Parma, 25 November 2008

MINUTES OF THE 2nd PLENARY MEETING OF THE SCIENTIFIC PANEL ON FOOD CONTACT MATERIALS, ENZYMES, FLAVOURINGS AND PROCESSING AIDS (CEF)

Held in Parma on 23-25 September 2008

Adopted on 31 October 2008 by written procedure

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MINUTES OF THE 2nd PLENARY MEETING OF THE SCIENTIFIC PANEL ON CONTACT MATERIALS, ENZYMES, FLAVOURINGS AND PROCESSING AIDS (CEF)

Held in Parma on 23-25 September 2008

PARTICIPANTS

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

Experts:
Wolfgang Dekant (for item 7.3, substances REF. No. 91530 and 91815), David Gott (for item 7.1) Jørn Gry (for items 6.1, 6.2 and 6.3) and Rainer Gürtler (for item 6.2).

Apologies:
Laurence Castle

EFSA:
Didier Verloo (AMU Unit) (item 7.1), Jean-Lou Dorne (CONTAM Unit) (item 7.1) and Andrew Cutting (Press office) (for items 6.1 and 7.1).

CEF Unit:
Alexandre Feigenbaum, Dimitrios Spyropoulos, Anne Theobald Kim Rygaard Nielsen, Eric Barthélémy, Marika Collin, Cristina Croera (scientific staff) – Hanne Pedersen, Marco Lannutti (administrative staff).

Commission:
Wim Debeukelaere (2nd day)

1. WELCOME; APOLOGIES FOR ABSENCE

In absence of the Chair, the Vice Chair Pr. Engel chaired for the first day. He welcomed the participants and the secretariat noted apologies.

2. ADOPTION OF THE AGENDA

The agenda was adopted.

3. DECLARATIONS OF INTEREST

The declarations concerning items on the agenda of this meeting are noted under the specific items 7.1 on bisphenol A and 7.3 on the 20th list of substances for food contact materials.

4. MATTERS ARISING FROM THE 1ST PLENARY MEETING HELD ON 10 JULY 2008

The minutes of the previous meeting have been adopted by written procedure. They can be seen on:
http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178718516776.htm

5. GENERAL INFORMATION FROM EFSA AND THE COMMISSION

The Secretariat informed the Panel members about the future expert survey.

An extranet will be accessible to experts by the next Panel meeting.

Members were invited to disseminate information about the call for new Panels in their Institute / University.

6. FLAVOURINGS

6.1. Presentation of the evaluation approach for substances currently on the market

A presentation of the ongoing Evaluation Programme was given.
The background of the evaluation approach was given and the Evaluation Procedure was presented. The interaction of FLAVIS and of the two Working Groups was described.
In addition the status of the Evaluation Programme and the future work after the finalisation of the Evaluation Programme was described.

6.2. Re-Evaluation of FGE.19 substances

6.2.1 Genotoxicity test strategy for substances belonging to subgroups of FGE.19$_{1\text{-}17}$
EFSA-Q-2008-710
(Statement of the CEF Panel)

The AFC Panel has classified 360 α,β-unsaturated aldehydes, ketones and precursors into FGE.19, for which genotoxicity data have to be examined before they can be evaluated through the usual procedure. FGE.19 has been divided into 28 subgroups. For the substances in 17 subgroups, the AFC Panel had concluded that further data on genotoxicity are needed (26th Plenary Meting November 2007: http://www.efsa.europa.eu/EFSA/Event_Meeting/afc_minutes_26thplen_en.pdf).

A document describing a genotoxicity test strategy for these substances has been prepared. It was presented and discussed by the Panel.

The list of substances to be tested will be published as another statement.

6.2.2 List of representative α,β-unsaturated aldehydes and ketones for genotoxicity testing EFSA-Q-2008-709

(statement of the CEF Panel)

The Panel decided that the genotoxicity data should be requested for substances considered as representative for each of the subgroups for which the AFC Panel had concluded that further data on genotoxicity are needed. A draft list of representative substances was prepared and discussed. In each subgroup, the representative substances were selected taking into account chain length, branching, lipophilicity and possible additional functional groups. Results of (Q)SAR studies were also considered.

This draft list will be completed taking into account comments received after the meeting and considering all subgroups of FGE.19. A revised list should be presented for adoption at the next Panel meeting.

6.2.3 Miscellaneous

The Panel took note of a recent publication on α,β-unsaturated aldehydes and related substances used as flavour ingredients (Adams *et al*., Food and Chemical Toxicology 46 (2008) 2935-2967). In this publication, the "Generally Recognized as Safe" (GRAS) status of these substances was reaffirmed. The Panel emphasizes that in the EU, the deliberate addition to food of substances which are both genotoxic and carcinogenic is considered not acceptable (Barlow *et al*., Food and Chemical Toxicology 44 (2006) 1636-1650), whatever the dose. Therefore, this publication does not change the requirement to provide data on the genotoxicity for selected substances from FGE.19 nor does it have any impact on the test strategy.

6.3. **Flavouring Group Evaluations (FGE)**

6.3.1. ***FGE.71***
EFSA-Q-2008-055

Consideration of aliphatic, α,β-unsaturated aldehydes, acids and related alcohols, acetals and esters evaluated by JECFA (63rd meeting)

This issue was deferred to the next Plenary meeting due to lack of time.

6.3.2. ***FGE.89***
EFSA-Q-2008-309

Consideration of phenyl-substituted aliphatic tertiary alcohols and related aldehydes and esters evaluated by JECFA (63rd and 68th meetings)

This issue was deferred to the next Plenary meeting due to lack of time.

6.3.3. ***FGE.201***
EFSA-Q-2008-758

2-Alkylated aliphatic acyclic α,β-unsaturated aldehydes and precursors with or without additional double-bonds from chemical subgroup 1.1.2 of FGE.19

The Flavouring Group Evaluation 201 (FGE.201) consists of 11 aliphatic acyclic 2-alkylated α,β-unsaturated aldehydes [FL-no: 05.033, 05.090, 05.095, 05.105, 05.107, 05.126, 05.130 and 05.178] or their precursors [FL-no: 02.174, 09.177 and 09.931], with or without additional double bonds, constituting the subgroup 1.1.2 of FGE.19.
For explanation of classification, please consult Minutes from the AFC Panel meeting November 2007, http://www.efsa.europa.eu/EFSA/Event_Meeting/afc_minutes_26thplen_en.pdf.

Owing to the positive results reported for 2-methyl-2-propenal and for the structurally related 2-ethyl, 2-propyl and 2 butyl substituted 2-propenal derivatives, the Panel concluded that a genotoxic potential of the 11 α,β-unsaturated aldehydes and alcohols and related esters in the present FGE.201 could not be ruled out. Accordingly, additional data are required. Pending submission of these data, the 11 substances cannot be evaluated through the usual Procedure.

Changes to the text of the draft opinion were noted. The opinion was adopted and will be published at
http://www.efsa.europa.eu/EFSA/ScientificPanels/efsa_locale-1178620753812_CEF.htm

6.3.4. ***FGE.202***
EFSA-Q-2008-759

3-Alkylated aliphatic acyclic α,β-unsaturated aldehydes and precursors with or without additional double-bonds from chemical subgroup 1.1.3 of FGE.19.

The Flavouring Group Evaluation 202 (FGE.202) consists of 37 substances, [FL-no: 05.020, 05.124 and 05.148] or precursors thereof [FL-no: 02.012, 02.029, 02.058, 02.109, 02.204, 06.004, 06.005, 09.011, 09.048, 09.067, 09.076, 09.128, 09.150, 09.167, 09.169, 09.212, 09.213, 09.382, 09.383, 09.405, 09.424, 09.431, 09.453, 09.471, 09.515, 09.691, 09.692, 09.693, 09.694, 09.695, 09.696, 09.704, 09.767 and 09.818], which are acyclic aliphatic 3-alkylated α,β-unsaturated aldehydes with and without additional double bonds.
For explanation of classification, please consult Minutes from the AFC Panel meeting November 2007, http://www.efsa.europa.eu/EFSA/Event_Meeting/afc_minutes_26thplen_en.pdf.

Based on the available data provided, the Panel concluded that there would be no safety concern with respect to genotoxicity or carcinogenicity for the 37 α,β-unsaturated substances presented in this FGE. Therefore the 37 flavouring substances in FGE.202 will be further evaluated, using the usual Procedure.

Changes to the text of the draft opinion were noted. The opinion was adopted and will be published at
http://www.efsa.europa.eu/EFSA/ScientificPanels/efsa_locale-1178620753812_CEF.htm

6.4. Presentation of the new Regulation on flavouring and certain food ingredients with flavouring properties for use in and on foods

The new regulation on flavouring substances was presented. When the regulation will enter in force, EFSA has a deadline of 6 months to adopt the new flavouring guidelines.
As the period of 6 months includes 2 months for public consultation, the discussion on these new guidelines has started and special working group meetings will be organised by the CEF Unit and by FLAVIS.

7. FOOD CONTACT MATERIALS

7.1. Bisphenol A

David Bell declared an interest because he has written a publication on Bisphenol A. This was not considered as a conflict. He also declared hat he conducts research on dioxins for which he receives funding from a company which is also a producer of bisphenol A. This was considered as a conflict of interest and he left the room during the discussion.

D. Gott, T. Husoy, M-R. Milana, K. Pfaff, K. Svensson and D. Woelfle declared that they have given scientific advice to their respective Ministry in the frame of their institutional activities. This was not considered as a conflict of interest.

7.1.1. Letter from Prof. Schönfelder, Prof. Chahoud and Dr. Gies to the EFSA Executive Director

The Panel discussed the arguments presented in a letter sent to EFSA by Prof. Schönfelder, Prof. Chahoud and Dr. Gies (July 31st 2008) and the nine literature references cited therein. In this letter it was suggested that the circulating free Bisphenol A (BPA) in maternal, fetal and neonatal blood is higher than anticipated and that the Opinion of the EFSA AFC Panel (July, 2008) concerning safety of BPA for neonates and unborn children would be incorrect.

However, in its opinion of 2006 on BPA, the AFC Panel had already highlighted that there are problems concerning some of the methods used for measurement of BPA in human blood and that the validity of reported high blood levels is questionable.

Five of the references cited in the Schönfelder letter have made use of a non-specific analytical ELISA method, which, as pointed out in the EFSA opinion of 2006, overestimates the concentration of free BPA in blood samples.

Two references have made use of HPLC-FLD. One (Lee *at al*, 2008) reported total BPA levels (free + conjugated) in fetal blood from non-detectable to 8.9 µg/L (mean value of 0.6 µg /L). The other (Kuroda *et al*, 2003) reported BPA levels in maternal and cord blood ranging from 0.2-0.8 µg /L (mean value of 0.5 µg /L). The problem of the BPA-conjugates splitting to give extra free BPA was not addressed.

The two other references (Schönfelder *et al.*, 2002; Padmanabhan *et al.*, 2008), one based on GC-MS and one on LC-MS, report levels of free BPA up to about 20 µg/L blood. Due to analytical deficiencies and inconsistencies in the reporting of the study results, it is not possible to evaluate if

these results are reliable for free BPA. The high blood levels of around 20 µg/L for free BPA reported in these two studies are not consistent with knowledge on the toxicokinetics (including BPA metabolism and the relationship between known intentional oral exposures and blood BPA levels in humans) and the estimated levels of actual exposure through the diet (EU RAR, 2003 and 2008; EFSA, 2006).

Given the doubts on the analytical methodology of the Schönfelder *et al.* (2002) and Padmanabhan *et al.* (2008) studies, it is equally questionable if the reported data on neonatal (cord) blood levels would be reliable, either. Therefore, these data do not demonstrate significant exposure of the human fetus to free BPA and the Panel does not see any need to revise the EFSA opinions of 2006 and 2008.

7.1.2. Exeter study (Lang *et al.*, 2008: Journal of the American Medical Association, 300, 1303-1310)
(EFSA-Q-2008-702)

The Panel took note of a study recently published in the Journal of the American Medical Association relating urinary BPA concentrations with medical disorders (Lang et al., 2008). The study makes use of the existing US National Health and Nutrition Examination Survey (NHANES) for 2003-2004, which comprises measurements of BPA in urine samples of individuals sampled once at the time the participants were asked about their health status. These data can be used as an estimation of the exposure to BPA within 24 hrs of sample collection. However, there is no information on exposure during the time needed for development of diseases such as diabetes and cardiovascular conditions or changes in plasma liver enzyme activities. Although the study authors attempted to rule out several commonly identified confounders of studies of this type, the observed association between urinary BPA elimination and the conditions mentioned above may have been a chance finding or may be due to non-identified confounders.

The Panel concluded that this single study does not provide proof for a causal link between exposure to BPA and the health conditions mentioned above. Therefore, the Panel concluded that there is no need to revise the TDI as derived by the AFC Panel in 2006.

The full statement as adopted can be seen on the EFSA website at:
http://www.efsa.europa.eu/cs/BlobServer/Statement/cef_ej838_statement%20on%20bpa_medical%20disorders_statem_en.pdf?ssbinary=true

7.2. Introduction to the evaluation of substances for use in Food Contact Materials

On the occasion of the second meeting of the new CEF Panel and in view of the discussions for first time in this Panel on food contact materials, the guidelines and the practices followed in EFSA for the evaluation of substances upon receipt of an application for authorisation of a substance for use in food contact materials were presented

7.3. Evaluation of substances for the 20th list of monomers and additives

M.-L. Binderup declared an interest for the substance REF. No. 33535, alpha-Alkenes(C20-C24) maleic anhydride-4-amino-2,2,6,6-tetramethylpiperidine, polymer, as her Institute had prepared the evaluation report of the substance under contract with EFSA. This was considered as a conflict of interest because she could not act at the same time as a representative of the contractor and a

member of the Panel with voting rights. She was allowed to stay in the room to answer questions specifically addressed to her but did not participate to the discussion of the opinion. Another Panel member presented the draft opinion.

R. Franz declared an interest for the substances REF. No. 91530, sulphosuccinic acid, alkyl (C4-C20) or cyclohexyl diesters, sodium salts, REF. No. 91815, sulphosuccinic acid mono-alkyl (C10-C16) polyethyleneglycol esters, sodium salts and REF. No. 93450, Titanium dioxide, coated with a copolymer of n-octyltrichlorosilane and [aminotris(methylenephosphonic acid), penta sodium salt], as his Institute had performed some of experimental work reported in the submitted dossiers. This was considered as a conflict of interest. Thus, he left the room during the discussions.

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

EFSA Question Number:	**EFSA-Q-2008-030**
Ref. No.:	30607
Name of the substance:	Acids, C2-C24, aliphatic, linear, monocarboxylic, from natural oils and fats, lithium salt
CAS number:	-
SCF_List:	3
Restriction:	In accordance with other lithium compounds this will be subject to a group SML of 0.6 mg Li/kg food
Remark for Commission:	None

EFSA Question Number:	**EFSA-Q-2006-183**
Ref. No.:	33105
Name of the substance:	Alcohols, C12-14 secondary, beta-(2-hydroxyethoxy), ethoxylated
CAS number:	146340-15-0
SCF_List:	3
Restriction:	5 mg/kg food
Remark for Commission:	The restriction may be exceeded in polyolephines

EFSA Question Number:	**EFSA-Q-2006-171**
Ref. No.:	33535
Name of the substance:	alpha-Alkenes(C20-C24) maleic anhydride-4-amino-2,2,6,6-tetramethylpiperidine, polymer
CAS number:	152261-33-1
SCF_List:	3
Restriction:	Not for contact with fatty or alcoholic foods
Remark for Commission:	No method for specific migration – only a method for determination of the content in polymer and a method for determination of the starting substances in food simulants are available.

EFSA Question Number:	**EFSA-Q-2007-013**
Ref. No.:	80510
Name of the substance:	Poly(3-nonyl-1,1-dioxo-1-thiopropane-1,3-diyl)-block-poly(x-oleyl-7-hydroxy-1,5-diiminooctane-1,8-diyl), process mixture with x=1 and/ or 5, neutralised with dodecylbenzenesulfonic acid
CAS number:	1010121-89-7
SCF_List:	3
Restriction:	Only to be used as a polymerization production aid in PE, PP and PS
Remark for Commission:	None

EFSA Question Number:	**EFSA-Q-2006-139**
Ref. No.:	81870
Name of the substance:	N,N''-1,3-propanediylbis(N'-octadecylurea)
CAS number:	35674-65-8
SCF_List:	3
Restriction:	0.05 mg/kg food
Remark for Commission:	None

EFSA Question Number:	**EFSA-Q-2007-019**
Ref. No.:	93450
Name of the substance:	Titanium dioxide, coated with a copolymer of n-octyltrichlorosilane and [aminotris(methylenephosphonic acid), penta sodium salt]
CAS number:	5283-66-9 for octyltrichlorosilane, 2235-43-0 for aminotris(methylenephosphonic acid), penta sodium salt and 13463-67-7 for titanium dioxide
SCF_List:	3
Restriction:	Specification: Content of the surface treatment copolymer of the coated titanium dioxide less than 1% w/w
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_1211902123216.htm

The draft opinions on the following substances:
REF. No. 91530, sulphosuccinic acid, alkyl (C4-C20) or cyclohexyl diesters, sodium salts
and
REF. No. 91815, sulphosuccinic acid mono-alkyl (C10-C16) polyethyleneglycol esters, sodium salts,
were discussed and many changes were made. The opinions were sent back to the working group for further consideration.

The draft opinions on the following substances:
REF. No. 49080, N-(2,6-diisopropylphenyl)-6-[4-(1,1,3,3-tetramethylbutyl)phenoxy]-1H-benzo[de]isoquinoline-1,3(2H)-dione and
REF. No.94985, trimethylolpropane, mixed triesters and diesters with benzoic acid and 2-ethylhexanoic acid,
were deferred to the next Plenary, due to lack of time.

8. ENZYMES (EFSA-Q-2007-080)

The scope of the new ad-hoc CEF Working Group was presented. The Working Group is preparing guidelines for the evaluation of enzymes. This work is expected to be completed by summer 2009.

9. SMOKE FLAVOURING

The discussion on the approach to assess the exposure to smoke flavourings is scheduled for the next Panel meeting.

10. IRRADIATION OF FOOD

(EFSA-Q-2006-034)

The former AFC Panel had received a mandate to evaluate the safety of irradiation of certain food products that is passed on to the CEF Panel. After clarification of the mandate with the Commission services it was decided to answer this request in two scientific opinions as the safety of irradiation of food is linked also to the efficacy of the process. The CEF and BIOHAZ Panel will provide scientific opinions on the safety of irradiation of food (mainly addressing chemical safety) and on the efficacy of irradiation (mainly addressing microbial safety), respectively. The opinions will be coordinated in terms of timing and cross-referring.

The adoption of these opinions is foreseen for December 2009.

11. ANY OTHER BUSINESS

The Panel members are advised to take note on the date of the next meeting: 25, 26 and 27 November.