



# New FCM and analytical tools for Risk Assessment

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# New FCM

- **Recycled polymers**
- **Bio-based polymers**
- **Natural materials**
- **Coated paper & board**
- **Silicones**

+

- **Adhesives**
- **Printing inks**



**To demonstrate the safety!!**

# Safety Evaluation of materials

- It implies the following tasks:
  - **Screening** in depth of potential contaminants: **Identification!**
  - Confirming the **absence** of BPA, PAAs, Phthalates, mineral oils, etc. (usually no detected in screening procedures)
  - Confirming the **absence** of NIAS
  - Confirming the **absence** of CMR chemicals
  - Confirming the **compliance** of the material (that involves **quantitative values** of migrants, including the oligomers)
- **RISK ASSESSMENT OF MATERIAL!**

# What happens with some new FCM

- **New unexpected migrants:**
  - pesticides
  - phytochemicals from plants & vegetables
  - allergens
- **Inappropriate simulants for testing**
- **Difficult selection of testing conditions**

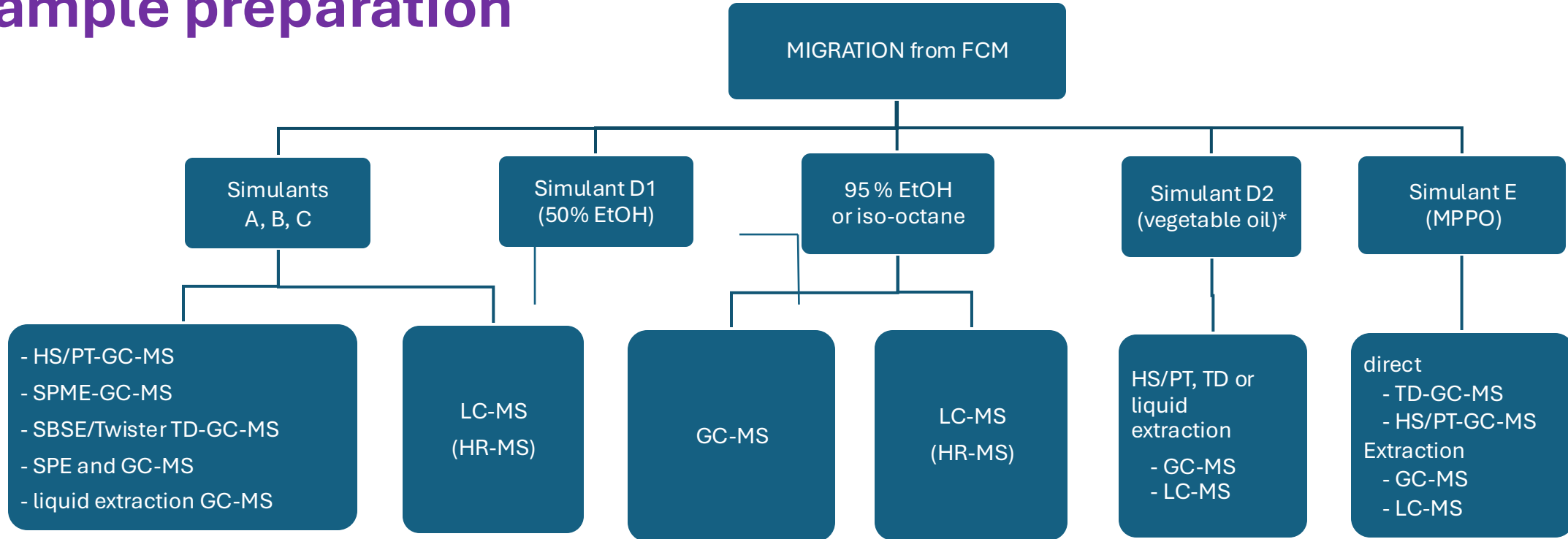
# The main points to consider

- **Decision** about the **migration tests** (leachables) to be applied
- **Decision about the analytical techniques** to be used
- Sample preparation
- Instrumental **analytical technique**
- **Data processing** and software tools required for identification.
- **Identification** of NIAS.
- **Calibration:** Instrument and substances
- **Quantification and semi-quantification**
- **Validation and Uncertainty**

**An Overview of Approaches for Analysing NIAS from different FCMs.** ILSI Europe Report Series ,  
05/04/2023. *Oldring, Peter Sherwin Williams ; Faust, Birgit; Gude,Thomas; Lesueur, Céline; Simat, Thomas;  
Stoermer, Angela; Van Hoek, Els; Nerin, Cristina*

# PROCEDURE FOR SCREENING NIAS IN MIGRATION SIMULANTS

## Sample preparation



HS headspace  
PT purge and trap, dynamic headspace  
TD thermal desorption  
SBSE stirr bar sorptive extraction  
SPME solid phase microextraction

\* Only for known NIAS, not for screening



# Identification using LIBRARIES

## In-House library (UNIZAR) in UPLC-IMS-QTOF

Using certified/pure standards in our lab. Experimental CCS values

+

Prediction models for Retention time and CCS (developed in UNIZAR)

Mol file

+

RT

+

CC

S

CPPdb (chemicals associated to plastic packaging) from Groh et al.

DOI: [10.1016/j.scitotenv.2018.10.015](https://doi.org/10.1016/j.scitotenv.2018.10.015)

FCCdb (food contact chemicals database) from Groh et al.

<https://doi.org/10.5281/zenodo.3240108>.

> 10,000 compounds with CCS and RT in the library

Song et al. J. Agric. Food Chem. 2022, 70, 9499–95

## In-House library (UNIZAR) UPLC-QTOF-MS

In-house MS/MS library  
and *mspcompiler R*  
package which contains

449 and 172 food  
packaging associated  
chemicals in positive and  
negative mode has been  
built. It Will be in public  
domain and available in  
<https://zenodo.org/record/4454648>

*Su et al 2023.*

*Anal. Chem. 2023, 95, 8780–8788*

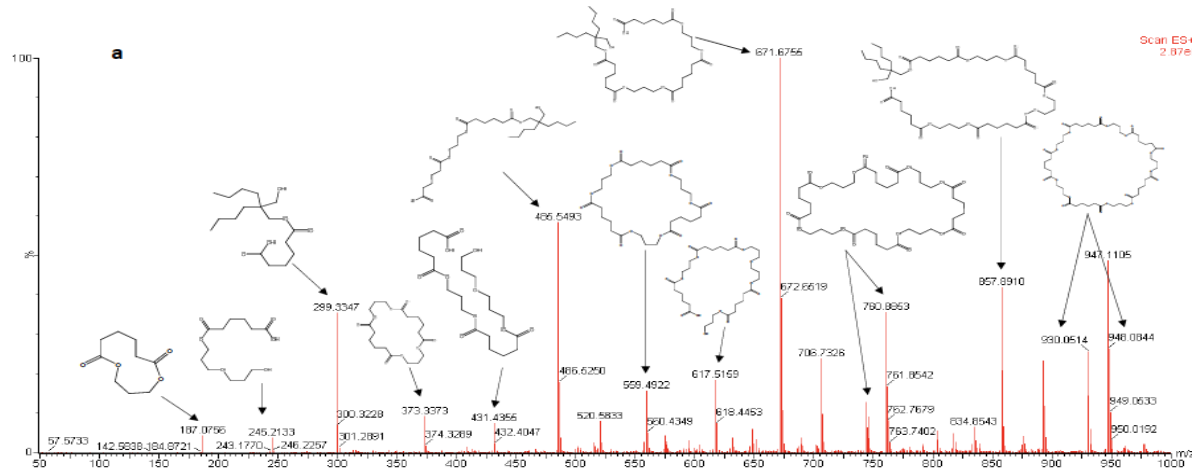


# Validation of analytical procedures

- **Use of pure/certified standards** corresponding to each compound found
- Determination of **LOD, LOQ and uncertainty**
- Determination of **recovery in case of extraction** or any sample treatment
- Use of **standard addition procedure** if it's possible (to know the matrix effect)
- **Confirm the absence of any concern** potential compound by spiking the migrants (leachables) with double and half concentration of LOD (FDA criteria)

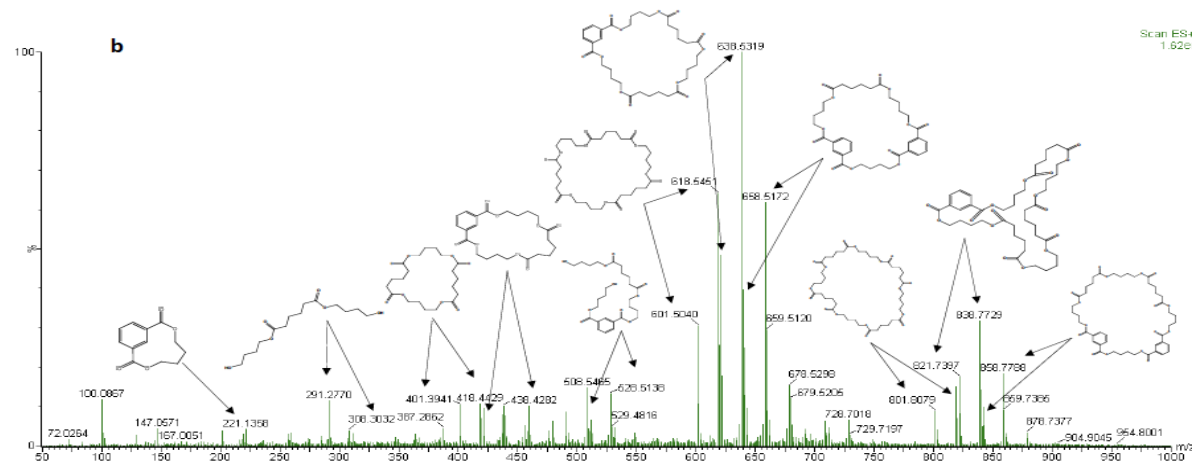
# Migration of oligomers from biopolymers

Simulant D2 (ethanol 95%)



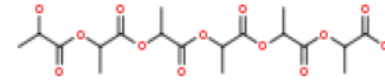
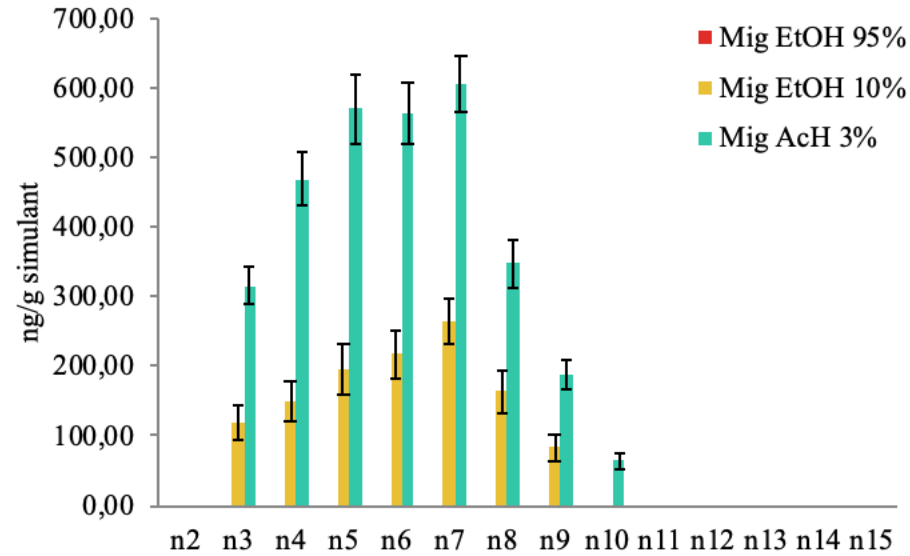
Identified by UPLC-QTOF-MS and DART-SVP

From PLA

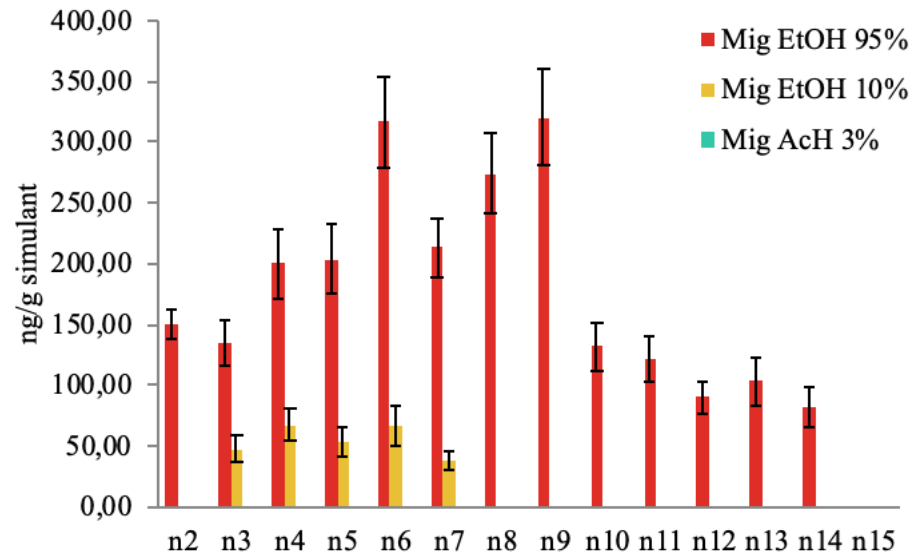
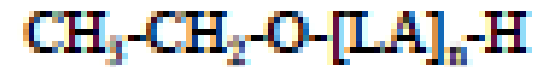
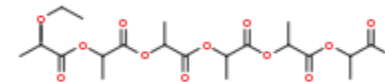


From starch-based biopolymer

# Migration from PLA



60°C, 10 days

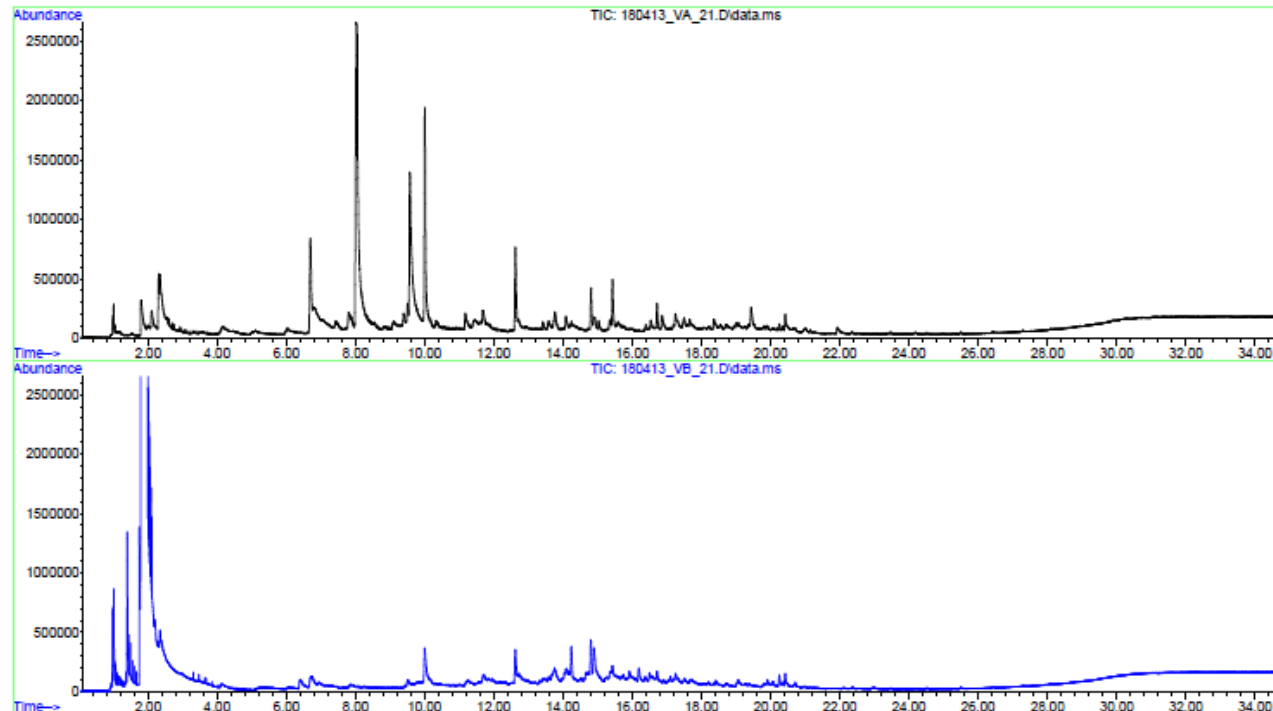


Ubada, S.; Aznar, M.; Alfaro, P.; Nerin, C. *Analytical and Bioanalytical Chemistry*, 2019, 411, 3521-3532  
DOI:10.1007/s00216-019-01831-0

## Migration from paper cups from coffee machines

2 h/70°C

Esther Asensio, Teresa Peiro and Cristina Nerín  
Determination of the set-off migration of ink in cardboard-cups used in coffee vending machines  
*Food and Chemical Toxicology*, **2019**, 130, 61-67;  
DOI: 10.1016/j.fct.2019.05.02



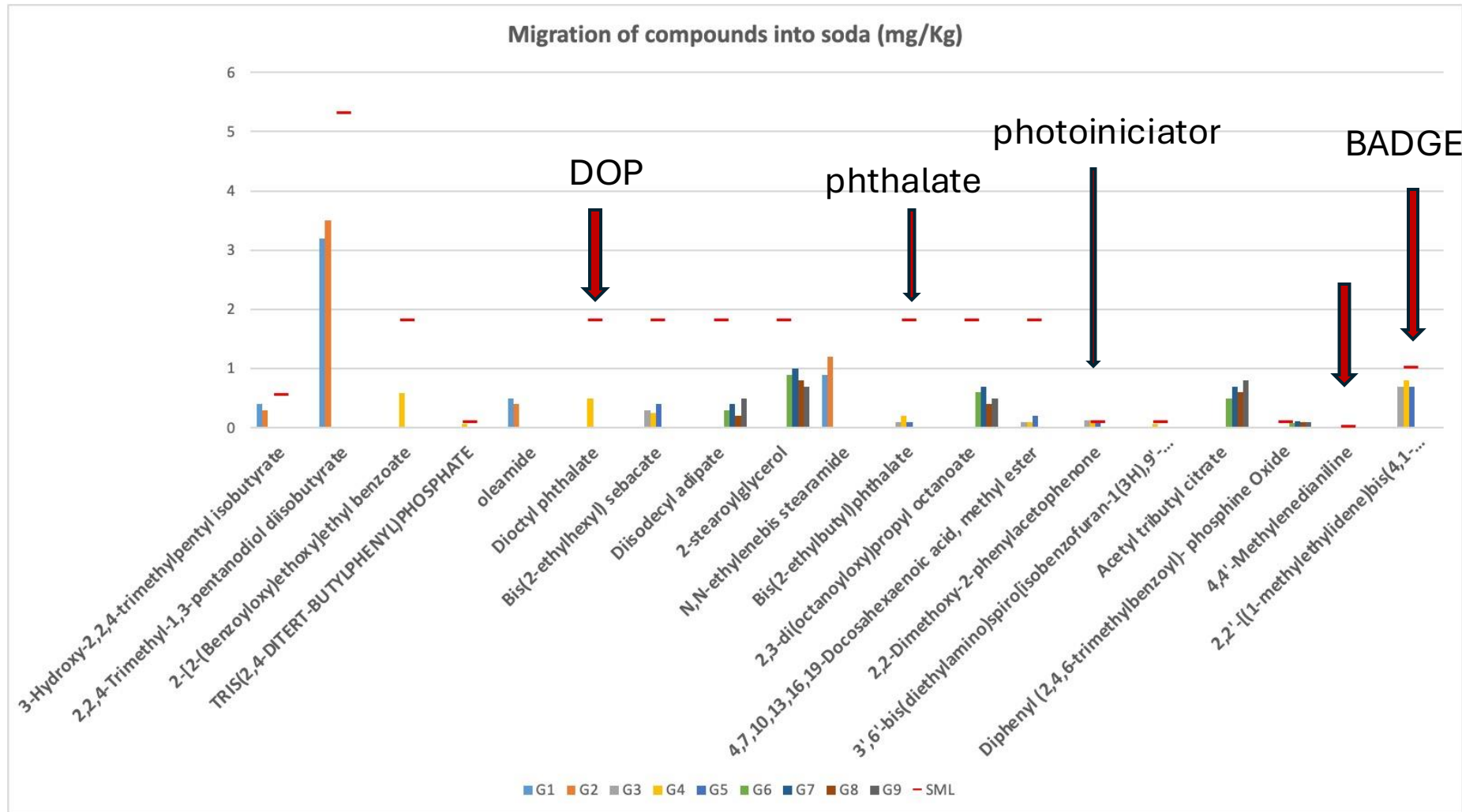
Sample A

Sample B

HS-SPME-GC-MS (DVB/CAR/PDMS) con columna capilar HP-5MS

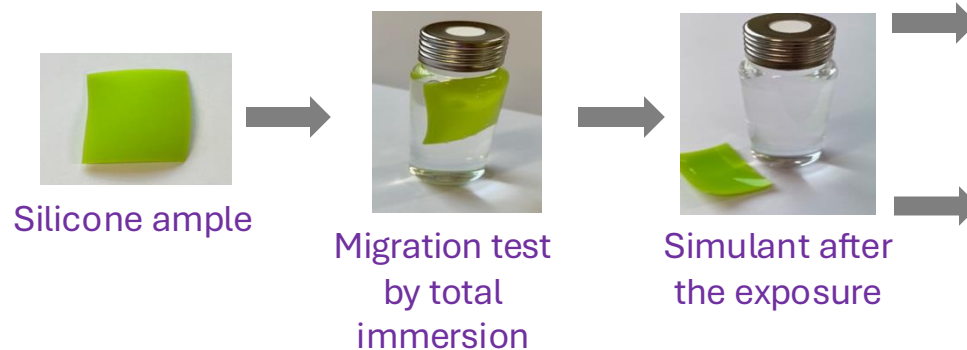
Migration from 0.48 ug/Kg para 3,5-di-tert-butyl-4-hydroxybenzaldehyde<sup>b,d</sup> in **simulant C** to  $1942.5 \pm 414.9$  ug/Kg for ATBC en **simulant D1**

## Migration of non volatile compounds from paper straws



## Migration tests and criteria applied

- Weight lost  $<0.5\%$  (To confirm the post-curation)
  - Dry in desiccator for 48 h at room temperature and heat at  $200^{\circ}\text{C}$  for 4 hours
- Migration tests:
  - 4 h at  $100^{\circ}\text{C}$  (baking molds)
  - 8 h at  $100^{\circ}\text{C}$  (molds for other applications)
  - Ethanol 50% (worst case scenario)
  - Ethanol 95% or edible oil are not appropriate



Analysis of volatile  
substances by HS-  
SPME-GC-MS

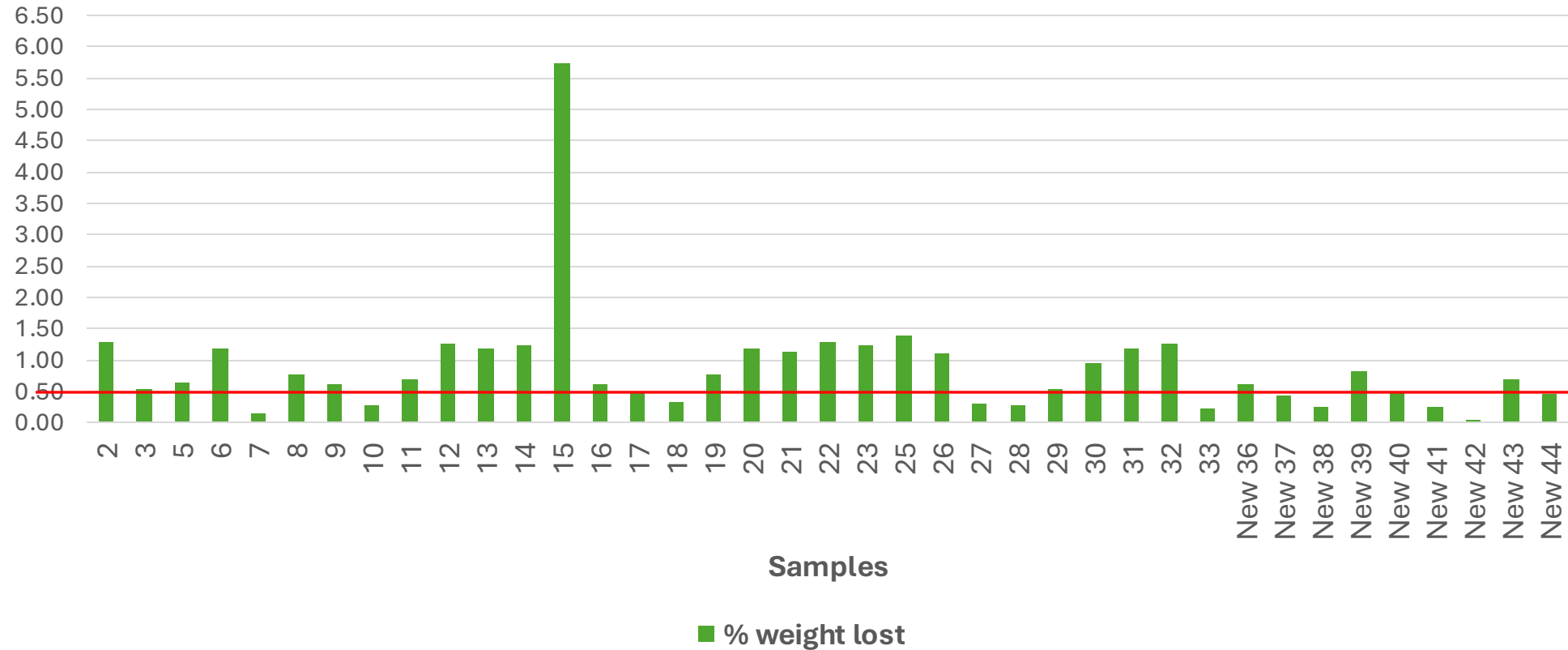


Analysis of non volatile substances by  
UPLC-IMS-QTOF/VION e UPLC-QTOF-MS<sup>E</sup>



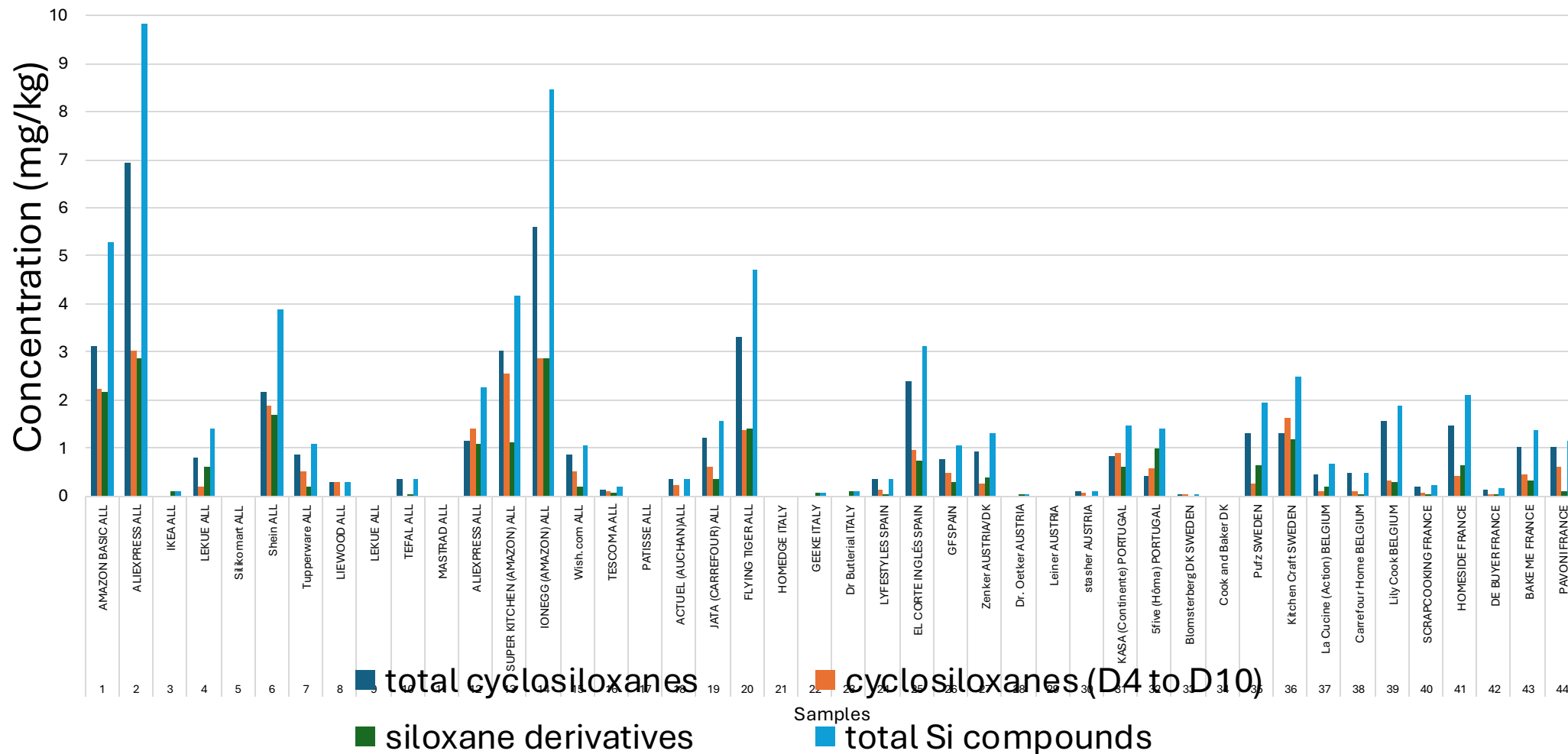
# Weight lost before using

% weight lost



The limit

# Quantitative analysis of volatile siloxanes after 3rd migration



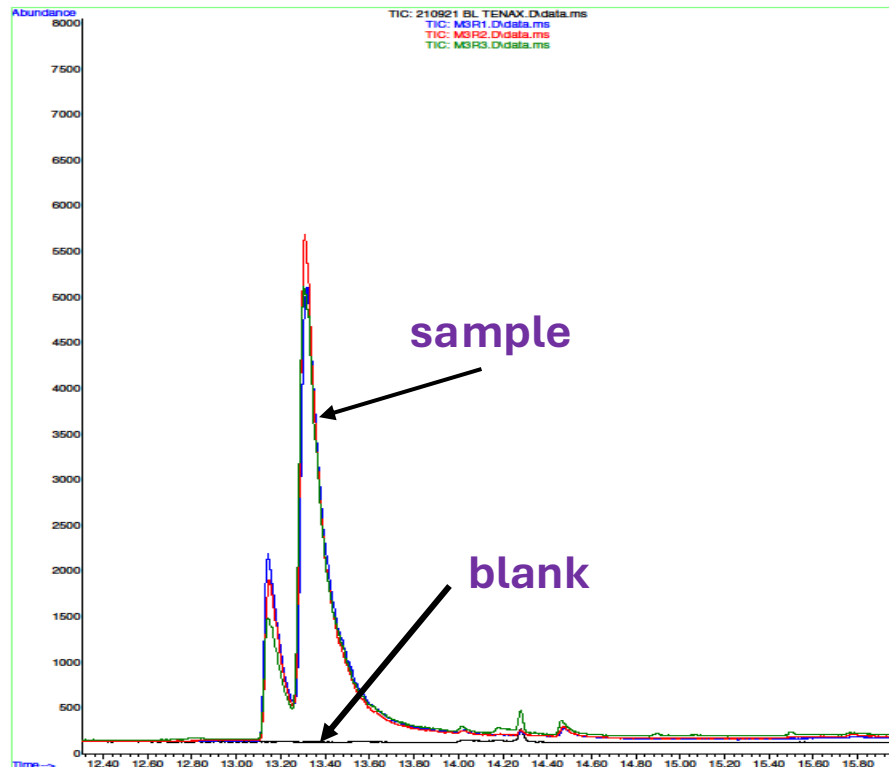


# Adhesives

## Migration of surfynol (surfactant) from adhesive

Surfynol: 2,4,7,9-tetrametil-5-decino-4,7-diol (CAS 126-86-3)

File :C:\gcms\1\data\QUIMOVIL\210921 BL TENAX.D  
Operator : MAGDA  
Acquired : 21 Sep 21 9:10 am using AcqMethod SIM QUIMOVIL.M  
Instrument : 5975B inert XL MSD  
Sample Name : 210921 BL TENAX  
Misc Info :  
Vial Number : 9



UPLC -qTOF-MS

Simulant	M1	M3	M5
Tenax	447 ± 8 µg/dm <sup>2</sup>	377 ± 7 µg/dm <sup>2*</sup>	370 ± 7 µg/dm <sup>2</sup>
Simulant	M1	M3	M5
Tenax	2.68 ± 0.7 mg/Kg	2.26 ± 0.5 mg/Kg*	2.22 ± 0.5 mg/Kg*

LOD 15 µg/Kg, ppb

SML = 50 µg/Kg

Nerin et al *Food and Chemical Toxicology* 113 (2018) 115–124  
<https://doi.org/10.1016/j.fct.2018.01.044>

García Calvo et al. *Food and Chemical Toxicology* 146 (2020) 111849  
<https://doi.org/10.1016/j.fct.2020.111849>



# RISK ASSESSMENT OF NIAS

EUROPEAN LEGISLATION (EU/10/2011)

NATIONAL LEGISLATION

TOXICITY REPORTS

**NO TOXICITY DATA**



Threshold of Toxicological Concern (TTC) approach  
(not suitable for carcinogenic, mutagenic or reprotoxic compounds)

**CRAMER RULES**

## TOXICITY CLASIFICACION-Cramer rules (Toxtree v1.51)

**Class I (Low)**

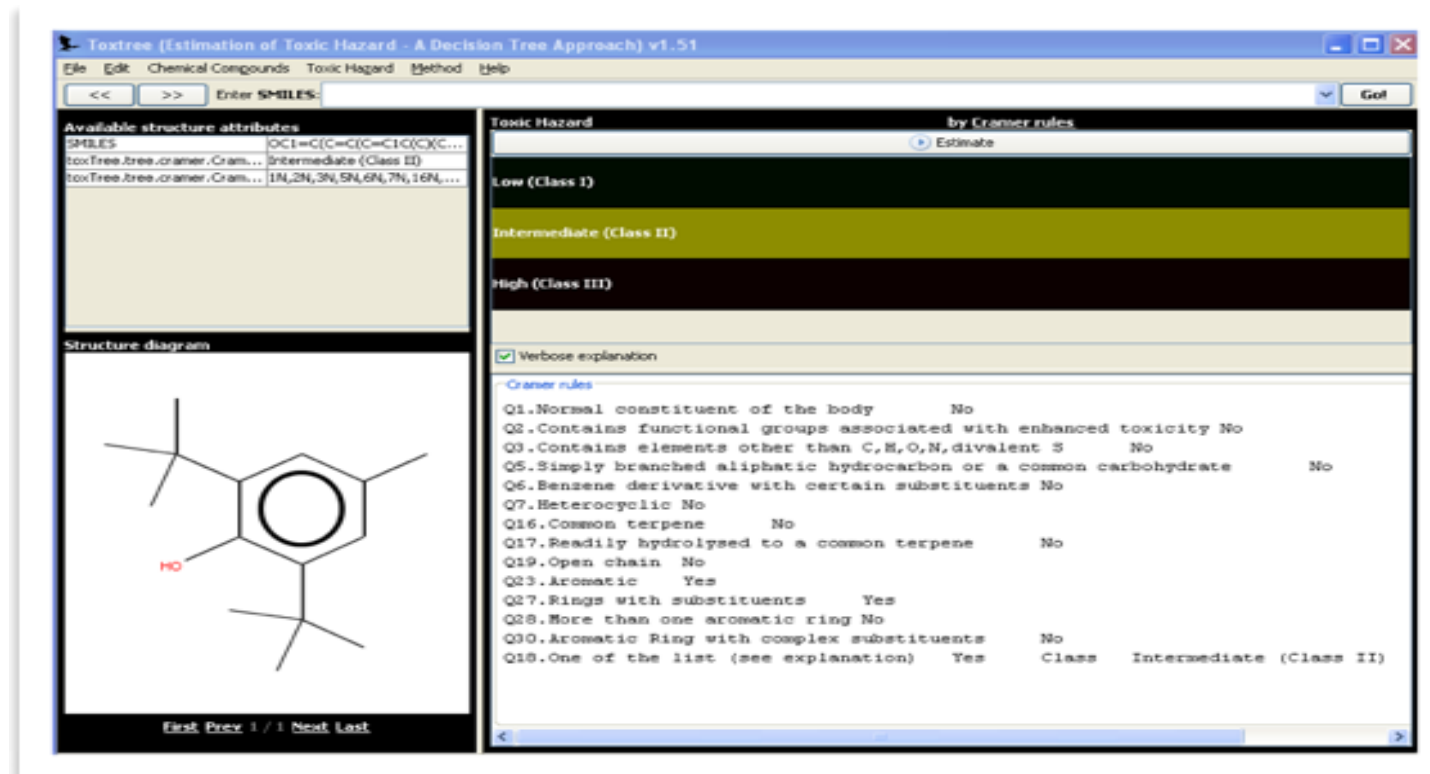
**<1.8 mg/person/day**

**Class II (Medium)**

**<0.54 mg/person/day**

**Class III (High)**

**0.09 mg/person/day**



The screenshot shows the Toxtree v1.51 interface. On the left, the 'Available structure attributes' section lists SMILES, and the 'Structure diagram' section displays a chemical structure of a substituted benzene ring with a hydroxyl group and two tert-butyl groups. On the right, the 'Toxic Hazard' section shows the classification 'Intermediate (Class II)' highlighted in yellow. Below this, the 'Cramer rules' section lists various rules (Q1-Q10) with their corresponding 'Yes/No' answers and the resulting classification 'Intermediate (Class II)'.

Rule	Answer
Q1. Normal constituent of the body	No
Q2. Contains functional groups associated with enhanced toxicity	No
Q3. Contains elements other than C, H, O, N, divalent S	No
Q5. Simply branched aliphatic hydrocarbon or a common carbohydrate	No
Q6. Benzene derivative with certain substituents	No
Q7. Heterocyclic	No
Q16. Common terpene	No
Q17. Readily hydrolysed to a common terpene	No
Q19. Open chain	No
Q23. Aromatic	Yes
Q27. Rings with substituents	Yes
Q28. More than one aromatic ring	No
Q30. Aromatic Ring with complex substituents	No
Q10. One of the list (see explanation)	Yes

Final classification: **Class Intermediate (Class II)**

**EDI (Estimated Daily Intake) (mg/person/day) = Mig (mg/Kg) x 1 Kg /day/person x CF**

# Interesting References

- **An Overview** of Approaches for Analysing NIAS from different FCMS

<https://ilsi.eu/publication/an-overview-of-approaches-for-analysing-nias-from-different-fcms/>

- **Guidance** in selecting analytical techniques for identification and quantification of non-intentionally added substances (NIAS) in food contact materials (FCMS)

Food Addit Contam Part A Chem Anal Control Expo Risk Assess 2022 Mar;39(3):620-643.

doi: 10.1080/19440049.2021.2012599. Epub 2022 Jan 26.

# Conclusions

- The number of migrants from FCM can be very high and the presence of recycled materials, bio-based polymers, natural materials with adhesives and printing inks add even more and **unexpected** potential migrants.
- There are **analytical tools** BUT a combination of different technologies and instruments is required.
- **High resolution** is an **essential key** for **identification** of chemical structures.
- **Critical interpretation** of the data are needed to avoid wrong identification.
- **Databases and libraries** as well as experience are extremely important for identifying the chemicals.
- **Confirmation** always with certified standards is required.

# R+D+i Projects

(the latest ones)

- **NATURALPACK (INTERREG)**
  - **MIGRESIVES Project (EU, VI FP, Collective Research Project)**
  - **NAFISPACK Project (EU, VII FP)**
  - **SAFEMTECH (EU, IAPP, Marie Curie)**
  - AGL-04363 and AGL- 2012-37886 (Spanish Ministry of R&D&i)
  - 4 INNPACTO Projects (Spain)
  - ACTIBIOPACK
  - NANOFLEXIPACK
  - AGL-2015
  - RTI-2018
  - (RTC2019-007161-2)
  - TED2021-129138B-C21
  - PID2021-128089OB-I00
  - **FOODYPLAST (EU)**
  - **POCTEFA-ALERT-PYR 2024-2027**
  - Several Companies...
- 
- Instituto de Investigación en Ingeniería de Aragón (I3A)
  - Gobierno de Aragón
- Grupo GUIA (T53\_20R) and  
Fondo Social Europeo



**GUIA group, University of Zaragoza, Spain**



**Thank you very much  
for your attention!  
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