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 CHRONIC EFFECTS ON THE THYROID

# General feedback

We appreciate the initiative to estimate the cumulative risk characterization of pesticides and the risk of chronic effects on the thyroid gland. 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. 18 – 20 "… does not exceed the threshold…" is a general statement indicating that there is no risk for negative health effects in any age group. Can this be equally true for hypothyroidism and development of thyroid, CNS and cognitive functions of children exposed in utero and in the age group 0-1 years of age? Please see arguments below: 1.2, 2.2.2.1, 2.2.2.3 and 4.

Suggest including that you have not performed the risk analysis for unborn children and children younger than 1 year.

# Summary

Line nr. 105 – 109: Suggest including that this risk analysis is not performed for unborn children and the age group 0 – 1 year.

# Introduction

No comments

## 1.1. Background and Terms of Reference

No comments

## 1.2. Input from Risk Managers and threshold for regulatory consideration

Line nr. 228 – 230: Our main concern is that neither the age group 0-1 year nor the unborn child in utero were included in this assessment. The developing CNS is at its most vulnerable phase in this period of life, and a normally functioning thyroid is important for normal CNS development. Although the exposure may be equal for children 1 - 3 years and for children 3 months - 1 year, the thyroid and the CNS may be more vulnerable for the younger age group and the unborn child in utero, i.e. the response may be stronger at equal exposure.

# 2. Methodology, data and uncertainty analysis

## 2.1. Methodology

Line nr. 246 onwards – Another major concern on this report is the choice of the N0AEL. In this case, a secondary effect (development of CNS and cogniticve function) is of major importance in the discussion. We suggest including a list per CAG and for each pesticide on what critical effect the NOAEL was based upon. We believe it would be better to use NOAELs based on psychological learning ability tests. The slope of the dose-response curve is also important in judging the NOAELs and this should be mentioned.

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

2.2.2.1 Cumulative exposure assessment for CAG-TCF

Line nr. 320: Table 1: The MOET for CAG-TCF (hypothyroidism) is decreasing with decreasing age for the 99.9th percentile. What will it be for children younger than 1 year and unborn children? Is NOAEL for hypothyroidism and cognitive functions established for these groups?

2.2.2.3 Sensitivity analyses

Line nr. 353 – 358: When left-censored data for CAG-TCF were imputed to be ½ LOQ the MOET dropped by 3 – 4 times. What will the effect of this be for the MOET for age group 0 – 1 year and unborn children?

## 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 characterising overall uncertainty

Line nr. 444, 774: Section 2.2.2.4 seems to be missing in the document, although reference is made to it. This applies also to the sections mentioned below.

Line nr. 458, 511, 695,726, 802: Section 2.2.2.5 seems to be missing.

Line nr. 466, 737, 915, 1030, 1091: Section 2.2.2.6 seems to be missing.

### 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 15, line nr. 515 onwards:

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 expertsassumed 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.

Line nr. 520: should probably be … exposure in the German…

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

No comments

### 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

## 3.1. Sources of uncertainty

No comments

## 3.2. Evaluation of individual uncertainties (EKE Question 1)

Tables 3 and 4 contain a total of 31 types of uncertainties.

However, on line nr. 772, a total of 32 is stated.

## 3.3. Combined impact of uncertainties (EKE Question 2)

Line nr. 806: should probably be …estimate of the…

### 3.3.1. Impact of uncertainties on the MOET estimates at the 99.9th percentile of exposure in the German adult population for CAG-TCF (hypothyroidism)

No comments

### 3.3.2. Impact of uncertainties on the MOET estimates at the 99.9th percentile of exposure in the German adult population for CAG-TCP (C-cell hypertrophy, hyperplasia and neoplasia)

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 hypothyroidism (CAG-TCF)

No comments

### 3.4.2. Overall uncertainty affecting the cumulative risk assessment of C-cell hypertrophy, hyperplasia and neoplasia (CAG-TCP)

No comments

# 4.Cumulative risk characterisation

## 4.1. Hypothyroidism

Line nr. 1240: Tab 13. There is an increasing uncertainty for MOET estimates with lower age. This adds to the concern for the situation for the unborn and children 0 – 1 years of age.

## 4.2. C-cell hypertrophy, hyperplasia and neoplasia

No comments

# 5. Conclusions

Line nr. 1294 – 1302: Considering the uncertainties concerning children and toddlers, and the lack of focus on unborn and 0 - 1 year old babies, we think this uncertainty should be stated in the conclusion. The statement "... does not exceed the threshold for regulatory consideration…" cannot be used for the aforementioned age groups.

# 6. Recommendations

No comments

# References

No comments

# Glossary and Abbreviations

Line nr. 1481: should probably be …CAG-TCP…

# Appendix A – Assessment of the individual sources of uncertainties affecting the cumulative risk assessment for active substances causing hypothyroidism (CAG-TCF) and C-cell hypertrophy, hyperplasia and neoplasia (CAG-TCP)

No comments

# Appendix B – Information used in the uncertainty analysis

Line nr. 2235, 2248: Note numbers do not seem to match the number of uncertainties in Tables 3 and 4.