RISK ASSESSMENT OF NON-INTENTIONALLY ADDED SUBSTANCES IN FOOD CONTACT MATERIALS

Triskelion tests and analyses chemical, pharmaceutical and biotechnology products, guaranteeing the safety and quality of the products we use every day. Triskelion ensures that we don't have to worry and that we can live safe and better lives.

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Introduction

The European Framework Regulation (EC) 1935/2004 states that materials and articles intended to be used for food contact should be safe, e.g. not harmful to health. To ensure this, entry of food contact materials (FCM) to the market is subject to many regulations in Europe and many other parts of the world. The regulations ensure a careful evaluation of the materials from the initial step in producing raw materials to making the final articles, throughout the supply chain.

Unfortunately, it's not sufficient to only take into consideration the substances intended for use as FCM themselves. During the production process, oligomers can be formed and impurities, reaction products and decomposition products may be incorporated in the material. During the life cycle of FCM, materials are being mixed, combined, applied and used together in varied ways and forms in order to ensure that materials meet the demanding expectations of the market.
As a consequence, reaction products, degradation products and further contaminations can be formed. All these substances fall under the definition of Non-Intentionally Added Substances (NIAS). Not all the NIAS are hazardous.
If the unexpected and potentially harmful NIAS subsequently migrate from FCM into food products, they can seriously damage the health of consumers. According to the Plastics Regulation (EU) No10/2011, NIAS have to be assessed using scientifically recognized principles of risk assessment.

However, a clear description of what NIAS are, and how the risk assessment should be performed for the many different types of materials that exist, is missing.

The risk assessment of NIAS in food contact materials is the responsibility of the manufacturer of the material. Guidelines for the risk assessment of NIAS were published by the International Life Sciences Institute (ILSI) in 2015[1]. These guidelines have been established in accordance with internationally recognized scientific principles on risk assessment and provide a maximum guarantee that your materials do not pose unwanted risks.

Analytical screening

After the introduction of these guidelines, extensive experience has been gained at Triskelion B.V in applying the ILSI guidelines to the risk assessment of NIAS in a range of materials. This involves plastics such as poly olefins, polyesters, polystyrene and several other types of materials.
The step-wise approach of NIAS screening at Triskelion is summarized in Figure 1. Based on the type of material, and the sample details (polymer pellet resin or end products), NIAS oligomer screening can be performed as residual content analysis or using a migration extract.
As a general approach, NIAS oligomer screening is performed using several analytical techniques to analyse, identify and semi-quantify NIAS, as summarized in table 1.

1. Guidance on Best Practices on the Risk Assessment of Non Intentionally Added Substances (NIAS) in Food Contact Materials and Artcles, ILSI, 2015

Figure 1: Step-wise illustration of NIAS screening approach

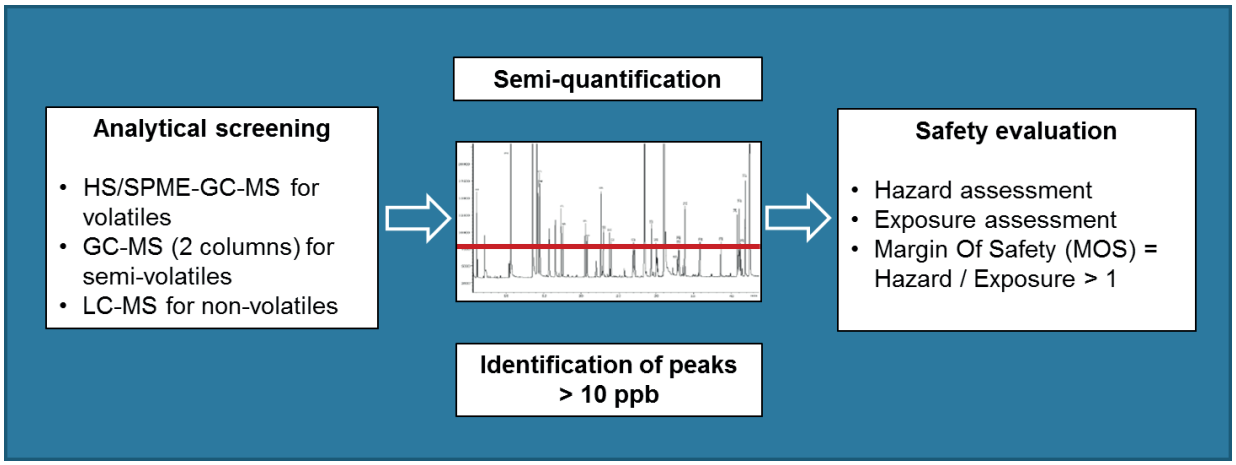


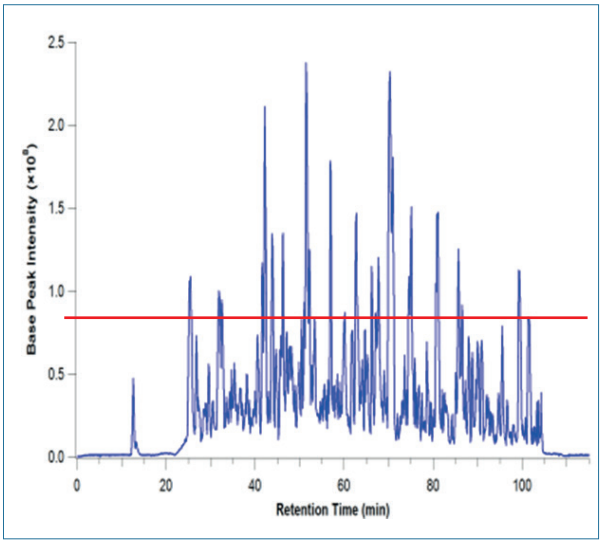
Table 1: Summary of analytical techniques for NIAS screening

Compound	Technique	Comments
	HS GC-MS	Semi-quantitative headspace analysis
Volatile	SPME GC-MS	More sensitive, qualitative headspace analysis
Semi-volatile	GC-FID/MS	Liquid injection GC. Broadest (polar-apolar) detection of NIAS
Non-volatile	LC-UV/MS	Suitable for detecting non-volatile components or oligomers
Metals or other elements	ICP-MS	

NIAS screening – (Semi) quantification and identification

A representative chromatogram of a result of a NIAS screening can be found in Figure 2. The red line indicates the limit of 10 ppb in food for the internal standard used during the analysis. Triskelion uses this internal standard for the (semi) quantification as well as to filter the peaks to be considered for further identification. Peaks will be identified using GC-MS libraries, our in-house library (accumulated knowledge in dealing with similar materials), the elemental composition obtained from LC-MS accurate mass, in-house organic chemistry knowledge and any relevant information obtained from the sponsor on the starting base materials and the production process. If needed, additional techniques (eg: chemical ionization MS), might be used for further identification.

Figure 2: A representative chromatogram of a NIAS screening



Risk assessment

After the identification and (semi) quantification of the NIAS present in the materials, the risk assessment starts. It is essential to know as much as possible about the toxicological properties of the NIAS found in order to ensure safety and comply with the legislation. The way to approach the risk assessment is highly dependent on the NIAS found.

Risk assessment consists of defining the hazardous properties of substances (hazard assessment) on one hand, and exposure to those chemicals (exposure assessment) on the other hand. On the hazard side of the risk assessment, REACH legislation has made a lot of information on chemicals available via the website of ECHA, the competent authority responsible for REACH implementation[2]. Within the database, it is possible to search for information on substances based on CAS number or EG number. Available information includes Classification and Labelling, summaries of toxicological information, and Derived No Effect Levels for the general public, which can be used directly in the risk assessment. Another valuable source of information is the CLP database, in which even more substances with accompanying classification and labelling can be found.

If the NIAS found are not known by CAS number or not (yet) registered under REACH, information in several open sources, e.g. Toxnet, IPCS, OECD chemportal and ECB can be used to fill data gaps. New methods of concluding the toxicological properties of chemicals are increasingly being accepted under REACH. These methods include the use of QSARS (Quantitative structure-activity relationship to model potential effects based on data on other substances) and Read Across, the use of data on structural analogue substances. Of course, the use of these new methodologies needs to be evaluated and recorded with care. The advantage of these methods is that it's also possible to look at parts of the chemical structure, without the need for a CAS number or other identifier. Furthermore, the Threshold of Toxicological Concern (TTC) concept and the Cramer classification approach may be used for hazard assessment of substances for which toxicological information is lacking.

2. https://echa.europa.eu/nl/information-on-chemicals

The exposure assessment aims to define the dose of a substance received by individuals in exposed populations. The assessment of food contact materials that come in contact with foods in non-repeated use applications e.g. food packaging, is complex and often requires more refined models and additional data. In both cases, tiered approaches are typically used in exposure assessments. Tiered approaches begin by using simple, conservative and widely applicable models of exposure (EuroCube[1], Matrix).
These models require relatively little data but tend to overestimate exposures. If the exposure estimates are found to be too large using the conservative models, then the assessor moves on to more refined (higher tier) methods (FACET).
In the final risk characterization step, the typical exposure level to the substance in the daily diet is compared with a toxicological limit value.
As long as the estimated exposure is below the value of the toxicological limit, the use of the substance is considered safe.

The Matrix exposure tool combines information on the composition and amount of food packaging in five EU countries (DE, UK, IT, FR, ES) with dietary surveys from the five countries. Stochastic modelling enables a value for the average daily consumer exposure to an area of food packaging, divided by food type and packaging type, to be calculated. The average exposure value of the packaging area is seen to represent a sizeable majority of consumers. Nevertheless, several factors of over-estimation remain (100% market share, 100% packaging loyalty, 100% packed foods, certain double-counting in the data, etc.). Measured migration levels of NIAS are used as input for the Matrix exposure assessment.

The FACET (Flavours, Additives, and food Contact materials Exposure Task) model may be considered the most refined model. The JRC's FACET exposure tool estimates consumer exposure to substances that can migrate from food contact materials into food.

It contains, among other things, databases of industry data on retail packaging composition, the market share of different packaging types and sizes used for each food, and food consumption diaries, which are then combined into probabilistic dietary exposure models. Measured residual content amounts of NIAS are used as input for the FACET exposure assessment. Dividing the value of the toxicological limit found through the hazard assessment step by the exposure value estimated by Eurocube, Matrix or FACET gives the Margin Of Safety (MOS). A MOS of >1 indicates that no consumer risk is to be expected.
The higher the MOS, the lower the estimated risk.

Conclusions

NIAS form a potential risk for consumers enjoying the benefits of complex and intelligent food contact materials. The risk assessment of NIAS is a constant outweighing of certainty on risk assessment on the one hand, and reasonability of efforts (and thus related costs) on the other hand. In many cases, it is possible to draw conclusions on the safety of FCM via the NIAS screening route. Using sensitive analytical methods in combination with libraries and extensive knowledge on polymer chemistry enables Triskelion experts to identify the majority of the NIAS found. By integrating information on chemicals generated for other legislations, e.g. REACH, as well as by applying the Threshold of Toxicological Concern (TTC) concept, a reliable hazard assessment of NIAS found can be performed in nearly all cases. Through a tiered approach of exposure assessment, involving calculations by the Matrix or FACET models, for most of the NIAS found a conclusion on safe use can be drawn.

3. The Eurocube model assumes that one person (bodyweight 60 kg) consumes one kg of food a day, which is packaged in 6 dm^2 of the food contact material under evaluation.