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Food contact materials, flavouring substances and smoke flavourings

Karl-Heinz Engel, Alexandre Feigenbaum, Jean-Claude Lhuguenot, Wim Mennes, Kim Rygaard Nielsen, Iona Pratt, Klaus-Dieter Jany, Dimitrios Spyropoulos, Anne Theobald[1, 2]

European Food Safety Authority (EFSA), Parma, Italy

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ABSTRACT

The EFSA Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food (AFC Panel) and the subsequent Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF Panel) have undertaken evaluations of the safety of flavourings (both chemically defined substances and mixtures such as smoke flavourings) and food contact materials (FCM), as well as assessments on other substances used in food. The major progress in methodologies for the evaluation of the safety of these substances is highlighted in this article. By December 2011, scientific opinions had been adopted for 247 substances for food contact materials, mainly plastics. Adoption of a series of opinions on active and/or intelligent packaging substances and on recycling processes of plastics is planned between July 2012 and December 2013. Panel opinions, EFSA statements/reports and guidance documents were published on specific issues and on substances for which there was an urgent request for safety evaluation (for example isopropylthioxanthone (ITX), bisphenol A (BPA), phthalates, epoxidised soybean oil (ESBO), benzophenone and 4-methylbenzophenone). By 2009, the AFC and CEF Panels had completed the safety review of 2 067 flavourings substances used in the EU. Additional data, which were requested for 404 substances, are currently under evaluation or have been generated. Eleven smoke flavourings have been evaluated, and the CEF Panel has prepared a guidance document on the future data required for the evaluation of flavourings.

KEY WORDS

Flavourings, flavouring substance, smoke flavourings, food contact materials, safety evaluation

[1] Correspondence: cef@efsa.europa.eu

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INTRODUCTION

The EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF Panel) deals with questions on the safety of use of materials in contact with food, enzymes, flavourings (both chemically defined substances and mixtures such as smoke flavourings) and processing aids, and also with questions related to the safety of processes. Prior to the establishment of the CEF Panel on 10 July 2008, this work was carried out by the Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food (AFC Panel). The safety evaluation methodologies used by the CEF Panel and the AFC Panel are based on methodologies initially developed by the Scientific Committee for Food (SCF) and the Joint FAO/WHO Expert Committee on Food Additives (JECFA). These methodologies have however been refined over the period of the Panels' work, as reflected in the assessment output and also in the development of guidance material for the industry, outlining the methodologies to be applied and the data required to be submitted by applicants or by interested parties to underpin the evaluations. This article focuses on the advances in assessment methodologies used for the safety evaluation of food contact materials and flavourings, including smoke flavourings, over recent years.

1. FOOD CONTACT MATERIALS

As substances used in food contact materials (FCM) may migrate into food, with a consequent potential for exposure of consumers, the SCF followed by EFSA have advised the European Commission since the early 1970s on the safety aspects of chemicals used in the production of FCM in view of the elaboration of the European Union (EU) lists of substances used in plastics FCM (Regulation (EU) No 10/2011[3]). The AFC Panel commenced the EFSA programme of safety evaluation of substances used in FCM in 2003; this work has been continued by the CEF Panel. For FCM, 247 opinions had been adopted by December 2011 for substances used in such materials (Figure 1).

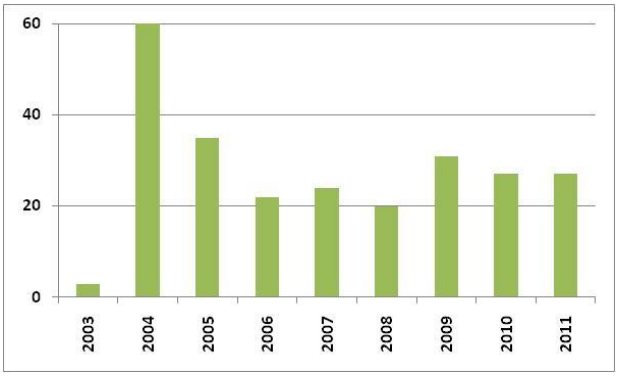

Figure 1: Numbers of FCM substances evaluated by EFSA between 2003 and 2011

1.1. Guidance for evaluation of substances used in plastics FCM

In 1990, the SCF published guidelines for evaluation of substances used in plastics FCM, clarifying which data were needed to assess their safety, depending on the extent of migration of the substance under evaluation into food stored in such FCM. These guidelines were last updated in 2001 (EC, 2001) and are still used by EFSA. More recently, they were complemented by an explanatory note for guidance with detailed technical information (EFSA, 2008a). The guidance recommends a core set of test data, considered sufficient to assess any main targets of toxicity, as follows: (i) a 90-day oral study in rodents, (ii) genotoxicity tests, (iii) data on absorption, distribution, metabolism and excretion (ADME), (iv) reproductive/developmental toxicity, and (v) long term toxicity/carcinogenicity studies.

[3] Commission Regulation (EU) 10/2011 of 14 January 2011 on plastic materials and articles intended to come into contact with food. OJ L 12, 15.1.2011, p. 1–89.

1.2. Default conservative exposure scenario and tiered approach

The above-mentioned core set of studies is required when the migration of the substance from the FCM exceeds 5 mg/kg food. As a default conservative exposure scenario, a conventional link between migration of the substance and exposure has been established by assuming that a 60-kg body weight consumer eats daily during their entire life one kg of food which is in contact with 6 dm² of the FCM containing the respective substance. Under this assumption, a migration of 5 mg/kg food is equivalent to a dietary exposure of 5 mg per person per day or 0.08 mg/kg body weight (b.w.) per day for a 60 kg adult. When migration is below 5 mg/kg food (dietary exposure lower than 0.08 mg/kg b.w. per day), long-term or reproductive toxicity are considered unlikely. Therefore only information on potential bioaccumulation (e.g. based on data on absorption, distribution, metabolism and excretion), genotoxicity data and the 90-day oral toxicity study are required for risk assessment. When migration is below 0.05 mg/kg food (0.001 mg/kg b.w. per day) the potential for exposure is low and substances can be used if they are considered to lack genotoxic potential. Only genotoxicity data are then requested.

Table 1: Toxicity data requested for the evaluation of FCM substances

Migration (mg/kg food)	**Reduced dossier < 0.05**	**Intermediate dossier 0.05-5**	**Full dossier >5**
Genotoxicity	X	X	X
90-day	-	X	X
Considerations on potential of the substance to bioaccumulate (e.g. information on lipophilicity)		X	-
Absorption, distribution, metabolism & excretion	-	X[1]	X
Reproductive toxicity	-	-	X
Long term & carcinogenicity	-	-	X
Developmental toxicity			X

[1] data requirement depends on considerations on bioaccumulative potential

The conservatism of the default exposure scenario used for the evaluation of FCM substances is being re-examined during the 2011-2014 mandate of the CEF Panel. It may not be protective enough for infants and children who have higher food consumption per kg body weight than adults. On the other hand, the assumption that a consumer eats daily the same food, packaged in the same packaging material, for all his life, is conservative and certainly offers a high degree of protection. A revision of the guidance is currently being examined in view of new data on exposure and the opinion of the EFSA Scientific Committee on the Toxicological Threshold of Concern (TTC) (EFSA Scientific Committee, 2012).

1.3. Guidance for recycling processes of plastics

In May 2008, following the publication of the Regulation (EC) No 282/2008[4], EFSA adopted its guidance for safety evaluation of processes to be included in a EU list of authorised processes to produce recycled plastic for FCM (EFSA, 2008b). This guidance applies to processes using mechanical recycling, whereby collected plastics are ground into small pieces and decontaminated before being processed into new food contact materials. Eighty-five valid applications for evaluation of processes have been received, of which 76 concern recycling of polyethylene terephthalate (PET)

[4] Commission Regulation (EC) 282/20008 of 27 March 2008 on recycled plastic materials and articles intended to come into contact with foods and amending Regulation (EC) No 2023/2006. OJ L 86, 28.3.2008, p. 9–18.

which is the most commonly recycled plastic. EFSA has published a methodology to assess the safety of recycled PET produced via mechanical recycling processes, requiring proof that the respective process can eliminate contaminants below a threshold considered as safe (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF), 2011). EFSA foresees the adoption of all recycling opinions over a period of 18 months starting from July 2012.

1.4. Guidance for active and/or intelligent packaging

In July 2009, following the publication of the Regulation (EC) No 450/2009[5], EFSA adopted its guidance for evaluation of substances to be included in a EU list of authorised substances, that can be used to manufacture an active or intelligent component of active and/or intelligent materials and articles (EFSA, 2009). The evaluation of substances follows the same principles as for other FCM regarding exposure assumptions and submission of toxicological data. However, information indicating the specific function of the substance or active component in the packaging has to be provided, and migration testing may be performed with simulants and conditions specifically selected and designed for the intended use of the active or intelligent packaging. Twenty-five valid applications have been received and they are currently under evaluation. EFSA has already published three opinions covering five applications.

1.5. ESCO Working Group on Non-Plastic Food Contact Materials

For non-plastic FCM such as paper, coatings, printing inks, adhesives, silicones and rubber, there is no specific EU legislation and no list of authorised substances exists. An EFSA Scientific Cooperation (ESCO) Working Group (WG) was established in December 2009, in order to collect information on the work carried out in Member States, to develop inventory lists of evaluated substances and classify them according to the approaches used for the evaluations (i.e. guidelines or risk assessments). The WG also identified gaps and strengths in the different approaches, established the principles for setting priorities for evaluations at EU level and identified appropriate experts in the field, who could be mobilised in case of further need. The final report of this ESCO WG was published in 2011 and updated in March 2012 (EFSA, 2012).

1.6. Urgent requests for safety evaluation of substances in FCM

In addition to the ongoing safety evaluation of a range of substances in FCM materials, the AFC and CEF Panels have received requests from the European Commission for urgent evaluation of substances of particular concern. These have included the chemical bisphenol A (BPA), a component in polycarbonate plastics including baby bottles, which is suspected of having endocrine-disrupting properties. BPA has been evaluated by EFSA in 2006, 2008, 2010 and is currently being re-evaluated against a deadline of May, 2013. In 2006, the AFC Panel derived a Tolerable Daily Intake (TDI) of 0.05 mg/kg b.w. per day for BPA and the subsequent EFSA risk assessments have not identified sufficient convincing scientific evidence of adverse effects of BPA to depart from this TDI. Similar urgent risk assessments have been carried out on certain phthalate plasticisers used in FCM, suspected of having endocrine-disrupting properties, semicarbazide (SEM) and epoxidised soybean oil (ESBO). All of these substances were of particular concern because of their presence in packaging materials used for food consumed by infants and young children. More recently, evaluations have been carried out urgently on isopropylthioxanthone (ITX), benzophenone and 4-methylbenzophenone, chemicals used in printing inks for (non-plastic) FCM, which were detected analytically in certain foods following migration from the packaging and the safety of which had not previously been evaluated.

[5] Commission Regulation (EC) 450/2009 of 29 May 2009 on active and intelligent materials and articles intended to come into contact with food. OJ L 135, 30.5.2009, p. 3–11.

2. FLAVOURING SUBSTANCES

2.1. Evaluation Procedure

Regulation (EC) No 1334/2008[6] of the European Parliament and of the Council provides for an EU list of flavouring substances, i.e. chemically defined substances with flavouring properties, approved for use in and on foods. In order to be included in that list, flavouring substances should be evaluated by EFSA, according to the programme laid down in Commission Regulation (EC) No 1565/2000[7]. The flavouring substances were divided into 34 structurally-related chemical groups and assessed in Flavouring Group Evaluations (FGEs). Substances within a group are considered to have some common metabolic and biological behaviours.

The approach for the safety assessment of chemically defined flavouring substances is based on a procedure developed by JECFA (WHO, 1996) and the SCF (EC, 1999), involving a stepwise decision tree-approach that considers information on structure-activity relationships, metabolism, intake and toxicity. A key feature of the procedure is the use of the TTC approach, in which flavouring substances are subdivided into three structural classes I, II and III (Cramer et al., 1978), for which specific thresholds of toxicological concern (1 800, 540 and 90 µg/person/day, respectively) have been derived (JECFA, 1996). After the assignment of the flavouring substance to one of the structural classes, the steps of the procedure cover the following issues:

- Can the substance be predicted to be metabolised to innocuous products?
- Do the conditions of use result in an intake greater than the threshold of toxicological concern for the structural class?
- Is the substance or are its metabolites endogenous?
- Does a no-observed-adverse-effect level (NOAEL) exist for the substance or structurally related substances, which provides an adequate margin of safety under conditions of intended use?

This procedure is not applied to flavouring substances with existing unresolved toxicity issues. In particular, flavouring substances for which a concern for genotoxic potential is raised are not put through the procedure, unless experimental evidence of absence of genotoxic potential is provided.

The intake assessment plays an important role in the application of the procedure. In its evaluations, the Panel, as a default, used the "Maximised Survey-derived Daily Intakes" (MSDI) approach to estimate *per capita* daily intakes of flavouring substances in Europe. Considering that the MSDI model may underestimate the intake of flavouring substances by certain groups of consumers, the Panel also performed an estimate of intakes using a "modified Theoretical Added Maximum Daily Intake" (mTAMDI) approach based on the normal use levels reported by industry. In those cases where the mTAMDI approach indicated that the intake of a flavouring substance might exceed its corresponding threshold of concern, it was concluded that more reliable exposure data were required. In such cases, the flavouring substance should be then re-evaluated using the procedure, after which additional toxicity data might become necessary.

By 2009, the Panel had completed the safety review of 2 067 flavourings substances used in the EU and concluded that the majority (1 663) of flavouring substances evaluated through the procedure would not give rise to safety concern at the estimated level of intake, using the default MSDI

[6] Regulation (EC) No 1334/2008 of the European Parliament and of the Council of December 2008 on flavourings and certain food ingredients with flavouring properties for use in and on foods and amending Council Regulation (EEC) No 1601/91, Regulations (EC) No 2232796 and (EC) No 110/2008 and Directive 2000/13/EC. OJ L 354, 31.12.2008, p. 34–50.

[7] Commission Regulation (EC) No 1565/2000 of 18 July 2000 laying down the measures necessary for the adoption of an evaluation programme in application of Regulation (EC) No 2232/96 of the European Parliament and of the Council. OJ L 180,19.07.2000, p.8–16.

approach. The Panel has also requested interested companies to provide further data on 404 substances to allow completion of the evaluations.

2.2. Guidance on future data required for the risk assessment of flavourings

The assessment of new flavourings (both chemically defined substances and mixtures) will change in the future. EFSA has adopted a guidance document on the future data required for the risk assessment of new flavourings (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF), 2010a). A basic element of the guidance is that new flavouring substances, which can be assigned to one of the existing FGEs on the basis of structural and metabolic similarities, should be evaluated according to the scientific principles underlying the evaluation programme described in section 2.1 above. However, the data requirements in the new guidelines are more stringent than those of the current evaluation programme, and data demonstrating absence of genotoxicity will be a prerequisite for all flavouring substances in the future, as well as data enabling a more accurate exposure assessment. For substances that cannot be assigned to one of the existing FGEs, an individual evaluation has to be performed, provided there is no safety concern with respect to genotoxicity. The type of toxicological data required depends on whether there are experimental data available for the substance to demonstrate that the metabolites can be considered as innocuous and whether the chronic dietary exposure, based on added use levels, is below or above the threshold of concern of the structural class to which the flavouring substance belongs (Table 2).

In the second part of the guidance document the Panel has elaborated for the first time on information to be supplied with applications for the authorisation of flavourings other than chemically defined flavouring substances.

Table 2: Toxicity data requested for the individual evaluation of flavouring substances

	Reduced	**Intermediate dossier**				**Full**
	Dietary exposure < TTC	**Dietary exposure 1-10 times the TTC**	**Dietary exposure > 10 times the TTC**	**Dietary exposure < TTC**	**Dietary exposure 1-10 times the TTC**	**Dietary exposure > 10 times the TTC**
Genotoxicity	X	X	X	X	X	X
Metabolites considered innocuous	Yes	Yes	Yes	No	No	No
90-day	-	X	X	X	X	X
Developmental toxicity	-	-	X	-	X	X
Long term toxicity & carcinogenicity	-	-	-	-	-	X

3. SMOKE FLAVOURINGS

Smoking has traditionally been applied to preserve certain foods such as meat or fish. In addition, the smoking process results in characteristic sensory properties of food. Nowadays, liquid smoke flavourings are increasingly added to foods to replace traditional smoking or to impart smoke flavour to foods that are not traditionally smoked. According to Regulation (EC) No 2065/2003[8], the use of a liquid smoke flavouring (defined as a primary product in the legislation) shall only be authorised if it does not present a risk to human health, based on EFSA's safety evaluation.

[8] Regulation (EC) No 2065/2003 of the European Parliament and of the Council of 10 November 2003 on smoke flavourings used or intended for use in or on foods. OJ L 309, 26.11.2003, p.1–8.

The AFC Panel of EFSA initially developed guidelines on the submission of a dossier on a smoke flavouring primary product laying down the administrative, technical and toxicological data required (EFSA, 2005), and dossiers were submitted by the industry based on these guidelines. In 2009, the CEF Panel completed the safety evaluation of eleven smoke flavouring primary products already in use in the EU, based on the data provided on production process, composition, use levels and toxicity. In order to determine "margins of safety" for each product, the Panel compared the highest intake levels at which the primary products did not show adverse effects in animals to the estimated intake levels for humans (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF), 2010b). For three of the evaluated primary products the margins of safety were large enough not to give rise to safety concerns at the levels of use as specified by the applicants, whereas for the others a safety concern was raised.

CONCLUSIONS AND OUTLOOK

A very large number of chemicals are used as flavourings in food, as additives or constituents of food contact materials. Specific methodologies for evaluation of safety have been developed by EFSA, JECFA and others, in order to enable these substances to be assessed in an efficient manner while still being protective of human health, and several thousand substances used in plastic FCM and as flavours have been assessed by the AFC and CEF Panels in the period 2002-2012. The CEF Panel faces new challenges in its risk assessment work over the coming years. The work on safety evaluation of food enzymes will commence in 2012, following introduction of specific EU legislation in 2008 as part of the Food Improvement Agents Package (FIAP)[9]. The outcome of EFSA's work will lead to a European Union list of food enzymes that can be used in food, in parallel with those already existing for food additives and flavouring substances. In preparation for this work the Panel has developed guidance for applicants on the data required to conduct a safety evaluation of food enzymes. Having completed its evaluation of chemically-defined flavouring substances, the Panel must now evaluate a large number of other flavourings including flavouring preparations, thermal process flavourings, flavour precursors, other flavourings and source materials other than food. Guidance on the data required for safety evaluation of these flavourings has already been developed, as described in section 2.2. of this article. Finally, an evaluation programme for substances used in non-plastic food contact materials, many of which have not been assessed at EU level, will have to be developed, based on the priorities established by the ESCO Working Group (Section 1.5).

About the authors

Karl-Heinz Engel*, Chair of the Flavourings Working Group (WG) from 2003 to 2009; **Alexandre Feigenbaum**, Head of the CEF Unit from 2008 to 2011, FIP (CEF) Team Leader since 2012; **Jean-Claude Lhuguenot***, Chair of the Food Contact Materials WG since 2008; **Wim Mennes***, Chair of the Flavourings WG since 2009; **Kim Rygaard Nielsen**, Scientific Secretary to the Flavourings WG; **Iona Pratt***, Chair of the CEF Panel since 2011; **Klaus-Dieter Jany***, Chair of the CEF Panel from 2008 to 2011; **Dimitrios Spyropoulos,** Scientific Secretary to the Food Contact Materials WG; **Anne Theobald**, Scientific Secretary to the Smoke Flavourings WG

*CEF Panel Member (2011-2014 mandate)

[9] Available from http://ec.europa.eu/food/food/fAEF/index_en.htm

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