Pesticide Action Network Europe

Brussels, 8 June 2023

Ms. Kyriakides
European Commissioner for Health and Consumer Policy
European Commission
B-1049 Brussels - Belgium

Concerns: neurotoxicity of pesticides

Dear Commissioner Kyriakides,

With this letter, we would like to express our concerns regarding the regulation of neurotoxic pesticides in the EU and request upon you to take action. Pesticides-related neurological diseases are rising in the EU (Parkinson's, autism, etc.), and specialists have raised alarms of an upcoming "Parkinson's epidemic"[1]. At the same time, scientific knowledge is evolving rapidly and therefore regulatory actions on the side of the Commission are urgent.

I. Neonicotinoids: new scientific evidence

Following our letter from 15 April 2022 on this matter, we appreciate that you sent a mandate to EFSA on acetamiprid in August last year. In the meantime, more information has been published on the health impact of neonicotinoids. We urge you to take action to phase out all neonicotinoid insecticides, including all agonists of nicotinic acetylcholine receptors, even if they haven't been allocated under this category. Such a case is the insecticide flupyradifurone that has the same mode of action as other neonicotinoids, nevertheless the pesticide industry arbitrarily created a new category for this substance[2].

[1] https://pubmed.ncbi.nlm.nih.gov/29131880/
https://www.thelancet.com/journals/laneur/article/PIIS1474-4422(20)30302-1/fulltext
[2]https://www.pan-europe.info/sites/pan-europe.info/files/public/resources/factsheets/201609%20Factsheet%20What%20is%20a%20neonicotinoid_Flupyradifurone_Sulfoxaflor_EN_PAN%20Europe.pdf

1. Acetamiprid

Since our letter from last year, a series of new scientific information have been published, pointing at the potential of neonicotinoids to cause carcinogenicity, endocrine disruption and reprotoxicity. One study also confirmed the presence of acetamiprid metabolites and other neonicotinoids in children's cerebrospinal fluid. These studies are:

- Li *et al*. 2022. Neonicotinoid insecticides promote breast cancer progression via G protein-coupled estrogen receptor: In vivo, in vitro and in silico studies. Environ Int. 10.1016/j.envint.2022.107568
- Mishani *et al*. 2022 The Effect of Increasing the Dose of Acetamiprid and Dichlorvos Pesticides on the Reproductive Performance of Laboratory Mice, Adv Biomed Res. 10.4103/abr.abr_199_22
- Yang and Liang 2023. Associations between neonicotinoids metabolites and hematologic parameters among US adults in NHANES 2015-2016. Environ Sci Pollut Res Int. 10.1007/s11356-022-23997-4
- Jing Li *et al*. 2022. Detection of Neonicotinoid Insecticides and Their Metabolites in Human Cerebrospinal Fluid. Environmental Health Perspectives, 10.1289/EHP11374
- Ma *et al*. 2022 Long-Term Exposure to Neonicotinoid Insecticide Acetamiprid at Environmentally Relevant Concentrations Impairs Endocrine Functions in Zebrafish: Bioaccumulation, Feminization, and Transgenerational Effects. Environ. Sci. Technol. 10.1021/acs.est.2c04014
- Mendy and Pinney 2022. Exposure to neonicotinoids and serum testosterone in men, women, and children, *Environ Toxicol* 10.1002/tox.23503 - Didenko *et al*. 2022. Dose dependence of subchronic influencing of acetamiprid on the organism of rats from data of morphological researches. *Wiad Lek* 10.36740/WLek202212116

2. Already banned neonicotinoids (imidacloprid, clothianidin, thiamethoxam and sulfoxaflor)

Apart from of the above-mentioned studies that also relate to other neonicotinoids, it seems that the human toxicity of neonicotinoids is a pattern that concerns several substances in this family:

- Santiago *et al*. 2023. Single and mixed exposure to distinct groups of pesticides suggests endocrine disrupting properties of imidacloprid in zebrafish embryos J Environ Sci Health B 10.1080/03601234.2023.2184158
. - Yang *et al*. 2022. Combined Reproductive Effects of Imidacloprid, Acetochlor and Tebuconazole on Zebrafish (*Danio rerio*). Agriculture 12(12), 1979; 10.3390/agriculture12121979
- Yue *et al*. 2022. Urinary neonicotinoid concentrations and pubertal development in Chinese adolescents: A cross-sectional study. Environ Int 10.1016/j.envint.2022.107186 - Suwannarin *et al*. 2021. Exposure to Organophosphate and Neonicotinoid Insecticides and Its Association with

Steroid Hormones among Male Reproductive-Age Farmworkers in Northern Thailand. Int J Environ Res Public Health 10.3390/ijerph18115599

Considering the consistent evidence of endocrine disruption on the one hand, and the fact that two different scientific studies confirm the presence of neonicotinoids in cerebrospinal fluids, we urge you to take action to protect our most vulnerable from exposure to these pesticides. In particular, we would like to highlight that the blood brain barrier is permeable at early stages of life and brain development[3]. Considering that neonicotinoid insecticides interact with mammalian neurons, we ask you to take action in order to protect the brain development of babies and children.

It has taken more than a decade for the EU to ban chlorpyrifos after the first evidence on its potential to cause developmental neurotoxicity. Considering the major impact it had on children's nervous system development, including the brain, we urge you not to repeat the same errors with neonicotinoids. Indeed, a strict implementation of the precautionary principle should lead you to ban and delete the maximum residue levels (MRLs) for all neonicotinoids (and neonicotinoid-like) insecticides in European food.

Finally, this new information should result in the implementation of sensitive neurodevelopmental toxicity tests in the frame of the pesticide risk assessment. An OECD test guideline exists[4] and should be included in regulation 284/2013 as mandatory, at least for insecticides. Scientific evidence on the impact of neurotoxic insecticides on humans is steadily increasing: how does the Commission justify to not yet having added this OECD guideline to the data requirements?

II. Thiacloprid MRLs

Thiacloprid was classified as Toxic to reproduction category 1B in 2015 and was banned in 2020 at EU-level for both health and environmental reasons. We have noticed, on the Commission MRLs database[5], that its MRLs were not set to the limit of determination (LOD) default value (0.01 mg/kg) for a series of foodstuffs. For instance, for berries the MRL goes up to 6 mg/kg. For mate and rooibos, it is up to 50 mg/kg, (5000 times higher than the LOD)!

Considering the risk posed by this substance to the unborn, as a substance toxic to reproduction category 1B, and considering that as it was banned for health reasons, its MRL should be set at the LOD for all foodstuff to ensure the high level of protection of consumers

[3] Saunders *et al.* 2012 Barrier Mechanisms in the Developing Brain, *Front Pharmacol* 10.3389/fphar.2012.00046

[4]https://www.oecd-ilibrary.org/environment/test-no-426-developmental-neurotoxicity-study_9789264067394-en

[5]https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/start/screen/mrls/details?lg_code=EN&pest_res_id_list=211&product_id_list=

required by regulation (EC) 396/2005 and (EC) 1107/2009. Could you please indicate to us why this is not yet the case?

Furthermore, considering the reprotoxicity of this substance, the fact that MRLs as high as 50 mg/kg are accepted for mate or rooibos poses a risk of EU citizens consuming these products but more importantly it indicates that people from third countries will be heavily exposed to this pesticide, with dramatic consequences on pregnant women and fetuses. This is morally unacceptable and not in line with the green diplomacy promoted by the green deal.

We thus respectfully ask you to make sure that the MRLs for thiacloprid are set to the limit of determination for all foodstuffs as soon as possible, included for imported ones.

III. Industry misconduct on reporting scientific evidence on the neurotoxicity of pesticide active substances

Recently, a new scientific publication highlighted pesticide industry misconduct and infringement of the pesticide regulation (EU) 1107/2009[6]. The authors highlighted that out of 35 developmental neurotoxicity studies (DNT) on 35 different active substances shared by the pesticide industry with the US environmental protection agency (USEPA), for 9 active substances[7] (26%), the DNT study was not shared with EU regulators in the frame of the regulatory procedure for approval or renewal of approval of the substances. To our knowledge, this information was also not shared in the frame of article 56 of the pesticide regulation, obliging companies to provide any scientific evidence that indicates that their products might not respect the safety requirements of the pesticide regulation.

The authors of the study notified EFSA and the Swedish national authorities (KEMI), and in 3 cases these originally undisclosed studies had regulatory consequences after they were requested and evaluated by the regulatory agencies (abamectin, ethoprophos, pymetrozine). Four DNT studies still have a potential effect on toxicological reference values or upcoming hazard classification (fenamidone, fluazinam, glyphosate-trimesium, pyridaben) and for one DNT study, the information available to assess the regulatory impact was insufficient.

It is not the first time that a scientific study reports misconducts from the pesticide industry. In 2018, following an analysis of the raw data of the DNT regulatory tests on chlorpyrifos and chlorpyrifos methyl from 2008[8], scientists identified that the pesticide industry had provided misleading conclusions on its studies, underreporting the adverse effects. This review resulted in the non-renewal of the authorisation of both substances in 2019, nevertheless with a 10 years of delay.

[6] Mie and Ruden 2023. https://ehjournal.biomedcentral.com/articles/10.1186/s12940-023-00994-9
[7] Abamectin, buprofezin, ethoprop, fenamidone, fenamiphos, fluazinam, glyphosate, pymetrozine and pyridaben
[8] Mie et al, 2018. https://pubmed.ncbi.nlm.nih.gov/30442131/

In the same vein, in the frame of the publication of internal communications[9] of Monsanto ('*Monsanto papers*'), it became evident that Monsanto employees were aware that POEA surfactants lead to important toxicity to humans but had never disclosed it to regulatory authorities.

To our knowledge, in the EU, none of these 2 previous examples of misconduct have led to any kind of administrative or judicial procedure 1. to suspend the EU approvals of these substances until the situation is clarified and 2. to issue a penalty for infringement to the companies for non-compliance with the requirements of the EU law (article 72) and putting EU citizens in danger. For the pesticide industry, the signal is very clear: in case of failing to comply with the law, there are absolutely no legal or financial consequences on their business and staff.

This inaction on the side of European regulatory authorities is in sharp contrast with EU law. Indeed, article 44 from the pesticide regulation (EU) 1107/2009 obliges Member States to withdraw national authorisations of products if the applicant has not respected the requirements of the pesticide regulation. In the present case, the fact that the applicant did not respect article 56 must lead to the immediate suspension of the authorisation of these products in all the EU, and the issue of penalties for the companies that committed these infringements of the EU law.

We consider that European regulatory authorities have been too friendly towards the pesticide industry over the last years: incomplete approval dossiers leading to data gaps or confirmatory information[10], non-disclosure of important scientific findings on the toxicity of pesticide active substances, co-formulants or products, etc. No form of penalty has ever been imposed upon them. By adopting such a friendly behaviour despite the accumulation of proof that the pesticide industry is behaving in an unlawful way, will only contribute to promoting more of this practice.

We would like to respectfully remind you that the European law on pesticides is meant to protect citizens' health and the environment. The inaction of the European Commission and Member States goes against this principle and against the rule of law.

[9] https://corporateeurope.org/sites/default/files/attachments/37-monsanto-executive-admits-studies-demonstrate-formulated-roundup-does-the-damage.pdf

[10] According to article 9, Rapporteur Member States (RMSs) are to carry out a completeness check when receiving a new approval or renewal of approval dossier. If regulatory studies are missing or incomplete, the application cannot be assessed but some RMSs go on with the assessment, leading to major data gaps during the EFSA peer review.

We therefore ask you to suspend the approval of the 5 remaining authorised substances, to make sure that all national authorisations will be withdrawn, in respect with article 44 from the pesticide regulation.

We also ask you to initiate a discussion with the Member States on the lack of implementation of articles 44 and 72.

Thank you in advance for your action.

Best regards,

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