Vitenskapskomiteen for mat og miljø
Norwegian Scientific Committee for Food and Environment

COMMENTS OF THE NORWEGIAN SCIENTIFIC COMMITTEE FOR FOOD AND ENVIRONMENT (VKM) ON THE CUMULATIVE DIETARY RISK CHARACTERISATION OF PESTICIDES THAT HAVE ACUTE EFFECTS ON THE NERVOUS SYSTEM

General feedback

We appreciate the initiative to estimate the cumulative risk characterization of pesticides and the risk of acute effects on the nervous system. We understand that this has been both a demanding and complicated process.

We think the process is well described and well-formulated. However, we have some suggestions for consideration.

Abstract

Line nr. 22 – Consider clarifying that the conclusions made here are solely based on the populations studied. For example by adding a statement such as "for the populations studied".

Summary

Line nr. 56 – Suggest including what the clinically observable adverse outcome associated with brain and or erythrocyte AChE inhibition are.

Line nr. 65 – What is the evidence that these models predict the real-life exposure to pesticides? Including discussions on this issue would be appreciated.

Line nr. 66 –Is there a reason why sensitive risk groups such as the elderly (with potential CNS related diseases as Parkinson and dementia) and pregnant women were not considered?

1. Introduction

No comments

1.1. Background and Terms of Reference

Line nr. 218 - Suggest mentioning the three additional effects on the nervous system in order for the reader to get an overview/better picture of the endpoints covered.
The CRA is a mixture of adverse outcomes (alteration of motor function) and MoA (AChE inhibition). What is the adverse outcome associated with AChE inhibition?

1.2. Input from Risk Managers and threshold for regulatory consideration

No comments

2. Methodology, data and uncertainty analysis

2.1. Methodology

Line nr. 268 – Our main concern on this report is the choice of the NOAEL. In most cases, the NOAEL is based on chronic studies and not on acute studies. In this case, acute exposure is probably more relevant as is mentioned in the discussion. We suggest including a list per CAG and for each pesticide on what critical effect the NOAEL was based upon. We assume that most NOAELs were not based on CNS related adverse outcomes and we believe it would have been better to use NoAELS based on either motor activity or AChE inhibition. The slope of the dose-response curve is also important in judging the NOAELs and this should be mentioned. It would be helpful to indicate for how many active substances motor activity and AChE inhibition data were available.

In general, the exposure and uncertainty analyses are well described in the report but the hazard identification and hazard characterization could be expanded. It is worth noting that in the uncertainty part of the document a number of uncertainties related to hazard are identified.

2.2. Data

No comments

2.2.1. Cumulative assessment groups (CAGs)

No comments

2.2.2. Cumulative exposure assessments

No comments

2.3. Uncertainty analysis

No comments

2.3.1. Identification of sources of uncertainty affecting the assessment

No comments

2.3.2. Model and process for characterizing overall uncertainty

No comments

2.3.3. Choice of probabilistic model output for use in the uncertainty analysis

No comments

2.3.4. Evaluation of individual uncertainties (EKE Question 1)

Page 16, line nr. 555 onwards:

The expert knowledge elicitation identified 34 sources of uncertainty affecting the input data.

Expert knowledge elicitation (EKE)

Seven experts participated in these assessments and provided independent replies to the elicitation questions for each CAG. Later, they considered differences in their judgements and developed a consensus assessment of the probability of the MOET for the 99.9th percentile of exposure in 2014 - 2016 being below 100 in each of the 10 populations under consideration. The consensus process was conducted partly during a physical meeting, and completed remotely. Our main concerns are as follows:

- *How did the experts identify the uncertainties, and how was the consensus developed?*
- *Is the identification of uncertainties based on scientific data?*

We are of the view that expert identification of uncertainties should be based on scientific evidence or the lack thereof.

For example, the seven experts state that the differences between populations are essentially induced by differences in food consumption. Based on this statement the experts assumed that the effect of peeling and/or washing of commodities with edible peel and eaten raw may be more pronounced for toddlers and children than for adults. This is especially the case for Dutch toddlers where apples and table grapes contribute about 30 and 10 % of total exposure above the 99th percentile, respectively. This would tend to shift the overall distribution of the multiplicative factor of the MOET towards higher values. It was assumed that the estimated 99.9th percentile of the MOET at 99.9th percentile of exposure would increase by at least 10 % in toddlers and children populations.

- *Is the judgment that peeling of apples would tend to shift the overall distribution of the multiplicative factor of the MOET towards higher values based on scientific data or is it a hypothesis?*

The seven experts state that the difference in occurrence of pesticide residues in food commodities between populations and countries are expected to have a lower impact, due to the common market.

- *Is this an evidenced-based expectation or is it an assumption?*

The EU monitoring in 2014, 2015 and 2016 may help to draw relatively firm conclusions regarding differences in exposures between countries. However, our main concern regarding the uncertainty analyses is that the report lacks information about sources (scientific data) and methods used by expert knowledge elicitation to identify sources of uncertainty.

2.3.5. Evaluation of combined uncertainties relating to exposure and toxicology (EKE Question 2)

Line nr. 655 – Miss a discussion regarding the application of dose addition to the selected endpoints (AChE inhibition and motor activity) since MoA is important.

2.3.6. 1-D Monte Carlo simulation to combine distributions quantifying uncertainties related to exposure and toxicology

No comments

2.3.7. Overall uncertainty analysis (EKE Question 3)

No comments

3.Results of uncertainty analyses

No comments

3.1. Sources of uncertainty

Line nr. 800, Table 5, row 3 - What is meant by "uncertainty regarding the combination of occurrence and consumption data"?

3.2. Evaluation of individual uncertainties (EKE Question 1)

No comments

3.3. Combined impact of uncertainties (EKE Question 2)

No comments

3.3.1. Impact of uncertainties on the MOET estimates at the 99.9th percentile of exposure in the German adult population for CAG-NAN (brain and/or erythrocyte AChE inhibition)

Line nr. 871 – Overall, the uncertainty part of the report is very well-written, but these tables are not easy to understand for people not familiar with this approach. Some description of the results and the consensus distribution in figure 3 would be helpful. This applies also for the other tables and figures presented in subsequent sections.

Line nr. 892- Why is toxicity overestimated for the group with gavage administration?

Line nr. 960 – In figure 5, it will be helpful to describe what 'both' and 'model' stand for.

3.3.2. Impact of uncertainties on the MOET estimates at the 99.9th percentile of exposure in the German adult population for CAG-NAM (functional alterations of the motor division)

No comments

3.4. Accounting for dependencies, population differences and additional uncertainties (EKE Question 3)

No comments

3.4.1. Overall uncertainty affecting the cumulative risk assessment of brain and/or erythrocyte AChE inhibition (CAG-NAN)

No comments

3.4.2. Overall uncertainty affecting the cumulative risk assessment of functional alterations of the motor division of the nervous system (CAG-NAM)

No comments

4.Cumulative risk characterisation

4.1. Brain and/or erythrocyte AChE inhibition

No comments

4.2. Functional alterations of the motor division of the nervous system

No comments

5. Conclusions

Line nr. 1373 Consider adding: "for the populations studied". See comments under Abstract.

6. Recommendations

No comments

References

No comments

Glossary and Abbreviations

No comments

Appendix A – Assessment of individual sources of uncertainties affecting the CRA for active substances causing brain and/or erythrocyte AChE inhibition (CAG-NAN) and functional alterations of the motor division of the nervous system (CAG-NAM).

No comments

Appendix B – Information used in the uncertainty analysis

No comments