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MINUTES OF THE 29th PLENARY MEETING OF THE SCIENTIFIC PANEL ON FOOD ADDITIVES AND NUTRIENT SOURCES ADDED TO FOOD (ANS)

Held in Parma on 6-8 December 2011

Adopted on 14 February 2012 at the 30th Plenary meeting

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MINUTES OF THE 29th PLENARY MEETING OF THE SCIENTIFIC PANEL ON FOOD ADDITIVES AND NUTRIENT SOURCES ADDED TO FOOD (ANS)

Held in Parma on 6-8 December 2011

Panel Members:

Riccardo Crebelli (1st and 2nd day), Birgit Dusemund, Pierre Galtier, John Gilbert, David Gott, Ursula Gundert-Remy, Jürgen König, Claude Lambré, Jean-Charles Leblanc, Alicja Mortensen (2nd and 3rd day), Pasquale Mosesso, Dominique Parent-Massin, Ivonne Rietjens, Ivan Stankovic, Paul Tobback, Ine Waalkens-Berendsen, Rudolf Woutersen and Matthew Wright (1st and 2nd day).

Apologies

Apologies for absence were noted from Fernando Aguilar.

EFSA

Hugues Kenigswald, George Kass, Ana Maria Rincon, Kim Petersen, (scientific staff), Anna Campanini, and Maria Correa (administrative staff).

European Commission

Jiri Sochor.

1. WELCOME; APOLOGIES FOR ABSENCE

The Chair welcomed the participants. Apologies for absence were noted.

2. ADOPTION OF THE AGENDA

The agenda was adopted without changes. The Panel were informed that the draft documents for agenda items 7.3. and 7.4 were not available sufficiently in advance of the meeting to be considered. The discussions will be postponed to a forthcoming meeting.

3. DECLARATIONS OF INTEREST

In accordance with EFSA's Policy on Declarations of Interests, EFSA screened the Annual Declaration of interest (ADoI) and Specific Declaration 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 of this document.

No additional interests were declared at the opening of the meeting.

4. ADOPTION OF THE MINUTES OF THE 28TH ANS PLENARY MEETING ON 25-27 OCTOBER 2011

The draft minutes were discussed and some changes were suggested. The adopted minutes can be seen on:

http://www.efsa.europa.eu/en/science/

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

5.1. Chair

The Chair informed the Panel that two plenary meetings of the Scientific Committee have taken place since the last plenary meeting of the Panel.

The draft revised policy of independence and its practical consequences for the declarations of Interests and their screening by EFSA have been discussed by the Scientific Committee.

The draft EFSA guidance on default values is progressing towards finalisation and a new proposed default body weight of 70 kg is considered.

The Scientific Committee is also working on an opinion on harmonised risk terminology to insure consistency between EFSA's Scientific Committee and the Panels.

Following the question raised by the ANS Panel on the risk assessment of regulated compounds voluntarily added to the diet with allergenic properties or containing impurities or by-products with allergenic properties, the Scientific Committee has decided to establish a new working group on the assessment approach for regulated compounds with by-products with allergenic properties. Since allergenicity is normally assessed by the NDA Panel this working group should focus on this specific issue which might be of interest for several Panels. The first meeting of the working group is expected to take place at the earliest in February 2012 and C. Lambre, D. Parrent-Massin and U. Gundert-Remy volunteered to join the working group.

Following the question raised by the ANS Panel on the use of the margin of exposure approach for the safety assessment of genotoxic and carcinogenic contaminants or residuals of food additives, the Scientific Committee has decided to organise a preparatory meeting in January 2012 on the applicability of the margin of exposure approach for the safety assessment of genotoxic and carcinogenic impurities in substances deliberately added to food or feed.

5.2. EFSA

H. Kenigswald updated the Panel on the progress of the merging of the CEF and ANS units. The Panel was furthermore informed that EFSA will move to its new Seat starting from January 2012.

The Panel was informed that the Commission and EFSA have clarified in a meeting the legal situation for food additives under re-evaluation resulting from article 6.3 of Regulation 257/2010/EC: if following a first public call for data, there are important data gaps that hinder the possibility to conclude on the safety of the authorised uses of a food additive, a specific call data shall be made by EFSA to request the missing data before the Panel can finalise its assessment. The Panel commented that this will delay the re-evaluation process and as a consequence additives that might cause public health concerns might be allowed to stay on the market longer.

5.3. European Commission

J. Sochor informed the Panel that following discussions between EFSA and the Commission data from the historical archives of the SCF relevant for the re-evaluation of food additives will be progressively made available to EFSA.

6. REPORT FROM THE WORKING GROUPS

6.1. Working Group A on Food Additives and Nutrient Sources

The Chair of Working Group A summarised the outcome of the discussions during the 30th Working Group A meeting on 15-16 November 2011.

6.2. Working Group B on Food Additives and Nutrient Sources

The Vice-Chair of Working Group B summarised the outcome of the discussions during the 20th Working Group B meeting held in Parma on 15-16-November 2011.

6.3. Working Group "Guidance on Food Additives"

The public consultation has been launched on 15 November 2011 and the deadline for comments is 15 January 2012. At least one meeting is planned to take place in early 2012 to discuss the comments. The revised draft guidance is foreseen to be discussed again by the Panel in the May 2012 plenary meeting.

6.4. Working Group "Exposure assessment"

A technical meeting with stakeholders on the exposure assessment of food additives has taken place in Brussels on 28 November 2011. The European Consumer's Organisation (BEUC), the Federation of European Specialty Ingredients (ELC), FoodDrink Europe, some of their member companies and associations and industry consultants participated to this meeting. The stakeholders were informed about the current and under development methodologies for the exposure assessment of food additives and these issues were discussed. In addition, FoodDrink Europe presented their process for collecting the data on actual use and use levels of authorised food additives.

On the same day a meeting of the working group took place dedicated to the finalisation of the draft correspondence table between the food classification systems of the Regulation on food additives and of the EFSA comprehensive food consumption database.

6.5. Working Group "Chemistry and specifications"

No meeting has taken place since the last Panel Plenary meeting.

7. FOOD ADDITIVES

7.1. Aspartame (*Question N° EFSA-Q-2011-00406)*

The acting Director of Scientific Evaluation of Regulated Products, P. Bergman, made a presentation of the current policy concerning conflict of interests. He highlighted that since the purpose of the declaration of interests is to enable EFSA to identify potential conflict of interests between external interests and EFSA activities, previous or ongoing EFSA involvements should not be declared. This addressed the question of the Panel on whether past involvement in EFSA assessments related to aspartame could generate any conflict of interests.

The Panel agreed to propose A. Mortensen for chairing the working group on aspartame and C. Lambré as Vice-Chair of this working group. The working group should start in January 2012 after assessment by EFSA of the declaration of interests of the Chair, Vice-Chair and members.

7.2. Indigo Carmine (E 132) (*Question N° EFSA-Q-2011-00358*)

The ANS unit has been recently informed that the FEEDAP Unit has received an application for the use of indigo carmine in feed and that following a specific request by EFSA, the applicant has indicated that they are considering providing the genotoxicity data that were requested in the public call for data for the re-evaluation of this colour as a food additive published on 26 January 2011 and closed on 30 September 2011. Therefore, the finalisation of the assessment by the ANS Panel is temporarily postponed until either the new data are provided or the deadline set for providing them is reached (March 2012). As a consequence the Commission has been asked to extend the deadline for the finalisation of evaluation of indigo carmine.

7.3. Revised exposure assessment of ethyl lauroyl arginate (*Question N° EFSA-Q-2011-00030*)

EFSA asked the Panel for guidance on a revised assessment of the exposure to ethyl lauroyl arginate because the request for technical assistance by the Commission makes reference to the use of this food additive in cosmetics.

7.4. Safety assessment of the exposure to lutein preparations based on new data on the use levels of lutein (*Question N° EFSA-Q-2011-00807*)

The draft statement to address this self-task mandate has not been finalised before the meeting and the discussion was postponed to the next plenary meeting of the Panel. Accordingly, the deadline will be extended to the end of February 2012.

7.5. Advantame (*Question N° EFSA-Q-2010-00943)*

The Panel discussed the answer received from the applicant following the request for clarification and additional data made in July 2011.

7.6. E 321 Butylated hydroxytoluene (BHT) (*Question N° EFSA-Q-2010-00344)*

The draft opinion was discussed. Further clarifications and improvements were suggested.

7.7. E153 Vegetable carbon (*Question N° EFSA-Q-2010-00355)*

The draft opinion was discussed. Further clarifications and improvements were suggested.

7.8. E 912 Montan acid esters (*Question N° EFSA-Q-2011-00708)*

Taking into account the legal situation for food additives under re-evaluation resulting from article 6.3 of Regulation 257/2010/EC (as described in section 5.2 of these minutes), the draft opinion was not discussed in detail. In this case, a general call for data for the waxes was launched in 2009 and even though no data were received for montan acid esters, a new public call for data must be launched to try to address the data gaps.

The Panel agreed that interested parties should be requested to provide a full data package on both toxicokinetics and toxicity including all other studies that could be relevant for the evaluation of montan acid esters. Furthermore interested parties should provide data on the uses and use levels of montan acid esters.

In cases where interested parties judge that some studies or tests are not necessary for the safety assessment they should provide a scientific justification.

7.9. E 160e *β*-apo-8' carotenal *(Question N° EFSA-Q-2011-00352)*

The draft opinion was discussed. Further clarifications and improvements were suggested and the opinion was adopted. Since the opinion on β-apo-8'-carotenal is connected to the opinion on mixed (E 160a(i) and beta-carotene (E 160a(ii) it was agreed by the Panel that the opinion on β-apo-8'-carotenal should be published together with the opinion on mixed carotenes and beta-carotene.

β-Apo-8'-carotenal (E 160e) is authorized as food additive in the EU and was previously evaluated by the JECFA in 1974 and the SCF in 1975 and 2000. The SCF and JECFA both established an ADI of 5 mg/kg bw/day, which was withdrawn by the SCF in 2000.

For the re-evaluation of β-apo-8'-carotenal several new studies appeared to be available. These studies included: i) additional in vitro genotoxicity studies that were generally negative, ii) an *in vivo* micronucleus study that was negative, iii) a 4 week and a 13 week toxicity study in rats performed according to OECD guidelines and under GLP, iv) two recent reproductive and developmental toxicity studies performed according to OECD guidelines and under GLP and v) data from old chronic toxicity studies which reported no adverse effects.

With the new data a full dataset has been made available for the re-evaluation of β-apo-8'-carotenal. The Panel discussed the available dataset and agreed that especially the 13 week study in rats which gives the lowest LOAEL should be used to derive the ADI. The formation of eosinophilic droplets in the kidneys was considered the critical effect in this study. However the data appeared not to be suitable for a BMD analysis. As a consequence the Panel concluded that based on the LOAEL of 10 mg/kg bw/day from the rat study and an uncertainty factor of 200 an ADI for β-apo-8'-carotenal of 0.05 mg/kg bw/day could be established.

7.10. E 160a(i) Mixed carotenes and E 160a(ii) beta-carotene *(Questions N° EFSA-Q-2011-00354, EFSA-Q-2011-00431)*

The draft opinion was discussed. Further clarifications and improvements were suggested.

7.11. E 904 Shellac *(Question N° EFSA-Q-2011-00705)*

Taking into account the legal situation for food additives under re-evaluation resulting from article 6.3 of Regulation 257/2010/EC (as described in section 5.2 of these minutes), the draft opinion was

not discussed in detail. In this case, a general call for data for the waxes was launched in 2009 and even though no data were received for shellac, a new public call for data must be launched to try to address the data gaps.

The Panel agreed that interested parties should be requested to provide a full data package on both toxicokinetics and toxicity including all other studies that could be relevant for the evaluation of shellac. Furthermore interested parties should provide data on the uses and use levels of shellac.

In cases where interested parties judge that some studies or tests are not necessary for the safety assessment they should provide a scientific justification.

8. NUTRIENT SOURCES

8.1. Heme iron *(Question N° EFSA-Q-2011-01107)*

The Chair presented the new mandate that has been received from the European Commission to provide a scientific opinion, based on its consideration of the safety and bioavailability of heme iron (blood peptonates) as a source of iron added for nutritional purposes to food for the general population, including food supplements.

In its opinion in 2010 on the same nutrient source, the ANS Panel concluded that the available data were insufficient to demonstrate the safety of the proposed use and use levels of heme iron (blood peptonates) as a source of iron for nutritional purposes in foods intended for the general population, including food supplements.

Compared to the previous application dossier evaluated by the Panel, the following three new *in vitro* tests have been provided: Comet assay, cell transformation assay and EST (Embryonic Stam Cell Test). The Chair indicated that EFSA asked for the views of the Panel because the new data provided have been generated by studies that do not correspond to the usually recognised tests.

The validity of these studies for the evaluation of this substance and the suitability of the overall data available to address the issues raised in the previous opinion of the Panel were discussed.

The Panel concluded that the data available were not sufficient to reach conclusions on the safety of the proposed uses of this nutrient source and that at least the following additional studies should be performed:

- a standard battery of *in vitro* genotoxicity tests in line with the recommendations of the Scientific Committee[i], the following two *in vitro* tests are required as the first step in genotoxicity testing: a bacterial reverse mutation assay (OECD TG 471), and an *in vitro* mammalian cell micronucleus test (OECD TG 487); in case of positive results a further *in vivo* test would be requested.
- a prenatal developmental toxicity study performed according to OECD Guidelines for Testing of Chemicals-Test Guideline 414[ii]

9. ANY OTHER BUSINESS

The EFSA report on "*Overview of the procedures currently used at EFSA for the assessment of dietary exposure to different chemical substances*" describes procedures to better harmonize exposure assessments between different panels. The ANS working group on exposure assessment had been consulted on the draft report and had provided comments.

The Commission asked if synergetic effects are considered when the Panel is evaluating food additives. The Panel indicated that synergetic effects are not necessarily easy to identify, test and

assess but that in cases where substances are known to have chemical similarities and/or share mechanistic endpoints like for parahydroxybenzoates or caramel colours the evaluation considers synergetic effects.

NEXT MEETINGS

The next ANS Panel Plenary meetings will take place on the following dates:

14 – 16 February 2012

17 – 19 April 2012

5 – 7 June 2012

3 – 5 July 2012

11 –13 September 2012

23 – 25 October 2012

4 - 6 December 2012

Annex I

INTERESTS AND ACTIONS RESULTING FROM THE SCREENING OF ADOI OR SDOIs

In his ADOI/SDoI, Dr D. Gott declared interest regarding to the agenda item « 7.1. Aspartame». carcinogenicity on aspartame. The expert declared an interest for aspartame because he is involved in the supervision of a pilot study on aspartame commissioned by his public employer, the UK FSA. This interest does not generate any potential conflict of interest with the discussion of the Panel since the discussion will not relate to the assessment of this study which is ongoing.

In her ADOI/SDoI, Dr D. Parent-Massin declared interest regarding to the agenda items « 7.1. Aspartame» and «7.5. Advantame». The interest of the expert with the company Ajinomoto generates a conflict of interests level C with the discussions on aspartame and advantame. Therefore, the expert was not able to participate in these discussions and left the room during these discussions.

In her ADOI/SDoI, Dr I. Waalkens-Berendsen declared interest regarding to the agenda items « 7.1. Aspartame» and «7.5. Advantame ». The expert declared an interest for aspartame and advantame because of the commercial relationship between her employer, TNO, and the company Ajinomoto for the realisation of studies on compounds to be used for feeding animals. This interest generates a potential conflict of interest level B for the discussions on aspartame and advantame. Therefore, the expert was not able to participate actively in the discussions on aspartame and advantame but was authorised to answer to questions addressed directly to her.

In his ADOI/SDoI, Dr. R. Woutersen declared interest regarding to the agenda items « 7.1. Aspartame» and «7.5. Advantame ». The expert declared an interest for aspartame and advantame because of the commercial relationship between his employer, TNO, and the company Ajinomoto for the realisation of studies on compounds to be used for feeding animals. This interest generates a potential conflict of interest level B for the discussions on aspartame and advantame. Therefore, the expert was not able to participate actively in the discussions on aspartame and advantame but was authorised to answer to questions addressed directly to him.

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[i] EFSA, 2011d. Scientific opinion on genotoxicity testing strategies applicable to food and feed safety assessment. EFSA Journal 2011;9(9):2379. http://www.efsa.europa.eu/en/efsajournal/doc/2379.pdf

[ii] OECD Guidelines for the Testing of Chemicals – Test Guideline 414. Prenatal Developmental Toxicity Study (adopted 22 January, 2001). Organisation for Economic Cooperation and Development, Paris. Available at: http://titania.sourceoecd.org/vl=11846807/cl=16/nw=1/rpsv/cgi-bin/fulltextew.pl?prpsv=/ij/oecdjournals/1607310x/v1n4/s14/p1.idx