Parma, 2 March 2011

EFSA/ANS/P_M21/MIN-0- 5625353

MINUTES OF THE 21st PLENARY MEETING OF THE SCIENTIFIC PANEL ON FOOD ADDITIVES AND NUTRIENT SOURCES ADDED TO FOOD (ANS)

Held in Parma on 1-3 February 2010

Adopted on 2 March 2011 at the 22nd Plenary meeting

AGENDA:

MINUTES OF THE 21st PLENARY MEETING OF THE SCIENTIFIC PANEL ON FOOD ADDITIVES AND NUTRIENT SOURCES ADDED TO FOOD (ANS)

Held in Parma on 1-3 February 2010

Panel Members:

Fernando Aguilar, Birgit Dusemund, Pierre Galtier, John Gilbert, David Gott (2nd and 3rd day), Sandro Grilli, Rainer Gürtler (2nd and 3rd day), Claude Lambré, John Christian Larsen (Chair), Jean-Charles Leblanc (1st and 2nd day), Alicja Mortensen , Dominique Parent-Massin, Iona Pratt (Vice-Chair), Ivonne Rietjens (Vice-Chair), Ivan Stankovic, Paul Tobback, Tatjana Verguieva, Ruud Woutersen.

Apologies

Apologies for absence were noted from Jürgen König.

EFSA

George Kass, Hugues Kenigswald, Majlinda Lahaniatis, Federica Lodi, Ana Maria Rincon, Kim Petersen, Alexandra Tard, Maria Luisa Escudero Hernandez, Anastasia Kesisoglou (scientific staff) and Anna Campanini (administrative staff).

European Commission

Stéphane Brion and Josiane Houins-Roulet.

1. WELCOME; APOLOGIES FOR ABSENCE

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

2. ADOPTION OF THE AGENDA

The agenda was adopted.

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 the Annex I of this document.

4. ADOPTION OF THE MINUTES OF THE 20TH ANS PLENARY MEETING ON 7-9 DECEMBER 2010

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

http://www.efsa.europa.eu/en/events/event/ans101207-m.pdf

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

5.1. Chair

The Chair informed the participants on the new mandates received by EFSA that fall within the remit of the ANS Panel:

- Request for technical assistance to provide comments on a refined intake assessment study on Quinoline Yellow, Sunset Yellow and Ponceau 4R in foodstuffs, as provided by the Union of European Beverages Association (UNESDA).

- Request for technical assistance to evaluate a new study related to the bioavailability of aluminium in food.

- Request for technical assistance to prepare a revised exposure assessment of ethyl lauroyl arginate (LAE) as a food additive.

- Request to provide a scientific opinion on the safety of iodized ethyl esters of poppy seed oil as a source of iodine added for nutritional purposes to foodstuffs and the bioavailability of iodine from this source, as well as on chromium (III) lactate trihydrate added for nutritional purposes to foodstuffs and the bioavailability of chromium from this source.

- Request for technical assistance to undertake a scientific evaluation of two articles published in 2010 has been sent by the EC to EFSA:

    1) Halldorsson et al.[1], which highlights that the daily intake of artificially sweetened soft drinks may be associated with an increased risk of preterm delivery. The authors consider that the artificial sweeteners might be the causal factor.

    2) Soffritti et al.[2], which concluded that Aspartame may induce carcinogenic effects in mice.

EFSA suggested that both studies are considered during this meeting and that the Panel prepare a statement in order to advise EFSA on the need for further work. Several members expressed that such advice could be made in the minutes of the plenary meeting rather than in a statement. There

[1] Halldorsson TI, Strøm M, Petersen SB, Olsen SF, 2010. Intake of artificially sweetened soft drinks and risk of preterm delivery: a prospective cohort study in 59,334 Danish pregnant women. American Journal of Clinical Nutrition 92, 626-633

[2] Soffritti M, Belpoggi F, Manservigi M, Tibaldi E, Lauriola M, Falcioni L, Luciano Bua L, 2010. Aspartame Administered in Feed, Beginning Prenatally Through Life Span, Induces Cancers of the Liver and Lung in Male Swiss Mice. American Journal of Industrial Medicine 53, 1197-1206.

were also discussions on the timing of the work, several members expressing the view that the normal timeline for a thorough assessment by the Panel should be respected. Finally, the Panel agreed to prepare a short preliminary statement.

5.2. EFSA

A few matters regarding the organisation of EFSA were briefly mentioned.

5.3. European Commission

S. Brion informed the Panel of the progress of the draft Commission Regulation on an implementing measure for Regulation (EC) No 1331/2008 establishing a common authorisation procedure for food additives, food enzymes and food flavourings.

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 20th Working Group A meeting in January 2011.

6.2. Working Group B on Food Additives and Nutrient Sources

The Chair of Working Group B informed the Panel that several natural colours and antioxidants were discussed at the last meeting in January.

The Chairs of Working Groups A and B expressed strong concern about the poor quality of some pre-assessment documents. In addition, on several occasions important references and studies have not been identified in these documents. H. Kenigswald indicated that the substandard quality of some pre-assessment documents has led to the anticipated termination of a procurement contract and that in the near future some of the new pre-assessment documents will be prepared by the ANS Unit.

6.3. Working Group "Guidance on Food Additives"

The Chair of the Working Group "Guidance on Food Additives" reported on the progress achieved during the last meeting in January. The working group has recommended using a tiered approach for the evaluation of core studies. The draft "Guidance on Food Additives" will be discussed during a forthcoming Panel meeting.

6.4. Working Group "Exposure assessment"

The Chair of the Working Group on the Exposure Assessment reported on the progress achieved during the last meetings in December and January.

The participants were informed that following a request from the European Commission, a revised exposure assessment of steviol glycosides, expressed as steviol equivalents, from its use as a sweetener, for children and adults, was carried out by EFSA based on the revised proposed use levels

defined in the terms of reference, and with reference to the exposure assessment presented in the former opinion on steviol glycosides by the EFSA's ANS Panel.

In the EFSA Statement approved on 13 January 2011[3] it is concluded that "*When considering the revised proposed maximum use levels, the mean dietary exposure to steviol glycosides, expressed as steviol equivalents, for European children (aged 1-14 years) ranged from 0.4 to 6.4 mg/kg bw/day, and from 1.7 to 16.3 mg/kg bw/day at the 95th percentile. The main contributors are the non-alcoholic flavoured drinks and the desserts including flavoured milk products. Taking into account uncertainties of non-alcoholic flavoured drink consumption, corrected exposure estimates for children high consumers (95th percentile) were calculated that range from 1.0 to 12.7 mg/kg bw/day. Exposure estimates for the UK adult population give a mean dietary exposure to steviol glycosides, expressed as steviol equivalents, of 1.9-2.3 mg/kg bw/day, and of 5.6-6.8 mg/kg bw/day for high level exposures (97.5th percentile), with main contributors being non-alcoholic flavoured drinks, tabletop sweeteners and beer and cider.*

The mean exposure estimates differ only slightly from the exposure estimates from the ANS Panel opinion (2010). By using data from the EFSA Comprehensive database, ranges of high level exposure estimates decreased from a maximum of 17.2 mg/kg bw/day from the ANS Panel opinion to 12.7 mg/kg bw/day for children but high level children exposures for several countries are still above the ADI of 4 mg/kg bw/day".

6.5. Working Group "Chemistry and specifications"

No meeting has taken place since the last Panel plenary meeting. The Chair of the Working Group J. Gilbert informed that B. Dusemund has joined the Working Group.

7. FOOD ADDITIVES

7.1. Caramels (E 150 a-d)

(Question N° EFSA-Q-2008-237; EFSA-Q-2008-238; EFSA-Q-2008-239; EFSA-Q-2008-240)

The draft opinion was discussed. The proposed changes to the text were noted and the opinion was adopted.

Caramel colours are colouring substances authorised as food additives in the EU, and are complex mixtures of compounds produced by heating carbohydrates under controlled heat and chemical processing conditions. The caramel colours are classified according to the reactants used in their manufacture as follows: Class I Plain Caramel or Caustic Caramel (E1 50a); Class II Caustic Sulphite Caramel (E 150b); Class III Ammonia Caramel (E 150c) and Class IV Sulphite Ammonia Caramel (E 150d).

Both JECFA and SCF have concluded that a numerical ADI was not necessary for Class I Plain Caramel, while both bodies have established an ADI of 200 mg/kg bw/day for Class III Ammonia Caramel and Class IV Sulphite Ammonia Caramel. This is also the ADI established by the SCF for Class II Caustic Sulphite Caramel, while JECFA have established an ADI of 160 mg/kg bw/day for this class.

The Panel concludes that, given the toxicological similarity of all four classes of caramel colours and the consistency in the toxicological database, the caramel colours can be considered as a single group

[3] Revised exposure assessment for steviol glycosides for the proposed uses as a food additive. Available from : http://www.efsa.europa.eu/en/efsajournal/doc/1972.pdf

in terms of assessing their safety, and that a group ADI can be derived. The Panel establishes a group ADI of 300 mg/kg bw/day for the caramel colours. Given, however, concerns regarding the immunotoxicity of THI, present in Class III Ammonia Caramel, the Panel decided to define an individual ADI of 100 mg/kg bw/day for this caramel within the group ADI, based on the currently available database. This means that within the group ADI of 300 mg/kg bw/day, only 100 mg/kg bw/day of this 300 mg/kg bw/day can be made up by Class III Ammonia Caramel.

The Panel notes that the anticipated dietary exposure of the adult population at the 97.5th percentile to Class I Plain Caramel exceeds the group ADI of 300 mg/kg bw/day proposed for the caramel colours. Similarly, the anticipated dietary exposure of the adult population at the 97.5th percentile to Class IV Ammonia Caramel exceeds this group ADI. For children, the upper end of both the mean intake ranges and also the 95th/97.5th percentile intakes for Class I Plain Caramel exceed the group ADI of 300mg/kg bw/day. Similarly, for children the upper end of both the mean intake ranges and also the 95th/97.5th percentile intakes for Class IV Sulphite Ammonia Caramel exceed the group ADI of 300 mg/kg bw/day.

The anticipated dietary exposure to Class II Sulphite Caramel for both adults and children was below the group ADI of 300 mg/kg bw/day.

For Class III Ammonia Caramel the upper end of the mean intake range for children exceeds the individual ADI of 100 mg/kg bw/day established for this colour within the group ADI, while the 97.5th percentile anticipated dietary exposures of both the child and adult populations are above this ADI of 100 mg/kg bw/day.

Anticipated combined dietary exposures of both adults and children to all caramel colours exceed the group ADI of 300 mg/kg bw/day at the 95th/97.5th percentile, while the ADI is also exceeded by the combined mean intake for children. In the case of children, this exceedance applies to the upper end of the exposure range only.

The Panel concludes overall that the exposure estimates for THI, 4-MEI or sulphur dioxide are not of concern, but notes remaining uncertainties regarding the effects of THI on the immune system. The Panel would welcome additional studies to clarify these effects.

The Panel notes that variations in the manufacturing processes of the caramel colours may result in a wide variability in the nature and levels of the various constituents, including constituents of toxicological concern such as 5-HMF and furan. Given this likely variability, the Panel considers that in order to further guarantee the safety of caramel colours with respect to their minor constituents, such as THI, 4-MEI, 5-HMF and furan, it would be prudent to reduce their levels as much as technologically feasible. The Panel considers therefore that the specifications for the caramel colours should be updated and extended to also include maximum levels for constituents of possible concern not yet included in the specifications, such as for example 5-HMF and furan.

The Panel additionally concludes that there is limited information about the relationship between processing parameters for the caramel colours and the formation and nature of heat-derived constituents which is also relevant for the control of manufacturing processes. Future research work is recommended in this respect.

7.2. Lutein

(Question N°EFSA-Q-2010-01491)

The item was not discussed due to lack of time.

7.3. Glycerol esters of tall oil rosin

(Question N°EFSA-2009-00880)

The item was not discussed due to lack of time.

7.4. Advantame

(Question N° EFSA-Q-2010-00943)

A preliminary discussion took place on the risk assessment approach proposed by the Working Group for the draft opinion.

7.5. Aspartame and other sweeteners: consideration of two new studies

The participants discussed two new articles published in 2010 in the scientific literature, describing potential adverse health effects of sweeteners.

The first article by Halldorsson et al. (2010) suggests an association between consumption of artificially sweetened soft drinks and increased risk of preterm delivery. The second article by Soffritti et al. (2010) reports that aspartame is a carcinogenic agent in mice.

In the Soffritti et al., 2010 study, Swiss mice were administered aspartame in feed beginning from gestational days 12 (through pregnant mice) until week 130 of life. The authors of the study reported a higher incidence of hepatocellular carcinoma in animals administered aspartame, statistically significant at the two higher doses tested (approximately 1900 and 4000 mg/kg body weight/day). The authors also reported a statistically significant higher incidence of alveolar/bronchiolar carcinomas at the dose of 4000 mg/kg body weight/day. The increase in liver and lung tumours was observed in male animals only, and no statistically significant change in tumour incidence was reported in female mice. There was no statistically significant increase in the incidence of adenomas of the liver or the lung in either sexes.

Soffritti et al. (2010) conclude that aspartame, administered under these conditions, induces significant dose-related increases in the incidence of carcinomas of both liver and lung in male Swiss mice. The authors suggest that methanol, a metabolite of aspartame, plays a possible role in the hepatocarcinogenic effects observed in male mice. No carcinogenic effects were observed in female mice.

The Panel noted that the type and incidence of the tumours reported by Soffritti et al. (2010) appear spontaneously at high rates in male mice. The Panel also observed that even though statistical significance was reported by the authors for male mice under the experimental conditions of this study, the increased incidence of both liver and lung carcinomas remained in all exposure groups within the historical control range of the tumours in these mice.

The Panel will undertake a detailed analysis of the study results and conclusions reported by Soffritti et al. (2010), including the suggested implication of methanol.

The Panel also discussed the recently published Danish prospective cohort study on the intake of artificially sweetened soft drinks and the risk of preterm delivery (Halldorsson et al., 2010). The Panel advised EFSA on the need for epidemiological expertise to provide additional insights on the methodology and statistical aspects of this study, taking into account confounding factors. EFSA will provide an assessment on the epidemiological and statistical methodology of the Halldorsson et al. study by the end of February 2011.

8. INFORMATION EXCHANGE PLATFORM (IEP)

The item was not discussed due to lack of time.

9. TECHNICAL GUIDANCE TO EXPLAIN THE TECHNICAL, EXPOSURE AND TOXICOLOGICAL DATA REQUIRED TO ESTABLISH THE SAFETY OF FOOD ADDITIVES PROPOSED FOR USE IN THE EUROPEAN UNION

The item will be discussed in a forthcoming ANS Panel Plenary meeting.

10. ANY OTHER BUSINESS

A few issues regarding the organisation of the work were discussed.

NEXT MEETINGS

The Panel members requested that all meetings take place in Parma, if possible. The next ANS Panel Plenary meetings will take place on the following dates:

1-2 March 2011
12 - 14 April 2011
24 - 26 May 2011
5 - 7 July 2011
20 - 22 September 2011
25 - 27 October 2011
6 - 8 December 2011

Annex I

INTERESTS AND ACTIONS RESULTING FROM THE SCREENING OF ADOI OR SDOIs

In her ADoI/SDoI, Prof. Dr. Dominique Parent-Massin declared interest regarding the agenda items « 7.4 Advantame » and « 7.5. Aspartame and other sweeteners: consideration of two new studies ».

The interest declared for advantame is related to financial links with Ajinomoto (the applicant), for the participation to a Panel choosing the winner of a prize. In accordance with EFSA's Policy on Declarations of Interests and Implementing documents thereof, and taking into account the specific matters discussed at the meeting in question, the interest above was deemed to represent a conflict of interest (level C).

Regarding the agenda item « 7.5. Aspartame and other sweeteners: consideration of two new studies ». the expert has also declared an interest with Ajinomoto (as mentioned above), a company that produces aspartame and is also involved in other sweeteners. This involvement generates a conflict of interest with the discussion by the ANS Panel on the aspartame and other sweeteners (level C).

Pursuant to EFSA's Procedure on Identifying and Handling Declarations of Interest, the said expert was excluded from participating in EFSA activities concerned by the potential conflicts in question.