To: members of the PAFF Committee - Section "Phytopharmaceuticals - Legislation”

Brussels, 24 September 2024

Subject: EU Standing Committee on Plants, Animals, Food and Feed (PAFF); 2-3 October - position of Pesticide Action Network (PAN) Europe

Dear members of the PAFF committee,

On October 2nd and 3rd, you are invited to the EU Standing Committee on Plants, Animals, Food and Feed to discuss and/or potentially adopt opinions on several proposals of the European Commission. In advance of this meeting, please find below PAN Europe's position on specific issues related to the protection of human health and the environment, which we kindly request you to give particular attention.

Agenda issues

1. Proposal for non-renewal of metribuzin (B.04)
2. Proposal for non-renewal of tritosulfuron (B.05)
3. Proposal for extension of the approval and several substances (B.06)
4. Draft renewal reports: pydiflumetofen, flutolanil and 8-hydroxyquinoline (A.05)
5. EFSA conclusions: flufenacet (A.04)
6. Working group on comparative assessment (A.15)

1. Proposal for non-renewal of metribuzin

PAN Europe welcomes the Commission's proposal for non-renewal of metribuzin despite recent delays resulting from exchanges with the "Metribuzin Task Force". In August 2023, EFSA published its conclusion of the peer review of the pesticide risk assessment of metribuzin. It listed three critical areas of concern, which in line with Article 4(1) to (3), preclude the reapproval of metribuzin:

- Metribuzin meets the endocrine disruption criteria for humans for the T-modality according to point 3.6.5 of Annex II of Regulation (EC) 1107/2009 and Commission Regulation (EU) 2018/605. No information was submitted by the applicant to demonstrate that dietary and non-dietary exposure to metribuzin is negligible or to demonstrate that the conditions for derogation under Article 4(7) of Regulation 1107/2009 are met during the eligible period for submission set out in Article 14(1)(a) of Commission Implementing Regulation 844/2012.
- Bystander and resident exposure estimates exceed the AOEL value.
- A high risk to bees could not be excluded based on the available studies.

Moreover, metribuzin is classified as acutely toxic when ingested (category 4, H302) and particularly toxic for aquatic organisms with long-term effects (Aquatic acute category 1; Aquatic chronic category 1) under Regulation (EC) 1272/2008. To ensure a high level of protection of human health, animal health and the environment, and in line with the approval criteria set out in Article 4(1) to (3), metribuzin must not be renewed. Considering its approval period was initially due to expire in September 2017 and has been continuously extended (now until February 2025), a non-renewal decision should occur as soon as possible.

We call on you **to <u>support</u>** the Commission proposal for **non-renewal of the approval of metribuzin**.

2. Proposal for non-renewal of tritosulfuron

PAN Europe welcomes the Commission's proposal for non-renewal of tritosulfuron, based on the applicant's withdrawal of its renewal applicable. We nevertheless regret that the proposal does not refer to the fact that tritosulfuron is a PFAS and to the risk of groundwater contamination by tritosulruton's relevant metabolite TFA at a level above 0.1 ug/L. This means that tritosulfuron does not meet the criteria of Article 4(1) and (2) of Regulation 1107/2009. In recent years, the persistence of PFAS has led to dangerous levels of pollution of our environment and living organisms, which the EU has recognised as an unacceptable risk and has taken action to address this under the proposal for a REACH restriction. Yet, an exception stands for now for pesticides although they constitute a deliberate and direct source of PFAS pollution of our environment and

the food chain and degrade into TFA. Our concerns regarding PFAS pesticides are confirmed in EFSA's conclusions on tritosulfuron published in August 2023. EFSA highlights that tritosulfuron is persistent as well as particularly toxic for aquatic organisms with long-term effects (Aquatic acute category 1; Aquatic chronic category 1) according to Regulation (EC) 1272/2008. Moreover, tritosulfuron is metabolised in soil to TFA, which is now proposed for classification as toxic for reproduction 1B, acute toxic 3, very persistent and very mobile (vPvM) and persistent, mobile and toxic (PMT) while being likely to contaminate groundwater above the limit value of 0.1 ug/L according to EFSA.

We call on you to **support** the Commission proposal for **non-renewal of the approval of tritosulfuron.**

3. Proposal for extension of the approval and several substances

PAN Europe is highly critical of the systematic practice of the Commission and Member States of extending substances' approval periods because the (re)approval procedure has not been completed within the legal timeframe. This practice is unacceptable, particularly when prolongations concern substances for which there is evidence of their toxicity indicating that their prolonged use is putting at risk human health and/or the environment. The extension of their authorisation period clearly contravenes the requirement of Articles 1(3) and 4(1) to (3) of Regulation (EC) 1107/2009 and its legal provisions of ensuring a high level of protection of human and animal health and the environment from harmful pesticides.

- 8-hydroxyquinoline is classified as toxic for reproduction 1B, as well as acute toxic 1 and chronic toxic 1.
- Imazalil is classified as carcinogen category 2 and chronic toxic 1. This antifungal substance is known to inhibit the enzyme aromatase[1], a key enzyme in the biosynthesis of estrogens, and is also an androgen receptor antagonist; a study showed that maternal exposure in mice can lead to endocrine disruption in offspring[2].
- Kresoxim-methyl is classified as carcinogen category 2 as well as acute toxic 1 and chronic toxic 1. This fungicide has been found to spread antimicrobial resistance at environmental concentrations, as it facilitates the transfer of antibiotic-resistant plasmids carrying clinically important antibiotic-resistant genes. This is not only serious in relation

[1] Vinggaard et al (2020). Screening of selected pesticides for inhibition of CYP19 aromatase activity in vitro. *Toxicol In Vitro*;14(3):227-34. https://doi.org/10.1016/S0887-2333(00)00018-7
[2] Jin et al (2019). Maternal exposure to imazalil disrupts the endocrine system in F1 generation mice. *Mol Cell Endocrinol.*15;486:105-112. https://doi.org/10.1016/j.mce.2019.03.002

to the antimicrobial resistant crisis and its implications for public health, but it also gives rise to pathogenic organisms in soil,[3] which can have a direct impact on crop yields.

- Azoxystrobin is aquatic acute toxic 1 and aquatic chronic toxic 1.
- Tefluthrin is aquatic acute toxic 1 and aquatic chronic toxic 1.
- Fluroxypyr is aquatic acute toxic 1 and aquatic chronic toxic 1.

We call on Member States to reject this Commission's proposal and proceed to immediate non-approvals of the above-mentioned substances in line with Regulation (EC) 1107/2009.

4. Draft renewal reports: pydiflumetofen, flutolanil, 8-hydroxyquinoline

a) Pydiflumetofen

PAN Europe is calling upon the Commission and Member States to ban the approval of pydiflumetofen, a succinate dehydrogenase inhibitor fungicide, by considering its very high persistence as an unacceptable effect. This demand is in line with the scientific recommendation that chemicals should be regulated based on their persistence alone to prevent irreversible impacts on human health and the environment. Moreover, pydiflumetofen has a difluoromethyl group and therefore is a PFAS according to the OECD 2021 definition of PFAS (contains at least one saturated CF2 or CF3 part).

The history of chemical regulation has indeed demonstrated that a number of chemical pollution problems we are facing nowadays result from the release of highly persistent chemicals, such as dichlorodiphenyltrichloroethane (DDT), chlordane and PFAS, due to an underestimation of their impacts during their risk assessment. The use of highly persistent substances leads to the risk of reaching particularly high concentrations when released in the environment, increasing thereby the risk of causing adverse effects on human health and the environment. In the case of pydiflumetofen, some toxicity concerns already exist. Namely, concerns remain regarding the genotoxic potential of its metabolite 2,4,6-TCP and the toxicity of three of its impurities. Moreover, while EFSA concluded that pydiflumetofen does not meet the criteria for endocrine disruption, some adverse effects were observed in fish (decreased VTG at all concentrations, decreased fecundity, change in female gonad histopathology, i.e. increased oocyte atresia), raising some clear "uncertainties" for its impact on non-target organisms other than mammals. These uncertainties and remaining unaddressed issues should have been addressed very carefully by risk managers for such a persistent substance to which concentration levels might be of high risk for humans and the environment. Moreover, chronic toxicity of persistent substances is insufficiently addressed in the context of pesticide risk assessment as such chronic studies are

[3] Zhu et al (2024). Investigation of the impact of widely used pesticides on conjugative transfer of multidrug resistance plasmids. J Hazard Mater. 2024 Oct 5;478:135436

not designed to particularly consider persistence and exposure to increasing background levels of the tested substance.

Finally, pydiflumetofen is a succinate dehydrogenase inhibitor (SDHI) fungicide. The potential adversity relative to an SDHI fungicide mode of action in humans was found inconclusive by EFSA, raising valid concerns. The latter is supported by the results of peer-reviewed studies published in independent scientific journals. Namely, pydiflumetofen was found to interact with drug transporters, notably by strongly reducing the activity of the renal organic anion transporter (OAT) 3, in a concentration-dependent manner[4]. It was also found to enhance CYP3A4 mRNA expression in human hepatic HepaRG cells and primary human hepatocytes[5]. Lastly, a study has pointed out the acute and developmental toxicity of pydiflumetofen toward embryos, larvae, and adult zebrafish[6].

Another concern with persistent substances is that it takes a lot of time to reverse contamination when these are found to be way more toxic than originally concluded in chemical assessment. For this reason and given the already high background exposure levels of chemicals for humans and the environment, a more precautionary approach from regulators is crucial to protect our health and that of the next generations. It would also be consistent with the current work on the proposal for a universal restriction of PFAS based on the persistence properties of this class of chemicals.

We call on you to invite the Commission to **propose the non-approval of pydiflumetofen** to prevent poorly reversible future impacts on human health and the environment.

b) Flutolanil

According to the OECD definition of PFAS and as confirmed by EFSA's peer review from June 2023, flutolanil belongs to this group of particularly problematic “forever pollutants”. Under its European Green Deal, the EU committed to phase out PFAS due to the unacceptable risk they pose to humans and the environment.

Such a concern applies to PFAS active substances including flutolanil. According to EFSA, flutolanil is a persistent (P) to very persistent (vP) substance and forms the very persistent and

[4] Kerhoas et al. 2024. Inhibition of human drug transporter activities by succinate dehydrogenase inhibitors, Chemosphere, Volume 358:142122 https://doi.org/10.1016/j.chemosphere.2024.142122

[5] Kerhoas et al. 2024. Induction of human hepatic cytochrome P-450 3A4 expression by antifungal succinate dehydrogenase inhibitors, Ecotoxicology and Environmental Safety, Volume 276:116261, https://doi.org/10.1016/j.ecoenv.2024.116261

[6] Wang et al. 2022. Comprehensive study of pydiflumetofen in *Danio rerio*: Enantioselective insight into the toxic mechanism and fate, Environment International, Volume 167: 107406 https://doi.org/10.1016/j.envint.2022.107406

very mobile metabolite trifluoroacetic acid (TFA). TFA is also proposed for classification as toxic for reproduction 1B and acute toxic 3, which makes it a relevant metabolite for groundwater and consumer risk assessment. This is worrying since numerous publications highlight high and widespread contamination of EU water bodies with this metabolite, at levels which largely exceed the 0.1µg/L threshold for groundwater and drinking water which apply to relevant metabolites. No data on the potential for groundwater contamination with TFA were submitted for flutolanil and renewing the substance would further increase the already high exposure to TFA. Moreover, the consumer risk assessment could not be finalised because of lacking data on the presence and toxicity of relevant metabolites, including TFA, for the residue definition in plants and animals. The concerns for consumers apply equally to the consumption of drinking water due to missing information on the effect of water treatment processes on the nature of the residues of flutolanil and metabolite M-11. The latter might be present in surface water when it is abstracted for the production of drinking water.

In addition, the potential for immunotoxicity of flutolanil could not be excluded based on existing data and should be further investigated according to EFSA.

We call on you to invite the Commission to **propose the non-renewal of flutolanil** to protect European citizens from direct and deliberate exposure to this PFAS substance.

c) 8-hydroxyquinoline

PAN Europe urges you to oppose the renewal of 8-hydroxyquinoline, a “cut-off” substance classified as presumed to "damage the unborn child" (i.e. toxic for reproduction 1B) since 2015. The Pesticide Regulation clearly establishes that reprotoxic substances cannot be approved in the EU unless negligible exposure to humans can be demonstrated under realistic conditions of use (Article 4(1), point 3.6.4 of Annex II). This provision and its exemption of negligible exposure must be interpreted very restrictively. This means that negligible exposure to all exposure groups should be clearly demonstrated prior to renewing a substance. This should be based on an objective, robust and comprehensive dataset. Worryingly, EFSA’s peer review on 8-hydroxyquinoline from March 2024 shows that these conditions for scientific rigour were not achieved due to the lack of reliable and realistic data.

- Workers and operators: the field study submitted by the applicant to assess non-dietary exposure for operators and workers had several limitations and could only be considered as supportive evidence for negligible exposure (technical deficiencies in the analysis recovery of the samples). It was considered non-reliable for quantitative risk assessment according to EFSA. Yet, this unreliable study was the main basis to conclude that workers’ and bystanders’ exposure does not exceed the negligible exposure. Even when applying an additional factor of 10, this situation does not ensure sufficient confidence in the assumption that workers and operators will be protected from this reprotoxic substance.

- Bystanders and resident children: the assessment of non-dietary exposure of bystanders and resident children could not be finalised due to a data gap for the representative use. Based on the best existing data (spray application), EFSA pointed out that the exposure of these vulnerable groups to vapour of 8-hydroxyquinoline is predicted to exceed the threshold for negligible exposure (120% of Acceptable Observed Effect Level. While this estimation may overestimate the level of exposure in the case of drip irrigation, it cannot be proven that residents' and bystanders' exposure will be negligible in that condition of use. Particularly, the risks of exposure *via* volatilisation cannot be ruled out based on the workers' and bystanders' study (mentioned above) as suggested in the Commission's renewal report. This is particularly worrying in that it concerns categories of the population that are particularly vulnerable.

In its renewal report, the Commission is proposing to request as confirmatory data a new non-dietary exposure study for workers and operators, this time under realistic conditions of use, which confirms the lack of robustness of the assessment carried out based on the current data. This proposal for confirmatory information about negligible exposure is unacceptable and fails to comply with point 3.6.4 of Annex II. Moreover, taking into consideration the precautionary principle, in line with Article 1(4) and Article 13(2), risk managers are entitled to issue a non-approval for this hazardous substance.

We call on you to request the Commission to propose a regulation on the **non-renewal of 8-hydroxyquinoline and require an immediate withdrawal from the EU market of products** containing this substance, in accordance with Article 20(2,3) of Regulation (EC) 1107/2009.

5. EFSA conclusions: flufenacet, mecoprop-P

a) Flufenacet

As highlighted in our to EFSA letter in July[7], we urge the imminent publication of the conclusions of EFSA's peer review of flufenacet, putting an end to a significant delay in its reassessment. After a prolongation of 11 years and 6 months of the approval of flufenacet, the conclusions on the assessment of its endocrine-disrupting properties require a swift ban of the substance.

According to EFSA's ED working group, flufenacet does not meet the approval criteria set out in points 3.6.5, 3.8.2 of Annex II of the Pesticide Regulation. In August/September 2022, based on the reporting table and the revised renewal assessment report submitted to EFSA, experts of the ED working group concluded that flufenacet meets the ED criteria via the T-modality. More specifically, adverse effects on haematological parameters (reticulocyte count and percentage,

[7] PAN Europe letter to EFSA's Director "Request to swiftly complete the peer review of flufenacet based on its endocrine-disrupting properties" July 2024.

met-haemoglobin and hematocrit) and organ weight (liver) were induced by flufenacet and a test-item-related perturbation of the hypothalamic-pituitary-thyroid (HPT) axis could not be excluded. In line with the hazard-based approach of the Pesticide Regulation. Further comparative thyroid assays (CTAs) were analysed to determine Triiodothyronine (T3) and Thyroxine (T4) concentration levels in rat serum samples collected during the in vivo phase. According to France (co-RMS) and the ED expert group, these CTAs confirmed T3 and T4 disruption, i.e. the former conclusion that flufenacet meets the ED criteria for humans via the thyroid as mode of action. Moreover, flufenacet was found to be an ED for non-target organisms. As a result, t it does not meet the requirements of Article 4(1) and points 3.6.5, 3.8.2 of Annex II of Regulation 1107/2009.

Another concern with flufenacet, which supports the critical need for its quick ban, is that it meets the OECD definition of PFAS. Moreover, its use leads to the formation in plants and soils of the very mobile and very persistent metabolite trifluoroacetic acid (TFA), resulting in groundwater contamination at significant levels. According to the flufenacet renewal report (2017), TFA was demonstrated to leach in groundwater above 0.75 µg/L in all of the FOCUS GW scenarios. This largely exceeds the legal threshold 0.1 µg/L which applies to relevant metabolites; a category to which TFA qualifies considering the proposal to classify this substance as toxic for reproduction category 1B and acute toxic 3. In a series of these scenarios, it was also found above 10 µg/L, which means it exceeds even the threshold for non-relevant metabolites.

Considering the above, we call on you to invite the Commission to **propose the non-renewal of flufenacet** without delay.

b) Mecoprop-P

In October 2023, EFSA published its updated peer review on mecoprop-p. EFSA concluded that the predicted exposure to residents is above the AOEL for children entering treated areas (75th percentile), even by applying a buffer strip of 10 m and a drift reduction during application. This critical area of concern indicates that the conditions set out in Article 4 of Regulation (EC) 1107/2009 are not met, particularly regarding the provisions of the Regulation aiming to ensure that products placed on the market and their residues *"shall not have any harmful effects on human health, including that of vulnerable groups"* (Recital 24; Article 4(2) & (3)). Moreover, mecoprop-p is classified as very toxic to aquatic life with acute and long-lasting effects (Aquatic Acute 1 and Aquatic Chronic 1) as well as harmful if swallowed and causing serious eye damage under Regulation (EC) 1272/2007. Therefore, it cannot be concluded that the use of the substance does not cause any harm to human health or does not have any unacceptable effects on the environment. In addition, the approval of mecoprop-p has been repeatedly extended for a total of 9 years and a half. It is high time that citizens, including agricultural workers, residents of agricultural areas, and the environment stop being exposed to this hazardous substance.

We call on you to invite the Commission to **propose the non-renewal of mecoprop-p** to ensure a high level of protection for children.

6. Working group on comparative assessment

We welcome the progress made by the working group before the summer. We acknowledge that the new draft Annex IV amendment proposal presents significant improvements over previous versions. In particular:

- Transparency and participation: the publication of a notice by Member States about the applications received and the requirement to ensure that interested parties are given the possibility to provide information on available alternatives.
- Minor use: carrying out the assessment of the effect of substitution on minor uses at the end of the comparative assessment and the fact that a decision to reject substitution on that ground should be evidence-based.
- Resistance risk assessment, the requirement to:
    - assess the risk of resistance developing in the targeted pest/crop combination in applications for authorisation;
    - base the number of available modes of action on the resistance risk for each target pest.

→ PAN Europe's recommendation: the conclusion on the risk of assessment should be based on experimental data in the Member States for the crops concerned. We propose to set three categories of resistance (low, medium and high). In case of high resistance, a maximum of three modes of action should remain available.

    - Moreover, we see as a positive development that each alternative method to chemical pesticides is considered alone or combined, as one different mode of action contributing to the minimisation of the occurrence of resistance.
- Significant practical or economic disadvantages: the short-term "lower efficacy" of non-chemical control or prevention methods, compared to chemical methods, should not be regarded as an inability to maintain adequate control in crop production, considering the long-term benefits of reducing chemical input.

PAN Europe will provide its more detailed position to the working group on comparative assessment and we support the continuation of the work. Namely, the amendment of Annex IV requires the revision of the guidance document on comparative assessment, including its part which relies on the EPPO standard, to ensure that the new provisions of Annex IV are implemented.

This call to speed up the work on substitution was a key recommendation by the EU Ombudsman in its decision on comparative assessment and substitution from 22 August 2024 (case 177/2023/VB). The EU Ombudsman decision underscores the Commission's longstanding

neglect in addressing these ineffective substitution rules and urges the European Commission to prioritise the substitution of most toxic pesticides. Moreover, should the Guidance document continue to rely on the EPPO standard on comparative assessment, the Commission - in coordination with Member States, should set its position within the EPPO to actively promote that:

- EPPO adopts more stringent rules on conflicts of interest, including requiring experts to submit declarations of interest and making such declarations publicly available online; and;
- EPPO allows the participation of stakeholders other than the pesticide industry in its work and ensures that these stakeholders are adequately informed of such a possibility.

Indeed, the Ombudsman's decision highlights EPPO's conflict of interest policies as grossly inadequate (compared to EFSA's standards).

Risk managers should adhere to the "independent, transparent, and objective assessment" mandated by EU law and implement measures to ensure a robust, independent policy in all working groups and collaborations with experts. This is crucial for the development of guidance documents and guidelines, safeguarding against conflicts of interest and commercial bias.

We call on you to work closely with the Commission to ensure that the Ombudsman's recommendations are implemented in relation to the comparative assessment, and beyond.

From beforehand, thank you for your consideration.

Sincerely yours,

On behalf of PAN Europe

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