European Food Safety Authority

Food Ingredients & Packaging Unit

SCIENTIFIC PANEL ON FOOD CONTACT MATERIALS, ENZYMES, FLAVOURINGS AND PROCESSING AIDS (CEF)

Minutes of the 29th plenary meeting of the Scientific Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids Held on 25-27 09 2012, Parma

(Agreed on 20 11 2012)

Participants

- **Panel Members**:

  Ulla Beckman Sundh, Mona Lisa Binderup, Leon Brimer, Laurence Castle, Karl-Heinz Engel, Roland Franz, Nathalie Gontard, Rainer Gürtler[1], Trine Husøy, Klaus-Dieter Jany, Svensson Kettil, Catherine Leclercq (Vice-Chair), Jean-Claude Lhuguenot, Wim C. Mennes (Vice-Chair), Maria Rosaria Milana[2], Fátima Pocas, Iona Pratt (Chair), Fidel Toldrá, Detlef Wölfle.

- **Hearing Experts**:

  Pia Lund (for Flavourings).

- **European Commission:**

  None

- **EFSA:**
  - **FIP Unit:**

    Eric Barthelémy, Anna F. Castoldi, Maria Carfi, Cristina Croera, Alina Lupu, Kim Rygaard Nielsen, Hanne Pedersen, Rositsa Serafimova, Dimitrios Spyropoulos, Elisavet Thessalonikeos, Anne Theobald.

  - **Other EFSA Units/Directorates:**

    None

- **Observers:**

  None.

- **Others:**

  None.

1. Welcome and apologies for absence

The Chair of the CEF Panel welcomed the members to the 29th CEF plenary meeting.

[1] Only present day 2 and 3.
[2] Only present day 1 and 2.

Apology for absence day 1 was received from Rainer Gürtler and for day 3 from Maria Rosaria Milana (CEF Panel Members).

2. Adoption of agenda

The draft agenda was adopted without changes.

3. Declarations of interest

In accordance with EFSA's Policy on Independence and Scientific Decision-Making Processes regarding Declarations of Interests (DoIs)[3] and the Decision of the Executive Director implementing this Policy[4], EFSA screened the Annual Declarations of interest (ADoI) and the Specific Declarations of interest (SDoI) filled in by the experts invited for the present meeting. For further details on the outcome of the screening of the ADoI and SDoI, please refer to Annex I.

No additional declarations were reported orally during the meeting.

4. Agreement of the minutes of the 28th Plenary meeting held on 3-5/07/2012, Parma

The draft minutes were discussed and some editorial changes were suggested. The agreed minutes can be seen on: http://www.efsa.europa.eu/en/events/event/120703b-m.pdf

5. Report on written procedures since 28th Plenary meeting

None

6. Feedback from the Scientific Committee/the Scientific Panel, Working Groups, EFSA, the European Commission

6.1 Scientific Committee

6.1.1 Risk assessment of chemical mixtures. For information and discussion.

The chair introduced the mandate of the Emerging Risk unit on a harmonised framework for the risk assessment of chemical mixtures and invited the Panel member to submit suggestions for priorities in the CEF area. The Panel felt that `combined exposure` would be more appropriate term to describe the scope of the project.

6.1.2 Update on work program and setting up of Working groups of the Scientific Committee. For information

The chair informed the Panel members about the participation in the various Working Groups of the Scientific Committee on Qualified presumption of safety (QPS) of botanicals (Karl-Heinz Engel), on the compendium of botanicals (Ulla Beckman Sundh), Review of Guidance documents (Catherine Leclercq), Emerging Risks (Klaus-Dieter Jany), Uncertainties in Risk Assessment (Iona Pratt), Environmental Risk Assessment (Leon Brimer). She informed also about the new mandate on endocrine disruptors received by the Scientific Committee, and on the opinion which is expected by March 2013 and might have implications on the CEF Panel's opinion on Bisphenol A.

6.1.3 Update on the recent International - Workshop on Low Dose Effects and Non-Monotonic Dose Responses for Endocrine Active Chemicals

The chair reported back from the recent International -Workshop on Low Dose Effects and Non-Monotonic Dose Responses for Endocrine Active Chemicals which took place in Berlin on 11-13 September 2012 and where she presented the outcome of the EFSA's 17th Scientific Colloquium on low dose response in toxicology and Alexandre Feigenbaums presentation on EFSA's approach to risk assessment. The event was perceived to be useful for exchange of information and opinions.

6.2 WG on Flavourings

The Panel was informed that data on more then 200 flavouring substances related to FGE 200 series are expected in 2013 and will lead to a heavy workload for the WG. Furthermore dossiers on flavourings which are covered by part B of the guidance document are also expected.

6.3 WG on Genotoxicity

The Panel was informed that the WG is going to continue its work on criteria for the acceptance of Comet assay reports as well as a scheme allowing identifying criteria for acceptance of genotoxicity studies with negative results.

6.4 WG on FCM

The Panel was informed on the new mandates received and on the progress of the evaluations of substances for plastic FCM and active and intelligent packaging.

6.5 WG on Recycling

The Panel was informed on the new mandates received and on the progress of the evaluations of recycling processes of plastics.

6.6 WG on BPA toxicology

The Chair of the WG on BPA Toxicology informed the Panel members of the outcome of the 3rd WG meeting and highlighted the need to hold an extra Plenary meeting on BPA in April 2013.

6.7 WG on BPA exposure

The Chair of the WG on BPA exposure reported about the work progress and future work plan of the WG.

6.8 EFSA

6.8.1 Information on the proposed CEF open plenary meeting in November

The Panel members were informed that the next Plenary in November will not be held as open session with observers. This event is postponed to mid 2013.

7. EFSA Scientific outputs submitted

7.1. Draft opinion on the substances carboxymethylcellulose, bentonite and aluminum potassium sulphate used as moisture and fluid absorbers in food packaging

(EFSA-Q- 2011-00302)

The EFSA had been requested to evaluate the risk for consumers health related to the use of the substances sodium carboxymethylcellulose, bentonite and aluminium potassium sulphate, used as moisture and liquid absorbers in food contact materials.

The rapporteur presented the draft opinion which was discussed, modified and adopted.

The CEF Panel concluded that the substances sodium carboxymethylcellulose and bentonite do not raise a safety concern for the consumer when used as moisture and liquid absorbers. Aluminium potassium sulphate dodecahydrate can be used in formulations with sodium carboxymethylcellulose (50-90% w/w) and bentonite (10-30% w/w) at levels up to 4% w/w. In all cases the absorbers must be placed in components in the food packaging preventing them from being in direct contact with food and the fluid absorption capacity of these absorbers must not be exceeded.

The full opinion is available through: http://www.efsa.europa.eu/en/efsajournal/pub/2904.htm

7.2. Draft opinion on the substances:

- **Terephthalic acid dimethyl ester, polymer with 1,4-butanediol, cyclized, polymers with glycidyl methacrylate, hydroxyl-terminated polybutadiene, methyl methacrylate and styrene and**
- **cobalt stearate**

  used in oxygen absorbing systems in food packaging

(EFSA-Q-2011-00967)

The EFSA had been requested to evaluate the risk for consumers health related to the use of the substance, (terephthalic acid, dimethyl ester, polymer with 1,4-butanediol, cyclized, polymers with glycidyl methacrylate, hydroxyl-terminated polybutadiene, methyl methacrylate and styrene) copolymer, used as oxygen absorber in food contact materials, and of the substance, cobalt stearate, used as oxidation catalyst, in materials in contact with food.

The rapporteur presented the draft opinion which was discussed, modified and adopted.

The Panel concluded that the use of the substance (terephthalic acid, dimethyl ester, polymer with 1,4-butanediol, cyclized, polymers with glycidyl methacrylate, hydroxyl-terminated polybutadiene, methyl methacrylate and styrene) copolymer in PET up to 1% w/w as oxygen absorber for contact with all types of foods at temperature up to 95°C and the use of cobalt stearate as oxidation catalyst in PET is not of safety concern for the consumer.

The full opinion is available through: http://www.efsa.europa.eu/en/efsajournal/pub/2905.htm

7.3. Draft opinion on the substance iron (II) modified bentonite used as oxygen absorber in food packaging

(EFSA-Q-2011-00193)

The EFSA had been requested to evaluate the risk for consumers health related to the use of the substance iron (II) modified bentonite used in oxygen absorbing components in food contact materials.

The rapporteur presented the draft opinion which was discussed, modified and adopted.

The Panel concluded that there is no safety concern if the substance is used as oxygen absorber incorporated without compatibilizers in polyolefin layers of food packages at levels up to 15% (w/w) or in sachets placed in the headspace of the packaging.

The full opinion is available through: http://www.efsa.europa.eu/en/efsajournal/pub/2906.htm

7.4. Draft opinion on the substance 2H-Perfluoro-[(5,8,11,14-tetramethyl)-tetraethyleneglycol ethyl propyl ether] (TFEE5)

(EFSA-Q-2011-00966)

Due to the lack of time the discussion was deferred to the next Plenary.

7.5. Draft opinion on the safety evaluation of the process, "INTERSEROH Step 1" used to recycle plastic for use in contact with food

(EFSA-Q-2010-00892)

This scientific opinion of EFSA deals with the safety evaluation of the recycling process "INTERSEROH Step 1" with the EC register number RECYC069. The process is deemed to recycle cleaned damaged food contact re-usable polypropylene (PP) crates which have been used in a closed and controlled product loop into new recycled crates.

The rapporteur presented the draft opinion which was discussed and editorial modifications were proposed. Due to lack of time it was decided that this opinion be circulated for adoption by written procedure.

7.6. Draft opinion on the safety evaluation of the following processes based on VACUREMA Prime® technology used to recycle post-consumer PET into food contact materials "Eco Plastics", "Vogtland", "Polowat" and "STF"

(EFSA-Q-2009-00898, EFSA-Q-2011-00135, EFSA-Q-2011-01119, EFSA-Q-2011-01131)

This scientific opinion of EFSA deals with the safety evaluation of the recycling processes Eco Plastics, Vogtland, Polowat and STF (EC register numbers RECYC016, RECYC067, RECYC078 and RECYC079 respectively) which are all based on the same VACUREMA Prime® technology. The input of the VACUREMA Prime® technology is washed and dried PET flakes originating from collected post-consumer PET bottles containing no more than 5% of PET from non-food consumer applications. The decontamination efficiency of all these processes was demonstrated using the same challenge test.

The draft opinion was discussed, modified and adopted.

The Panel concluded that the recycling processes Eco Plastics, Vogtland, Polowat and STF are able to reduce any foreseeable accidental contamination of the post-consumer food contact PET to a concentration that does not give rise to concern for a risk to human health.

The full opinion is available through: http://www.efsa.europa.eu/en/efsajournal/pub/2907.htm

7.7. Draft opinion on FGE.07Rev4 - Saturated and unsaturated aliphatic secondary alcohols, ketones and esters of secondary alcohols and saturated linear or branched-chain carboxylic acids

(EFSA-Q-2012-00510, EFSA-Q-2012-00509, EFSA-Q-2012-00508, EFSA-Q-2012-00507, EFSA-Q-2012-00506)

The present revision of FGE.07, FGE.07Rev4, includes the assessment of five additional candidate substances 2,6-dimethylocta-1,5,7-triene-3-ol [FL-no: 02.145], octa-1,5-dien-3-ol, [FL-no: 02.194], undeca-1,5-dien-3-ol [FL-no: 02.211], pseudo-ionone [FL-no: 07.198] and 3,3,6-trimethylhepta-1,5-dien-4-one [FL-no: 07.204]. These substances have been considered with respect to genotoxicity in FGE.206, where the Panel concluded that the data available ruled out the concern for genotoxicity and thus that the substances could be evaluated through the Procedure. The Panel concluded now that all 49 substances do not give rise to safety concerns at their levels of dietary intake, estimated on the basis of the MSDI approach.

The draft opinion was discussed. The Panel considered the possible problems arising from intake of food flavouring substances with a known potential for dermal contact sensitization. It was concluded that gastrointestinal contact allergic sensitization and reactions appear to

be very rare. A statement was made, which is attached to these minutes (s. Annex II). The Panel wishes to thank Martinus Løvik for his contribution to this statement.

The draft opinion was modified and adopted. The full opinion is available through: http://www.efsa.europa.eu/en/efsajournal/pub/2899.htm

7.8. Draft opinion on FGE.12Rev3 - Primary saturated or unsaturated alicyclic alcohols, aldehydes, acids and esters

(EFSA-Q-2012-00682)

Due to lack of time, the opinion was postponed to a further Plenary meeting.

7.9. Draft opinion on FGE.20Rev4 - Benyl alcohols, benzaldehydes, a related acetal, benzoic acid, and related esters

(EFSA-Q-2012-00621, EFSA-Q-2012-00620, EFSA-Q-2012-00619, EFSA-Q-2012-00618)

Due to lack of time, the opinion was postponed to a further Plenary meeting.

7.10. Draft opinion on FGE.63Rev1. Consideration of aliphatic secondary alcohols, ketones and related esters evaluated by JECFA (59th and 69th meetings)

(EFSA-Q-2012-00518, EFSA-Q-2012-00517, EFSA-Q-2012-00516, EFSA-Q-2012-00515, EFSA-Q-2012-00514, EFSA-Q-2012-00513)

This revision is due to inclusion of six additional substances, 4,8-dimethyl-3,7-nonadien-2-ol, 6-methylhepta-3,5-dien-2-one, octa-1,5-dien-3-one, (E,E)-3,5-octadien-2-one, (3Z)-4,8-dimethyl-3,7-nonadiene-2-one and 4,8-dimethyl-3,7-nonadien-2-yl acetate [FL-no: 02.252, 07.099, 07.190, 07.247, 07.256 and 09.936]. These substances have been cleared for genotoxicity concern in FGE.206. The Panel concluded that all substances considered in this FGE would present no safety concern at estimated levels of intake as flavouring substances based on the MSDI approach.

The draft opinion was discussed, modified and adopted. The full opinion is available through: http://www.efsa.europa.eu/fr/efsajournal/pub/2900.htm

7.11. Draft opinion on FGE.99. Consideration of Furanone derivatives evaluated by the JECFA (63th and 65th meetings).

(EFSA-Q-2007-00608, EFSA-Q-2007-00597, EFSA-Q-2007-00595, EFSA-Q-2007-00594, EFSA-Q-2007-00577)

This opinion deals with five furanone derivatives, 4-hydroxy-2,5-dimethylfuran-3(2H)-one [FL-no: 13.010], 2-ethyl-4-hydroxy-5-methyl-3(2H)-furanone [FL-no: 13.084], 4-hydroxy-5-methylfuran-3(2H)-one [FL-no: 13.085], 4-acetoxy-2,5-dimethylfuran-3(2H)-one [FL-no: 13.099] and furaneyl butyrate [FL-no: 13.176].

The Panel concluded that there is no safety concern for the candidate substances in this FGE, based on the MSDI approach.

The draft opinion was discussed, modified and adopted. The full opinion is available through: http://www.efsa.europa.eu/it/efsajournal/pub/2901.htm

7.12. Draft opinion on FGE.205. Consideration of genotoxicity data on representatives for 13 alpha,beta-unsaturated aliphatic ketones with terminal double bonds and precursors from chemical subgroup 1.2.2 of FGE.19

(EFSA-Q-2012-00390, EFSA-Q-2012-00389, EFSA-Q-2012-00105, EFSA-Q-2012-00104, EFSA-Q-2012-00103, EFSA-Q-2012-00102, EFSA-Q-2012-00101, EFSA-Q-2012-00100, EFSA-Q-2012-00099, EFSA-Q-2012-00098, EFSA-Q-2012-00097, EFSA-Q-2012-00096, EFSA-Q-2012-00095)

The 13 substances under consideration in the present evaluation are α,β-unsaturated ketone structures, or can be metabolised to such, which are structural alerts for genotoxicity. The data on genotoxicity previously available did not rule out the concern for genotoxicity.

The European Flavour Association (EFFA) has submitted genotoxicity studies for the two representative substances, oct-1-en-3-one [FL-no: 07.081] and pent-1-en-3-one [FL-no: 07.102]. Both substances were tested in mammalian cells for gene mutations at the *hprt* locus and for structural and numerical chromosomal aberrations in the micronucleus assay. The Panel considered that the positive effects seen in the bacterial mutagenicity assays of the two representative substances cannot be overruled by the one negative and one equivocal gene mutation test in mammalian cells and the Panel recommend that an *in vivo* Comet assay on the first site of contact (*e.g.* the stomach) and on the liver is requested on the most potent of the representative substances, pent-1-en-3-one.

The draft opinion was discussed, modified and adopted. The full opinion is available through: http://www.efsa.europa.eu/de/efsajournal/pub/2902.htm

7.13. Draft opinion on FGE.304 - Five carboxamides

(EFSA-Q-2009-00406, EFSA-Q-2009-00407, EFSA-Q-2010-01111, EFSA-Q-2010-01559, EFSA-Q-2010-01560)

This group evaluation deals with five carboxamides, N-p-benzeneacetonitrile-menthanecarboxamide [FL-no: 16.117], N-(2-(pyridine-2-yl)ethyl)-3-p-menthanecarboxamide [FL-no: 16.118], (1R,2S,5R)-N-(4-methoxyphenyl)-5-methyl-2-(1-methylethyl)cyclohexanecarboxamide [FL-no: 16.123], (1R,2S,5R)-N-cyclopropyl-5-methyl-2-isopropyl cyclohexanecarboxamide [FL-no: 16.124] and (2S,5R)-N-[4-(2-amino-2-oxoethyl)phenyl]-5-methyl-2-(propan-2-yl)cyclohexanecarboxamide [FL-no: 16.125].

The Panel concluded that three substances [FL-no: 16.117, 16.123 and 16.125] do not give rise to safety concerns at their levels of dietary intake, estimated on the basis of the MSDI approach. For the remaining two candidate substances [FL-no: 16.118 and 16.124], no appropriate NOAEL was available and additional data are required.

The draft opinion was discussed, modified and adopted. The full opinion is available through: http://www.efsa.europa.eu/en/efsajournal/pub/2903.htm

8. New Mandates

The Panel members were informed about the new mandates received since the last Plenary. They can be found also on EFSA´s webpage:

http://www.efsa.europa.eu/en/request/requests.htm

9. Other scientific topics for information and/or discussion

9.1. Revision of Food contact material (FCM) guidelines – Exposure assessment

The rapporteur presented the new proposal on the exposure assessment of the revision of the FCM guidelines for information and possible comments. This proposal considers various food types and covers three age groups, infants, children and adults. The food consumption data for each food type and age class are retrieved from the EFSA Comprehensive European Food Consumption Database. Uncertainties pertinent to the conservativeness of

the model due to the combination of high consumption with maximum migration values need still to be discussed in the FCM WG.

The new exposure scenarios could have a significant impact on the presentation of the dossiers for evaluation and also on the authorisation of substances for FCM, e.g. different migration limits depending on the food type.

The Panel requested the FCM WG to present some examples of the consequences from the application of the exposure model and be in dialog with the European Commission to have their views on the applicability of the model for authorisation purposes.

9.2. Scientific report on minimum criteria for the acceptance, interpretation and reporting of the *in vivo* alkaline Comet Assay.

The scientific report was presented. The Panel was informed that also the other EFSA Panels will have the opportunity to send comments on this scientific report.

9.3. External evaluation of EFSA by Ernst & Young for information

The Panel members were informed that EFSA has commissioned an external evaluation of its performance. The report is available through: http://www.efsa.europa.eu/en/keydocs/docs/efsafinalreport.pdf

10. Any Other Business

The meeting dates for the scheduled meeting in May were changed to 14-16 May and an additional CEF Plenary is planned for 9-10 April 2013.

Annex I

INTERESTS AND ACTIONS RESULTING FROM THE SCREENING OF ADOI OR SDOI

a) **CONFLICT OF INTEREST:** In his SDoI Dr Franz declared interests for the draft group opinion on “recycling processes based on Vacurema Prime technology (“Eco Plastics”, “Vogtland”, “Polowat” and “STF”)” and for the substance “terephthalic acid, dimethyl ester , polymer with 1,4-butanediol, cyclized, polymers with glycidyl methacrylate, hydroxyl-terminated polybutadiene, methyl methacrylate and styrene”, as his organisation has prepared the dossiers for these applications. These were considered as conflicts of interest and the expert left the room when the opinions were discussed.

Annex II

CEF Panel statement on contact dermatitis after peroral intake

The Panel considered the possible problems arising from intake of food flavouring substances with a known potential for dermal contact sensitization; an example being pseudo-ionone [FL-no: 07.198].
Allergic contact dermatitis is due to a cell-mediated immune reaction. Allergic contact dermatitis is largely confined to the skin, but has also been described in the oral cavity (allergic contact stomatitis). Apart from the stomatitis, contact dermatitis-like reactions to low molecular weight substances in food have not been well described. In relation to food allergy, contact dermatitis-like reactions have not been considered to be of importance.
The normal mode of immune system response to peroral exposure is tolerance (which is an active immune process). This is the case with proteins in food, as well as with low-molecular weight substances.

a) With proteins, tolerance sometimes fails to become established or is later broken, and IgE-mediated food allergy will result. Even with the strongest food allergens (e.g. peanut allergens) tolerance is the usual, normal response, but in a few individuals (~ 0.5%) tolerance fails and food allergy is the result. The reasons that tolerance fails are unclear, environmental factors appear to play a role, and genetic predisposition is important (as always with IgE-mediated allergy).
b) With low-molecular weight substances giving allergic contact dermatitis on the skin, allergy development is less influenced by genetic factors, and exposure is the main determinant for allergy developent.

Sensitization to contact allergens on the skin is not dependent on the total dose, but on the local concentration of the substance, i.e. under given conditions a low concentration of a substance spread over a large surface will not sensitize, while the same total amount of substance concentrated on a smaller area may sensitize a high proportion of exposed individuals. Sensitization is facilitated by prolonged contact, illustrated among the cosmetic products; the risk of sensitization is largest with products that are intended to stay on for a longer time.
The reasons why allergic contact stomatitis is seen relatively seldom are in addition to the cellular composition of the oral mucosa thought to be that saliva will dilute and quickly wash away allergenic substances in the mouth. Further, the oral mucosa is highly vascularized so that substances that have penetrated into the mucosa also will be quickly removed this way (Greenberg, 2003).
Allergic contact stomatitis is most often caused by allergens from sources being in the mouth permanently or frequently applied in high concentrations, like dental products, some hygienic products (mouthwashes, toothpaste) and remedies (Brailo et al., 2006), and components in chewing gum, e.g. cinnamon (Tremblay & Avon, 2008; Georgakopoulou 2010).
With regard to contact allergic manifestations from the lower gastro-intestinal tract, it is known that in rather exceptional cases of strong contact allergy (mainly described for nickel), peroral intake may lead to exacerbations of skin manifestations, presumably because of intestinal absorption. Local symptoms from the bowels are sometimes claimed by patients, but are not common even in strong contact allergy and local intestinal reactions to contact allergens have not been well described and documented.
The reason why gastrointestinal contact allergic sensitization and reactions appear to be very rare, may be the same as those cited for the oral mucosa: dilution and short contact time (for an intestinal segment draining to the same lymph node), and quick removal via blood. In

addition there are the anatomical and immune system differences between skin, buccal mucosa and intestinal mucosa, and the strong tendency to develop tolerance to substances after peroral intake ('oral tolerance'). While there is a strong genetic component in IgE-mediated food allergy, development of dermal contact allergy is not so much dependent on genetic factors; one may speculate that a consequence of this may be that induction and maintenance of oral tolerance to low-molecular weight substances resulting in contact allergy in skin, rarely fails in the gut.

REFERENCES

Brailo V, Boras VV, Alajbeg I, Juras V (2006). Delayed contact sensitivity on the lips and oral mucosa due to propolis – case report. Med Oral Patol Oral Cir Bucal 11;E303-4.

Georgakopoulou EA (2010). Cinnamon contact stomatitis. J Dermatol Case Rep. 2010; 2:28-29.

Greenberg MS. Ulcerative, vesicular, and bullous lesions. In: Greenberg MS, Glick M, editors. Burket's oral medicine, diagnosis and treatment. 10th ed. Hamilton, Ontario: BC Decker; 2003. pp. 50-84.

Tremblay S, Avon SL (2008). Contact allergy to cinnamon: Case report. JCDA 74;445-448. www.cda-adc.ca/jcda/vol-74/issue-5/445.html