SCIENTIFIC COMMITTEE AND EMERGING RISKS UNIT

Minutes of the 3rd meeting

Scientific Committee cross-cutting Working Group

Genotoxicity (2018-2021)

Held on 27th-28th Feb 2019 in EFSA, Parma (IT)

(agreed on 26 March 2019)

Participants

- **Working Group Members:**

Diane Benford (Chair), Gabriele Aquilina, Claudia Bolognesi, Tamara Coja*, Riccardo Crebelli, Rainer Gürtler, Elsa Nielsen, Josef Schlatter, Christiane Vleminckx, Francesca Marcon* .

- **EFSA:**

SCER Unit: Daniela Maurici, Jenny Maner

FIP Unit: Maria Carfì, Carla Martino

NUTRI Unit: Annamaria Rossi

FEED Unit: Paola Manini and Fabiola Pizzo

PREV Unit: Juan Parra Morte

*participated only day 1

1. Welcome and apologies for absence

The Chair welcomed the participants. Apologies were received from Margherita Bignami.

2. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence and Scientific Decision-Making Processes1 and the Decision of the Executive Director on Declarations of Interest2 EFSA screened the Annual Declaration of Interest filled in by the working group members invited for the present meeting. No Conflicts of Interest related to the issues discussed in this meeting were identified during the screening process or at the Oral Declaration of Interest at the beginning of this meeting.

3. Request for an advice from the Pesticides Unit on para-chloroaniline

In the context of the renewal for the substance diflubenzuron, EFSA is in the process of assessing comments of Member States and applicant, identifying points where clarification is needed. EFSA requested the view of the WG genotoxicity for some aspects related to the possible genotoxicity Mode of Action for 4-chloroaniline (PCA - a potential residue of the pesticide diflubenzuron) and related uncertainty analysis.

Background information were shared with the WG, namely:

In 2012, EFSA concluded that PCA is an in vivo genotoxic substance.

In 2015, EFSA concluded that PCA is genotoxic and carcinogenic.

The EFSA WG Gentox was provided with the following data:

- UK COMM 2009, statement on genotoxicity of Para-chloroaniline (COM/09/S3). Assessment done on available data on PCA. The outcome of this assessment proposed testing strategy to follow up the results. It was the basis for the EC to set confirmatory data requirement on which new in vivo studies were conducted by the applicant (i.e. original studies in vivo UDS, in vivo comet, in vivo MN) on which EFSA concluded that PCA is an in vivo genotoxic substance (EFSA, 2012).
- Krsmanovic, 2011. Study report on genotoxicity assessment of para-chloroaniline following oral administration (in vivo MNT)
- Pant and Celestin, 2011. Study report on para-chloroaniline: Comet assay in rat peripheral blood liver and spleen cells following oral administration
- Pant and Celestin, 2011. Study report on para-chloroaniline: Unscheduled DNA synthesis (UDS) test with mammalian cells in vivo
- Brown and Ciubotaru, 2017. Study report on in vivo mutation assay at the cII locus in Big Blue transgenic F344 rats and micronuclei analysis in peripheral blood
- Beevers and Parsons, 2019. Statement on Mode of Action and human relevance assessment of genotoxicity and carcinogenicity observed in rodents.

[1] http://www.efsa.europa.eu/en/keydocs/docs/independencepolicy.pdf
[2] http://www.efsa.europa.eu/en/keydocs/docs/independencerules2014.pdf

- Hendriks et al. 2016: The Extended ToxTracker assay discriminates between induction of DNA damage, oxidative stress and protein misfolding. Toxicological sciences 2016, p190-203.

The data was reviewed by the WG. The lack of access to the original data in some instances was noted. It was agreed to draft a report by mid-March to be discussed in a dedicated teleconference with representatives from EMA, ECHA, and the RMS Greece on 22nd March 2019. A final report will be then sent to the requestor.

4. Request for an advice from the PPR panel on triazine amine

The PPR panel requested the support of the WG Gentox in relation to the EC mandate on the genotoxic potential of triazine amine (M-2018-0207).

Data provided by the applicant were presented and discussed. The draft contributions of the WG members to the report summarising the assessment were also discussed. It was agreed to send a revised version of the report to the PPR panel secretariat by the end of March. The draft report providing the view of the WG Gentox will be tabled and discussed at the PPR panel plenary in the beginning of April.

5. AOB

Possible statement/opinion on aneugenicity assessment

The WG discussed the aneugenicity self task mandate and considered the possibility to invite hearing experts at one of the next meetings. The search strings for the literature search on this matter were discussed.

6. Next meeting(s)

Dates of next meetings in 2019:

- 22nd March: teleconference
- 11th April: placeholder for teleconference
- 29th-30th April: Parma
- 27th-28th June: Parma

Minutes of the 2nd meeting

Scientific Committee cross-cutting Working Group

Genotoxicity (2018-2021)

Held on 31st Jan - 1st February 2019 in Parma
(Agreed on 27th February 2019)

Participants

- **Working Group Members:**

Diane Benford (Chair), Gabriele Aquilina, Claudia Bolognesi, Riccardo Crebelli, Rainer Gürtler, Elsa Nielsen, Josef Schlatter, Christiane Vleminckx.

- **EFSA:**

SCER Unit: Daniela Maurici
FIP Unit: Maria Carfì, Carla Martino
NUTRI Unit: Annamaria Rossi
FEED Unit: Paola Manini and Fabiola Pizzo
PREV Unit: Juan Parra Morte

- **Observers**

Raffaella Corvi (DG JRC) and Frank Le Curieux (ECHA), only on 1 February 2019.

1. Welcome and apologies for absence

The Chair welcomed the participants. Apologies were received from Margherita Bignami and Francesca Marcon.

2. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence and Scientific Decision-Making Processes[1] and the Decision of the Executive Director on Declarations of Interest[2] EFSA screened the Annual Declaration of Interest filled in by the working group members invited for the present meeting. No Conflicts of Interest related to the issues discussed in this meeting were identified during the screening process or at the Oral Declaration of Interest at the beginning of this meeting.

[1] http://www.efsa.europa.eu/en/keydocs/docs/independencepolicy.pdf
[2] http://www.efsa.europa.eu/en/keydocs/docs/independencerules2014.pdf

3. Request for an advice from the PPR panel – update from the last meeting

The PPR panel requested the support of the WG gentox in relation to the EC mandate on the genotoxic potential of Triazine amine (M-2018-0207). The WG reviewed all the available genotoxicity data and discussed the results in the meeting. It was agreed to draft a report that summarises the discussion; the report will be sent to the PPR panel who will discuss it in its plenary meeting in the beginning of April. If necessary, the WG genotoxicity will be requested to provide additional clarification. The aim for the PPR panel is to adopt the opinion by end of June to respect the deadlines set by the Commission for this mandate.

4. Request for an advice from the Pesticides Unit

In the context of the renewal for the substance diflubenzuron, EFSA is in the process of assessing comments of Member States and applicant, identifying points where clarification is needed. EFSA requested the view of the WG genotoxicity for some aspects related to the possible genotoxicity Mode of Action for 4-chloroaniline (PCA) and related uncertainty analysis.

The WG was presented with 2 papers on the ToxTracker assay (Hendriks G. et al. Toxicol. Science, 2012; Hendriks G. et al. Toxicol. Science, 2016) a test that has been proposed to give an insight on the mechanisms of action of genotoxic compounds and therefore clarifying some issues related to PCA as a potential residue of diflubenzuron.

5. Possible statement/opinion on aneugenicity assessment

The WG was presented with a draft self-task mandate on aneugenicity assessment and discussed the specific terms of reference. The mandate was finalised and will be presented at the SC plenary meeting in the end of February for final approval.

The group discussed the various issues related to genotoxicity assessment especially in relation to the in vivo follow up of substances that have shown potential for aneugenicity in vitro. It was agreed to do some literature searches and to invite hearing experts in one of the next meetings to seek views outside the group.

The aneugenicity will be again on the agenda in April.

6. Next meeting(s)

Dates of next meetings in 2019:

- 27-28 February, Parma
- 11 April, placeholder for teleconference
- 29-30 April, Parma,
- 27-28 June, placeholder, Parma

SCIENTIFIC COMMITTEE AND EMERGING RISKS UNIT

Minutes of the KICK OFF MEETING

of the re-established Scientific Committee

cross-cutting Working Group on Genotoxicity

Held on 3-4 December 2018 in Parma
(Agreed on 4 January 2019)

Participants

- **Working Group Members:**

Diane Benford (Chair), Gabriele Aquilina, Claudia Bolognesi, Riccardo Crebelli, Rainer Gürtler, Francesca Marcon, Elsa Nielsen, Josef Schlatter, Christiane Vleminckx,

- **EFSA:**

SCER Unit: Daniela Maurici

FIP Unit: Maria Carfì, Carla Martino, Ana Rincon

NUTRI Unit: Annamaria Rossi

FEED Unit: Paola Manini and Fabiola Pizzo

PESTICIDES Unit: Federica Crivellente and Danièle Court Marques

1. Welcome and apologies for absence

The Chair welcomed the participants. Apologies were received from Margherita Bignami, Raffaella Corvi (DG JRC) and Frank Le Curieux (ECHA).

2. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence and Scientific Decision-Making Processes[1] and the Decision of the Executive Director on Declarations of Interest[2] EFSA screened the Annual Declaration of Interest filled in by the working group members invited for the present meeting.

Elsa Nielsen declared an interest in relation to Quillaia extract. Denmark Technical University was the contractor of an EFSA procurement to prepare the "Draft preparatory documents, including toxicological and non-toxicological data, to support the preparatory work for the re-evaluation of food additives permitted in the European Union". Elsa was the team coordinator not directly involved in the preparatory work. The final version of the external report was submitted to EFSA 1 March 2013.
No Conflicts of Interest related to the issues discussed in this meeting were identified during the screening process or at the Oral Declaration of Interest at the beginning of this meeting.

[1] http://www.efsa.europa.eu/en/keydocs/docs/independencepolicy.pdf
[2] http://www.efsa.europa.eu/en/keydocs/docs/independencerules2014.pdf

3. Request for an advice from the FIP Unit

The FAF WG on the "re-evaluation of the remaining food additives other than colours and swetteners" submitted a request to the WG via the FIP unit secretariat. The request for advice related to the evaluation of the available genotoxicity studies for the re-evaluation of Quillaia extract (E999) as a food additive and the preliminary assessment done by the FAF WG. The dataset was presented and explained by Rainer Gürtler and Ana Rincon. The WG gentox agreed with the conclusions of the FAF WG.

4. Request for an advice from the Pesticides Unit

Danièle Court Marques presented data on 4-Chloroaniline (PCA) as a metabolite potentially present in the residues resulting from the application of the pesticide diflubenzuron.

In the context of the renewal for the substance diflubenzuron, EFSA is in the process of assessing comments of Member States and applicant, identifying points where clarification is needed. In this context, EFSA would like to seek the view of the WG genotoxicity for some aspects related to the possible genotoxicity Mode of Action for PCA and related uncertainty analysis. Detailed data will be provided to the WG that will express its view in the next meetings.

5. Possible statement/opinion on aneugenicity assessment

Maria Carfì presented an overview of genotoxicity assessment in relation to substances that have provided indication of aneugenicity in *in vitro* testing. The issue of appropriate follow up *in vivo* for these substances has been discussed. The WG agreed to prepare an opinion/statement that clarifies and complement the EFSA Genotoxicity Testing Strategies published in 2011 (EFSA 2011, link here) in relation to the issue of aneugenicity assessment. The Term of Reference of a self task mandate of the Scientific Committee will be drafted by the secretariat and shared with the WG for possible comments.

6. Request for an advice from the PPR panel

The PPR panel requested the support of the WG gentox in relation to the EC mandate on the genotoxic potential of Triazine amine (M-2018-0207). The mandate was presented to the WG by Federica Crivellente. The deadline to deliver an opinion is July 2019. The WG will review all the available genotoxicity data and will provide an advice to the PPR Panel by spring 2019.

7. Next meeting(s)

Dates of next meetings in 2019:

- 31 Jan- 1 Febr, Parma
- 27-28 Febr, Parma
- 11th April, placeholder for teleconference
- 29-30 April, Parma,
- 27-28th June, placeholder, Parma