PESTICIDE PEER REVIEW UNIT

Scientific Panel on Plant Protection Products and their Residues

Minutes of the 113th Plenary meeting

Held on 10 November 2021 (webconference)

(Agreed on 26 November, 2021)

Participants

- Panel Members:

  Paulien Adriaanse, Annette Aldrich, Philippe Berny, Tamara Coja, Sabine Duquesne, Andreas Focks, Antonio Hernandez-Jerez (chair), Marina Marinovich, Maurice Millet, Olavi Pelkonen, Silvia Pieper, Aaldrik Tiktak, Christopher Topping, Anneli Widenfalk, Martin Wilks, Gerrit Wolterink.

- Hearing Experts:

  Not Applicable

- European Commission and/or Member States representatives:

  Not Applicable

- EFSA:

  PREV Unit: Maria Arena, Domenica Autieri, Jorge Borroto, Anna Castoldi, Arianna Chiusolo, Federica Crivellente, Guilhen de Seze, Isabella De Magistris, Alessio Ippolito, Dimitra Kardassi, Alberto Linguadoca, Christopher Lythgo, Marco Marchesi, Maria Masoura, Laura Padovani, Martina Panzarea, Juan Parra Morte, Rositsa Serafimova, Andrea Terron, Manuela Tiramani

  PRES Unit: Lucien Ferreira da Costa

- Observers:

  See Annex I

- Others:

  Not Applicable

OPEN SESSION (9:00-12:45 CET)

1. Welcome and apologies for absence

The Chair welcomed the participants.

2. Adoption of agenda

The agenda was adopted without changes.

3. Declarations of Interest of Scientific Committee/Scientific Panel/ Members

In accordance with EFSA's Policy on Independence and the Decision of the Executive Director on Competing Interest Management, EFSA screened the Annual Declarations of Interest filled out by the Panel members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process. At the beginning of the meeting an interest related to agenda item 7.1 was declared orally by Tamara Coja, as team member of the beneficiaries for an EFSA grant in support to the development of the PPR Panel output. The Chair asked Tamara to disconnect from the webconference during the agenda item 7.1.

4. Brief introduction of Panel Members and Observers

Panel members and EFSA introduced themselves to the observers.

5. Presentation of the EFSA guidelines for Observers

EFSA presented the guidelines for observers for open plenary meetings.

6. Scientific outputs submitted for discussion and/or possible adoption, updates on ongoing activities, new projects

6.1 Comparative in vitro metabolism studies (EFSA-Q-2020-0055)

The Panel was informed on the comments received from reviewers (Martin, Philippe and Tamara) and how they were addressed. The Scientific Opinion was adopted unanimously.

6.2 Development of Adverse Outcome Pathways relevant for the identification of substances having endocrine disruptors properties (EFSA-Q-2019-00492)

The Panel was updated on the progress of the project, including the related outsourced activity and the planning for the next steps.

6.3 Update on the Working Group 'IATA DNT - VGSC AOP' (EFSA-Q-2019-00100)

The Panel was updated on the status of activities and planning for the Development of a DNT-AOP using VGSC inhibition as a molecular initiating event (MIE).

7. New mandates

7.1 Use and reporting historical control data (HCD) for regulatory studies

The Panel was informed on the recently initiated one-year grant (GP/EFSA/ENCO/2020/02) with public institutions from two Member States (AGES and BPI) as preparatory work on how to report, use and interpret historical control data in (eco)toxicity studies. The terms of reference of the self-task mandate for the development of a Scientific Opinion on the use and reporting of historical control data in regulatory studies were agreed.

7.2 Request for a Statement on the design and conduct of groundwater monitoring studies supporting groundwater exposure assessments of pesticides

The Panel was informed on the mandate from the Commission, asking the public consultation of a SETAC publication (Gimsing et al. 20191) before the development of the Statement.

8. Q&A

Questions received upon registration as well as questions posed during the meeting were answered by the Panel and EFSA (see Annex II).

[1] Gimsing, A.L., Agert, J., Baran, N. et al. Conducting groundwater monitoring studies in Europe for pesticide active substances and their metabolites in the context of Regulation (EC) 1107/2009. J Consum Prot Food Saf 14, 1–93 (2019). https://doi.org/10.1007/s00003-019-01211-x

CLOSED SESSION (14:00-18:00 CET)

6. Scientific outputs submitted for discussion and/or possible adoption, updates on ongoing activities, new projects [cont.]

6.4 Statement on the active substances flupyradifurone and acetamiprid (EFSA-Q-2021-00159 and 2021-00160)

The Panel was updated on the main comments received by the reviewers (Sabine, Andreas and Olavi) for the two Statements (one for each active substance) and how they were addressed. The Panel was also informed that the two outputs will be shared on 18th November for possible adoption via written procedure.

6.5 Opinion on the toxicity profile of PBA and PBA(OH) (metabolites common to several pyrethroid substances) (EFSA-Q-2021-00118)

The Panel was informed on the progress for the development of the output and the planning for the next meetings.

9. On-going activities of the Scientific Committee

The Panel was updated on the activities of the EFSA Scientific Committee and in particular on the following:

- Draft opinion on non-monotonic dose response;
- Draft opinion on evaluation of existing guidelines for their adequacy for the food and feed risk assessment of microorganisms obtained through synthetic biology;
- Review of the existing health-based guidance values for copper and its exposure assessment from all sources;
- Guidance on Expert Knowledge Elicitation (EKE);
- Follow up on the GMO workshop on allergenicity assessment;
- EFSA international workshop on chemical mixtures (18-20 October 2021).

10. Update on the ARchitecture Transformation (ART) Programme

The Panel was updated on the EFSA re-organisation and the changes introduced for the implementation of the transparency Regulation.

11. Implementation of the agreed SPG for honeybees in risk assessment

The Panel was informed on an approach for the implementation of the specific protection goal for honeybees which was developed under the on-going revision of the Guidance on the risk assessment for bees.

12. AOB

A member informed the Panel on the recently conducted Johns Hopkins Center for Alternatives to Animal Testing (CAAT) workshop 'Challenges and Opportunities for Overcoming Dog Use in Agrochemical Evaluation and Registration'. The Panel asked EFSA staff to share in a next Plenary the 'Analysis of Dog Data from European Pesticide Registration' presented at the workshop.

ANNEX I

List of observers

Last Name	First Name	Name of Employer	Affiliation
Ålander	Johan	Swedish food agency	National Authority
Blagaia	Anna	Bogomolets National Medical University	University/public research
Buca	Valdete	National Veterinary and Plant Protection Authority	National Authority
Collina	Marina	University of Bologna	University/public research
COOLS	Andrea	Essenscia	Other
Corvaro	Marco	Corteva Agriscience	Private sector
De Lima e Silva	Claudia	Wageningen Environmental Research	University/public research
Delijaj	Naim	Kosovo Food and Veterinary Agency	International organisation
Đermic	Edyta	University of Zagreb Faculty of Agriculture	University/public research
Edwards	James	LKC Switzerland Ltd	Private sector
Fatur	Tanja	National Institute of Public Health	National Authority
Frunzareanu	Bogdan	Institute for Control of Biological Products and Veterinary Medicines	Other
Galbusera	Carmen	CHEMSERVICE	Private sector
Garcin	Jean-Christophe	Bayer	Private sector
GINER	Marta	DEVREG	Private sector
Graham	Paul	Eurofins	Private sector
Himmelstein	Matthew	Corteva Agriscience	Private sector
Hiroko	Matsumoto	Nihon Nohyaku Co., Ltd.	Other
Hofmann	Thomas	BASF SE	Other
Isacco	Luca	Expedia MRCC	Private sector
Janusauskaite	Dalia	The State Plant Service under the Ministry of Agriculture, Lithuania	National Authority
Kluxen	Felix	ADAMA Deutschland GmbH	Private sector
Kozmos	Martin	University of Maribor, Faculty of Agriculture and Life Science	University/public research
Ksiazkiewicz	Agnieszka	LKC Switzerland Ltd.	Private sector
Lamshoeft	Marc	Bayer AG, Crop Science	Private sector
Lupi	Daniela	University of Milan	University/public research
Maranghi	Francesca	Istituto Superiore di Sanità	University/public research
Marie	Pauline	Eurofins	Private sector
metruccio	francesca	A:O fatebenefratelli Sacco	EFSA Panel/WG/Network
Moisac	Alexandru	ICA Research & Development	Private sector
Nallani	Gopinath	FMC	Private sector
Neumann	Birgit	Bayer AG	Private sector

Noel	Laetitia	Eurofins Agroscience Regulatory	Private sector
Pálka	Václav	Ministry of Agriculture	National Authority
Paltanaviciene	Audra	The State Plant Service under the Ministry of Agriculture	National Authority
Porta	Giovanni	Politecnico di Milano	University/public research
Pribu	Mihaela	National Institute of Public Health	National Authority
Ramirez	Kelvin	LKC Ltd	Private sector
Rutten	Joost	Triskelion	Private sector
Sabah	Ahmed	Swedish Food Agency	National Authority
Soviero	Giovanna	DR.ssa Giovanna SOVIERO	Private sector
Tena	David	Eurofins Agroscience Services Regulatory Spain S.L.	Private sector
Mammone	Teresa	Hospital Sacco - ASST Fatebenefratelli - Sacco	Other
Tosti	Luca	Department of Biomedical and Clinical Sciences – Università degli Studi di Milano	University/public research
Tulcan	Camelia	USAMVB TIMIȘOARA ROMÂNIA	University/public research
Vidotto	Francesco	Università di Torino. Department of Agriculture, Forestry and Food Science	University/public research
Zarn	Jürg	Federal Food Safety and Veterinary Office FSVO	International organisation
Zusková	Eva	National Institute of Public Health	National Authority

ANNEX II

List of questions from observers and answers

Question maker	Question	Answer
General question		
Bogomolets National Medical University	Endocrine disruptors-official definition, express assessment models, legal aspects	In 2018, Commission Regulation 2018/605, setting out scientific criteria for the determination of endocrine disrupting properties was published. Based on those criteria, an active substance, safener or synergist shall be considered as having endocrine disrupting properties, if: it shows an adverse effect in [an intact organism or its progeny]/[non-target organisms], which is a change in the morphology, physiology, growth, development, reproduction or life span of an organism, system or (sub)population5 that results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress or an increase in susceptibility to other influences; it has an endocrine mode of action, i.e. it alters the function(s) of the endocrine system; the adverse effect is a consequence of the endocrine mode of action. The text laying down the scientific criteria is amending Annex II of the Regulation 1107/2009 and in particular point 3.6.5 for humans and 3.8.2 for non-target organisms. A Regulation (2017/2100) laying down scientific criteria for the determination of endocrine disrupting properties was also published pursuant to the Biocidal Products Regulation (EU) No 528/2012. Following the publication of the scientific criteria for both biocidal products and plant protection products, EFSA and ECHA issued a common guidance document describing how to perform hazard identification for endocrine-disrupting properties by following the scientific criteria.
University of Maribor, Faculty of Agriculture and Life Science	Since all higher living beings use microbiomes to influence their health, could using specific microbial, fungal and phytoplasmic entities in combination with	Formulations containing micro-organisms are used as Plant Protection Products (PPPs). The rules for their assessment are also described under Regulation EC (No)1107/2009. Please, note that under the Green Deal, the Commission will take actions to reduce the use and risk of chemical pesticides and to facilitate the placing on the market of pesticides containing biological active substances. Concerning the role of microbiomes in plant health, research aiming to increase the understanding of the role of microbiomes in human/animal/plant health is still ongoing, and it expected to play a role in the future regulatory science (EFSA Journal 2020;18(6):e18061).

Question maker	Question	Answer
	use of wide plant species end the use of chemically synthetic substances used in plant protection nowadays?	
Eurofins	In the section of plant and animal metabolism, it is mandatory to submit study summaries for EU dossiers using MSS composer software. Will IUCLID replace MSS composers for the default way in which metabolism study summaries shall be submitted and if so, when?	Currently and still for short and mid-term, MSS composers (for residues metabolism studies) and DER composer (for rat metabolism studies) are used to enter the metabolism study data and to create XML-files that are attached in IUCLID submissions. This is defined in the IUCLID manual: https://zenodo.org/record/5091464#.YYJrqWDMLD4 (see Section 6.2.1, page 1265). However, for the longer term, the question is still open whether the structure of the DER/MSS composers might be embedded directly in the metabolism study records (OHT) of IUCLID or if MSS/DER composers should still co-exist. This question, among others, was analysed by Germany (BfR) and a draft report has been issued in September. If you are interested in this topic, you may find the following documentation useful: https://www.bfr.bund.de/en/analysis_of_the_information_flow_in_metabolism_studies_on_pesticides-272198.html. Kindly note that the commenting period is over. However, several comments were received so far and the next step is to discuss this analysis and the different views at the MUG (MetaPath User Group) meeting in November.
Questions related to item 6.2.- 6.2 Development of Adverse Outcome Pathways relevant for the identification of substances having endocrine disruptors properties		
Bayer AG	How do you rate the certainty/uncertainty related to the new AOP?	Thanks for the question. The OECD AOP guidance and the AOP wiki template is describing how to handle uncertainties as part of the overall WOE for the biological plausibility of the pathway. In a former SO dealing with AOP we tested a methodology for the quantification of the uncertainties, which was very comprehensive but also very resource demanding. For the current AOP we have developed a protocol to be followed along the different steps. The protocol is including the qualitative assessment of the uncertainties that should be listed for each KER. For critical KER, we will likely use an expert knowledge elicitation to quantify them. A possibility is to quantify the overall uncertainties for the full pathway and include it as part of the overall WOE for the pathway.
Questions related to item 6.3.- IATA DNT - VGSC AOP		
Bayer AG	Thank you for the clear presentation on the AOP development.	Thanks for the question and I assume your question refers to the VGSC AOP. Although AOP, are agnostic, indeed your question is relevant when thinking about the regulatory applicability of the AOP. This is indeed a complex AOP as it is dealing with an AO which is very complex and difficult to

Question maker	Question	Answer
	To put it into perspective - is there any adversity evidence related to chemistry or other biochemical triggers and factors that would trigger this AOP? How is it possible to differentiate?	measure in the regulatory studies and to translate to the human situation (Papparella et al. 2019). The initial effort was done using the VGSC but it is clear that the downstream KEs are showing commonalities with many other pathways and alteration of the NNF is by itself a downstream KE sharable to many pathways. Though the KER between KE4 and KE5 has a high biological plausibility, the empirical support is less certain mainly because testing beyond MEA is not so easy and the morphological association is difficult to prove. However, when moving to the KER for KE5 to AO, both biological plausibility as well as empirical support are robust. There is evidence for many chemicals interacting with the glutamatergic and GABAergic pathway that are affecting this KER. In addition, knockout models are available (e.g. Fragile X syndrome).
Questions related to item 7.1.- Use and reporting historical control data (HCD) for regulatory studies		
ADAMA	Specifying an acceptable HCD time range has some benefits but it would be good to allow some flexibility: for example, If a laboratory goes out of business and only HCD before study conduct is available, would this be acceptable and used or rejected? If an endpoint is only rarely investigated in a lab, can the time range be expanded to built up a more informative database for HCD? Older studies often refer to peer-reviewed	Thanks for the questions/observations. Data requirements on HCD are specified in Regulation (EU) No 283/2013. "The data submitted shall be for endpoints that could represent critical adverse effects, and shall be strain-specific and from the laboratory which carried out the index study. They shall cover a five-year period, centred as closely as possible on the date of the index study". The HCD project aims to explore the landscape as regards HCD use and to collect scientific community views on their use. Outcome of the literature review and survey feedbacks will be discussed in the stakeholders' workshop to agree on basic principles for the use, reporting and interpretation of HCD. This piece of evidence will be then taken into consideration by the PPR Panel for the drafting of the Scientific Opinion.

Question maker	Question	Answer
	publications containing HCD information and HCD from other labs, how would new HCD requirements affect study acceptability? Generally, if there is scarce information on control variation available, can published data be used in a weight-of-evidence assessment? While the range as an HCD descriptor has limitations, would it also be in the future a practical descriptor of HCD, maybe in combination with a mean or median? Because estimation intervals strongly depend on statistical assumptions that are hard to support by typical tox data with small observation numbers	
Corteva Agriscience	May I suggest to include pharma sister regulatory agencies (at least EMA/FDA/MHLW/PMDA	Thanks for the observation. Please note CROs are considered relevant stakeholders and their experience will be taken on board through the survey and workshop.

Question maker	Question	Answer
	as ICH core agencies) since CRO do collect HCD for multiple sectors and certainly pharma drives most of their business, interest and procedures. This will allow easier implementation.	