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Role of food contact materials in the safety assessment of potentially hazardous substances and in the dietary exposure of infants

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ABSTRACT

The largest application area of food contact materials is the packaging of foodstuff, being an essential element in the preservation of the microbiological and sensory quality of the packaged goods. However, chemical compounds present in the packaging material, either intentionally added or non-intentionally present, may migrate into the food during packaging and storage. With a large variety of materials used in the production, food packaging requires safety assessments with respect to the migration of packaging compounds into the packaged goods. The present article deals with the safety assessment of potential migrants from food contact materials, approaches to migration testing and summarizes European food regulatory requirements with special focus on infants' dietary exposure.

Introduction

Food may contact a broad range of different materials or articles during its production, storage, preparation and serving, before the food is finally consumed.

By legal definition of the European Framework Regulation (EC) No 1935/2004,[1] these food contact materials (FCMs) are "a) materials intended to be brought into contact with food, b) materials that are already in contact with food or c) materials that can reasonably be expected to be brought into contact with food or transfer their constituents to the food under normal or foreseeable use".

FCMs comprise of a large variety of materials from glass, paper/cardboard and metals to polymers like polyethylene terephthalate, polypropylene, styrene and silicone or combinations thereof. Although food contact materials and articles have an important function in daily life (e.g. to prolong the shelf life of food, facilitate storage, consumer information), most materials are chemically not fully inert. In contact with food, substances present in these materials, either intentionally added or non-intentionally present, may be released from the food contact material into the food by a process called migration.

Scientifically, migration can be described as the mass transfer from a packaging material into food caused by a concentration gradient between the packaging and the filling good. The extent of the migration process is dependent on several parameters including the intrinsic properties of the food contact material, the physicochemical properties of the migrating substance, the characteristics of the food and the conditions of food contact. Migration takes place until an equilibrium throughout the whole system is reached. The process, following well-known laws of diffusion, can be calculated precisely.

Consequently, consumers of all ages are indirectly exposed to chemicals present in food contact materials via the migration process.

Hence, dietary exposure to potentially hazardous chemicals of various origins has been in the public focus in the past years.[2–5] Although this matter should be monitored closely for all age groups, infants are particularly vulnerable to impairments induced by contaminated foodstuff as they have a higher intake of food per kg body weight compared to adults. Hence, several studies have been performed[6–8] focussing on the exposure of children to food-related contaminants.

In the more recent and comprehensive "Infant Total Diet Study" (iTDS)[8,9] carried out and published by Anses in 2016, the health risks associated with the potential presence of a wide variety of chemical contaminants in food (metal and mineral trace elements, polychlorinated dibenzo-p-dioxins and polychlorinated dibenzofurans (PCDD/Fs), polychlorinated biphenyls (PCBs), perfluoroalkyl acids (PFAAs), brominated flame retardants, mycotoxins, phyto-oestrogens, heat-induced compounds, pesticide residues and food additives) were assessed. Out of the nine chemicals or chemical groups of high concern, none of these were likely to originate from materials used for food packaging. Bisphenol A only, a component of widespread use in the fabrication of food contact materials, was considered a substance for

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which a risk cannot be ruled out. Other chemicals under investigation that originated in food contact materials were deemed as components with "tolerable or acceptable risks" or substances with no feasible risk assessment.

To protect the consumer's health and the quality of the food from FCM-related hazards, binding legal rules and requirements have been established in Europe for over 40 years dating back to the definition of safety requirements of FCMs as early as in the 1976 Council Directive 76/893/EEC.

Any material or article to come into contact (regardless of the material's identity) is subject to the provisions of the European Framework Regulation (EC) No 1935/2004, which establishes the basic principles of safety and risk management concerning food contact materials, providing a harmonised legal EU framework.

The general safety requirements are laid down in Article 3 of the Framework Regulation. According to this, "materials and articles, including active and intelligent materials and articles, shall be manufactured in compliance with good manufacturing practice so that, under normal or foreseeable conditions of use, they do not transfer their constituents to food in quantities which could:

(a) endanger human health; or
(b) bring about an unacceptable change in the composition of the food; or
(c) bring about a deterioration in the organoleptic characteristics thereof."[1]

The Framework Regulation also authorizes the adoption of specific requirements for individual materials listed in Annex 10 of the Regulation in order to further harmonize individual materials at EU level.

The most comprehensive specific EU measure, Commission Regulation (EU) No 10/2011,[10] is in place for materials and articles made of plastics.

Food contact materials composed of plastics or including a plastic layer play a major role in the infant and baby food area with products ranging from plastic bottles or spoons to multilayer laminates for the packaging of cereal-based food and milk powder.

Regulation (EU) No 10/2011, commonly known as the *Plastics Regulation*, sets forth rules on the composition of plastic FCMs and establishes a Union List of substances that are permitted to be used in the manufacture of plastic FCMs. This Regulation also sets out restrictions on the use of these substances and defines rules to determine the compliance of plastic materials and articles made thereof. The Regulation is amended on a regular basis.

As for substances used to manufacture articles intended for young children, tightened rules and conditions may apply: By means of example, 2,2-bis(4-hydroxyphenyl)propane (Bisphenol A) is an authorized monomer used to produce polycarbonate plastics and is also used for coatings for food and beverage cans. However, according to the Plastics Regulation, Bisphenol A is "not to be used for the manufacture of polycarbonate infant feeding bottles" and is "not to be used for the manufacture of polycarbonate drinking cups or bottles which, due to their spill proof characteristics, are intended for infants and young children". Bisphenol A has been in the focus of scientists, toxicologists and legislators for many years due to potential adverse health effects.[11] Back in 2013, France adopted a law banning the use of Bisphenol A for food contact materials for children below the age of three years. Amending the law in 2015, the ban of Bisphenol A was extended to all food contact materials on the French market.[12]

In 2015, the European Food Safety Authority (EFSA) has derived a temporary tolerable daily intake (TDI) of 4 μg per kg body weight per day following an evaluation on potential health risks of Bisphenol A in foods.[13] The TDI is defined as the estimated amount of a substance that can be consumed daily over the entire life without a significant risk to human health.[14] Based on a recent comprehensive re-evaluation, EFSA discusses a tolerable daily intake of 0.04 ng per kg body weight per day, which is 100 000 times lower compared to the previous assessment performed in 2015.[15]

An essential instrument to ensure the safety of plastic materials is the use of migration limits. These limits specify the maximum amount of substances allowed to migrate into foodstuff. Commission Regulation (EU) No 10/2011 establishes these maximum amounts in the form of "Specific Migration Limits" (SMLs). These SMLs are derived by EFSA based on the toxicity data of each specific substance. To ensure the overall quality of the plastic, two criteria have to be met: in the first place, the overall migration into food of all substances together must not exceed the "Overall Migration Limit" (OML) of 10 mg/dm^2 contact surface of the material (or 60 mg/kg food in specific cases). Secondly, the specific migration limit of each constituent present in the material and listed in Annex I of the Plastics Regulation may not be exceeded either.

SMLs of substances intended to be used in articles for young children or infants may be significantly lower than in articles intended to be used for adults: As for the plasticizer ESBO (epoxidized soybean oil) used in PVC materials, the specific migration limit is lowered from 60 mg/kg to 30 mg/kg when applied in PVC gaskets used to seal glass jars containing infant formulae, follow-on formulae, processed cereal based foods or baby foods for infants and young children.

In the context of specific migration (limits), the Plastics Regulation provides detailed migration testing rules. Although migration testing in the food prevails, migration is usually tested using '*simulants*' due to analytical challenges caused by the food matrices. These simulants, as outlined in Table 1, shall mimic the characteristics of real food (due to similar physicochemical properties of food and simulant) and are therefore representative for a certain food category.

The migration testing is done under standardised time and temperature conditions, representative for a certain food packaging application and shall cover the time and temperature of food contact under real-life application.

As an example, for the specific migration testing of a plastic pouch that is intended for the packaging of vegetables in the form of purée for long term storage at room temperature, the migration experiment shall be performed with food simulants C and B (if the pH value of the product is below 4.5) for 10 days at a temperature of 60 °C according to the provisions of Regulation (EU) No 10/2011.

Following the migration contact, specific analytical methods are applied in order to determine the concentration of the migrants in the obtained migration solution.

Depending on their physicochemical properties (e.g. volatility and polarity), the concentrations of the respective analytes in the migration solutions can be quantified using a variety of analytical techniques, ranging from headspace and liquid injection flame ionization gas chromatography/ mass spectrometry (GC-FID/MS) to liquid chromatography-mass spectrometry (LC-MS) for organic compounds and atomic absorption spectrometry (AAS) and inductively coupled plasma (ICP) analyses for inorganic compounds.

However, in addition to intentionally added substances (IAS), FCMs

Table 1
Assignment of food simulants to food according to Regulation (EU) No 10/2011.

Food simulant	Abbreviation	Food category (examples)
10% Ethanol	Food simulant A	Aqueous food (pH above 4.5)
3% Acetic acid	Food simulant B	Acidic food (pH below 4.5)
20% Ethanol	Food simulant C	Clear drinks, Fruit or vegetable pureé
50% Ethanol	Food simulant D1	Oil in water emulsions (milk products), cloudy drinks
Vegetable oil	Food simulant D2	Fatty food
poly(2,6-diphenyl-p-phenylene oxide)	Food simulant E	Dry food (cereal)

made of plastics may contain substances that are not used intentionally and that are not listed as authorized monomers or additives in Commission Regulation (EU) No 10/2011. These substances are commonly referred to as NIAS (non-intentionally added substances) and must also comply with the general safety requirements of Article 3 of the European Framework Regulation 1935/2004.[1] Assessment of these components shall be performed in accordance with internationally recognised scientific principles on risk assessment (Article 19 of Regulation (EU) No 10/2011).

Unlisted substances found in plastic FCMs may include impurities in the starting materials used to make the plastic, reaction intermediates formed during the polymerisation processes, decomposition or reaction products formed during polymerisation, substances formed during thermal processing of package fabrication and chemicals that are applied to the non food contact side (like printing inks) that might be transferred to the food contact side. In such cases, non target screening assays are commonly used that are suitable for detection, identification and quantification of a wide range of potentially migratable chemicals differing in structure, polarity and molecular weight. Such screening analyses[16] include, among others, the analytical techniques outlined in Table 2.

For the assessment of NIAS for which no other basis for evaluation is available, the threshold for the migration of unauthorised substances beyond a functional barrier may be used in accordance with Article 13 of Regulation (EU) No 10/2011. Accordingly, the migration must not exceed a limit of 10 µg/kg (ppb) of food. However, this limit does not apply to substances classified as "mutagenic", "carcinogenic" or "toxic to reproduction" (CMR) according to the criteria set in Regulation (EC) No 1272/2008.

In a conservative approach for risk assessment of genotoxic substances, EFSA has derived a threshold limit of 0.15 µg per kg in food for an adult person, based on a worst-case scenario of a person with a default body weight of 60 kg, a consumption of 1 kg foodstuff per day and taking into account the TTC (Threshold of Toxicological Concern) of 0.0025 µg per kg body weight per day below which the exposure to an unknown contaminant would have negligible consequences for the human health.[17]

For infants, a worst-case scenario based on 5 kg body weight and a consumption of 0.75 kg of food (baby bottle contents such as reconstituted milk formula and water) each day,[18] a much lower threshold limit of 0.017 µg per kg in food can be calculated when taking into account the aforementioned TTC (Threshold of Toxicological Concern) of 0.0025 µg per kg per day.

However, this TTC approach is only intended for substances where no specific toxicological data are available. In the case of substances with an existing toxicological profile, evaluations from other fields of application can be referred to for the risk assessment.[19]

Detection, quantification and regulatory assessment of both intentionally and non-intentionally added substances of high concern and low threshold limits can present a challenging task for both analytical laboratories and supervisory authorities. Analyses of individual components or complex mixtures might require time-consuming and complex analytical techniques such as high resolution gas chromatography mass spectrometry (HR-GC–MS), liquid chromatography Fourier transformation mass spectrometry (LC-FT MS) and two-dimensional gas chromatography mass spectrometry (GCxGC MS).

Hence, integrated approaches to enable the identification, assessment, detection and mitigation of safety risks raised by food contact materials have become increasingly important in recent years.[20–22] At present, safety risks brought about by FCMs are studied extensively within the framework of the SAFFI project,[23] a multinational cooperation to benchmark the main safety risks throughout the food chain of infants' food. With partners from industry and university research centres and funded by the European Union, joint studies such as SAFFI may, in turn, make a valuable contribution to food safety if their results are translated into the legal framework - to distinguish those substances of very high concern from the wide range of substances of minor importance, thus making food contact materials safe in every respect, but in particular for young children and infants.

Table 2
Analytical approaches to determine Specific Migration.

Type of substance	Predominant Analytical Method	Examples
Very volatile organic compounds (b.p. <50 −100 °C)	Headspace, SPME or purge and trap with GC with FID or MS detection	Monomers, residual solvents
Volatile organic compounds (50- 100 °C < b.p. < 250°−300 °C)	Liquid injection (split, splitless, PTV, on-column etc.) with GC with FID or MS detection	Plasticizers, glycols, additives
Semivolatile organic compounds 250–300 °C < b.p. <~400 °C)	Liquid chromatography with diode array, fluorescence or MS detection	Antioxidants, additives, oligomers
Inorganic compounds	Atomic Absorption spectrometry (AAS) or inductively coupled plasma (ICP) with MS detection	Heavy metals

b.p.: boiling point.

Declarations of Competing Interest

None

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