Scientific Panel on Plant Protection Products and their Residues

Minutes of the 88th Open Plenary meeting

Held on 05-06 July 2017, Parma (Italy)

(Agreed on 15 September 2017)

Participants

- Panel Members

  Paulien Adriaanse, Theodorus Brock, Sabine Duquesne, Sandro Grilli, Antonio Hernandez-Jerez, Susanne Hougaard Bennekou, Michael Klein, Thomas Kuhl, Ryszard Laskowski, Kyriaki Machera, Colin Ockleford, Olavi Pelkonen, Silvia Pieper, Robert Smith, Ingvar Sundh, Ivana Teodorovic, Aaldrik Tiktak, Christopher Topping, Gerrit Wolterink

- Hearing Experts [1]:

  Not Applicable

- European Commission and/or Member States representatives:

  Not Applicable

- EFSA:

  Pesticides Unit: Maria Arena, Arianna Chiusolo, Danièle Court-Marques, Federica Crivellente, Marcella De Maglie, Mark Egsmose, Dimitra Kardassi, Luc Mohimont, Alexandre Nougadère, Franz Streissl, Jose Tarazona and Andrea Terron

  Scientific Committee and Emerging Risks Unit: Georges Kass

[1] As defined in Article 11 of the Decision of the Executive Director on Declarations of Interest: http://www.efsa.europa.eu/en/keydocs/docs/independencerules2014.pdf.

- Observers:

  30 observers were registered to attend remotely, of which 18 actually attended:

  Aiad Alkhatib (Nestle, Switzerland), Anthony Tweedale (NGO, Belgium), Bill Pickering (Nichino-Europe, United Kingdom), David Parker (Syngenta, United Kingdom), Eleftherios Meletis (Student, Greece), Eva Kaminski (Canadian Food Inspection Agency), Felix Badea (Affiliation unknown), Felix Kluxen (Adama, Germany), Frank Hamburger (Trifolio-m, Germany), Gerrit Dreyersdorff (Ministry of Rural Affairs, Estonia), Gregor Spickermann (Adama, Germany), Laurent Oger (ECPA, Belgium), Miguel Escribano (Veterinary Medicines Directorate, DEFRA, UK), Niall O'Brien (Veterinary Medicines Directorate, DEFRA, UK), Peter Dohmen (BASF, Germany), Reinhard Fischer (Consultant, Germany), Seamus Taylor (Adama, Germany) and Stephanie Melching-Kollmuss (BASF, Germany).

- Others:

  Not Applicable

1. Welcome and apologies for absence

The Chair welcomed the participants.

Apologies were received from Michael Stemmer.

2. Brief introduction of Panels members and Observers

The Panel members and EFSA staff introduced themselves. The Secretariat communicated the list of observers registered to attend the meeting via web streaming.

3. Adoption of agenda

The agenda was adopted without change.

4. Declarations of Interest Scientific Panel Members

In accordance with EFSA's Policy on Independence and Scientific Decision-Making Processes[2] and the Decision of the Executive Director on Declarations of Interest[3], EFSA screened the Annual Declarations of Interest and the Specific Declarations of Interest filled in by the Scientific Panel Members invited for the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process or at the Oral Declaration of Interest at the beginning of this meeting.

5. Presentation of the Guidelines for Observers

The secretariat presented the EFSA guidelines for observers and provided information on the code of conduct during and after the plenary meeting.

6. Agreement of the minutes of the 87th Plenary meeting held on 17-18 May 2017, Parma (Italy)

The minutes of the 87th plenary meeting held on 17 and 18 May 2017 were under written agreement procedure.

7. Report on the written procedures since 87th Plenary meeting

The draft Scientific Opinion of the PPR Panel on the follow-up of the findings of the External Scientific report 'Literature review on epidemiological studies linking exposure to pesticides and health effects' (University of Ioannina Medical School, 2013), as revised following the input of the Scientific Committee was re-endorsed by written procedure on 6 June 2017.

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

8.1. Scientific opinion on pesticides in foods for infants and young children (EFSA-Q-2016-00702)

The Scientific Committee and Emerging Risks Unit presented the Guidance on the risk assessment of substances present in food intended for infants below 16 weeks of age recently adopted by the Scientific Committee.

The Chair of the Working Group informed the Panel on the outcome of the second meeting of the Working Group.

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

[3] http://www.efsa.europa.eu/en/keydocs/docs/independencerules2014.pdf

At the Working Group meeting, food consumption data for baby food and conventional food available in the EFSA Comprehensive Database were presented and age classes were defined for exposure calculation. The status of the on-going development for RAC model (tool to match occurrence and food consumption data) was also presented. The WG was updated on the on-going EFSA work for the Cumulative Risk Assessment of pesticides and in particular the methodology for cumulative assessment groups (CAGs) and establishment of CAGs for nervous system and thyroid was presented. The methodology for the literature review on physiology of developing systems (nervous, immune, reproductive, endocrine, ADME) was agreed by the Working Group. Moreover, preliminary information on the developing functions in brain and brain barriers were presented, including data gaps and future research needs. In the end, the Working Group was informed about the outcome from public consultation on the draft Scientific Committee guidance on the 'risk assessment of substances present in food intended for infants below 16 weeks'.

Two specific questions from observers were addressed:

• Have you ever evaluated pesticide residue impact on health by expressing your result in DALY's (Eva Kaminski)?

Reply: The question was not related to the specific mandate. The secretariat is not aware of any study using the DALY (Disability Adjusted Life Years) methodology for the evaluation of pesticides residues effects. However, the observer was informed that EFSA commissioned a literature review to identify and characterise available methodologies for risk ranking in the fields of food and feed safety and nutritional hazards, as well as in the field of socio-economics. From the screening of the literature, the disease burden methods (such as DALY) appeared to be applicable mainly for relevant substances not intentionally added to food (i.e. pathogens or contaminants). The External Scientific Report 'Critical review of methodology and application of risk ranking for prioritisation of food and feed related issues, on the basis of the size of anticipated health impact' is available in the EFSA website.

• Wouldn´t a 2-Generations study (OECD TG 416; possibly including enhanced specific thyroid or neurotoxic parameter) also be able to answer some of the specific questions regarding infants/neonate exposure (Stephanie Melching-Kollmuss)?

Reply: As reported in section 6.2 of the Scientific Committee guidance on the 'risk assessment of substances present in food intended for infants below 16 weeks', the extended one-generation reproductive toxicity study (EOGRTS) (OECD TG 443) is warranted, when standard toxicological studies do not show adverse effects and the ADME studies

show that a substance or its metabolite(s) is (are) absorbed. Deviations are possible, if scientific justification is provided: for example, when the two-generation reproductive toxicity study (OECD TG 416) is available instead of an EOGRTS, the former can be complemented with appropriate post-natal developmental studies addressing e.g. neurotoxicity and immuno-toxicity.

8.2. Scientific Opinion of the PPR Panel on the follow-up of the findings of the External Scientific report 'Literature review on epidemiological studies linking exposure to pesticides and health effects' (University of Ioannina Medical School, 2013) (EFSA-Q-2014-00481)

The Chair of the Working Group summarised for the observers the context and the content of the draft opinion which was under public consultation and consultation of the Pesticide Steering network until 28 July 2017.

8.3. Scientific Opinion addressing the state of the science on risk assessment for amphibians and reptiles (EFSA-QN- 2011-00985)

The Chair of the Working Group informed the Panel on the outcome of the public consultation which closed on 24 May 2017. The Working Group is addressing the 295 comments which were submitted. The main changes resulting from the public consultation will include a better explanation of the choice of focal species, the introduction of new section summarising in detail the prerequisites for the development of a guidance document, suggesting options to refine the risk assessment and describing the requirements for a good field-effects study.

Two specific questions from observers were addressed:

• What has been the area where the Working Group thinks that most changes will be needed (Peter Dohmen)?

Reply: Most changes in the opinion will be needed in the areas related to future risk assessment. It is for example planned to add sections on what is needed for developing a future Guidance Document, possible refinement options and a description of the necessary information for a reliable field study.

• Concerning modelling, by when does the Panel think a working and tested model will be available (Peter Dohmen)?

Reply: The scientific opinion does not include details of the model testing, sensitivity and uncertainty analysis as this would have gone beyond the scope of the scientific opinion. However, this work has been done for the Great Crested Newt model and publications are in process. Hence, for the terrestrial stages of Great Crested Newt a

working and tested model is therefore close. Inclusion of aquatic stages will be dependent on development of an improved exposure model for ponds in the ALMaSS framework.

For the other five focal species suggested in the opinion there are no current plans for model development and this is one of the recommendations for work to be done before a GD can be finalised.

8.4. Scientific Opinion of the PPR Panel on the state of Toxicokinetic/Toxicodynamic (TK/TD) and Simple Food Chain effects modelling for regulatory risk assessment of pesticides for aquatic organisms (EFSA-Q-2012-00960)

The Chair of the Working Group informed the Panel on the outcome of the last meetings of the Working Group. The outline of the Opinion was presented. A brief overview of the already available chapters was given e.g. overview of the models in the remit of the Opinion (TK/TD for survival, TK/TD for growth and reproduction and TK/TD for primary producers), problem formulation for the use of TK/TD models in the risk assessment of aquatic organisms, documentation and testing of the models and model implementation. The Panel was also informed that in the Working Group meeting foreseen on November, hearing experts covering the 3 different model types will be invited. Two rapporteurs were nominated in consultation with the Secretariat.

Following consultation of the Secretariat and considering the unavailability of external expertise related to simple food chain models, the Chair of the Working Group proposed to restrict the scope of the opinion to state of Toxicokinetic/Toxicodynamic (TK/TD) effects modelling. The Panel agreed to propose this revision of the mandate to the Executive Director, with a recommendation to cover simple food chain models in a future activity focussed on a tiered approach for the risk assessment of secondary poisoning of non-target organisms.

One specific question from observers was addressed:

- Considering the discussion about worst-case scenarios, is it considered that such models provide value if primarily based on worst-case assumptions (Peter Dohmen)?

Reply: The TK/TD models can be used to model every possible exposure scenario provided that they are properly validated and calibrated on the basis of worst-case assumptions. Those worst-case assumptions can discriminate toxicologically dependent and independent pulses and they can vary between species. Every model is substance and species-specific. This approach is not considered to differ from other refinement approaches such as micro/mesocosms.

For active substances evaluation, in theory, one safe use only is necessary. But it should be for worst-case intended use so that

evaluation of refinements based on TK/TD modelling is performed at EU level rather than at Member State level for product authorization.

8.5. Scientific Opinion on the Guidance proposal on how aged sorption studies for pesticides should be conducted, analysed and used in regulatory assessments (Chemical Regulation Directorate, UK, 2016)

The Secretariat summarised for the observers the context and the earlier activities conducted in the area of aged soil sorption studies and informed the Panel on the progress of the establishment of the Working Group.

8.6. EFSA scientific reports on cumulative assessment groups of pesticides for the effects on the nervous system and the thyroid (EFSA-Q-2017-00434, EFSA-Q-2017-00436)

The Pesticides unit summarised for the observers the past activities of the PPR Panel related to the elaboration of a methodology to conduct cumulative risk assessments resulting from the exposure of consumer to pesticide residues in food, and reminded the key points of this methodology.

A detailed presentation was given on the progress of the EFSA scientific reports on cumulative assessment groups addressing the effects of pesticides on the nervous system and the thyroid. In particular, the Pesticides Unit presented an approach to conduct an uncertainty analysis on the applicability of the dose-addition model to cumulative assessment groups, and relying on the identification and integration of lines of evidence.

Two specific questions from observers were addressed:

• You mentioned, that observed thyroid hormone decreases were in some cases considered to be not specific but secondary effects to liver enzyme induction, but that these compounds were nevertheless included in the thyroid CAG. Will those compounds be removed from the thyroid CAG (Stephanie Melching-Kollmuss)?

Reply:

Thyroid effects associated to liver induction are considered human relevant in terms of hazard (histology and decreased thyroid hormones) and metabolic mechanisms (CAR, PXR, UDPGT). Although qualitatively similar, the effect is recognised to be quantitatively different amongst species.

Characterisation of the mode of action will be necessary to establish a liver threshold or that the substance is not liver inducer in human. If a mechanism of action can be established, the uncertainties of working by dose addition would be likely restricted to the compound with the same mode of action.

• Where there may be diverse MOAs, would there be more uncertainty surrounding the assumption that each individual would be equally sensitive to each substance? And therefore increased uncertainty in the quantitative outcome of the cumulative risk assessment (David Parker)?

Reply:

Indeed the existence of different modes of action is expected to increase the uncertainty regarding the assumption of dose addition.

In addition, EFSA replied to the written question 10.1 sent by Stephanie Melching-Kollmuss (see point 10).

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

9.1. Scientific Committee and/or Scientific Panel(s) including their Working Groups

Feedback from the plenary meeting of the Scientific Committee of 26 and 27 April 2017 has already been given during the 87th Plenary meeting of the PPR Panel.

The forthcoming plenary meeting of the Scientific Committee will take place on 12 and 13 July as an open session.

9.2. EFSA including its Working Groups /Task Forces

The Pesticides unit summarized for the observers past activities in the area of developmental neurotoxicity (DNT). This included an opinion of the PPR panel in 2014 on the developmental neurotoxicity potential of acetamiprid and imidacloprid, an outsourced literature review on in-vivo and alternative DNT testing methods and an EFSA/OECD workshop on integrated approach for testing and assessment of DNT. EFSA is now preparing a call for tender on the implementation and interpretation of in vitro testing battery for the assessment of developmental neurotoxicity. If successful, the result of this outsourced activity will be used as scientific background for the development of OECD guidance.

The Pesticides unit informed the Panel on a number of follow up activities and noteworthy impacts of the scientific opinion investigating experimental toxicological properties of plant protection products having a potential link to Parkinson's disease and childhood leukaemia. EFSA is fully engaged in disseminating the AOP conceptual framework by organising a 2 days AOP development course which is now at its 8th edition. The chair of the former Working Group also presented EFSA activities on AOP at the New Zealand EPA. The Scientific Opinion is

already used for providing recommendations in the context of REACH and pesticide re-evaluation and advice on environmental toxicants and Parkinson's disease. One of the AOPs developed by the Working Group is core in one of the case studies of the EU-ToxRisk project (European Union's Horizon 2020 research and innovation programme). The Scientific Opinion has been quoted so far in one scientific paper (Tipping points and endogenous determinants of nigrostriatal degeneration by MPTP, Trends in Pharmacological Science, June 2017). The Panel was also informed of letters sent by PAN Europe to EFSA and to the Chair of the former Working Group and of the follow-up given to these letters.

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

10.1. *How many CAGs are planned to be defined in addition to the ones seen (thyroid, nervous system, reproduction, liver, eyes, adrenals) or indicated (heart, liver, testes)? What are the timelines for definition and publication of the CAGs? Does EFSA have an idea, how these presumably large groups of CAGs (based on level 2 effects) can be refined based on mechanistic data in order to achieve CAGs at levels 3/4 to make CRAs more achievable and meaningful? Some compounds have been included in the thyroid and nervous system CAGs, although in the EFSA conclusion eventual findings in these organs were not considered to be adverse and/or treatment-related. How will this inconsistency be handled in the final definition of the CAGs? It would seem evident, that cumulative risk assessment calculations for "new" pesticide uses (e.g., new active substance approvals; setting new MRLs) must be significantly more conservative than for calculations based on monitoring data, as only "prospective" calculations presumably using field trial residues data can be used. Does EFSA have any ideas how cumulative risk assessment calculations can be done so as not to heavily disadvantage innovation (Stephanie Melching-Kollmuss)?*

Reply by EFSA:

EFSA is willing to prepare the following Scientific Reports with their respective deadlines (including Public Consultation):

- Establishment of CAGs of pesticides regarding their combined effects on the nervous system (December 2017)
- Establishment of CAGs of pesticides regarding their combined effects on the thyroid (December 2017)
- Establishment of CAGs of pesticides regarding their combined effects on the liver (February 2018)

- Establishment of CAGs of pesticides regarding their combined effects on the adrenals (May 2018)
- Establishment of CAGs of pesticides regarding their combined effects on the eyes (May 2018)
- Establishment of CAGs of pesticides regarding their combined effects on reproduction (February 2019)
- Establishment of CAGs of pesticides regarding their combined effects on development (February 2019)
- Establishment of CAGs of pesticides regarding their combined effects on the kidneys (May 2021)
- Establishment of CAGs of pesticides regarding their combined effects on the testes (September 2021)
- Establishment of CAGs of pesticides regarding their combined effects on the hematopoietic system (February 2022)

For the time being no cumulative assessment groups are planned for the heart.

No refinement has been planned for the different CAGs on the basis of mode/mechanism of action information, since in many instances such information is not available. Considerations on mode/mechanisms of actions, if available, will be part of uncertainty analysis included in the EFSA Scientific Reports. During the update of the CAGs for effects on the nervous system and the thyroid, a revision of the following evidence has been completed: original study reports, EFSA Conclusions, new data submitted in accordance with article 21 and some published papers. As a consequence, some substances have been removed from the original CAGs. However, any additional comments which might improve the CAGs may be submitted during the Public Consultation phase.

With respect to the regulatory context in which cumulative risk assessment is done, there is indeed a clear distinction between pre- and post-authorisation situations. With respect to the post-authorisation situation, EFSA will progressively perform analyses of chronic and acute risks to the health of consumer from pesticide residues, as provided in article 32 of the MRL regulation. With respect to the pre-authorisation, it is initially the responsibility the risk managers to formulate the exact assessment question to be addressed and the respective level of protection to achieve. This will later govern the use of the methodology for cumulative risk assessment.

10.2. *You communicated that you own a vast amount of data on pesticide contamination. Have you ever used these data for quantitative assessment, especially for chronic exposure (remote question by Eva Kaminski)?*

Reply by EFSA:

Yes, this is one of the baseline activities of the Pesticides unit. On the basis of the results of official monitoring of pesticide residues in food conducted by Member States, EFSA drafts an annual report on pesticide residues. This report includes an analysis of chronic and acute risks to the health of consumer from pesticide residues.

This report is published each year on the EFSA website. The latest one considered the monitoring results of 2015 and can be found at this link: http://www.efsa.europa.eu/en/efsajournal/pub/4791

11. Any other business

The following was brought to the attention of the Panel:

- The Norwegian Scientific Committee for food safety and EFSA will co-organise a joint symposium on risk assessment and risk management cooperation on environmental protection goals on 26 and 27 October in Oslo.
- An internal workshop took place in EFSA on the trial of the EFSA guidance document on uncertainty on 22 and 23 June. The feedback from this workshop will help to shape the final guidance planned to be adopted by the Scientific Committee in November 2017.
- The EFSA guidance on dermal absorption has been approved on 24 May 2017. An info-session for stakeholders will be organised in Parma on 27 and 28 September 2017.
- The call for application for the renewal of the Scientific Committee and Scientific Panels is open. The deadline for submission of applications is 8 September 2017.
- The dates of plenary meetings of the PPR Panel in 2018 are established as follows: 7(PM) and 8(AM) February, 21(PM) and 22(AM) March, 16(PM) and 17(AM) May, 27(PM) and 28(AM) June, 26(PM) and 27(AM) September, 28(PM) and 29(AM) November.