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Indoor air quality – materials inside the car cabin

WP6 Case Study Summary

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MISTRA SAFECHEM

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Cover photo: Volvo Cars

About the case study

Task D6.2. was a collaboration between IVL and Volvo Cars to use the SafeChem toolbox with a focus on ensuring a high indoor air quality in the car and that the materials used inside the car are safe. The focus in this case study was on the evaluation of exposure to specific substances as well as the identification of strategies to decrease or substitute said substances with safer and sustainable alternatives. The aim was to achieve a substitution with a systems perspective, assuring not only increased safety but also improved environmental performance of the alternatives without changing the material properties.

To reach these goals, two main tracks were pursued in this case study:

1. An assessment of current and alternative plasticizers used in artificial leather to investigate safe substitution.

2. An analysis of CMR (Carcinogenic, Mutagenic, Reprotoxic) substances present in the indoor air environment and an analysis of which substances to be prioritized for substitution with a safer alternative.

The case study had three internal deliverables within the project:

D6.2.1 Toxicological and biological information from mixtures or substances in the car cabin

D6.2.2 Feedback on implementation of tools and methods from the case study to WP3 and WP5

D6.2.3 Internal documentation for decision making in case of substitution and choice of substitute

In addition, the case study also delivered:

- A master thesis by Tomáš Slaný, focusing on the assessment of current and alternative plasticizers used in artificial leather to investigate safe substitution (not publicly available)
- A side-by-side comparison of Usetox and Proscale results
- An internal tool developed by Volvo Cars, based on findings from the case study, to aid in the decision-making process to map and substitute hazardous substances
- Additional data coupled to D.6.2.1. based on two sampling campaigns in the car cabin, testing a new approach for passive contact samplers (results partly available in this report).

Methods and tools used

Case study D6.2 has mostly focused on testing the tools that fall under the Safety branch of the Mistra Safechem Toolbox and those that fall under Sustainability (See Figure 1). Tools included under "Process" were the focus of WP4.

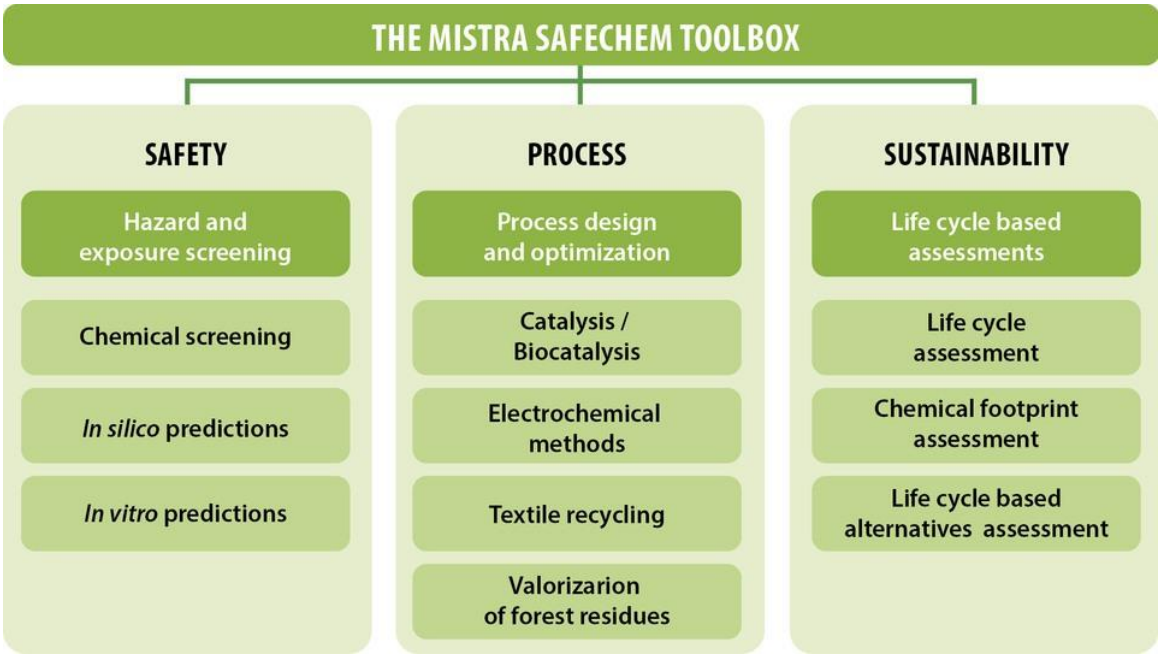

Figure 1: Overview of the Mistra Safechem Toolbox. D6.2 focused mostly on Safety and Sustainability.

Chemical screening

To map substances of interest and potential alternatives in tracks one and two, the study mostly relied on literature analyses and expert input.

For the CRM assessment in track 1, a selection of hazardous substances was identified as potentially occurring in the indoor car environment using literature analysis and expert input (see Table 1).

Table 1: Overview of chemicals included in the CRM assessment

Chemical name	CAS	Chemical function
(1,1'-Biphenyl)-4,4'-diol	92-88-6	Used for the manufacture of plastic products and chemicals
2,6-Di-tert-butyl-p-cresol	128-37-0	Used in food, cosmetics and industrial fluids to prevent oxidation and free radical formation
4-(1,1,3,3-Tetramethylbutyl)phenol	140-66-9	Used in plasticizers, fuel oils, to make fungicides and disinfectants, dyes, adhesives, rubber chemicals and to make other detergents
4,4'-Isopropylidenediphenol (Bisphenol A)	80-05-7	Used in liners, lacquers, adhesives, plastics, and the coating of drinks and food cans
4,4'-Methylenediphenol (Bisphenol F)	620-92-8	Used in liners, lacquers, adhesives, plastics, and the coating of drinks and food cans
6,6'-Di-tert-butyl-2,2'-methylenedi-p-cresol	119-47-1	Antioxidant. Used in polymers adhesives and sealants, lubricants and greases, fuels, hydraulic fluids and metal working fluids
Bis(2-propylheptyl) phthalate	53306-54-0	Plasticizer
Diundecyl phthalate	3648-20-2	Plasticizer
Octabenzone	1843-05-6	UV stabilizer
PFOA	335-67-1	Surfactant / repellent
PFOS	1763-23-1	Surfactant / repellent
Triphenyl phosphate	115-86-6	Flame retardant / plasticizer
Tris[2-chloro-1-(chloromethyl)ethyl] phosphate	13674-87-8	Flame retardant

The other part of the case study relates to the measurement of substances within a car cabin, since it contains different components and materials, many of which are polymeric materials. Polymeric materials often need different additives to create specific functional properties of the plastic. These are mixed into the materials and not chemically bound to the polymer molecules. These substances can be emitted from the materials, and they are often categorized as volatile organic compounds VOC or semi volatile organic compounds SVOC. The classification of the substances is connected to vapor pressures, sizes and their properties. The VOCs are quite well studied, while the SVOCs are less studied. SVOCs often have a slower release rate, which can be boosted by increasing the temperature in the surrounding environment. The SVOCs also tend to adsorb to airborne particles, dusts and sometimes also other surfaces.

To map the substances found in the car cabin in track two, passive samplers (PDMS sheets) were placed in the car cabin to either collect migration samples from materials, air samples or deposition (air + particles). PDMS sheets were chosen based on the project's previous experience with the media and the suitability of PDMS as a passive sampler for many semi-volatile organic contaminants which were the main focus in this study.

The samples were analyzed by targeted screening for a list of CMR substances reported in the literature from measurements in car environments (Table 1), with a few additions. The substances included in the analyses are presented in Table 2.

Table 2: Overview of CMR substances in focus for this study.

Pthalates	Bisphenols	Organophosphates	UV-Filters	Anti-Oxidants
DMP	BPAF	TDCPP	Octabenzone	4-tert-Octylphenol
DEP	BPF	TCEP		BHT
DiBP	BPA	TCPP		Anti-oxidant 2246
DnBP	BPS	TEHP		
BBzP	TBBPA	TBEP		
DEHP		TPhP		
DPHP		EHDPP		
DuDP		ToCrP		

Two sampling campaigns were carried out within the scope of the case study, with a different vehicle each time. The vehicles differed in model, size and material specifications. Each car was prepared by removing all lose items from inside the cabin. Thereafter, the passive samplers were placed on different surfaces (See figures 2-6 for an illustration of the placement of the sheets).

The PDMS sheets were used for both air sampling as well as for contact sampling of the material surfaces inside of the car cabin. The PDMS sheets used as contact samplers, were placed directly in contact with a surface of interest and then covered with aluminum foil to exclude uptake from the air. The PDMS sheets used for air sampling were hung in the open air and those used for deposition sampling were placed on a clean aluminum sheet. The handling of the PDMS was done using pre-cleaned metal tweezers along with pre-cleaned aluminum foils to reduce contamination.

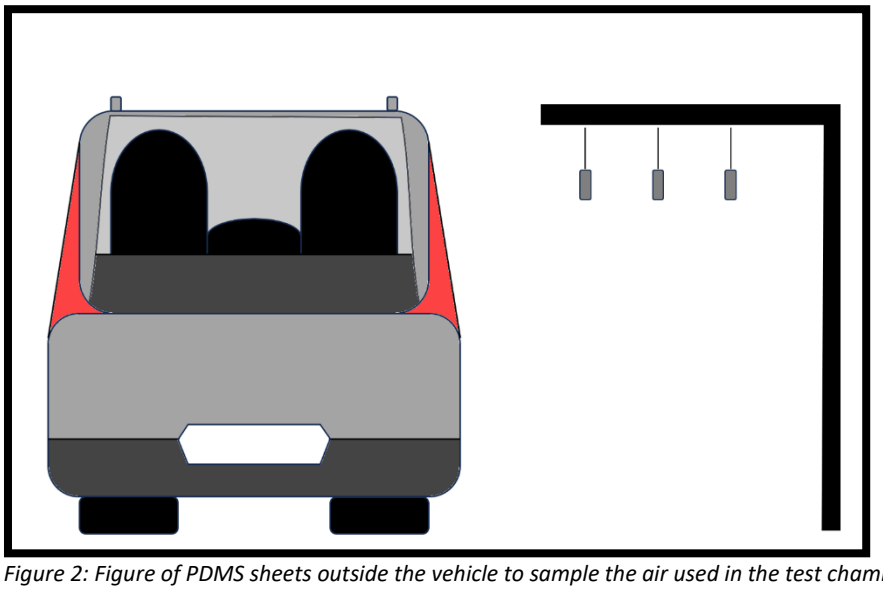

Figure 2: Figure of PDMS sheets outside the vehicle to sample the air used in the test chamber

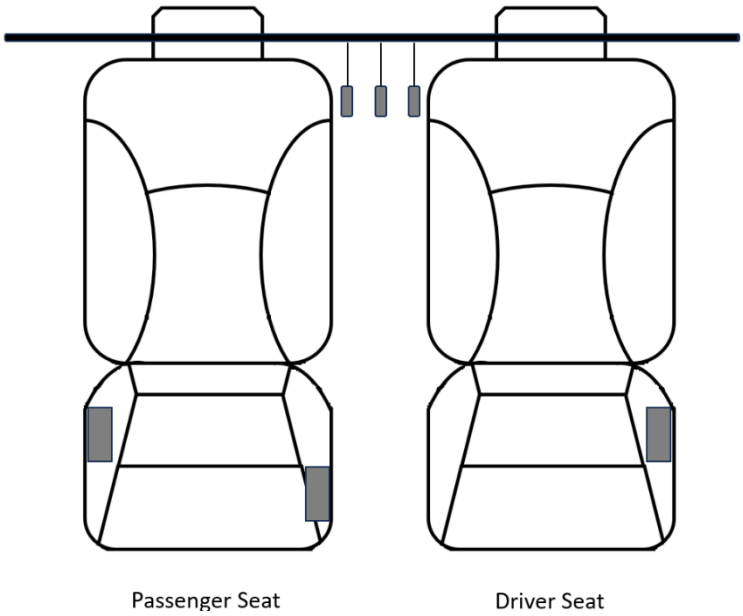

Figure 3: Showing the placement of the PDMS sheets inside the front of the car cabin. Three sheets in between the front row seats that measure the air. Three sheets were also placed directly on the seats to get migrational effects and then covered by aluminum.

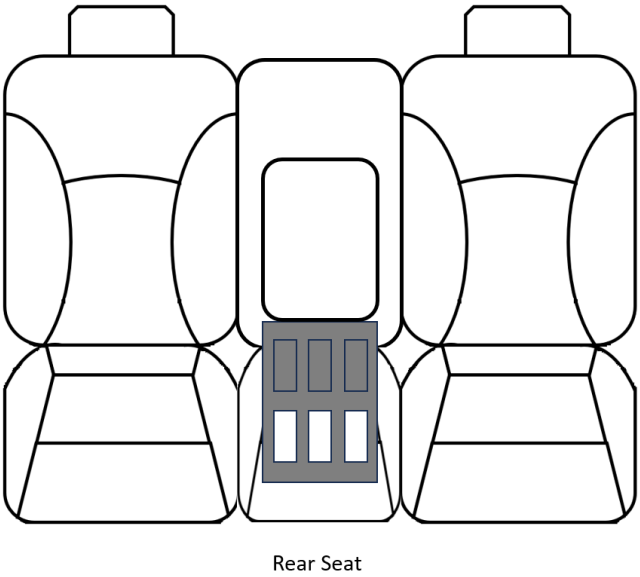

Figure 4: Showing the placement of the PDMS sheets inside the back of the car cabin. The PDMS sheets are placed on an aluminum covered rear seat armrest console inside the car. Three blanks were covered totally with aluminum. Additional three deposition sheets were laid on the aluminum to sample air in between the back row seats.

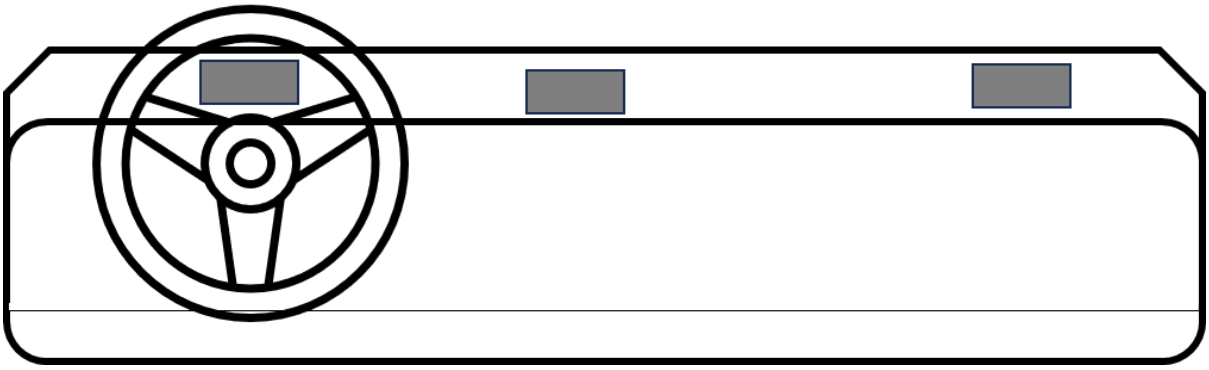

Figure 5: Placement of the PDMS sheets on the dashboard, where the sheets were spread out evenly on the instrument panel and directly placed on the surface to get migrational effects and then covered with aluminum.

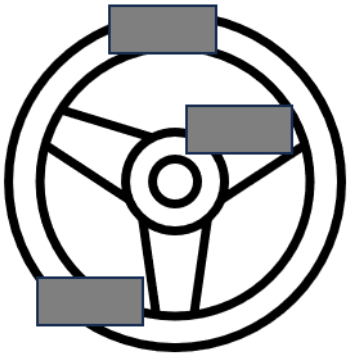

Figure 6: Placement of the PDMS sheets on the dashboard. The PDMS sheets were placed on three different positions, upper, middle and lower, shown by the figure above. They were covered and held by aluminum around the steering wheel to sample migrational effects.

During the sampling occasion the vehicles were subjected to different temperatures. This was possible with the help of a test chamber equipped with UV-lamps and the possibility to control the incoming air temperature and humidity of the air in the chamber. The temperature was measured on three places inside the vehicle: on the instrument panel, between the front seat and in the rear seat. The rigg was then heated according to a cycle shown in Table 3 (first event) and Table 4 (second event) below, where the PDMS was placed in the vehicle at the start of the sampling and removed at the end and sent for analysis.

To reach in cabin air temperatures of 80 degrees Celsius, one must have air temperatures of 35 degrees outside the car and have an UV intensity in the lamps for around 1100W/m2. That solar radiation intensity equals direct sunlight hitting the ground when the sun is at zenith (at the height of the day). Thus, during the sample occasions that were performed, the car was under this high solar radiation for 24 hours straight. This is not a real world scenario, but it was used to get a controlled temperature in the vehicle that can be similar to that found in certain areas if the car is parked in the sun, with closed doors and windows and with the ventilation turned off. These high temperatures help speed up the transfer kinetics and enable measurement of potential emissions with the passive samplers during a short sampling period.

Table 3: Temperature scheme for first sampling event

Day	Rigg temperature (°C)	Humidity %	Inside car temperature (air) (°C)
0	Sampling starts	Sampling starts	Sampling starts
0	25	10	25
1	25	10	40
2	35	10	80
3	25	10	25
4	Rigg turned off		
Cool down	Rigg turned off		

Table 4: Temperature scheme for second sampling event

Day	Rigg temperature (°C)	Humidity %	Inside car temperature (air) (°C)
0	Sampling starts	Sampling starts	Sampling starts
0	25	10	25
1	25	10	40
2	35	10	80
3	35	10	80
4	Rigg Turned off		
Cool down	Rigg Turned off		

Details for the materials and methods

PDMS sheets:

The PDMS sheets in the first campaign were supplied by Altec Extrusions Limited (UK) and were prepared as described in Papazian et al.:

- Papazian, S., Fornaroli, C., Bonnefille, B., Pesquet, E., Xie, H., & Martin, J. W. (2022). Silicone foam for passive sampling and nontarget analysis of air. *Environmental Science & Technology Letters*, 10(11), 989-997.

The PDMS sheets (SSP-M823) in the second campaign were supplied by Specialty Silicone Products, Inc. (US) and were prepared by overnight Soxhlet extraction in methanol and subsequent drying in a fume hood. Due to the lack of a vacuum oven to dry the PDMS sheets after cleaning, higher blank levels were found for several substances in these sheets. This was accounted for by the use of blank subtractions.

The PDMS sheets were stored in glass jars / vials until use. After use, they were kept frozen at -20 degrees Celsius, until analysis.

Aluminum foil and glassware:
All glassware and aluminum foil used in the study was washed and burned before use.

Chemical analysis:
The targeted analysis was performed in-house by IVL with the extraction of the PDMS sheets based on that in Papazian et al. (2022), which was supplied by Stockholm University.

Before extraction, the PDMS sheets for the samples, field blanks and procedural lab blanks were spiked with a mixture of isotope-labelled internal standards (1ppm, 10 µL) in methanol. The PDMS sheets were then left to absorb the droplet.

After spiking, the samples were extracted using ultrasound. Each sample was extracted using 4 cycles of 30 minutes of ultra sonification:

- Solvent volume (MTBE: n-hexane) = 5mL each round (x2 = 10 mL in total), for GC-MS analysis.
- Solvent volume (MeOH) = 5mL each round (x2 = 10 mL in total), for LC-MS analysis pooled together with the previous fraction for GC-MS.

After every 10 minutes of ultrasonication, the samples were vortexed.

After extraction, the samples were concentrated using a stream of N_2 gas at room temperature to a volume of 1 mL after which they were transferred to a 1.5 ml vial and filtered using a 0.2 µm polypropylene filter.

The analytical methods used for the analyses are described in more detail in the following publications:

Phthalates and alternatives, OPEs, Bisphenols and BFRs

- Giovanoulis G., Nguyen M. A., Arwidsson M., Langer S., Vestergren R., Lagerqvist A. (2019) Reduction of hazardous chemicals in Swedish preschool dust through article substitution actions. *Environmental International* 130: 104921

UV filters

- Silva, C. P. D., Emídio, E. S., & de Marchi, M. R. (2013). UV filters in water samples: experimental design on the SPE optimization followed by GC-MS/MS analysis. Journal of the Brazilian Chemical Society, 24, 1433-1441.
- Remberger M., Bibi M., Kaj L., Brorström-Lundén E. (2015), Screening 2014 - Analysis of UV-filters (and fragrances) used in cosmetics and textiles, IVL report C 138
- Remberger M., Kaj L., Victor T., Brorström-Lundén E. (2011), Results from the Swedish National Screening Programme 2009. Subreport 3: UV-filters*, IVL report* B 1971

Antioxidants

- Teoh, W. Y., Yong, Y. S., Razali, F. N., Stephenie, S., Dawood Shah, M., Tan, J. K., Gnanaraj C. & Mohd Esa, N. (2023). LC-MS/MS and GC-MS Analysis for the Identification of Bioactive

Metabolites Responsible for the Antioxidant and Antibacterial Activities of Lygodium microphyllum (Cav.) *R. Br. Separations*, 10(3), 215.

Life cycle based alternative assessments and chemical footprint assessments

For the LCA based alternative assessment, the project used USEtox version 3.0 beta 6c and the LCAA framework by Peter Fantke et al.. It also made use of SciFinders Reactions database (External tool) to map possible chemical production pathways.

In silico predictions

In silico prediction tools were used for hazard assessments as well as to generate data to be used in the different tiers of the life cycle based alternative assessments. Both *in silico* prediction tools from the SafeChem toolbox as well as a range of external tools were used.

In silico prediction tools used from the SafeChem toolbox:

- AI-based prediction tools, developed by Swapnil Chavan, RISE
- Machine learning tools, developed by Ziye Zheng, Cytiva
- Machine learning tools, developed by Ulf Norinder, Stockholm University

The *in silico* models provided predictions for 35 endpoints with 18 of these endpoints represented in two or more models (See Table 5). The models have been trained on the same dataset but have used different approaches for the predictions. For that reason, predictions using different models for the same endpoints can differ. These differences can be more pronounced for endpoints coupled to for example endocrine toxicity, where the training data may be more uncertain and include for example both agonistic as well as antagonist effects on the same endocrine receptor (Based on discussion with the developers of the tools).

Having different output values for the same endpoint makes it difficult to do a direct assessment of the chemical's hazards, based on the raw data. The *in silico* output was therefore assessed and ranked according to the certainty of the predictions. The following ranking, from "most certain" to "least certain" was used in this report:

1. Expert data (e.g. Literature) included in the training data
2. Predictions with a high confidence, resulting in a positive result for the endpoint (e.g., the chemical is likely to be an AR-agonist)
3. Predictions with a high confidence, resulting in a negative result for the endpoint (e.g., the chemical is most likely not at an AR-agonist)

Using this ranking, the assumption was made that expert data is the most reliable and that the precautionary principle should be to deal with chemicals that have conflicting but high confidence predictions. All other data was interpreted as a negative result due to the uncertainty in the predictions.

Table 5: Overview of the endpoints covered by the different prediction models, as of October 2023. Note that endpoints are sometimes named differently in the three models. For transparency, these have been kept as is.

Ulf Norinder, Stockholm University	Swapnil Chavan, RISE	Ziye Zheng, Cytiva
RXR_agonists_pred_class		
RAR_agonists_pred_class	retinoic acid receptor agonist_class	RAR_agonist_pred
RAR_antagonists_pred_class	retinoic acid receptor antagonist_class	RAR_antagonist_pred
CAR_agonists_pred_class		
CAR_antagonists_pred_class		
PXR_agonists_pred_class		
PR_agonists_pred_class	progesterone receptor agonist_class	PR_agonist_pred
PR_antagonists_pred_class	progesterone receptor antagonist_class	PR_antagonist_pred
FXR_agonists_pred_class		
FXR_antagonists_pred_class		
GR_agonist_pred_class	glucocorticoid receptor agonist_class	GR_agonist_pred
GR_antagonist_pred_class	glucocorticoid receptor antagonist_class	GR_antagonist_pred
AR_agonist_pred_class	androgen receptor agonist_class	AR_agonist_pred
AR_antagonist_pred_class	androgen receptor antagonist_class	AR_antagonist_pred
	thyroid receptor-beta agonist_class	TR_agonist_pred
TR_antagonist_pred_class	thyroid receptor-beta antagonist_class	TR_antagonist_pred
ERA_agonist_pred_class	estrogen receptor-alpha agonist_class	ER_agonist_pred
ERA_antagonist_pred_class	estrogen receptor-alpha antagonist_class	ER_antagonist_pred
	estrogen receptor-beta agonist_class	
	estrogen receptor-beta antagonist_class	
AHR_activator_pred_class		
PPARg_agonist_pred_class		
PPARg_antagonist_pred_class		
PPARd_antagonist_pred_class		
PPARd_agonist_pred_class		
VDR_antagonist_pred_class		
readily_biodegradation_pred_class		Biodegradation_pred
reprotox_pred_class	reproductive toxicity_class	Reprotox_pred
carcinogen_pred_class	carcinogenicity_class	Carcinogencity_pred
mutagenicity_pred_class	mutagenicity_class	Mutagenicity_pred
bioconc_factor_fish_pred_class		BCF_pred
persistence_soil_pred_class		Persistence_(soil)_pred
	skin sensitization_class	
	eye irritation_class	
	eye corrosion_class	

Note that the tools in WP3 were not ready to be tested by the case study group, e.g. it was not possible to use the models directly. But rather information on substances was distributed to the tool owners in the form of SMILES codes and results were then provided to the case study group.

The case study also used the following external *in silico* prediction tools:

- VEGA
- TEST
- EPISUITE
- APROBA-Plus model

In addition to the use of *in silico* tools, the project also relied heavily on chemical parameters found in the literature and in online databases as input for the different tools:

Public databases used to collect chemical property data:

- US EPA Chemical dashboard
- EPISUITE
- US EPA's Toxicity Value Database (ToxValDB)
- OECD eChemPortal's Chemical Substance Search
- USEtox database (database incorporated in the USEtox model)
- ECHA Registration Dossiers

Public databases to collect chemical hazard data and information on chemical legislation:

- ED Lists
- ECHA C&L Inventory
- ECHA Candidate List of SVHC for Authorization
- ECHA Authorization List
- GADSL
- SIN List
- OEHHA Proposition 65
- DTSC Candidate Chemicals List
- IARC List of Classifications

Results and discussion

An assessment of current and alternative plasticizers used in artificial leather - investigate safe substitution.

The work by Tomáš Slaný, in his master thesis, focused on the assessment of current and alternative plasticizers used in artificial leather to investigate their safe substitution. In his work he used the following SafeChem tools: the SafeChem in silico toolbox (through the developers), the life cycle alternative assessment workflow developed by Peter Fantke et al. and the USEtox model. In addition, a wide range of other tools and databases were used to provide Thomas with the data needed to do his assessment.

In his hazard assessment of alternative plasticizers, Tomáš identified four alternatives to have a lower hazard compared to the others. However, the uncertainty associated with the hazard classification, mostly based on QSAR predictions was very high. Therefore, the results indicated that the differences in the potential human toxicity impacts (calculated using USEtox) were too small in relation to the estimated uncertainty, to draw any conclusions. The differences observed for the tested alternatives on the potential impact on freshwater ecosystems was larger and could potentially indicate which substances would be safer from an environmental point of view. The work performed in the thesis should be seen as a preliminary but very valuable first screening of the alternatives and evaluation of the toolbox.

An analysis of CMR substances present in the indoor air environment and an analysis of which substances to be prioritized for substitution with a safer alternative

The results reveal that only a small subset of the substances is likely to be carcinogenic (3 substances), mutagenic (1 substances) or bio accumulative (1 substance). Three substances were identified as being persistent, but only one substance was estimated to be readily biodegradable. A higher fraction of the substances is likely to be reprotoxic (7 substances) and all substances were predicted to have 1 or more endocrine disrupting effect. Several of the substances are also likely to have the potential to cause skin sensitization or eye irritation. For a condensed summary of the results, see Table 6.

Table 6: Summary of the in silico predictions and ranking procedure as described in the method section. Scores of 1 indicate a positive prediction, e.g. the chemical is an endocrine disruptor, the chemical is reprotoxic. Note that for "Readily_Biodegradability", a 0 means that the chemical is not readily biodegradable.

Chemical Name	EDC potential	Readily Biodegradability	Repro-tox	Carcino-genicity	Muta-genicity	BCF	Per-sistence	Skin sensiti-zation	Eye irrita-tion	Eye corro-sion
4,4'-Biphenyldiol	**1**	0	0	0	0	0	0	**1**	**1**	0
Butylated hydroxytoluene	**1**	0	0	0	0	0	0	**1**	**1**	0
4-(1,1,3,3-Tetramethylbutyl) phenol	**1**	0	0	0	0	0	0	**1**	**1**	0
Bisphenol A	**1**	0	**1**	0	0	0	0	0	**1**	0
Bis(4-hydroxyphenyl) methane	**1**	0	0	0	0	0	0	**1**	**1**	0
2,2'-Methylenebis (4-methyl-6-tert-butylphenol)	**1**	0	**1**	0	0	0	0	0	**1**	0
Bis(2-propylheptyl) phthalate	**1**	0	0	0	0	0	0	0	0	0
Diundecyl phthalate	**1**	0	0	0	0	0	0	0	0	0
Octabenzone	**1**	0	**1**	0	0	0	0	0	0	0
Perfluorooctanoic acid	**1**	0	**1**	**1**	0	0	0	0	**1**	**1**
Perfluorooctane-sulfonic acid	**1**	0	**1**	**1**	0	**1**	**1**	0	**1**	0
Triphenyl phosphate	**1**	**1**	**1**	0	0	0	**1**	0	0	0
Tris(1,3-dichloro-2-propyl) phosphate	**1**	0	**1**	**1**	**1**	0	**1**	0	0	0

The results from the *in silico* predictions therefore confirm that the substances in focus (See Table 1) are likely either CMR substances or have an endocrine disrupting potential. Based on these results, all substances looked at, should be prioritized for substitution, if they are found to be present in the car cabin.

The assessment of the data can be considered arbitrary however, as it relies on the assumption that expert data is the most reliable and that the ranking approach used is the best. To avoid uncertainty in the future in how the in silico data is used and interpreted, the in silico toolbox could be complemented with the addition of a summary function in which the data is automatically summarized according to best practices, as developed by experts in the SafeChem project. Summarizing the data also took a few hours and could easily be automated.

Ideally the data would also include information on if expert data was available to help evaluate the predictions. Some of the prediction models mentioned if expert data for the chemicals was available, but not all.

Measurement of substances in a car cabin

The measurements carried out within the project are summarized below.

Most of the phthalates (Figure 7) have been observed in all sample positions. Car 2 shows overall higher levels compared to car 1. Phthalates detected in the highest levels in car 2 were: DEHP found in the steering wheel, DPHP found in the seat and the steering wheel, and DuDP found in the seat. The lowest levels were detected in the dashboard in both cars. The low inside air levels indicate that the deposition samples (air + particles) provide more data than just taking air samples with PDMS. DEHP and DPHP particularly seem to be deposited in higher levels. All levels are based on the concentrations measured in the PDMS and do not represent actual concentrations in the air / surfaces as these concentrations are influenced by the uptake kinetics of the chemicals into the PDMS, as no equilibrium sampling was performed.

Not all chlorinated phosphates (Figure 8) were detected in the PDMS samples in levels above the level of detection. The lowest levels were detected in the dashboards while the car seats and the steering wheels had higher levels. Substances detected in the highest levels were TCPP in the car 2 seat and TDCPP in the car 1 seat. TCPP was present in almost all the materials and deposition samples but not in the inside air. Again, car 2 shows higher levels of chlorinated phosphates.

BPA (Figure 9) was only found in significant levels in the deposition sample and the inside air of car 2. This indicates that BPA may be released from the surfaces in the car, aside from the dashboard, steering wheel, and seat, as no elevated sources of BPA inside the test chamber were found. BPF and BPS were not detected above detection limits.

From UV filters and antioxidants (Figure 10), only octabenzone was found in higher levels in the car seat and the steering wheel of car 2, as well as in the deposition sample. It is unlikely that this is due to the contamination from the test chamber, as levels there were low.

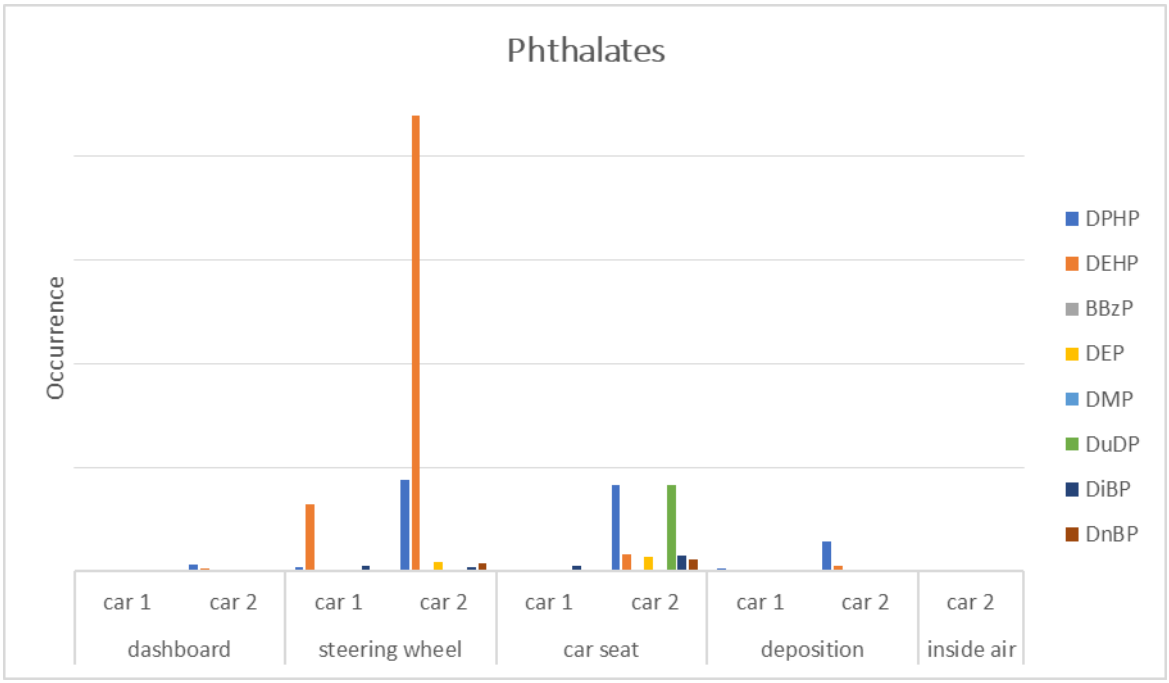

Figure 7: Levels measured for phthalates during the two sampling campaigns Due to confidentiality, no y-axis is given and no information on the materials in the car cabin can be supplied. Levels were blank corrected. Occurrence is used on the y-axis as it represents the concentrations measured in the PDMS which does not directly reflect concentrations in the materials.

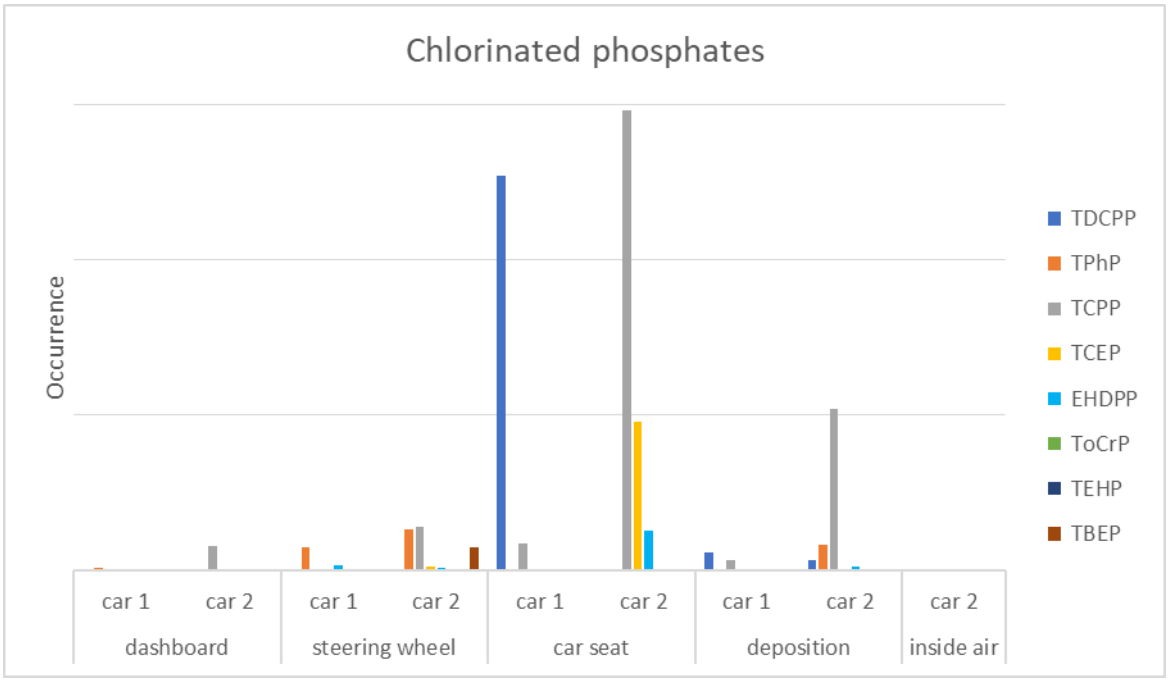

Figure 8: Levels measured for chlorinated phosphates during the two sampling campaigns. Due to confidentiality, no y-axis is given and no information on the materials in the car cabin can be supplied. Levels were blank corrected. Occurrence is used on the y-axis as it represents the concentrations measured in the PDMS which does not directly reflect concentrations in the materials.

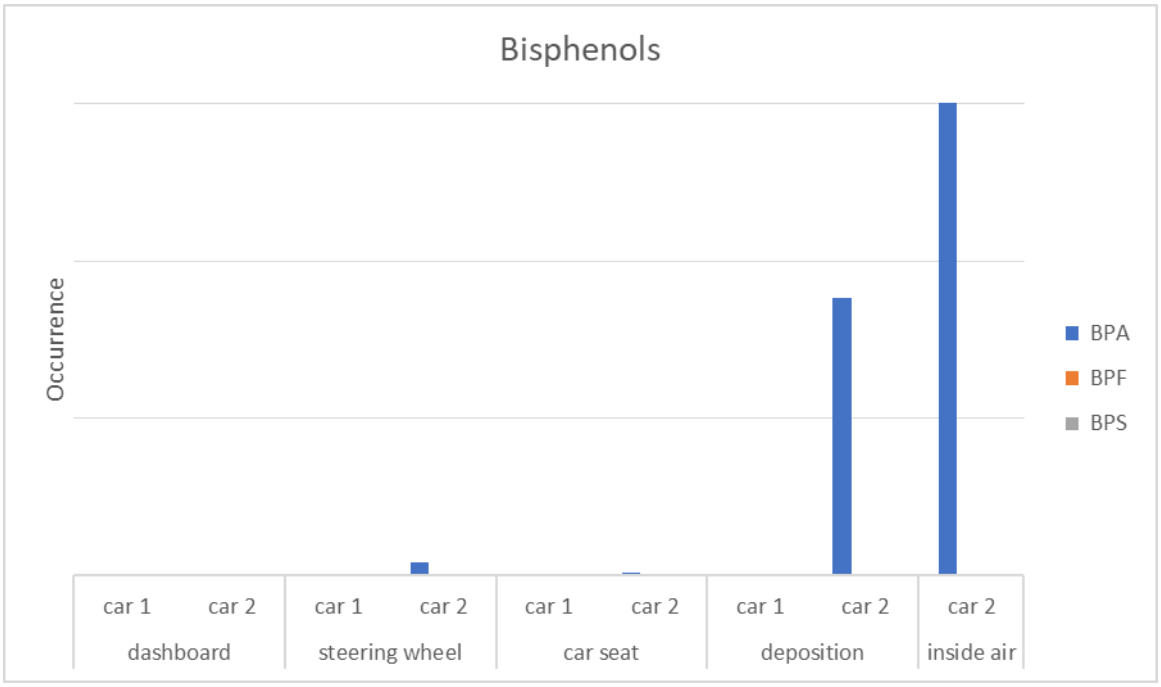

Figure 9: Levels measured for bisphenols during the two sampling campaigns. Due to confidentiality, no y-axis is given and no information on the materials in the car cabin can be supplied. Levels were blank corrected. Occurrence is used on the y-axis as it represents the concentrations measured in the PDMS which does not directly reflect concentrations in the materials.

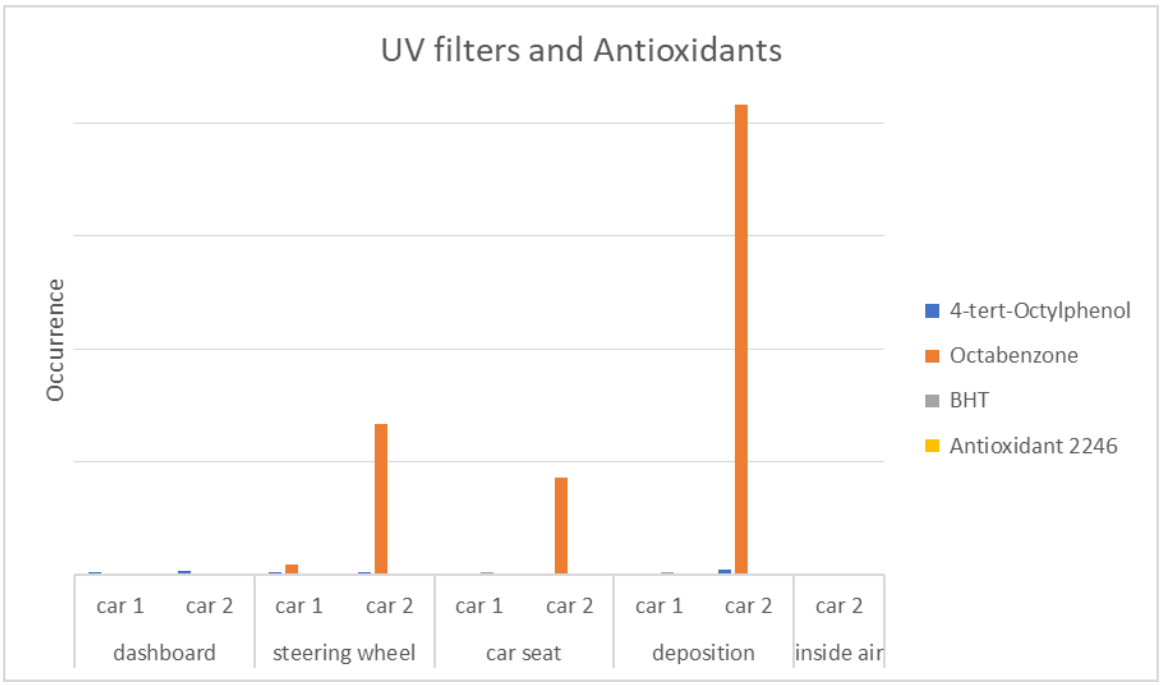

Figure 10: Levels measured for UV filters and Antioxidants during the two sampling campaigns. Car 1 was a car with leather surfaces while car 2 had artificial leather. Due to confidentiality, no y-axis is given. Levels were blank corrected. Occurrence is used on the y-axis as it represents the concentrations measured in the PDMS which does not directly reflect concentrations in the materials.

Substances belonging to chlorinated phosphates group were detected in almost all the locations and showed the highest levels (Figure 11). Generally, dashboards of both cars were cleanest, while steering wheels and seats were at the other end of the scale. Car 2 showed overall higher levels of

detected substances, which could be explained by longer time for the samplers at 80 degrees and the use of different materials and parts between the two cars.

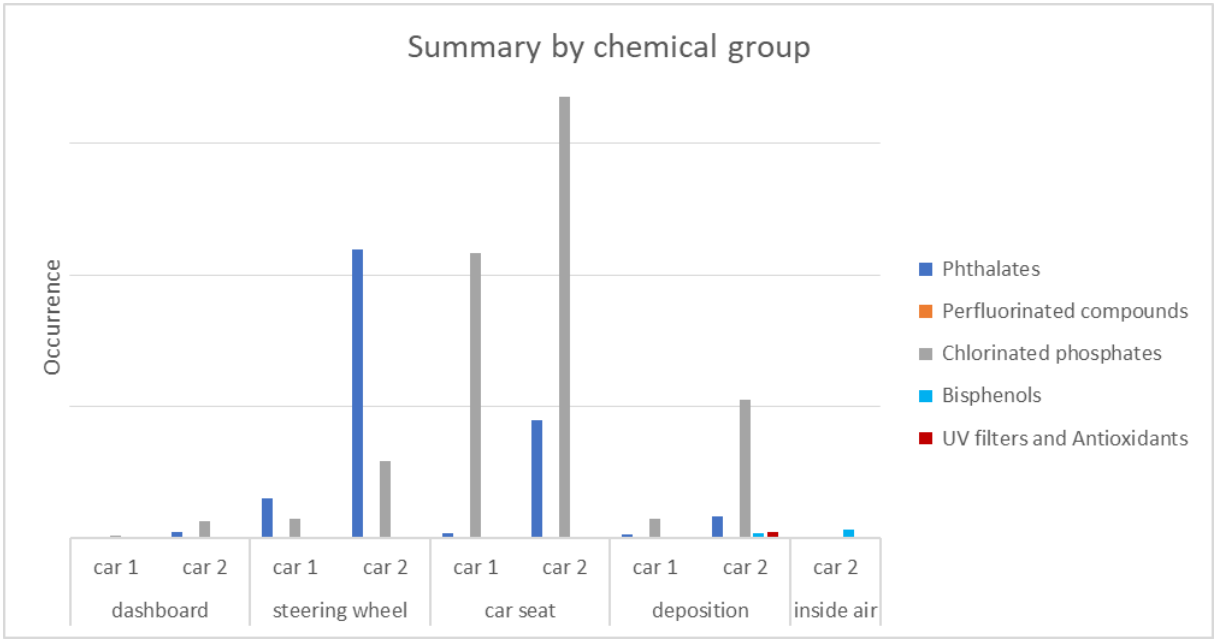

Figure 11: Level of phthalates, chlorinated phosphates, bisphenols and antioxidants found on the surface of dashboard, steering wheel, seat, in deposition sample, and in the air inside of the tested cars. Due to confidentiality, no y-axis is given and no information on the materials in the car cabin can be supplied. Levels were blank corrected. Occurrence is used on the y-axis as it represents the concentrations measured in the PDMS which does not directly reflect concentrations in the materials.

The measurements show that differences can be observed between the different areas in relation to the emission from the specific surfaces. The measurements are in line with what would be expected from the various parts (engineering judgement). To be able to assess how the substances affect human health, not only the presence of a substance is enough, firstly the level needs to be measured, and then combine that with the route of exposure and time of exposure. This has not been part of the scope of this study; however, initial calculations made by Volvo Cars show no health effects from the levels measured during exposure time.

SVOCs found previously in gas phase (unpublished data) inside tested cars were also detected using surface diffusion sampling (See Table 7), confirming that these substances come from the car's interior. Note that here as well, very high temperatures were used to provide measurable levels of these substances.

Table 7: Comparison of substances found with surface diffusion sampling and SVOCs in the gas phase.

Substance CAS no.	Substance short name	Passive diffusion surface sampling	SVOC in gas phase (temp. at the highest concentration)
53306-54-0	DPHP	car 1 seat	80˚C
3648-20-2	DuDP	car 1 seat	80˚C
115-86-6	TPhP	car 1 steering wheel	80˚C
13674-87-8	TDCPP	car 1 seat	80˚C
25068-38-6	BPA	car 2 inside air	80˚C
128-37-0	BHT	car 1 seat & deposition	40˚C
1843-05-6	Octabenzone	car 2 deposition	80˚C

Review of the Mistra SafeChem tools

In silico prediction tools from the SafeChem toolbox

What worked well regarding the *in silico* prediction tools:

- The ease of use and the range of endpoints covered by the models. WP3 was contacted and supplied with a list of SMILES for the substances of interest and could in short time provide the case study with a large list of *in silico* predictions for these substances. The models will be even easier to use in the future as WP3 is working on creating a common interface, connecting all three of the models, making the in silico toolbox a valuable addition to already existing models.

- Experts from WP3 were available for providing feedback regarding the results from their models.

- Model outputs were provided with predictions regarding the confidence in the results, e.g. “Prediction with high confidence” or “Out of domain”.

- The results were provided in an easy-to-use format (Excel).

Limitations of the in silico prediction tools, for this case study were that:

- The tools are limited to hazard predictions (qualitative data) and do not yet match all needs for an LCAA (quantitative data). External tools and databases need to be used to generate additional input data required for the use of the USEtox model.

- The hazard predictions from the tools can sometimes be hard to interpret and the tools can feel like a black box. It is not always clear which data is used to train the models and how certain outputs, e.g., substances predicted to have both antagonistic as well as protagonist effects for a certain endocrine disrupting endpoint, should be interpreted.

- The existing models currently cannot be used to predict hazards for substances such as metals, nanomaterials or natural oils as they fall outside the domain of these models. This is a general limitation of many existing *in silico* prediction tools. For companies focusing on screening alternative substances and materials using a different type of chemistry, this can be an issue.

- The interface for the users was not developed at the time of testing and can therefore not be evaluated by the case study. This is important to make the tool industry friendly.

Recommendations for further development:

- Better documentation for the tools and more transparency regarding the input data and data quality.
    - In older models such as EPISUITE for example, the user would often be presented with two or more values for the suggested molecule. One would be the predicted value and the others would be existing expert data, where available, that was used to train the model. It could be helpful for the user to be more transparent with conflicting results if they were presented with this data where available. This was supplied in some of the models, but not all.
- Integration of other SafeChem tools such as those for the prediction of biodegradability and transformation products. In that way, the toolbox can automatically screen for potentially hazardous transformation products.
- Further development of the toolbox to generate quantitative data that can then be used as input to other tools, such as USEtox.
- Further development of the toolbox to generate all results in a default format. So that the output can easily be used for further processing. Now all three models generate results in their own format.
- To avoid uncertainty in the future in how the in silico data is used and interpreted, the in silico toolbox could be complemented with the addition of a summary function in which the data is automatically summarized according to best practices, as developed by experts in the SafeChem project
- Experimental data driving the models used can also come with a large uncertainty, see for example the predictions for endocrine disrupting potential where experimental data can sometimes be hard to interpret. Reliable experimental data is essential for correctly training new models.

Life cycle based alternative assessments and chemical footprint assessments

What worked well regarding these tools:

- The workshops and presentations on USEtox were very informative and helped users understand the thinking behind the models and how they could be used.
- Direct contact with the USEtox developers that supplied the case study with input data (where available), bug fixes and feedback on the use of the model and recommendations regarding the data generation.
- The adaptability of the USEtox model. In this case a scenario had to be built to better reflect the indoor car environment. It was easy to setup a basic environment.

Limitations of the toolbox for this case study were:

- The data requirements for running the USEtox model. When data is readily available, it can be relatively easy to get started with USEtox. However, when the data wasn't available, the data generation process is complex and tedious.

- It was difficult to assess the propagated uncertainty from the model output and put it into relation to the observed differences between different alternatives. In this case study, the model uncertainty was assumed to be larger than the observed differences between many of the alternatives screened, thereby limiting its use.

- The USEtox model could not be used for screening some of the alternatives (e.g. the natural oil derivatives) as these were outside of its domain, making it difficult to screen all the alternatives in the same way.

- The absence of a user-friendly interface creates problems for incorporating the tool in regular work streams in the industry.

- While the USEtox model is flexible enough to simulate different environment, some parameters such as changing ventilation rates were harder to model within the time constraints of the project.

Recommendation for further development:

- To set-up clear guidelines or a data pipeline for generating input data to USEtox

    - This work is ongoing in a collaboration between WP3 and WP5 and will greatly improve how easy it is to use models like USEtox for substances that are not yet included in its database.

    - The USEtox team is also working on putting together a large dataset with input data for a wide range of substances.

- Implement a new tab, in which the outcome from USEtox is automatically processed into a summary with graphs, that makes it easy to compare between alternatives and that avoids user from overinterpreting the results.

- Set up a general workflow on how SafeChem recommends proceeding for the assessment of alternatives. While some of the tools used are similar, each of the case studies so far seems to solve the alternative assessment issue in their own way. A streamlined workflow might help avoid common pitfalls, save time by reducing the need to re-invent the wheel and help align the process so that the quality of the results can be assured.

- Develop guidelines on how to screen substances that are outside the domain of USEtox.

Passive sampling tools:

What worked well regarding these tools:

- The passive samplers offer a low cost and easy method to screen for the occurrence of SVOCs in the car cabin.

- The use of contact samplers provides a new dimension to screen for potential chemical sources which can aid in the identification of materials containing substances in need to be phased out.

- PDMS is an easy matrix to work with for the chemical analysis.

Limitations of the toolbox for this case study were:

- Suitable PDMS sheets can be challenging to obtain and prepare for use, if not ordered weeks/months in advance. This resulted in the use of two difference sources of PDMS in the study. For labs working more frequently with PDMS, this is likely not an issue.

- The use of the vacuum oven seems to significantly affect the background contamination in the PDMS sheets, that can occur during the drying phase. Not all labs will have a vacuum oven available and other options should be explored further.

Recommendation for further development:

- The use of the passive samplers for contact sampling should be explored further as it provides a valuable input to the screening process. Different media should be tested, in addition to PDMS, to provide a broader chemical spectrum.

The substitution process

The case study aimed at addressing the substitution process in an industry context, going from the identification of a substance in need of substitution, via the evaluation of alternatives to ending up with a new substitute. This was done by assessing two different cases, first based on the migration, deposition and air samples collected in a car cabin to find possible sources of suggested substances. We showed that specific substances can be traced to certain surfaces, as seen above. The second part was looking into assessment of a known substance that needed to be substituted, for example a phthalate, and looking at the in literature suggested substitute. Here we used the tools developed within Mistra SafeChem to assess the usage of looking at such an evaluation. Taking both these different processes into consideration we assessed the way for setting requirements for substances in materials.

To understand the challenges the industry is facing with a rapid change in the need for substitution the background must be taken into consideration. Substitution was and is generally mainly driven by legal requirements on different markets, along with customer demands. Together with that different specific initiatives by companies the substitutions are addressed. In the event of a substitution action, the relevant components are identified, and the substitution process is started, see Figure 12.

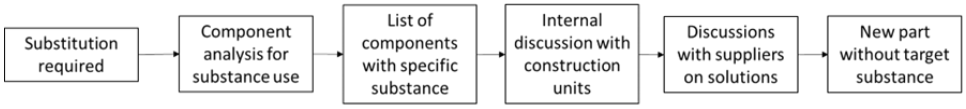

Figure 12: Overview of the substitution process.

Described here is how a possible substitution might look. A substitution action is a cooperation between different stakeholders within the company depending on the company set up. The process usually starts with identifying the target substance, the first step is to look at the relevance for the product in question. That is followed by a component analysis, where the component containing the targeted substances are identified. After identifying the components, a collaboration between the company and the supplier starts, to find the best suitable substitute. This will lead to a change in component composition and then the component with new content will be introduced.

The need seen by the industry is to increase the accuracy of the available tools to make safe substitution and contribute to the sustainable transition. The tools developed need to be user-friendly and provide results that are easy to interpret. Uncertainties in the result also need to be addressed in a clear way. The tools developed within the project are still too complex to be implemented into industrial use as they are now. However, during the project the tools have matured and become more user-friendly. The discussions between researchers developing the tools and industry using them have a great benefit in identifying the needs from both sides. This has been a strength of the project. The tool that has evolved the most is USEtox where several parts have been implemented for ease of use and a common goal for the future has been discussed, however there is still work that needs to be done.

From the industry side the need is now and waiting for a tool was not an option, so other possible ways forward were investigated. It ended up with a digital tool connecting the substances to different assessments carried out by a third party. The substances were divided into three groups, ok to use, possible use but restrictions apply and do not use, depending on the third-party assessment. This work was carried out in parallel to the thesis work by Tomáš Slaný assessing the USEtox model more in depth. As stated in his report, a lot of the assessed substances didn't show a difference and therefore third-party assessments were used in his work as well. Both these conclusions lead to the lists in Table 8 being used as a basis for the developed tool.

Table 8: Names of lists used and their references.

List name	Ref.
Global Automotive Declarable Substance List GADSL	https://www.gadsl.org/
EU Candidate List	https://echa.europa.eu/candidate-list-table
SIN List (Chemsec)	https://sinsearch.chemsec.org/
EU REACH Annex XIV	https://echa.europa.eu/authorisation-list
EU REACH Annex XVII	https://echa.europa.eu/sv/substances-restricted-under-reach
EU ELV Annex II	https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A02000L0053-20230330
EU POP Substances	https://echa.europa.eu/list-of-substances-subject-to-pops-regulation

By making this tool it is possible to proactively work with phase-outs, and make sure we have an overview of what substances to address. The lists in the tool are under constant review to make additions and deletions.

In a perfect world substitution would not be an issue and all parts and materials were already in line with circular use. However, that is not the case right now and might still take some time to achieve as the knowledge increases. Here the increased knowledge in human- and eco-toxicology, circularity and environmental impacts needs to be taken into consideration. The industry must have the tools to work proactively with substitution to increase the speed for the circular transition when it comes to chemical usage. These tools include both screening tools for chemical toxicology along with increased focus on safe substitutes which could have the wanted properties. This environmental challenge needs to be addressed as a whole.

Conclusion

At the moment, it is difficult to see an immediate widespread use for the industry for working with similar case studies due to its complexity. The data generation for further use in the LCAA can be very complex and time consuming, but also the lack of a common step by step procedure to do an alternative assessment using the tools can be a challenge. In this case study, for example, it took a master student half a year to do an assessment without reaching a clear answer on which alternatives that were preferred.

That said, the toolbox does show a strong potential to be able to meet industry needs (e.g. Volvo Cars) and several of the challenges and limitations that were mapped in this deliverable are already being addressed in ongoing work packages.

The passive sampling approach using the contact samplers also showed great potential to be used in identifying emission sources of hazardous substances in the car cabin environment. While this approach will not work for all substances, it will likely be useful for many semi-volatile organic substances.

A recommendation from our case study would be to focus on the following key points:

- Expand the in silico predictions to also include quantitative data that can be used for USEtox
- Focus on the usability of USEtox for non-researchers
- Develop a common step by step workflow that companies can follow for their LCAA, using the SafeChem toolbox
- Further develop and standardize the use of the passive samplers used for contact sampling

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About Mistra SafeChem

Mistra SafeChem is a research programme with the vision
to enable and promote the expansion of a safe, sustainable, and green chemical industry.

The programme is developed with the twelve principles of green chemistry as a fundament.

The research combines the potential of innovative manufacturing processes,
tools for hazard and risk screening, and life cycle assessment
with ambitions and opportunities for the development and growth
of a safe and sustainable chemical industry.

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