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NIAS Exposure Assessment: Comparison of Different Tools

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Food contact materials (FCMs) can contain Non-intentionally added substances (NIAS) as a result of break down, side product or impurities. NIAS can migrate into food and this might cause a risk for human health. Thus, their presence has to be evaluated, but currently there are no protocols to establish how to perform a risk assessment. Then, in this work, three different strategies to make a NIAS exposure assessment were compared: the European Food Agency Authority (EFSA) food consumption database, the Matrix Tool and the FACET tool. 2,4-Di-tert-butylphenol (2,4-DTB), an identified and quantified NIAS, was used as the case study. Differences between these tools were highlighted, but for all the strategies tested the estimated exposure to 2,4-DTB was lower than its threshold value indicating that there are no risk for the consumers.

1. Introduction

The safety to chemical hazard is a theme of great interest that affects all the supply chain (Ju, 2017). Particularly, it has a great impact on the food safety. Foods can be contaminated by several pollutant of different origins (Ling, 2018) and one the possible sources of contamination could be the packaging material itself. In fact, food contact materials can release their constituents, which can be intentionally but also non intentionally added in it. The latter are the so-called Non-intentionally added substances (NIAS), which are compounds present in food contact materials (FCMs), but not added for a technical reason during the production process. Often their presence is not known by the consumer and neither by the FMC producer. NIAS can be generated at any level of the supply chain, e.g. during the syntheses of raw materials, transport and process. In fact, they can have different origins: they can be break-down products, side products and can be originated from contaminants present in the equipment. NIAS, as all the constituents of FCMs, could migrate into food and this might cause a risk for human health, so their presence have to be assessed. However, the regulation 10/2011 / EU is the first that recognises that NIAS can be formed in the FCMs and, according to article 3 of the Framework Regulation EC 1935/2004, the FCM manufacturer is obliged to ensure the food packaging safety, but no clear advice is given by authorities on how their safety should be assessed, except for art.19 in Reg EU 10/2011 where internationally recognised protocols are required for in house risk assessment. An available guidance for the NIAS risk assessment has been made by International Life Sciences Institute (ILSI) Europe Packaging Materials Task Force (2015) (Koster et al., 2016). Moreover, NIAS identification is a very difficult analytical task. One of the main difficulties is related to the lack of knowledge of the packaging composition. A packaging material can be formed with several layers of different materials which can also be coated with inks or vanishes. Furthermore, very often these layers are produced by different manufacturers and the composition of a material is generally confidential. Therefore, it's almost impossible to know exactly the composition of a packaging material. Moreover, in each layer there are many intentionally added-substances (IAS) (e.g. antioxidant, UV absorbers, plasticizers, antimicrobials, etc.) and know the formula is more difficult than the materials (Ubeda et al., 2018). Another difficulty is related to the analytical work which is one of the most challenging steps: NIAS can be present in very low concentrations (ppb or ppt), thus, complex analytical techniques are required to detect them, and it's necessary the help of chemical databases for their identification. So, it's almost impossible to identify all the NIAS present in a food contact material; in fact, also using sophisticated analytical techniques there will be NIAS detected but not identified or not detected. In this context, several works have been done to identify NIAS in FCMs. Different breakdown products of PET have been identified in water bottles (Cincotta et al., 2017). Ubeda et al. (2018) and Brenz et

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al. (2018) determined different oligomers respectively in PET and PBT samples. Degradation products of Polycarbonate have been identified in FCMs (Bignardi et al., 2014). Furthermore, also additive degradation products have been found in different packaging materials (Bradley and Coulier, 2007). However, most of these articles are focused on the analytical methodology for NIAS identification, but there are other difficulties related to this topic. In fact, just because a NIAS is a non-listed substance some business operators have adopted the threshold value of 10 µg/kg food, which is the Limit of Detection indicated for same cases in Reg EU 10/2011. This low limit could represent a challenge with some FCMs as they may release many NIAS. Thus, the so-called exposure based approach could be adopted, setting a level corresponding to a safe exposure threshold and determining the estimated exposure to the given substance. If the exposure to a given substance doesn't exceed such an exposure threshold, there are no risks for the consumer, otherwise countermeasures are needed in order to reduce NIAS concentration. However, few articles deal with this exposure assessment and there are no protocols made by public authorities to establish how it can be done and which strategy should be adopted. In this context, it could be useful to test the possible strategies to perform the exposure assessment with the aim to create a model useful to ensure NIAS safety. Thus, the aim of this work is to make an exposure assessment basing on an identified and quantified NIAS using different methods: using the European Food Agency Authority (EFSA) food consumption database (EFSA, 2016), using the Matrix Tool (Eisert, 2011) or using the FACET tool (Oldring et al., 2009).

2. Materials

2,4-Di-tert-butylphenol (2,4-DTB) was chosen as case study since it is a non-listed substance and a breakdown product of a widely used antioxidant: Tris (2,4-ditert- butylphenyl) phosphite (Irgafos 168) and it has been identified in several polyolefin FCMs (Alin and Hakkarainen, 2011). This NIAS was industrially identified and quantified in 20 (on 37 containing Irgafos 168) polyethylene's film samples intended for food contact. The mean concentration of Irgafos 168 was 186 µg/dm^2, while the mean concentration of its breakdown product in the films was 2 µg/dm^2. The method used for NIAS identification and quantification cannot be specified for companies privacy reasons.

3. Determination of the "Level of Interest" (LOI)

The "Level of Interest" is the threshold amount of a substance to which the health risk is negligible.
The determination of 2,4-DTB LOI was done according to the "Threshold of Toxicological Concern" (TTC) which is a decision tree that is based on the principle of establishing a human exposure threshold value for all chemicals below which there is a very low probability of an appreciable risk to human health (Kroesa et al., 2004). Substances are divided, basing on their chemical structure, in three Cramer classes (Cramer et al., 1976), each of them has its TTC value (class I – 1.8 mg/person/day; class II – 0.54 mg/person/day; class III – 0.09 mg/person/day). However, substances that are carcinogenic, mutagenic or reprotoxic (CMR), substances that accumulate and proteins are excluded from Cramer classification. The LOI of 2,4-DTB is equal to 1.8 mg/person/day (it belongs to the class I) and this value has been determined using the Toxtree application (Patlewicz et al., 2008) in which the decision tree is automated.

4. Exposure Assessment

Exposure estimation of NIAS is based on migration and consumption data, as reported in the Eq. (1)

$$\text{Exposure} = \text{Migration} * \text{Food consumption} \quad (1)$$

Where exposure is reported in $\mu g_{NIAS}/(person*day)$, migration in $\mu g_{NIAS}/Kg_{Food}$ and food consumption in $Kg_{Food}/(person*day)$. Migration data can be derived from worst case calculations, migration calculation models or migration studies in food simulants, whereas consumption data can be derived from assumptions, e.g. a person eats every day 1 kg food which is packed in 6 dm^2 of a single type of plastics material (EU No 10/2011), or using specific databases. As above mentioned, in this work three different tools were compared: EFSA Database, Matrix Tool and Facet Tool. The results of these software were compared for three countries: Italy, France and UK because they are the only ones in common for the tools.
Furthermore, the surveys used to compare these tools for EFSA and FACET are:

- Italy INRAN-SCAI 2005
- France INCA 2
- UK NDNS 200 19-64

4.1 Migration into food

As above reported, the migration levels of substances from plastics into the food can be derived in different ways. In this case, the migration of the NIAS into food has been calculated using the worst case migration, according to the guidelines developed by Plastics Europe. The worst case migration assumes that all the NIAS contained in the film pass into the food.

$$C_{Food} = C_{Film} * S/V \quad (2)$$

Where:

- C_{Food} [µg/Kg] is the concentration of the NIAS into the food;
- C_{Film} [µg/dm^2] is the concentration of the NIAS into the film, in this case it is known and is equal to 2 µg/dm^2;
- S/V [dm^2/Kg] is the surface / volume ratio, in this case is not known but the conventional value of 6 dm^2/Kg ((EU) No 10/2011) has been assumed.

Applying the Eq. (2), the concentration of the NIAS into the food was estimated and it was equal to 12 µg/Kg food.
The selected foods are the followings: Cheese, Butter, Potatoes, Chocolate, Dried Pasta, Processed meat, Processed fish, Honey, Vinegar, Beer, Yoghurt.

4.2 EFSA Comprehensive Database

The EFSA Comprehensive Database (EFSA Comprehensive Database, 2018) is a food consumption database of 61 different dietary surveys in 25 different Member States. Foods are classified according to "FoodEx2", which is a hierarchical system based on 21 main food categories that are further divided into subgroups up to a maximum of 7 levels. Food consumption statistics are reported both in grams/day and in grams/kg body weight per day, for both chronic and acute consumption. For each country, food consumption data are presented per age class (Infants, Toddlers, Other children, Adolescents, Adults, Elderly and Very elderly); and for the total population and for consumers only. The summary statistics include the total number of individuals and, for each level, age classes, number of consumers, the mean, median and the standard deviation, as well as low and high percentiles. High percentiles (95th, 97.5th, 99th and even 99.9th) are often used to identify high-level consumers. The use of summary statistics from this database is intended to produce conservative estimates of exposure (EFSA, 2016). In this work the chronic consumption of different foods (which belong from the 2nd to 5th level) was estimated per consumers in terms of mean and 95th percentile. To be conservative, the selected population class was the one with the highest consumption value. After, for each food, the NIAS exposure was estimated multiplying the consumption value by the migration value (12 µg/Kg food).

4.3 Matrix Tool

Matrix (Matrix Tool, 2014) is a tool for risk assessment of non – listed substances (NLS) and not - intentionally added substances (NIAS) under Article 19 of the European Commission Regulation (EU) No 10/2011 on plastic materials and articles intended to come into contact with food. The Matrix database was jointly initiated, financed and supported by Cefic-FCA, European Plastics Converters (EuPC), Flexible Packaging Europe (FPE) and Plastics Europe and is publicly available (Eisert, 2011) .
Matrix calculation tool derived country data from five European countries (Italy, Spain, France, UK and Germany) with the respective packaging surface to which consumers are exposed per plastic material group and per consumed food (dm^2 / person*day). This area is then used to calculate exposure (µg / person*day) of identified substances based on their migration data or residual content level (µg / dm^2).

$$\text{Exposure} = \text{Migration} * \text{Surface Area} \quad (3)$$

Where Exposure is reported in μg_{NIAS}/(person*day), migration in μg_{NIAS}/(dm^2) and surface area in dm^2/(person*day).
The Matrix calculation tool allows to select the country, food type selection by simulant, packaging and substance concentration (µg / dm^2) for exposure calculation.
In this case, the exposure values was obtained for each simulant and for each country, selecting "PE multilayer" as packaging material, and 2 µg / dm^2 as NIAS residual content. The obtained results are reported in Table1.

Table 1: Exposure values (μg/person/day) to 2,4-DTB for each simulant

Simulant	Italy	France	UK
A	0.536	1.772	0.63
B	0.316	1.6	0.532
C	0	0.002	0
D1	0	0.172	0
D2	0.224	0.896	0.228
E	0.934	1.406	0.758

It has to be noted that there are no consumption data available for Multilayer PE in Italy and UK for simulants C and D1. A Possible reason could be that at the time of data collection there was no packaging of material type Multilayer PE on the market for these simulants. However, each food was associated to one or more simulants, to obtain the exposure values.

4.4 FACET Tool

The FACET project developed the FACET (Flavourings, Additives, and food Contact materials Exposure Tool) exposure tool in response to a call by the European Commission to produce a risk management tool consisting of a database containing information on concentrations of food additives and food flavourings, potential migrants in food contact materials and food consumption data (Oldring et al., 2009). This tool (FACET Tool, 2017) contains food consumption data for eight EU countries for different age groups with 15 surveys. It also has databases on packaging composition, formula and usage. However, there is no database on the occurrence and concentrations of NIAS. Estimates of exposure to NIAS could be derived in three ways: (i) NIAS associated with an existing foodstuff. This is used when the concentration of a migrant in the food is already\ known. (ii) NIAS associated with an existing packaging material. It uses the existing data within FACET for which this packaging material is used in which applications, and what the surface to volume ratios are for these applications (ii) NIAS associated at a fixed ratio with a substance that exists in the FACET substance database. This can be optionally restricted to specific material categories (adhesives, inks, other coatings, paper & board, plastic).
In this work, only the third approach was tested for all the above-mentioned foods with a migration value of 12 μg/Kg food and the exposure values were estimated per consumers and in terms of mean and 95th percentile. In all the cases, the selected packaging is “Flexible Wrapper / Bag / Pouch”.

5. Comparison of the different tools

The exposure values in (μg/person/day) are reported for each country per consumer and in terms of mean, for Figures 1a, 2a and 3a, and in terms of 95^{th} percentile, for Figures 1b, 2b, 3b. However, these distinctions can be made only using EFSA and FACET approach, the MATRIX values are always the same.

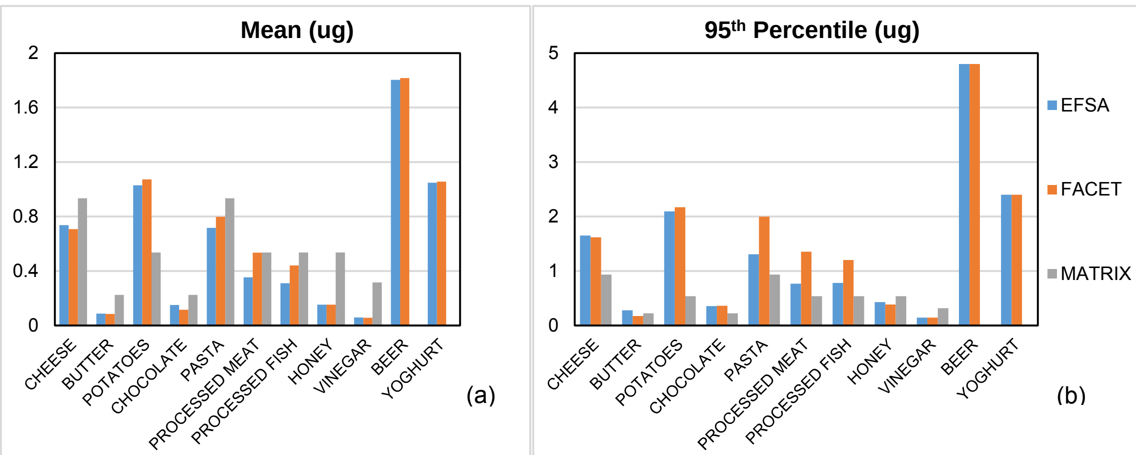

Figure 1: Exposure values to 2,4-DTB for (a) mean and (b) high-level consumers in Italy.

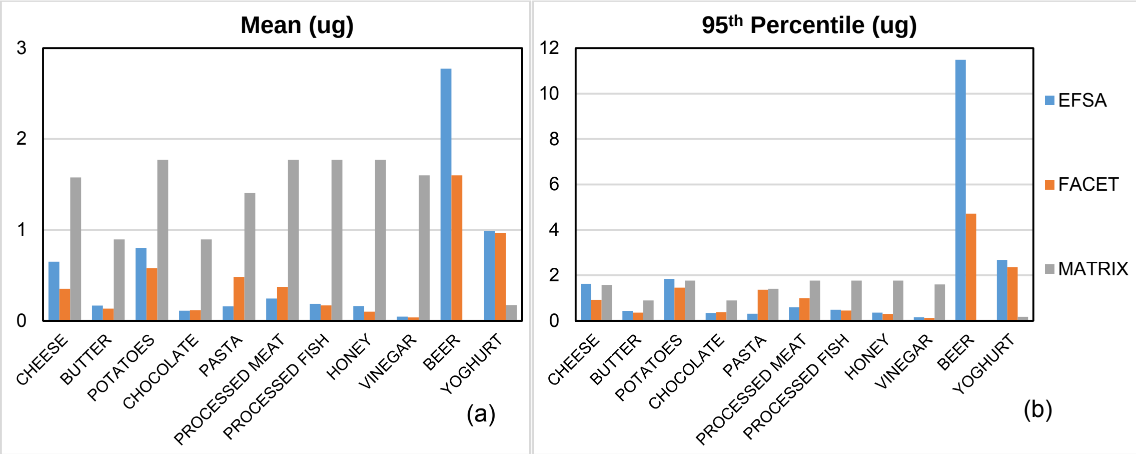

Figure 2: Exposure values to 2,4-DTB for (a) mean and (b) high-level consumers in France.

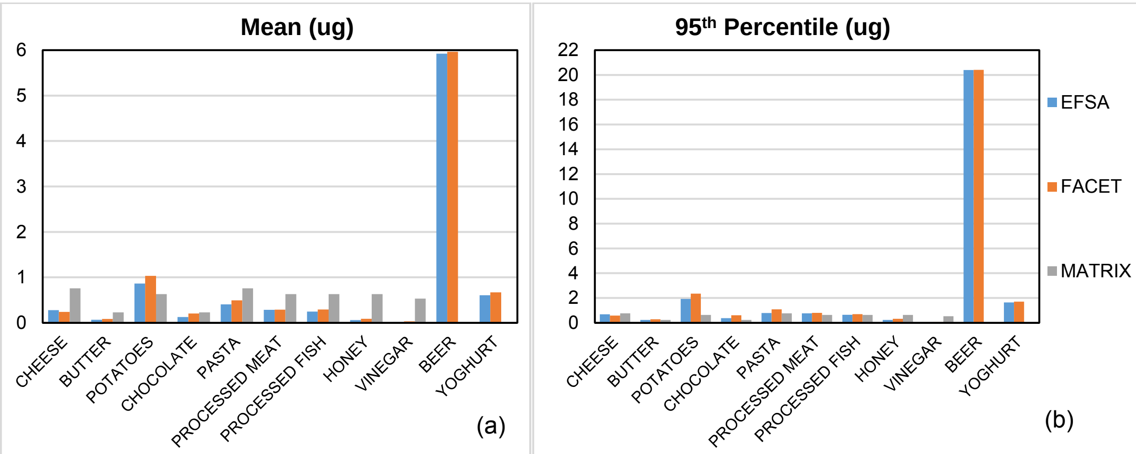

Figure 3: Exposure values to 2,4-DTB for (a) mean and (b) high-level consumers in UK.

From Figures 1, 2 and 3 it is evident that EFSA and FACET tools, give similar results for both mean and 95th percentile (some differences can be observed only for French beer and this could be due to the choice of the EFSA population group that has very few consumers). It has to be reminded that EFSA and FACET are compared using the same interviews, but the food classification is different for the two systems and EFSA database also divides the food consumption for different age classes (among them, the population group with the highest consumption value has been chosen). Moreover, using EFSA database, the package usage factor has not been considered. For this reasons, there are some differences in the exposure value between EFSA and FACET. Matrix gives different value from the other approaches. Looking at the mean value, for Italy and UK, the choice of the simulant and not of the specific food lead to an overestimation in the case of low consumption foods (e.g. butter, honey, vinegar) and to an underestimation in the case of high consumption foods (e.g. potatoes, beer). Instead, in the case of France, Matrix gives higher values than the mean of the other approaches (except for C and D1 simulants). This could be due to a medium surface / volume ratio, for packaged French food, higher than the assumed value (6 dm^2/Kg) because in the MATRIX database also this data is included. Furthermore, the MATRIX exposure values are always lower than the 95th percentile of the other systems. It must be reminded that these approaches are conservative and require little data because of the assumption of the worst case migration. However, also in the worst case conditions, the exposure to 2,4-DTB is lower than its LOI indicating that there are no risk for the consumers.

6. Conclusions

In this work three tools for NIAS exposure assessment were compared basing on an identified and quantified NIAS: 2,4-DTB. The LOI of this migrant has been calculated using the TTC approach and it is equal to 1800 µg/person/day. The migration into the food, was calculated using the worst case assumption. Then, the three tools were compared for Italy, France and UK. Since that there are different options of FACET tool, the one in which the concentration of the NIAS into the food is already known was used to compare these methods. From the comparison of these tools, it emerged that EFSA and FACET tools give similar results for both mean and 95th percentile, some differences can be due to the different food classification system and to the fact that EFSA database also divide the food consumption for different age classes (among them, the population group with the higher consumption value was selected). Matrix gives, for Italy and UK, higher values in the case of low consumption foods and lower values in the case of high consumption foods compared to the mean exposure value of FACET and EFSA tools. Instead, in the case of France, Matrix gives higher values than the mean of the other approaches. This could be due to a medium surface / volume ratio, for packaged French food, higher than the assumed value (6 dm^2/Kg). Furthermore, the MATRIX exposure values are always lower than the 95th percentile of the other systems. Anyway, also in the worst case conditions, the exposure to 2,4-DTB is lower than its LOI indicating that there are no risk for the consumers. However, if using this approach the estimated exposure of given substance is too large, more refined models (e.g. the other functions of the FACET tool) have to be used.

References

Alin J. and Hakkarainen M., 2011, Microwave Heating Causes Rapid Degradation of Antioxidants in Polypropylene Packaging, Leading to Greatly Increased Specific Migration to Food Simulants As Shown by ESI-MS and GC-MS, Journal of Agricultural and Food Chemistry, 59, 5418–5427.

Bignardi C., Cavazza A., Corradini C., Salvadeo P., 2014, Targeted and untargeted data-dependent experiments for characterization of polycarbonate food-contact plastics by ultra high performance chromatography coupled to quadrupole orbitrap tandem mass spectrometry, Journal of Chromatography A, 1372, 133-144.

Bradley E. and Coulier L., 2007, An Investigation into the Reaction and Breakdown Products from Starting Substances Used to Produce Food Contact Plastics, Report FD07/01, London (UK): Central Science Laboratory.

Brenz F., Susanne L., Simat T., 2018, Linear and cyclic oligomers in polybutylene terephthalate for food contact materials, Food Additives & Contaminants: Part A, 35 (3), 583-598.

Cincotta F., Verzera A., Tripodi G., Condurso C., 2017, Non-intentionally added substances in PET bottled mineral water during the shelf-life, European Food Research and Technology, 244, 433–439.

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

Eisert R., 2011, “EU Exposure Matrix Project - Results” presentation at PIRA Conference on “Global Food Contact 2011”, Frankfurt, Germany.

European Food Safety Authority, 2016, Use of the EFSA Comprehensive European Food Consumption Database in Exposure Assessment, EFSA Journal, 9(3), 2097.

EFSA Comprehensive Database, 2018, <www.efsa.europa.eu/it/food-consumption/comprehensive-database>.

FACET Tool, 2017, <expofacts.jrc.ec.europa.eu/facet>.

Ju H., 2017, Research on the risk assessment of hazardous chemical supply chain and the application, Chemical Engineering Transactions, 59, 1123-1128.

Kroesa R., Renwickb A.G., Cheesemanc M., Kleinerd J., Mangelsdorfe I., Piersmaf A., Schilterg B., Schlatterh J., Van Schothorste F., Vosf J.G., Wu¨rtzen G., 2004, Structure-based thresholds of toxicological concern (TTC): guidance for application to substances present at low levels in the diet; Food and Chemical Toxicology; 42, 65-83.

Koster S., Bani-Estivals M., Bonuomo M., Bradley E., Chagnon M., Garcia M. L., Godts F., Gude T., Helling R., Paseiro-Losada P., Pieper G., Rennen M., Simat T., Spack L., 2016, Guidance on best practices on the risk assessment of non-intentionally added substances (NIAS) in food contact materials and articles, ILSI Europe Report Series.

Ling W., 2018, Risk assessment of chemical pollution in organic food, Chemical Engineering Transactions, 67, 145-150.

Matrix Tool, 2014, <matrixcalculation.eu>.

Oldring P., Castle L., Franz R., 2009, Exposure to substances from food contact materials and an introduction to the FACET project. Deutsche Lebensmittel-Rundschau, 105, 501-07.

Patlewicz G., Jeliazkova N., Safford R.J., Worth A.P., Aleksiev B., 2008, An evaluation of the implementation of the Cramer classification scheme in the Toxtree software; SAR QSAR Environ Res., 19(5-6):495-524.

Ubeda S., Aznar M., Nerín C., 2018, Determination of oligomers in virgin and recycled polyethylene terephthalate (PET) samples by UPLC-MS-QTOF; Analytical and Bioanalytical Chemistry, 410, 2377–2384.