



Brussels, 21.11.2018

Contact : Martin Dermine,
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To: Mr. Vytenis Andriukaitis
European Commissioner for Health and Consumer Policy
European Commission
B-1049 Brussels.

Concerning: Unreported neurodevelopmental adverse effects of chlorpyrifos and chlorpyrifos-methyl on rodents in toxicity studies

Dear Commissioner,

A recent publication¹ highlights the fact that the authors of two neurodevelopmental toxicity studies on chlorpyrifos and one on chlorpyrifos-methyl, commissioned by for regulatory purposes to evaluate the safety of these substances, have failed to correctly report all the adverse effects observed in pre- and post-natally exposed rat pups. The industry-sponsored studies² in question are in line with the international OECD test guideline protocol and they were funded by (at the time) Dow Chemicals in the frame of the registration process for these 2 substances for approval. Today, Dow Chemicals has been rebranded "Corteva"³, the agricultural division of DowDupont.

In their critical studies, among others, the authors indicate a series of misconducts:

1. They reported that no neurodevelopmental adverse effects were observed while the raw data from these studies indicates that effects on brain morphology were observed at all doses.

¹ Safety of Safety Evaluation of Pesticides: developmental neurotoxicity of chlorpyrifos and chlorpyrifos-methyl. Mie A, Rudén C, Grandjean P. Environ Health. 2018 Nov 16;17(1):77. doi: 10.1186/s12940-018-0421-y.

² Anon. Developmental neurotoxicity study of chlorpyrifos administered orally via gavage to Crl:CD@BR VAF/Plus® presumed pregnant rats. 1998.

Maurissen JPJ, Hoberman AM, Garman RH, Hanley TR. Lack of selective developmental neurotoxicity in rat pups from dams treated by gavage with Chlorpyrifos. Toxicol Sci. 2000;57(2):250-63.

Anon. A Dietary Developmental Neurotoxicity Study of Chlorpyrifos-Methyl in Rats; 2015.

Mattsson JL, Maurissen JP, Nolan RJ, Brzak KA. Lack of differential sensitivity to cholinesterase inhibition in fetuses and neonates compared to dams treated perinatally with chlorpyrifos. Toxicol Sci. 2000;53(2):438-46.

³ <https://www.corteva.com/>

2. The DNT studies were not done according to the guidelines. The authors failed to detect effects on their positive control and selected a very low statistical cut-off value, to dismiss the findings as non-significant, without justification
3. The DNT study on chlorpyrifos-methyl was missing two exposures, the low and medium one, without providing justification. Furthermore, 50% of the data points concerning cerebellum height are missing.

This is not the first time that independent scientists highlight such misconduct concerning widely used pesticides. Indeed, in 2017, Christopher Portier found that the Glyphosate-Task-Force did not correctly report cases of tumours in a carcinogenicity study and neither the Rapporteur Member State nor the European Institutions European food Safety Authority (EFSA) and European Chemical Agency (ECHA) identified this misconduct. In 2017, you received a copy⁴ of the letter Dr. Portier sent to President Jean-Claude Juncker. At the time, despite the fraudulent reporting of the study results carried out by the pesticide industry, the European Commission did not initiate any legal action against the authors. To our knowledge, the European Commission did not even complain to the glyphosate-task-force for this misconduct.

Chlorpyrifos and Chlorpyrifos-methyl are currently in the process of re-assessment at the EFSA-level. We thus request you to ask EFSA to dismiss the 3 studies in question in their review. Furthermore, we respectfully ask you to send a mandate to the EFSA and ask them to systematically review the reporting of the raw data of the regulatory studies as the applicants repeatedly show dishonesty. Finally, we ask you to suspend the use of chlorpyrifos and chlorpyrifos-methyl in the EU at once. Indeed, the previous risk assessment has been based on misleading results and a series of scientific evidence⁵ shows that chlorpyrifos induces important neurodevelopmental effects, such as autism or a lowered IQ in children. A tribunal has forced the United States of America to ban this substance, we ask you to swiftly evaluate the arguments that led to such a ban.

The health costs of the use of pesticides are difficult to properly assess but studies show they are considerable (146 billion euros in the EU, just for chlorpyrifos!)⁶. Manipulation of data by the applicant, as we've seen in the cases of glyphosate and chlorpyrifos, is unacceptable. By not reacting strongly to such misconducts, we consider that, as the guardian of EU citizens' health, you are missing to comply with an important duty of yours. Therefore, we ask you to initiate a legal action towards Corteva as they are responsible for providing misleading information considering major health damages the use of their products entails.

In 2017, we sent you a letter complaining that important endpoints were not properly assessed under the current risk assessment procedure. The letter we received in January 2018 was answered by the pesticide head of unit from DG Sante, on your behalf (in Annex to this letter). In this letter, it is indicated that neurodevelopmental toxicity is addressed by the

⁴ <https://www.nrdc.org/sites/default/files/open-letter-from-dr-christopher-portier.pdf>

⁵ Grandjean P, Landrigan PJ. Neurobehavioural effects of developmental toxicity. *Lancet Neurol.* 2014;13(3):330-8.

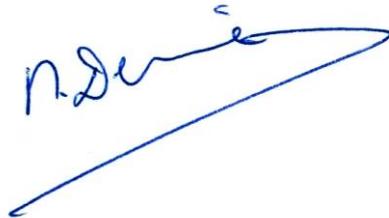
⁶ Bellanger M, Demeneix B, Grandjean P, Zoeller RT, Trasande L. Neurobehavioral deficits, diseases and associated costs of exposure to endocrine disrupting Chemicals in the European Union. *J Clin Endocrinol Metab.* 2015;100(4):1256-66.

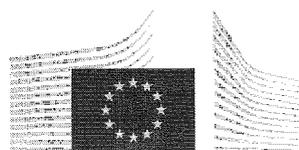
pesticide regulation and that Member States and EFSA can request additional information during the assessment procedure. We have here another good example that the system does not work: the studies in question were biased and of poor quality and this has not been identified by the risk assessors. Impeding biases in the risk assessment of pesticides is an important request NGOs are having for a long time. The fact that the industry is running its own regulatory testing creates an enormous bias by default. It carries out the evaluation, based on its own data and sends it to the Rapporteur Member States together with its own biased assessment. Member States that are, for most of them, understaffed, do not have the capacity to properly verify in dozens or hundreds of studies that no fraud took place. This also led to the “glyphosate copy-paste” scandal at German BfR-level. Therefore, we ask you to change this unacceptable situation by changing the procedure: raw data must systematically be assessed by Member States and EFSA and low quality data must systematically be rejected. Incomplete dossiers must be rejected. This situation is not tenable and must be changed, for the sake of citizens’ health and that of the environment.

This new example of pesticide industry’s misconduct is one more reason for the more than 120 EU NGOs, institutions and organizations that have joined the [Citizens for Science in Pesticide Regulation](#) to ask the European Commission and Member States for a major upgrade of the way pesticides are assessed.

From beforehand, thank you for your action.

Best regards,
Martin Dermine
PAN Europe





EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

Food and feed safety, innovation
Pesticides and biocides

Brussels,
SANTE/E4/WR/df (2017) 7159269

Dear Mr Muilerman,

Subject: Your letter dated 30 August 2017 to Commissioner Andriukaitis

thank you for your letter addressed to Commissioner Andriukaitis, who asked me to reply on his behalf. I would like to apologise for the long delay in replying, which has been caused by resource constraints due to several very work-intensive dossiers with strict legal deadlines that had to be treated with priority throughout the last quarter of 2017.

I would also like to note that during our meeting on 12 November 2017 we discussed among other topics also the issue raised in your mail.

Let me first confirm again that the Commission clearly pursues the objective to assure the highest level of protection to health and the environment whilst at the same time reducing the amount of testing animals to the absolute minimum necessary. However, this does in no way mean 'an absolute ban on further animal testing' as you state in your letter.

I disagree with your allegation, that EU citizens would be exposed to plant protection products which are not properly tested. It is generally recognised that the EU system is the most protective authorisation system worldwide, providing the highest safety standards. Decision-making under that system is based on very conservative, worst-case assumptions. I would like to note in particular that the data requirements for pesticides set out in the relevant Commission Regulations include immunotoxicity, endocrine disruption and developmental neurotoxicity and relevant test methods are listed in the accompanying Commission Notices. Even if not systematically required in all cases, there are triggers for when the relevant tests have to be provided – furthermore, both the evaluating Rapporteur Member State and EFSA can request additional tests to be conducted during the assessment procedure.

The European Commission, together with the scientists from the European Food Safety Authority and from Member States are continuously developing these high safety

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standards further: e.g. scientific criteria for the determination of substances with endocrine disrupting properties are adopted for biocides, substantial progress has been made towards their adoption for plant protection products and a revision of the data requirements, which were last revised in 2013, will be prepared in the near future.

All these processes take place in full transparency and are open for input from all stakeholders willing to contribute. For example, the draft revised data requirements will be made available for stakeholders to comment on via the feedback mechanism created in the context of the Commission's Better Regulation agenda.

As to your question regarding AOPs, I take note of the views expressed in your letter of 10 May 2017. However, please note that any such concept – as every other alternative method - can only be applied for regulatory purposes, once it has gone through the required validation processes at EU and OECD level, which among others involve the Commission's Joint Research Centre (in particular the European Union Reference Laboratory for Alternatives to Animal Testing - EURL ECVAM), and are then listed in the Commission Notices referred to above.

Yours sincerely,

A handwritten signature in black ink, appearing to read 'Klaus Berend', written in a cursive style.

Klaus Berend
Head of Unit