Scientific Panel on Food Additives and Nutrient Sources added to Food (ANS)

Minutes of the 81st Plenary meeting

Held on 15-17 May 2018, Parma (Italy)

Meeting open for Observers

(Open session: 16 May 2018, 09:00-18:00h

17 May 2018, 09:00-15:30h)

(Agreed on 07 June 2018)

Participants

- **Panel Members:**

  Peter Aggett, Fernando Aguilar[1], Riccardo Crebelli, Birgit Dusemund, Metka Filipic, Maria José Frutos Fernandez, Pierre Galtier, David Gott, Ursula Gundert-Remy, Gunter Georg Kuhnle, Claude Lambré, Jean-Charles Leblanc[2], Inger Therese Lillegaard, Peter Moldeus, Alicja Mortensen, Agneta Oskarsson, Ivan Stankovic, Ine Waalkens-Berendsen, Rudolf Antonius Woutersen, Matthew Wright and Maged Younes

- **Hearing Experts:**

  Agenda item 10.1: Agnes Oomen, Henk Van Loveren, Gretchen Mahler, Eric Houdeau[3]

  Agenda item 10.2: Patrizia Restani[4]

  Agenda item 10.5: Pasquale Mosesso[5]

- **European Commission representatives:**

  DG SANTE (Health and Food Safety), E2 Food processing technologies and novel foods: Guillermo Cardon

- **EFSA:**

  FIP Unit: Claudia Roncancio Peña, Anna Christodoulidou, Dimitrios Chrysafidis, Alessandra Giarola, Federica Lodi, Fabiola Pizzo, Ana Maria Rincon, Camilla Smeraldi, Alexandra Tard

[1] Participated by web-conference on 15.05 and 16.05
[2] Participated on-site on 15.05 and by web-conference 16.05 am and 17.05 am
[3] Participated on 16 May pm
[4] Participated on 16 May am
[5] Participated on 17 May am

DATA Unit: Claudia Cascio

- **Observers[6] (in brackets affiliation, when known)**

  Attending physically in Parma:

  Vincent Rudigar Battersby (EBRC Consulting GmbH), Stefanie Geiser (EAS Stategies), Stella Krashia (TEAM Mastery), David Lockley (Venator Materials – Representing TDMA – part of Cefic), Federica Manini (Soremartec Italia), Maria Vittoria Nanni (Eville & Jones), Silvia Toia (GB Foods), Lorenza Anna Varraso (University of Parma)

  Attending via web-streaming:

  Enza Baldo, Federica Bargna, Fabiana Bariselli (SISTE), Barbara Barlozzini, Clara Bollain (Generalitat Valenciana), Friederike Buehre-Weck (Evonik), Maria Grazia Camana (Meda Pharma), Elena Cogalniceanu (EAS Strategies), Lorene Courrege (Food Supplement Europe), Simona De Lucia (AMITALIA SRL), Nora Debraise (Cefic/TDMA), Eloise Devillers (Tilman), Dino Fantinel (UNIFARCO SPA), Beatriz Fernandes, Isabella Fontana (Piam Farmaceutici S.p.A.), Matteo Gaglianone (Piam Farmaceutici S.p.A.), Stefanie Geiser (EAS Strategies), Maryse Herve (EU Specialty Food Ingredients), Kevin Hughes (Colorcon Ltd), Pilvi Jalonen (Bayer), Joanna Jaskolska (Biopolymer International), Sven Johannes (Kronos International, Inc.), Alice Kindl (Mylan), Stefanie Knerr (Merck), Simone Koenig (Bayer), Orjeta Kuci, Sara Levorato (Unilever), Irene Lupi, Farrah Malik (Perrigo), Marella Manzini (Meda Pharma), Stefania Mariani (Meda Pharma), Francesco Meschini, Marta Miks (Glycom A/S), Deborah Montrasio (Scharper), Yasmine Moraca (A.C.R.A.F. SpA), Giuseppina Morgante (DIFASS International SRL), Phaik Morgenthaler (Bayer), Cristian Paone, Maud Perrudin (AESGP), Ines Pisanelli, Pierre Rigal (MBR), Giulia Sanapo (Teva), Tobias Schuster (Evonik), Colette Shortt (J&J), Tania Soenens (Eastman), Marco Terrile (Piam Farmaceutici S.p.A.), Amy-Jane Troy, Maria Wilhelm (Pfizer)

1. Welcome and apologies for absence

The Chair welcomed all participants.

Apologies were received from Gunter Kuhnle, Therese Lillegaard and Agneta Oskarsson who did not participate in the morning session on 15 May 2018 and from Fernando Aguilar who did not attend the plenary meeting on 17 May 2018.

2. Adoption of agenda

The agenda was adopted without any changes related to its content.

A change in the order of discussion of the agenda items was agreed by the Panel, resulting in the discussion and adoption of the scientific opinion on the refined exposure assessment for polyethylene glycol (E 1521) (item 10.4 in the draft agenda) being anticipated to the first day of the plenary, i.e. during the closed session.

3. Declarations of Interest of Scientific Panel Members

In accordance with EFSA's Policy on Independence and Scientific Decision-Making Processes[7] and the Decision of the Executive Director on Declarations of Interest[8], EFSA screened the Annual Declarations of Interest and the Specific Declarations of Interest filled in by the Panel Members invited for the present meeting.

[6] http://www.efsa.europa.eu/en/stakeholders/observers
[7] http://www.efsa.europa.eu/en/keydocs/docs/independencepolicy.pdf
[8] http://www.efsa.europa.eu/en/keydocs/docs/independencerules2014.pdf

Oral Declaration of Interest was asked at the beginning of the meeting and no additional interest was declared.

4. Agreement of the minutes of the 80th Plenary meeting held on 13-15 March 2018 - Parma (Italy)

The minutes of the 80th Plenary meeting held on 13-15 March 2018 were agreed by written procedure on 13 April 2018[9].

5. Report on the written procedures since 80th Plenary meeting

No scientific outputs were adopted by written procedure since the last plenary meeting.

6. Scientific outputs submitted for discussion and possible adoption

6.1. Di-calcium malate as a novel food ingredient and as a source of calcium (EFSA-Q-2016-00240)

The draft opinion on the evaluation of the safety of di-calcium malate (DCM) as a novel food ingredient proposed as a source of calcium to be added for nutritional purposes to food, food supplements and food for special medical purposes and on the bioavailability of calcium from the proposed source was discussed by the Panel.

The ANS Panel discussed the different parts of the assessment and unanimously adopted the opinion, subject to incorporation of changes as suggested during the meeting.

The full opinion is available on the Authority's webpage[10].

6.2 Di-magnesium malate as a novel food ingredient and as a source of magnesium (EFSA-Q-2016-00115)

The draft opinion on the evaluation of the safety of di-magnesium malate (DMM) as a novel food ingredient proposed as a source of magnesium to be added for nutritional purposes to food, food supplements and food for special medical purposes and on the bioavailability of calcium from the proposed source was discussed by the Panel.

The ANS Panel discussed the different parts of the assessment and unanimously adopted the opinion, subject to incorporation of changes as suggested during the meeting.

The full opinion is available on the Authority's webpage[11].

6.3 Refined exposure assessment for polyethylene glycol (E 1521) (EFSA-Q-2013-00698)

The draft opinion on the refined exposure assessment of the permitted food additive polyethylene glycol (E 1521) was presented to the members of the ANS Panel together with the main points for discussion.

The ANS Panel discussed the refined exposure assessment and unanimously adopted the opinion, subject to incorporation of changes as suggested during the meeting.

The full opinion will be available on the Authority's webpage.

[9] https://www.efsa.europa.eu/en/events/event/180313
[10] http://www.efsa.europa.eu/en/efsajournal/pub/5291
[11] http://www.efsa.europa.eu/en/efsajournal/pub/5292

OPEN SESSION

16 May 2018, 09:00-18:00h

17 May 2018, 09:00-15:30h

7. Welcome

The Chair welcomed all observers who attended the open session of the plenary. Participants were informed that a change in the order of discussion of the agenda items had to be made resulting in the discussion and adoption of the scientific opinion on the refined exposure assessment for polyethylene glycol (E 1521) during the closed session. Observers were presented with the adopted opinion during the open plenary session.

8. Brief introduction of Panel members and Observes

A tour de table followed the Chair's welcome to enable the participants physically attending the plenary meeting to introduce themselves.

9. Presentation of the EFSA Guidelines for Observers[12]

The Head of FIP Unit presented the rules for observers to be followed during and after the open plenary meeting. Observers were given the possibility to send questions when submitting their registration and these questions would be answered in a dedicated session at the meeting. Observers were also informed that the Chair would grant opportunity for additional questions at the end of each discussion topic.

10. Scientific outputs submitted for discussion and/or possible adoption

10.1. Titanium dioxide (E 171) evaluation of four new publications (EFSA-Q-2018-00271)

A new mandate was received at EFSA on 22 March 2018 requesting EFSA to carry out a scientific evaluation of four new studies[13] on the potential toxicity of titanium dioxide used as a food additive (E 171), published after the publication of the 2016 ANS Panel opinion, in accordance with Article 29 (1)(a) of the Founding Regulation (EC) No 178/2002, and to indicate whether these would merit re-opening the existing opinion on the safety of the food additive E 171 adopted by the Panel in June 2016[14].

Further to the receipt of this mandate, the Standing Working Group (SWG) on the re-evaluation of food colours was tasked with the assessment of these new data and with the drafting of the scientific opinion which, according to the deadline indicated in the mandate, should be adopted by the ANS Panel no later than 30 June 2018.

During the initial discussion on the four studies at the 11th meeting of the SWG held on 23 April 2018, a number of questions were raised that would deserve some clarifications from the authors of the publications. It was therefore agreed to invite one author for each of the four publications as hearing experts to join the current

[12] https://www.efsa.europa.eu/sites/default/files/observersguidelines.pdf

[13] Bettini S. et al., 2017. Food-grade TiO2 impairs intestinal and systemic immune homeostasis, initiates preneoplastic lesions and promotes aberrant crypt development in the rat colon. doi: 10.1038/srep40373.
Guo Z. et al., 2017. Titanium dioxide nanoparticle ingestion alters nutrient absorption in an in vitro model of the small intestine. https://doi.org/10.1016/j.impact.2017.01.002
Heringa MB et al., 2016. Risk assessment of titanium dioxide nanoparticles via oral exposure, including toxicokinetic considerations. doi: 10.1080/17435390.2016.1238113
Proquin H. et al., 2017. Titanium dioxide food additive (E171) induces ROS formation and genotoxicity: contribution of micro and nano-sized fractions. doi: 10.1093/mutage/gew051.

[14] https://www.efsa.europa.eu/it/efsajournal/pub/4545

Panel plenary meeting, to present an overview on their studies and to answer to the questions and remarks from the experts.

After a short presentation by EFSA to the Panel on the new mandate received, the Chair of the Panel welcomed the four hearing experts attending the plenary for this agenda item and thanked them for their availability.

The floor was given to Dr Oomen from the Netherlands National Institute for Public Health and the Environment who presented the main findings from the Heringa et al., 2016 study and a brief overview of two other related publications from her research group (Rompelberg et al., 2016[15] and Heringa et al., 2018[16]). Dr. Oomen replied to the questions identified by the Working Group and others from the Panel rose during the discussion.

Prof van Loveren from the Maastricht University (the Netherlands) presented an overview on the background work with respect to the publication by Proquin et al. (2017), and replied to the questions identified by the Working Group and others from the Panel rose during the discussion In response to one of these questions, he explained that there must have been a mistake in one of the figures included in the publication and that an erratum has been signalled to the journal that had published the study.

Prof Mahler from the Binghamton University (New York, US) presented the main findings from the Guo et al. (2017) paper, and replied to the questions identified by the Working Group and others from the Panel rose during the discussion.

Finally, Dr Houdeau from the INRA Toxalim Research centre (France) presented the main findings from the Bettini et al. (2017) study, and replied to the questions identified by the Working Group and others from the Panel rose during the discussion.

When asked by the Panel to comment on the significance of their findings to the overall risk assessment of titanium dioxide when used as a food additive, all the four authors acknowledged that their studies would not allow for conclusive risk assessment.

The main points rose during the discussion will be reflected in the current scientific opinion which will be finalised and discussed at a forthcoming WG Colours meeting in June, and scheduled for adoption by the ANS Panel at the next plenary meeting at the end of June 2018.

In addressing the terms of reference of this new mandate in the scientific opinion which is currently being drafted, the Panel will concentrate on those four studies as requested by the European Commission. On the other hand, the Panel is aware of the large number of new publications on titanium dioxide that have emerged since the finalisation of the re-evaluation opinion and acknowledged that each publication should be assessed in respect to the whole dataset available, considering a weight of evidence approach based on the totality of the information.

The Panel noted that these studies highlighted some concerns as well as some uncertainties. Further research would be needed to decrease these uncertainties, as also recognised by the authors.

The Chair thanked again the four hearing experts and opened the floor to the questions received from the observers in advance to the meeting. The following ones related to this agenda item:

[15] Rompelberg et al., 2016. Oral intake of added titanium dioxide and its nanofraction from food products, food supplements and toothpaste by the Dutch population. Nanotoxicology. 2016 Dec;10(10):1404-1414. doi: 10.1080/17435390.2016.1222457

[16] Heringa et al., 2018. Detection of titanium particles in human liver and spleen and possible health implications. Part Fibre Toxicol. 2018 Apr 11;15(1):15. doi: 10.1186/s12989-018-0251-7.

- Will EFSA consider the limitations of the sample preparation methods in the INRA (Bettini) study when assessing this study and it's relation to the types of actual aggregate particles of TiO2 that will be experienced in the gut? Sonication of the samples prior to feeding is not appropriate since the aggregates will not break down in the body in this manner or be absorbed as has been demonstrated in many other studies.
- Could this discussion have an impact on other food additives?

In answer to the first question, it was explained that the experimental conditions of the four studies will be discussed in the scientific opinion which is currently being developed, in particular with respect to their relevance to the actual dietary exposure to the food additive.

In answer to the latter question, it was explained that the mandate received from the EC and currently being addressed is limited to the food additive titanium dioxide (E 171).

The following questions were made by some of the observers attending the plenary:

- In its assessment of the studies, will EFSA be considering results from *in vitro* studies showing that after 2 hours in simulated gastric juice, titanium dioxide is soluble?
- In its assessment of the studies, will EFSA be considering that *i.v.* administration is not a suitable model for extrapolating to the oral intake of titanium dioxide?
- With respect to the background exposure to titanium dioxide, will EFSA be considering that this is very high, as humans are constantly exposed to titanium dioxide by inhaling air, by soil, by ingesting milk, by medication and dental implants?

As above, it was explained that the experimental conditions of the four studies will be discussed in the scientific opinion.

A final remark was made by one of the observers representing the titanium dioxide manufacturers' association (TMDA) wishing to clarify that only anatase is used as a food additive (E 171), whereas all the other forms of titanium dioxide (including rutile and coated titanium dioxide) are not used as a food additive.

The presentations given by Dr Oomen, Prof Mahler and Dr Houdeau are available on the EFSA website at the following address: https://www.efsa.europa.eu/it/events/event/180515

10.2. Scientific opinion on the safety of monacolins in red yeast rice (EFSA-Q-2017-00138)

Further to the discussion held at the previous plenary meeting on the safety evaluation of monacolins in red yeast rice performed under the framework of Article 8 of Regulation (EC) No1925/2006, the draft opinion was presented to the members of the ANS Panel for the first time together with the main points for discussion

The ANS Panel discussed the technical part and the biological and toxicological data included in the assessment and suggested some changes to the draft scientific opinion to be further elaborated by the WG.

The revised draft opinion will be scheduled for discussion and possible adoption at the next plenary meeting.

The Chair opened the floor to a question received from the observers in advance to the meeting in relation to this agenda item:

- Is it true that Monacolin K, in a near future will be classified like medicine and no longer as a food supplement?

EFSA explained that on the basis of the scientific opinion of EFSA it will be up to the European Commission to formulate a proposal for inclusion of these substances in Part A, B or C of Annex III to Regulation (EC) No 1925/2006, however after publication of the scientific opinion EFSA has no role on the subsequent risk management steps.

10.3. Draft Guidance on Nutrient Sources (EFSA-Q-2016-00150)

Further to the closure of the public consultation on the draft guidance, endorsed by the Panel at its 77th Plenary meeting in November 2017, a revised document was distributed for adoption.

The public consultation had been kept open from 15 December 2017 until 25th February 2018, but has gathered very few comments.

At the current meeting, the ANS Panel discussed the minor amendments made to the guidance document to address the comments received and unanimously endorsed the document.

The final guidance document will be available on the Authority's webpage. Its publication will be accompanied by an EFSA report detailing the comments received during the public consultation and how they have been addressed in the document.

The Chair of the Panel thanked the Chair and the members of the ad hoc Working Group tasked with the preparation of this updated guidance.

10.4. Re-evaluation of gellan gum (E418) (EFSA-Q-2011-00517)

The ANS Panel was presented for the first time with a draft scientific opinion on the re-evaluation of the already permitted food additive gellan gum (E 418) together with the main points for discussion

The ANS Panel discussed the different parts of the assessment and unanimously adopted the opinion, subject to incorporation of changes as suggested during the meeting.

The full opinion will be available on the Authority's webpage.

10.5. Re-evaluation of stannous chloride, stannous chloride dihydrate (E 512) (EFSA-Q-2011-00661)

The ANS Panel was presented for the first time with a draft scientific opinion on the re-evaluation of the already permitted food additive stannous chloride, stannous chloride dihydrate (E 512) together with the main points for discussion

The ANS Panel discussed the different parts of the assessment and unanimously adopted the opinion, subject to incorporation of changes as suggested during the meeting.

The full opinion will be available on the Authority's webpage.

11. New Mandates

The Secretariat informed the members of the ANS Panel that no new mandates were received since the last plenary meeting, in addition to the one already presented under the agenda item 10.1.

12. Feedback from the Scientific Committee/Scientific Panels, EFSA, the European Commission

12.1. Scientific Panel(s) including their Working Groups

The Chair briefly reported on the main topics dealt by the Scientific Committee at its 88th plenary meeting held on 11-12 April 2018, open to the observers.

Attention was drawn in particular to the establishment of a standing working group on nanotechnologies which should facilitate the implementation of the guidance document for assessing nanotechnology in the food and feed chain which will undergo a pilot phase until June 2019 and the upcoming update of the guidance on the threshold of toxicological concern.

12.2. EFSA including its Working Groups /Task Forces

The Chairs of the ANS Panel Working Groups and EFSA scientific secretariat provided feedback from their latest meetings:

12.2.1. ANS Panel SWG Applications

No specific issue was brought to the attention of the Panel in addition to what already recorded in the minutes of the WG

12.2.2. ANS Panel SWG on the re-evaluation of Gums and Food Additives from Natural Sources 2017-2018

No specific issue was brought to the attention of the Panel in addition to what already recorded in the minutes of the WG.

12.2.3. ANS Panel SWG on the re-evaluation of food additives other than gums and colours

No specific issue was brought to the attention of the Panel in addition to what already recorded in the minutes of the WG.

12.2.4. ANS Panel SWG re-evaluation of other miscellaneous food additives with 2018 deadline

No specific issue was brought to the attention of the Panel in addition to what already recorded in the minutes of the WG.

12.2.5. ANS Panel *ad hoc* WG on the re-evaluation of phosphates

No specific issue was brought to the attention of the Panel in addition to what already recorded in the minutes of the WG.

12.2.6. ANS Panel SWG Procedures under Article 8 of Regulation (EC) No 1925/2006

No specific issue was brought to the attention of the Panel in addition to what already recorded in the minutes of the WG.

12.2.7. ANS Panel SWG Exposure Assessment

No specific issue was brought to the attention of the Panel in addition to what already recorded in the minutes of the WG.

12.2.8. ANS Panel SWG Re-evaluation of Food Colours

No specific issue was brought to the attention of the Panel in addition to what already recorded in the minutes of the WG.

12.2.9. ANS Panel WG on the Re-evaluation of food additives for use in foods for infants below 16 weeks of age

In addition to what already recorded in the minutes of the WG, the Chair of the WG presented the mandate and the short term work plan of the WG.

12.2.10. ANS Panel WG Guidance on Nutrient Sources

In addition to what already recorded in the minutes of the WG, the Panel noted that after the publication of the guidance (see agenda item 10.3), this WG will be closed.

12.3. European Commission

The EC representative provided feedback to the Panel on the programme for the follow-up of scientific opinions on the re-evaluation of the safety of permitted food additives for which some concerns have been identified by the ANS Panel:

- Further to the publication of the follow-up call for scientific and technical data on the permitted food additive indigotine, indigo carmine (E 132) on 09/03/2018, registration of the contact details of business operators interested in submitting data (step 1) has been completed. The deadline for the confirmation of data submission, deadlines and milestones (step 2) of the follow up call will be closing on 9/9/2018.
- Further to the publication of the two follow-up calls for scientific and technical data on the permitted food additives silver (E 174) and gold (E 175) on 06/03/2018, no business operator indicated interest in submitting the requested data on either silver (E 174) or gold (E 175). The EC will therefore start the procedure for removing both substances from the list of permitted food additives.
- Further to the publication of the follow-up call on the permitted food additives propyl gallate (E 310), octyl gallate (E 311) and dodecyl gallate (E 312) on 30/05/2017, no business operator indicated interest in submitting the requested data on octyl gallate (E 311) and dodecyl gallate (E 312). The EC will therefore start the procedure for removing both substances from the list of permitted food additives.

13. Other scientific topics for information and/or discussion

None

14. Questions from and answers to Observers (in application of the guidelines for Observers)

The Chair opened the floor to any additional question from the observers attending the meeting. No additional questions were raised.

15. Any Other Business

None