How to assess non-intentionally added substances in food contact materials?

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The content of this lecture does not necessarily represent the position of the European Food Safety Authority

Workshop TTC for risk assessment of food contact material chemicals

Food Packaging Forum

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Overview

- Food contact materials: regulatory context, risk assessment process and revision of guidelines
- What are non-intentionally added substances (NIAS)?
- Approaches to consider NIAS in the risk assessment of food contact materials
- Assessment of NIAS by EFSA´s CEF/AFC Panel

Regulatory context: Food contact materials

Framework Regulation (EC) No 1935/2004

General requirements for all Food contact materials (FCM) and Mandate for specific measures

COMMISSION REGULATION (EU) No 10/2011

of 14 January 2011

on plastic materials and articles intended to come into contact with food

(Text with EEA relevance)

- Article 1, 2, and 5 outlines what is a plastic food contact material and lays down which substances are subject to the authorisation scheme and makes reference to the Union list

“Substances” on the Union list

- Commission Regulation (EU) No. 10/2011, Art. 5
  - monomers or other starting substances;
  - additives excluding colorants;
  - polymer production aids excluding solvents;
  - macromolecules obtained from microbial fermentation

- Regulation 1935/2004, Articles 7, 9 and 10 lays down the workflow and risk assessment by EFSA and makes reference to guidelines for the safety assessment of a substance by EFSA

Food contact materials applications

APDESK

CEF Panel

30 working days
Feedback on Completeness check
(Internal EFSA deadline

6 month by legislation;
Additional information might be requested

Applicant → **MS** → **Reception EFSA** → **Validity (by EFSA)** / **Not valid**

Risk Assessment → **Adoption by the Panel** → **Publication**

15 working days
(Internal EFSA deadline)

Guidance documents

FOOD CONTACT MATERIALS

NOTE FOR GUIDANCE

("NOTE FOR GUIDANCE FOR PETITIONERS PRESENTING AN APPLICATION FOR THE SAFETY ASSESSMENT OF A SUBSTANCE TO BE USED IN FOOD CONTACT MATERIALS PRIOR TO ITS AUTHORISATION")

(Updated on 30/07/2008)

The EFSA Journal (2009) 1208

Opinion of the Panel on food contact materials, enzymes, flavourings and processing aids (CEF)

Guidelines on submission of a dossier for safety evaluation by the EFSA of active or intelligent substances present in active and intelligent materials and articles intended to come into contact with food

Question number EFSA-Q-2005-041

Adopted on 21/07/2009

Guidance documents of EFSA´s Scientific Panels providing steering on the submission of an applications for the safety assessment of a substance.

Food contact material guidelines (EFSA, 2008) – toxicological information

As a general principle, the greater the exposure through migration, the more toxicological information will be required

	< 0.05 mg/kg food	< 5 mg/kg food	> 5mg/kg food
	< 0.83 µg/kg bw/d	< 83.3 µg/kg bw/d	> 83.3 µg/kg bw/d
genotoxicity	+	+	+
90-day study		+	+
Accumulation information		+	+
ADME			+
reproduction study			+
developmental studies			+
long term study			+

Food contact material guidelines (EFSA, 2008): exposure assessment

Based on Scientific Committee on Food guidelines of 2001:

- human exposure data are not readily available
- use of data on migration into food or food simulants
- for reasons of prudence, it is assumed that a person may consume daily up to 1 kg of food in contact with the relevant food contact material
- person weighs 60 kg
- surface packaging:food mass = 6 dm^2:1 kg

Revision of the food contact material (FCM) guidelines

- Guidelines are based on the Scientific Committee on Food opinion from 2001;
- To take into account new scientific knowledge in the area of exposure assessment;
- To align with respective EFSA´s Scientific Committee (SC) opinions such as threshold of toxicological concern (TTC), nanotechnology, genotoxicity;
- To have a more robust scientific basis for the safety assessment.

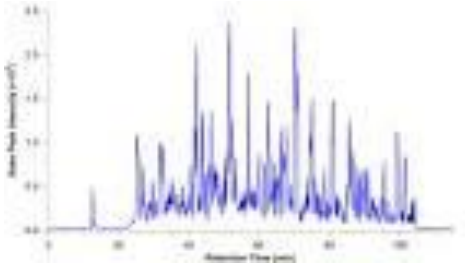
Timetable for revision of FCM guidelines

- EFSA´s CEF Panel aims to endorse the FCM guidelines for public consultation in 2013 and aiming to adopt the guidelines during 2014

- Art. 36 grant "implications on requirements for submission of toxicological information, restrictions and administrative consequences" of draft FCM guidelines was launched on 23/10/2013 with a closing date for submission of offers by 5/11/2013
  http://www.efsa.europa.eu/en/art36grants/article36/gpefsafip201301.htm

Non-intentionally added substances (NIAS)

- Commission Regulation (EU) No. 10/2011, Article 3 (9) defines non-intentionally added substances (NIAS) as impurities, reaction and degradation products which should be considered in the risk assessment if relevant
- Art. 6 (4) and 19 sets out the requirements for NIAS
- NIAS can be present in the starting material or occur during the manufacturing process



Information on NIAS in applications

- Starting material, purity, chemical synthesis, impurities
- Quantification of the impurity
- Estimation of the likely maximum daily intake of the substance, its impurities, its breakdown and reaction products and if possible concentration in the food itself
- Analytical methods to determine impurities

Assessment of NIAS in FCM

- Toxicological information on the substance to be evaluated needs to be available. However, NIAS are often
  - present in very low concentrations,
  - multiple chemical species,
  - structurally interrelated and/or related to the parent compound

A possible challenge in risk assessment ?

- Applicant is asked to provide sufficient information on NIAS particularly related to genotoxicity

Approaches to assess NIAS

Preliminary toxicological assessment of NIAS can be based on:

- Grouping & read-across
- Computational methods (SARs, QSARs)
- Threshold of Toxicological Concern (TTC)
- Margin of Exposure (MOE)

EFSA´s SC opinion on TTC (2012)

- EFSA´s SC was requested to evaluate the relevance and reliability of the TTC approach as a tool for providing scientific advice about possible human health risks from low level exposures

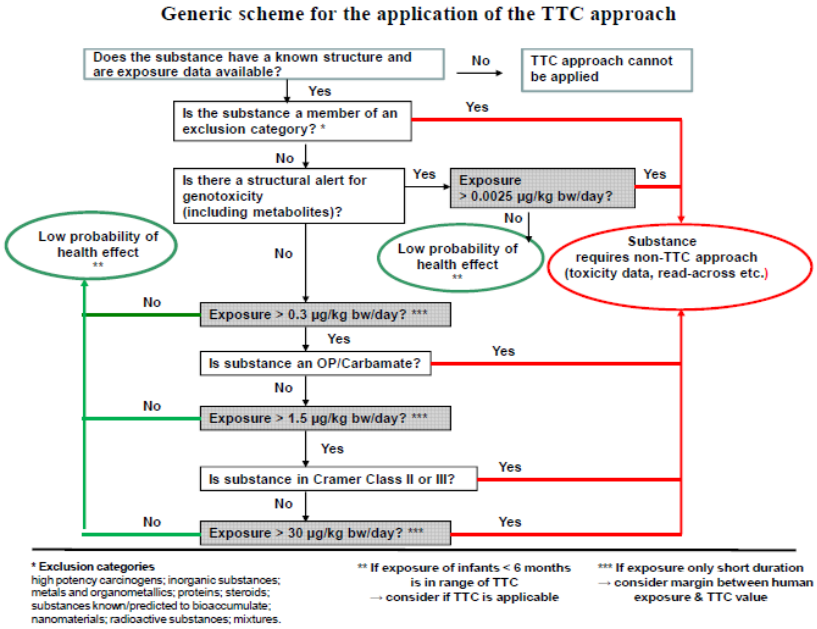
- The EFSA´s SC concluded that

– The science supports the application of the TTC approach in any area of chemical risk assessment for which human exposures are low and structure known

– TTC would not be used for substances for which EU legislation requires the submission of toxicity data

EFSA´s SC opinion on TTC (2012)

- TTC can be used to assess impurities, breakdown and reaction products, metabolites, and low-level contaminants, where exposure assessment can be conducted, but on which there are few or no toxicological data (EFSA, 2012)



Thresholds of Toxicological Concern

The following human exposure threshold values are sufficiently conservative to be used in EFSA's work (EFSA, 2012)

	Substances	µg/kg bw/day
Carcinogen	with a structural alert for genotoxicity	0.0025
Non-carcinogen	Organophosphates, carbamates	0.3
	Cramer Structural TTC Class II & III	1.5
	Cramer Structural TTC Class I	30

TTC approach for NIAS

- Genotoxicity data may be not necessary if human exposure to NIAS in food is below the threshold value of 0.0025 µg/kg body weight per day, unless there are structurally related to high potency carcinogens (i.e. aflatoxin-like, azoxy- or N-nitroso-compounds).

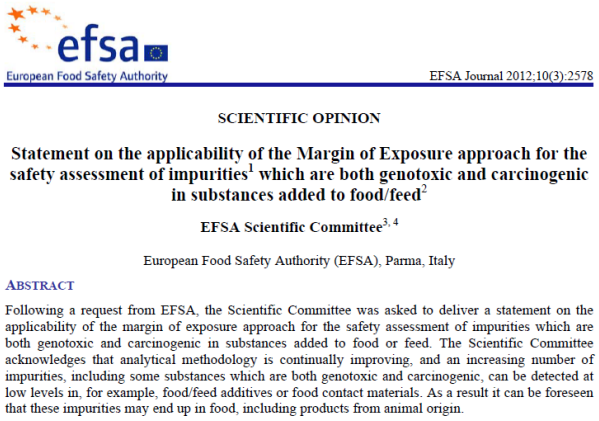
Margin of Exposure (MOE)

The MOE is a reference point on the dose-response curve* (usually based on animal experiments in the absence of human data) divided by the estimated human intake (exposure scenarios e.g. mean intake, high intake…)

*) e.g. benchmark dose lower confidence limit, LOAEL, NOAEL

Use of MOE for impurities

- The MOE approach can be applied to impurities which are both genotoxic and carcinogenic, irrespective of their origin (EFSA, 2012),
- EFSA´s SC reiterates its view and recommendations from 2005:
  - discussion on the weighting of the potential health significance of the magnitude of MOEs needed;
  - how to band MOEs with respect to conclusions using terms such as high or low concern or unlikely to be of safety concern.



European Food Safety Authority EFSA Journal 2012;10(3):2578

SCIENTIFIC OPINION

Statement on the applicability of the Margin of Exposure approach for the safety assessment of impurities[1] which are both genotoxic and carcinogenic in substances added to food/feed[2]

EFSA Scientific Committee[3, 4]

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

Following a request from EFSA, the Scientific Committee was asked to deliver a statement on the applicability of the margin of exposure approach for the safety assessment of impurities which are both genotoxic and carcinogenic in substances added to food or feed. The Scientific Committee acknowledges that analytical methodology is continually improving, and an increasing number of impurities, including some substances which are both genotoxic and carcinogenic, can be detected at low levels in, for example, food/feed additives or food contact materials. As a result it can be foreseen that these impurities may end up in food, including products from animal origin.

NIAS and approaches taken by EFSA´s CEF/AFC Panel

- The EFSA´s CEF/AFC Panels have assessed the safety of app. 250 FCM substances
- Generally NIAS have been addressed by using read across and SARs/QSARs
- MOEs for impurities were calculated in only few cases (e.g. N,N-bis (2-hydroxyethyl) dodecamide)
- The TTC approach has not yet been used to evaluate NIAS




Thank you!