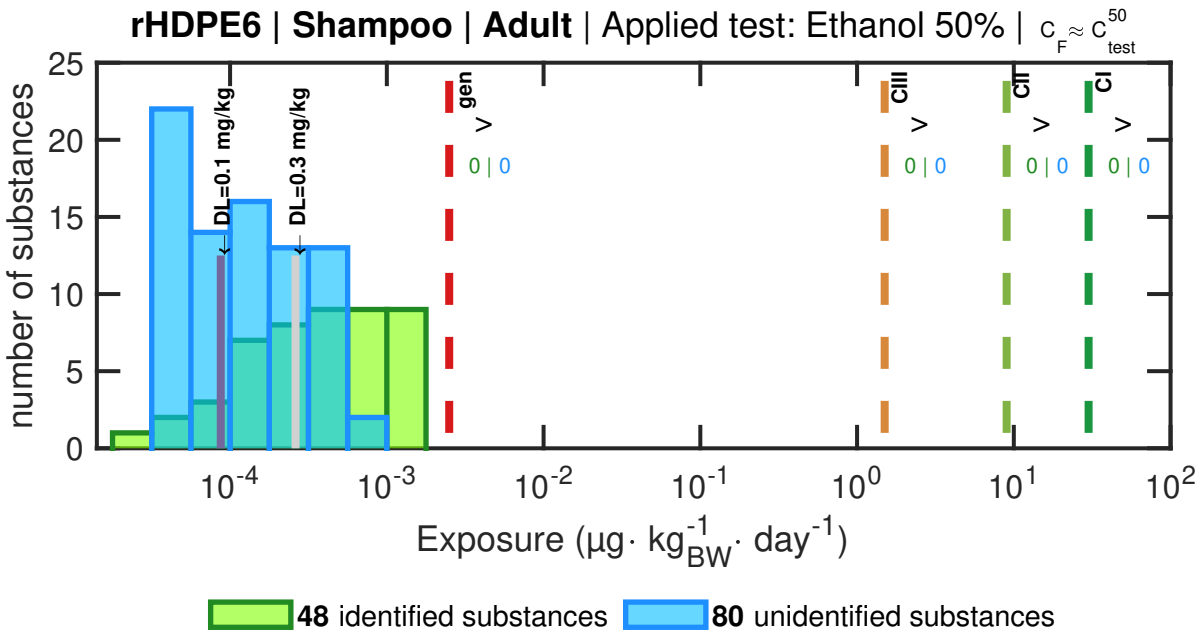

rHDPE4 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
46 | 63
0 | 0
0 | 0
0 | 0
54 identified substances
94 unidentified substances

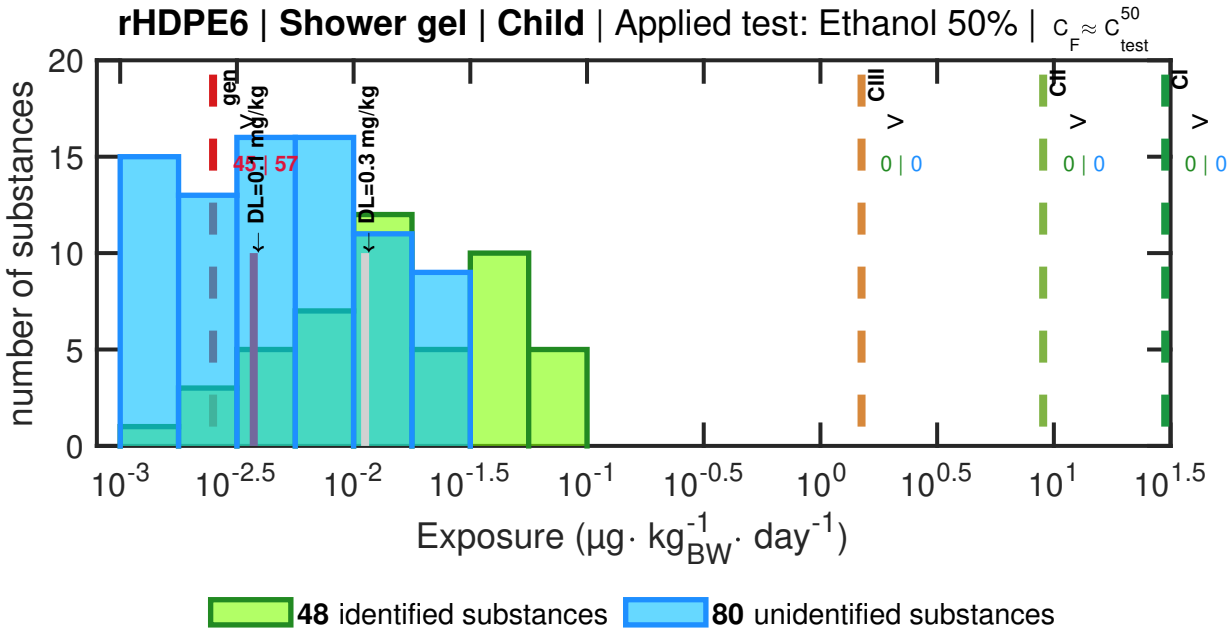

rHDPE4 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
104 | 135
3 | 0
0 | 0
0 | 0
106 identified substances
155 unidentified substances

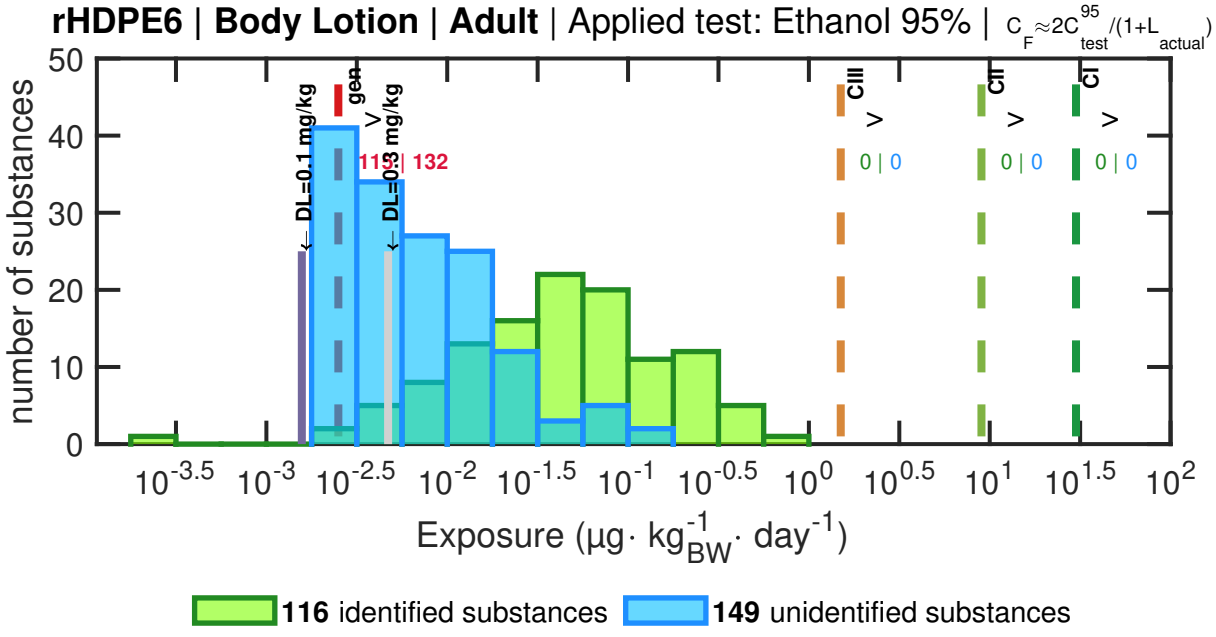

rHDPE5 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg$^{-1}_{BW}$· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
3 | 0
0 | 0
0 | 0
0 | 0
57 identified substances
94 unidentified substances

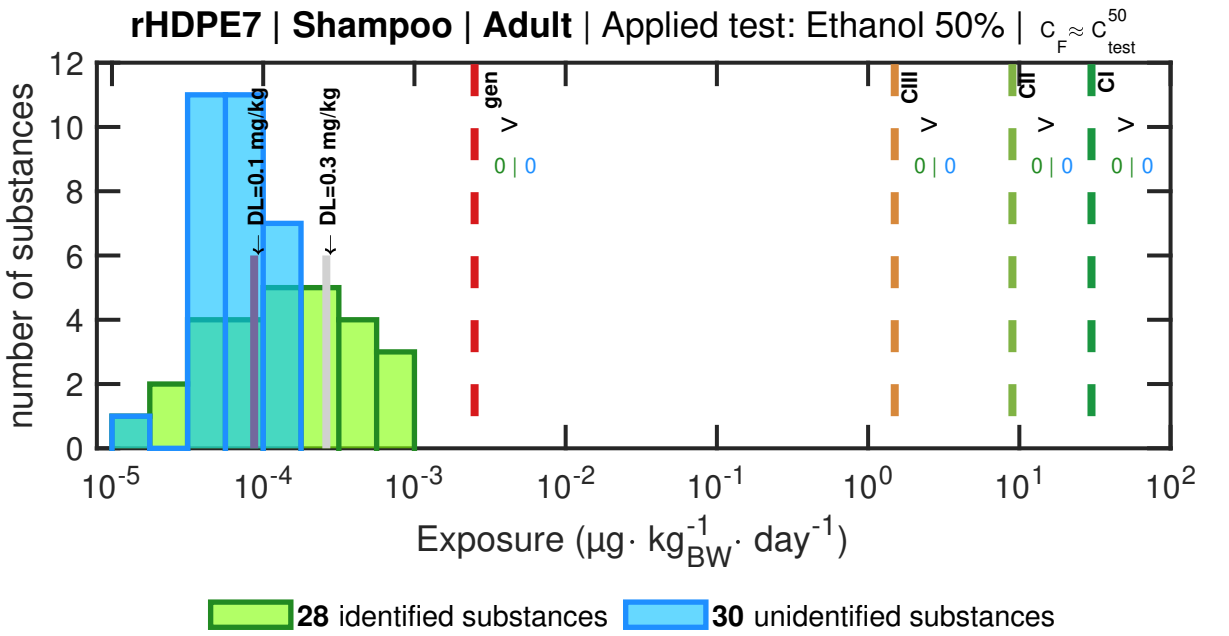

rHDPE5 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg$^{-1}_{BW}$· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
57 | 71
0 | 0
0 | 0
0 | 0
57 identified substances
94 unidentified substances

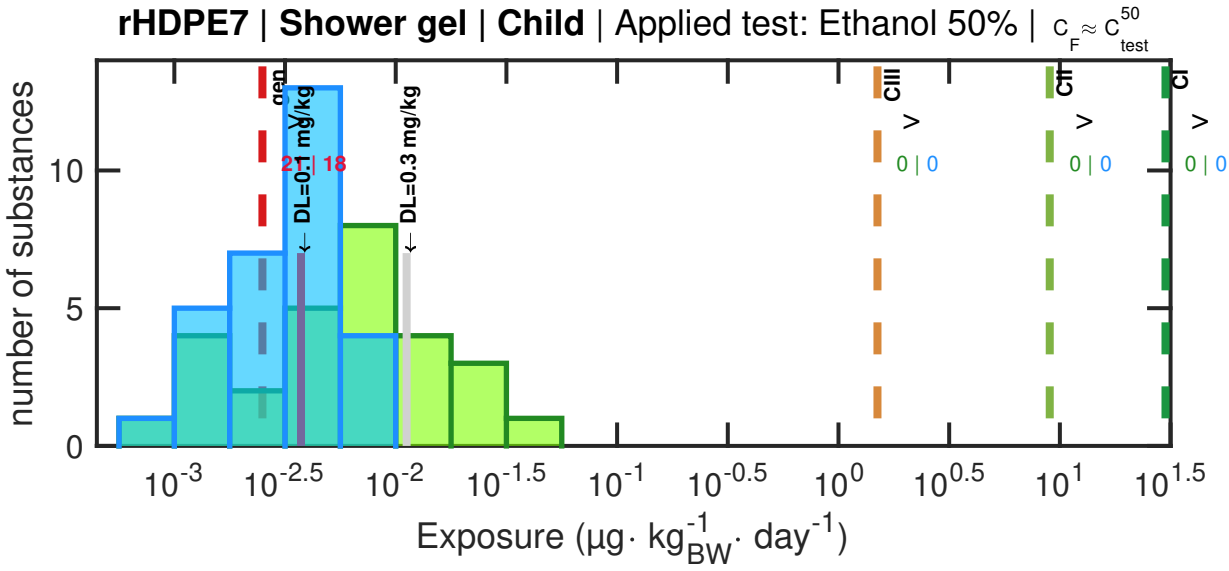

rHDPE5 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
Exposure (µg· kg$^{-1}_{BW}$· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
127 | 165
0 | 0
0 | 0
0 | 0
129 identified substances
198 unidentified substances

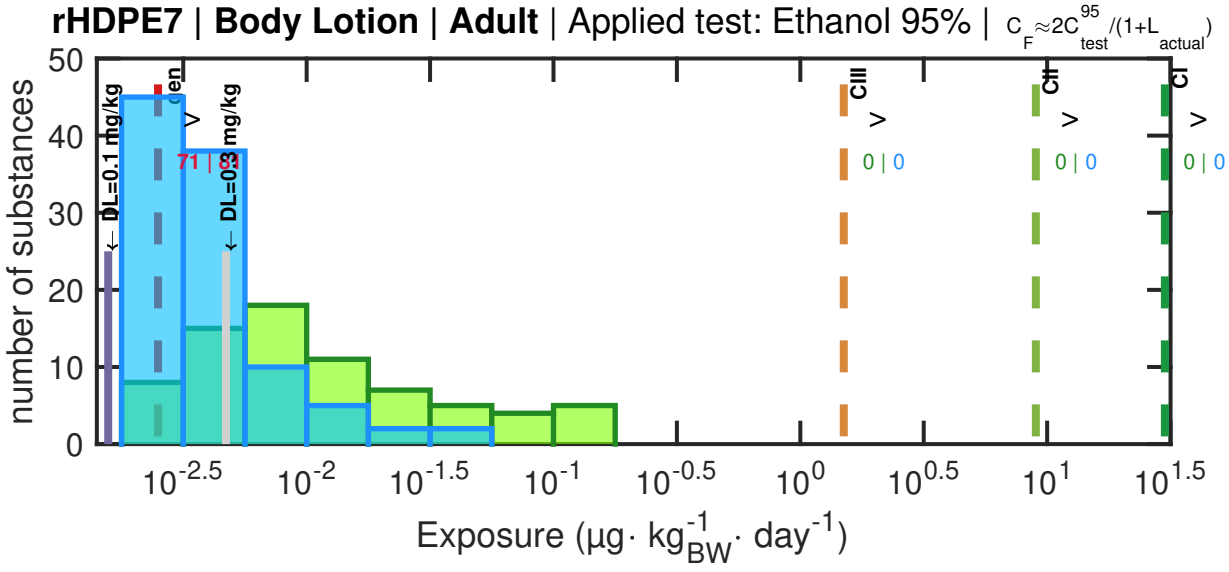

rHDPE6 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
0 | 0
48 identified substances
80 unidentified substances

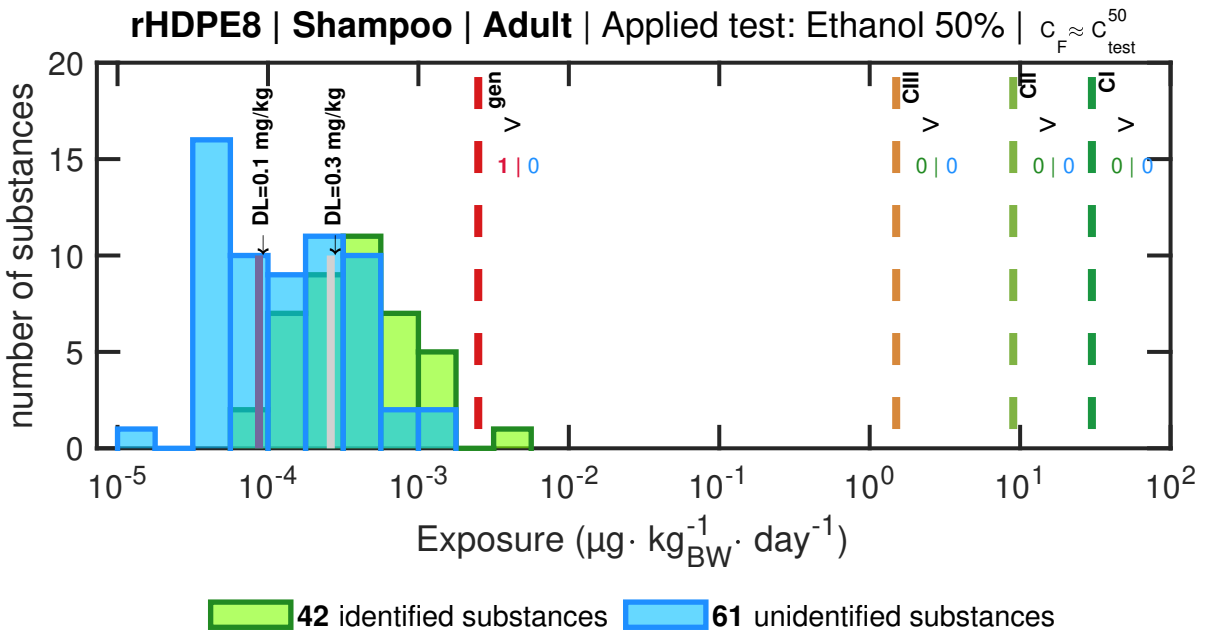

rHDPE6 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
gen
DL=0.1 mg/kg
DL=0.3 mg/kg
45 | 57
CIII
CII
CI
0 | 0
48 identified substances
80 unidentified substances

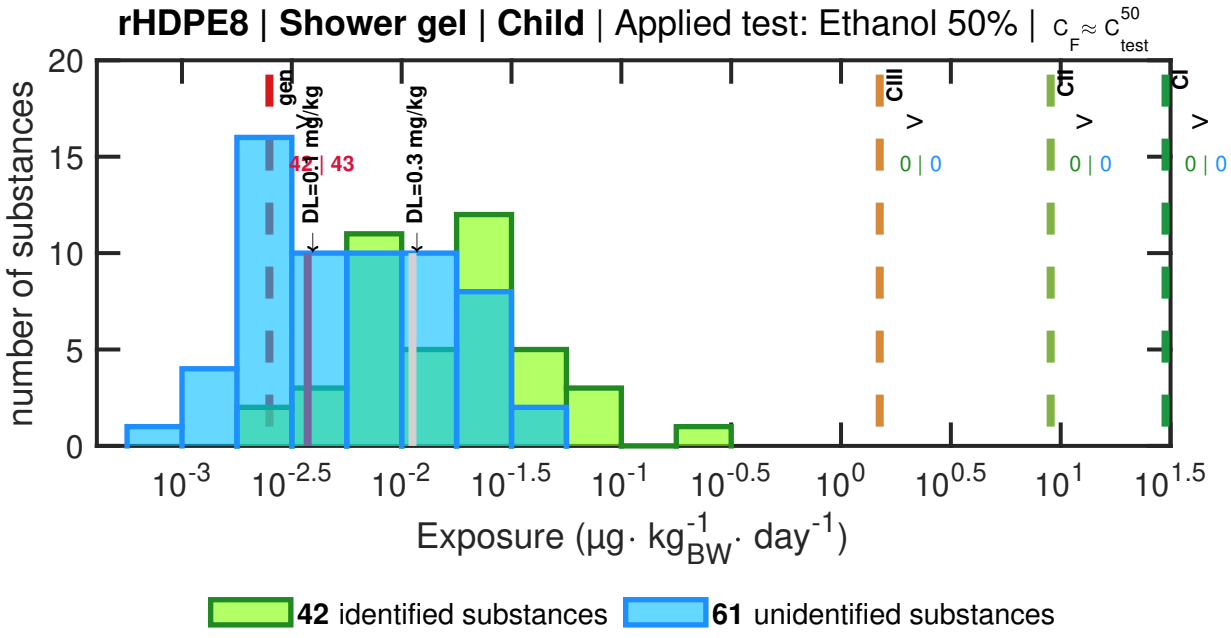

rHDPE6 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
gen
DL=0.3 mg/kg
115 | 132
CIII
CII
CI
0 | 0
116 identified substances
149 unidentified substances

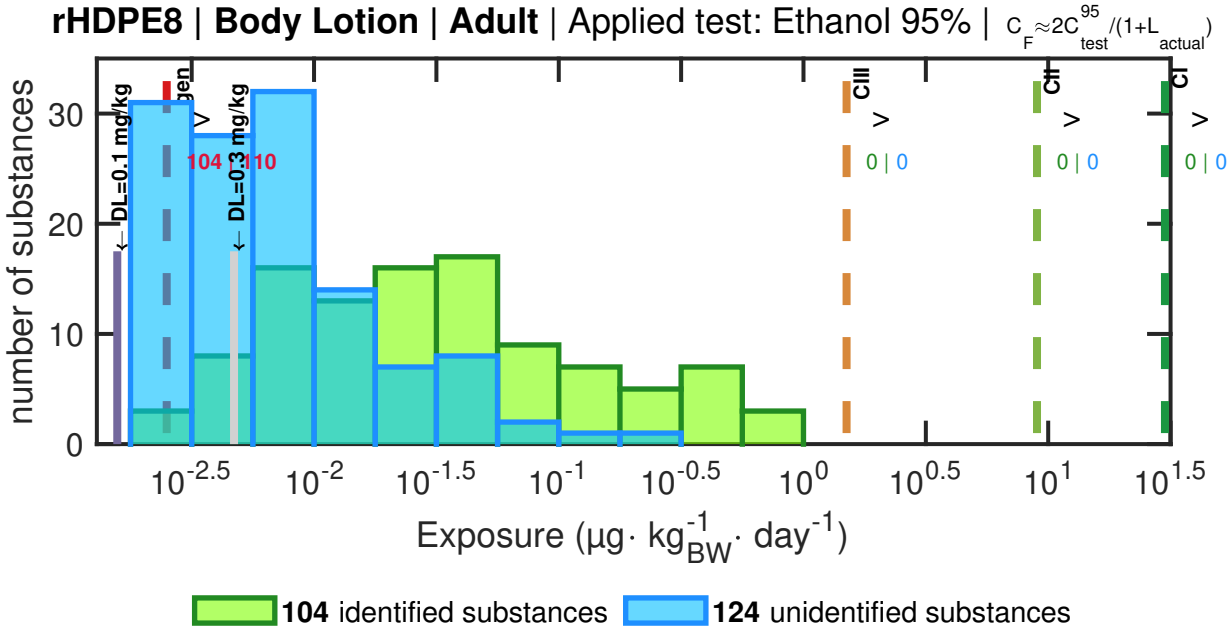

rHDPE7 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
0 | 0
Exposure (µg· kg$^{-1}_{BW}$· day^{-1})
28 identified substances
30 unidentified substances

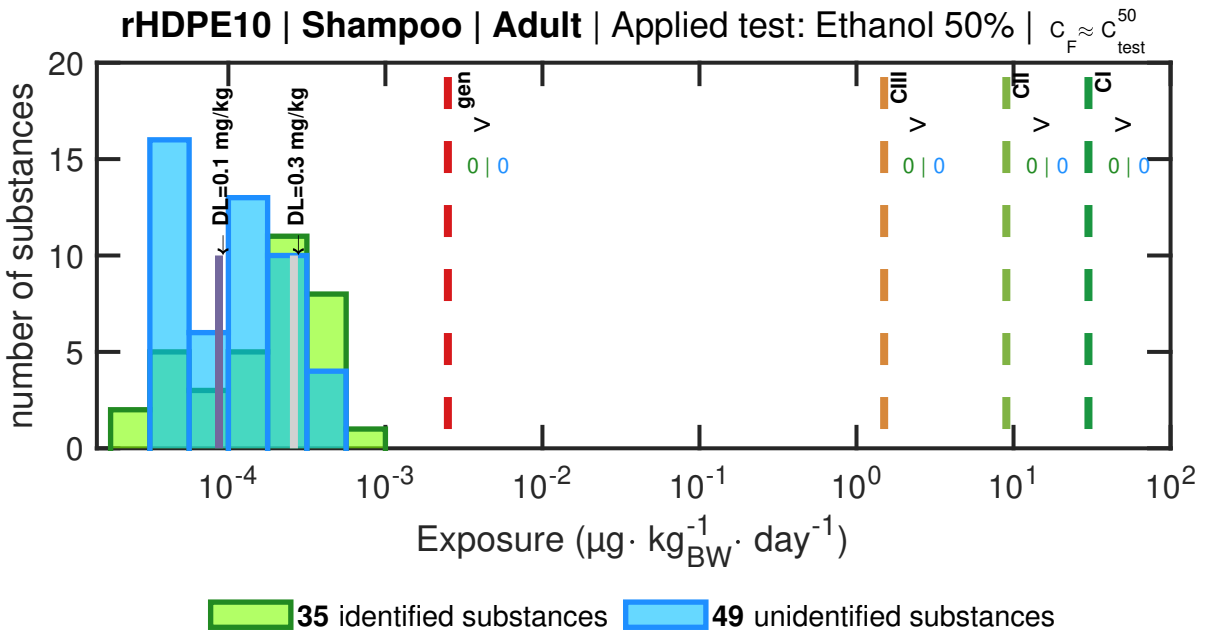

rHDPE7 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
gen
21 | 18
DL=0.1 mg/kg
DL=0.3 mg/kg
CIII
CII
CI
0 | 0
Exposure (µg· kg$^{-1}_{BW}$· day^{-1})
28 identified substances
30 unidentified substances

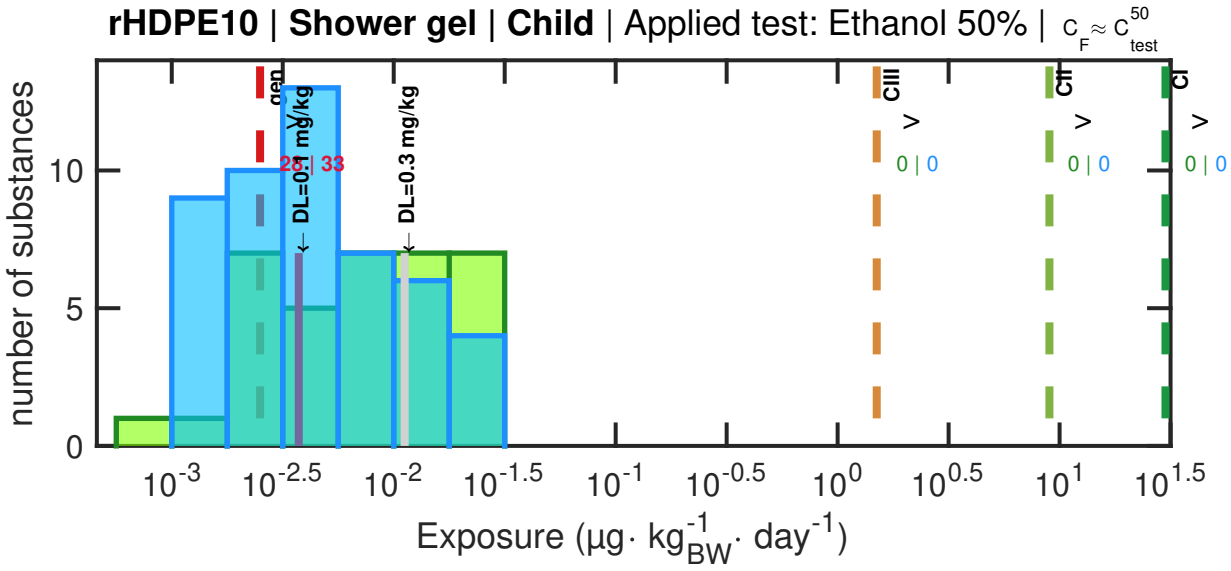

rHDPE7 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
DL=0.1 mg/kg
gen
71 | 53
DL=0.3 mg/kg
CIII
CII
CI
0 | 0
Exposure (µg· kg$^{-1}_{BW}$· day^{-1})
73 identified substances
102 unidentified substances

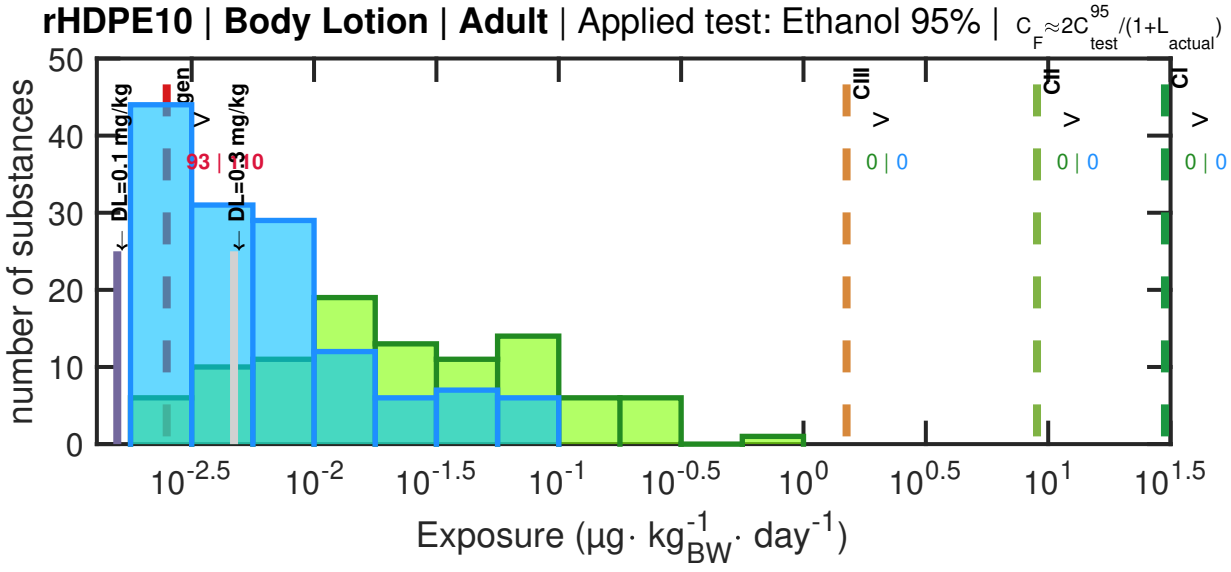

rHDPE8 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
1 | 0
0 | 0
0 | 0
0 | 0
42 identified substances
61 unidentified substances

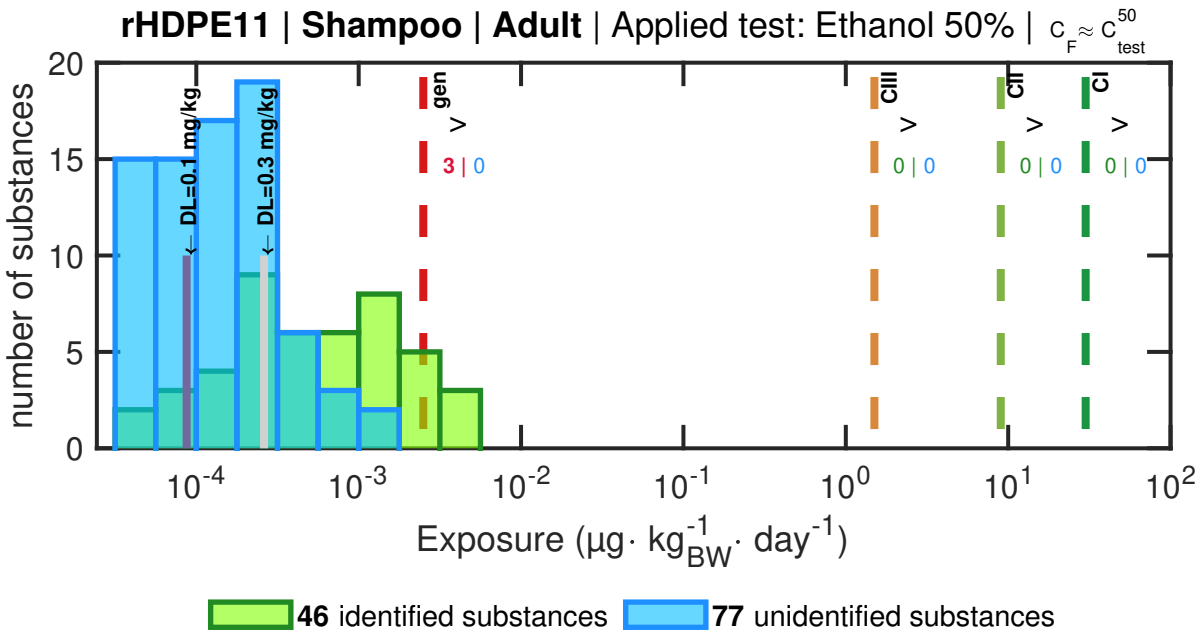

rHDPE8 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
gen
DL=0.1 mg/kg
DL=0.3 mg/kg
CIII
CII
CI
41 | 43
0 | 0
0 | 0
0 | 0
42 identified substances
61 unidentified substances

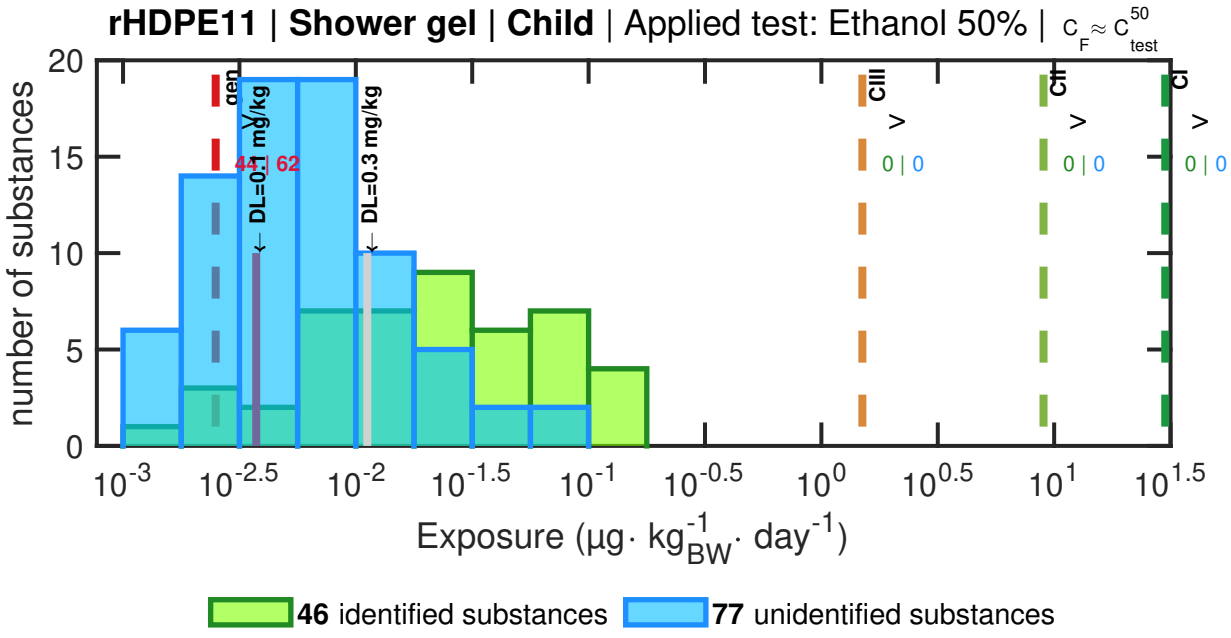

rHDPE8 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
gen
DL=0.3 mg/kg
CIII
CII
CI
104 | 110
0 | 0
0 | 0
0 | 0
104 identified substances
124 unidentified substances

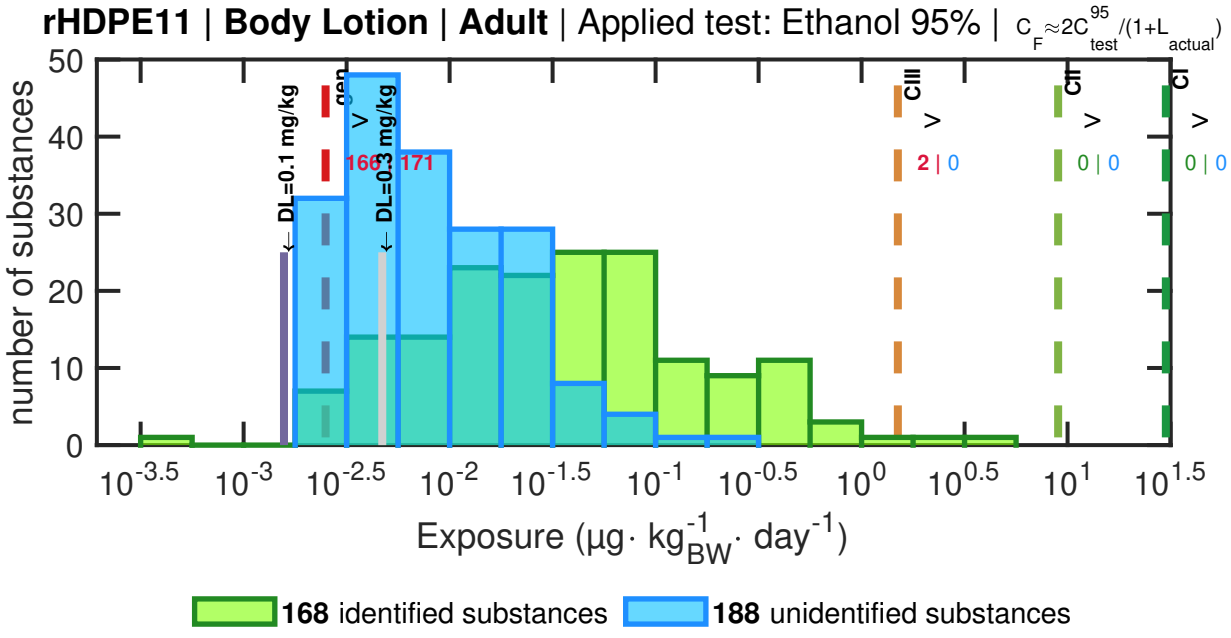

rHDPE10 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
0 | 0
Exposure (µg· kg^{-1}_{BW}· day^{-1})
35 identified substances
49 unidentified substances

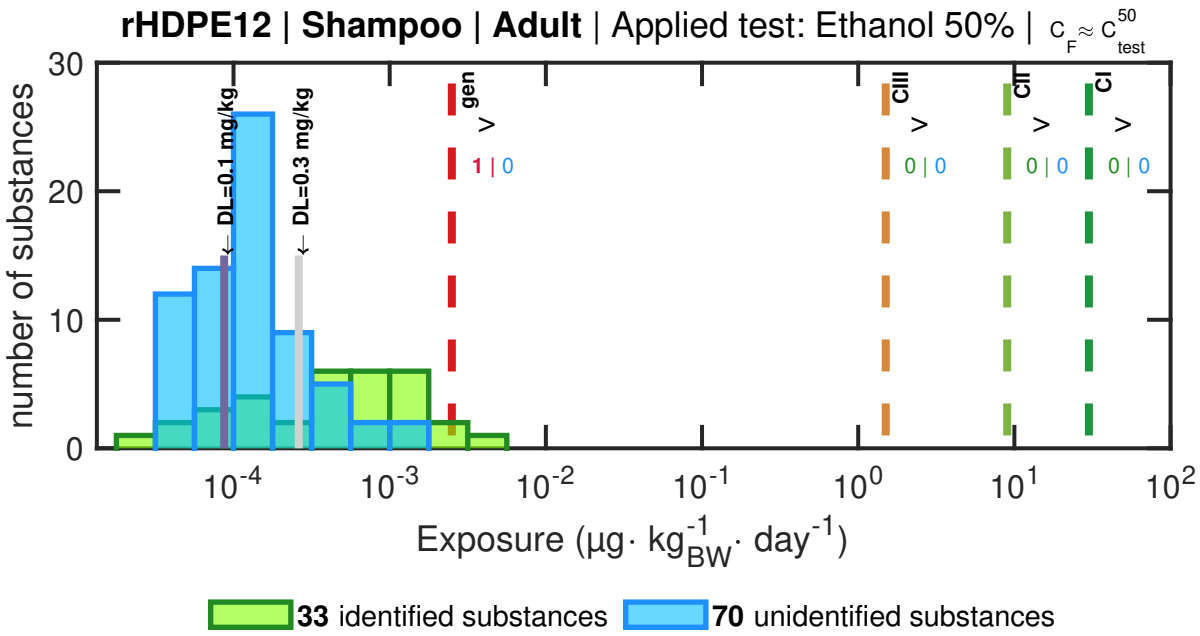

rHDPE10 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
gen
DL=0.1 mg/kg
DL=0.3 mg/kg
CIII
CII
CI
0 | 0
Exposure (µg· kg^{-1}_{BW}· day^{-1})
35 identified substances
49 unidentified substances

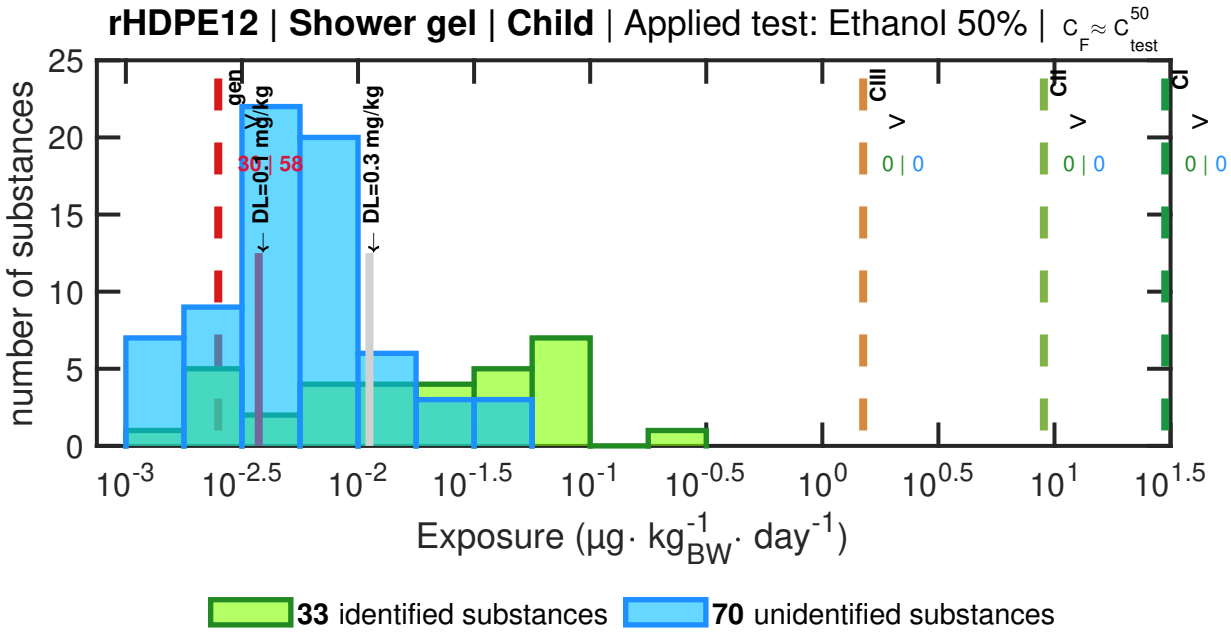

rHDPE10 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
DL=0.1 mg/kg
gen
DL=0.3 mg/kg
93 | 10
CIII
CII
CI
0 | 0
Exposure (µg· kg^{-1}_{BW}· day^{-1})
97 identified substances
135 unidentified substances

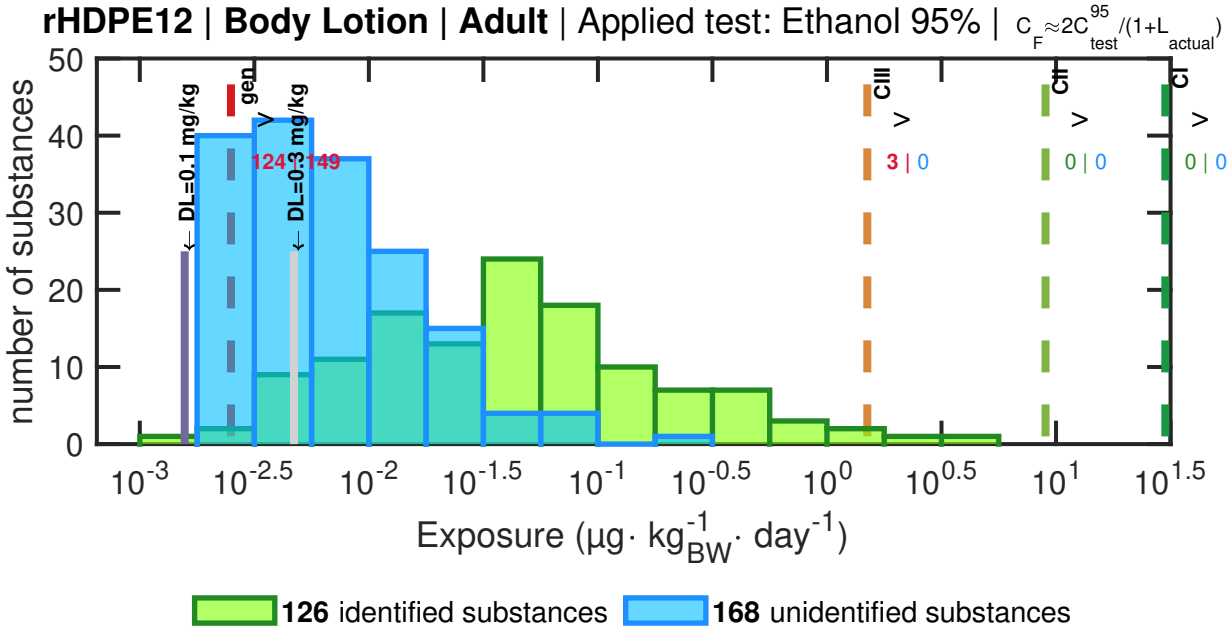

rHDPE11 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
3 | 0
CIII
0 | 0
CII
0 | 0
CI
0 | 0
46 identified substances
77 unidentified substances

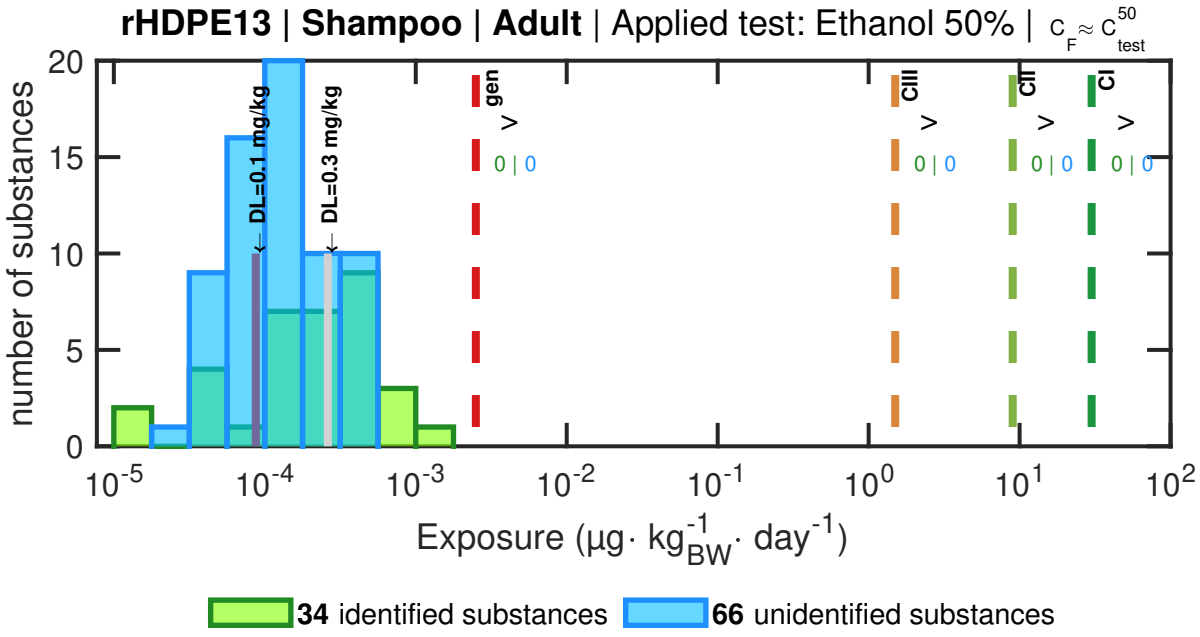

rHDPE11 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
gen
41 | 62
DL=0.1 mg/kg
DL=0.3 mg/kg
CIII
0 | 0
CII
0 | 0
CI
0 | 0
46 identified substances
77 unidentified substances

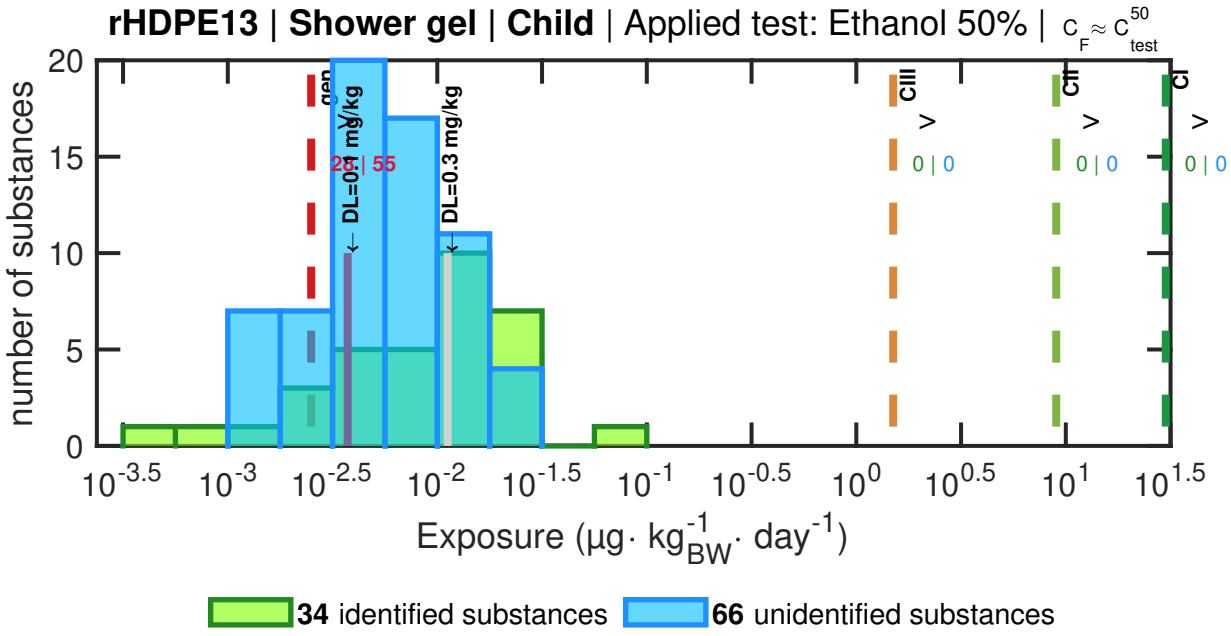

rHDPE11 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
gen
166 | 171
DL=0.3 mg/kg
CIII
2 | 0
CII
0 | 0
CI
0 | 0
168 identified substances
188 unidentified substances

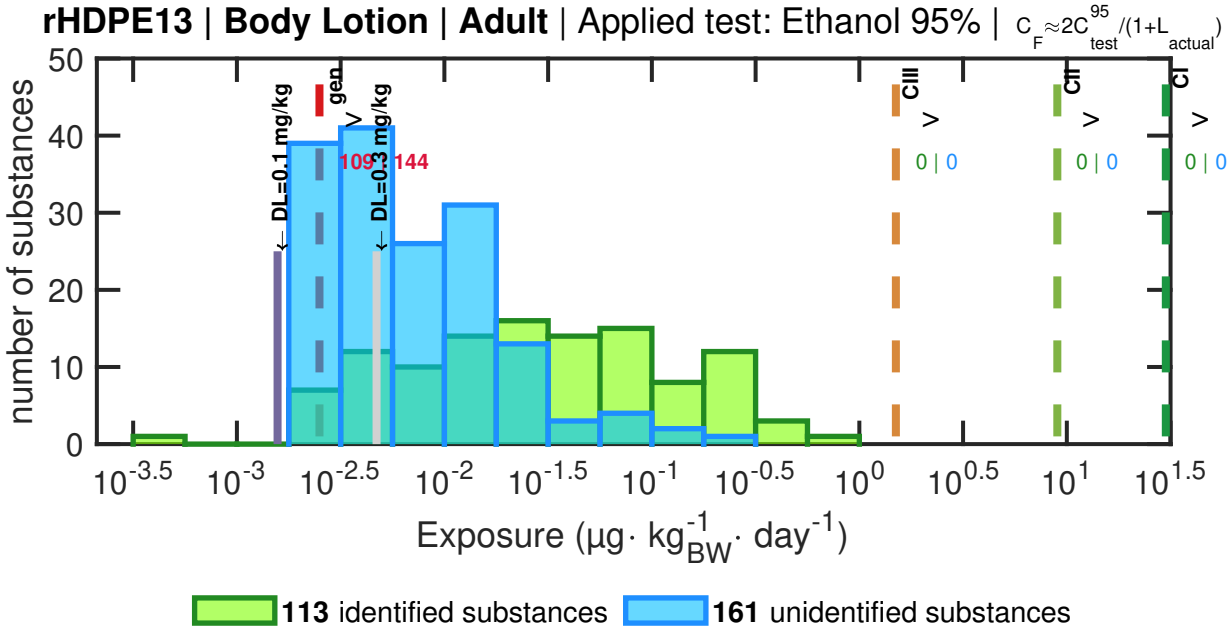

rHDPE12 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CIT
CI
1 | 0
0 | 0
0 | 0
0 | 0
Exposure (µg· kg^{-1}_{BW}· day^{-1})
33 identified substances
70 unidentified substances

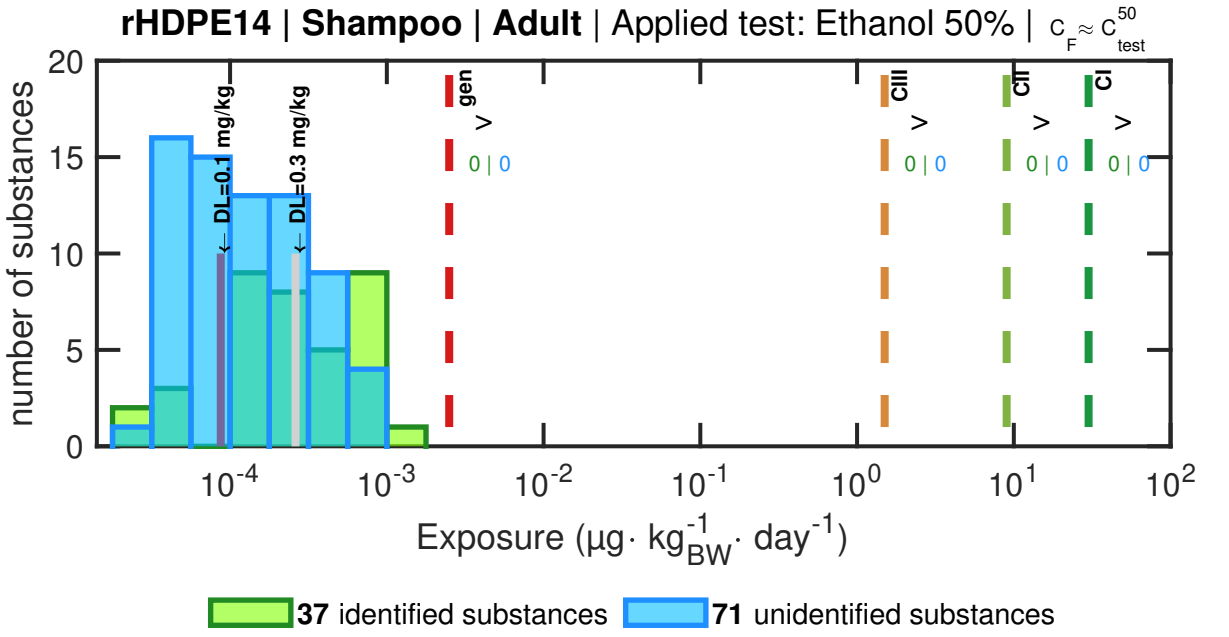

rHDPE12 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
gen
30 | 58
DL=0.1 mg/kg
DL=0.3 mg/kg
CIII
CIT
CI
0 | 0
0 | 0
0 | 0
Exposure (µg· kg^{-1}_{BW}· day^{-1})
33 identified substances
70 unidentified substances

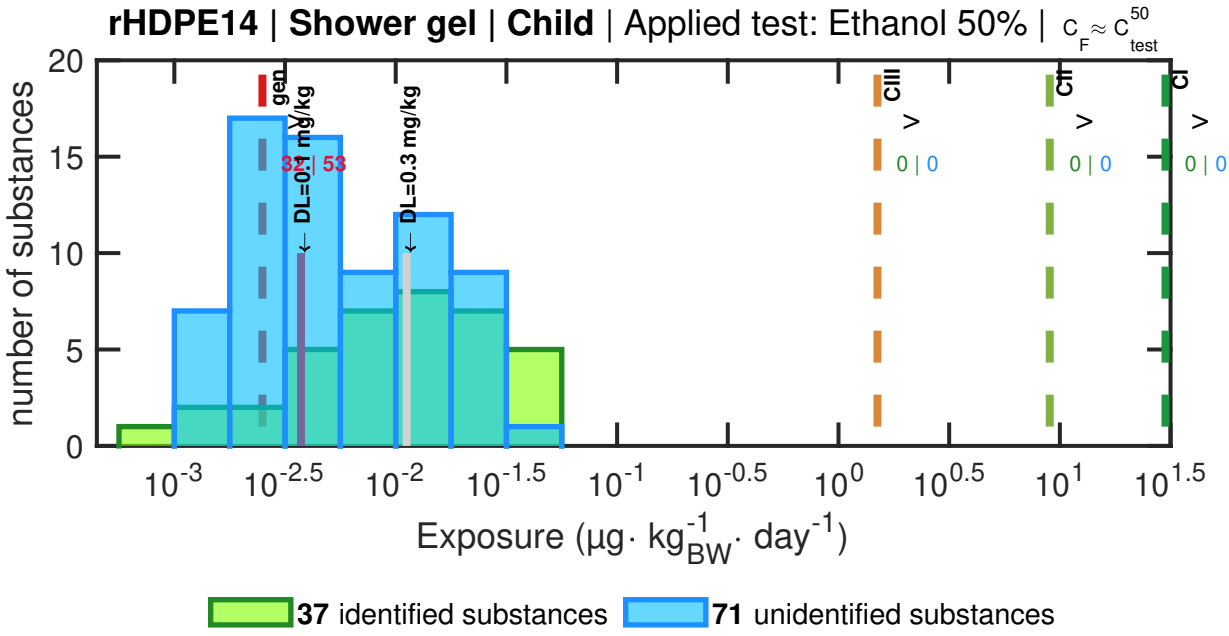

rHDPE12 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
DL=0.1 mg/kg
gen
124 | 149
DL=0.3 mg/kg
CIII
CIT
CI
3 | 0
0 | 0
0 | 0
Exposure (µg· kg^{-1}_{BW}· day^{-1})
126 identified substances
168 unidentified substances

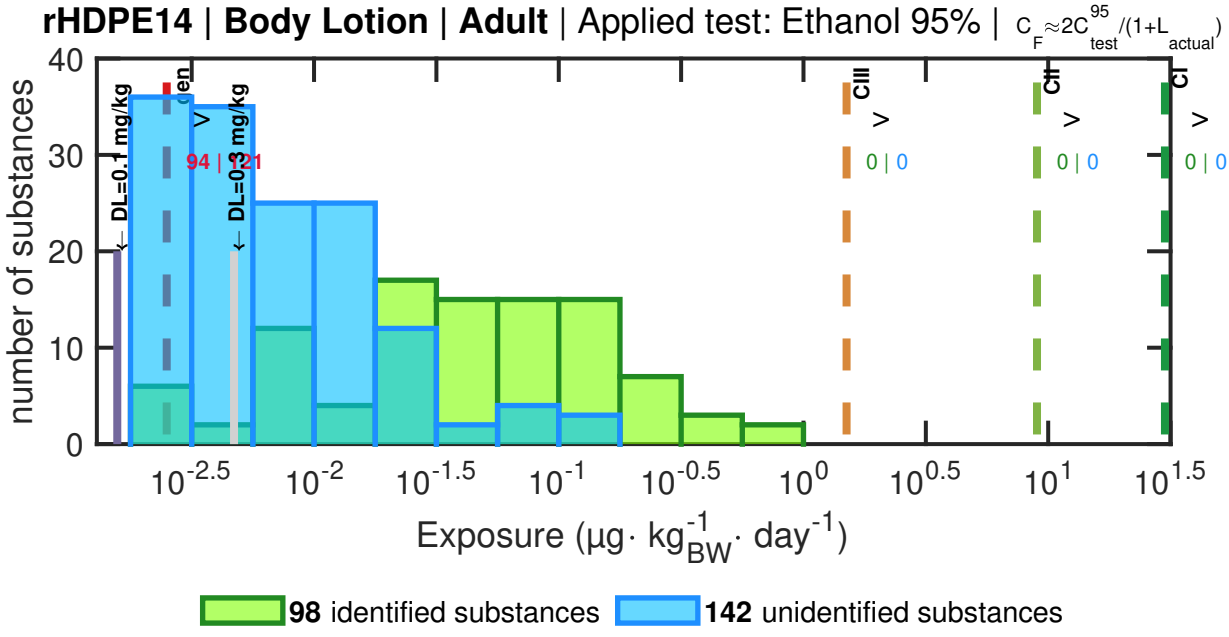

rHDPE13 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
0 | 0
34 identified substances
66 unidentified substances

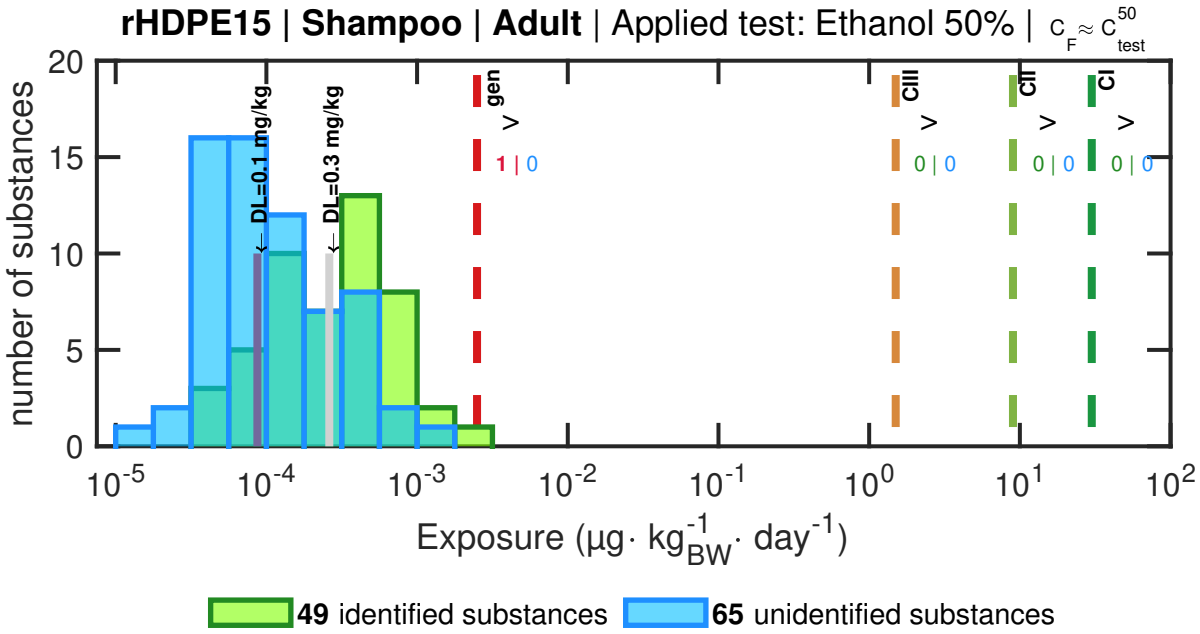

rHDPE13 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
25 | 55
CIII
CII
CI
0 | 0
34 identified substances
66 unidentified substances

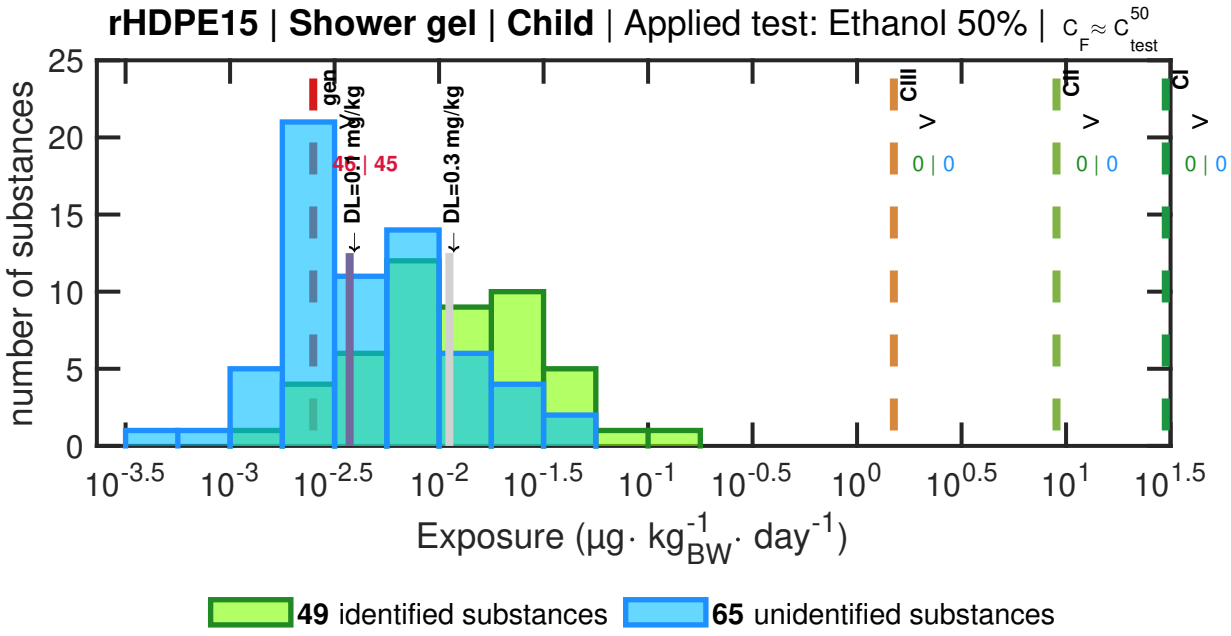

rHDPE13 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
109 | 144
CIII
CII
CI
0 | 0
113 identified substances
161 unidentified substances

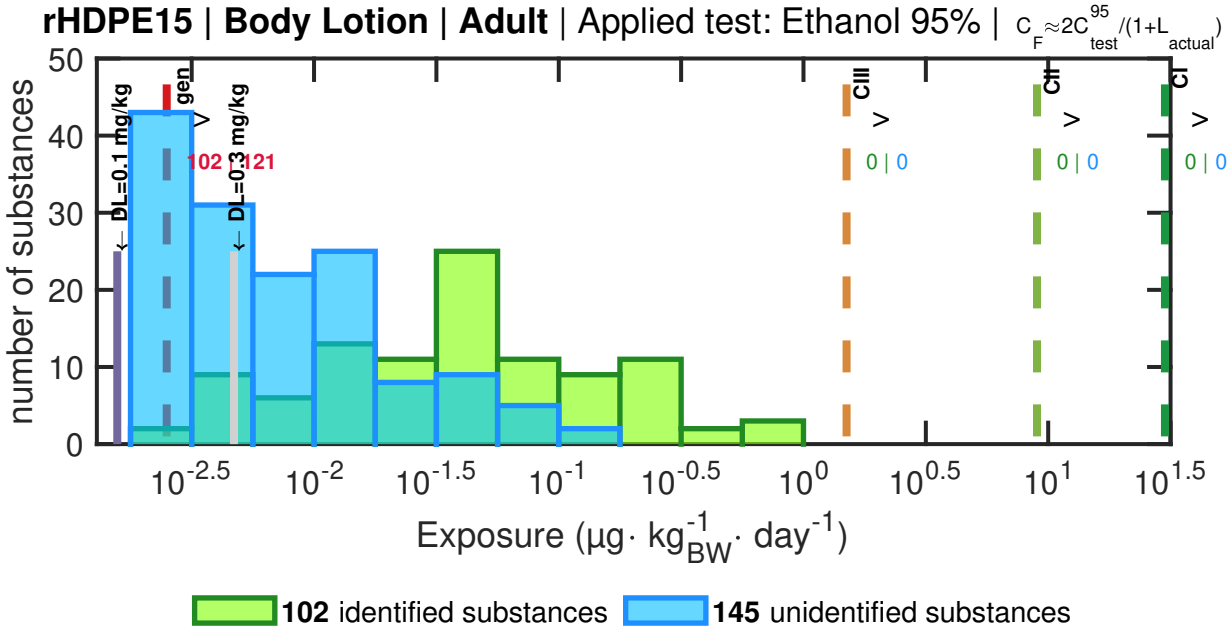

rHDPE14 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
← DL=0.1 mg/kg
← DL=0.3 mg/kg
gen
CIII
CII
CI
0 | 0
37 identified substances
71 unidentified substances

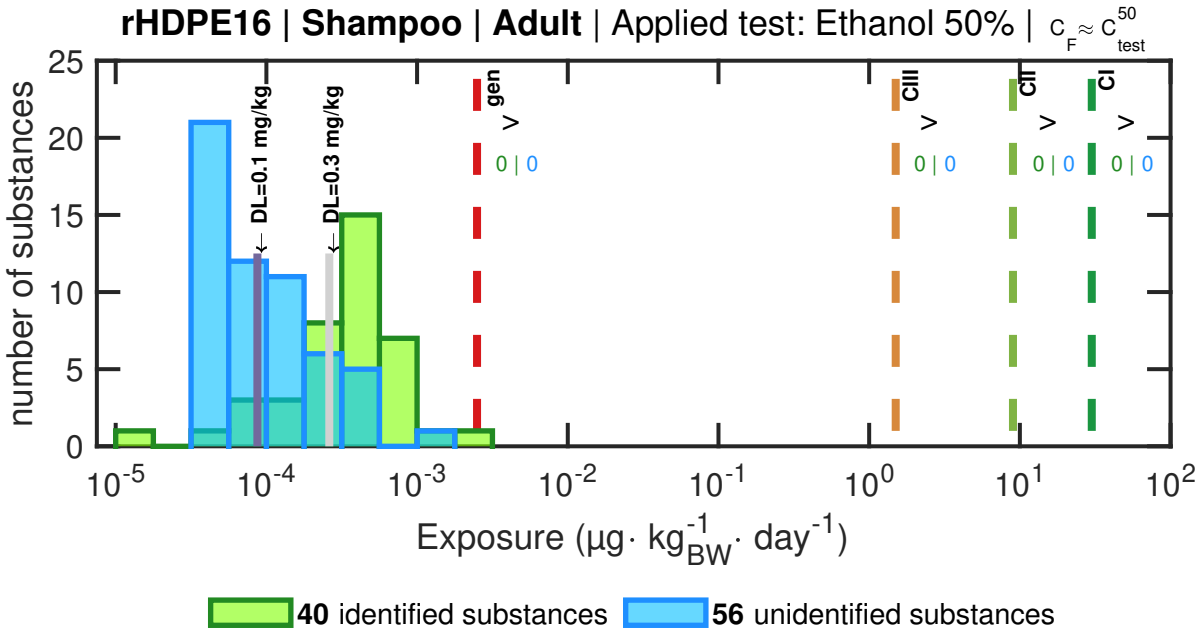

rHDPE14 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
gen
32 | 53
← DL=0.1 mg/kg
← DL=0.3 mg/kg
CIII
CII
CI
0 | 0
37 identified substances
71 unidentified substances

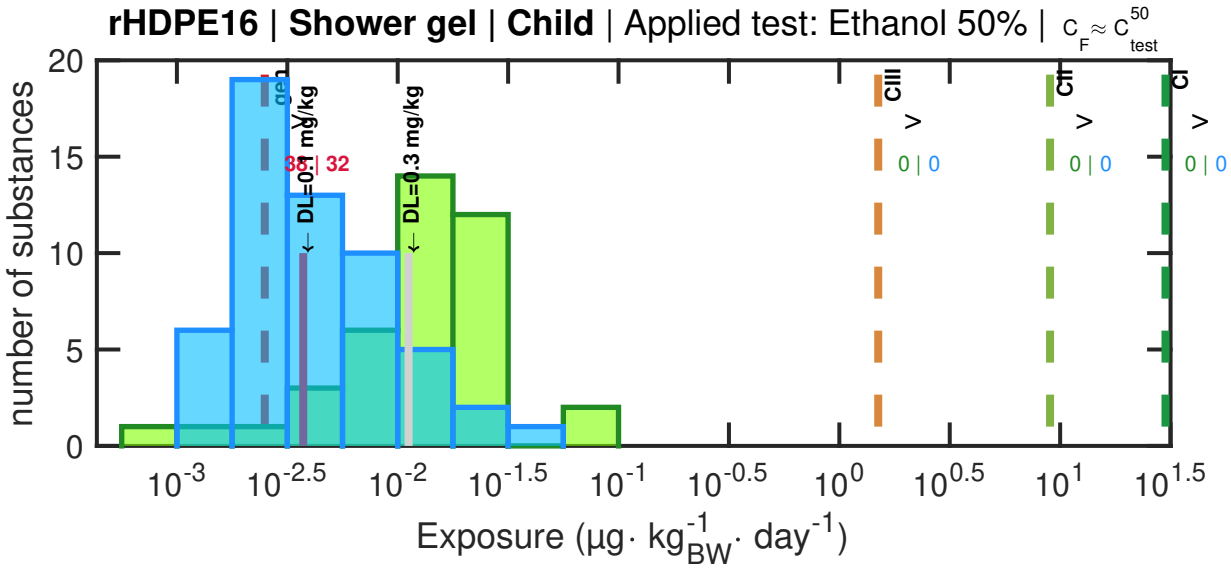

rHDPE14 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
← DL=0.1 mg/kg
gen
94 | 121
← DL=0.3 mg/kg
CIII
CII
CI
0 | 0
98 identified substances
142 unidentified substances

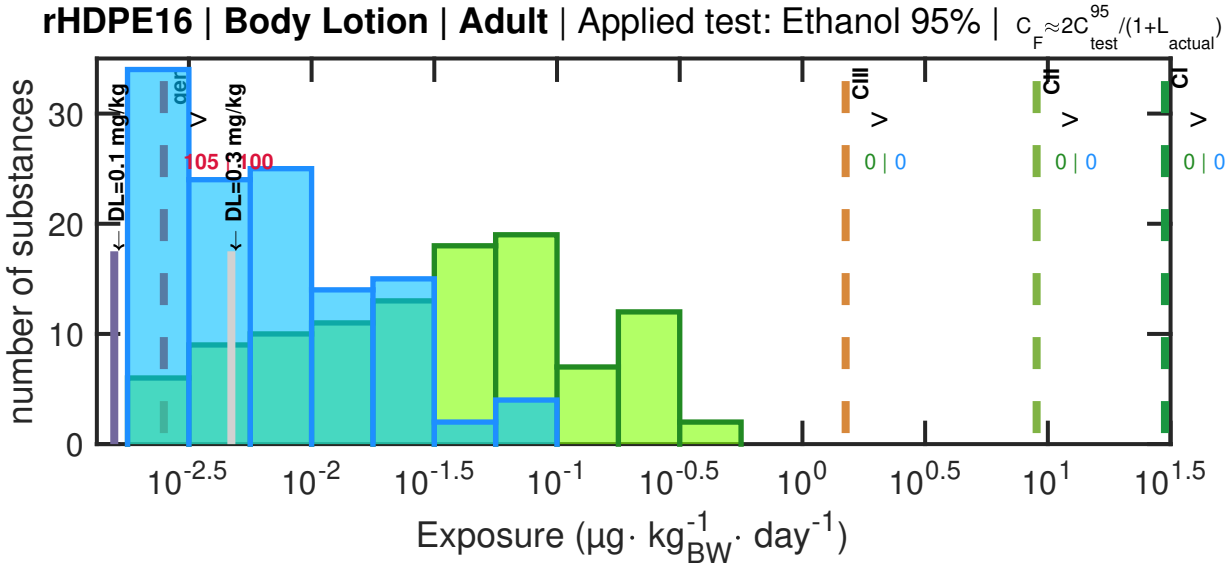

rHDPE15 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
1 | 0
0 | 0
0 | 0
0 | 0
49 identified substances
65 unidentified substances

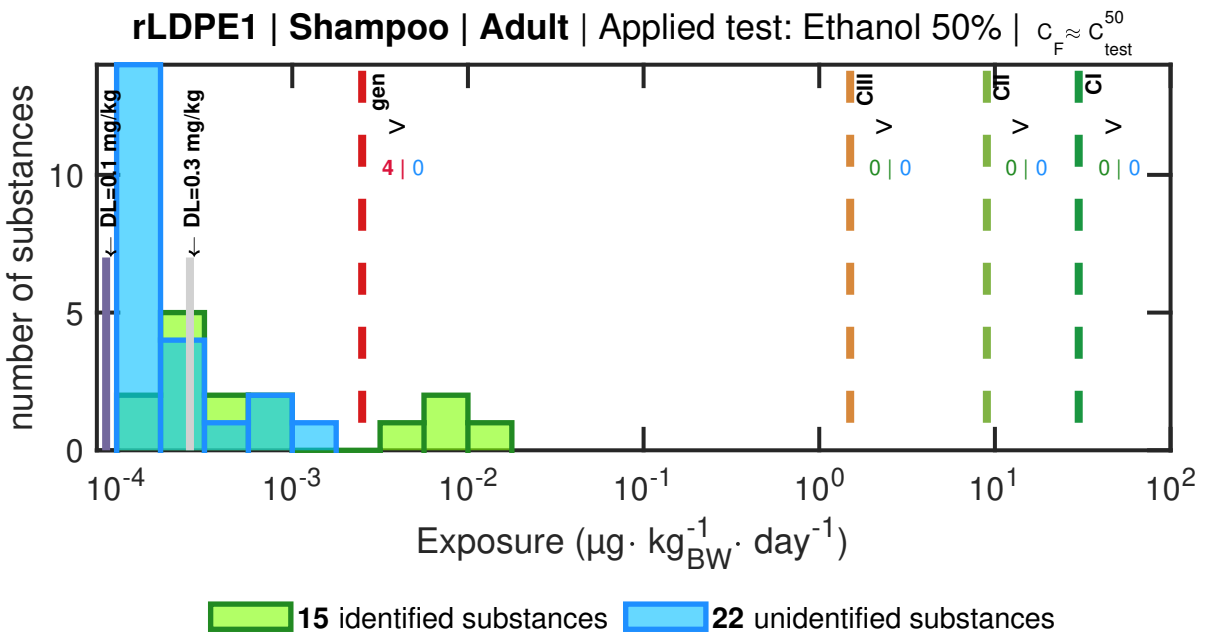

rHDPE15 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
45 | 45
0 | 0
0 | 0
0 | 0
49 identified substances
65 unidentified substances

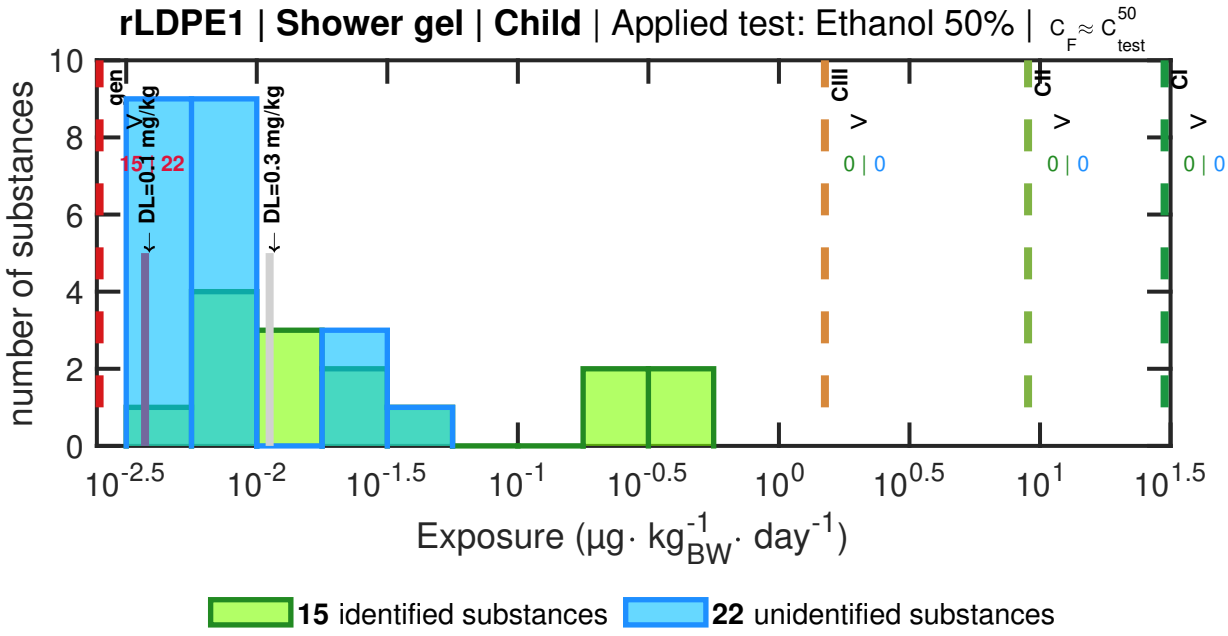

rHDPE15 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
102 | 121
0 | 0
0 | 0
0 | 0
102 identified substances
145 unidentified substances

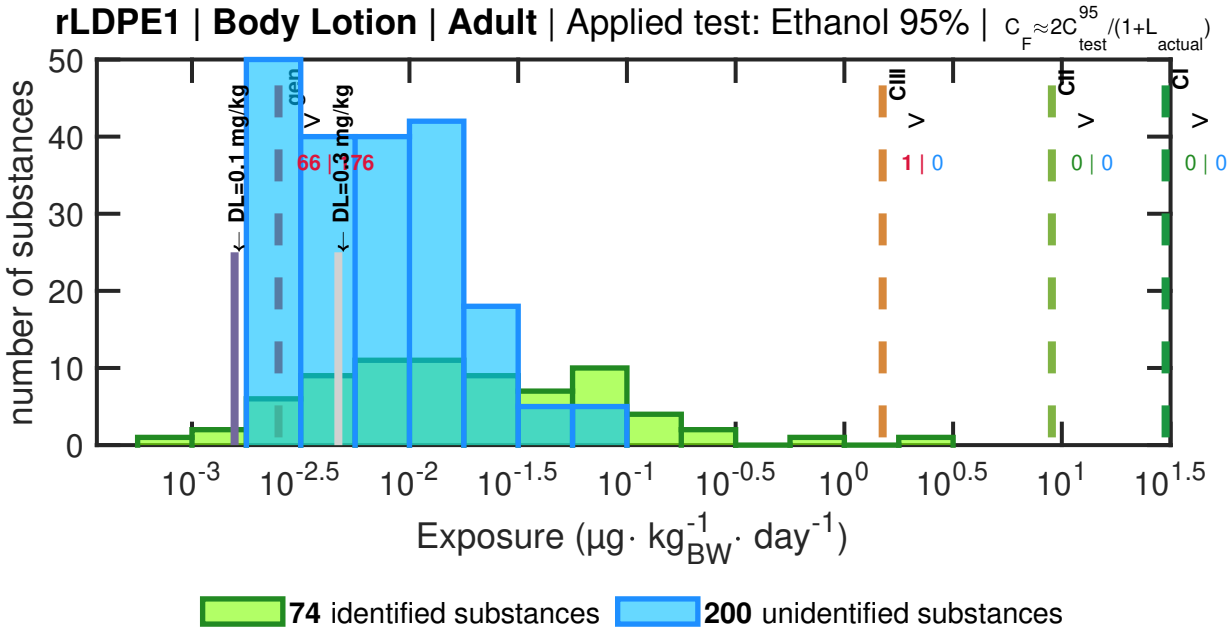

rHDPE16 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
0 | 0
Exposure (µg· kg$^{-1}_{BW}$· day^{-1})
40 identified substances
56 unidentified substances

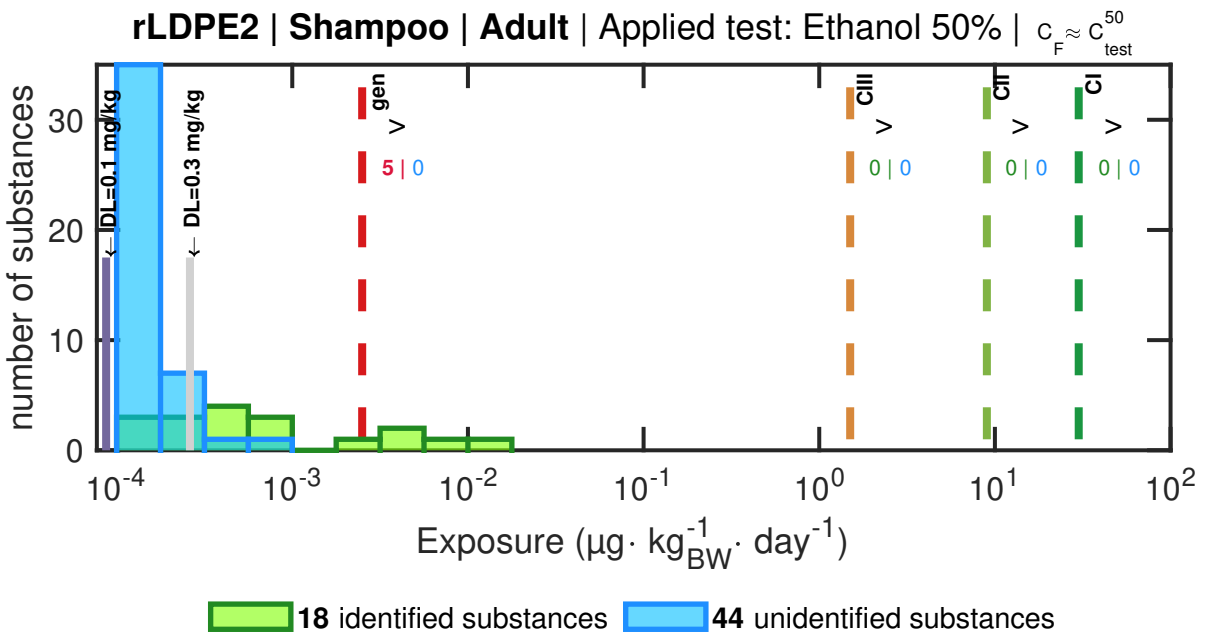

rHDPE16 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
DL=0.1 mg/kg
DL=0.3 mg/kg
38 | 32
CIII
CII
CI
0 | 0
Exposure (µg· kg$^{-1}_{BW}$· day^{-1})
40 identified substances
56 unidentified substances

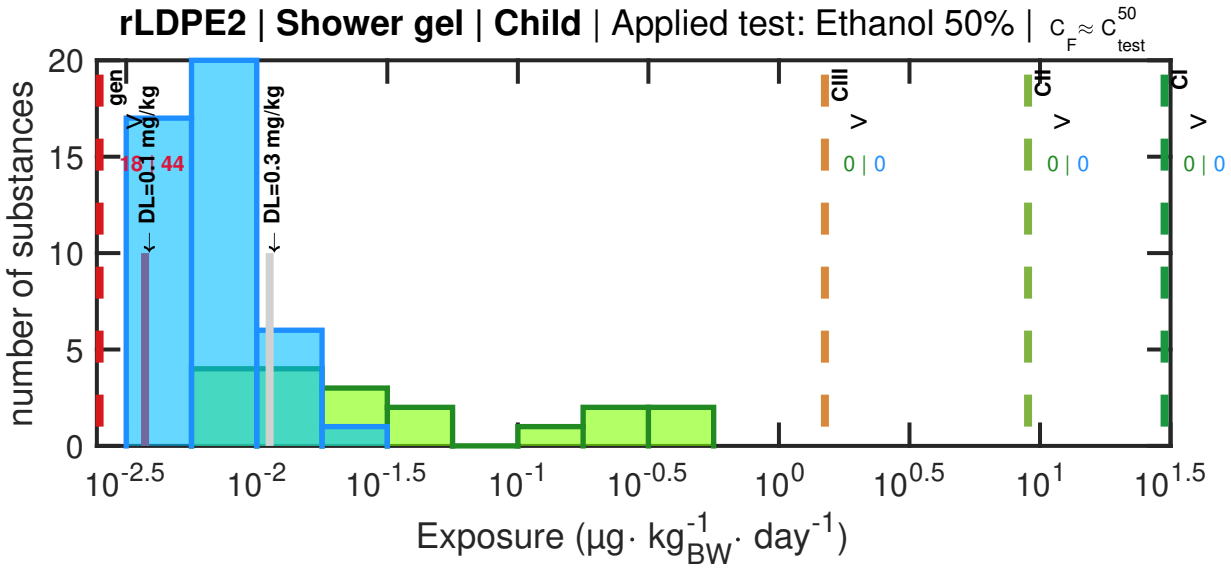

rHDPE16 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
DL=0.1 mg/kg
DL=0.3 mg/kg
105 | 100
CIII
CII
CI
0 | 0
Exposure (µg· kg$^{-1}_{BW}$· day^{-1})
107 identified substances
118 unidentified substances

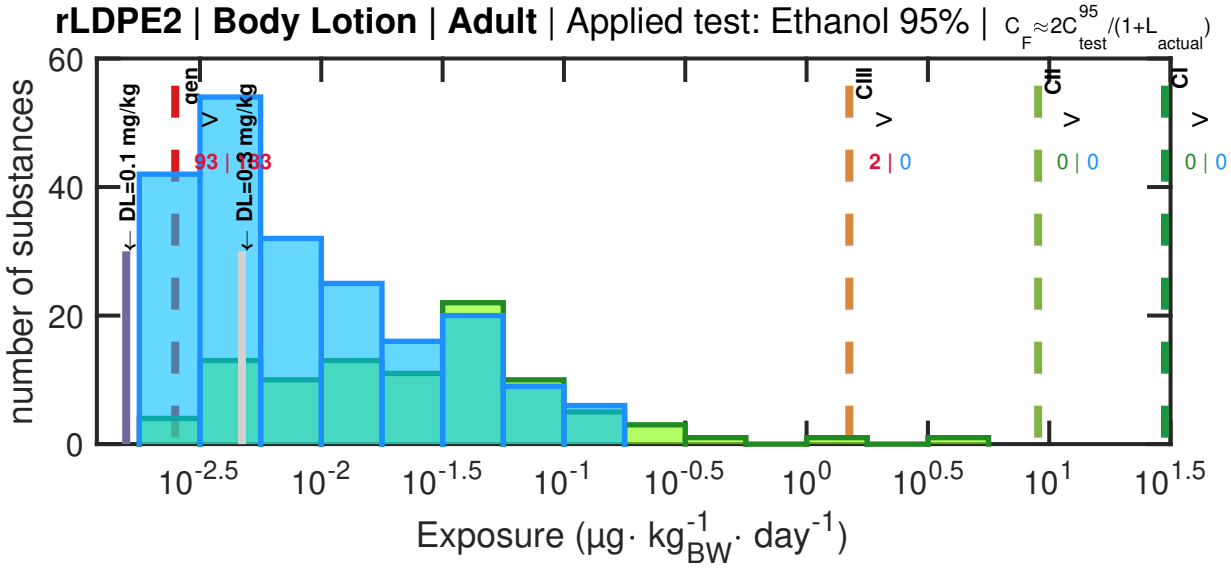

rLDPE1 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
4 | 0
CIII
0 | 0
CII
0 | 0
CI
0 | 0
Exposure (µg· kg$^{-1}_{BW}$· day^{-1})
15 identified substances
22 unidentified substances

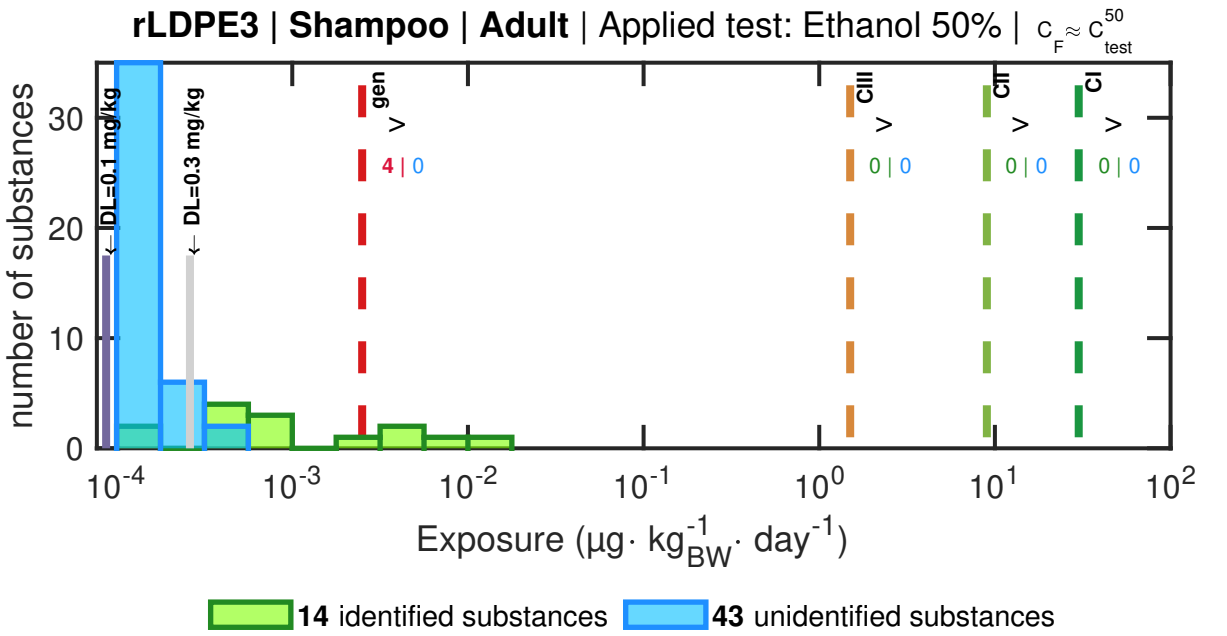

rLDPE1 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
gen
15 | 22
DL=0.1 mg/kg
DL=0.3 mg/kg
CIII
0 | 0
CII
0 | 0
CI
0 | 0
Exposure (µg· kg$^{-1}_{BW}$· day^{-1})
15 identified substances
22 unidentified substances

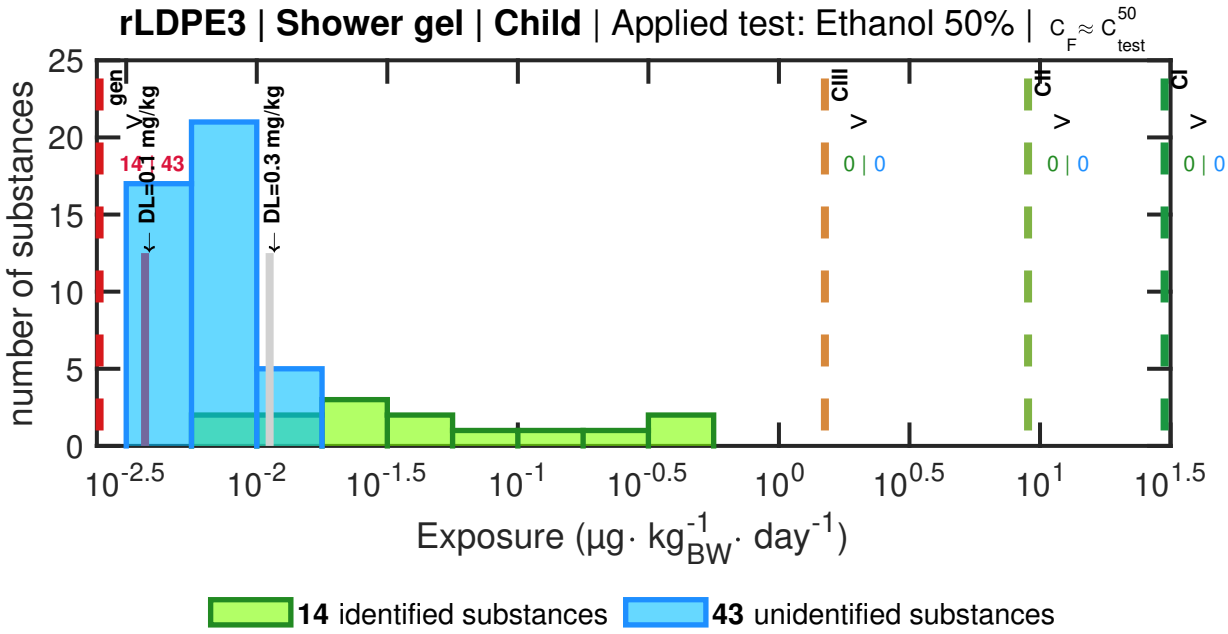

rLDPE1 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
DL=0.1 mg/kg
gen
66 | 176
DL=0.3 mg/kg
CIII
1 | 0
CII
0 | 0
CI
0 | 0
Exposure (µg· kg$^{-1}_{BW}$· day^{-1})
74 identified substances
200 unidentified substances

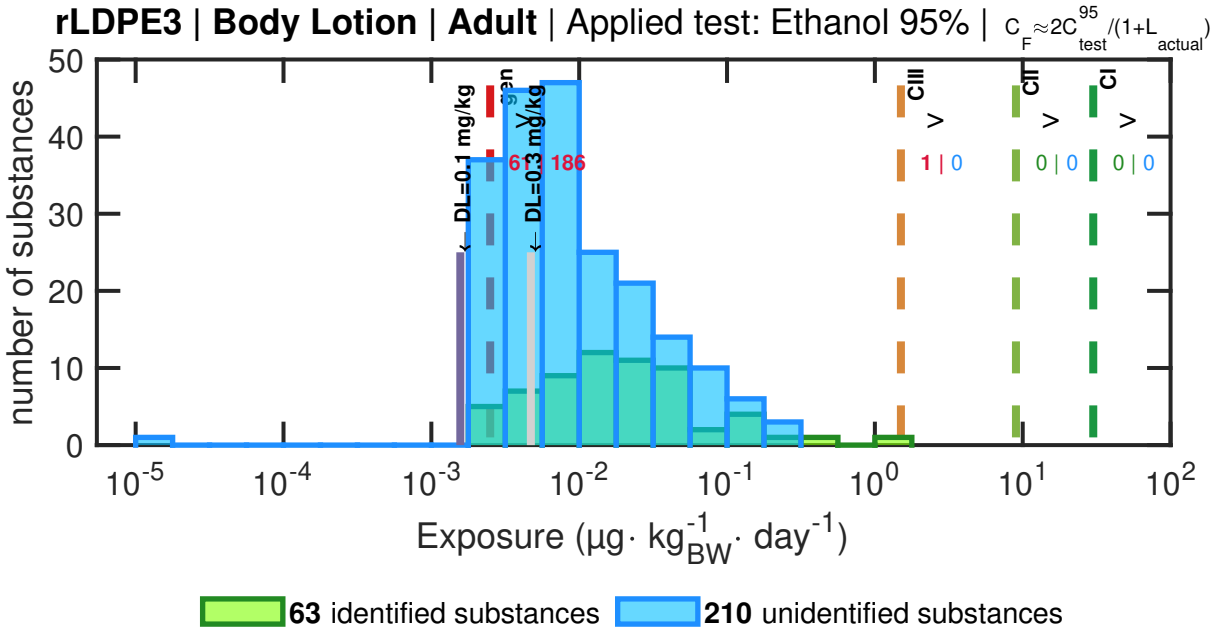

rLDPE2 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
5 | 0
CIII
0 | 0
CII
0 | 0
CI
0 | 0
Exposure (µg· kg^{-1}_{BW}· day^{-1})
18 identified substances
44 unidentified substances

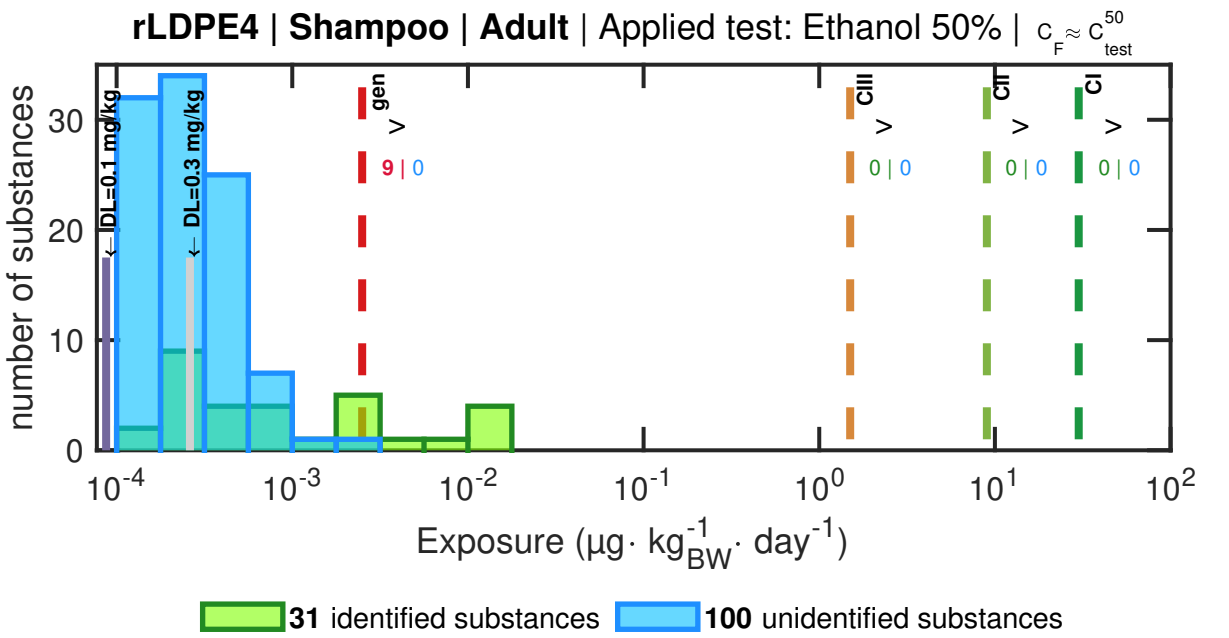

rLDPE2 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
gen
18 | 44
DL=0.1 mg/kg
DL=0.3 mg/kg
CIII
0 | 0
CII
0 | 0
CI
0 | 0
Exposure (µg· kg^{-1}_{BW}· day^{-1})
18 identified substances
44 unidentified substances

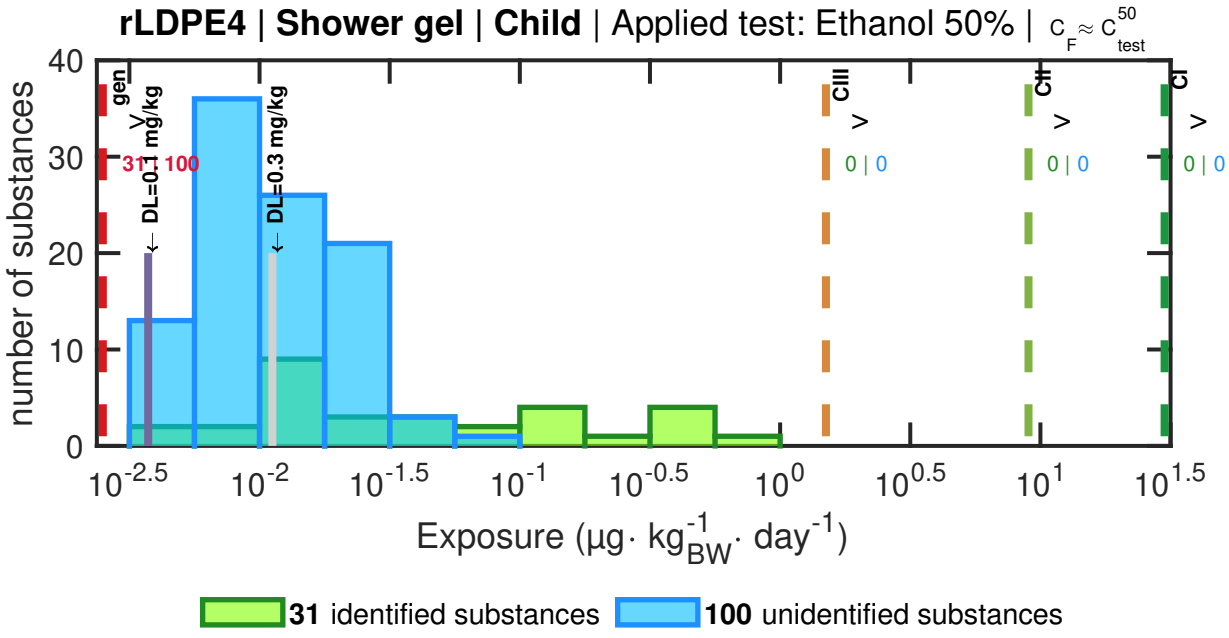

rLDPE2 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
DL=0.1 mg/kg
gen
93 | 133
DL=0.3 mg/kg
CIII
2 | 0
CII
0 | 0
CI
0 | 0
Exposure (µg· kg^{-1}_{BW}· day^{-1})
94 identified substances
204 unidentified substances

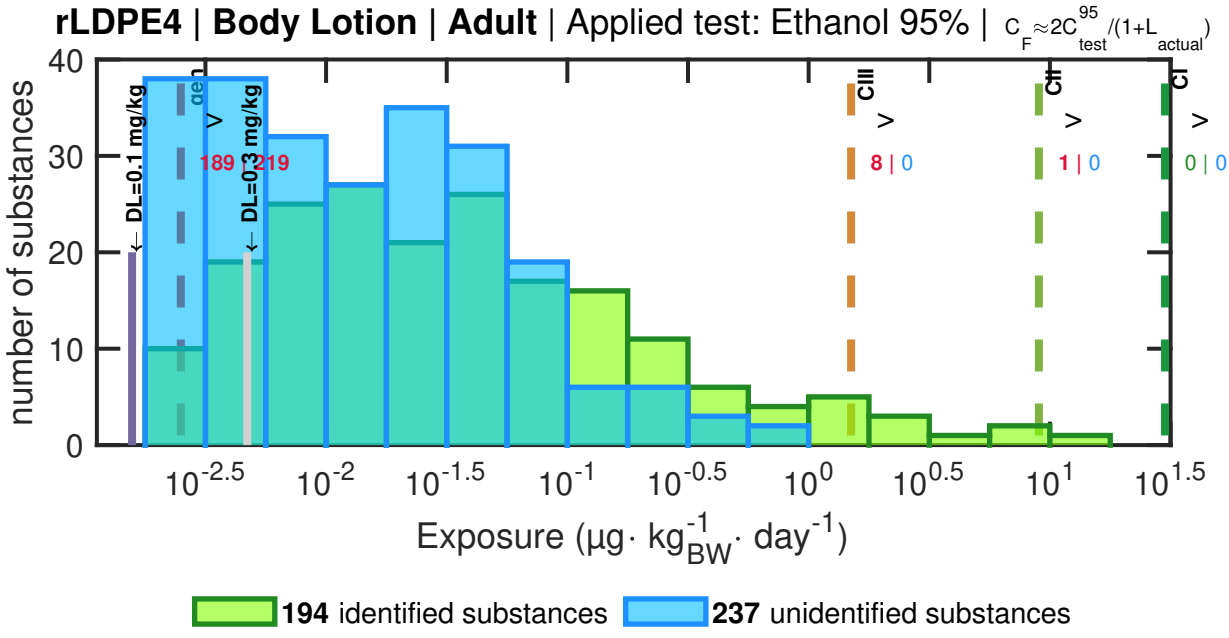

rLDPE3 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
4 | 0
0 | 0
0 | 0
0 | 0
14 identified substances
43 unidentified substances

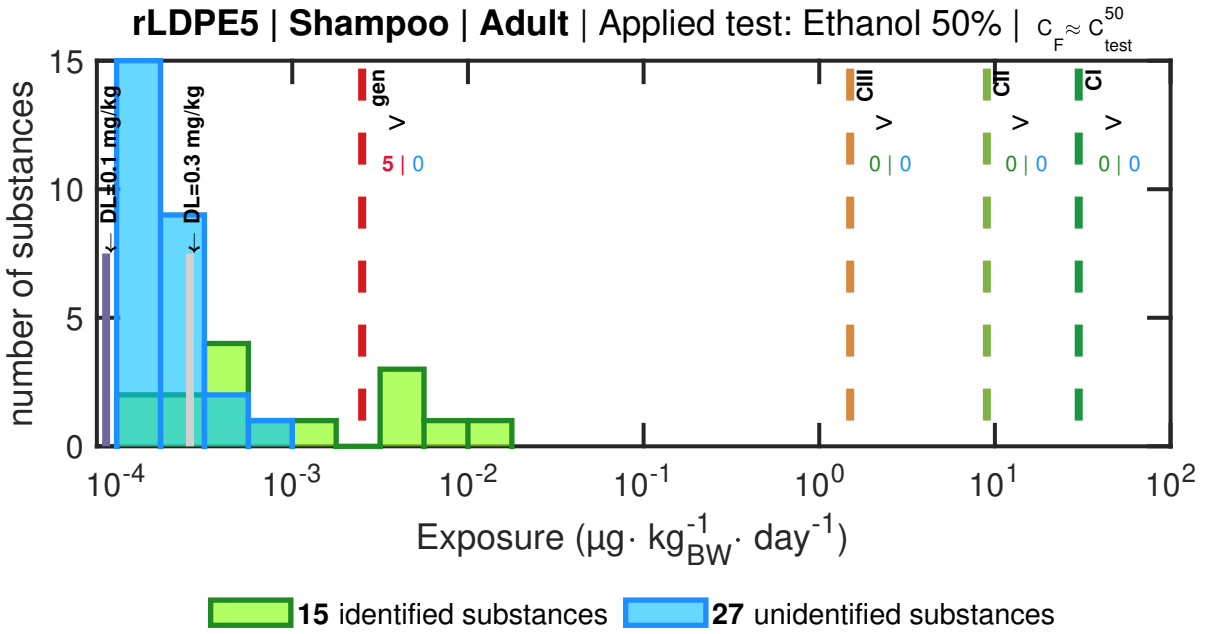

rLDPE3 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
gen
DL=0.1 mg/kg
DL=0.3 mg/kg
CIII
CII
CI
14 43
0 | 0
0 | 0
0 | 0
14 identified substances
43 unidentified substances

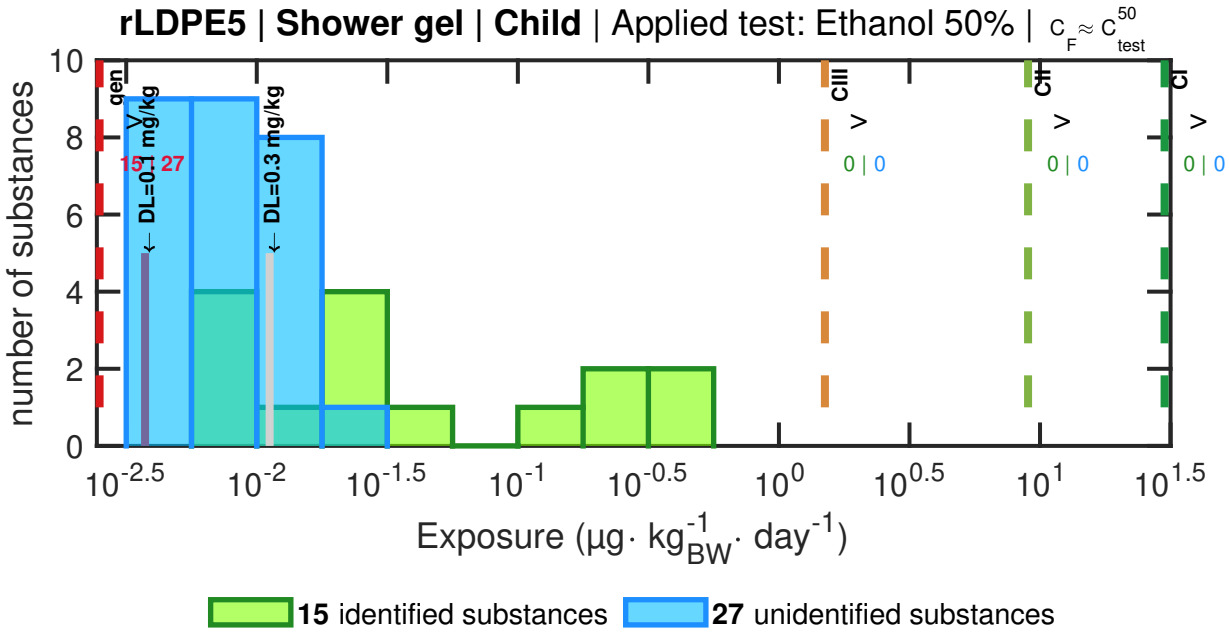

rLDPE3 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
gen
DL=0.3 mg/kg
CIII
CII
CI
61 186
1 | 0
0 | 0
0 | 0
63 identified substances
210 unidentified substances

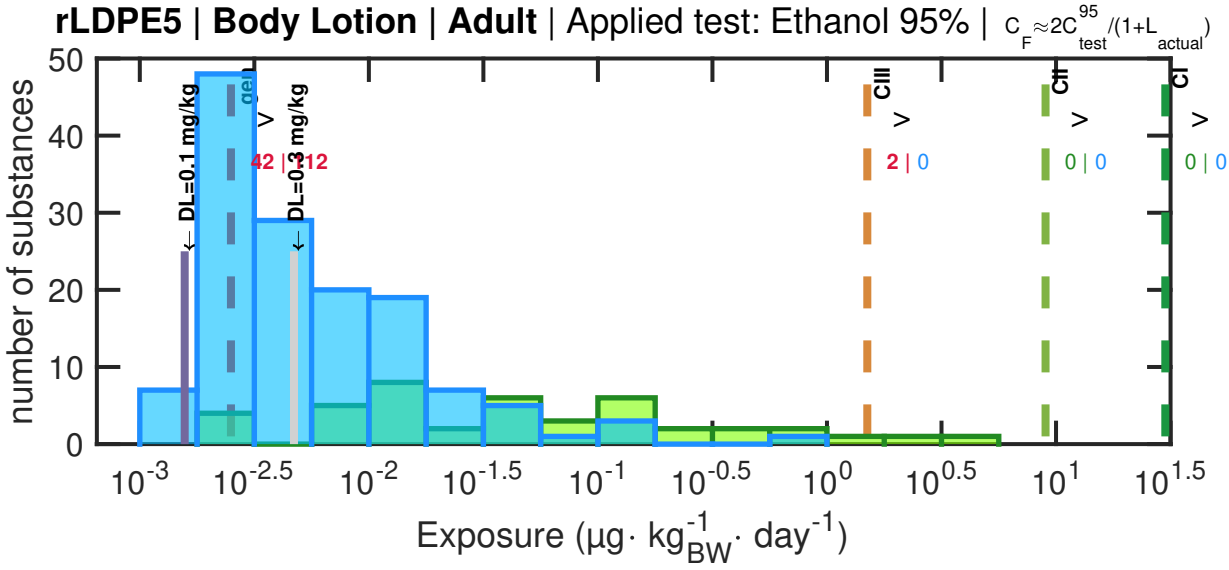

rLDPE4 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
gen
CIII
CII
CI
DL=0.1 mg/kg
DL=0.3 mg/kg
9 | 0
0 | 0
0 | 0
0 | 0
Exposure (µg· kg^{-1}_{BW}· day^{-1})
31 identified substances
100 unidentified substances

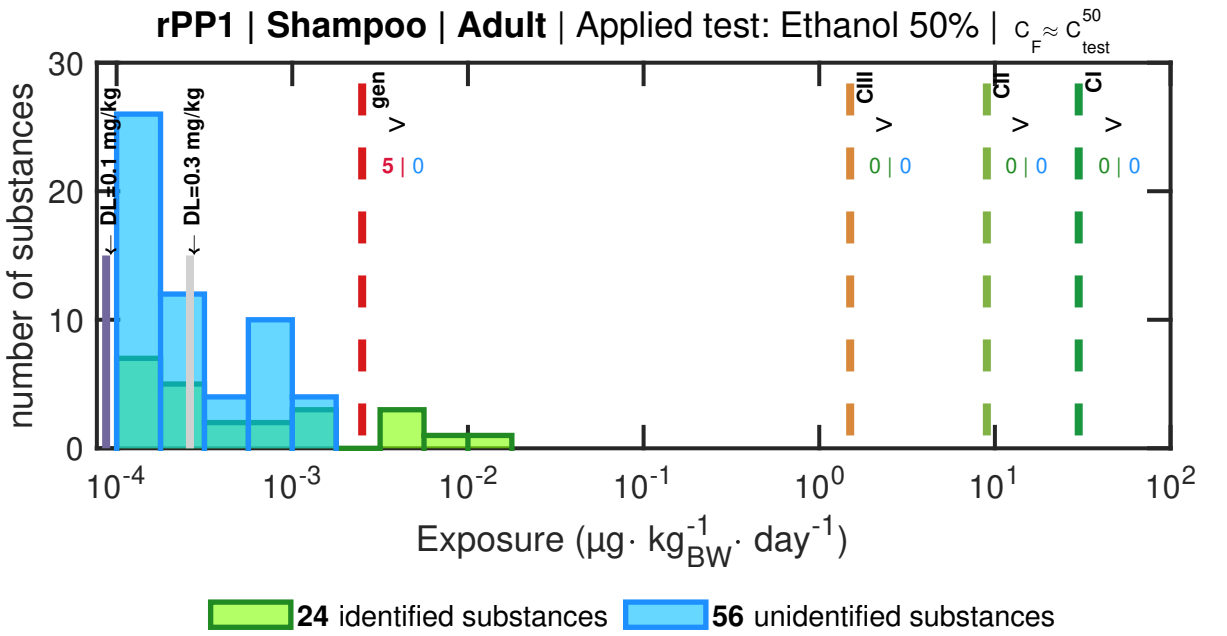

rLDPE4 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
gen
CIII
CII
CI
DL=0.1 mg/kg
DL=0.3 mg/kg
31 | 100
0 | 0
0 | 0
0 | 0
Exposure (µg· kg^{-1}_{BW}· day^{-1})
31 identified substances
100 unidentified substances

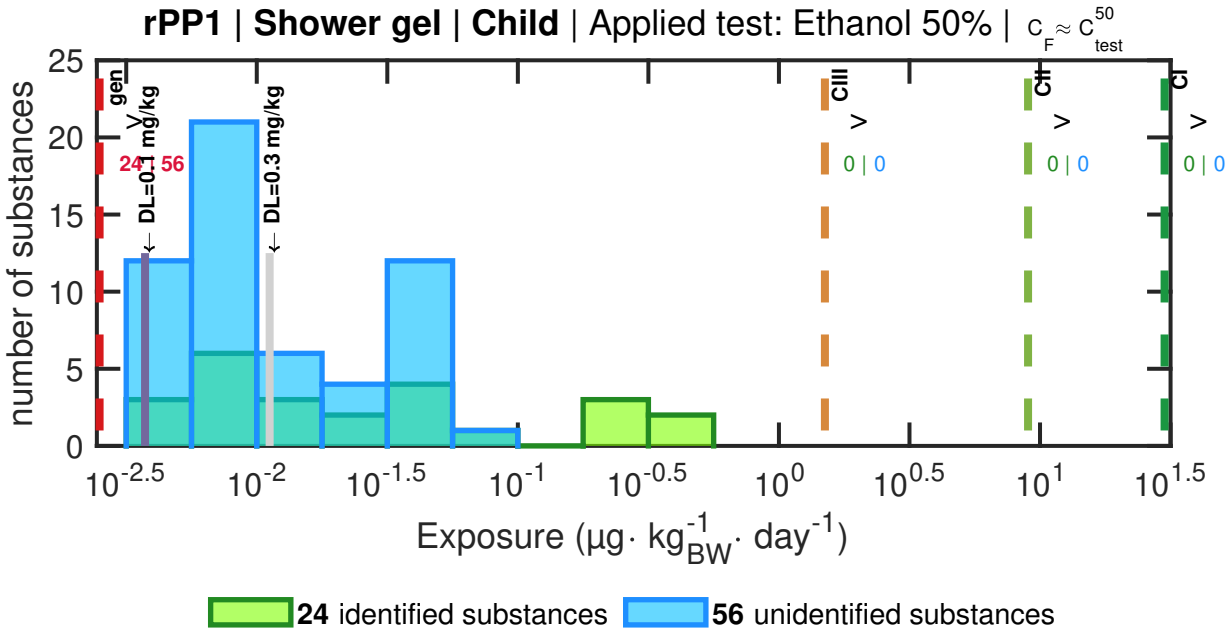

rLDPE4 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
gen
CIII
CII
CI
DL=0.1 mg/kg
DL=0.3 mg/kg
189 | 219
8 | 0
1 | 0
0 | 0
Exposure (µg· kg^{-1}_{BW}· day^{-1})
194 identified substances
237 unidentified substances

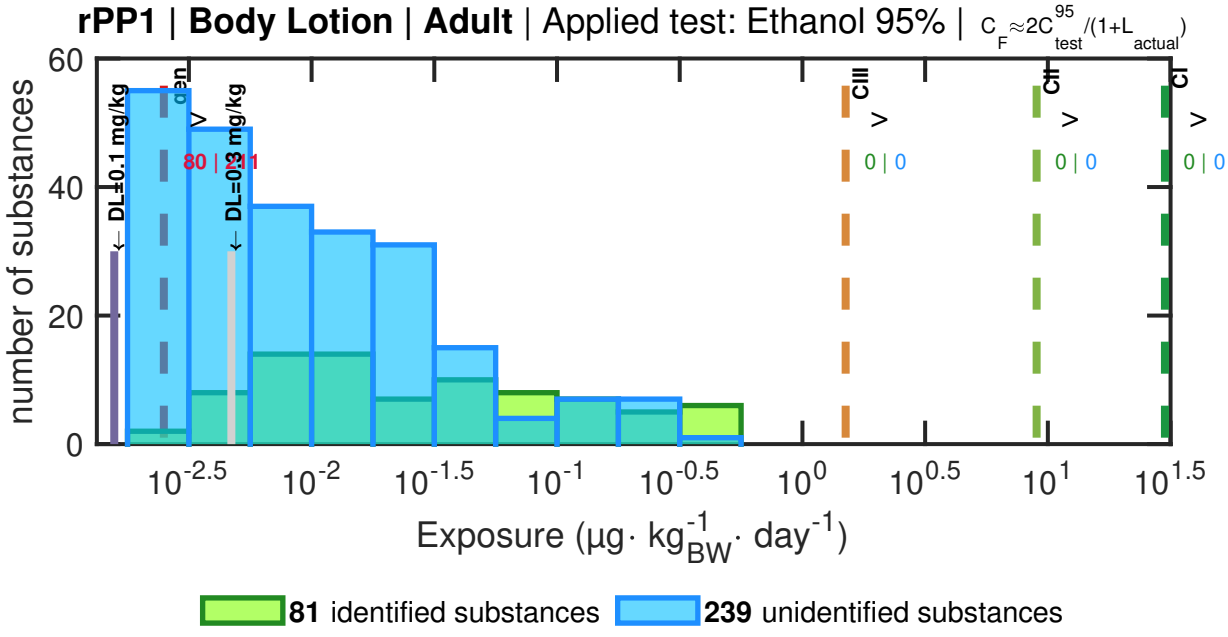

rLDPE5 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg$^{-1}_{BW}$· day^{-1})
← DL=0.1 mg/kg
← DL=0.3 mg/kg
gen
5 | 0
CIII
0 | 0
CII
0 | 0
CI
0 | 0
15 identified substances
27 unidentified substances

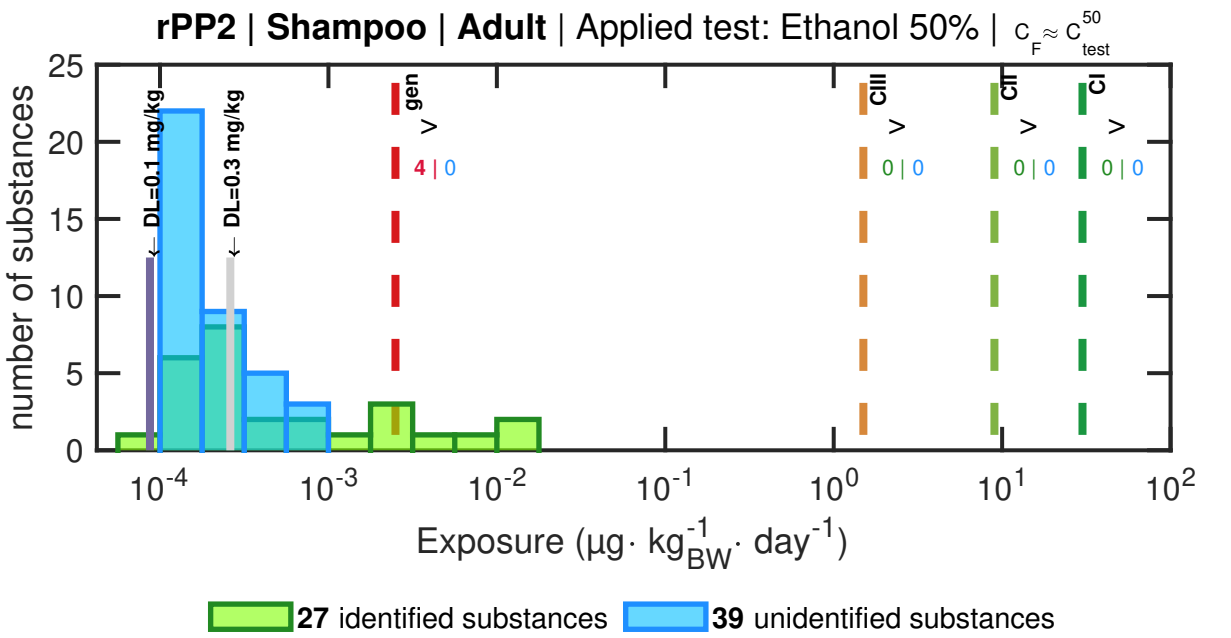

rLDPE5 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg$^{-1}_{BW}$· day^{-1})
gen
15 | 27
← DL=0.1 mg/kg
← DL=0.3 mg/kg
CIII
0 | 0
CII
0 | 0
CI
0 | 0
15 identified substances
27 unidentified substances

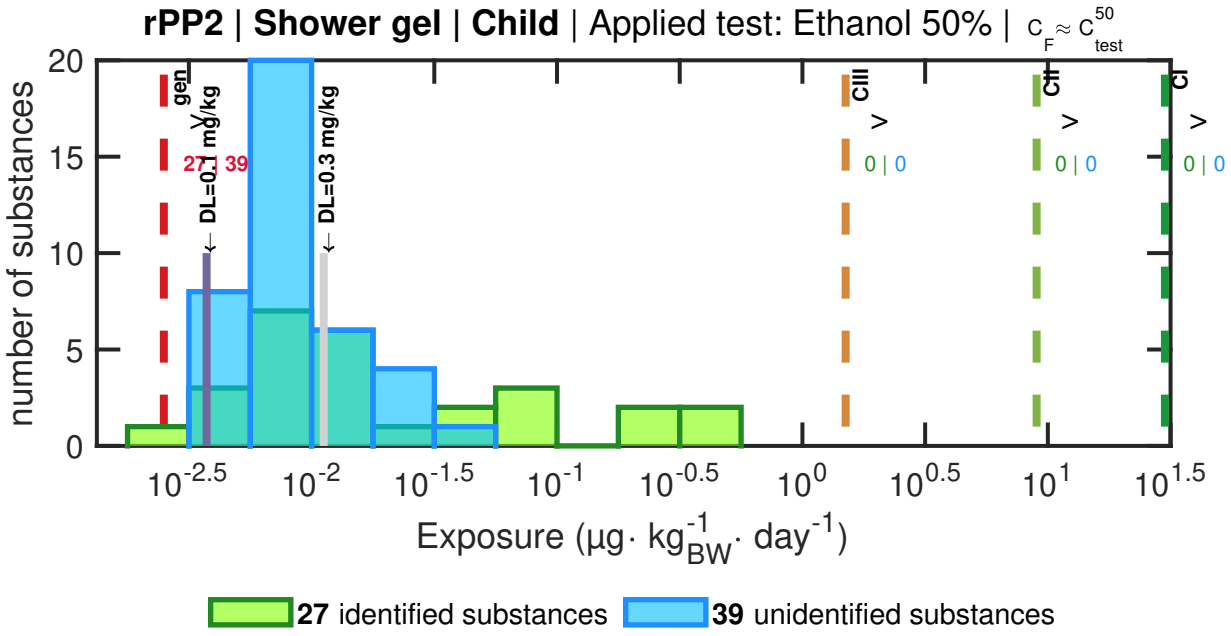

rLDPE5 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
Exposure (µg· kg$^{-1}_{BW}$· day^{-1})
← DL=0.1 mg/kg
← DL=0.3 mg/kg
gen
42 | 212
CIII
2 | 0
CII
0 | 0
CI
0 | 0
43 identified substances
140 unidentified substances

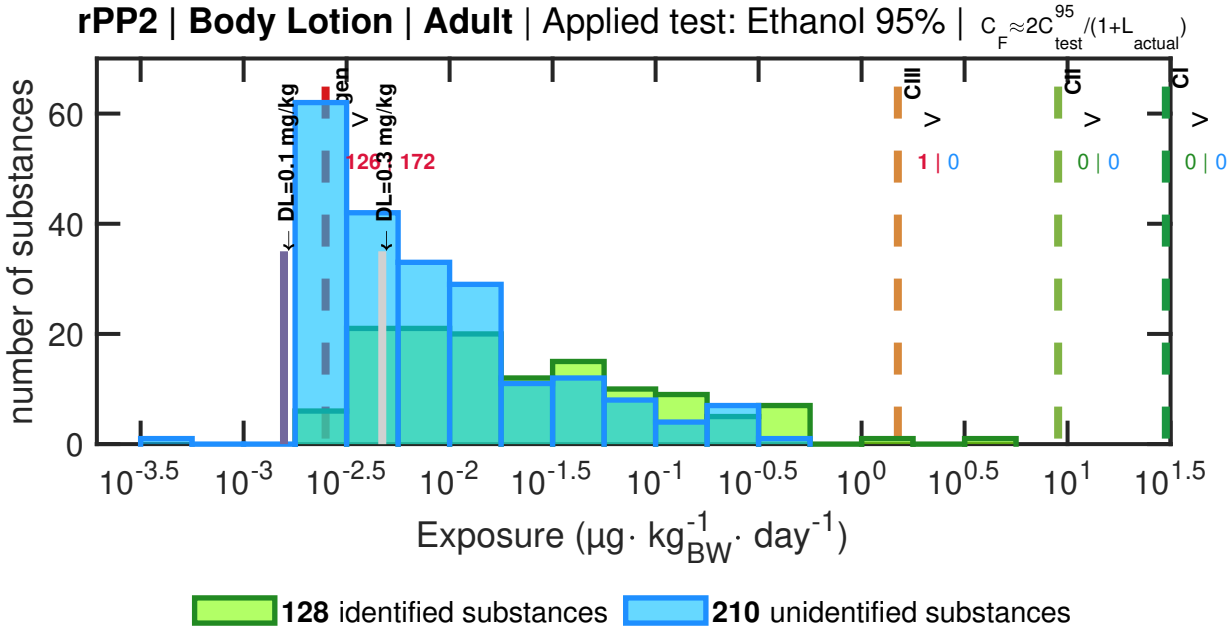

rPP1 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
5 | 0
0 | 0
0 | 0
0 | 0
24 identified substances
56 unidentified substances

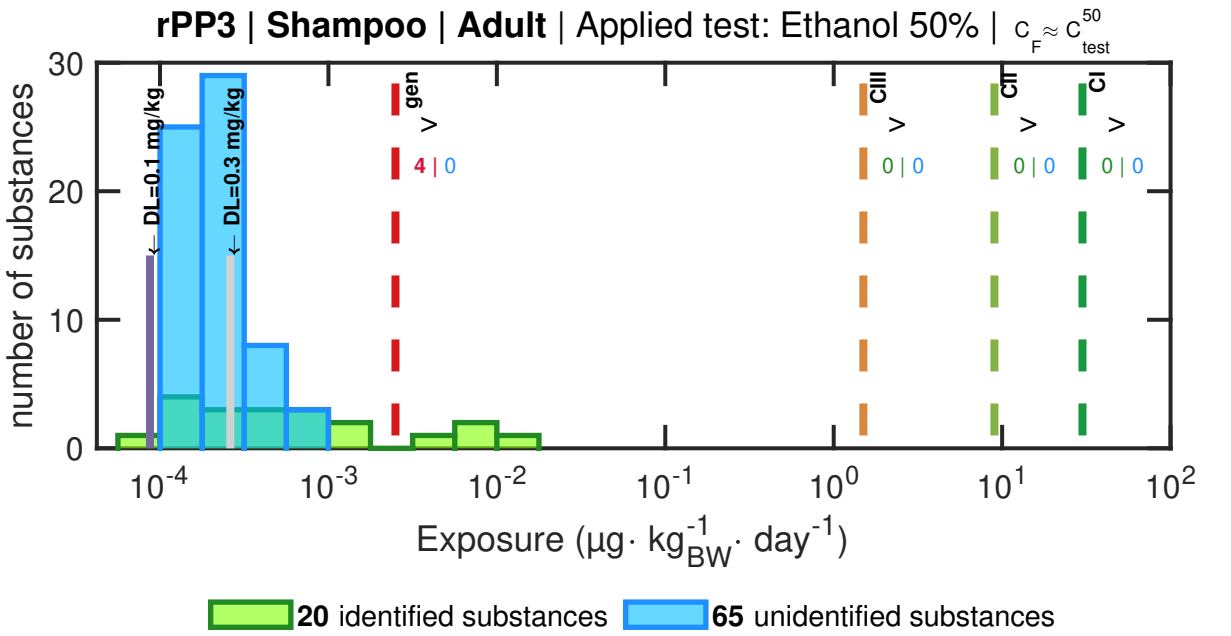

rPP1 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
gen
DL=0.1 mg/kg
DL=0.3 mg/kg
CIII
CII
CI
24 | 56
0 | 0
0 | 0
0 | 0
24 identified substances
56 unidentified substances

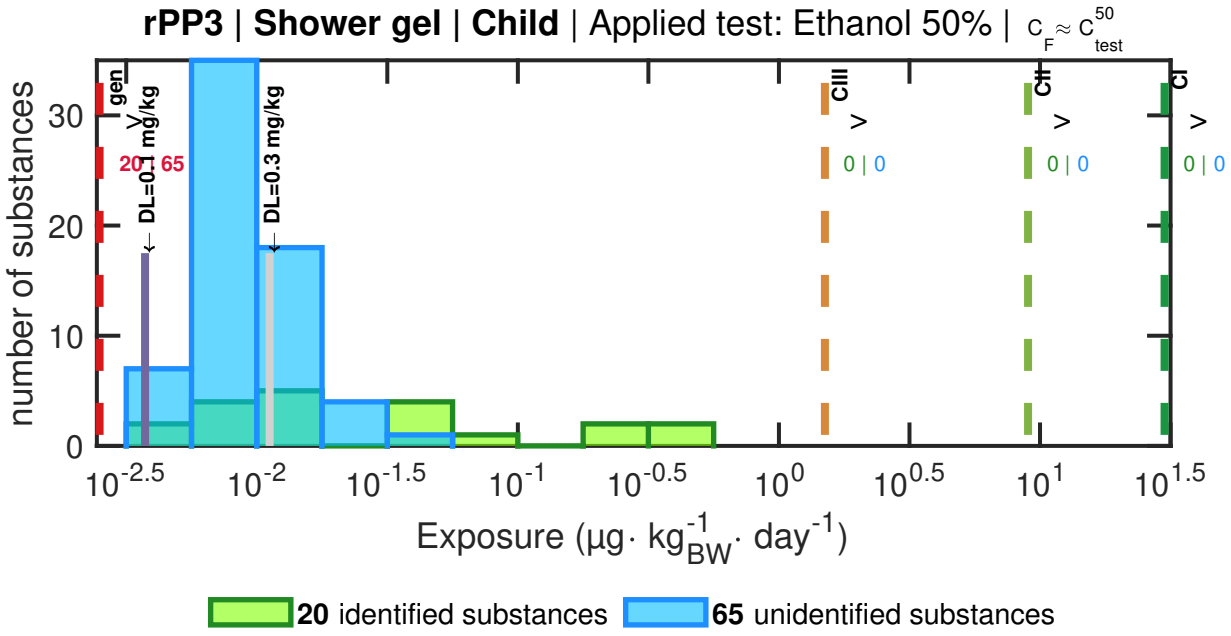

rPP1 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
gen
DL=0.3 mg/kg
CIII
CII
CI
80 | 81
0 | 0
0 | 0
0 | 0
81 identified substances
239 unidentified substances

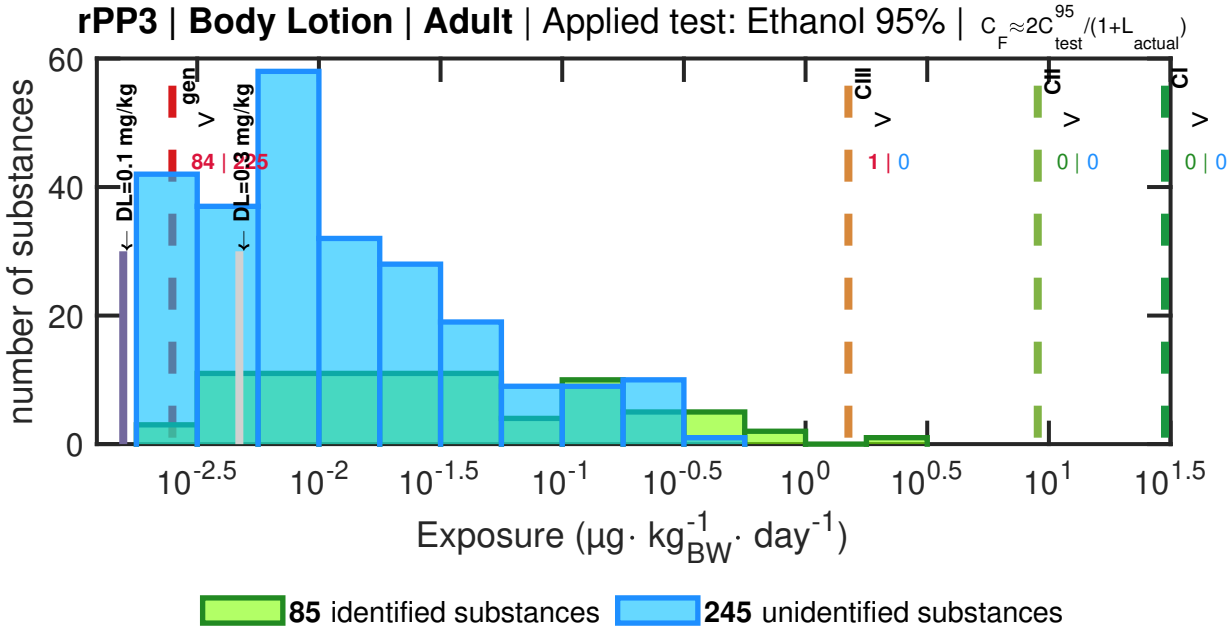

rPP2 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
4 | 0
CIII
0 | 0
CII
0 | 0
CI
0 | 0
27 identified substances
39 unidentified substances

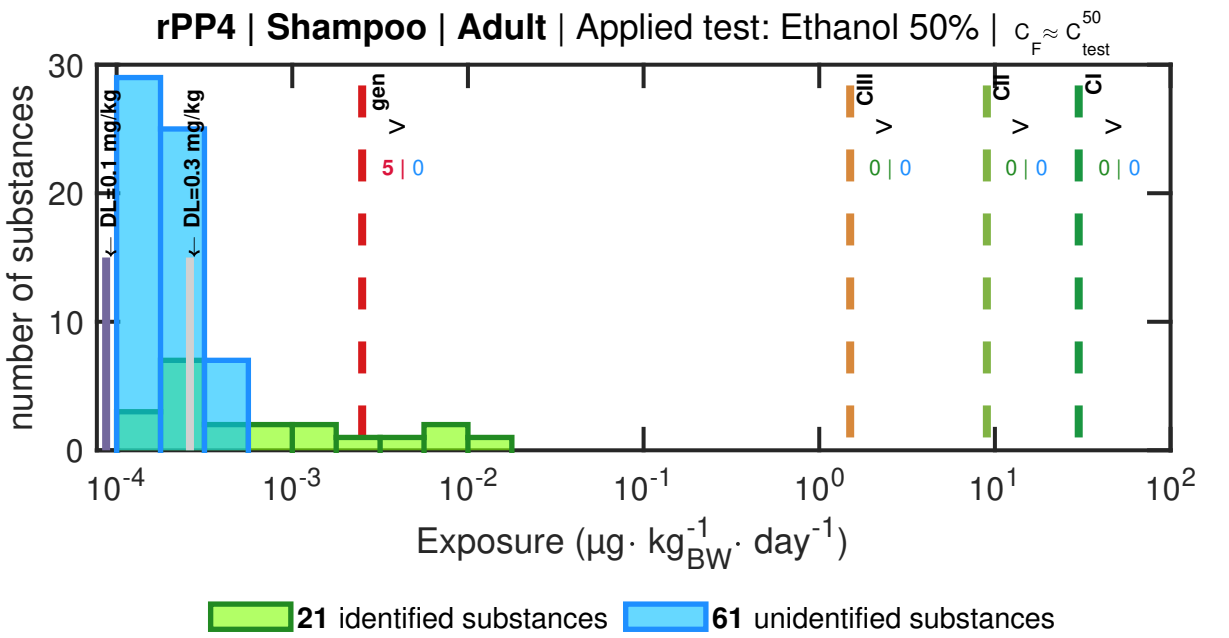

rPP2 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
gen
27 | 39
DL=0.1 mg/kg
DL=0.3 mg/kg
CIII
0 | 0
CII
0 | 0
CI
0 | 0
27 identified substances
39 unidentified substances

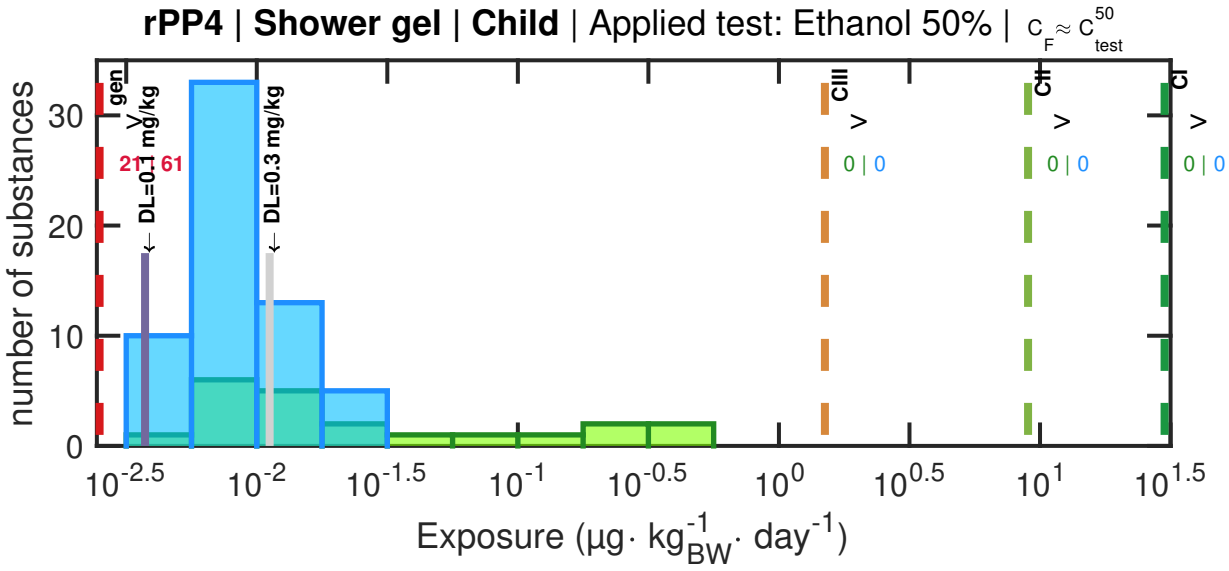

rPP2 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
gen
126 | 172
DL=0.3 mg/kg
CIII
1 | 0
CII
0 | 0
CI
0 | 0
128 identified substances
210 unidentified substances

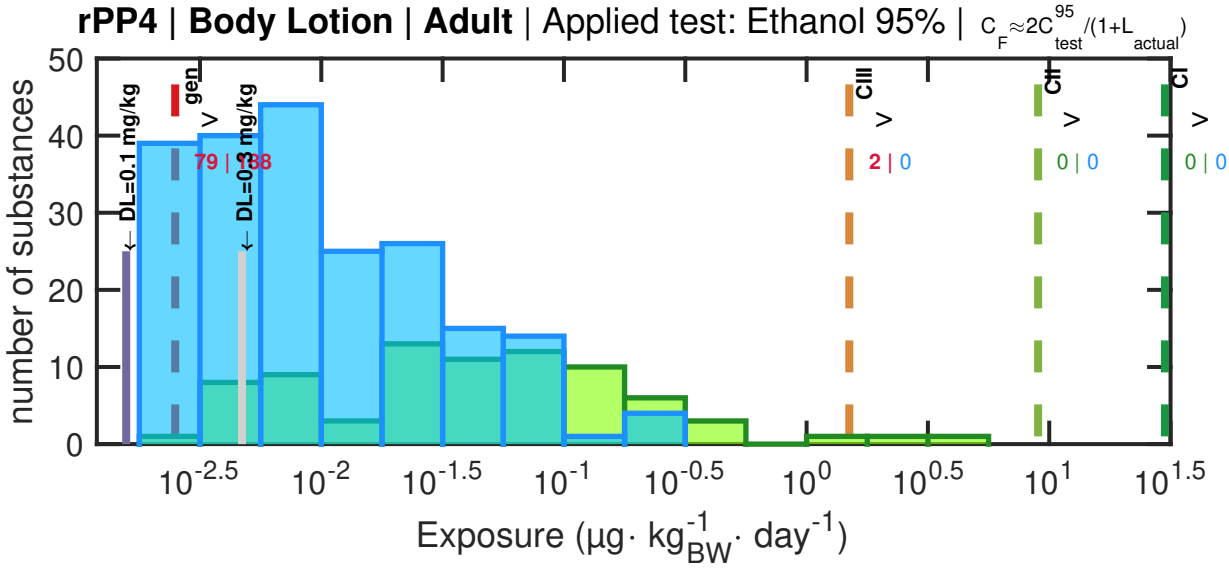

rPP3 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
4 | 0
0 | 0
0 | 0
0 | 0
20 identified substances
65 unidentified substances

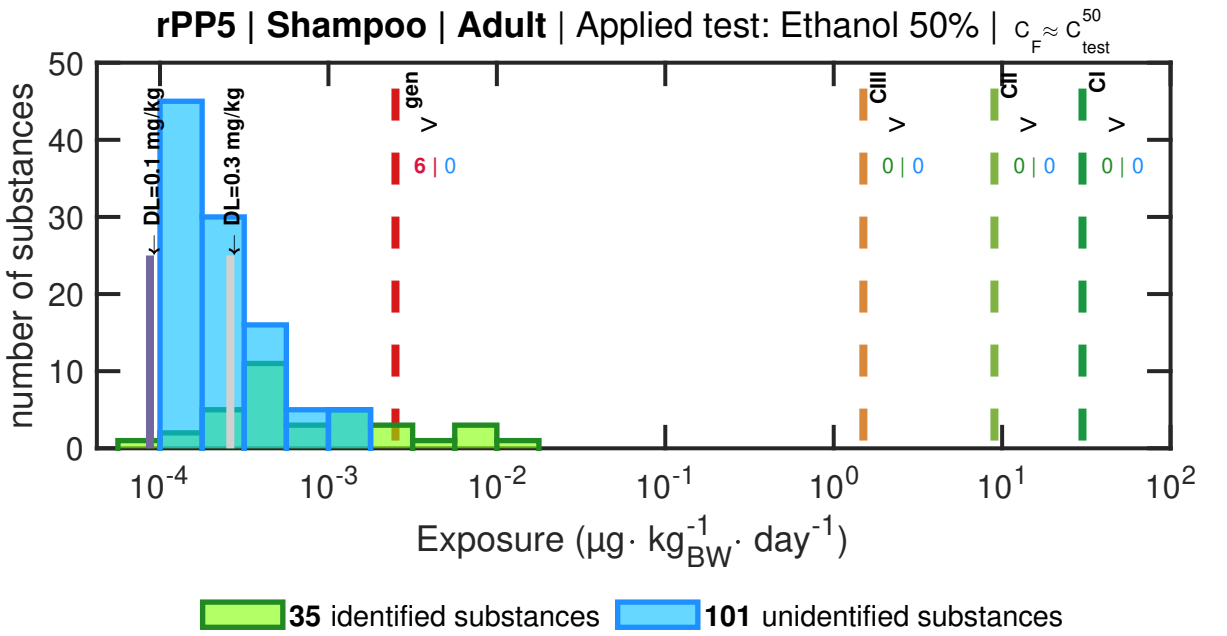

rPP3 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
gen
DL=0.1 mg/kg
DL=0.3 mg/kg
CIII
CII
CI
20 | 65
0 | 0
0 | 0
0 | 0
20 identified substances
65 unidentified substances

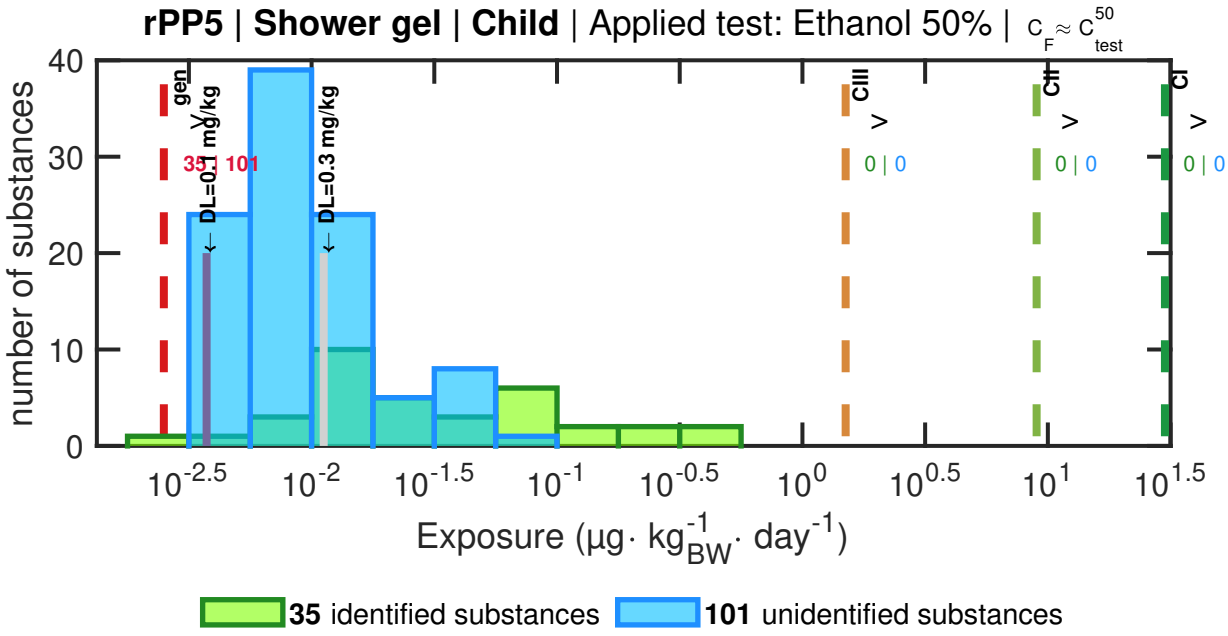

rPP3 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
gen
DL=0.3 mg/kg
CIII
CII
CI
84 | 25
1 | 0
0 | 0
0 | 0
85 identified substances
245 unidentified substances

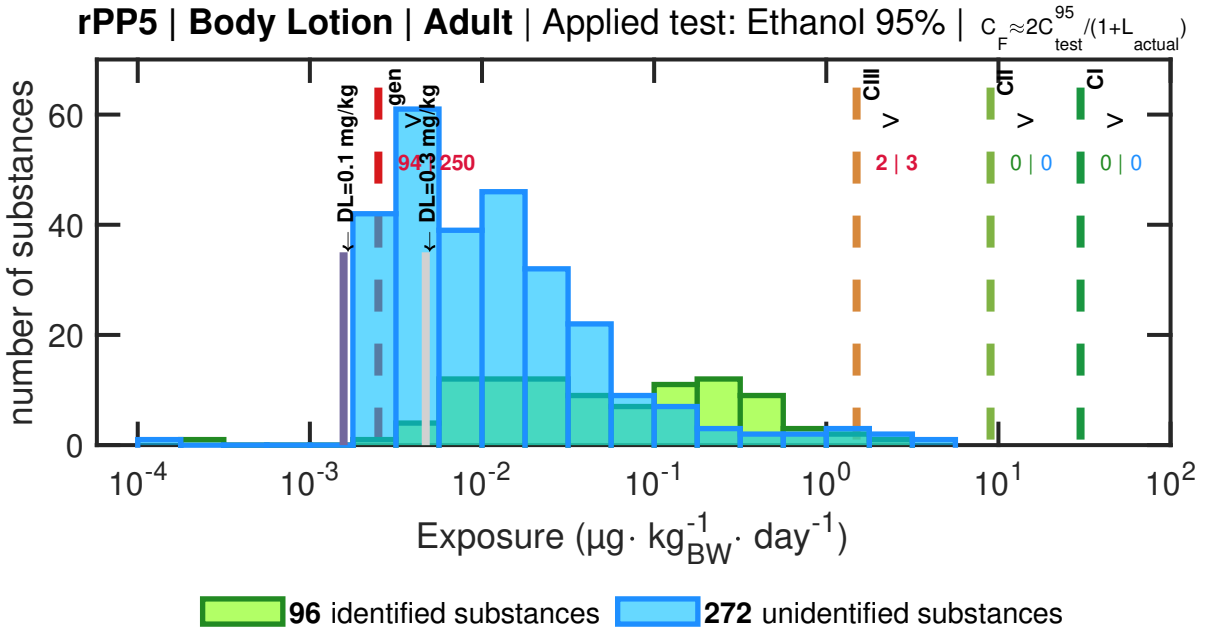

rPP4 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
5 | 0
0 | 0
0 | 0
0 | 0
21 identified substances
61 unidentified substances

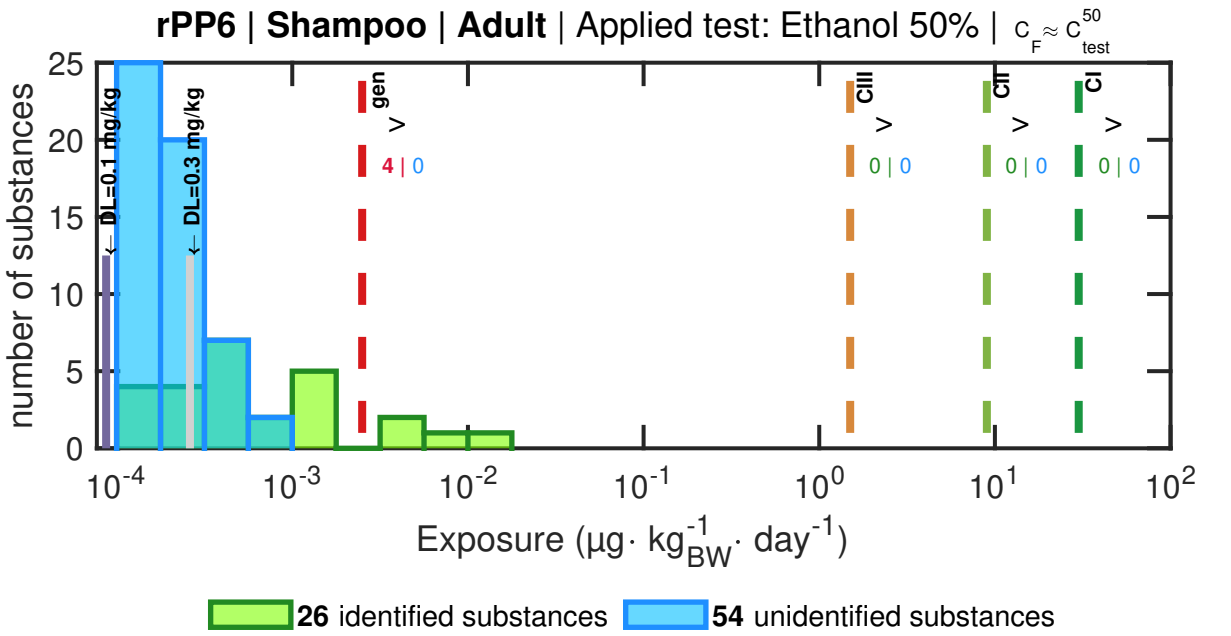

rPP4 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
gen
DL=0.1 mg/kg
DL=0.3 mg/kg
21 | 61
CIII
CII
CI
0 | 0
0 | 0
0 | 0
21 identified substances
61 unidentified substances

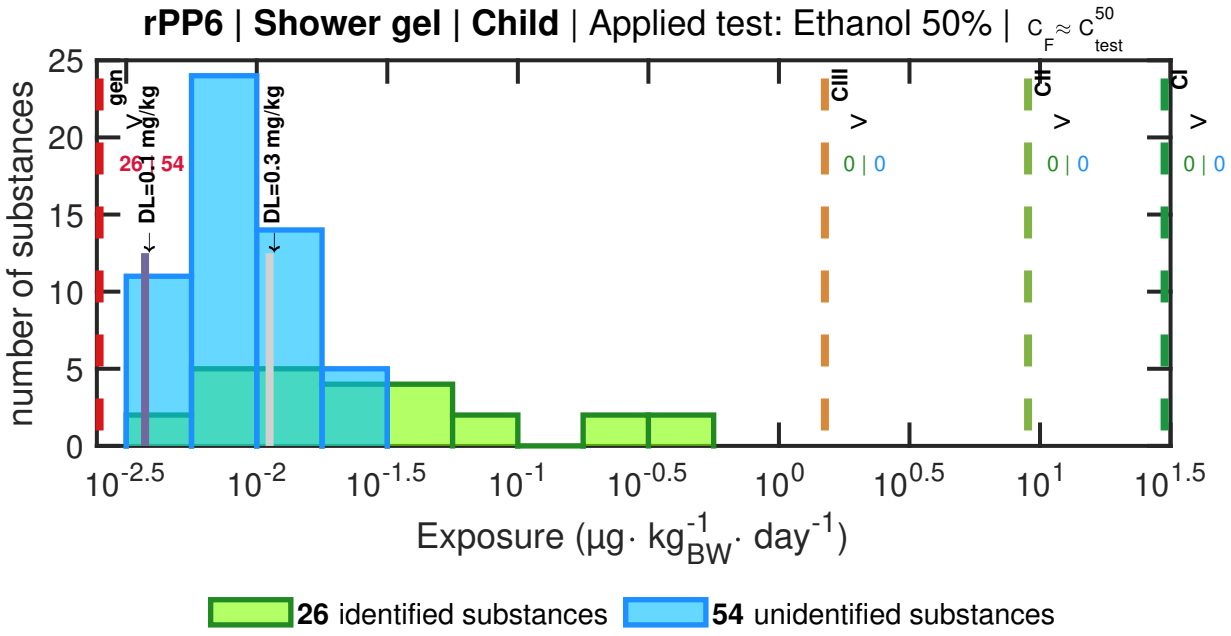

rPP4 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
gen
DL=0.3 mg/kg
79 | 208
CIII
CII
CI
2 | 0
0 | 0
0 | 0
79 identified substances
208 unidentified substances

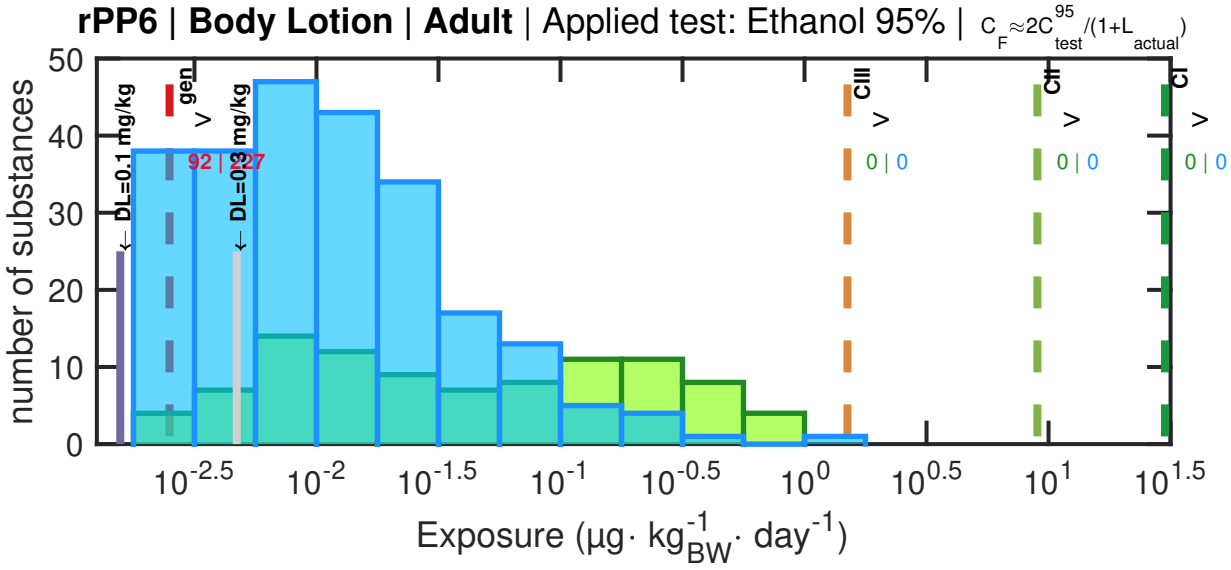

rPP5 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg$^{-1}_{BW}$· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
6 | 0
CIII
0 | 0
CII
0 | 0
CI
0 | 0
35 identified substances
101 unidentified substances

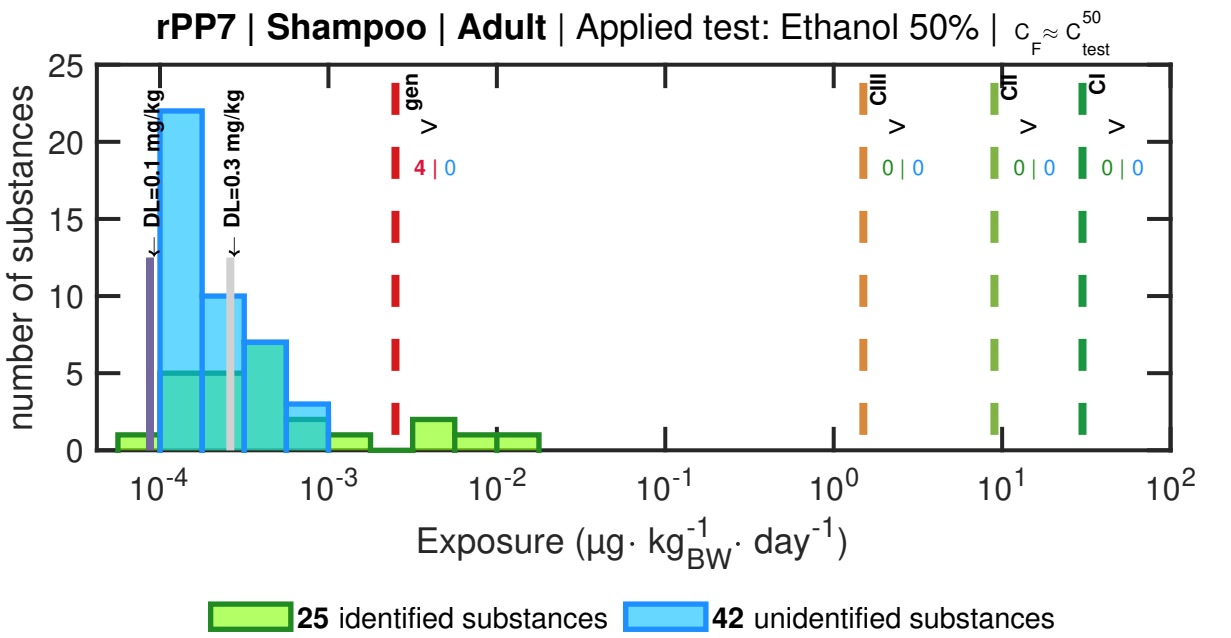

rPP5 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg$^{-1}_{BW}$· day^{-1})
gen
35 | 101
DL=0.1 mg/kg
DL=0.3 mg/kg
CIII
0 | 0
CII
0 | 0
CI
0 | 0
35 identified substances
101 unidentified substances

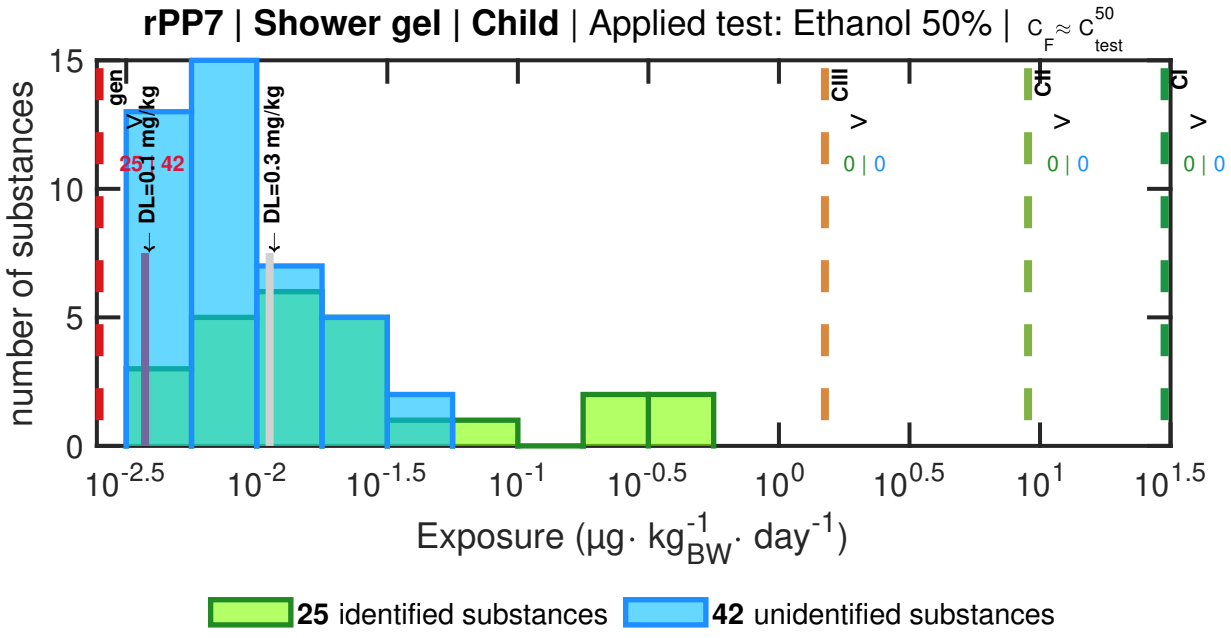

rPP5 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
Exposure (µg· kg$^{-1}_{BW}$· day^{-1})
DL=0.1 mg/kg
gen
94 | 250
DL=0.3 mg/kg
CIII
2 | 3
CII
0 | 0
CI
0 | 0
96 identified substances
272 unidentified substances

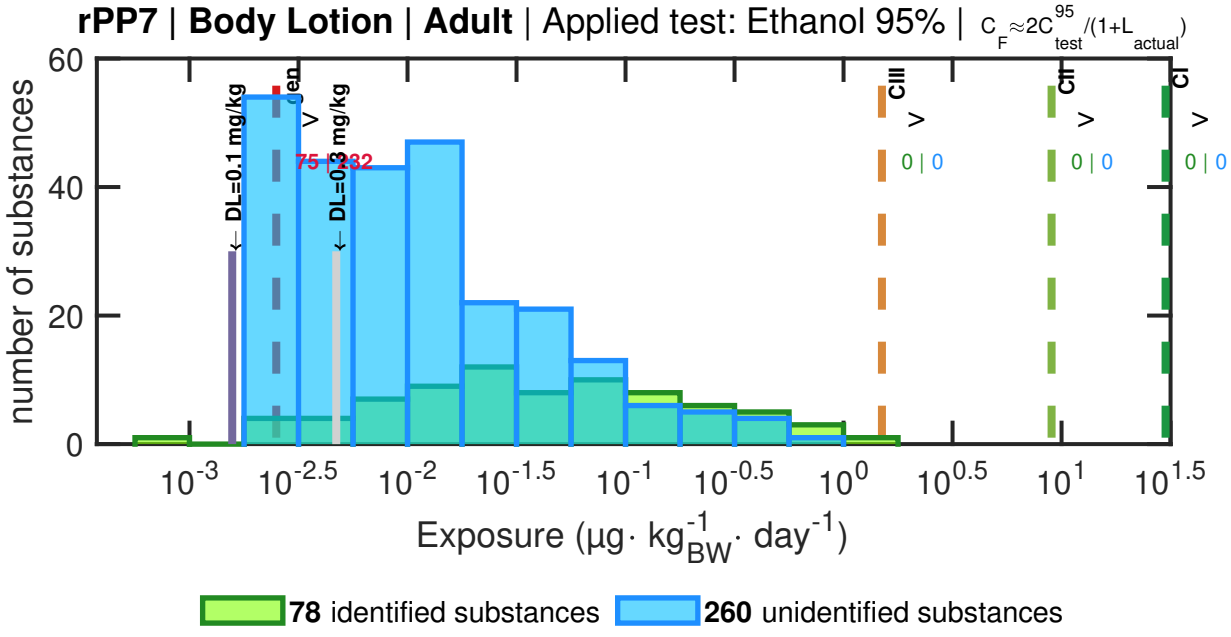

rPP6 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
← DL=0.1 mg/kg
← DL=0.3 mg/kg
gen
4 | 0
CIII
0 | 0
CII
0 | 0
CI
0 | 0
26 identified substances
54 unidentified substances

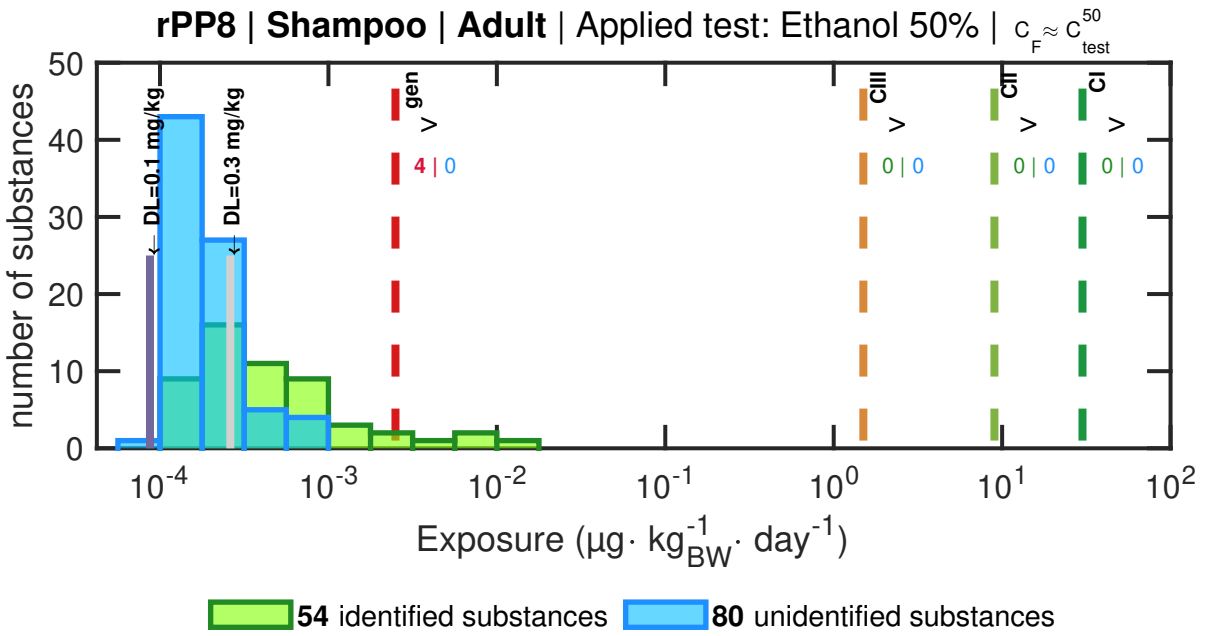

rPP6 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
gen
26 | 54
← DL=0.1 mg/kg
← DL=0.3 mg/kg
CIII
0 | 0
CII
0 | 0
CI
0 | 0
26 identified substances
54 unidentified substances

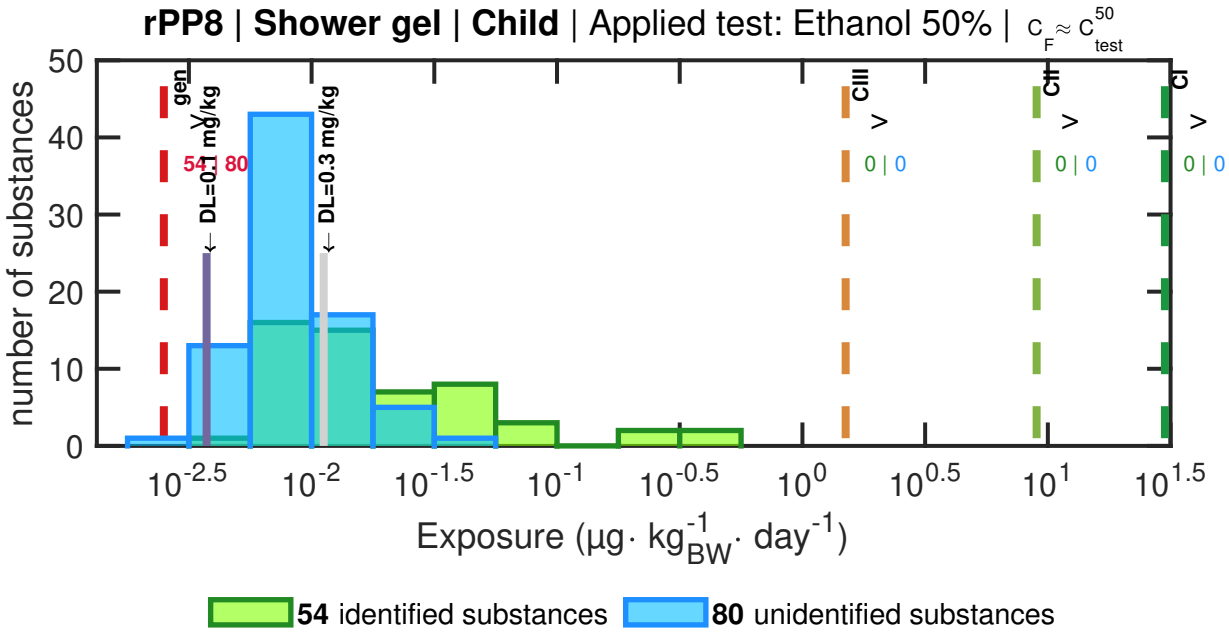

rPP6 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
← DL=0.1 mg/kg
gen
92 | 27
← DL=0.3 mg/kg
CIII
0 | 0
CII
0 | 0
CI
0 | 0
95 identified substances
241 unidentified substances

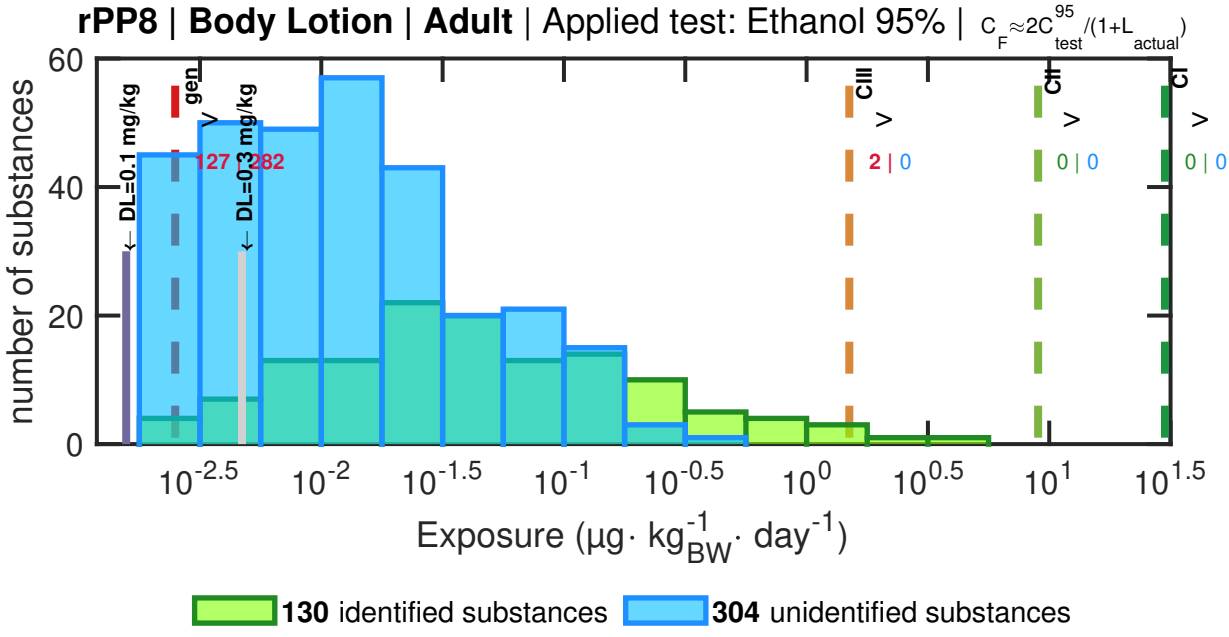

rPP7 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
4 | 0
0 | 0
0 | 0
0 | 0
25 identified substances
42 unidentified substances

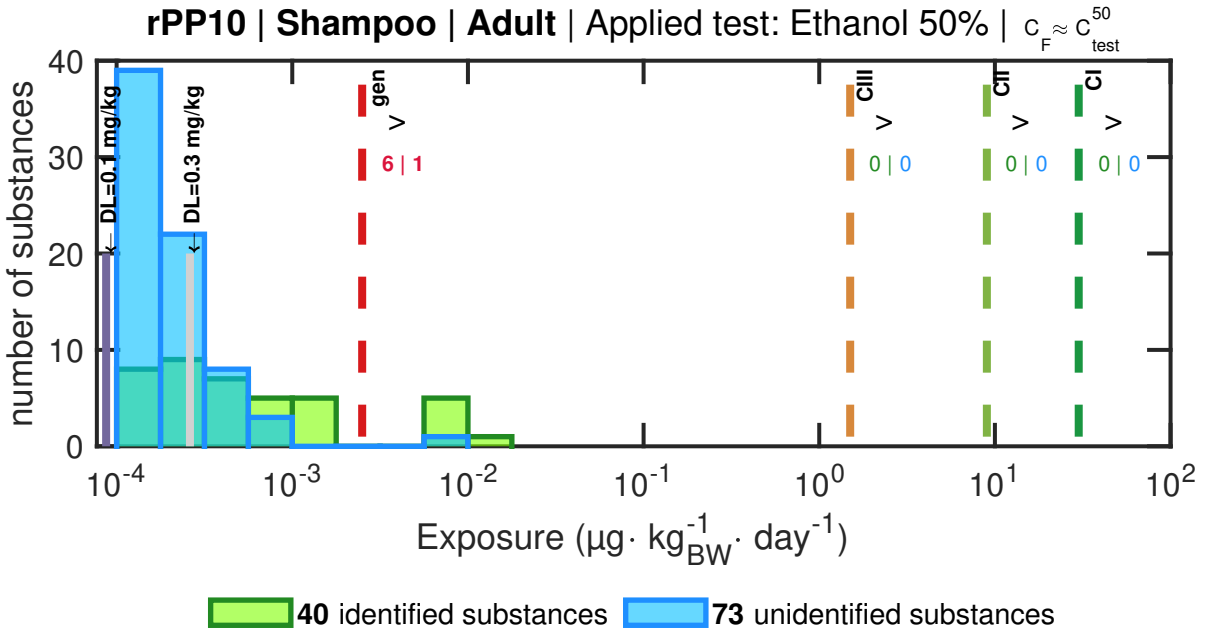

rPP7 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
25 | 42
0 | 0
0 | 0
0 | 0
25 identified substances
42 unidentified substances

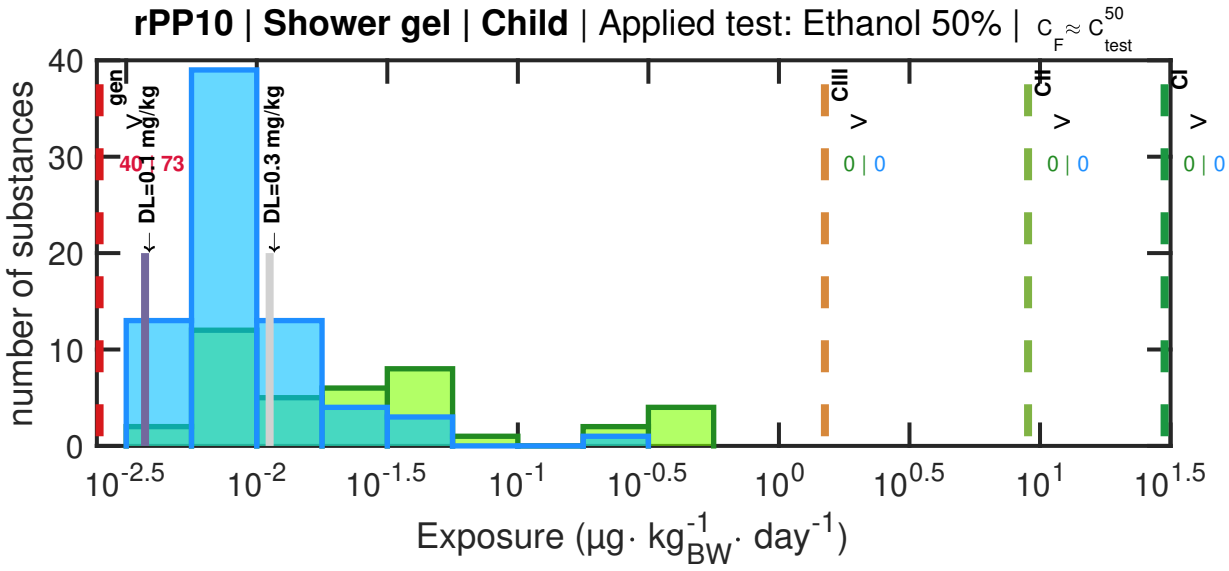

rPP7 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
75 | 232
0 | 0
0 | 0
0 | 0
78 identified substances
260 unidentified substances

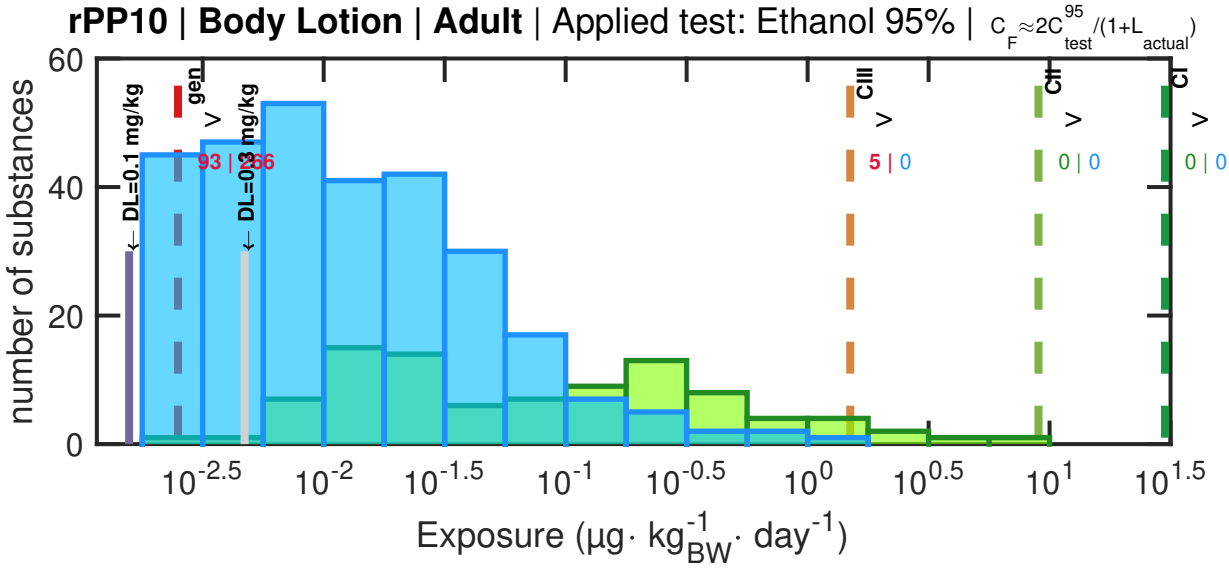

rPP8 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
4 | 0
0 | 0
0 | 0
0 | 0
54 identified substances
80 unidentified substances

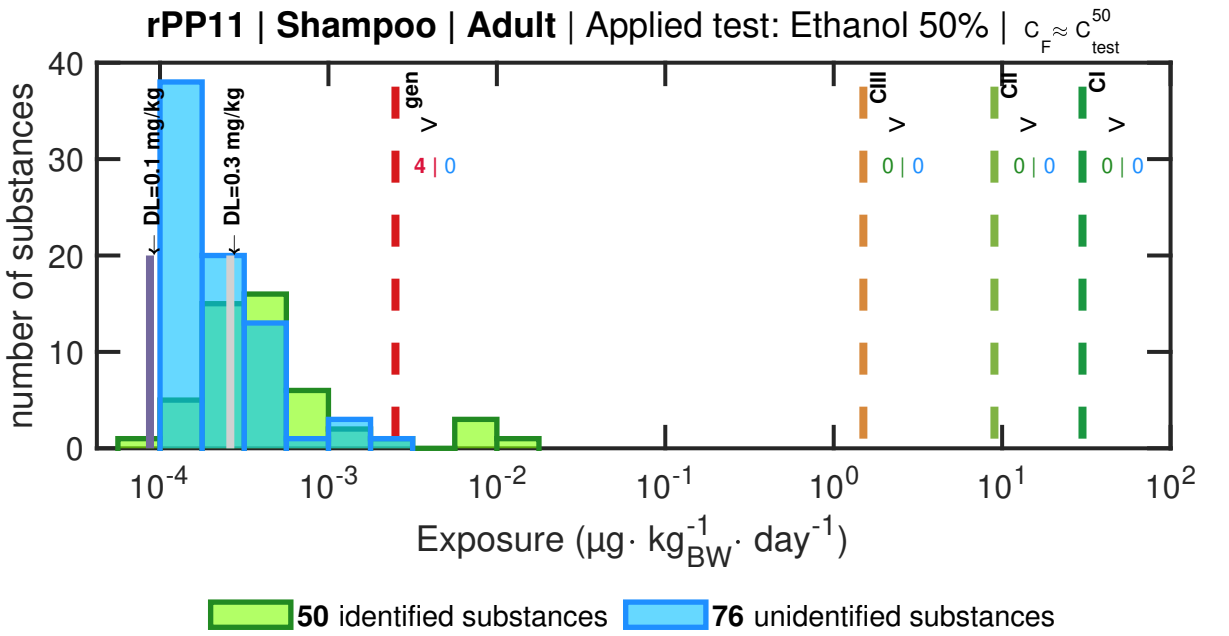

rPP8 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
gen
DL=0.1 mg/kg
DL=0.3 mg/kg
CIII
CII
CI
54 | 80
0 | 0
0 | 0
0 | 0
54 identified substances
80 unidentified substances

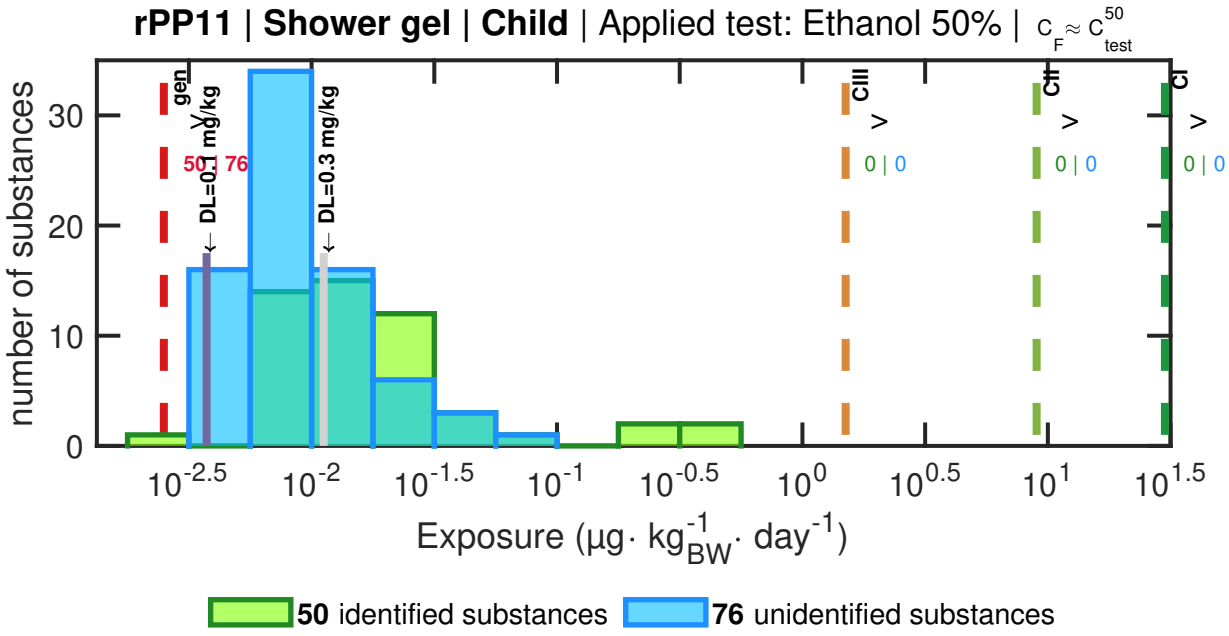

rPP8 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
gen
DL=0.3 mg/kg
CIII
CII
CI
127
282
2 | 0
0 | 0
0 | 0
130 identified substances
304 unidentified substances

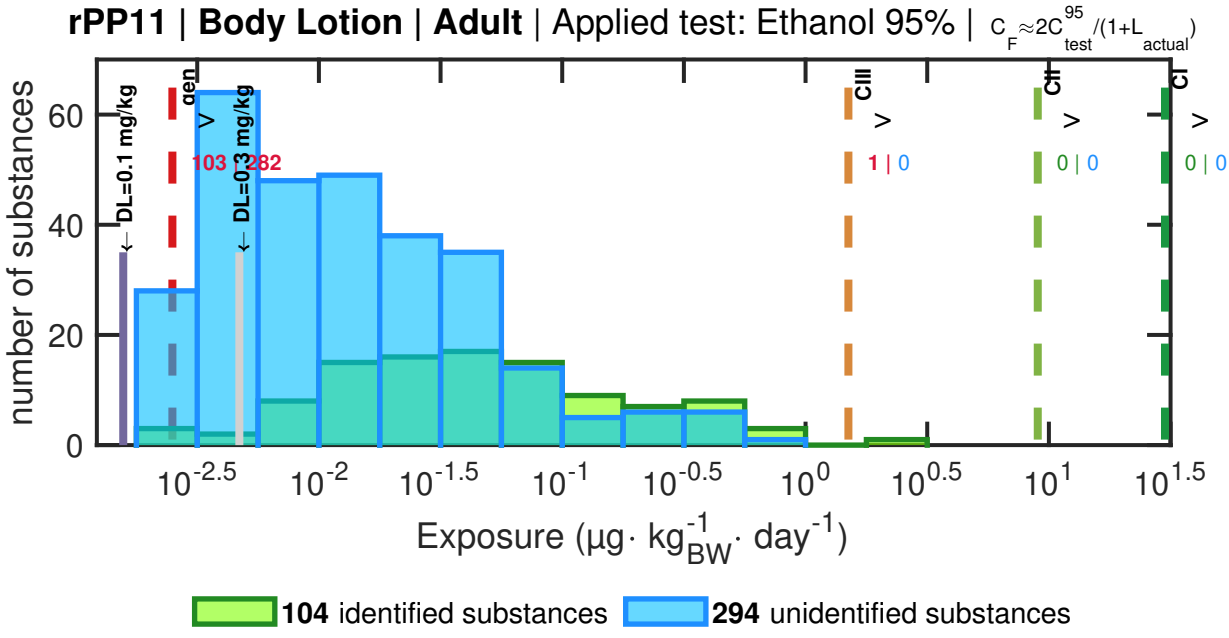

rPP10 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
6 | 1
CIII
0 | 0
CII
0 | 0
CI
0 | 0
Exposure (µg· kg^{-1}_{BW}· day^{-1})
40 identified substances
73 unidentified substances

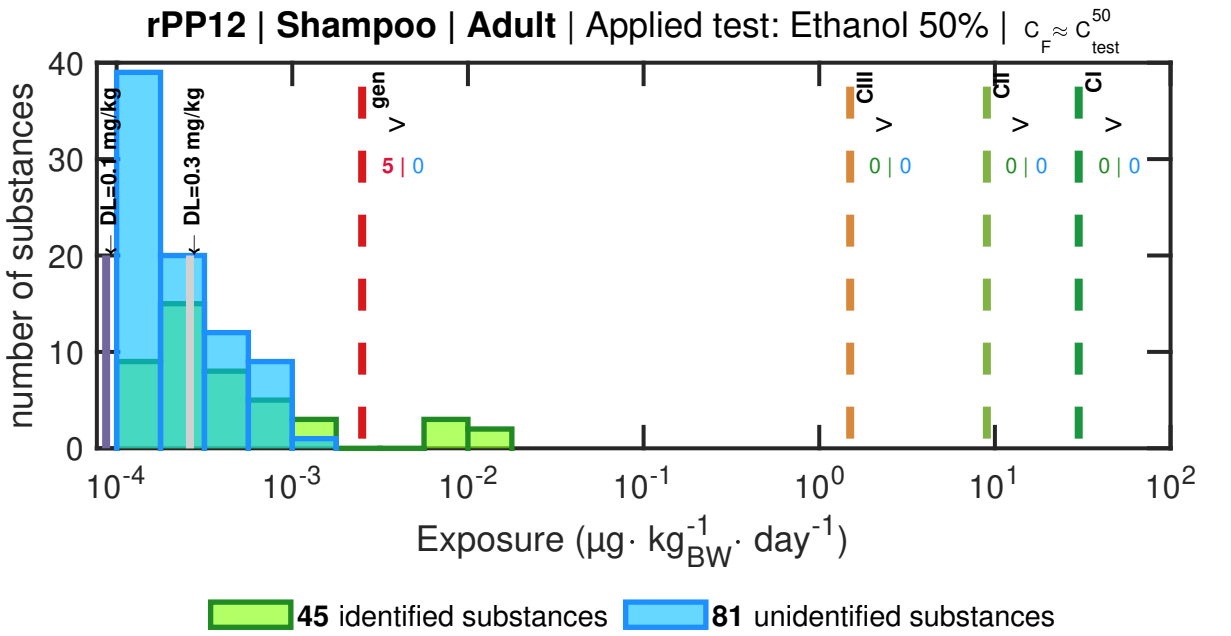

rPP10 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
gen
40 | 73
DL=0.1 mg/kg
DL=0.3 mg/kg
CIII
0 | 0
CII
0 | 0
CI
0 | 0
Exposure (µg· kg^{-1}_{BW}· day^{-1})
40 identified substances
73 unidentified substances

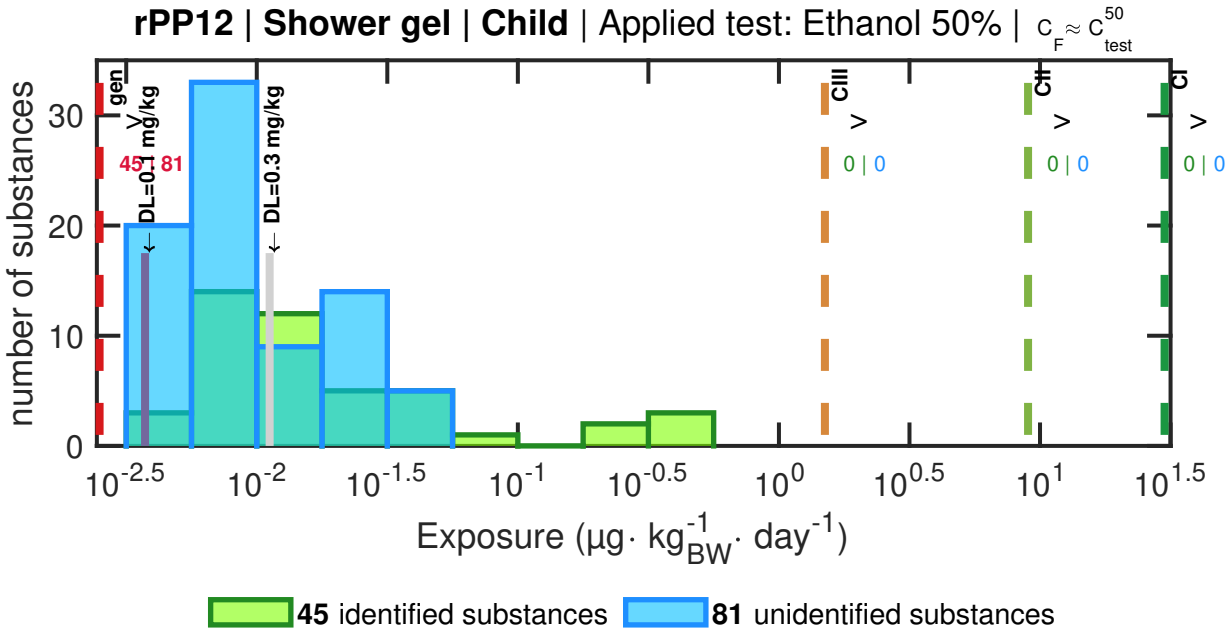

rPP10 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
DL=0.1 mg/kg
gen
93 | 292
DL=0.3 mg/kg
CIII
5 | 0
CII
0 | 0
CI
0 | 0
Exposure (µg· kg^{-1}_{BW}· day^{-1})
93 identified substances
292 unidentified substances

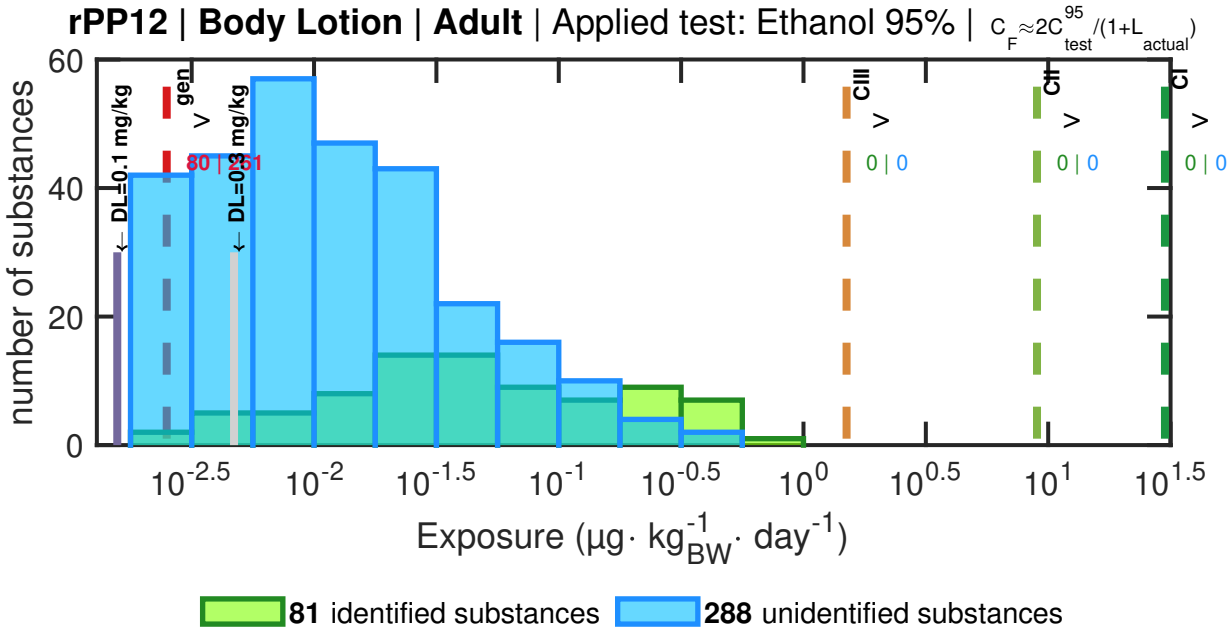

rPP11 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
4 | 0
0 | 0
0 | 0
0 | 0
50 identified substances
76 unidentified substances


rPP11 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
gen
DL=0.1 mg/kg
DL=0.3 mg/kg
CIII
CII
CI
50 | 76
0 | 0
0 | 0
0 | 0
50 identified substances
76 unidentified substances


rPP11 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
gen
DL=0.3 mg/kg
CIII
CII
CI
103 | 282
1 | 0
0 | 0
0 | 0
104 identified substances
294 unidentified substances


rPP12 | Shampoo | Adult | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
DL=0.3 mg/kg
gen
CIII
CII
CI
5 | 0
0 | 0
0 | 0
0 | 0
45 identified substances
81 unidentified substances


rPP12 | Shower gel | Child | Applied test: Ethanol 50% | $C_F \approx C^{50}_{test}$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
gen
DL=0.1 mg/kg
DL=0.3 mg/kg
CIII
CII
CI
0 | 0
0 | 0
0 | 0
45 identified substances
81 unidentified substances


rPP12 | Body Lotion | Adult | Applied test: Ethanol 95% | $C_F \approx 2C^{95}_{test}/(1+L_{actual})$
number of substances
Exposure (µg· kg^{-1}_{BW}· day^{-1})
DL=0.1 mg/kg
gen
DL=0.3 mg/kg
CIII
CII
CI
0 | 0
0 | 0
0 | 0
81 identified substances
288 unidentified substances