7 December 2023 – BelTOX

Advances in the Risk Assessment of Chemical Mixtures

CRA FOR PESTICIDE RESIDUES

STATUS OF EFSA-SANTE ACTION PLAN

Germán Giner Santonja

EUROPEAN FOOD SAFETY AUTHORITY

EFSA-SANTE ACTION PLAN

- **Prioritisation:** 2023 (to be repeated every 3 years)
- **Estimated organs**: 8 to 16

Development of new CAGs

Retrospective CRA

- **Timeline:** 2022 onwards
- Repeated on a regular basis based on CAGs update and exposure changes
- MS Capacity Building

- **Timeline:** 2025 onwards
- Assess the risks related to new authorisations
- Mock assessment initiated

Prospective CRA

Integration of non-dietary exposure

- **Timeline:** 2024 onwards
- Work programme under elaboration

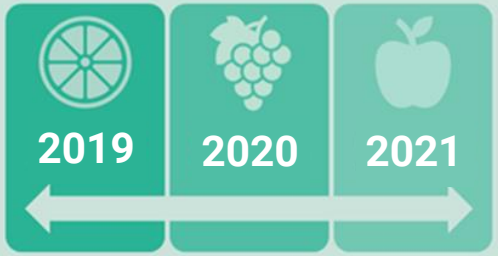
https://ec.europa.eu/food/sites/food/files/plant/docs/pesticides_mrl_cum-risk-ass_action-plan.pdf

CRA PRIORITIZATION (TO BE REPEATED EVERY 3 YEARS)

2021 — 2022 — 2023

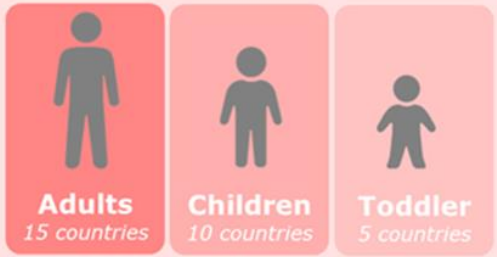
Monitoring data

3-year cycle / 36 commodities



Population groups

30 groups / 17 countries



Target organs

To be compiled by DTU

Preliminary analysis

- Identify pesticides with measurable findings
- **371** pesticides were retained for prioritisation

Substance screening

- Probabilistic assessment for each single pesticide
- **67** pesticides were retained for next step (>10% HBGV)

Organ screening

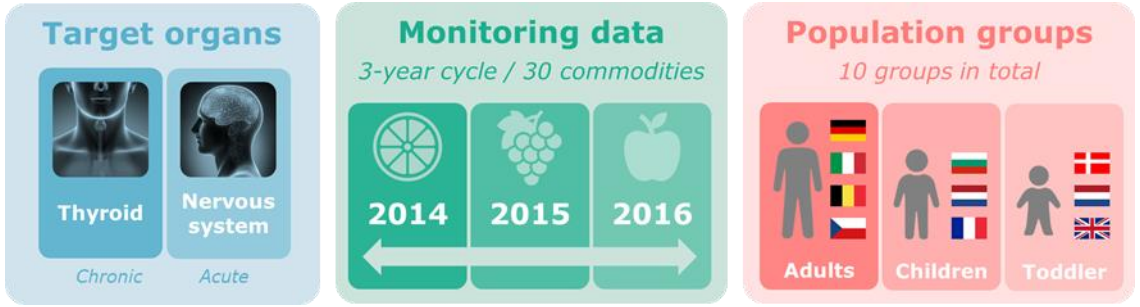
- Create assessment groups by organ
- Probabilistic assessment for **16** target organ systems

Scientific Report

List of pesticides and organs/systems that require establishment of CAGs and CRAs

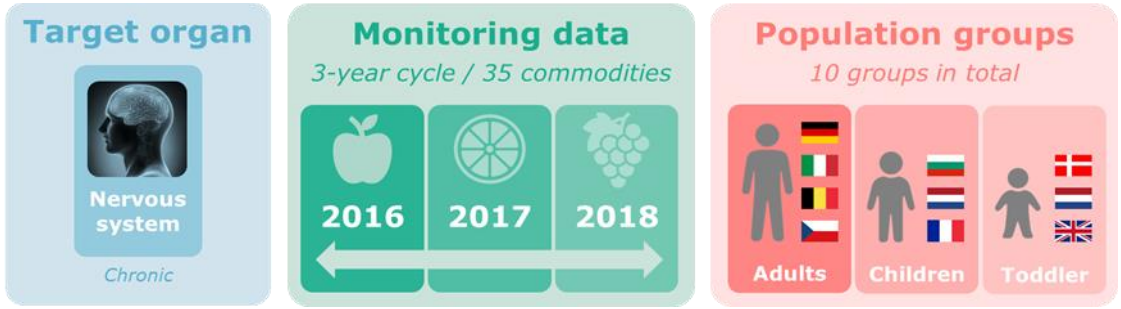
RETROSPECTIVE CRA, ALREADY PERFORMED

Pilot assessment



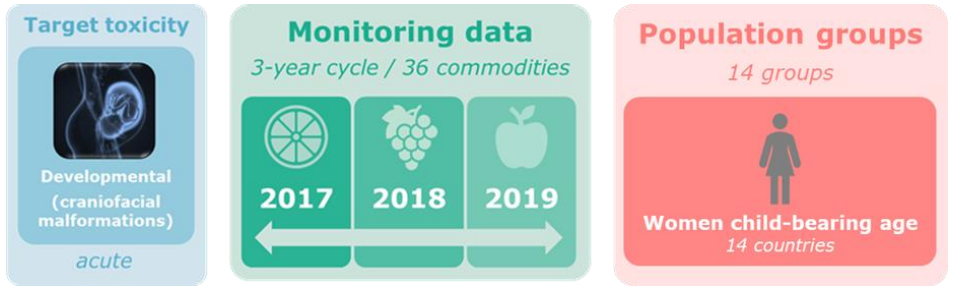
2019

Chronic AChE inhibition



2020

Craniofacial malformations



2021

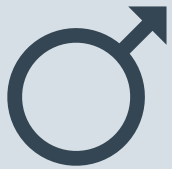
2022

RETROSPECTIVE CRA, TO BE PERFORMED

Kidney: Ongoing

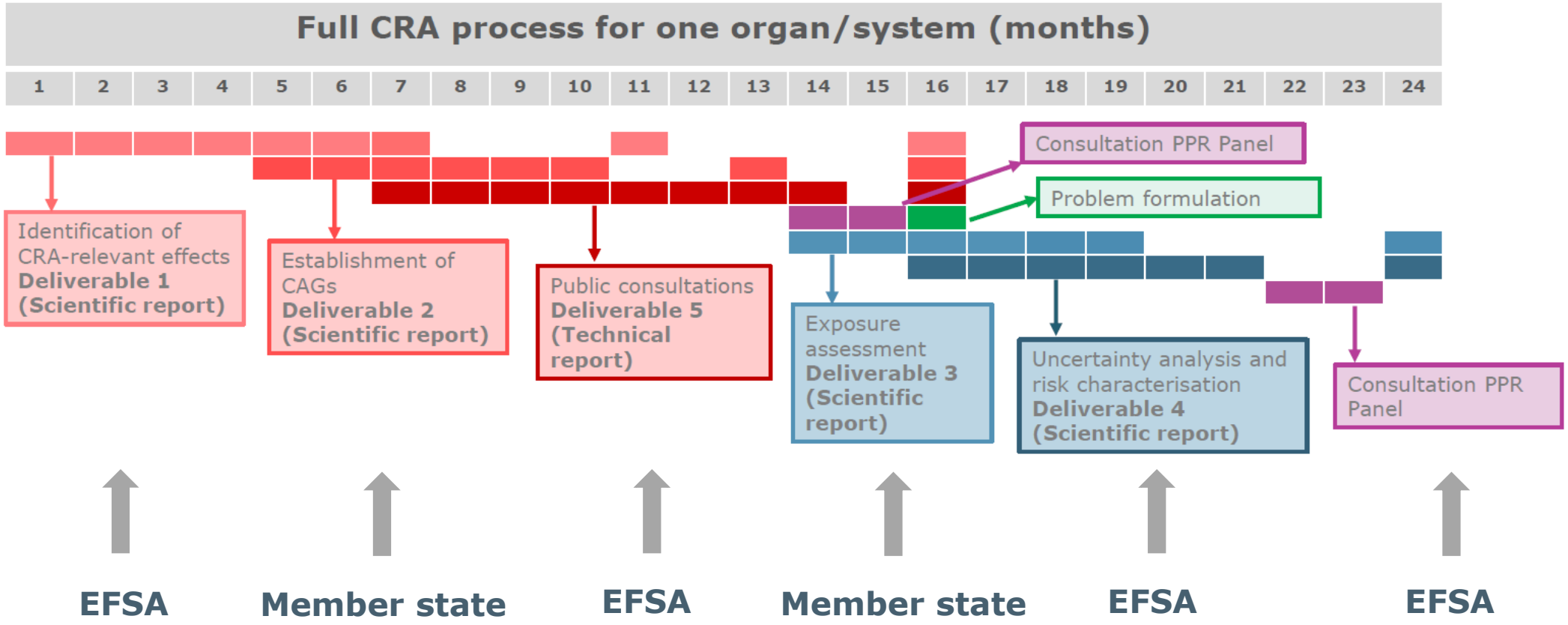
Liver: Ongoing

Reproductive and developmental effects: start in 2023-2024



Male reproductive system: start in 2025

RETROSPECTIVE CRA, WORK SHARING



Call for cooperation with EFSA on CRA: Evaluation of the applications completed and results communicated to applicants – Ongoing preparation of the first specific agreement

PROSPECTIVE CRA, PRELIMINARY ACTIONS

Case studies → SANTE WG → PAFF

EXTERNAL SCIENTIFIC REPORT

APPROVED: 23 July 2021

doi:10.2903/sp.efsa.2021.EN-6811

Proposed prospective scenarios for cumulative risk assessment of pesticide residues

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Abstract

To ensure a high level of consumer protection, Article 14 of Regulation (EC) No. 396/2005 stipulates that decisions on applications concerning the setting, modifying and deletion of maximum residue levels (MRLs) of pesticides shall take into account the cumulative effects, when the methods to assess such effects are available. This report investigates the feasibility of a tiered approach for prospective cumulative risk assessment (CRA). This report describes 15 case studies for the cumulative assessment group (CAG) associated with an effect on the motor division of the nervous system and 15 for the CAG associated with an effect on hypothyroidism. For each case study, Tier 0, Tier I and Tier II calculations were performed. The Tier II assessment was performed for three different scenarios representing three different risk assessment questions related to the exposure of a focal substance/focal commodity combination: 1) the MRL scenario assessing exposure at the MRL, 2) the Good Agricultural Practice (GAP) scenario assessing exposure to the focal commodity treated with the focal substance at the critical GAP and 3) the actual scenario, assessing actual exposure of pesticides, and taking into account use frequency of the focal substance. Additionally, three sensitivity analyses were performed addressing the impact of changing parameters or assumptions made in the comparison. The results revealed that prospective CRA could be performed more efficiently if a trigger value (e.g. a certain percentage of the Health Based Guidance Value (HBGV)) is implemented at Tier 0. For the tiered approach, however, although Tier II calculations should in principle result in a higher total Margin of Exposure compared to Tier I, this was not the case for all scenarios and case studies. Final criteria will need to be discussed and agreed by the Standing Committee of Plants, Animal, Food and Feed.

Key words: prospective cumulative exposure assessment, pesticide residues, acute effects, chronic effects, probabilistic, Monte Carlo Risk Assessment

Question number: EFSA-Q-2020-00759

Correspondence: data.collection@efsa.europa.eu

WG CRA 29 June 2020, Meeting Minutes

MINUTES OF THE WORKING GROUP MEETING ON CUMULATIVE RISK ASSESSMENT OF PESTICIDE RESIDUES

Monday 29 June 2020 (Webex)

MINUTES OF THE WORKING GROUP MEETING ON CUMULATIVE RISK ASSESSMENT OF PESTICIDE RESIDUES

Thursday 18 March 2021 (Webex)

Participants

COM DG S
EFSA: Bru
RIVM: Jac
AT: Ingo G
BE: Chanta
CY: Despo
CZ: Petr Se
DE: Marlee
DK: Bodil
FR: Alexan
FI: Juha La
GR: Christo
HR: Zdravk
IE: Finbarr
LU: Danny
NL: Arie To
SE: Niklas

MINUTES OF THE WORKING GROUP MEETING ON CUMULATIVE RISK ASSESSMENT OF PESTICIDE RESIDUES

Wednesday 26 May 2021 (Webex)

Participants:

COM DG SANTE: Almut Bitterhof and Stephanos Kirkagaslis

EFSA: Bruno Dujardin, Hermine Reich

RIVM: Jacob Van Klaveren, Gerda van Donkersgoed, Trijntje van der Velde, Annick van der Brand

AT: Ingo Großsteiner

BE: Chantal Vervaet

BG: Ralitsa Ganeva

CY: Despo Louca Christodoulou

CZ: Petr Sedlak

DE: Christian Sieke, Karsten Hohgardt, Angela Göbel

DK: Bodil Hamborg Jensen, Nina Nørgaard Sørensen

FR: Alexandra Mienné, Florence Gerault

FI: Tiia Makinen-Toykka, Johanna Rajasärkkä

GR: Christos Anagnostopoulos, Maira Gaspari

IE: Finbarr O'Regan

IT: Angela Santilio

LT: Elena Barzdėnienė, Eglė Vegienė

NL: Arie Ton, Judith Hulst

SE: Niklas Montell

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MRL-SETTING (PROSPECTIVE) CUMULATIVE RISK ASSESSMENT

TENTATIVE APPROACH REGARDING CERTAIN PARAMETERS FOR EFSA'S "CRA MRL-SETTING MOCK EXERCISE 2022"

Standing Committee for Plants, Animals, Food and Feed – Section Phytopharmaceuticals, Pesticide Residues, 22-23 February 2022

At the meetings of Experts on Cumulative Risk Assessment on 18 March 2021 and 26 May 2021, it was announced that the European Food Safety Authority (EFSA) would perform a "mock" exercise for the MRL-setting scenario within 2022. EFSA will pick an application for the setting of a Maximum Residue Level (MRL) and will perform acute and chronic consumer exposure assessments using the CRA methodology as developed until today.

It is important to note that the selected application needs to concern a crop included in the EU coordinated multi-annual monitoring programmes, as background exposure calculations are based on them, and a pesticide included in the currently established Cumulative Assessment Groups.

During the Experts' meetings, EFSA highlighted four parameters in the methodology for which the views of risk managers were necessary in order to further advance and are key-points for EFSA's 'mock' exercise. The discussions on those parameters were not conclusive, however there was consensus on a tentative approach for some of them. Table 1 below lists those parameters and the tentative approach from the Experts.

This *'tentative approach'* for some parameters is the outcome of an initial exchange and convergence of ideas expressed during the Experts' meetings. **The approaches listed below only serve the purpose of supporting the execution of the 'mock' exercise from EFSA. They are subject to review and update from the Experts following the results of the exercise,** in order to further fine-tune the approach.

#	Parameter	Tentative Approach	Status
1	Uncertainty of background exposure	Use uncertainty factors at the 99.9th in Tier 1 and Tier 2.	Consensus
2	Tier 1	PRIMo estimates to be summed with the 99.9th percentile of the background exposure distribution	No agreement. Awaiting results from 'mock' exercise.
3	Tier 2	GAP-scenario including the 20% use frequency.	Consensus
4	Condition to trigger CRA?	If focal exposure >10% ADI/ARfD	No agreement. Awaiting results from 'mock' exercise.

A fifth point was raised by DG SANTE as whether it would be imperative to use the same (MRL) approach in both IESTI and CRA (Tier 2), however, this is pending discussions on an international level and will be further evaluated following the conclusion of those discussions.

PROSPECTIVE SCENARIOS

Mock assessments

(Anses, EFSA tasking grant)

Acute prospective CRA

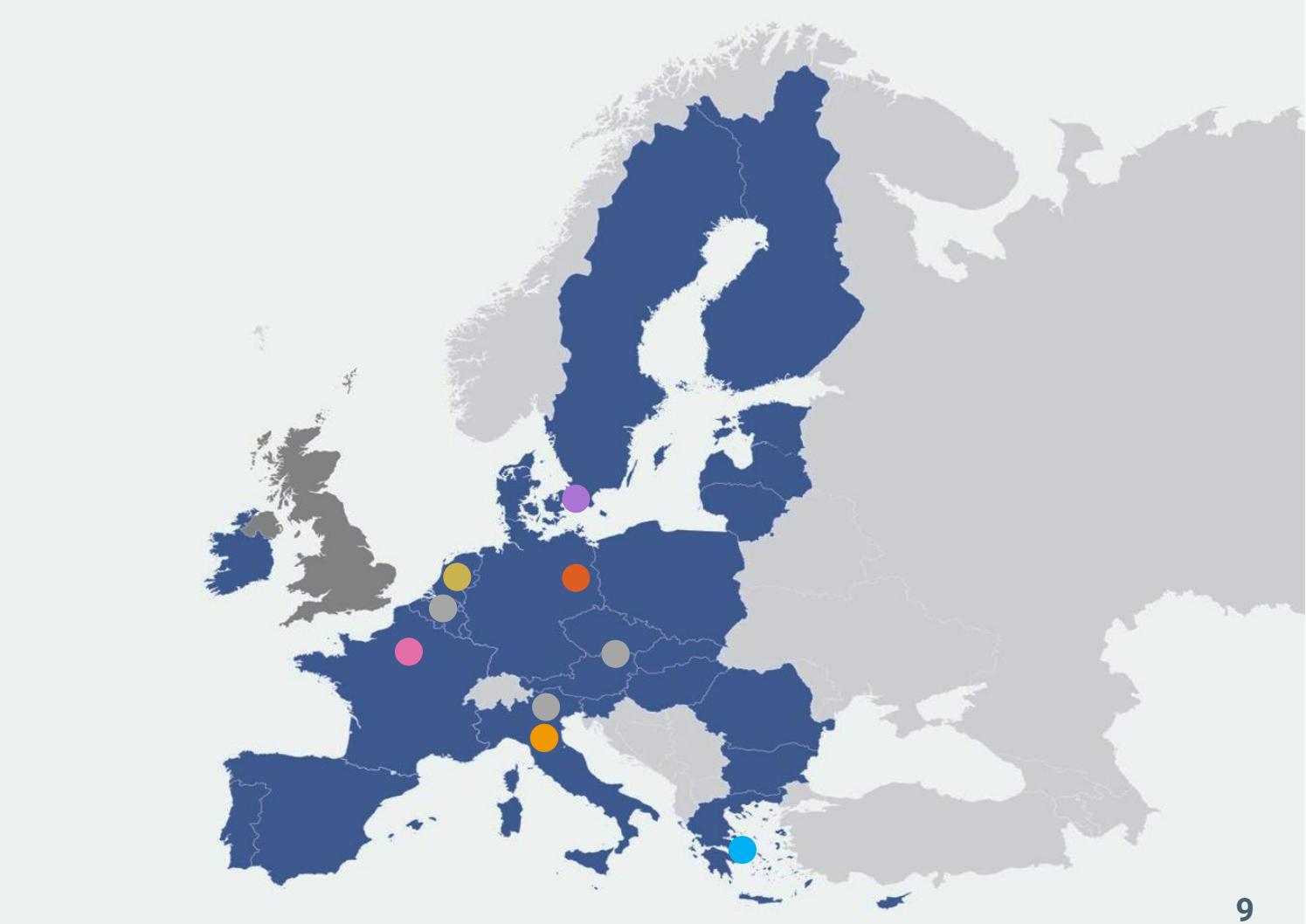
- Effects on motordivision: tefluthrin/carrot, 9 populations
- December 2022 to November 2023

Chronic prospective CRA

- Hypothyroidism: fenamidone/lettuce, 9 populations
- April 2023 to April 2024

EU CAPACITY BUILDING ON CRA OF PESTICIDES

- EFSA
- RIVM
- DTU
- BfR
- BPI
- Anses
- WG Experts
- …



INTEGRATION OF NON-DIETARY EXPOSURE

Work programme under elaboration - 6 years starting in 2024

Work package 1 (Methodology, toxicology)	Adaptation of the methodologies regarding the hazard identification and hazard characterisation developed for retrospective dietary CRA
Work package 2 (Methodology, exposure)	Development of the methodology to perform non-dietary cumulative exposure assessments, linked to the methodology in WP1
Work package 3 (Prototype calculation tool)	Translating the model developed in WP2 into a calculation tool (MCRA)
Work package 4 (prioritisation)	Prioritisation of pesticides, toxicological effects and population groups of concern
Work package 5 (Pilot assessment)	Survey for non-dietary exposure in a representative sample of population Non-dietary cumulative exposure assessment and uncertainty analysis using the prototype calculator

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