Reviewer’s report

Title: Safety of Safety Evaluation of Pesticides: Developmental neurotoxicity of chlorpyrifos and chlorpyrifos-methyl

Version: 0 Date: 26 Aug 2018

Reviewer: Susanne Bennekou

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Major Critiscisms:

The data analysis, is not fully contextualized. The study evaluated, was only assessed as a supplementary study during the EU pesticide review. More robust data was relied on for the EU assessment that is currently ongoing. This is important information in the context and also for the further conclusion drawn by the authors. Therefore, not being fully guideline compliant is of a lesser problem since appropriate guideline compliant data will be required. Also, in regard to contextualizing the data analysis, it is important to notice that the study was performed before the current more specified guidelines and therefore, the notions in regard to the assessment of the study director as not being compliant to current standards is not valid. That a re-analysis has not been requested might be seen in the context of the study only being assessed as "supplementary".

Referring to one of the publications that is referenced (Garman et al.), specific recommendations should be considered when assessing DNT data. As such, if the recommendations of the study referred to was to be followed, the lack of a dose response, the absence of treatment-related microscopic alterations, and also the lack of finding of different time points would often be assessed as "ambiguos". The authors did not discuss the data in these respects.

Overall, the data-analysis conducted on Chlorpyriphos and methyl-chlorpyriphos is not thorough and contextualized enough to support the overall claim, that "Evaluations of pesticides are not safe".

The background information should be more precise and comprehensive. For example, it is important information that the required regulatory studies must comply to relevant guidelines as set in the data requirements of the regulation (EU 283/2013). Furthermore, the whole discussion of the data -analysis would have benefitted from more detail on the actual status and timings of the different assessments of Chlorpyriphos. Thus, in discussing the current ADI's, it would be helpful to notice when the US ADI was set and on which basis, and also that the EU ADI is currently undergoing re-evaluation and as such could be revised soon. Also, as the authors have access to the draft EU re-assessment report, the authors could have indeed mentioned that due to lack of robust DNT data, the recommendation of the assessment so far, is to require a new DNT study.
To further substantiate the point, the authors should have discussed more comprehensively the specific reasons for the different conclusions reached by academia and industry-sponsored studies.

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