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Food Safety

Emerging Residues and Contaminants Control

9 May 2024

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AOAC Europe Section

- **AOAC stands for:**
  ASSOCIATION OF OFFICIAL ANALYTICAL COLLABORATION (AOAC) INTERNATIONAL

- **Our Mission**
  - AOAC Europe brings together government, industry, and academia to establish standard methods of analysis that ensure the safety and integrity of foods and other products that impact public health around the world

- **Our Activities**
  - We are organizing regularly meetings together with other European Societies
  - We are organizing workshops based on working group activities:
    - Q3 2024: Bioassay – Harmonization
    - Q3 2024: Chemical Analysis Non-Target Methods

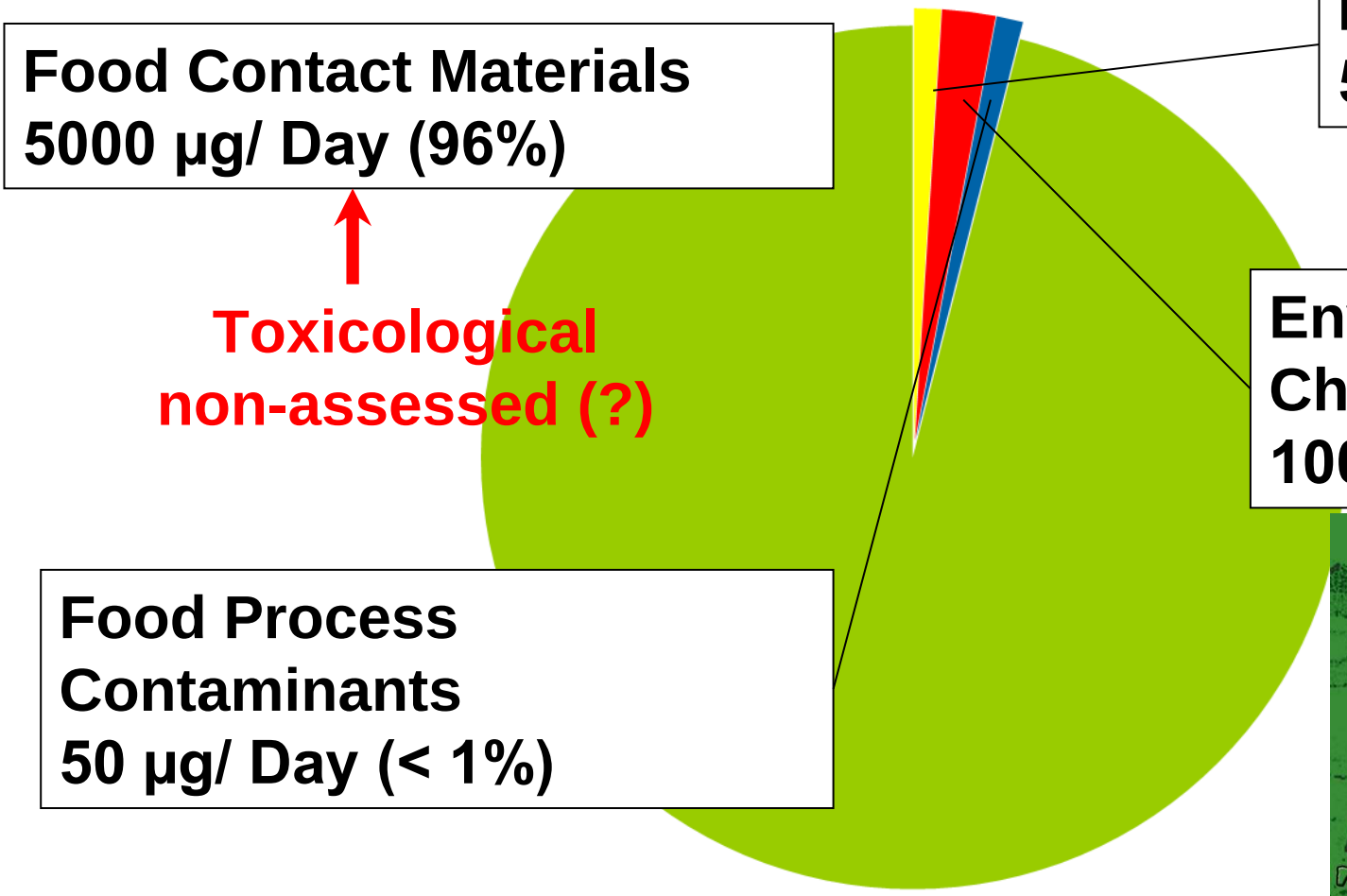
    Taking place in Nov 2024 in Prague as part of the RAFA Conference

The Future of Food Safety*

- **FOOD SAFETY IS FOOD SECURITY**
  - If it is not safe, it is not food. Food security is achieved when all people, at all times, have physical and economic access to food that meets their dietary needs for an active and healthy life.
- **FOOD SAFETY IS SCIENCE CENTRED**
  - Science-based decision-making increases public health and protects trade. Risk assessment provides policy makers with the information and evidence they need for effective and transparent decision-making, contributing to better food safety outcomes and improvements in public health.
- **FOOD SAFETY REQUIRES SHARED SOLUTIONS**
  - Human health is closely interlinked with the health of animals and the environment around us.
- **FOOD SAFETY IN EMERGENCIES**
  - International emergency response systems ensure coordinated action when combatting outbreaks of foodborne illness globally.

*FAO/WHO/AU International Food Safety Conference, 2019

Risks from a Toxicological Point



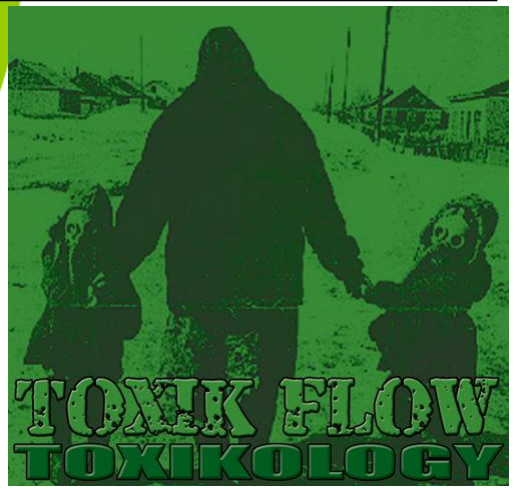
Food Contact Materials
5000 µg/ Day (96%)

Toxicological non-assessed (?)

Pesticides
50 µg/ Day (1%)

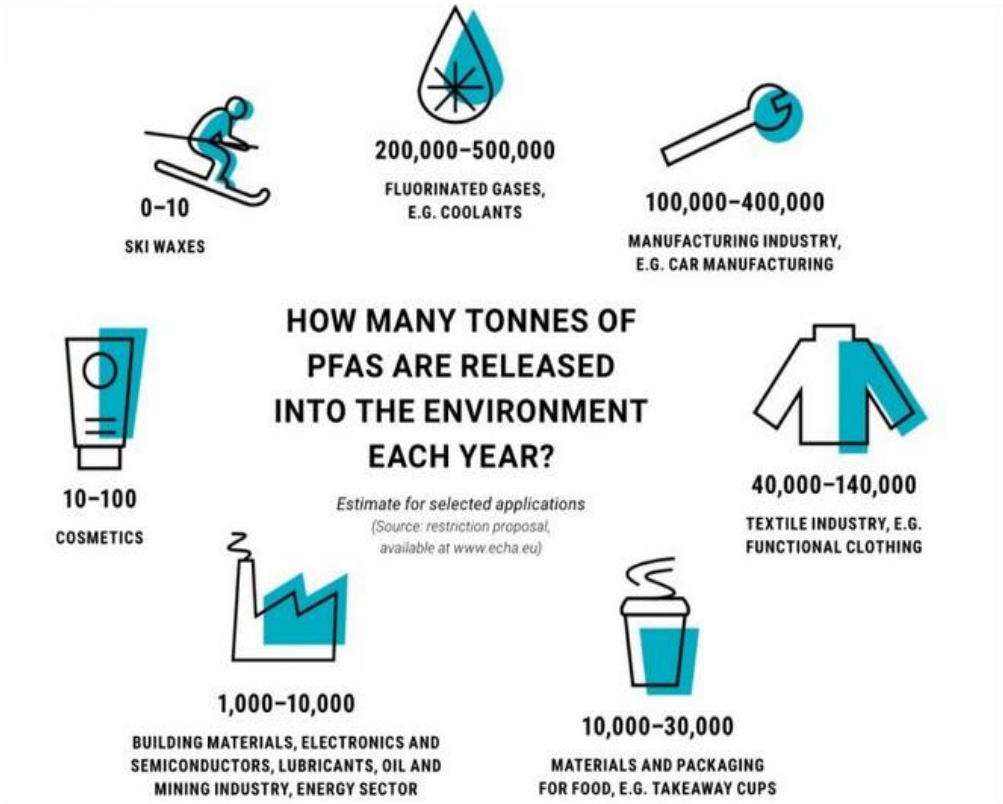
Enviromental Chemicals
100 µg/ Day (2%)

Food Process Contaminants
50 µg/ Day (< 1%)



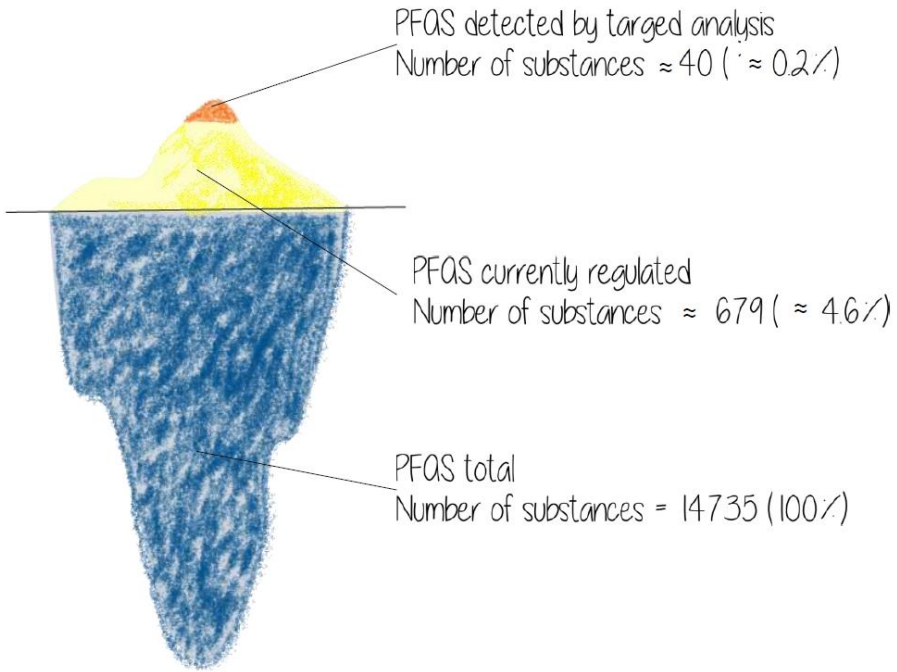
Lets Talk about PFAS

- Poly- and per-fluoroalkyl substances
  - Generic family of chemicals
  - Manmade and do not occur naturally
  - Used since 1940 (Critical for the Manhattan Project)
  - Can be branched or unbranched
  - Short chain or long chain
  - Used to make products that resist heat, oils, grease, stains, and water
- Most prevalent and researched: PFOA and PFOS



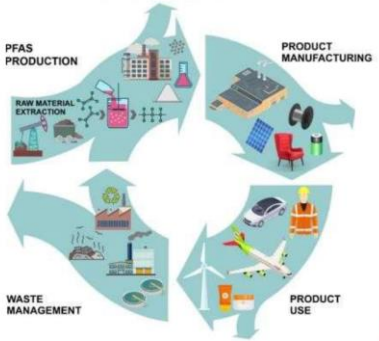
The Iceberg
Know Who or What are PFAS?

- According to the OECD definition (2021), “per- and polyfluoroalkyl substances” (PFAS) are defined as fluorinated substances that contain at least one fully fluorinated methyl or methylene carbon atom (with no H/Cl/Br/I atom attached), meaning with few exceptions, any chemical with at least one perfluorinated methyl group (−CF 3) or one perfluorinated methylene group (−CF 2 −) is a PFAS.”
- The “mentioned exceptions” refer to a carbon atom with an H/Cl/Br/I atom attached to it (Wang et al., 2021).



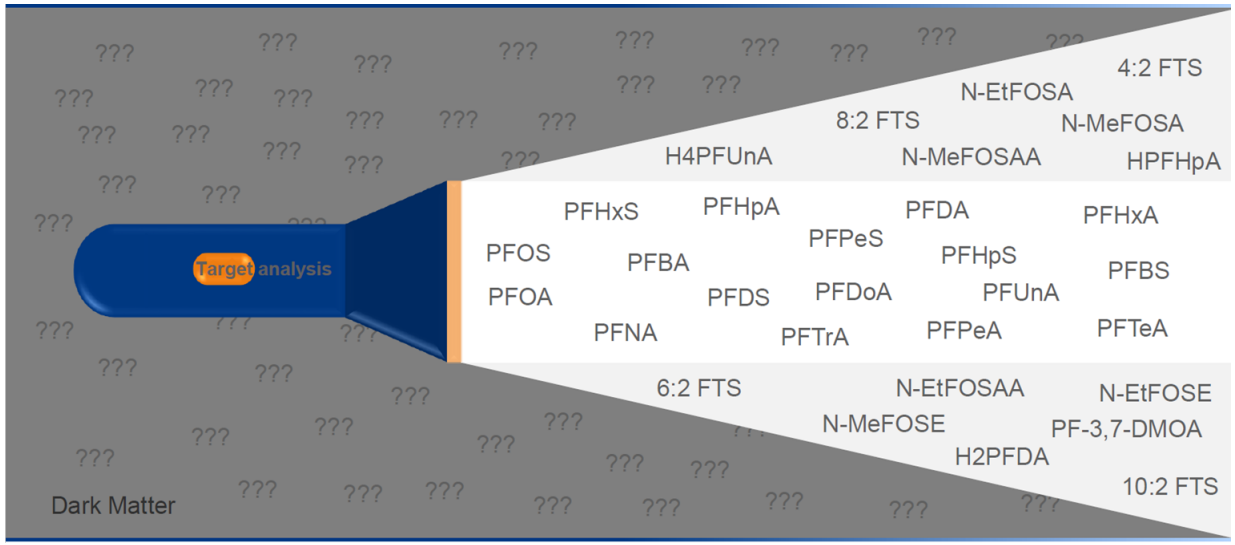
75 000 tons of emissions in 2020

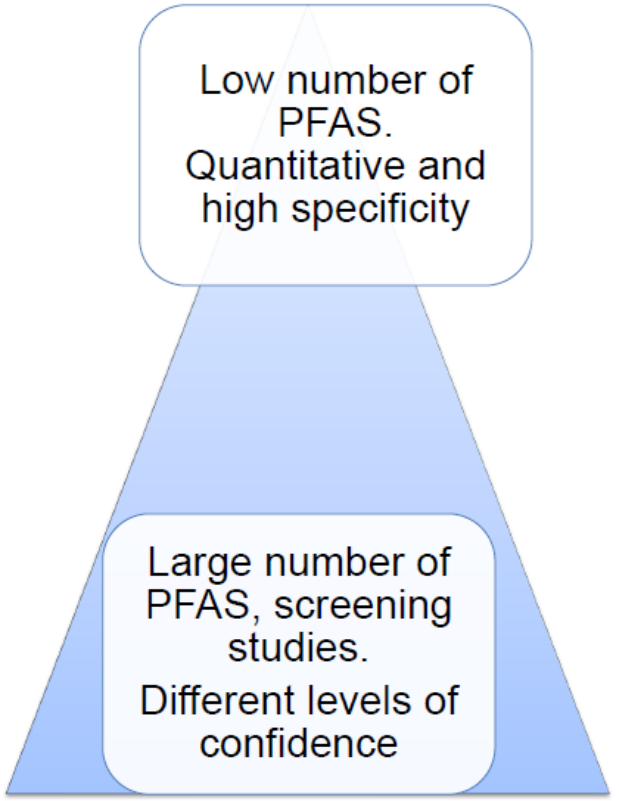
4.5 mio tons of emissions over 30 years



Source: https://ec.europa.eu/environment/pdf/chemicals/2020/10/SWD_PFAS.pdf

The Analytical Dilemma





REGULATION (EU) 2022/2388
Maximum levels of PFAS in Food

Foodstuff	PFOS*	PFOA*	PFNA*	PFHxS*	Sum of PFOS*, PFOA*, PFNA* and PFHxS* (**)
Eggs	1,0 µg/kg	0,30 µg/kg	0,70 µg/kg	0,30 µg/kg	1,70 µg/kg
Fishery products: a) Muscle meat of fish, group A [1] b) Muscle meat of fish, group B [1] c) Muscle meat of fish, group C [1]	 2,0 µg/kg 7,0 µg/kg 35,0 µg/kg	 0,20 µg/kg 1,0 µg/kg 8,0 µg/kg	 0,50 µg/kg 2,5 µg/kg 8,0 µg/kg	 0,20 µg/kg 0,20 µg/kg 1,5 µg/kg	 2,0 µg/kg 8,0 µg/kg 45,0 µg/kg
Crustaceans and bivalve molluscs	3,0 µg/kg	0,70 µg/kg	1,0 µg/kg	1,50 µg/kg	5,0 µg/kg
Meat and edible offal: a) Meat of bovine animals, pig and poultry b) Meat of sheep c) Offal of bovine animals, sheep, pig and poultry d) Meat of game animals (not bear meat) e) Offal of game animals (not bear offal)	 0,30 µg/kg 1,0 µg/kg 6,0 µg/kg 5,0 µg/kg 50 µg/kg	 0,80 µg/kg 0,20 µg/kg 0,70 µg/kg 3,50 µg/kg 25 µg/kg	 0,20 µg/kg 0,20 µg/kg 0,40 µg/kg 1,50 µg/kg 45 µg/kg	 0,20 µg/kg 0,20 µg/kg 0,50 µg/kg 0,60 µg/kg 3,0 µg/kg	 1,30 µg/kg 1,6 µg/kg 8,0 µg/kg 9,0 µg/kg 50 µg/kg

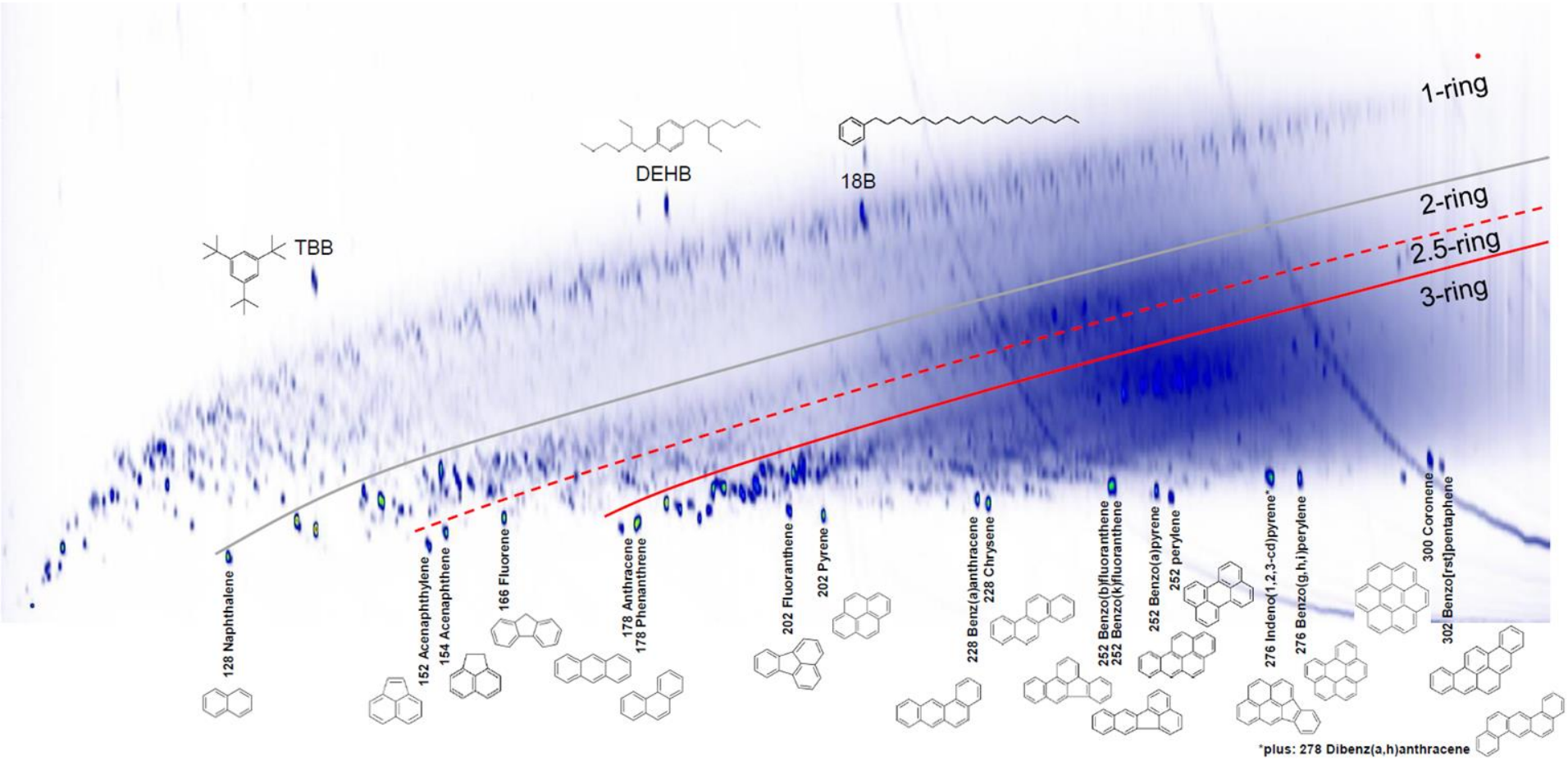
[1] see next slide for details

* Sum of linear and branched stereoisomers, ** Lower-bound concentrations

Let’s Talk About Mineral Oil

- The European Food Safety Authority (EFSA) has published an updated risk assessment on mineral oil residues in food.
- According to current knowledge, there are no health concerns regarding the amount of saturated mineral oil hydrocarbons (MOSH) consumed in food.
- However, the EFSA still believes that the intake of aromatic mineral oil hydrocarbons (MOAH) is too high, especially for infants and young children.
- **Separation between 1-2 ring and 3-7 ring systems?**

Analytical Challenge



mixture of mineral oil fractions (crude, DAE, waxes) + 16 EPA PAHs + individual components, MOAH LC fraction, GC column set: mid-polar–apolar

Taken from M. Biedermann

Non-Intentionally Added Substances (NIAS) – The Box of Pandora

Listed Substances

In the EU specifically covered Substances

In the EU controlled Substances

Food Contact Materials (FCM)

Size of EU industry:

~€100 billion/ annum

Plastics €30 bn	Paper €25 bn	Glass €20 bn	Other €18 bn	Metal €7 bn

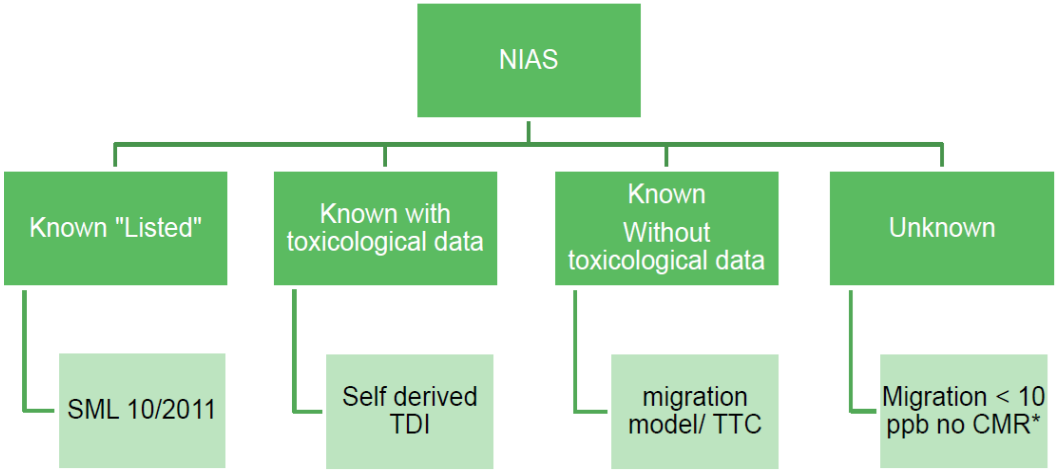
What toxicological limit must be reached?

Analytical detection limit

- **So far:** threshold given by analytical possibility
  - Idea: No evidence necessary below the detection limit because it cannot be verified
  - **Detection limit of 0.01 mg/kg** set in the EU
- **Present/future**
  - LoDs can/must be reduced below the toxicological relevance

High Degree of Purity (Article 3a- Draft to Reg 10/2011)

they are unknown or have not been subject to an assessment specified in points (ii) or (iii) but are present at a level in the plastic material or article that, assuming their full migration into food, cannot give rise to individual migration into food of any of them resulting in their presence **in food exceeding 0.00015 mg/kg.**



*When migration < 10 ppb, no further considerations are necessary dependent on exclusion of CMR substances based on expert judgement. http://fca.cefic.org/images/Documents/FCA.pdf

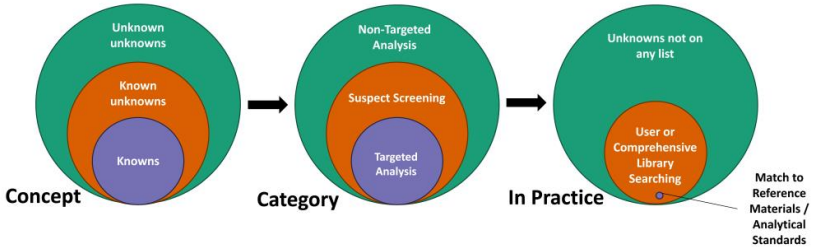
Challenges

- Safety is insufficiently defined at EU/Worldwide level for most FCMs (lack of harmonisation)
- No capacity for risk assessment and management of all FCM substances.
- Lack of priority on most hazardous substances; the use of certain chemicals is increasingly no longer accepted
- Safety of migrating substances is not transparent
- Public authorities have insufficient capacity to comprehensively enforce compliance and safety in accordance with current rules
- Environmental challenges call for more sustainable production and use.
- New products are entering the market that challenge present categories
- **No harmonized analytical test methods, especially for screening**

Residues and Contaminants Control

Target Testing versus Non-Target Testing

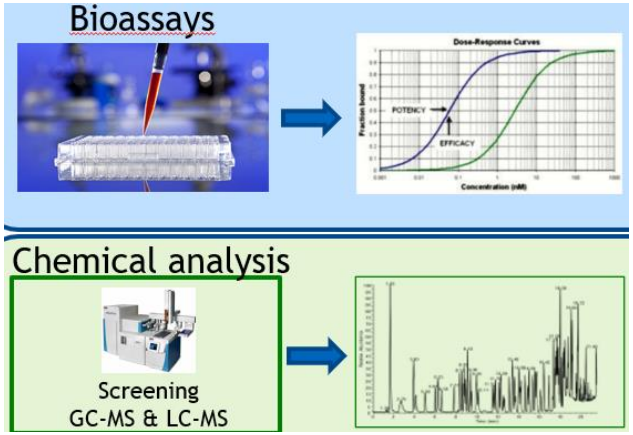
- Target:
  - limitation of the target analysis technique is in terms of the number and variety of compounds for which qualitative as well quantitative analysis can be achieved
- Non-Target:
  - Non-target screening is useful for screening and identifying compounds that have not yet been discovered



https://nontargetedanalysis.org/reference-content/methods/study-design/

Chemical versus Biological Testing

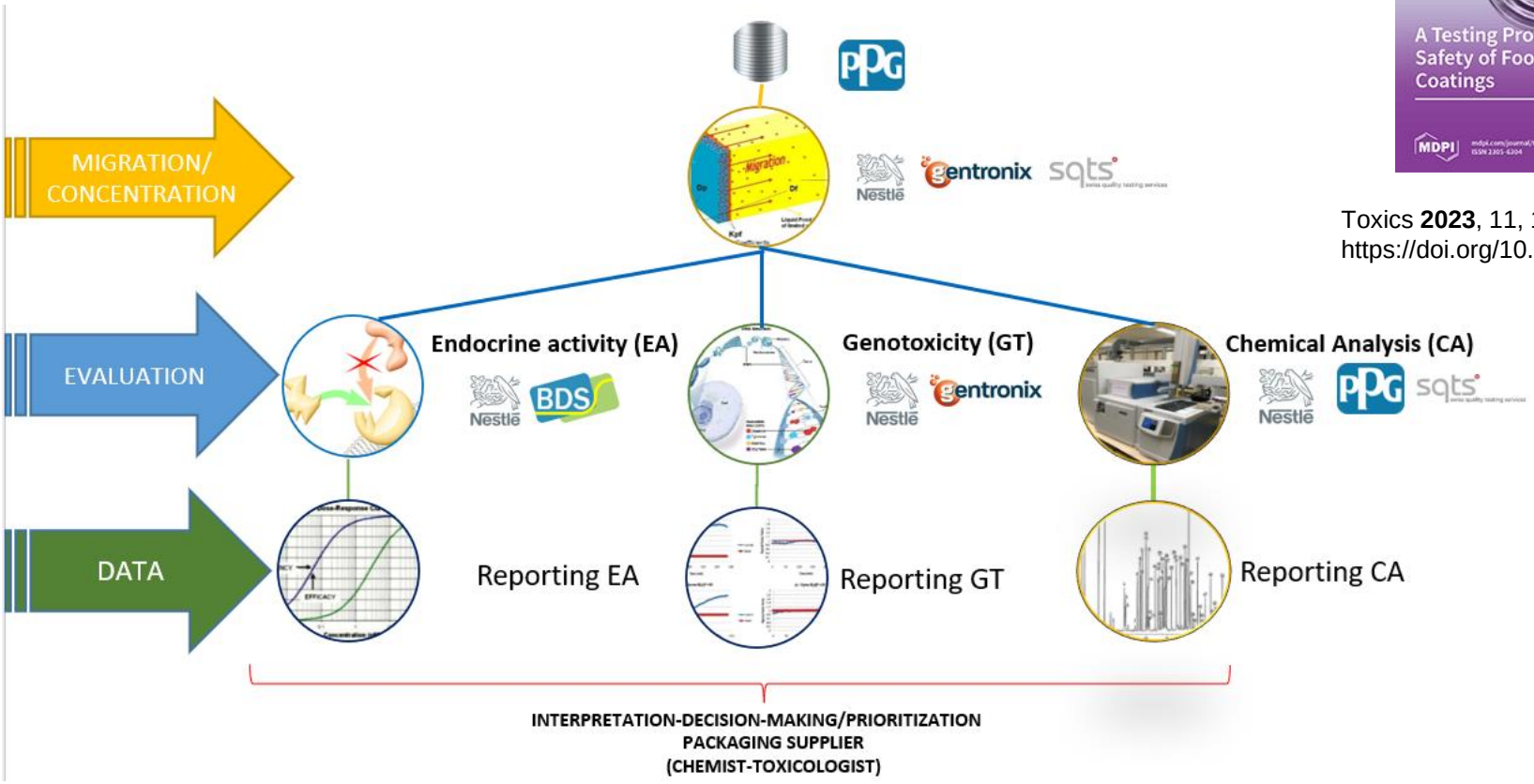
- A contrast or complementary?

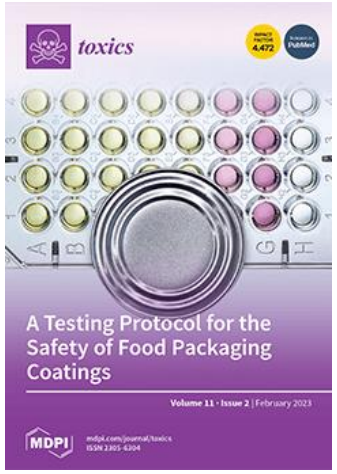


Toxics **2023**, 11, 156.
https://doi.org/10.3390/toxics11020156

A Comparison

Workflow of Interlaboratory Study





Toxics **2023**, 11, 156.
https://doi.org/10.3390/toxics11020156

Chemical Analysis

GC-MS

- Different instruments and methods between labs.
- EI
- 12 main peaks (highest areas) reported without identification of the chemicals.

LC-MS

- Different instruments and methods between labs.
- ESI positive mode
- 100 main peaks (highest areas) reported without identification of the chemicals.

LC-MS DATA

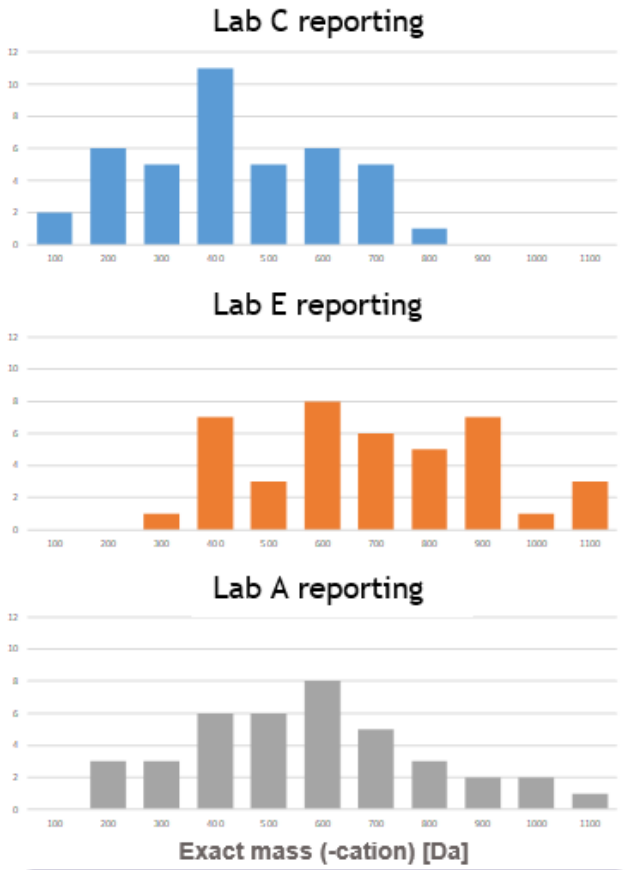
Lab C
100 peaks
89 distinct peaks*

Lab E
109 peaks
72 distinct peaks*

Lab A
41 peaks
38 distinct peaks*

*Distinct peaks: Difference on exact mass (-cation) > 0.05 Da

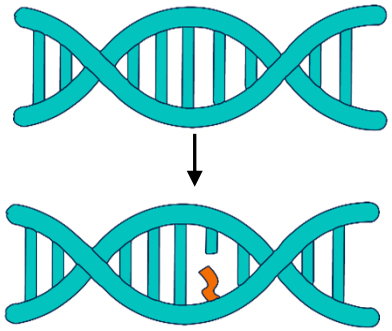
Distribution top 100 peaks



Distribution top 41 peaks

Not all genotoxic substances are critical at very low doses

1. **Direct-DNA reactive / mutagen:**
   direct changes in the DNA sequence

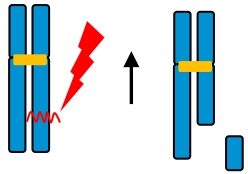


Mutation

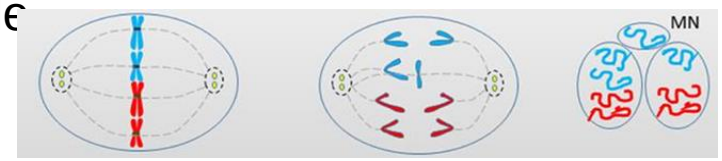
- Tolerated intake very low
- (0.15 µg/day for 60 kg person)
- Detection: Ames test (bacteria-based)

2. **Clastogens/Aneugens:**
   indirect DNA damage at the chromosomal level

- **Clastogens:** chromosome breakage (Deletion, Insertion, Chromosome rearrangement)



- **Aneugens:** disrupt cell division/mitotic spindle

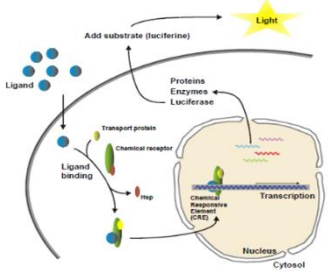


- A safe threshold can be set up
- Covered by Cramer Class III
- Undetectable with bacteria-based tests

Bioassays Analysis

ENDOCRINE ACTIVITY

Transcription activation CALUX bioassays: Receptor mediated Chemically Activated LUciferase eXpression

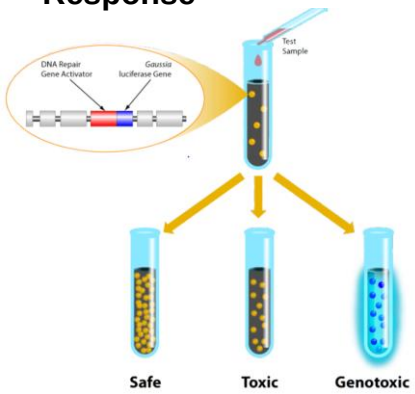


CALUX cell lines to assess activation or inhibition:

Estrogen Receptor ✓
Androgen Receptor ✓

GENOTOXICITY

Cellular DNA Damage Response



Bluescreen TM
(Gadd45a)

Broad Genotoxicity Evaluation

Overall Interlab Study Conclusions

The interlab study allowed to identify critical steps for Best Practices Framework

- Migration
- Triplicate, Solvent control — Sample preparation
- Sample contamination
- Bioassays
- Qualified bioassays
- Avoid technical differences
- Chemical analysis
- Instrument/method differences
- Use of internal standard
- Reproducibility
- Data analysis/ID/ Reporting
- Qualified Recommendations

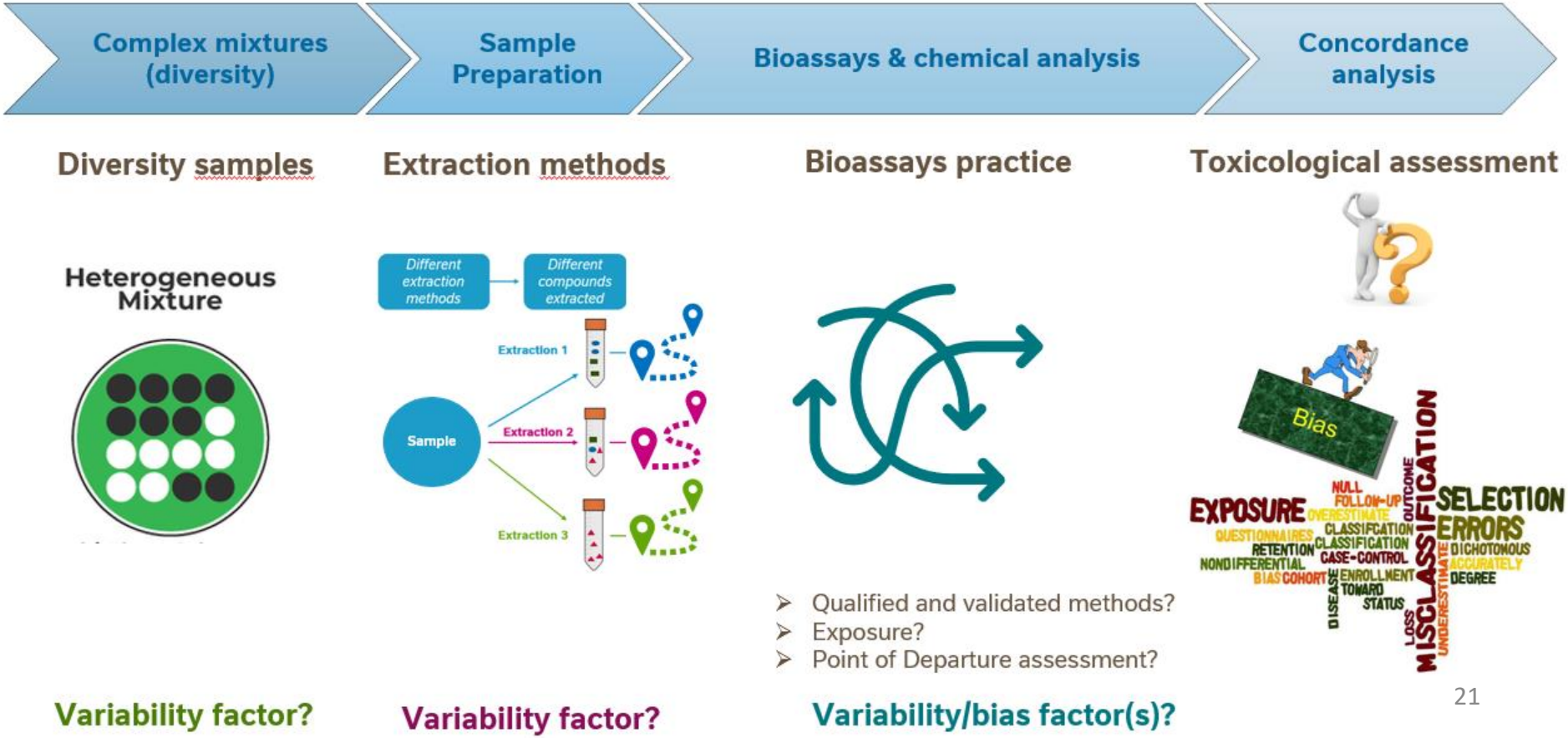
Harmonization of protocols with detailed precision of conditions are needed

Skilled laboratories for packaging safety assessment of IAS and NIAS has been identified as crucial to reduce laboratory variability and to improve concordance.

"Different methodologies can give different results and it can be difficult to make meaningful comparisons".

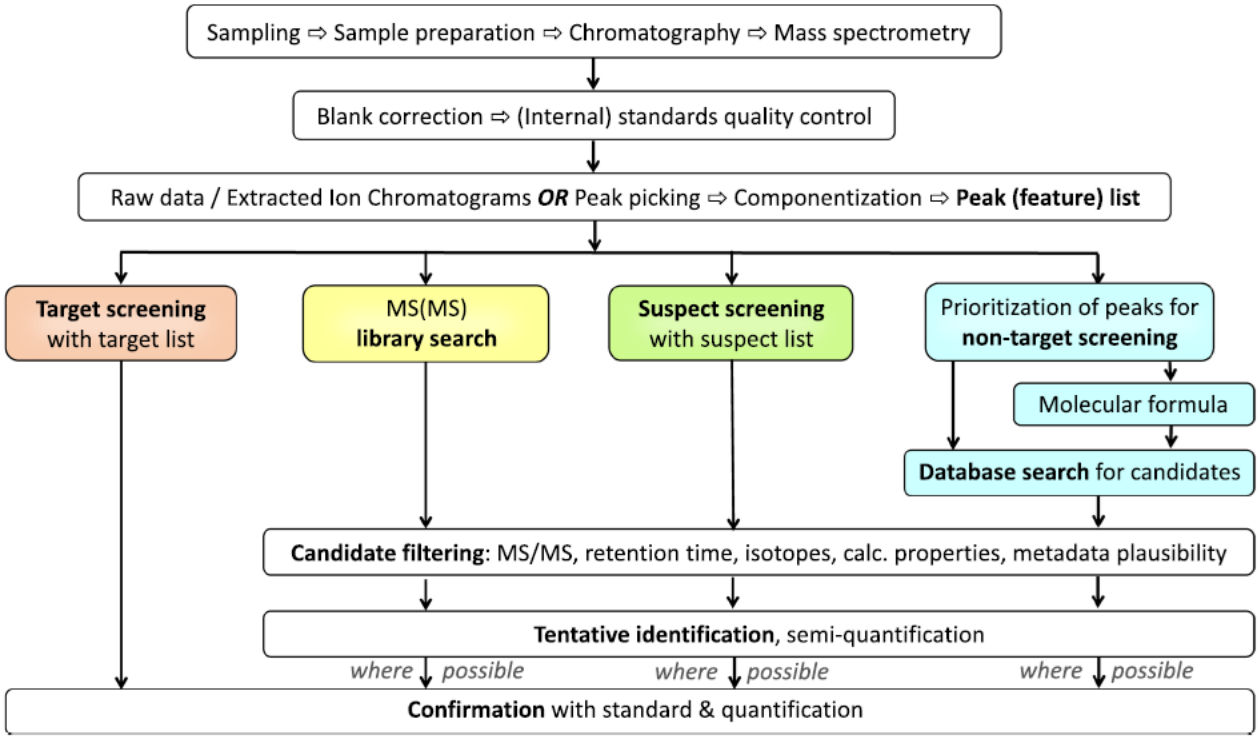
Harmonisation Activities

Bioassays: 4 working groups within AOAC Europe Section are formed to achieve a “Broader harmonization at each stage to reduce bias/misinterpretation?!”



Harmonisation Activities

Screenings: working groups covering environment, food, food contact materials, metabolomics and forensic within AOAC Europe Section are formed to achieve a “Broader harmonization at each stage to reduce bias/misinterpretation?!”



Hollender *et al., Environmental Sciences Europe (2023) 35:75,* https://doi.org/10.1186/s12302-023-00779-4

To be presented

AOAC Annual Meeting & Exposition

138th Annual Meeting • August 23-28, 2024 • Baltimore, MD

- Report out to and engagement with the AOAC INTERNATIONAL annual meeting attendees
- Possibility of having a scientific session focused on bioassays

11th International Symposium on Recent Advances in Food Analysis

November 5-8, 2024; Prague, Czech Republic

- Report out during the AOAC INTERNATIONAL session at 2024 RAFA
- Possibility of having a face-to-face AOAC Europe Section meeting