



EFSA-RIVM Symposium on the future of risk assessment and toxicity testing of chemical mixtures – 18-19 May 2016

Ongoing work on implementing cumulative risk assessment in European decision making

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Overview

- Cumulative risk assessment in current EU legislation
- Current status:
 - EFSA
 - RIVM
 - COM
- Outcome of WG on risk management aspects related to CRA
- Future plans

CRA in current legislation

Regulation (EC) No 1107/2009 on the placing on the market of plant protection products

Regulation (EC) No 396/2005 on maximum residue levels of pesticides in food and feed

CRA in current legislation

Reg. (EC) No. 1107/2009

Art. 4 (Approval criteria for active substances):

*The residues of plant protection products shall not have any harmful effects on human health, including that of vulnerable groups, ..., **taking into account known cumulative and synergistic effects where the scientific methods accepted by the Authority to assess such effects are available, ...***

CRA in current legislation: Reg. (EC) No. 396/2005

*Rationale for Art. 14 in **Recital (6)**:*

*"It is also important to carry out further work **to develop a methodology to take into account cumulative and synergistic effects**. In view of human exposure to combinations of active substances and their cumulative and possible aggregate and synergistic effects on human health, MRLs should be set after consultation of the European Food Safety Authority..."*

CRA in current legislation: Reg. (EC) No. 396/2005

Art. 14 (Decision on applications concerning MRLs)

"...account shall be taken of:

(a) the scientific knowledge available

*(b) the possible presence of pesticide residues arising from other sources than current plant protection uses of active substances, **and their known cumulative and synergistic effects, when the methods to assess such effects are available...**"*

CRA in current legislation: Reg. (EC) No. 396/2005

Art. 36 on support measures relating to harmonised pesticides MRLs – studies aimed at developing methods for cumulative risk assessment

CRA in current legislation: Reg. (EC) No. 396/2005

Future use of CRA

- Approval of active substances
- MRL setting
- Authorisation of PPPs
- Assessment of high residue events
- Annual reviews of monitoring data

Current status: EFSA and RIVM

- EFSA: opinions on the methodology
 - Grouping on the basis of a common effect
 - Probabilistic calculation methodology
- EFSA work on cumulative assessments groups (CAGs)
 - 2 CAGs established focusing on effects on thyroid and nervous system
 - EFSA work on other CAGs is ongoing
- ACROPOLIS on-line IT tool (RIVM- FP7 2010-2013)
- EFSA-RIVM grant agreement (2015-2016)
 - Upscaling of Acropolis
 - CRA calculations on thyroid and neurotoxicity CAG

Current status: COM

- Working group of MS experts for discussing risk management questions related to CRA
 - In the 2015 and 2016 meetings progress has been made on defining the risk managers point of view regarding the methodology to assess cumulative effects of pesticides residues.
- Working document summarising the outcome of the discussions on risk management aspects related to cumulative risk assessment.

Current status: COM

- DG SANTE concluded a grant agreement with RIVM to continue the work of the ACROPOLIS project during 2015 and 2016
 - Provide calculation examples to support the discussions in the working group.
 - Implement the tiered approach in the Acropolis tool.
 - Enable the output for the whole EU and not only country by country
 - Provide clear user instructions

Outcome of WG on risk management aspects related to CRA

- Subjects under discussion in the working group:
 - Specific regulatory questions on actions to be undertaken when a cumulative risk is identified
 - Threshold for regulatory consideration
 - Probabilistic versus deterministic methodology
 - Tiered approaches
 - Different procedures
 - Acute ↔ chronic
 - Exposure assessment post approval ↔ MRL setting
 - Other international systems
 - Communication

Outcome of WG on risk management aspects related to CRA

- Issues agreed by risk managers:
 - The combined margin of exposure concept will be used for expressing the risk with a probabilistic assessment instead of a CAG ADI or ARfD (concept no true tox ref value)
 - MoE = the ratio between the estimated exposure and a relevant toxicological endpoint taken from an animal study.
 - A threshold for regulatory consideration will be identified: Xth percentile of the population should have a combined margin of exposure above Y

Main challenges for risk managers

- Issues agreed by risk managers:
 - Tiered approach
 - First tier: scenario A
 - » Conservative scenario (less conservative than the EFSA pessimistic scenario)
 - » No risk: OK
 - » Risk identified: calculate scenario B
 - Second tier: scenario B
 - » Less conservative scenario than tier 1 (refinements on e.g. non-detects)
 - » No risk: OK
 - » Risk identified: take a risk management decision whether regulatory action is needed taking into account the uncertainties of the assessment or further refined analyses.

Outcome of WG on risk management aspects related to CRA

- Issues agreed by risk managers:
 - Probabilistic versus deterministic approach
 - Second tier calculation should be a probabilistic one.
 - First tier calculation: deterministic or probabilistic?
 - » With an easy to use computerised probabilistic model, in case of a tiered approach, a deterministic step might not be needed.
 - » A comparison of a deterministic and a probabilistic methodology will be made for the assessments on the neurotoxicity and thyroid CAG.

Plans for the near future

- Testing of the Acropolis tool and the methodology for their suitability for carrying out exposure assessments of multiple pesticide residues.
 - Thyroid and neurotoxicity CAG
- Intense interactions between risk managers and EFSA to define the appropriate parameters for the tier 1 and 2 scenarios.
- If the initial assessments are successful EFSA hopes to start progressively incorporating tests on cumulative risk assessment into its consumer exposure assessments that are conducted for the EFSA annual report on pesticides residues in food.

Plans for the near future

- The outcome of the first examples and assessments by EFSA and RIVM will form the basis for further discussions in the working group.
- The experiences gained in the EFSA-RIVM tests will be used for further optimising the methodology.

Plans for the longer term

- Use of the methodology for taking into account cumulative effects of pesticides for regulatory purposes in future after
 - Demonstration of fitness-for-purpose of the methodology
 - Definition of detailed procedures
 - The establishment of all cumulative assessment groups by EFSA
 - Impact assessment of the new methodology including impact on health, agriculture and international trade

⇒ **First still a lot of works needs to be done by both risk managers and risk assessors.**

Questions

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