Parma, November 30, 2009

MINUTES OF THE 9th PLENARY MEETING

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

Held in Parma on 22-24 September 2009

Adopted on 26 November 2009

AGENDA:

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PARTICIPANTS

Panel Members:

Arturo Anadón (1st day), David Bell (2nd and 3rd days), Mona-Lise Binderup, Wilfried Bursch, Laurence Castle (1st and 2nd days), Riccardo Crebelli, Roland Franz, Nathalie Gontard, Thomas Haertlé, Trine Husøy, Klaus-Dieter Jany, Catherine Leclercq (1st and 2nd days) , Jean-Claude Lhuguenot, Wim C. Mennes, Maria Rosaria Milana (1st and 2nd days), Karla Pfaff, Kettil Svensson, Fidel Toldrá (1st and 2nd days), Rosemary Waring, Detlef Wölfle.

Invited Experts, hearing experts:

David Gott (for item 8.3), Rainer Gürtler (for item 8.1), Ada Knaap (for item 8.3), Iona Pratt (for item 8.2).

Apologies: Karl-Heinz Engel

European Commission: Sirkku Heinimaa

EFSA:

CEF Unit Scientific staff: Alexandre Feigenbaum, Dimitrios Spyropoulos, Anne Theobald, Eric Barthélémy, Cristina Croera, Kim Rygaard Nielsen;

Administrative staff: Hanne Pedersen, Marco Lannutti.

SCA unit Carola Sondermann

Communication Andrew Cutting

1. WELCOME, APOLOGIES FOR ABSENCE

2. ADOPTION OF THE AGENDA

The agenda was adopted.

3. DECLARATIONS OF INTEREST

In accordance with EFSA's Policy on Declarations of Interests, the EFSA secretariat screened the Specific Declarations of Interests (SdoIs) completed by the scientific experts invited to this meeting. For further details on the outcome of this screening please refer to Annex I of these minutes.

4. MATTERS ARISING FROM THE 8TH PLENARY MEETING, 21-23 JULY 2009

The minutes of the 8th Plenary meeting were adopted. They can be seen on http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902694089.htm

5. GENERAL INFORMATION FROM THE EFSA, THE COMMISSION AND THE CHAIR

5.1 EFSA technical report on dissociation of acids and salts used in FCM *(EFSA-Q-2009-00683)*

The Commission has sent a request for technical assistance regarding the extension of a rule already applied in the legislation on plastics in contact with food for the salts of authorised acids, phenols and alcohols with some cations to salts with five other cations, namely lithium, barium, cobalt, copper and manganese. The Panel agreed that the Secretariat could provide technical assistance in any format EFSA considers.

6. FLAVOURINGS

6.1. Flavouring group evaluations

According to Regulation 1565/2000 of 18 July 2000.

6.1.1. Flavouring Group Evaluation 25Rev1 (FGE.25Rev1):

Aliphatic and aromatic hydrocarbons from chemical group 31.

(*EFSA-Q-2009-00565)*

The FGE.25Rev1 includes the assessment of 3 additional candidate substances [FL-no: 01.059, 01.070 and 01.078] compared to FGE.25. The present FGE.25Rev1 deals with 34 flavouring substances in total.

Data on the genotoxicity of the flavouring substances in this group are limited and the genotoxicity could not be assessed adequately for these substances. However, the Panel

concluded that the available data do not preclude an evaluation of the 34 candidate substances using the Procedure.

The Panel concluded that eight candidate substances are expected to be metabolised into innocuous substances, [FL-no: 01.027, 01.028, 01.033, 01.034, 01.038, 01.039, 01.054 and 01.057]. They would not give rise to safety concerns at their estimated intakes arising from their use as flavouring substances based on the "Maximised Survey-derived Daily Intake" (MSDI) approach.

For the remaining 26 candidate substances, [FL-no: 01.022, 01.023, 01.030, 01.031, 01.032, 01.035, 01.036, 01.037, 01.042, 01.043, 01.044, 01.047, 01.050, 01.051, 01.052, 01.053, 01.055, 01.056, 01.058, 01.059, 01.060, 01.064, 01.066, 01.067, 01.070 and 01.078], evaluated through the Procedure, or structurally related supporting substances, no adequate No Observed Adverse Effect Level (NOAEL) were available. Therefore, additional toxicological data are required.

In order to determine whether these conclusions could be applied to the materials of commerce, it is necessary to consider the available specifications. For one substance [FL-no: 01.078] an identification test (ID) and minimum assay value is missing. For eight substances [FL-no: 01.027, 01.032, 01.034, 01.035, 01.050, 01.055, 01.056 and 01.060] information on the stereoisomeric composition has not been specified. Thus, the final evaluation of the materials of commerce cannot be performed for nine substances [FL-no: 01.027, 01.032, 01.034, 01.035, 01.050, 01.055, 01.056, 01.060 and 01.078] pending further information on isomerism and/or specifications.

Thus, for 28 of the 34 substances [FL-no: 01.022, 01.023, 01.027, 01.030, 01.031, 01.032, 01.034, 01.035, 01.036, 01.037, 01.042, 01.043, 01.044, 01.047, 01.050, 01.051, 01.052, 01.053, 01.055, 01.056, 01.058, 01.059, 01.060, 01.064, 01.066, 01.067, 01.070 and 10.078] the Panel has reservations (additional toxicity data are needed, and/or lack of data on stereoisomerism and/or missing data on specifications).

For the remaining six candidate substances [FL-no: 01.028, 01.033, 01.038, 01.039, 01.054 and 01.057] the Panel concluded that they would present no safety concern at their levels of intake estimated on the basis of the MSDI approach.

Changes to the text of the draft Opinion were noted. The opinion was adopted and will be published on http://www.efsa.europa.eu.

6.1.2. Flavouring Group Evaluation 40 (FGE.40):

Alicyclic and aromatic derivatives of 2-hydroxypropionamide from chemical group 16.

(EFSA-Q-2008-044)

FGE.40 deals with one flavouring substance, 2-hydroxy-N-[2-(4-hydroxyphenyl)ethyl]-propionamide [FL-no. 16.107].

It is considered on the basis of the default "Maximised Survey-derived Daily Intake" (MSDI) approach that the candidate substance [FL-no: 16.107] evaluated through the Procedure, will not give rise to safety concerns at the estimated level of intake arising from its use as a flavouring substance at its estimated European daily *per capita* intake (MSDI) is below the threshold of concern for its structural class.

In order to determine whether the conclusion for the candidate substance can be applied to the materials of commerce it is necessary to consider the available specifications. Information on the stereoisomeric composition has not been specified. Thus, the final evaluation of the materials of commerce cannot be performed for the candidate substance, pending further information.

Changes to the text of the draft Opinion were noted. The opinion was adopted and will be published on http://www.efsa.europa.eu.

6.1.3. Flavouring Group Evaluation 42 (FGE.42):

Iron containing organic substances from chemical group 30.

(*EFSA-Q-2008-046*)

This Opinion was formally adopted at the 6th Plenary, but the wording of a paragraph had to be rediscussed before publication. Minor changes have since been introduced.

The two candidate substances, ferrous lactate [FL-no: 16.096] and ferric ammonium citrate [FL-no: 16.089], are organic non-haem iron complexes. The Panel considered it inappropriate to evaluate these two substances using the Procedure for their evaluation as flavouring substances, because neither the classification into structural classes nor the thresholds of concern seem to be sufficiently underpinned. Instead, the Panel decided to evaluate the safety of these two flavouring substances on the basis of data on iron toxicity in general and on toxicity data available for several iron salts and complexes, including the candidate substances.

The data available indicate that, upon ingestion or absorption, the two candidate flavouring substances will be converted into iron ions on one hand and citrate, lactate and ammonium on the other hand. It may thus be anticipated that any adverse effects of these substances would be related to the separate components, rather than the parent substances. No adverse effects are expected from citrate, lactate and ammonium at the anticipated levels of exposure. The possibility of adverse effects elicited by iron has been further considered.

For people with normal iron homeostasis, high levels of exposure should not raise a safety concern, not even if these levels are additional to a background exposure that would suffice to cover the daily iron requirement. However, for people suffering from hereditary haemochromatosis (inadequate down-regulation of iron absorption) a safety concern is concluded. The same holds for patients undergoing regular blood transfusions (e.g. in thallasaemia or ineffective erythropoiesis) which may also lead to (secondary) haemochromatosis.

In order to determine whether these conclusions can be applied to the materials of commerce, the Panel examined the available specifications. Specifications provided were incomplete for the two materials of commerce: for [FL-no: 16.089], no assay value and no ID test have been provided and for [FL-no: 16.096] no ID test is available and no information on stereochemical composition has been submitted. Thus, the final evaluation of the materials of commerce cannot be performed for both candidate substances, pending further information.

Changes to the text of the draft Opinion were noted. The opinion was adopted and will be published on http://www.efsa.europa.eu.

6.1.4. Flavouring Group Evaluation 90 (FGE.90):

Aliphatic, acyclic and alicyclic terpenoid tertiaty alcohols and structurally related substances evaluated by JECFA (68th meeting)

(*EFSA-Q-2009-00561*)

This FGE.90 is a consideration of six flavouring substances [FL-no: 02.018, 02.245, 02.250, 02.251, 13.076 and 13.087] evaluated by the JECFA. These six substances are structurally related to the aliphatic, alicyclic and aromatic saturated and unsaturated tertiary alcohols, aromatic tertiary alcohols and their esters, evaluated by EFSA in FGE.18Rev1.

The Panel agrees with the way the application of the Procedure has been performed by the JECFA for four of the six substances [FL-no: 02.018, 02.245, 02.250 and 02.251].

For the remaining two substances [FL-no: 13.076 and 13.087], no metabolism data are available, neither for the substances themselves nor for related substances. Therefore, in contrast to the JECFA, the Panel cannot conclude that these substances are metabolised to innocuous products. They were therefore evaluated *via* the B-side of the Procedure scheme. A NOAEL could not be identified for these two substances nor for structurally related substances. Accordingly, additional data are required for these substances.

In order to determine whether these conclusions can be applied to the materials of commerce, it is necessary to consider the available specifications. For two substances [FL-no: 02.250 and 02.251], information on the stereoisomeric composition has not been specified and an ID test is missing. Data on solubility in ethanol is lacking for three substances [FL-no: 02.245, 13.076 and 13.087] and in water for one substance [FL-no: 02.245].

Thus, for two substances [FL-no: 02.250, 02.251] the Panel has reservations (missing information on stereoisomerism and missing ID test). For two substances [FL-no: 13.076 and 13.087] the Panel concluded that additional data are needed before they can be evaluated as flavouring substances.

For the remaining two substances [FL-no: 02.018 and 02.245] the Panel agrees with the JECFA conclusion “No safety concern at estimated level of intake as flavouring substance”, based on the MSDI approach.

Changes to the text of the draft Opinion were noted. The opinion was adopted and will be published on http://www.efsa.europa.eu.

6.1.5. Flavouring Group Evaluation 91 (FGE.91):

Simple aliphatic and aromatic sulphides and thiols evaluated by JECFA (68th meeting).

(EFSA-Q-2009-00774)

This FGE.91 is a consideration of 45 flavouring substances evaluated by the JECFA. All the 45 substances are structurally related to the aliphatic and alicyclic mono-, di-, tri-, and polysulphides with or without additional oxygenated functional groups evaluated by EFSA in FGE.08Rev1, in which the substances were divided into ten subgroups (I-X).

Eight substances (the seven tertiary thiols [FL-no: 12.038, 12.085, 12.137, 12.138, 12.145, 12.252 and 12.259] and the sulphonate [FL-no: 12.272]) are structurally related to substances in FGE.08 {[FL-no: 12.172, 12.174] (subgroup III, monothiols), [FL-no: 16.057] (subgroup VII, mono-, di-, tri- and polysulphides with thioacetal structure) and [FL-no: 12.159] (subgroup X, sulphoxides/sulphones and sulphonates)} for which the Panel had identified concerns with respect to genotoxicity. Consequently these substances were not evaluated using the Procedure and adequate genotoxicity data are needed.

Therefore only 37 substances are evaluated through the Procedure.

Furthermore, for the trisulphides [FL-no: 12.114 and 12.256], contrary to the JECFA, the Panel concluded that no adequate NOAEL exists and that additional toxicity data are required.

For the remaining 35 substances the Panel agrees with the JECFA conclusion “No safety concern at estimated levels of intake as flavouring substances” based on the MSDI approach.

In order to determine whether the conclusion for the 37 substances evaluated through the Procedure can be applied to the materials of commerce, it is necessary to consider the available specifications. Information on the stereoisomeric composition has not been specified for 14 substances [FL-no: 12.108, 12.264, 12.267, 12.273, 12.274, 12.284, 12.285, 12.286, 12.287, 12.289, 12.290, 12.292, 12.297 and 15.049] and compositional information of mixture is lacking for one substance [FL-no: 12.274]. Boiling point is missing for two substances [FL-no: 12.253 and 12.256] and for [FL-no: 12.284] an ID test is missing and the range for the boiling point is too wide.

Thus, for 17 of the 37 materials of commerce [FL-no: 12.108, 12.114, 12.253, 12.256, 12.264, 12.267, 12.273, 12.274, 12.284, 12.285, 12.286, 12.287, 12.289, 12.290, 12.292, 12.297 and 15.049], the Panel has reservations (additional toxicity data are needed, missing data on stereoisomerism and/or compositional information of mixture and/or missing data on specifications).

For the remaining 20 materials of commerce [FL-no: 12.012, 12.017, 12.021, 12.126, 12.130, 12.134, 12.139, 12.146, 12.153, 12.240, 12.242, 12.243, 12.254, 12.265, 12.275, 12.276, 12.288, 12.293, 12.294, and 17.036] the Panel agrees with the JECFA conclusion “No safety concern at estimated levels of intake as flavouring substances” based on the MSDI approach.

Changes to the text of the draft Opinion were noted. The opinion was adopted and will be published on http://www.efsa.europa.eu.

6.1.6. Flavouring Group Evaluation 94 (FGE.94):

Aliphatic and aromatic amines and amides evaluated by JECFA (68th meeting).

(*EFSA-Q-2009-00560)*

This FGE.94 is a consideration of 12 flavouring substances [FL-no: 16.090, 16.095, 16.098, 16.099, 16.100, 16.101, 16.102, 16.103, 16.104, 16.105, 16.111 and 17.035] evaluated by the JECFA.

The Panel estimated that evaluations of the substances in the present FGE.94 cannot be supported by any other existing FGE.

The Panel agrees with the way the application of the Procedure has been performed by the JECFA for nine of the 12 substances [FL-no: 16.098, 16.099, 16.100, 16.101, 16.102, 16.103, 16.104, 16.105 and 17.035].

For the three other substances [FL-no: 16.090, 16.095 and 16.111], the Panel did not agree with the application of the Procedure by the JECFA for the following reasons:

- For two substances [FL-no: 16.095 and 16.111], the JECFA used No Observed Effect Level (NOEL) derived from 28 days studies in rats and calculated margins of safety. However, according to the practice of the Panel, the margin of safety can only be derived from a study of at least 90 days duration.

- For [FL-no: 16.090], the JECFA used a NOEL from a 90 days study in rats for *N*-nonanoyl-4-hydroxy-3-methoxybenzylamide ([FL-no: 16.006] of FGE.86) for the estimation of a margin of safety. However, the Panel considers that this substance cannot be used as a supporting substance since is not sufficiently structurally related to [FL-no: 16.090].

Therefore, for these three flavouring substances [FL-no: 16.090, 16.095 and 16.111] the Panel concluded that additional toxicity data are needed before they can be evaluated as flavouring substances.

In order to determine whether the conclusion for the 12 substances can be applied to the materials of commerce, it is necessary to consider the available specifications. For three substances [FL-no: 16.090, 16.102 and 16.104] information on the stereoisomeric composition has not been specified. For two substances [FL-no: 16.100 and 16.101] an ID test is missing. Thus, for seven of the 12 substances [Fl-no: 16.090, 16.095, 16.100, 16.101, 16.102, 16.104 and 16.111] the Panel has reservations (additional toxicity data are needed, and/or missing data isomerism and/or ID test).

For the remaining five substance [FL-no: 16.098, 16.099, 16.103, 16.105 and 17.035] the Panel agrees with the JECFA conclusion “No safety concern at estimated levels of intake as flavouring substances” based on the MSDI approach.

Changes to the text of the draft opinion were noted. The opinion was adopted and will be published on http://www.efsa.europa.eu.

6.2. Opinion on data needed for the evaluation of flavourings

The opinion on data needed for evaluation of flavourings was thoroughly discussed at the previous Plenary, but due to lack of quorum at the moment of the discussion, the opinion was formally adopted with additional minor changes at the current Plenary.

The opinion will be fine-tuned through a public consultation in November till 7 December 2009, followed by a Workshop with stakeholders on 4 and 5 March 2010.

7. FOOD CONTACT MATERIALS

7.1. Evaluation of substances of the 26th list

The draft opinions on the following substances were discussed, modified and adopted:

EFSA Question Number:	**EFSA-Q-2008-020**
Ref. No.:	15180
Name of the substance:	3,4-Diacetoxy-1-butene
CAS number:	18085-02-4
SCF_List:	3
Restriction:	0.05 mg/kg food (including the hydrolysis product 3,4-dihydroxy-1-butene) Only to be used as a comonomer for EVOH copolymers.
Remark for Commission:	Analytical method was provided only on the residual content of the substance and its hydrolysis product.

EFSA Question Number:	**EFSA-Q-2007-077**
Ref. No.:	22074
Name of the substance:	3-Methyl-1,5-pentanediol
CAS number:	4457-71-0
SCF_List:	3
Restriction:	0.05 mg/kg food Only to be used in materials in contact with food at a surface to volume ratio up to 0.5 dm^2/kg (e.g. sealing gaskets).
Remark for Commission:	None

The full opinions as adopted can be seen on the EFSA website at:
http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902959201.htm

7.2. Creation of WG on plastics recycling

Following the publication of the Commission Regulation (EC) No 282/2008 on recycled plastic materials and articles intended to come into contact with foods and the corresponding EFSA guidelines, industry has submitted the first applications for evaluation of recycling processes. Nine applications have been received up to now and till the end of the year are

expected 35 applications in total. These applications belong to the initial phase of the evaluation project which ends by the 31st December of 2009. The Commission will publish a Register of all valid applications received by the EFSA in this initial phase.

The Panel endorsed the creation of a new CEF working group (wg) on "Recycling processes for plastics" to draft the evaluation reports of the dossiers expected to come to EFSA.

Dr. Maria Rosaria Milana and Dr. Karla Pfaff will be the Chair and the vice Chair of the wg respectively.

The wg will maintain strong links with the standing wg on FCM and especially in this initial phase of the work, the evaluation reports and the evaluation principles should be commented by the FCM wg before their presentation to the Panel.

7.3. Update on Bisphenol A (BPA) - EFSA Statement

Letter of Antidote

Following a letter of Antidote Company (Dr. Claude Reiss, 28 July 2009) to EFSA, the Panel discussed the data presented by Antidote on BPA and took note of the following Statement of EFSA.

The letter of Antidote refers to an exchange of correspondence in written and by e-mail. The letter points out weaknesses in the 2008 opinion of the Panel, as "*the Panel ignores toxicogenomics data obtained in cultured human cells, which Antidote Europe sent to EFSA on May 15, 2008*". Dr. Reiss "*urged EFSA to base its recommendations on the risk posed by BPA to humans, on data obtained from human cell cultures to begin with, using methods that are now well established, in place of unreliable animal tests*."

Dr. Reiss referred to results deposited in ArrayExpress (ref E-TOXM-31 and A-MEXP-798) and a "*toxicogenomics data sheet on BPA*". EFSA noted that there was no sufficient reporting of procedures, no method validation, no peer reviewed data or reports, no data interpretation.

More specifically, the study (from what can be seen from the web site in the absence of any other public report: http://www.ebi.ac.uk/microarray-as/ae/browse.html?keywords=E-TOXM-31+) has many flaws in the experimental design and many limitations: e.g. only two human cancer cell lines of hepatic and neuronal origin were used and not "normal" primary cells , just two test concentrations of BPA, one as high as the IC50, exposure medium for neuronal cells (i.e. cell culture supernatant of HEPG2 cells containing bisphenol A and possible "metabolites", while HepG2 cells do not conjugate) not characterized in its composition, no dose-response provided, only raw data available (no processed data). Furthermore, the concentrations of BPA (200 mM = IC50 and 20 mM = 1/10 of the IC50) used in their *in vitro* study have no physiological relevance for the *in vivo* situation, as these high levels will never be reached in humans.

Overall, this study does not support the statements of Antidote in their correspondence and represents a poor contribution to the risk assessment of BPA.

In the short discussion which followed the presentation of this Statement, Panel Members emphasized that according to the EU regulations a TDI cannot be based on *in vitro* studies.

8. SMOKE FLAVOURINGS

8.1. Draft opinion on Smoke Flavouring Primary Product Scansmoke R909

EFSA-Q-2005-262

The rapporteur presented the draft opinion. It was discussed and some changes were suggested. The suggested changes will be introduced to the draft and it will be forwarded to the next Plenary meeting for final discussion and adoption.

8.2. Draft opinion on Smoke Flavouring Primary Product Fumokomp

EFSA-Q-2005-265.

The Panel considered that there were major deficiencies in the summary of the 90-day study in rats submitted as part of the application dossier for Fumokomp, and that since the detailed report of this study was not provided, the validity of the study could not be confirmed. Furthermore the identity of the material tested in the study is unknown. For these reasons the study could not be used in the safety evaluation of Fumokomp.

The Panel concluded that the toxicological data do not enable the safety of use of Fumokomp to be established.

The full opinions as adopted can be seen on the EFSA website at:
http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902942587.htm

8.3. Statement on the Interpretation of the Margin of Safety

EFSA-Q-2009-764

The draft statement on how to interpret the margins of safety in the context of the evaluation of smoke flavourings was presented. The Panel members discussed the approach and changes were suggested. The document will be forwarded to the next Plenary meeting for final discussion and expected adoption.

9. DOSSIERS ON FOOD ENZYMES FOR EVALUATION BY CEF

The Chair of the WG reported to the Panel about a meeting with stakeholders which took place after the session of 23 September.

10. IRRADIATION

The chair of the Working Group reported from the first meeting which was held 21-22 September in Parma. The members of the WG were informed about the scope of the opinion. It is agreed with the European Commission that two separate scientific opinions on irradiation of food will be expressed: one on the efficacy and microbiological safety of the process (by the

Panel on Biological Hazards - BIOHAZ) and one on the chemical safety of the process (by the Panel on Food Contact Materials, Enzymes, Flavourings and Processing aids - CEF). December 2010 is proposed as deadline for the delivery of the two opinions.

11. OTHER BUSINESS

No other business

12. ANNEX 1: INTERESTS AND ACTIONS RESULTING FROM THE SCREENING OF SPECIFIC DECLARATION OF INTERESTS

In her Specific Declaration of Interests, Dr. M.-L. Binderup declared an interest for the substance 2,3,6-Trimethylphenol (REF. No. 46630) and 1,10-Diaminodecane (15260). These substances were not discussed during the Plenary and postponed.
In her Specific Declaration of Interests, Dr. M-R Milana declared an interest for the substance Zeolite silver (86437). This substance was also postponed.

INTERESTS AND ACTIONS RESULTING FROM DECLARATIONS DONE AT THE MEETINGS

Concerning the issue of BPA (item 7.3), Dr. Milana, Pfaff, Svensson and Wölfle declared interest because they advise their National Authorities on the issue. Dr. Bell declared interest because his University gets funding from a Company producing BPA (but for another purpose) and since he wrote a publication on Risk Assessment on BPA.

However since the item 7.3 is a Statement of EFSA, there was no vote and no conflict for this meeting.