Journal Pre-proof

Assessment of baby Bibs. GC-MS screening, migration into saliva and insight of toxicity with QSAR tools

Chandisree Rajbux, Joel Pereira, Maria do Céu Selbourne, Ana Rita Pinto, Fátima Poças

PII:	S0956-7135(19)30540-7
DOI:	https://doi.org/10.1016/j.foodcont.2019.106951
Reference:	JFCO 106951
To appear in:	*Food Control*
Received Date:	21 August 2019
Accepted Date:	12 October 2019

Please cite this article as: Chandisree Rajbux, Joel Pereira, Maria do Céu Selbourne, Ana Rita Pinto, Fátima Poças, Assessment of baby Bibs. GC-MS screening, migration into saliva and insight of toxicity with QSAR tools, *Food Control* (2019), https://doi.org/10.1016/j.foodcont.2019.106951

Title
Assessment of baby Bibs. GC-MS screening, migration into saliva and insight of toxicity with QSAR tools

Chandisree Rajbux[1], Joel Pereira[1], Maria do Céu Selbourne[1], Ana Rita Pinto[2], Fátima Poças[1,2]*
1- Universidade Católica Portuguesa, CINATE, Escola Superior de Biotecnologia
2- Universidade Católica Portuguesa, CBQF - Centro de Biotecnologia e Química Fina – Laboratório Associado, Escola Superior de Biotecnologia, Rua Diogo Botelho 1327, 4169-005 Porto, Portugal

* Corresponding author: mpocas@porto.ucp.pt

1. Introduction

Plastic baby Bibs are used extensively today, having replaced the traditional textile ones. According to the European framework legislation (Regulation (EC) No 1935/2004), a food contact material (FCM) is: i) an article or material which is intended to be in contact with food; ii) is already in contact with food and were intended for that purpose; iii) can reasonably be expected to be brought into contact with food or to transfer their constituents to food under normal or foreseeable conditions of use. During its use, the baby spilt food and saliva on the Bib, which is then typically fed again into the baby mouth, by the parent (care-taker). The migration of chemical substances directly into the food that the baby spilled on the Bib before swallowing it or the migration into the saliva following ingestion mixed with the food is the main concern. Baby plastic Bibs should, therefore, be considered FCM materials and should comply with the applicable rules laid down in regulation (EU) No 10/2011, namely the overall migration limit of 60 $mgkg^{-1}$ of food and any specific migration limit for each authorized substance entering the composition of the material.

However, often stakeholders do not consider Bibs as FCMs and tend to frame these products in the clothing sector or as toys because they may be handled by the baby, and not as FCMs. Consequently, these products are not always subjected to safety evaluation, and the ones often entering Europe from third world countries, may not comply with the rules applicable to FCMs. Studies focusing in baby Bibs in the context of FCM have not been reported. Most studies targeted baby bottles, nipples and teethers or toys, and assessed migration of phthalates, bisphenol A, generally endocrine disruptors (Simoneau et al., 2011 and 2012, Simon et al., 2016, Onghena et al. 2016, Szczepańska et al. 2016, 2017), and more recently silver nanoparticles (Jeong et al. 2018). Bibs were included in a Canadian study but specific to polyfluoroalkyl substances (PFASs) in consumer

products (clothing, apparel, and children's Items) (CEC, 2017). The present work aimed at to detect and identify, by GC-MS analysis, potential migrants in Bib samples from several European countries, and to determine the migration of the chemicals into the artificial saliva.

To evaluate health risks of a migrating substance, its toxicological properties have to be considered together with the exposure of consumer. For FCM assessment, the European Food Safety Authority (EFSA) demands that the greater the extent of migration, the more toxicological information is required on the substance, but genotoxicity data, commonly evaluated through the bacterial reverse mutation assay (Ames test) is always required (Poças et al., 2007). It is well recognised that only a limited number of substances used in FCMs, particularly in those non-plastic without harmonised legislation chemicals, have been assessed (EFSA, 2012; Geueke et al., 2014). Furthermore, for non-intentionally added substances (NIAS) or when FCMs referentials are not followed, it can be anticipated a lack of toxicological data required for risk assessment.

Quantitative Structure-Activity Relationship (QSAR) modelling is being increasingly developed and applied to screen, prioritise and replacing the efforts in toxicity testing (Van Bossuyt et al., 2017; Pieke et al., 2018; Honma et al., 2019). This approach was followed for further analysing the substances detected in the Bibs. The chemical structure-based classification of Cramer Classes (Cramer, 1976), with increasing degree of potential oral systemic toxicity (Pavan et a.l, 2008) was applied to all substances detected in the Bibs samples. For the detected substances lacking a legal background support, namely those that were not listed and not evaluated, in order to gain insight on the possible adverse health effects QSAR models were applied to the three endpoints carcinogenicity, mutagenicity and reproductive toxicity (CMR).

2. Materials and Methods

2.1. Samples

Twenty-two Bibs (Figure 1) were purchased from all around Europe through various commercial stores and through members of the JRC EURL-NRL network for food contact materials. Most of the Bibs were made of PEVA and a few of them were composed of PA and PE. Some of the samples included a back or a rim in cotton. Table 1 presents the main characteristics of the Bibs. The samples were analysed by chromatography coupled with mass spectrometry (GC-MS) to screen the chemicals entering the composition of the plastic materials or the printing inks that could migrate into the food, saliva or be transferred into the baby skin.

2.2. Sample preparation for qualitative and semi-quantitative analyses

Approximately 1 g of each sample was cut into small pieces and extracted with 10 mL of DCM with internal standard for 24 hours at 40 °C. DCM was subjected to ultrasound (30 min), followed by centrifugation 5 min at 690 g and filtration using 0.045 mm Polytetrafluoroethylene (PTFE) filter into the GC vials. Benzophenone deuterated-10 (BP-d10) (Isotec-Sigma Aldrich®) was used as internal standard for semi-quantification (final concentration in the extraction medium was 0.047 mgL^{-1}), assuming the same response factor for all substances. The results were then translated into the concentration in the Bib and into the migration assuming a total mass transfer and the conventional ratio of 6 dm^2/Kg food.

2.3. GC-MS analyses of the DCM extracts

A GC system Bruker GC456 (Bremen, Germany) in combination with a triple quadrupole SCION TQ mass spectrometer and equipped with a Combi-pal (CTC analytics, Switzerland) automatic injector was used for analysis. The vector gas used was helium of high-purity grade (99.999%) at a constant flow rate of 1 $mLmin^{-1}$, and the transfer line

temperature was set at 300 °C while the source temperature was 320 °C. MS detection was carried out in Electronic Impact (EI) at 70 eV and full scan mode between 33 and 700 m/z. The mass spectra for each compound was collected and compared with those from NIST Mass Spectral Library (Version 2.2, built in June 2014)and a Match factor higher than 700 was considered. Furthermore, most of the identified substances were already included in the laboratory self-developed library allowing matching mass spectra and retention time.

The injection volume was 1 µL, the splitless injection time was 0.5 min, the inlet temperature was set at 320 °C and oven program was 40 ºC for 5 min, 10 ºC/min up to 320 ºC for 25 min. The separation column was Supelco SLB-5ms 30 m * 0.25 mm ID, Df 0.25 µm column (Sigma-Aldrich).

2.4. Migration into artificial saliva

Artificial saliva was brought into contact with printed and non-printed region of the Bibs (6 pieces of 1 cm^2 of Bib per 6 mL of saliva, according to Standard EN 1186). Migration was set at 37 ºC for 24 h in a water stirring bath. Temperature corresponds to the baby body temperature. The time period selected considered the frequency of meals, the possibility of keeping the Bib between meals and the testing repetitions required to represent migration over repeated use of the Bib. It may be considered an overestimation of the real contact time but somehow compensating the use of saliva in the replacement of food simulants specified in the legislation and the potential chewing/sucking of the Bib by the baby. Three replicas of each extract were taken for analysis. The artificial saliva (4 mL) was extracted in DCM (2 mL) containing the internal standard (BP-d10 at 0.1 mgL^{-1}). Further vortexed for 1 min; separated by centrifugation for 5 min at 2500 rpm. The lower phase was collected and analysed by GC-MS analysis.

The artificial saliva was prepared according to the BS 6684 - Specification for Safety Harnesses (Steiner et al., 1998): 4.5 g sodium chloride, 0.3 g potassium chloride, 0.3 g sodium sulphate, 0.4 g ammonium chloride, 0.2 g urea and 3.0 g lactic acid dissolved in 1000 mL distilled water adjusted to pH 4.5 to 5.0 with 5M sodium hydroxide in water. Chemicals were supplied by Sigma Aldrich and Merck.

2.5. Tools for information regarding the substances found in the samples

Regulatory status (Decernis database)

Decernis is a non-free online database, specific for substances used in food contact applications (Decernis, 2018). This database was searched to check the regulatory status of the substances according to the EU Regulations and Swiss Ordinance on printing inks.

QSAR software

The open source software application ToxTree Toxic Hazard Estimation by Decision Tree Approach of the Joint Research Centre of the European Union (www.toxtree.sourceforge.net) was used to classify the substances into the Cramer Class according to specific molecular structures that are known to trigger toxicity alerts (Bhatia et al., 2015).

The VEGA (https://www.vegahub.eu/) platform (by Istituto di Ricerche Farmacologiche Mario Negri IRCCS) includes a series of QSAR models (Benfenati et al., 2013). The substances detected in Bibs were evaluated for mutagenicity with the CONSENSUS model 1.0.2, for carcinogenicity with the model (CAESAR) 2.1.9 and for developmental toxicity with the model (CAESAR) 2.1.7.Based on the results obtained from QSAR and bibliographic survey, four Bibs were shortlisted accordingly to be subjected to migration into artificial saliva.

2.6. Statistics

A Principal component analyses (PCA) of the TIC chromatograms was performed to verify possible clustering and highlight differences between samples (Matlab R2013b, MathWorks Inc).

3. Results and discussion

3.1. Composition of Bibs – qualitative assessment

An overall number of 106 chemicals were detected in 22 baby Bib samples. The substances can belong to the plastic material or to the printing inks applied. Table 2 gives an overview of all the chemicals detected, its potential role and origin in the product and the frequency of detection. Occurrence of some compounds could be due to the polymer degradation or intermediate products used in the Bibs. Information on the status of these substances regarding their regulatory restriction or inclusion in inventories is also presented. If the substance is listed in the Regulation EU 10/2011 relative to plastics is labelled as "EU – SML" or if it is listed in Swiss legislation on printing inks as "'Swiss – SML". A label as "not evaluated" is attributed if no information regarding restrictions was found, but the substance is included in chemical inventories, such as ECHA or other industrial listings. The substance is labelled as "not listed" when it is absent from both legislation and ECHA or other inventories. In Table 2, the classification of each substance regarding its Cramer Class is also presented.

The major chemical categories of the compounds detected were cyclic ketones, alkyl benzenes, ortho phthalates, fatty acid esters, other esters, oligomers and siloxanes. Substances used as monomers, solvents and other categories such as plasticizers, UV stabilizers, antioxidants, lubricants, photoinitiators and few other known intermediate compounds from the photo initiators or the printing inks were detected in the Bibs.

The most common chemicals found were cyclohexanone (14/22) which can be used as a solvent. Alkanes were found in all Bibs, which are naturally associated to the polyolefin

materials of the Bibs and several additives were observed that are commonly used in plastic articles. Butylated Hydroxytoluene (BHT - an antioxidant) was found in 14/22, benzophenone (a photo-initiator) was found in 10/22, Benzyl butyl phthalate (BBP - a plasticiser) was found in 9/22, Tris(2,4-ditert-butylphenyl)phosphite (Irgafos 168) (16/22) and Benzenepropanoic acid, 3,5-bis(1,1-dimethylethyl)-4-hydroxy-, octadecyl ester (Irganox 1076) was found in nearly all the samples. In association with these additives, their degradation products were also detected: 2,6-DI(Tert-butyl)-4-hydroxy-4-methyl-2,5-cyclohexadien-1-one (degradation product of BHT and found in 9/22 samples), 2,4-di-tert-butylphenol (found in 10/22 samples), 7,9-Di-tert-butyl-1-oxaspiro(4,5)deca-6,9-diene-2,8-dione an impurity or degradation of Irganox (7/22) and Tris(2,4-di-tert-butylphenyl) phosphate, which is the oxidised form of Irgafos 168 (found in 20/22 samples).

Plasticizers found included the authorised substances: 2,2,4-Trimethyl-1,3-pentanediol di-isobutyrate (Eastman TXIB), Di-butyl phthalate (DBP), Tri-butyl acetylcitrate (ATBC), Benzyl butyl phthalate (BBP), Bis(2-ethylhexyl) phthalate (DEHP) and Di-octyl terephthalate (Eastman 168).

Non-authorized substances for usage as plastic FCMs in Europe were also found: Diethyl phthalate (DEP), Di-isobutyl phthalate (DIBP), which are known for their reproductive toxicity (Yost et al., 2019). Tributyl aconitate is a NIAS substance that is present in ATBC. Whereas, Bis(2-ethylhexyl) Iso-phthalate (Iso-DEHP), which is an iso-phthalate of DEHP was reported before as it was tested for its emission from vinyl flooring (Liang et al, 2015) and Di-decyl phthalate (DDP).

Another relevant group are the substances used in printing inks, particularly photoinitiators and whitening agents and respective impurities or degradation products: benzophenone and 2,5-Bis(5-tert-butyl-2-benzoxazolyl)thiophene (UVITEX OB),

authorised in the European plastics legislation; and Methyl-2-benzoylbenzoate, 2-Ethylhexyl-4-dimethylaminobenzoate (Padimate O) and 9H-Thioxanthen-9-one, 2-(1-methylethyl)- (ITX), which are included in Swiss legislation for printing inks with specific migration limits. Sample 4210 contained several photoinitiators at the highest concentration among all Bibs.

Several other substances, that are listed in the Swiss legislation but with the restriction of a SML lower than 10 μgkg^{-1}, were also found. 1-Propanone, 2-methyl-1-[4-(methylthio) phenyl]-2-(4-morpholinyl)- (Irgacure 907); Methanone, (1-hydroxycyclohexyl) phenyl- (Irgacure 184), which was found in 4 Bibs and Ethylene glycol diphenyl ether (Leuco dye) and Benzoxazole, 2,2'-(1,2-ethenediyl) bis[5-methyl- (Brightner 135), both substances found in one sample only.

Aniline and Isophorone, that were recently excluded from the Swiss legislation due to suspicion of being CMR (Bomhard and Herbold, 2005), were detected in 1 and in 4 samples, respectively. Caprolactam a monomer of polyamide was detected in sample 4211 which was unexpected as the Bib was made of PEVA. 2-(2-Hydroxy-5-methylphenyl) benzotriazole (Tinuvin P) and 2-((2H-benzotriazo)-2-yl)-4-(1,1,3,3-tetramethylbutyl) phenol (Tinuvin 329) are known to be the UV absorbers were found in 1 and 4 samples respectively.

Di-isocyanates which can be used as monomer in polyurethane materials were found: Isophorone diisocyanate in 3 samples and the aromatic 2,4-Diisocyanate toluene and 4,4'-Methylenediphenyl diisocyanate were detected in 8 out of 22 samples. It should be noted that these latter can give origin to the formation of primary aromatic amines (but this was not tested).

Substances used as flame retardants were also detected such as tributyl phosphate and 2-Ethylhexyl diphenyl phosphate (octicizer), which are authorised in Swiss legislation with

SML. However, others like triphenyl phosphate which has a non-detectable limit (< 10 ppb) and Di-n-octyl phenyl phosphate that was "not evaluated", were also detected. In 2 of the Bibs, a cyclic dimer of Polyethylene terephthalate (PET) was found. This may be explained by the usage of recycled plastics in the production of the baby Bibs.

Further, a number of 30 substances were labelled either "non-listed" or "non-evaluated". Substances which can be related to inks (Table 2) but that were not listed or not evaluated were: Azocine, octahydro-1-nitroso-; 4-Methyl-3-phenyl-1,3-oxazolidine; 5-Methyl-3-phenyl-1,3-oxazolidine. The predicted toxicity of these non-evaluated or not listed substances is discussed in the following section. A number of substances that were not possible to identify or to attribute a potential structure were also detected.

Figure 2A shows the projection plot of PC1 and PC2 scores (first and second principal components) of the Bibs chromatograms. These PCs extracted 67% of the total variance in the samples. The scatter points indicate a main cluster with most of the samples and a differentiation of a few: samples 4221 and 4227 from the others along PC1 and a differentiation between these two along PC2. In order to highlight, PC1 and PC2 loadings are represented in Fig. 3B. Isophorone diisocyanate at 20.3 min and Oleamida at 28.1 min seems to be the substances responsible for this discrimination according to the PC1 loadings, and Erucamide at 31.3 min in PC2 loadings (Figure 2B).

3.2. Composition of Bibs – semi-quantitative assessment and estimation of migration

The concentration of each substance detected in the Bibs was semi-quantified with respect to BP-d10. The migration of each substance was then estimated by assuming migration of the total concentration determined in the Bib material and assuming a surface area of contact corresponding to 6 dm^2 per kg of food. The highest concentration detected for each substance along with its estimated migration and in which Bib those values occurred are presented in Table 2. The highest concentration of substances that occurred more

frequently (in more than 10 Bibs) such as Cyclohexanone; Benzene, 1,3-bis(1,1-dimethylethyl)-; Butylated Hydroxytoluene; 2,4-Di-tert-butylphenol; Benzophenone; Tris(2,4-ditert-butylphenyl) phosphite; Tris(2,4-di-tert-butylphenyl) phosphate; Benzenepropanoic acid, 3,5-bis(1,1-dimethylethyl)-4-hydroxy-octadecyl ester, was in a range between 0.005 to 11 $\mu g g^{-1}$ of Bib, while their estimated migration ranged from 3.87 to 65.54 $\mu g kg^{-1}$ of food, respectively.

From Table 2, it is observed that sample 4227 contained most of the compounds of interest and those showed an estimated migration from 0.005 to 167.6 $\mu g kg^{-1}$ of food. It is then followed by Bib 4219 which presented an estimated migration range between 0.005 to 12.19 $\mu g kg^{-1}$ of food. The highest estimated migration was seen in sample 4214 for butyl palmitate. This butyl ester has no restriction regarding its migration limit (Table 2). Also, another fatty acid ester - Isobutyl stearate - had a very high estimated migration of 103.9 $\mu g kg^{-1}$ of food. For the aromatic diisocyanate such as 4,4'-Methylenediphenyldiisocyanate a limit of lower than 10 $\mu g kg^{-1}$ of food applies (Table 2), but a migration of 81.24 $\mu g kg^{-1}$ of food was estimated. Additionally, a limit of 1 $m g kg^{-1}$ in the plastic material needs to be observed.

Irgafos 168 and its degradation product Irgafos 168ox had estimated migration values of 65.54 and 53.33 $\mu g kg^{-1}$ of food, respectively. There is no specific limit defined for these substances in EU legislation, which means that a 60 $m g kg^{-1}$ applies. Nevertheless, the estimated results are far below that limit. Irganox 1076 had an estimated migration of 64.38 $\mu g kg^{-1}$ of food, which is below the limit as described in the regulatory status of the substances. It was seen that most compounds were under the migration limit of 10 $\mu g kg^{-1}$ of food, they ranged between 0.005 to 10 $\mu g kg^{-1}$ of food.

Furthermore, the compounds which belonged to Cramer class 3 and labelled as “non-listed” or “non-evaluated” were checked regarding their estimated migration level in

comparison with the tier levels triggering toxicity tests for safety assessment of substances by EFSA. All substances fall in the lower tier level for which a minimum dossier with toxicity information would be required. The minimum and maximum concentrations were in the range of 0.00097 to 2.61 $\mu g g^{-1}$ of Bib. The estimated migration corresponds to 0.009 to 20.65 $\mu g kg^{-1}$ of food assuming 6 dm^{-2} of Bib in contact with food.

3.3. Predicted Toxicity

The Cramer class of each compound was identified with ToxTree. This tool indicated, that out of the 30 substances that were not evaluated or not listed, 13 belong to class I, 2 to class II and 15 to class III. The outcomes of the QSAR for predicted carcinogenicity, mutagenicity and developmental toxicity (CMR) are presented in Table 3.

In a total number of 30 substances, 5 substances were positive for CMR activity and Class 3: 2H-1,3-Benzoxazine, 6-chloro-3,4-dihydro-3-phenyl-; Azocine, octahydro-1-nitroso-; 4-Methyl-3-phenyl-1,3-oxazolidine; 5-Methyl-3-phenyl-1,3-oxazolidine; and 9,10-Anthracenedione, 1,8-dimethoxy-. All these substances except the first are probably related to printing inks or dyes used in the Bibs. The structures of these substances are depicted in Figure 3.

In terms of developmental/reproductive toxicity, it was observed that 23 compounds from different Cramer classes were predicted as toxic. The 7 compounds which were non-toxic belonged to class I, and were also not predicted as mutagenic nor carcinogenic. Exception for 1,2-Cyclohexanedione belonging to class III and was found to be positive for mutagenicity and carcinogenicity.

3.4. Migration into saliva

From the overall results above, 4 Bibs were selected to be tested for experimental migration into artificial saliva: samples 4210, 4217, 4219 and 4227. A full scan was run

for screening the compounds present in the migration solutions, and a semi-quantification against deuterated benzophenone standard was performed. Results are shown in Table 4. In all cases the experimental migration was much lower than that estimated from the concentration in the Bibs.

In sample 4210, Methanone, (1-hydroxycyclohexyl) phenyl- (Irgacure 184) was detected in an average concentration of 0.006 and 0.008 mgL^{-1} of artificial saliva in non-printed regions and printed regions, respectively. Irgacure 184 is listed in printing inks Swiss regulation with a limit of migration lower than 10 μgkg^{-1}. The experimental value is lower than this limit. As this substance is used as a photo-initiator, these results indicate set-off mechanism of ink transfer, defined as the transfer of components from printing inks into the non-printed areas of the plastic by rubbing or any other accidental activity (Aznar et al., 2016).

In sample 4217, the detected compounds were Cyclohexanone, an unknown (non-identified peak) and the additive Decanedioic acid, bis(2,2,6,6-tetramethyl-4-piperidinyl) ester (Tinuvin 770), with similar concentration values in migration solutions of both printed and non-printed regions.

In sample 4219, there were four compounds detected namely Cyclohexanone, Isophorone, a similar unknown substance as detected in sample 4217 and Tinuvin 770. Cyclohexanone was detected in both printed and non-printed extracts, although at a much higher concentration in the printed extract case - 0.182 mgL^{-1} of artificial saliva. The other three compounds were detected only in the printed regions of the Bibs. Isophorone was detected at 0.013 mgL^{-1}.

In 4227, only two compounds were detected in the migration solutions from the printed region of the sample: Cyclohexanone and 9-Octadecenamide, (Z)- (Oleamide) in concentrations of 0.004 mgL^{-1} and 0.002 mgL^{-1} of artificial saliva. Oleamide is a common

migrant used as slip agent in polyolefin and other materials (Hahladakis, Velis, Weber, Iacovidou, and Purnell, 2018). Oleamide is authorised in EU without restriction for plastic food contact materials and it is classified as Cramer class III. Cyclohexanone has a migration limit lower than 10 μgkg^{-1} in Swiss regulation. This limit is exceeded in samples 4217 and 4219, even if a conventional surface area of material per food amount is considered. Therefore, these Bib samples are not complying with legislation, regarding to cyclohexanone. Tinuvin 770 is not authorised to be used in plastics according to the EU legislation. However, is authorised as a component in printing inks according to the Swiss legislation with a SML lower than 10 μgkg^{-1}. This limit is also exceeded in sample 4217 and therefore the same considerations made above apply for this migrant. Isophorone which migrated at 13 μgkg^{-1} in sample 4219 has already been excluded from the Swiss regulation as it is a CMR positive compound.

4. Conclusions

This study focused on the assessment of chemical migration potential on baby Bibs collected in different European countries. Bibs are considered, accordingly to European legislation, as FCMs and therefore, they should comply with the applicable rules, restrictions and limits.

The Bibs were made in PEVA, except one that was in polyamide, with printed graphics. The chemical assessment showed that several components not authorised for plastics in contact with foods according to European legislation are present as intended use or as contaminants.

The chemical analyses showed as most frequently detected, the substances: cyclohexanone, alkylbenzene, alkyphenols, benzophenone and several additives and corresponding impurities or degradation products. Several non-authorised substances were detected in the Bibs, namely phthalates, light stabilizer and flame retardants.

Substances requiring further attention were the substances found that were not evaluated or not listed in either the European or Swiss legislation. Around 30 substances were detected and some of them can possibly be related to printing inks.

Results of migration into saliva indicate that migration do occur in the tested conditions. The following substances were detected in the saliva after contact with four (4/22) selected Bibs: Irgacure 184, Cyclohexanone, Tinuvin 770, Isophorone, 9-Octadecenamide, (Z)- and an unknown. The migration values for Cyclohexanone, Tinuvin 770, Isophorone, render two samples non-compliant. These results should be regarded as indicative because they are semi-quantitative and because the migration conditions used may be more severe than those in the FCMs legislation: while migration into saliva is expected to be lower than that into the prescribed simulants, the time of contact applied in the migration experiments was considerably longer than the required.

Nevertheless it can be concluded that compliance of baby Bibs with the European and Swiss legislation should be monitored. Market surveillance, monitoring Bibs composition, migration and the use of GMP by industry, seems to need reinforcement. Measures to guaranty traceability are required. It should be considered that the sensitivity to hazardous chemicals is relatively higher in babies. Studies of specific substances found are required, namely on phthalates and substances from printing inks such as photoinitiators and others are of great interest.

Acknowledgments

The authors thank to Dr. A.C. Ferreira for his assistance on chromatography data treatment.

5. References

Aznar, M., Nerín, C., Bosetti, O. (2016). Migration from printing inks in multilayer food packaging materials by GC-MS analysis and pattern recognition with chemometrics. Food Additives & Contaminants: Part A, 33(4), 703-714. doi:10.1080/19440049.2016.1155757

Bhatia, S., Schultz, T., Roberts, D., Shen, J., Kromidas, L., Marie Api, A. (2015). Comparison of Cramer classification between Toxtree, the OECD QSAR Toolbox and expert judgment. Regul Toxicol Pharmacol, 71(1), 52-62.

Benfenati, E, Manganaro, A, Gini, G. (2013). VEGA-QSAR: AI inside a platform for predictive toxicology. in CEUR Workshop Proceedings. vol. 1107, CEUR-WS, pp. 21-28, 2nd Workshop on Popularize Artificial Intelligence, PAI 2013, Held in Conjunction with AI*IA 2013, Turin, Italy, 12/5/13

CEC. 2017. Furthering the Understanding of the Migration of Chemicals from Consumer Products – A Study of Per- and Polyfluoroalkyl Substances (PFASs) in Clothing, Apparel, and Children's Items. Montreal, Canada: Commission for Environmental Cooperation. 201 pp.

Cramer, G. M., Ford, R. A., Hall, R. L. (1976). Estimation of toxic hazard—A decision tree approach. Food and Cosmetics Toxicology, 16(3), 255-276.

EFSA, European Food Safety Authority; Report of ESCO WG on non-plastic Food Contact Materials. Supporting Publications 2012:139 [63 pp.].

Geueke, B., Wagner, C.C., Muncke, J., 2014. Food contact substances and chemicals of concern: a comparison of inventories. Food Addit. Contam. Part A Chem. Anal. Control. Expo. Risk Assess 31, 1438–1450

Honma, M., Kitazawa, A., Cayley, A., Williams, R., Barber, C., Hanser, T., Saiakhov, R., Chakravarti, S., Myatt, G., Cross, K., Benfenati, E., Raitano, G., Mekenyan, O., Petkov, P., Bossa, C., Benigni, R., Battistelli, C., Giuliani, A., Tcheremenskaia, O., DeMeo, C., Norinder, U., Koga, H., Jose, C., Jeliazkova, N., Kochev, N., Paskaleva, V., Yang, C., Daga, P., Clark, R., Rathman, J. (2019). Improvement of quantitative structure–activity relationship (QSAR) tools for predicting Ames mutagenicity: outcomes of the Ames/QSAR International Challenge Project. Mutagenesis, 34, 3–16

Jeong In Choi, Song Ji Chae, Jung Min Kim, Jae Chun Choi, Se Jong Park, Hee Ju Choi, Hojae Bae & Hyun Jin Park (2018) Potential silver nanoparticles migration from commercially available polymeric baby products into food simulants, Food Additives & Contaminants: Part A, 35:5, 996-1005

Liang, Y., Caillot, O., Zhang, J., Zhu, J., Xu, Y. (2015). Large-scale chamber investigation and simulation of phthalate emissions from vinyl flooring. Building and Environment, 89, 141-149.

Onghena, M.; Van Hoeck, E.; Negreira, N.; Quirynen, L.; Van Loco, J.; Covaci, A. (2016). Evaluation of the migration of chemicals from baby bottles under standardised and duration testing conditions. Food Additives and Contaminants Part A-Chemistry Analyses Control Exposure & Risk Assessment; 33; 5; p893-p904

Pavan, M. and Worth, A. P.(2008) 'Publicly-accessible QSAR software tools developed by the Joint Research Centre', SAR and QSAR in Environmental Research, 19: 7, 785 — 799

Pieke, E.N., Granby, K., Teste, B., Smedsgaard, J., Rivière, G. (2018). Prioritization before risk assessment: The viability of uncertain data on food contact materials. Regulatory Toxicology and Pharmacology 97, 134–143.

Poças, M. d. F., & Hogg, T. (2007). Exposure assessment of chemicals from packaging materials in foods. Trends in Food Science & Technology 18(4):219-230.

Simon, C., Onghena, M., Covaci, A., VanHoeck, E., Van Loco, J., Vandermarken, T., Van Langenhove, K., Demaegdt, H., Mertens, B., Vandermeiren, K., Scippo, ML., Elskens, M. (2016) Screening of endocrine activity of compounds migrating from plastic baby bottles using a multi-receptor panel of in vitro bioassays. Toxicology in Vitro 37, 121–133

Simoneau, C.; Valzacchi, S.; Morkunas, V.; Van den Eede, L. (2011). Comparison of migration from polyethersulphone and polycarbonate baby bottles. Food Additives & Contaminants. Part A: Chemistry, Analysis, Control, Exposure & Risk Assessment, Vol. 28 Issue 12, p1763-1768.

Simoneau, C.; Van den Eede, L.; Valzacchi, S. (2012). Identification and quantification of the migration of chemicals from plastic baby bottles used as substitutes for polycarbonate Food Additives and Contaminants - Part A Chemistry, Analysis, Control, Exposure and Risk Assessment, 29(3):469-480

Steiner, I., Scharf, L., Fiala, F., Washüttl, J. (1998) Migration of di-(2-ethylhexyl) phthalate from PVC child articles into saliva and saliva simulant, Food Additives &Contaminants, 15:7, 812-817

Szczepańska, N., Namieśnik, J.,& Kudłak, B. (2016). Assessment of toxic and endocrine potential of substances migrating from selected toys and baby products. Environmental Science and Pollution Research, 23, 24890–24900.

Szczepańska, N., Kudłak, B., Nedyalkova, M., Simeonov, V., Namieśnik, J. (2017). Application of chemometric techniques in studies of toxicity of selected commercially available products for infants and children. Environ Monit Assess.189: 309

Van Bossuyt, M., Van Hoeck, E., Raitano, G., Manganelli, S., Braeken, E., Ates, G., . . . Rogiers, V. (2017). (Q)SAR tools for priority setting: A case study with printed paper and board food contact material substances. Food Chem Toxicol, 102, 109-119.

Yosta, E., Euling, S., Weaver, J., Beverly, B., Keshava, N., Mudipalli, A., Arzuaga, X., Blessinger, T., Dishaw, L., Hotchkissa, A., Makris, S. (2019). Hazards of diisobutyl phthalate (DIBP) exposure: A systematic review of animal toxicology studies. Environment International 125, Pages 579-594

Conflict of Interest and Authorship Conformation Form

Please check the following as appropriate:

√ All authors have participated in (a) conception and design, or analysis and interpretation of the data; (b) drafting the article or revising it critically for important intellectual content; and (c) approval of the final version.

√ This manuscript has not been submitted to, nor is under review at, another journal or other publishing venue.

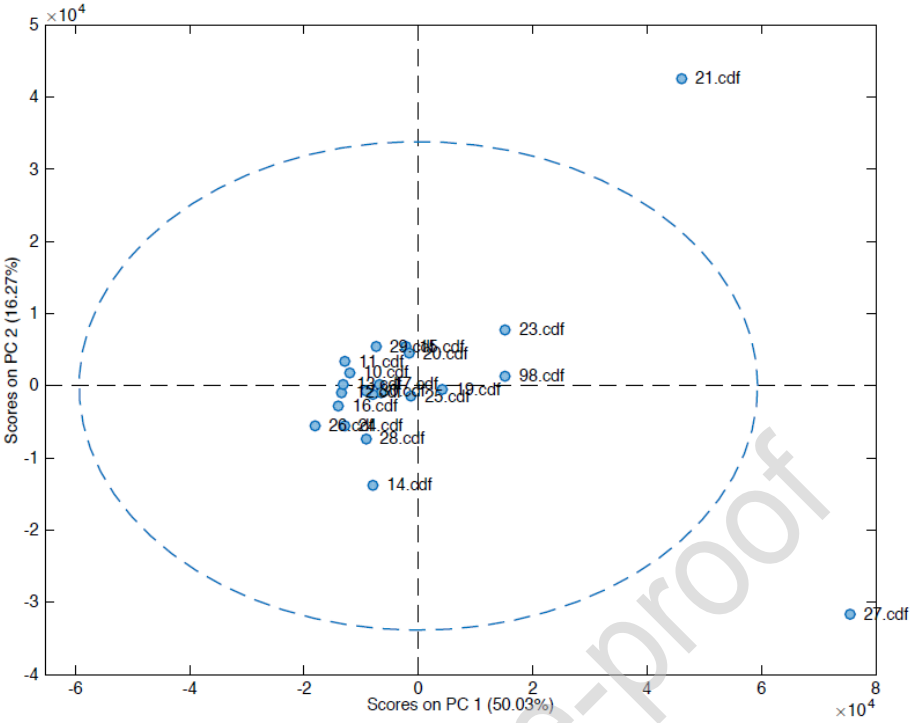
√ The authors have no affiliation with any organization with a direct or indirect financial interest in the subject matter discussed in the manuscript

- The following authors have affiliations with organizations with direct or indirect financial interest in the subject matter discussed in the manuscript:

Author's name	Affiliation

Figure 1. Examples of baby Bib samples from European market.

A)



B)

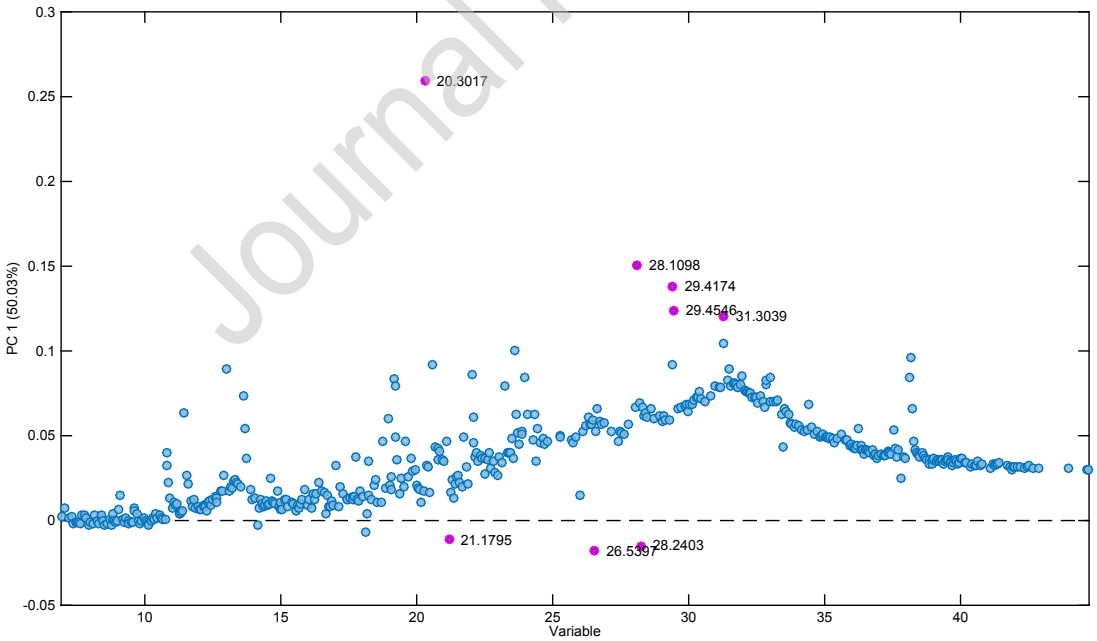


Figure 2. Plot of PC1 and PC2 scores (A) and loadings of PC1 (B)

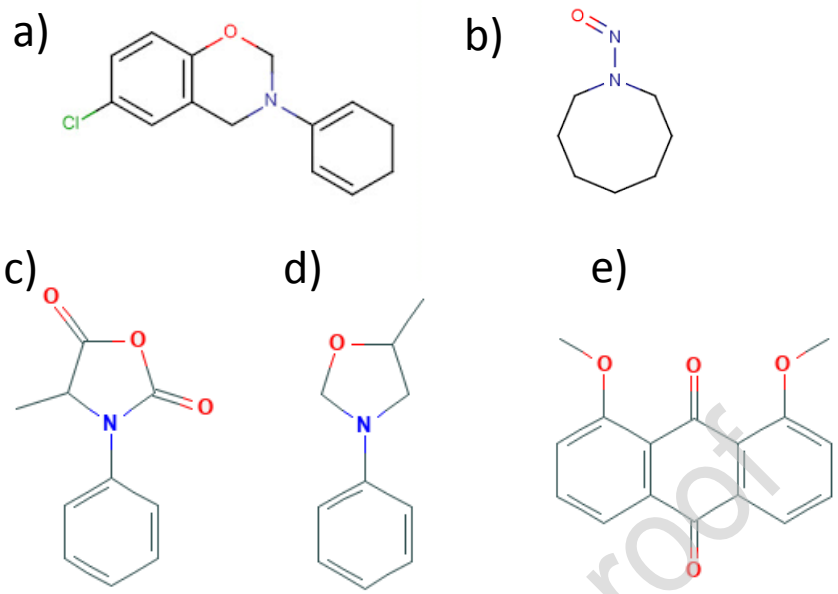


Figure 3. Structures of non-authorised substances detected in Bibs Cramer Class 3 and predicted CMR.

Title

Assessment of baby Bibs. GC-MS screening, migration into saliva and insight of toxicity with QSAR tools

Chandisree Rajbux[1], Joel Pereira[1], Maria do Céu Selbourne[1], Ana Rita Pinto[2], Fátima Poças[1,2]*

1- Universidade Católica Portuguesa, Edifício de Biotecnologia - CINATE

2- Universidade Católica Portuguesa, Edifício de Biotecnologia, CBQF - Centro de Biotecnologia e Química Fina – Laboratório Associado, Rua de Diogo Botelho, 1327 4169-005 Porto

* Corresponding author: mpocas@porto.ucp.pt

Highlights

- Baby Bibs from Europe were screened for potential migrants
- Migration into saliva render two samples non-compliant
- Thirty substances non-authorised in European or Swiss legislation were detected
- These include phthalates, light stabilizers, flame retardants and photoinitiators
- Monitoring Bibs compliance, industry GMPs and traceability are required

Abstract

Plastic baby Bibs are, according to the European legislation, food contact materials. Therefore, compositional and migration limits applicable to plastics should be observed. This work aimed at identifying potential migrants in Bibs from European market and determining the migration into artificial saliva. Bibs were subjected to screening analyses (GC-MS). Thirty substances non-authorised in European or Swiss legislation were detected: phthalates, light stabilizers, flame retardants and photoinitiators. Irgacure 184, Cyclohexanone, Tinuvin 770, Isophorone and 9-Octadecenamide, (Z)- were detected in saliva after contact with selected Bibs. The migration values render two samples non-compliant. In order to gain insight on the toxicity of migrants, QSAR tools were applied. Substances non-evaluated or not-listed were analysed with free software regarding their Cramer class (ToxTree) and their predicted mutagenicity, carcinogenicity and developmental toxicity (VEGA). Results indicate that surveillance is required: monitoring Bibs' compliance, application of GMPs and traceability.

Key words: Food contact materials; Baby bibs; Migration; QSAR; Safety evaluation; Plastics; NIAS

Table 1. Bibs samples used and some characteristics

Origin	Material	Grammage (gdm^{-2})
Italy	PEVA 100%	1.77
Italy	PEVA 100%	1.04
Italy	PE/PEVA 100%	1.86
Italy	PEVA 100%	1.38
Spain	PEVA 100%	1.57
Spain	PEVA 100%	1.59
Spain	PEVA 100%	1.37
Spain	PEVA 100%	1.64
Spain	PEVA 100%	1.66
Portugal	PEVA 100%	1.61
Portugal	PEVA 100%	1.32
Portugal	PEVA 100%	1.44
Portugal	PEVA 100%	1.28
Portugal	PEVA 100%	1.28
UK	PEVA 100%	1.43
UK	PEVA 100%	1.34
UK	PEVA 100%	1.68
Slovenia	PA 100%	0.72
Slovenia	PEVA 100%	1.28
Germany	PEVA 100%	1.91
Germany	PEVA 100%	1.60
Denmark	PEVA 85%, PE 15%	2.17

Table 2. Substances detected in the Bibs, role, legal status, Cramer Class (CC) and the number of occurrences (N), SML – specific migration limit; CMR - Carcinogenic, Mutagenic and Toxic to Reproduction; QM- maximum permitted quantity, C_{max} - highest concentration, $\mu g g^{-1}$ of Bib, M_{max} – estimated migration ($\mu g kg^{-1}$ of food)

Peak	CAS	NAME	Role	Legal status/Limit	CC	N	Cmax	Mmax	Occurrence in Bib
1	120-92-3	Cyclopentanone	Food additive/ Flavouring substance	Reg.EU.No. 1334/2008	II	1	0,06	0.26	4227
2	95-47-6	o-Xylene	Precursor	Swiss - SML < 10ppb	I	1	0,13	0.55	4227
3	108-94-1	Cyclohexanone	Solvent, precursor, food additive	Swiss - SML < 10ppb	II	14	3,20	31.5	4217
4	930-68-7	2-Cyclohexen-1-one	Precursor, flavouring	Swiss - SML < 10ppb	II	1	0,06	0.56	4219
5	126-30-7	Neopentyl glycol	Additive, monomer	EU - SML = 0.05 mg/kg	I	2	0,74	5.91	4225
6	51892-04-7	2H-1,3-Benzoxazine, 6-chloro-3,4-dihydro-3-phenyl-		Not listed	III	1	0,51	2.22	4227
7	110-63-4	1,4-Butanediol	Solvent, other	EU - SML = 5 mg/kg	I	1	0,06	0.60	4219
8	103-71-9	Benzene, isocyanato-	Monomer	Not listed	I	1	0,04	0.17	4227
9	95-63-6	Benzene, 1,2,4-trimethyl-	Solvent, precursors	Swiss - SML < 10ppb	I	1	0,03	0.31	4210
10	556-67-2	Cyclotetrasiloxane, octamethyl-	Adhesives, lubricants	Swiss - SML < 10ppb	III	1	0,03	0.32	4214
11	62-53-3	Aniline	Intermediate for dyes and polymers	Excluded from Swiss because CMR	I	1	0,24	1.04	4227
12	765-87-7	1,2-Cyclohexanedione	Flavouring/ Food additive	Not listed	III	1	0,02	0.10	4227
13	104-76-7	2-Ethyl-1-hexanol	Precursor of DEHP	EU - SML = 30 mg/kg	I	1	0,05	0.47	4219
14	5989-54-8	Limonene	Natural compound/Flavouring substance	Reg.EU.No. 1334/2008	I	1	0,11	0.90	4220
15	na	Alkane				22	--	--	All
16	933-12-0	Cyclohexene, 3,5,5-trimethyl-			I	1	1,26	5.43	4227
17	111-92-2	1-Butanamine, N-butyl-		Swiss - SML < 10ppb	III	1	0,03	0.14	4227
18	541-02-6	Cyclopentasiloxane, decamethyl-	Adhesives, lubricants	Swiss - SML < 10ppb	III	4	0,94	9.29	4217
19	78-59-1	Isophorone	Solvent, inks	Excluded from Swiss because CMR	II	4	0,35	3.41	4219
20	91-20-3	Naphthalene		Present in other compounds	III	1	0,07	0.71	4219
21	1014-60-4	Benzene, 1,3-bis(1,1-dimethylethyl)-		Not evaluated	I	16	0,51	3.87	4223
22	105-60-2	Caprolactam	Monomer polyamide	EU - SML = 15 mg/kg	III	1	0,04	0.23	4211

Peak	CAS	NAME	Role	Legal status/Limit	CC	N	Cmax	Mmax	Occurrence in Bib
23	540-97-6	Cyclohexasiloxane, dodecamethyl-	Adhesives, lubricants	Swiss - SML < 10ppb	III	1	2,10	16.6	4220
24	5779-72-6	Benzaldehyde, 2,4,5-trimethyl-	Solvent, degradation of antioxidants	Not evaluated	I	1	0,03	0.36	4210
25	102-76-1	Triacetin	Solvent	EU - SML - no restriction	I	2	0,12	1.00	4216
26	4771-80-6	3-Cyclohexene-1-carboxylic acid		Not evaluated	I	1	0,02	0.17	4210
27	584-84-9	2,4-Diisocyanate toluene	Adhesives, polyurethane	EU - SML < 10ppb QM=1mg/kg	I	1	0,04	0.39	4217
28	20917-49-1	Azocine, octahydro-1-nitroso-	Possible NIAS from printing ink	Not evaluated	III	1	0,13	0.54	4227
29	20241-60-5	4-Methyl-3-phenyl-1,3-oxazolidine	Possible from pigments	Not listed	III	1	0,06	0.27	4227
30	480-63-7	Benzoic acid, 2,4,6-trimethyl		Not evaluated	I	2	0,05	0.67	4598
31	73861-82-2	5-Methyl-3-phenyl-1,3-oxazolidine	Possible from pigments	Not listed	III	1	0,31	1.36	4227
32	107-50-6	Cycloheptasiloxane, tetradecamethyl-	Silicone oligomer	Not evaluated	III	1	2,61	20.6	4220
33	10396-80-2	2,6-DI(Tert-butyl)-4-hydroxy-4-methyl-2,5-cyclohexadien-1-one	Degradation of BHT	Not listed	III	9	0,15	1.90	4598
34	128-37-0	Butylated Hydroxytoluene	UV stabilizers, antioxidant	EU - SML = 3 mg/kg	II	14	2,57	24.5	4221
35	96-76-4	2,4-Di-tert-butylphenol	UV stabilizers, antioxidant and degradation	Swiss - SML < 10ppb	I	10	2,07	8.93	4227
36	1011-12-7	Cyclohexanone, 2-cyclohexylidene-	--	Not evaluated	II	1	0,51	3.91	4228
37	1502-22-3	2-(1-Cyclohexenyl) cyclohexanone	--	Not evaluated	II	1	0,07	0.29	4227
38	4130-42-1	2,6-Di-tert-butyl-4-ethylphenol	Natural compound	EU - SML = 4.8 mg/kg	II	1	0,13	1.34	4226
39	4098-71-9	Isophorone diisocyanate	Coatings, polyurethane, adhesives	EU - SML < 10ppb QM=1mg/kg	III	3	38,79	167	4227
40	6846-50-0	2,2,4-Trimethyl-1,3-pentanediol diisobutyrate	Plasticiser (Eastman TXIB)	EU - SML = 5 mg/kg	I	2	0,39	5.05	4598
41	na	Pentanoic acid, 2,2,4-trimethyl-3-carboxyisopropyl, isobutyl ester			I	1	0,17	1.37	4225
42	84-66-2	Diethyl Phthalate	Solvent, plasticiser	Swiss - SML < 10ppb	I	6	0,79	4.94	4211
43	556-68-3	Cyclooctasiloxane, hexadecamethyl-	Silicone oligomer	Not evaluated	III	1	1,32	10.4	4220
44	10233-13-3	Dodecanoic acid, 1-methylethyl ester		Swiss - SML < 10ppb	I	1	0,01	0.07	4230

Peak	CAS	NAME	Role	Legal status/Limit	CC	N	Cmax	Mmax	Occurrence in Bib
45	126-73-8	Tributyl phosphate	Flame retardant	Swiss - SML = 0.05 mg/kg	III	2	0,34	3.94	4229
46	119-61-9	Benzophenone	Photoinitiator, UV absorber	EU - SML = 0.6 mg/kg	III	10	1,00	10.1	4226
47	24157-81-1	2,6-Diisopropylnaphthalene	Dye and pigments	Not evaluated but listed in inventories related to paper and board (BFR XXXVI)	III	1	0,01	0.05	4230
48	57122-16-4	1,3-Diisopropylnaphthalene	Related to 2,6-Diisopropylnaphthalene	Not evaluated but listed in inventories related to paper and board (BFR XXXVI)	III	1	0,00	0.03	4230
49	947-19-3	Methanone, (1-hydroxycyclohexyl)phenyl-	Photoinitiator (Irgacure 184)	Swiss - SML < 10ppb	I	4	0,28	3.61	4598
50	131-17-9	Diallyl phthalate	Monomer, cross-linking agent	EU - SML < 10ppb	II	1	0,03	0.35	4210
51	5809-91-6	Myristic acid vinyl ester		Not evaluated	I	2	0,11	0.87	4222
52	556-71-8	Cyclononasiloxane, octadecamethyl-	Silicone oligomer	Not evaluated	III	1	1,01	8.02	4220
53	1620-98-0	3,5-di-tert-Butyl-4-hydroxybenzaldehyde	Antioxidant degradation	If related to alkylbenzenes is listed Swiss - SML < 10ppb	II	1	0,01	0.06	4230
54	104-66-5	Ethylene glycol diphenyl ether	Leuco dye	Swiss - SML < 10ppb	III	1	0,09	0.40	4227
55	84-69-5	Diisobutyl phthalate	Plasticiser	Excluded from Swiss because CMR	I	3	0,03	0.29	4229
56	38061-92-6	2-Methyl-oct-2-enedial		Not listed	I	1	2,03	8.76	4227
57	na	Adipic acid, isohexyl 2-methoxyethyl ester			I	1	0,20	0.87	4227
58	18772-36-6	Cyclodecasiloxane, eicosamethyl-	Silicone oligomer	Not evaluated	III	1	0,55	4.32	4220
59	82304-66-3	7,9-Di-tert-butyl-1-oxaspiro(4,5)deca-6,9-diene-2,8-dione	Degradation, impurity of Irganox 1076	Not listed	III	7	0,56	4.31	4223
60	112-39-0	Hexadecanoic acid, methyl ester	Food additive/ Flavouring substance	Reg.EU.No. 1334/2008	I	3	0,70	9.07	4598
61	606-28-0	Methyl-2-benzoylbenzoate	Photoinitiator	Swiss - SML = 0.05 mg/kg	III	1	0,42	4.41	4210
62	693-38-9	Palmitic acid vinyl ester			I	1	0,07	0.56	4224
63	84-74-2	Dibutyl phthalate	Plasticiser	EU - SML = 0.3 mg/kg	I	1	0,00	0.02	4230
64	1235-74-1	Methyl dehydroabietate	Degradation of abietic acid (tackifier)	Not evaluated	I	1	0,03	0.11	4227
65	32624-67-2	10,18-Bisnorabieta-8,11,13-triene	Degradation of abietic acid (tackifier)	Not listed	I	1	0,01	0.14	4226

Peak	CAS	NAME	Role	Legal status/Limit	CC	N	Cmax	Mmax	Occurrence in Bib
66	2440-22-4	2-(2-Hydroxy-5-methylphenyl) benzotriazole	UV stabiliser, Drometrizole (Tinuvin P)	EU - SML = 30 mg/kg	III	1	0,05	0.53	4229
67	101-68-8	4,4'-Methylenediphenyl diisocyanate	Monomer	EU - SML < 10ppb; QM=1mg/kg	III	8	8,45	81.2	4225
68	112-61-8	Methyl stearate	Lubricant/Flavouring substance	Reg.EU No. 1334/2008	I	1	0,02	0.13	4213
69	7568-58-3	1-Propene-1,2,3-tricarboxylic acid, tributyl ester	Plasticiser (Tributyl aconitate)	Not evaluated	I	2	0,07	0.70	4219
70	5466-77-3	2-Ethylhexyl 4-methoxycinnamate	UV absorber (Parsol, Univul)	Swiss - SML < 10 ppb	I	1	0,14	1.17	4221
71	111-06-8	Butyl palmitate		EU - SML - no restriction	I	1	24,79	234	4214
72	77-90-7	Tributyl acetylcitrate	Plasticiser (ATBC)	EU - SML = 60mg/kg	III	5	0,74	7.12	4219
73	10541-83-0	Benzoic acid, 4-(methylamino)-	Photoinitiator, UV absorber	Not evaluated	I	1	0,02	0.17	4210
74	21245-02-3	2-Ethylhexyl-4-dimethylaminobenzoate	Photoinitiator, UV absorber (Padimate O)	Swiss - SML = 2.4 mg/kg	I	2	0,14	1.49	4210
75	71868-10-5	1-Propanone, 2-methyl-1-[4-(methylthio)phenyl]-2-(4-morpholinyl)-	Photoinitiator (Irgacure 907)	Swiss - SML < 10 ppb	III	1	0,05	0.55	4210
76	110-39-4	Butanoic acid, octyl ester		Swiss - SML < 10 ppb	I	1	0,09	0.87	4226
77	85-68-7	Benzyl butyl phthalate	Plasticiser	EU - SML = 30 mg/kg	I	9	0,41	4.13	4218
78	301-02-0	9-Octadecenamide, (Z)-	Slip agent (Oleamide)	EU - SML - no restriction	III	5	2,80	12.1	4227
79	646-13-9	Isobutyl stearate	Lubricant/Flavouring substance	Reg.EU.No. 1334/2008	I	2	11,01	103	4214
80	124-26-5	Octadecanamide	Surfactant	EU - SML - no restriction	III	1	0,12	0.50	4227
81	115-86-6	Triphenyl phosphate	Flame retardant, plasticiser	Swiss - SML < 10 ppb	III	1	0,08	0.77	4219
82	5495-84-1	9H-Thioxanthen-9-one, 2-(1-methylethyl)-	Photoinitiator	Swiss - SML = 0.05 mg/kg	III	3	0,05	0.46	4223
83	1241-94-7	2-Ethylhexyl diphenyl phosphate	Flame retardant (Octicizer)	EU - SML = 2.4 mg/kg	III	1	0,07	0.68	4219
84	6161-81-5	Di-n-octyl phenyl phosphate	Flame retardant	Not evaluated	III	1	0,10	0.98	4219
85	16958-85-3	Hexadecanoic acid, octyl ester		Not evaluated but in inventaries EUPIA	I	1	0,59	6.80	4229
86	117-81-7	Bis(2-ethylhexyl) phthalate	Plasticiser	EU - SML = 1.5 mg/kg	I	2	0,00	0.03	4213
87	6407-55-2	9,10-Anthracenedione, 1,8-dimethoxy-	Dyes	Not evaluated	III	1	0,02	0.18	4210
88	3147-75-9	2-((2H-benzotriazo)-2-yl)-4-(1,1,3,3-tetramethylbutyl) phenol	UV absorber (Tinuvin 329)	Swiss - SML < 10ppb	III	4	0,48	4.74	4218

Peak	CAS	NAME	Role	Legal status/Limit	CC	N	Cmax	Mmax	Occurrence in Bib
89	109-36-4	Octadecanoic acid, octyl ester		Not evaluated but listed Synoptic Document 2005	I	1	0,32	3.68	4229
90	6422-86-2	Dioctyl terephthalate	Plasticiser (Eastman 168)	EU - SML = 60mg/kg	I	1	0,16	1.51	4219
91	137-89-3	Bis(2-ethylhexyl) Isophthalate	Plasticiser (Flexol plasticizer 380)	Not listed	I	1	0,20	1.55	4228
92	1041-00-5	Benzoxazole, 2,2'-(1,2-ethenediyl) bis[5-methyl-	Whitening agent (Fluorescent Brightener 135)	Swiss - SML < 10ppb	III	1	0,03	0.13	4227
93	112-84-5	13-Docosenamide, (Z)-	Slip agent (Erucamide)	EU - SML - no restriction	III	8	2,72	23.5	4221
94	1843-05-6	Octabenzone	UV absorber (Chimassorb 81)	EU - SML - 6 mg/kg	III	2	0,07	0.58	4216
95	111-02-4	Squalene	Natural compound	Not listed	I	2	1,49	11.4	4223
96	84-77-5	Didecyl phthalate	Plasticiser	Swiss - SML < 10 ppb	I	1	Traces	--	4228
97	777-95-7	1,6-Dioxacyclododecane-7,12-dione	NIAS from polyurethane adhesive	Not evaluated but is listed in US FDA CEDI Database	I	7	1,26	12.2	4219
98	52829-07-9	Bis(2,2,6,6,-tetramethyl-4-piperidyl)sebaceate	HALS (Tinuvin 770)	Swiss - SML < 10 ppb	III	4	0,69	6.92	4218
99	na	Adipic acid, pentadecyl trans-hex-3-enyl ester			I	1	2,54	11.0	4227
100	31570-04-4	Tris(2,4-ditert-butylphenyl)phosphite	Antioxidant (Irgafos 168)	EU - SML - no restriction	III	16	8,55	65.5	4223
101	na	Ethylene Terephthalate Cyclic Dimer	Degradation from PET		NA	2	Traces	--	4227
102	95906-11-9	Tris(2,4-di-tert-butylphenyl) phosphate	Oxidised form of antioxidant (Irgafos 168ox)	EU - SML - no restriction for CAS 31570-04-4	III	20	6,62	53.3	4221
103	2082-79-3	Benzenepropanoic acid, 3,5-bis(1,1-dimethylethyl)-4-hydroxy-, octadecyl ester	Antioxidant, heat stabilizer (Irganox 1076)	EU - SML = 6mg/kg	II	21	8,40	64.4	4223
104	1662-01-7	1,10-Phenanthroline, 4,7-diphenyl		Not evaluated	III	1	0,13	0.54	4227
105	2615-18-1	1,4-Bis(4-cyanostyryl)benzene	Whitening agent	Not evaluated	III	1	0,05	0.23	4227
106	7128-64-5	2,5-Bis(5-tert-butyl-2-benzoxazolyl) thiophene	Whitening agent (Uvitex OB)	EU - SML = 0.6 mg/kg	III	3	0,16	1.54	4217

Table 3. Predicted toxicity of chemical compounds which were labelled as "not-listed" as "not-evaluated". CC – Cramer class

Peak	CAS	Name	CC	Mutagenicity (Ames test)	Carcinogenicity	Developmental Toxicity
6	51892-04-7	2H-1,3-Benzoxazine, 6-chloro-3,4-dihydro-3-phenyl-	III	Mutagenic	Carcinogen	Toxic
8	103-71-9	Benzene, isocyanato-	I	Non-Mutagenic	Non-Carcinogen	Toxic
12	765-87-7	1,2-Cyclohexanedione	III	Mutagenic	Carcinogen	Non-Toxic
21	1014-60-4	Benzene, 1,3-bis(1,1-dimethylethyl)-	I	Non-Mutagenic	Non-Carcinogen	Non-Toxic
24	5779-72-6	Benzaldehyde, 2,4,5-trimethyl-	I	Non-Mutagenic	Non-Carcinogen	Toxic
26	4771-80-6	3-Cyclohexene-1-carboxylic acid	I	Non-Mutagenic	Carcinogen	Toxic
28	20917-49-1	Azocine, octahydro-1-nitroso-	III	Mutagenic	Carcinogen	Toxic
29	20241-60-5	4-Methyl-3-phenyl-1,3-oxazolidine	III	Mutagenic	Carcinogen	Toxic
30	480-63-7	Benzoic acid, 2,4,6-trimethyl	I	Non-Mutagenic	Non-Carcinogen	Non-Toxic
31	73861-82-2	5-Methyl-3-phenyl-1,3-oxazolidine	III	Mutagenic	Carcinogen	Toxic
32	107-50-6	Cycloheptasiloxane, tetradecamethyl-	III	Non-Mutagenic	Non-Carcinogen	Toxic
33	10396-80-2	2,6-DI(Tert-butyl)-4-hydroxy-4-methyl-2,5-cyclohexadien-1-one	III	Non-Mutagenic	Non-Carcinogen	Toxic
36	1011-12-7	Cyclohexanone, 2-cyclohexylidene-	II	Non-Mutagenic	Non-Carcinogen	Toxic
37	1502-22-3	2-(1-Cyclohexenyl)cyclohexanone	II	Non-Mutagenic	Non-Carcinogen	Toxic
43	556-68-3	Cyclooctasiloxane, hexadecamethyl-	III	Non-Mutagenic	Non-Carcinogen	Toxic
51	5809-91-6	Myristic acid vinyl ester	I	Non-Mutagenic	Non-Carcinogen	Non-Toxic
52	556-71-8	Cyclononasiloxane, octadecamethyl-	III	Non-Mutagenic	Non-Carcinogen	Toxic
56	38061-92-6	2-Methyl-oct-2-enedial	I	Non-Mutagenic	Non-Carcinogen	Non-Toxic
58	18772-36-6	Cyclodecasiloxane, eicosamethyl-	III	Non-Mutagenic	Carcinogen	Toxic
59	82304-66-3	7,9-Di-tert-butyl-1-oxaspiro(4,5)deca-6,9-diene-2,8-dione	III	Non-Mutagenic	Carcinogen	Toxic
64	1235-74-1	Methyl dehydroabietate	I	Non-Mutagenic	Non-Carcinogen	Toxic
65	32624-67-2	10,18-Bisnorabieta-8,11,13-triene	I	Non-Mutagenic	Carcinogen	Toxic
69	7568-58-3	1-Propene-1,2,3-tricarboxylic acid, tributyl ester	I	Non-Mutagenic	Non-Carcinogen	Non-Toxic
73	10541-83-0	Benzoic acid, 4-(methylamino)-	I	Non-Mutagenic	Non-Carcinogen	Toxic
84	6161-81-5	Di-n-octyl phenyl phosphate	III	Non-Mutagenic	Non-Carcinogen	Toxic
87	6407-55-2	9,10-Anthracenedione, 1,8-dimethoxy-	III	Mutagenic	Carcinogen	Toxic
91	137-89-3	Bis(2-ethylhexyl) Isophthalate	I	Non-Mutagenic	Carcinogen	Toxic
95	111-02-4	Squalene	I	Non-Mutagenic	Carcinogen	Non-Toxic

Peak	CAS	Name	CC	Mutagenicity (Ames test)	Carcinogenicity	Developmental Toxicity
104	1662-01-7	1,10-Phenanthroline, 4,7-diphenyl	III	Mutagenic	Non-Carcinogen	Toxic
105	2615-18-1	1,4-Bis(4-cyanostyryl) benzene	III	Non-Mutagenic	Non-Carcinogen	Toxic

Table 4. Compounds detected in the artificial saliva migration solutions and concentration mgL-1

Sample	Compounds detected	Non-printed	Printed
4210	Irgacure 184	0.006	0.008
4217	Cyclohexanone	0.049	0.051
	Unknown	0.001	0.001
	Tinuvin 770	0.032	0.027
4219	Cyclohexanone	0.071	0.182
	Isophorone	ND	0.013
	Unknown	ND	0.002
	Tinuvin 770	ND	0.001
4227	Cyclohexanone	ND	0.004
	9-Octadecenamide, (Z)-	ND	0.002