EXECUTIVE DIRECTOR

Ref. BU/GdS/MT/AT/ss (2021) OC-2021-24570142

Ir. J.F. de Leeuw
Chairman of the Board
for the Authorisation of
Plant Protection Products
and Biocides – ctgb
Bennekomseweg 41,
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Subject/Re.: possible relation between the use of specific pesticides and the development of Parkinson's disease

Ref. IC-2021-24570142 – your email dated 09/03/2021

Dear Dr de Leeuw,

Thank you for approaching EFSA on this important topic.

The area of environmental neuroscience and the impact of chemical exposure on brain health are a growing field, which includes the assessment of plant protection products as a potential risk factor.

EFSA is engaged in this area, recognising the complexity of the different environmental contributors to the several neurodegeneration processes.

EFSA and its PPR Panel published two Scientific Opinions in 2015 as a follow up of a meta-analysis contracted by EFSA to the University of Ioannina, where a positive relationship was highlighted between exposure to pesticides and Parkinson's disease. In agreement with your position, the Panel concluded that a causality link cannot be established with the available information, and that a different approach for hazard identification and characterization should be undertaken.

One of the activities undertaken by the PPR Panel culminated in the development of adverse outcome pathways (AOP) for Parkinsonian disorders. The measurable key events (KEs) included in the AOP can be used to test and identify chemicals that might contribute to the disease via the identified pathway. An AOP approach is considered important in the study of mechanisms of toxicity to enable linking those mechanisms through epidemiological studies to neurological disorders. Therefore, data on biological processes occurring in the context of adverse outcomes is essential to show their relevance in the disease aetiology. This mechanistic understanding enables the development of tools for a predictive toxicology approach, which can support regulatory decisions.

This approach was applied and implemented in a work package of the EU-ToxRisk[1] project, and for the ongoing assessment of the active substance Tebufenpyrad; while the two activities have different regulatory problem formulations, they are both based on New Approach Methodologies (NAMs). Similar methodologies are used by EFSA for the developmental neurotoxicity (DNT) assessment of chemicals. In this case, an Integrated Approach for Testing and Assessment (IATA), informed by AOP, was used to answer different regulatory problem formulations (e.g. screening of many chemicals or

[1] https://www.eu-toxrisk.eu/

single substance hazard characterization), and NAMs were developed to measure selected KEs in DNT adverse outcome pathways. This project is in an advanced state, and can serve as a valid experience also for other environmental neuroscience endpoints. A key lesson learned from these parallel projects is that they require the interaction of specialists from different fields to be successful. This is therefore an opportunity for a multidisciplinary collaboration between regulators, academics, laboratory experts and stakeholders. The preliminary results of the DNT project are promising, and indicate that the approach could be used to support regulators in identifying substances of potential concern, and to change the current testing paradigm for the assessment of the potential link between neurodegenerative adverse outcomes and chronic low-level exposure of environmental contaminants, including pesticides.

We therefore believe that the acquired expertise can also be useful to tackle the problem of the Parkinsonian syndromes which, however, requires an even greater multidisciplinary approach, given that genetic predispositions and epidemiological data are essential for a better definition of the problem. In addition, a more elaborated plan is necessary to move to the screening of large chemical classes, to define a tiered approach for the identification of neurodegenerative hazards, and for the assessment of mixtures.

For this purpose, we believe it is necessary to take stock of the situation from a scientific and multidisciplinary point of view. Our aim is to identify the gaps in research, collect feedback on the availability of suitable test methods and test systems to be used in the screening programme, and estimate the policy implications for environmental neuroscience. We are therefore considering the organisation of a scientific event that would have the aim of exploring the current knowledge landscape and future opportunities in neurotoxicology, and would create the basis for a series of scientific projects with the collaboration of the Member States. The debate should also focus on the need to prioritize chemicals to be tested, and to develop higher throughput methods using molecular or cellular approaches. Testing pesticides through these tools would represent a first step towards understanding the complexity of the mechanisms that regulate neurological functions, and, subsequently, towards developing regulatory action.

We aim at defining a plan to be shared with you in the upcoming weeks, and remain available for further discussions. EFSA looks forward to working with CTGB and MSs on this topic.

Yours sincerely,

efsa
European Food Safety Authority

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