Webinar | 26th May 2025

WEBINAR ON THE OPEN MCRA TOOL FOR PROSPECTIVE CUMULATIVE RISK ASSESSMENT

STARTING AT 09:30 (CEST)

efsa
EUROPEAN FOOD SAFETY AUTHORITY

HOUSEKEEPING RULES

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One-way audio
(listen only mode)

Post your **questions** in the Q&A section, they will be answered during the Q&A session

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After the event, attendees will receive a **link to a survey** to evaluate the EFSA's event & services

TODAY'S CHAIR, SPEAKERS AND MODERATORS

Bruno Dujardin

Chair, Team Leader

EFSA

Angelo Cafaro

Presenter, Data Scientist

EFSA

Jacob van Klaveren

Presenter, Senior Scientific Advisor

RIVM

Anne Zwartsen

Presenter, Toxicologist

RIVM

Marloes Schepens

Moderator, Risk Assessor

RIVM

Luc Mohimont

Moderator, Scientific Officer

EFSA

AGENDA

Starting time 09:30

Introductory remarks
Bruno Dujardin, EFSA

Cumulative Risk Assessment of Pesticides: An Overview
Angelo Cafaro, EFSA

Cumulative Risk Assessment performed using MCRA
Jacob van Klaveren, RIVM

Demonstration of prospective CRA using MCRA
Anne Zwartsen, RIVM

Q&A
EFSA & RIVM

Closing remarks
Bruno Dujardin, EFSA

Ending time 11:20

Cumulative risk assessment of pesticide residues: An Overview

Angelo Cafaro, EFSA

OVERVIEW

- Background
- Prospective CRA Methodology
- Open MCRA

BACKGROUND

Regulation 396/2005
Setting of MRLs for pesticides

Regulation 1107/2009
Placing on the market of PPPs

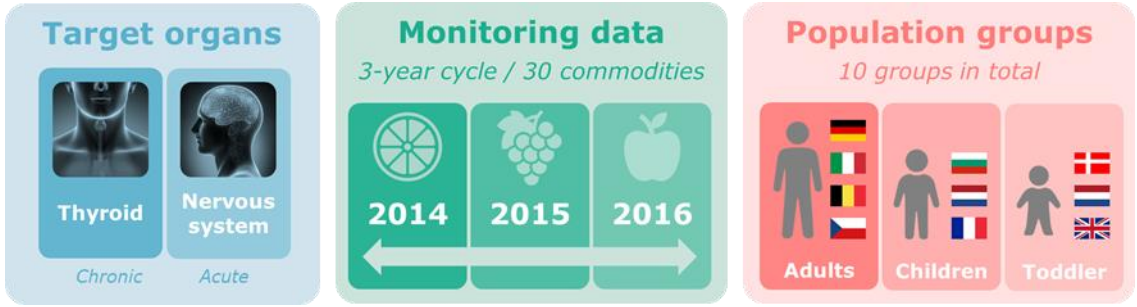
Open MCRA 10.0
Implementing retrospective CRA as standard regulatory action in MCRA

Methodological developments → **Pilot assessments** → **Implementation**

"…take into account known cumulative and synergistic effects of pesticides when the methods are available…"

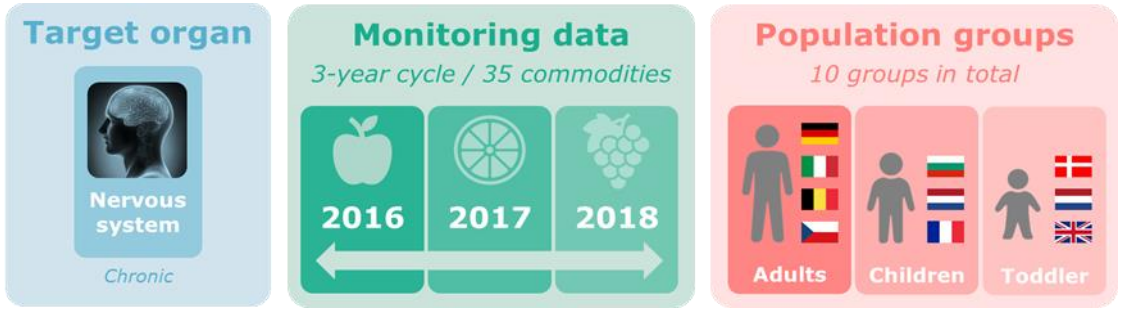
RETROSPECTIVE CRA, SO FAR…

Pilot assessment



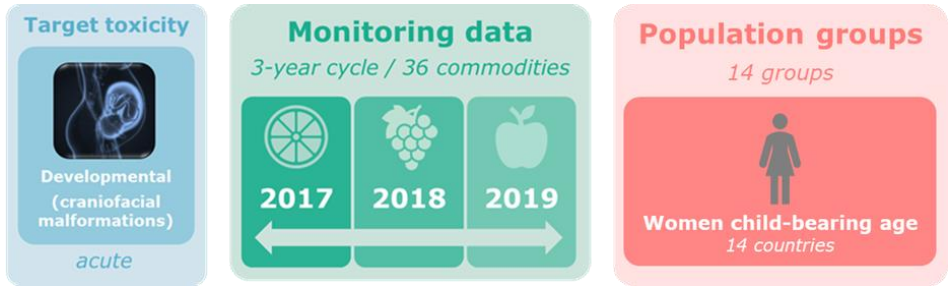
2019

Chronic AChE inhibition



2020

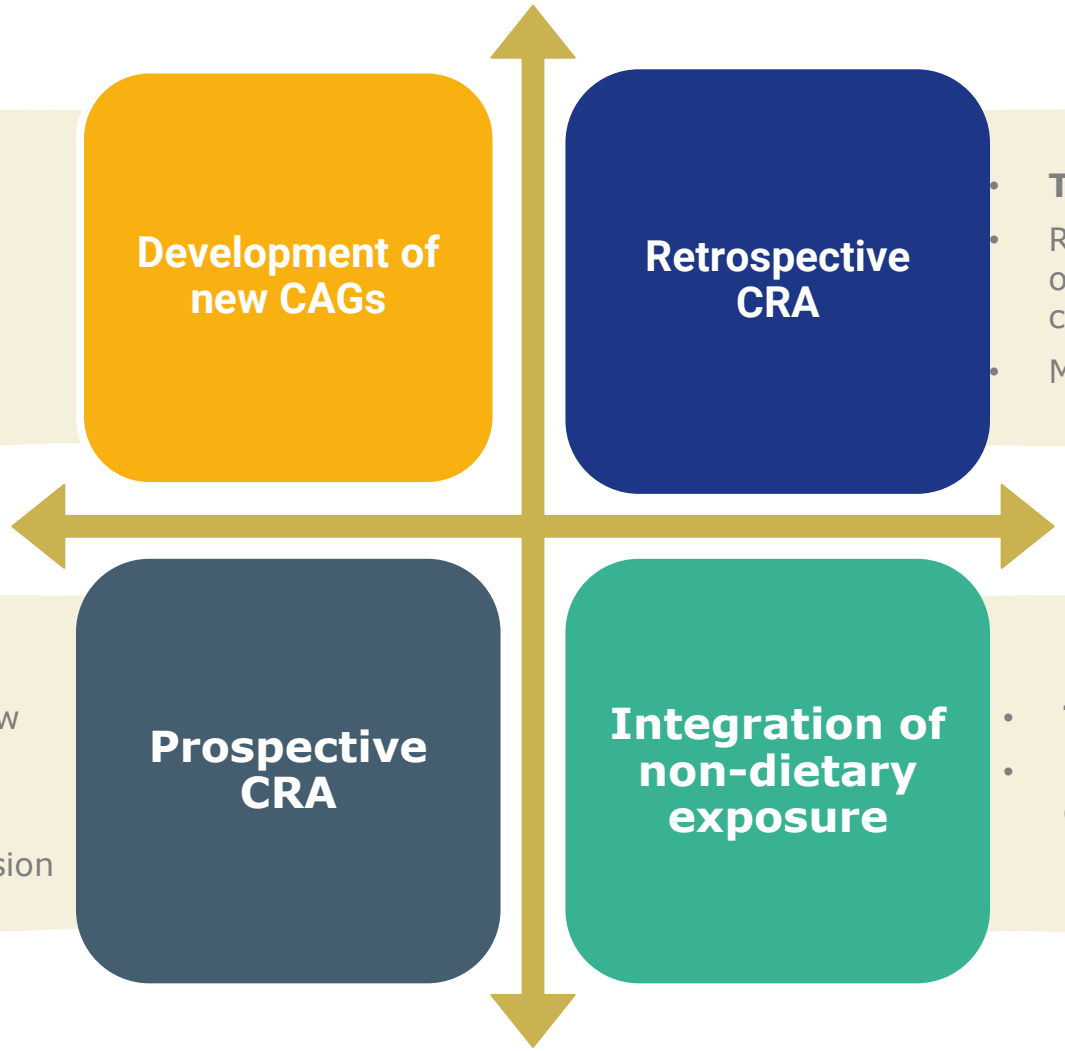
Cranio-facial malformations



2021

2022

EFSA-SANTE ACTION PLAN



- **Prioritisation:** 2022 (to be repeated every 3 years)
- **Prioritised organs**: 2 + 5
- **Timeline:** 2024–2030

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

- **Timeline:** 2024 onwards
- Assess the risks related to new authorisations
- Mock assessment finalised
- Implementation under discussion

- **Timeline:** TBC
- Further methodological developments and data are needed

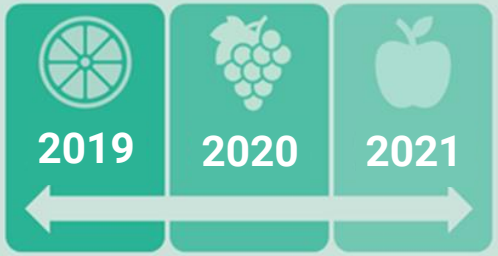
https://ec.europa.eu/food/sites/food/files/plant/docs/pesticides_mrl_cum-risk-ass_action-plan.pdf

CRA PRIORITISATION

2021 — 2022 — 2023

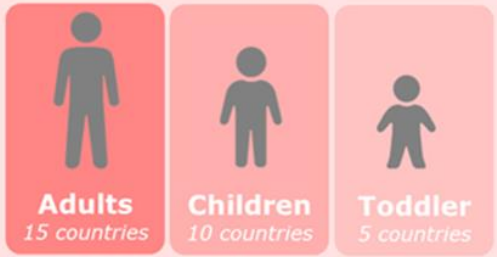
Monitoring data

3-year cycle / 36 commodities



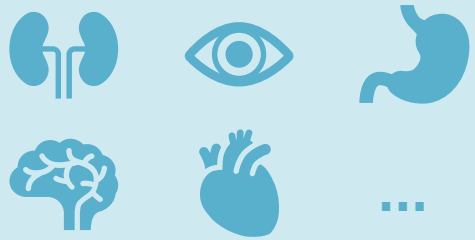
Population groups

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
- Retain pesticides with HQ≥0.1 at P99.9

Organ screening

- Probabilistic assessment for **16** target organ systems
- Retain target organ system with HI≥1 at P99.9

Scientific Report

Establishment of CAGs and CRA execution is required for:

67 pesticides

5 target organ systems

https://doi.org/10.2903/j.efsa.2024.8554

ONGOING AND NEXT RETROSPECTIVE CRA

Thyroid (repetition): Ongoing (risk characterisation)

Liver: Ongoing (CAG establishment)

Kidney: Ongoing (CAG establishment)

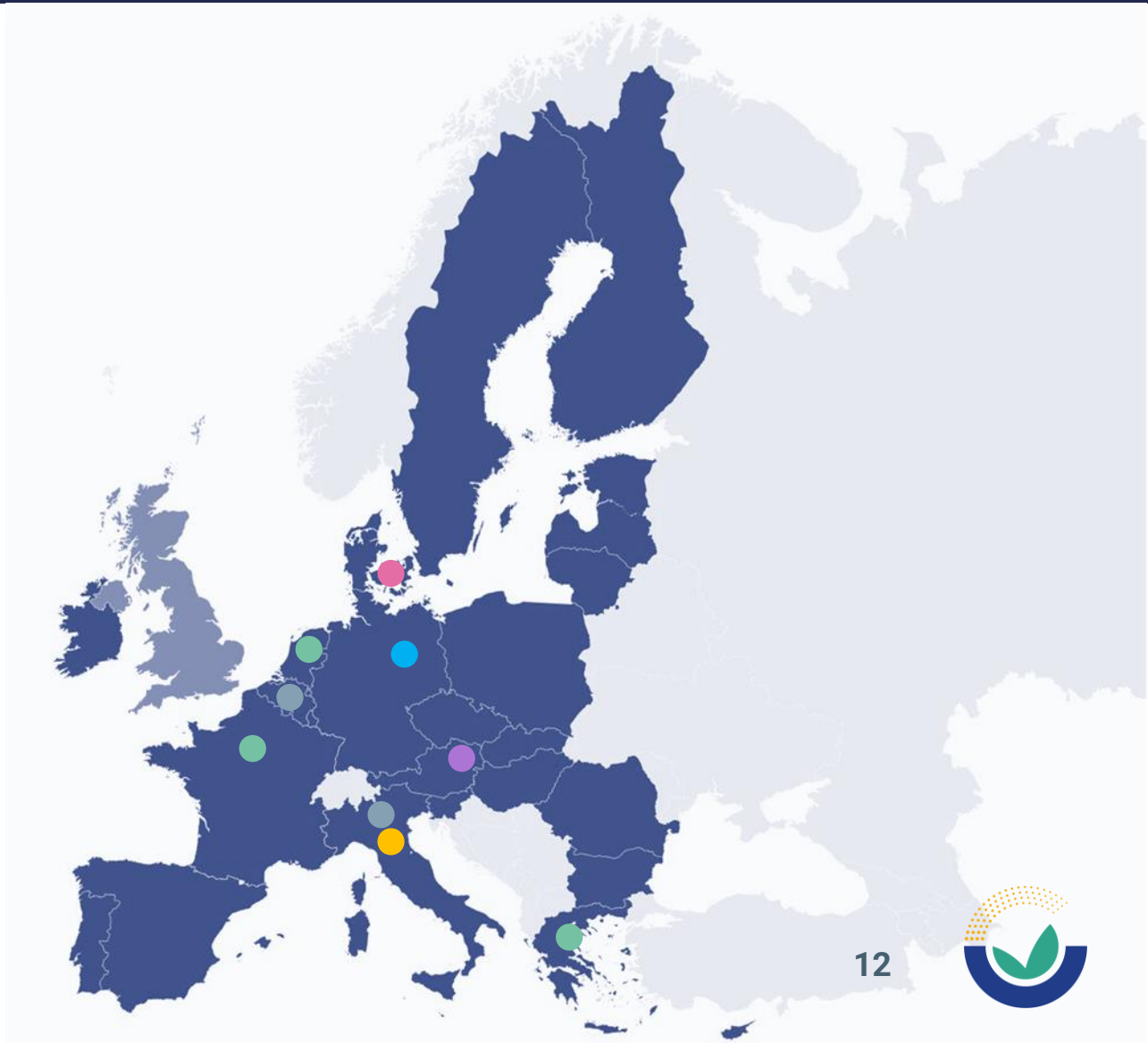
Reproductive toxicity (including fertility):
Ongoing (WG identification of specific effects)

Developmental toxicity and haematopoietic system toxicity: Ongoing (WG identification of specific effects)

+ CRA update every 3 years for organs already assessed

EU CAPACITY BUILDING ON CRA OF PESTICIDES

- EFSA
- Exposure assessment
  - RIVM
  - Anses
  - BPI
  - WUR
- Hazard assessment
  - Ages
  - BfR
  - DTU
  - WG Experts



OVERVIEW

- Background
- Prospective CRA Methodology
- Open MCRA

PROSPECTIVE CRA - TIMELINES

2020

EFSA, RIVM, European Commission and Member States initiate discussions on possible scenarios

2021

RIVM releases a first scientific report exploring feasibility of prospective CRA with 30 case studies

2022

European Commission and Member States on a first set of criteria for a tiered approach

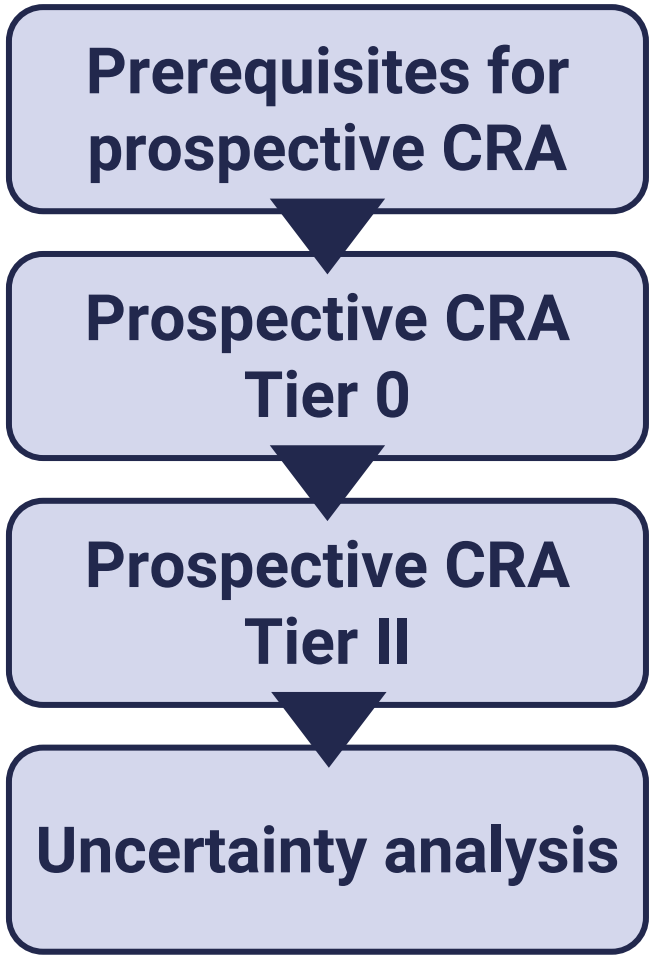
2024

ANSES issues two mock assessments investigating main uncertainties for the proposed scenarios

2025

European Commission and Member States endorse scenarios for prospective CRA of pesticides

PROSPECTIVE CRA – TIERED APPROACH



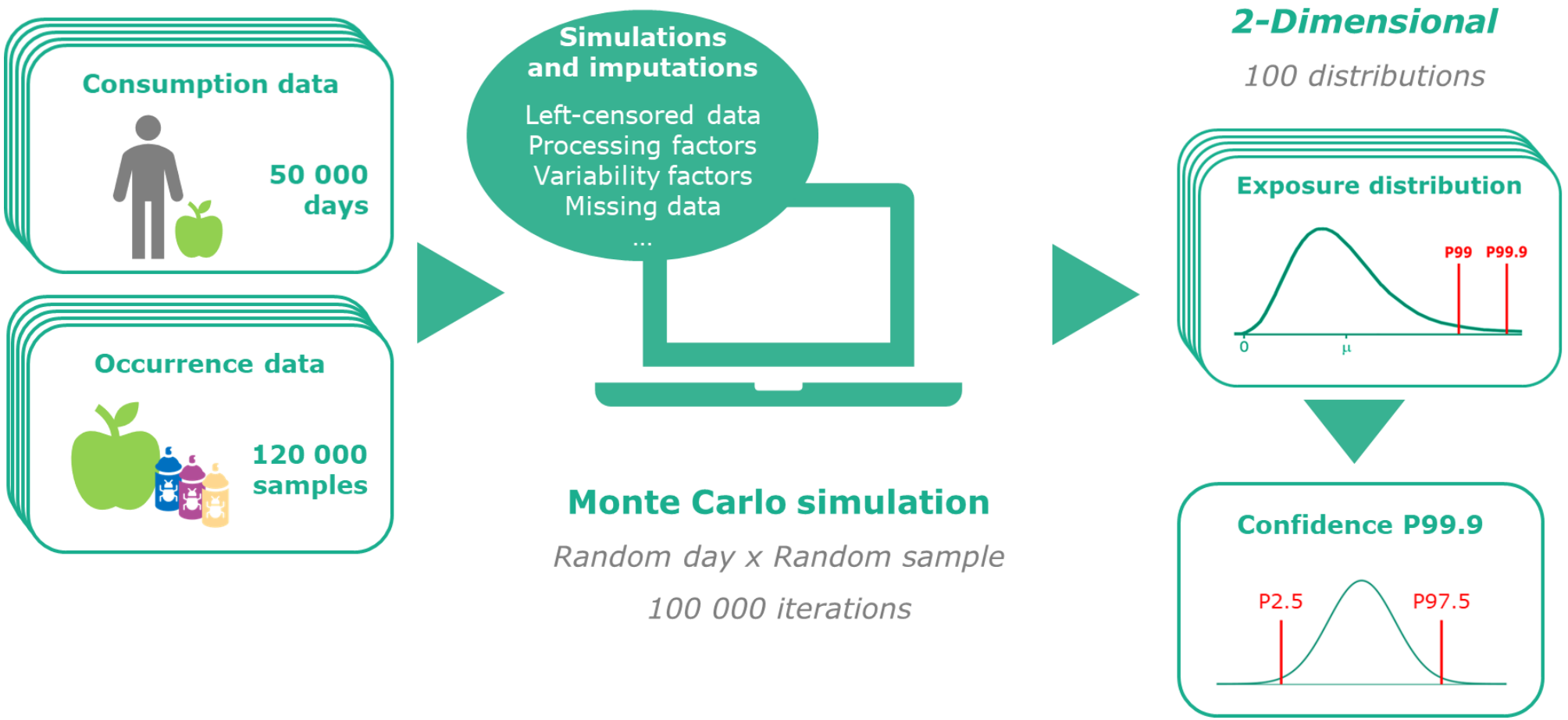
Today's webinar will focus on the execution of prospective CRA Tier II with MCRA

Important notes:

- EFSA is currently elaborating a cookbook that will provide further instructions on how to perform prospective CRA in a tiered approach, including the uncertainty analysis.
- Prospective CRA complements and does not replace deterministic assessment with PRIMo of single substance (e.g., IESTI ≤ 100% ARfD or IEDI ≤ 100% ADI).
- Tier I scenario was removed during the elaboration process as it was not demonstrated to be effective.

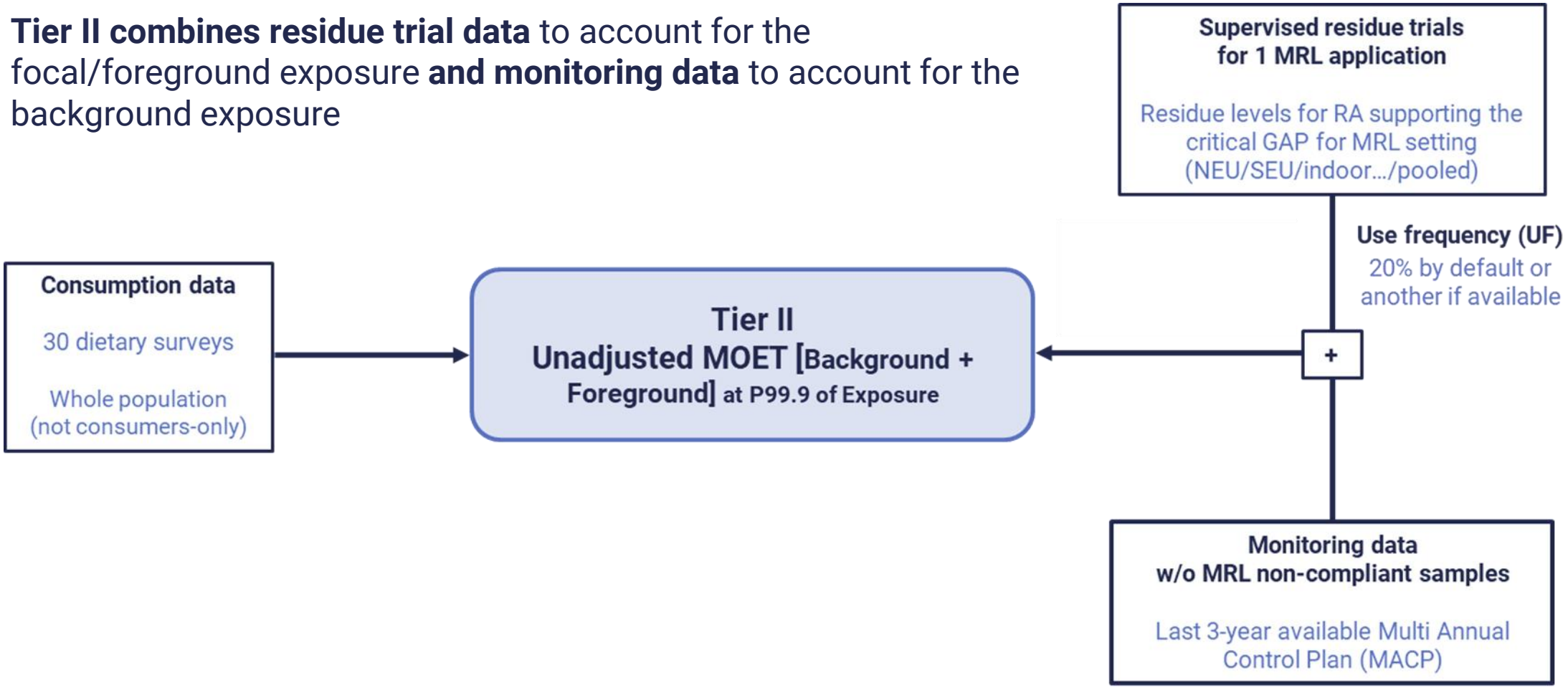
TIER II – BASIC PRINCIPLES

Tier II relies on the same probabilistic principles as the retrospective CRA



TIER II - FINAL SCENARIO

Tier II combines residue trial data to account for the focal/foreground exposure **and monitoring data** to account for the background exposure



OVERVIEW

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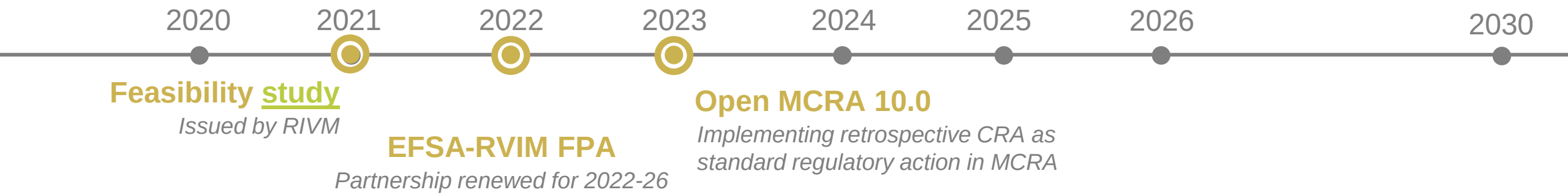
- Open MCRA

MONTE-CARLO RISK ASSESSMENT (MCRA) PLATFORM

- Web-based tool that can be used for the cumulative risk assessment of pesticides.

- Need for a common EU **efficient**, **transparent**, **accessible**, **harmonized** and **user-friendly** software tool for supporting human health risk assessments for combined exposure to multiple chemicals.

EFSA-RIVM PARTNERSHIP: FROM MCRA TO OPEN MCRA



PILLARS OF DEVELOPMENT PHASE

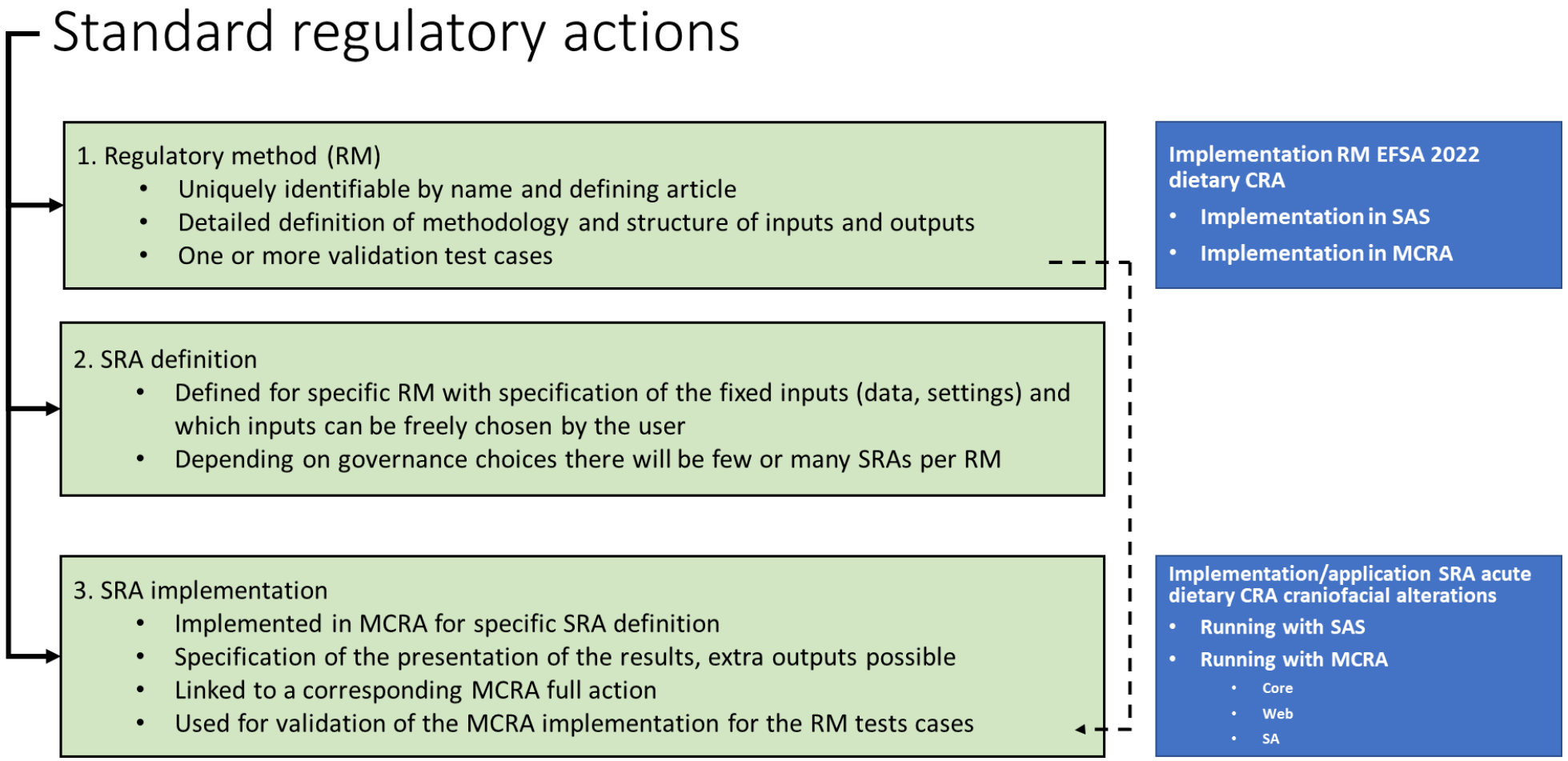
Transparency: open source, governance.

Interoperability: data connectivity, co-creation.

Accessibility: user groups, dedicated & simplified interfaces.

Harmonisation: standard regulatory actions, capacity building & training.

STANDARD REGULATORY ACTIONS (SRAS)



TIMELINE OF DEVELOPMENT PHASE

Action	2022	2023	2024	2025	2026
Transparency					
Interoperability					
Accessibility (Part I)					
Accessibility (Part II)					
Harmonisation & maintenance					

Achieved

Ongoing

Planned

ACHIEVEMENTS

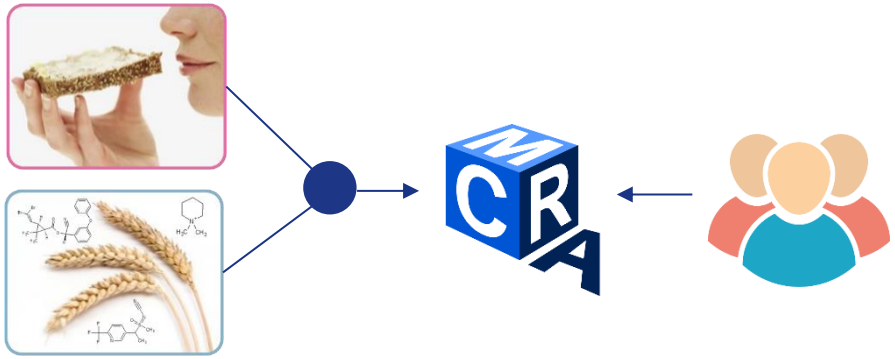
- External scientific reports:
  1. The MCRA platform for EU regulatory actions: governance, user guidance and FAIRification (2023).
  2. Standard regulatory action for retrospective cumulative risk assessment of pesticides in MCRA (2023).
  3. Update of the MCRA platform: enhancing data connectivity, security, interoperability, and accessibility (2024).
  4. Update of the SRAs for prospective and retrospective dietary CRA of pesticides in MCRA (2024).

- Release of MCRA version 10 (June 2023) and 10.1 (July 2024):
  - Core models published in openly accessible repository.
  - Web application to interface with MCRA core models.

- Trainings:
  - Relevant EFSA networks (2023, 2024 and 2025).
  - DG SANTE staff, e-working group, SCoPAFF member and/or appointed experts (May 2023).

ONGOING

Enhance data connectivity.
Develop a framework for co-creation.



Implementation of the SRA for prospective CRA with endorsed methodology.
Refinement of the SRA for retrospective CRA.

PLANNED

May 2025
- ❑ This webinar to provide an overview of prospective CRA methodology and implementation in MCRA.

July 2025
- ❑ External scientific reports about updates in MCRA developments and updates in SRAs 2025.
- ❑ Open MCRA web version 10.2.0.

Sep. – Dec. 2025
- ❑ Ensure accessibility of Open MCRA and a sustainable financial model to operate the platform and maintain it.
- ❑ Renewed EFSA-RIVM partnership to transition in operational phase.

Jan. 2026 - onwards
- ❑ Update CAGs when needed.
- ❑ Start limiting options for ProsCRA scenarios in MCRA.
- ❑ Start implementing sensitivity analyses.
- ❑ Improve features in MCRA.

CREDITS

- This presentation has been designed using icons made by Pixel Perfect from Flaticon.

National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

Cumulative Risk Assessment performed using MCRA

Webinar on the open MCRA Tool for prospective cumulative risk assessment

26-05-2025, Online

Jacob van Klaveren

Department of Chemical Food Safety, RIVM

Content

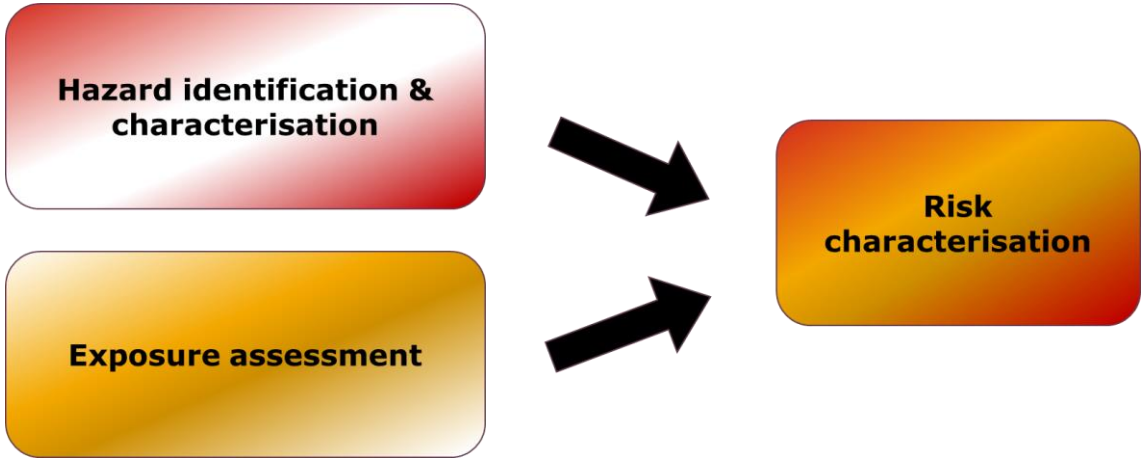
- Recap on cumulative risk assessment methodology
- Prospective cumulative risk assessment methodology
- Uncertainties

Content

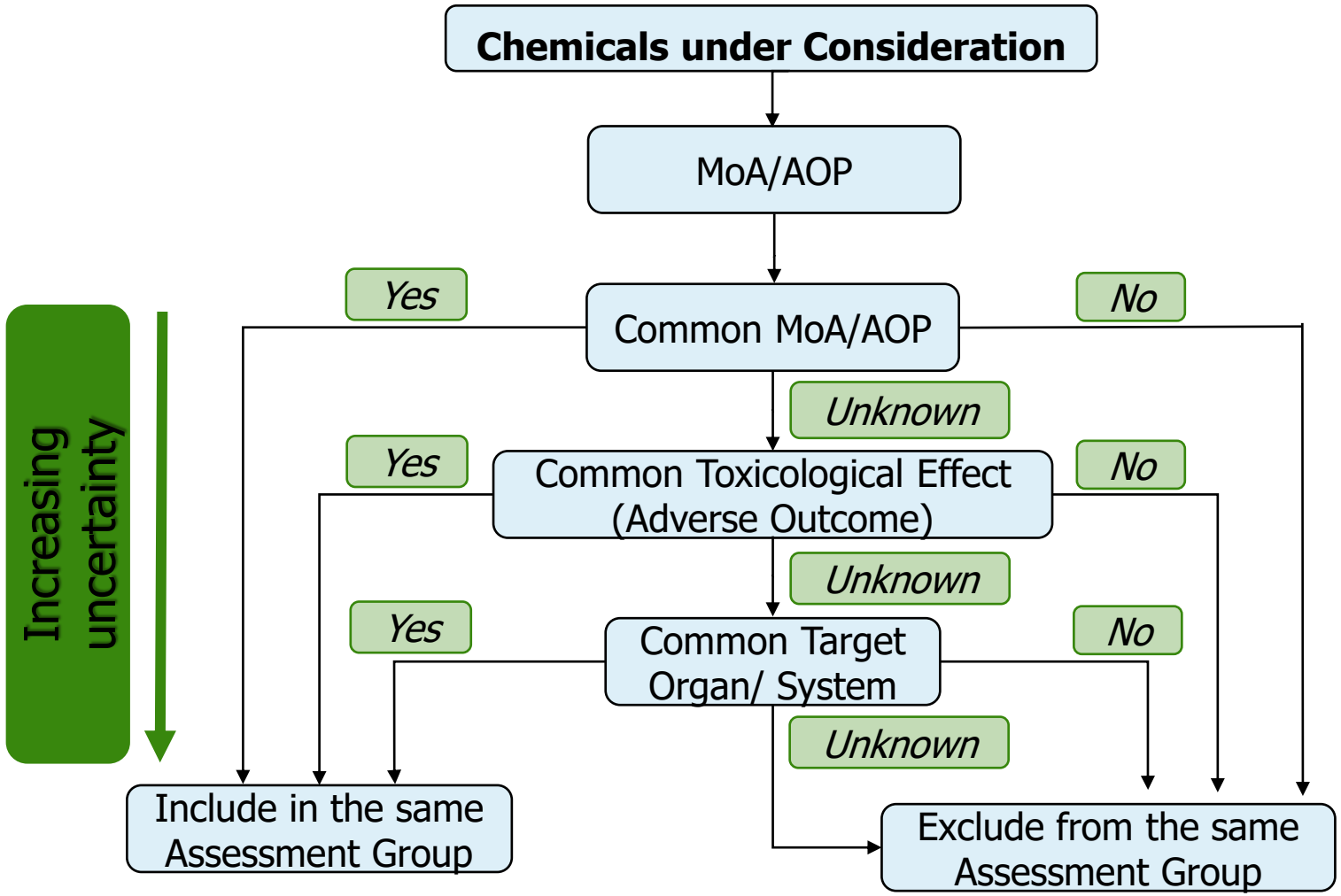
- Recap on cumulative risk assessment methodology
- Prospective cumulative risk assessment methodology
- Uncertainties

Retrospective CRA method in short

- Combine risk for all chemicals with a similar effect
  - Chemicals with the same effect are grouped in Cumulative Assessment Groups (CAGs)
  - The exposure of the individual chemicals in the CAG is expressed as the concentration of the CAGs index chemical
  - Risk is calculated by dividing hazard of the index chemical by the exposure



Retrospective CRA – hazard assessment (1/2)



- Grouping of chemicals into assessment groups
- Top-down hierarchical process for grouping chemicals into Assessment Groups using hazard-driven criteria
- Gold standard Common MoA/AOP for grouping into assessment group
- Then move to common toxicity or target organ
- Publication in December 2021
  https://doi.org/10.2903/j.efsa.2021.7033

Retrospective CRA – hazard assessment (2/2)

Cumulative Assessment Groups (CAGs)

- Nervous system
- Thyroid
- Craniofacial
- Liver
- Kidney
- Repro
- Developmental and haematopoietic system

For each active substance in a CAG:

- Toxicological Point of Departure (PoD)→ NOAEL
- Relative potency factors (RPF)

Exposure assessment

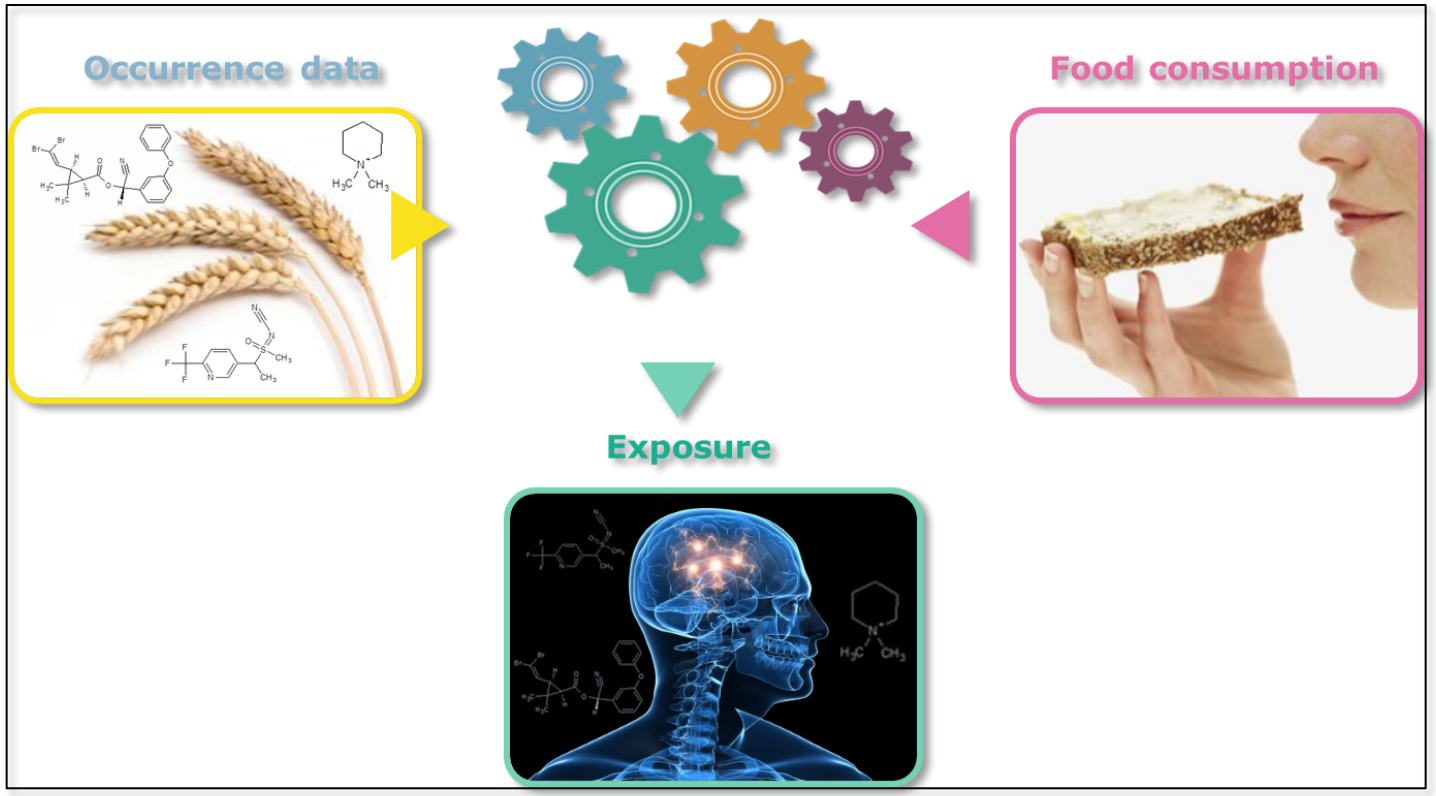
Retrospective CRA – exposure assessment (1/3)
Food consumption data

- Food consumption data
  - 16 countries
  - 30 populations

NETWORK ON FOOD CONSUMPTION DATA

AGENDA OF THE 14th MEETING

Meeting date:	**06 April 2022**
Meeting hours:	**09:30 – 17:30**
Meeting venue:	**Online *(MS Teams)***
Chair:	***Sofia Ioannidou***



Exposure assessment

Retrospective CRA – exposure assessment (2/3)
Monitoring/occurrence data

- Concentration data from MS pesticide monitoring programmes
  - 30 different countries
  - 36 different commodities
  - Will be updated, and new 3-year cycles will become available over time

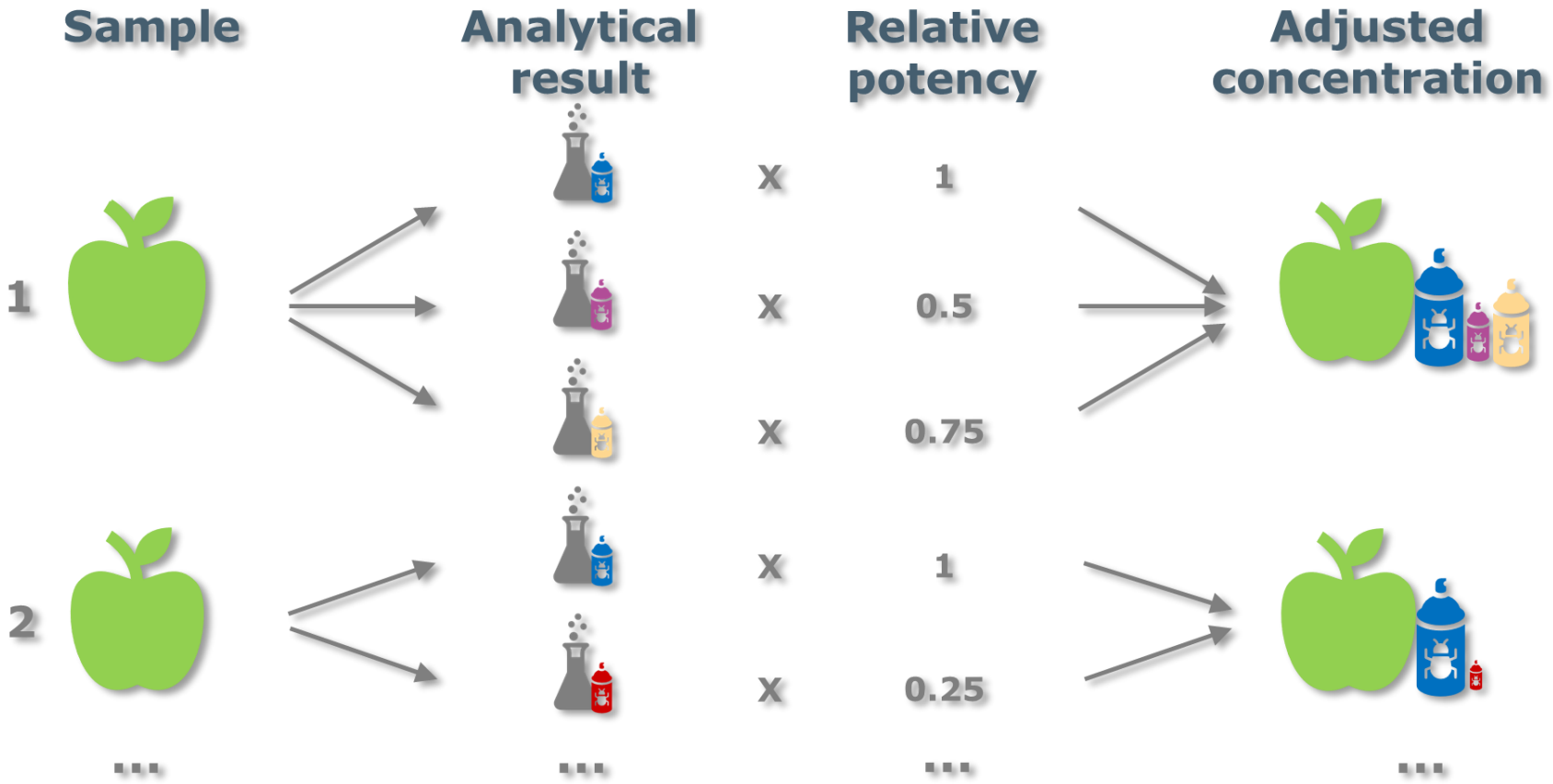
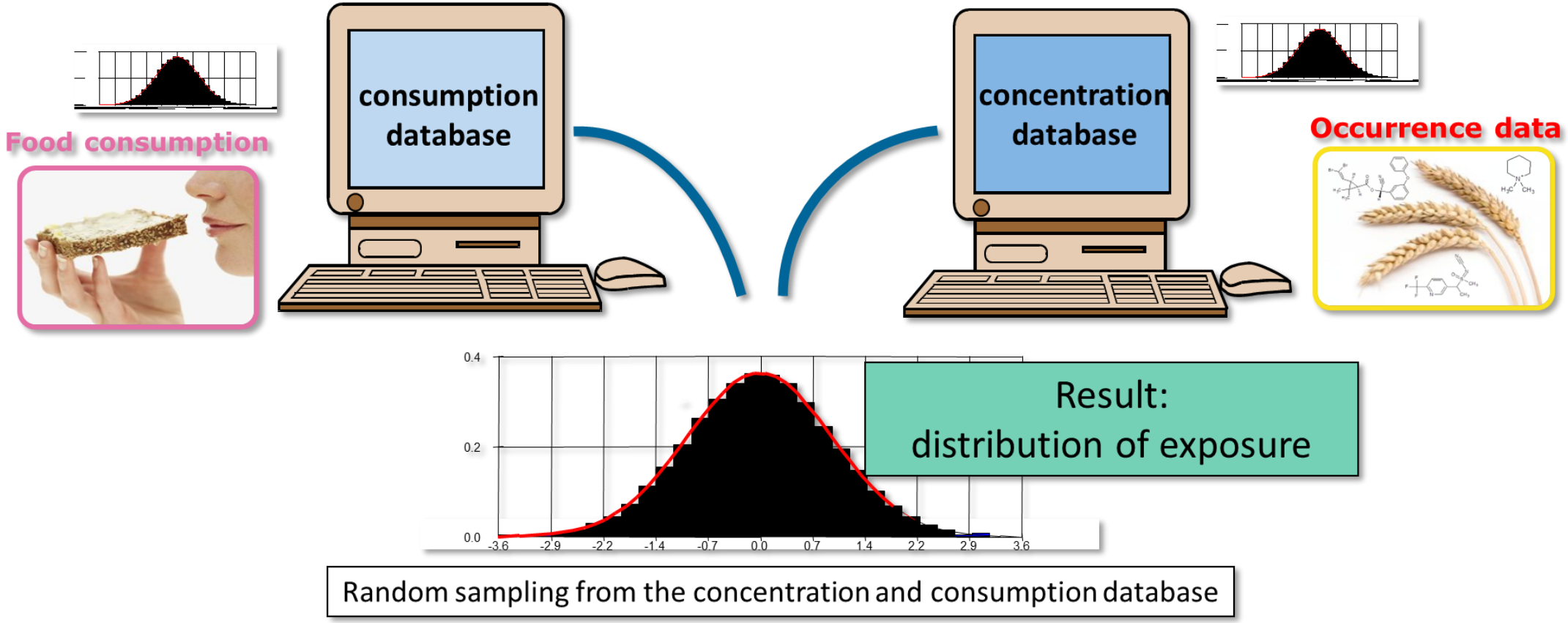


Figure from EFSA

Exposure assessment

Retrospective CRA – exposure assessment (3/3)



Risk characterisation

Retrospective CRA – Risk characterisation

Risk matric: Total margin of exposure (MOET)

Calculated based on the MOEs for each chemical in the CAG

- **Threshold of regulatory concern**: MOET for the 99.9th percentile of the exposure distribution of > 100

Content

- Recap on cumulative risk assessment methodology
- Prospective cumulative risk assessment methodology
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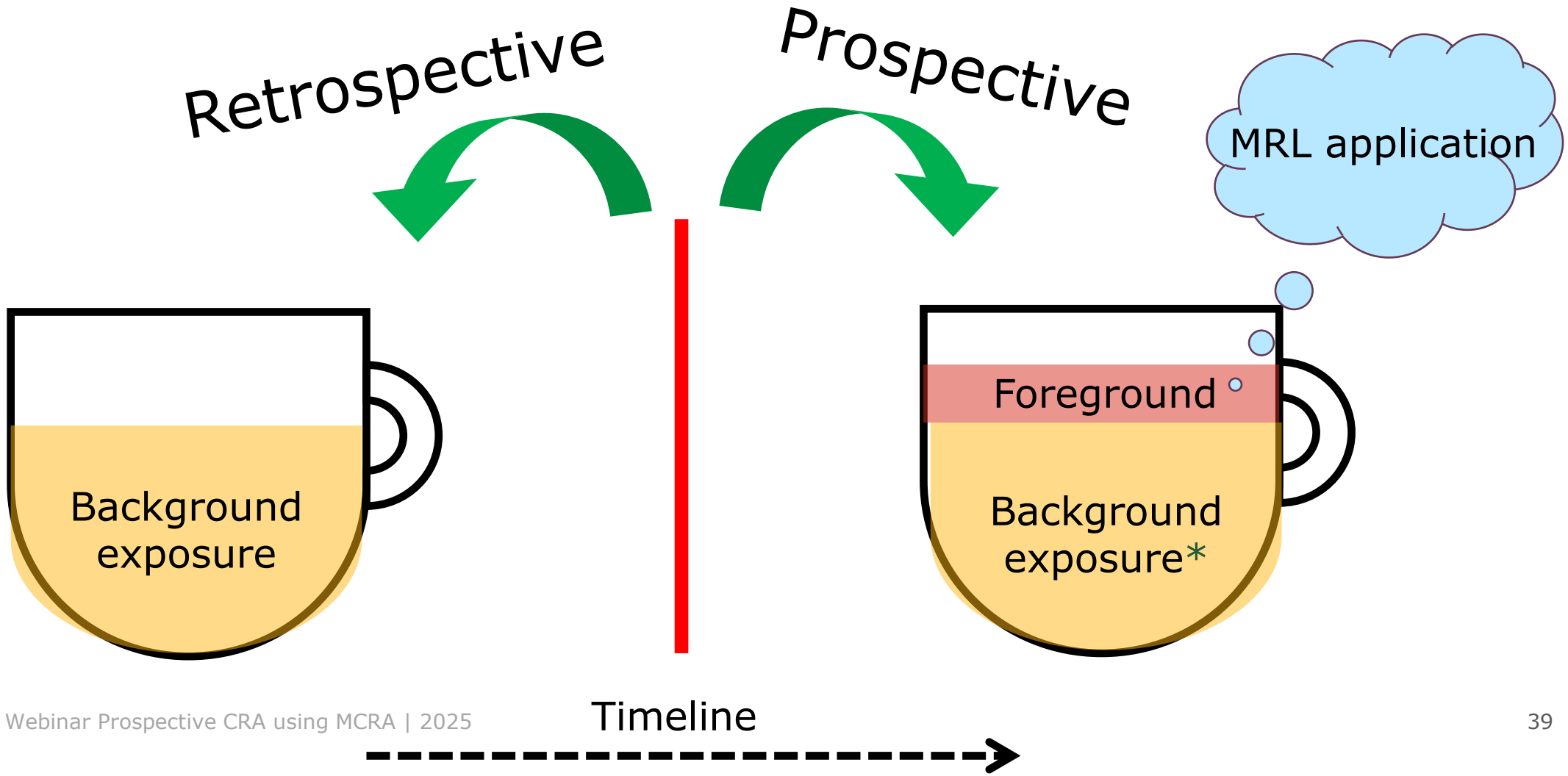
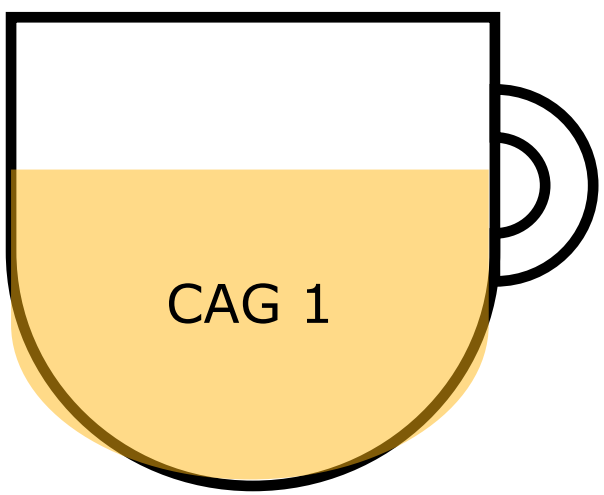
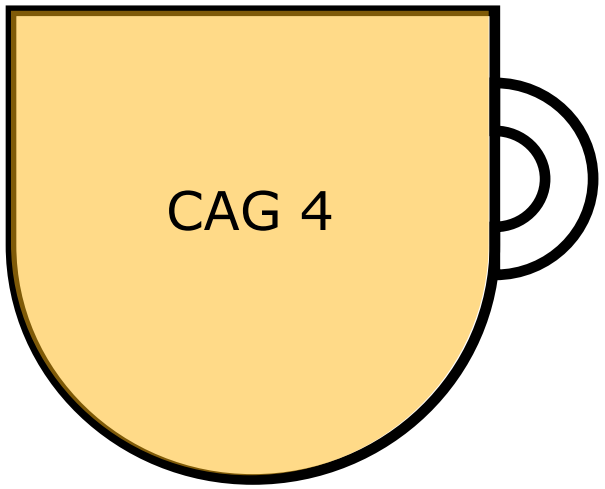
Retrospective vs. prospective CRA



Cumulative risk cup-conceptual approach

- Once the risk cup is full for a given population and for a specific CAG, a risk to human health cannot be excluded





When is CRA using MCRA needed?

Start with deterministic assessment (Tier 0; IESTI/IEDI)

MOE = 0-100
Health risk cannot be excluded

MOE = 100-1000
Perform probabilistic CRA using MCRA (Tier II), if possible

MOE = >1000
No health concern identified

When is CRA using MCRA performed?

› When CAG is flagged OR when MOE TIER 0 = 100-1000

However, CRA can only be performed when:
✓ The active substance is in priority list, AND
✓ The active substance is included in CAG, AND
✓ A retrospective CRA for this CAG is available

If not available → no CRA performed

Where do these requirements come from?

Prioritisation exercise

(identification of pesticides and organ systems with the **highest risk in terms of dietary exposure**)

Establishment/update of Cumulative Assessment Groups (CAGs)

Based on **common adverse outcome** (similar MoA or dissimilar MOA but same tox endpoint) and definition of **Reference Value for each group**

Every 3 years

Retrospective CRA

1. **Assess the risk from actual exposure** to pesticides using monitoring data;
2. **Provide baseline for the prospective CRA**

EFSA

When needed

Prospective CRA

Predict cumulative risk within regulatory decision making to understand how new authorisations may impact on cumulative risk estimated under the retrospective assessments

Applicable for example to:

- **MRL setting processes** – Art 10 Reg (EC) 396/2005
- **Approval processes** – Reg (EC) No 1107/2009
- (possible) **Authorisation of PPPs at MS level**

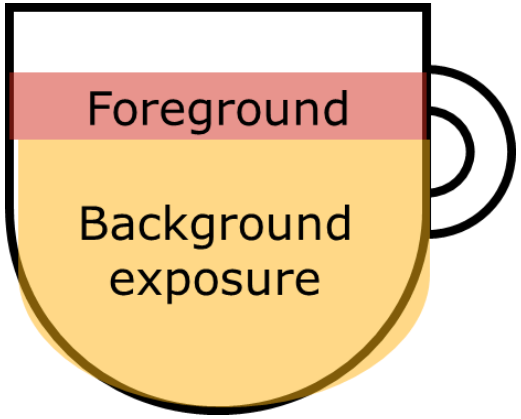
MS

Hazard for prospective CRA

For each active substance in a CAG:

- Toxicological Point of Departure (PoD)→ NOAEL
- Relative potency factors (RPF)

Exposure for prospective CRA



Background occurrence data
→ Most recent 3 years of monitoring
→ Exclusion of samples not compliant to MRL
→ Concentration data focal food/focal substance removed

Foreground occurrence data
→ Field trial data focal food/focal substance according to cGAP
→ Safety of GAP with 20% use frequency
→ Processed focal food

Whole population consumption data

Field trial data + conversion factor templates

Template can be downloaded after selecting settings for prospective CRA, and is partly filled in

	A	B	C	D	E	F	G	H	I	J	K
1	labSampCode	prodCode	prodName	paramCode	paramName	sampY	resUnit	resLOD	resLOQ	resVal	resType
2	Sample-01	prod X code	prod X	chemical Y code	chemical Y	2024	mg/kg		0.01		LOQ
3	Sample-02	prod X code	prod X	chemical Y code	chemical Y	2024	mg/kg		0.01		LOQ
4	Sample-03	prod X code	prod X	chemical Y code	chemical Y	2024	mg/kg		0.01		LOQ
5	Sample-04	prod X code	prod X	chemical Y code	chemical Y	2024	mg/kg		0.01		LOQ
6	Sample-05	prod X code	prod X	chemical Y code	chemical Y	2024	mg/kg		0.01		LOQ
7	Sample-06	prod X code	prod X	chemical Y code	chemical Y	2024	mg/kg		0.01		LOQ
8	Sample-07	prod X code	prod X	chemical Y code	chemical Y	2024	mg/kg		0.01		LOQ
9	Sample-08	prod X code	prod X	chemical Y code	chemical Y	2024	mg/kg		0.01		LOQ
10	Sample-09	prod X code	prod X	chemical Y code	chemical Y	2024	mg/kg		0.01		LOQ
11	Sample-10	prod X code	prod X	chemical Y code	chemical Y	2024	mg/kg		0.01		LOQ
12											
13											

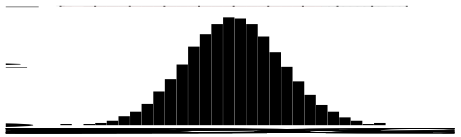
	A	B	C	D	E	F	G
1	ParamCodeMeasuredSubstance	MeasuredSubstanceName	ParamCodeActiveSubstance	ActiveSubstanceName	idFood	FoodName	ConversionFactor
2	Residue definition of MeasuredSubstance code	Residue definition of MeasuredSubstance	ActiveSubstance 1 code	ActiveSubstance 1	idProd X	prod X	a
3	Residue definition of MeasuredSubstance code	Residue definition of MeasuredSubstance	ActiveSubstance 2 code	ActiveSubstance 2	idProd X	prod X	b
4	Residue definition of MeasuredSubstance code	Residue definition of MeasuredSubstance	ActiveSubstance 3 code	ActiveSubstance 3	idProd X	prod X	c
5	Residue definition of MeasuredSubstance code	Residue definition of MeasuredSubstance	ActiveSubstance 4 code	ActiveSubstance 4	idProd X	prod X	d
6	Residue definition of MeasuredSubstance code	Residue definition of MeasuredSubstance	ActiveSubstance 5 code	ActiveSubstance 5	idProd X	prod X	e
7	Residue definition of MeasuredSubstance code	Residue definition of MeasuredSubstance	ActiveSubstance 6 code	ActiveSubstance 6	idProd X	prod X	f
8							
9							

Content

- Recap on cumulative risk assessment methodology
- Prospective cumulative risk assessment methodology
- Uncertainties

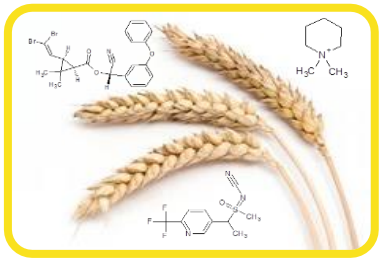
Uncertainties already addressed

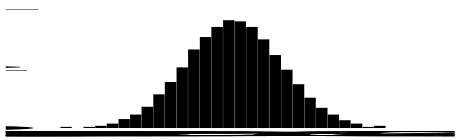
Food consumption

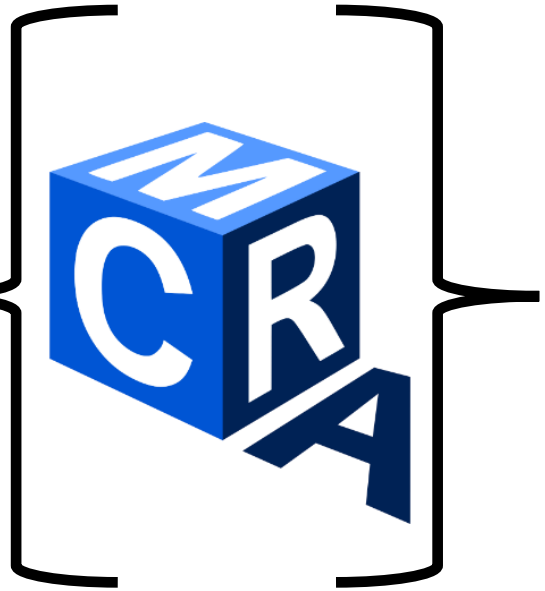


Random day x
random sample
(100.000 iterations)

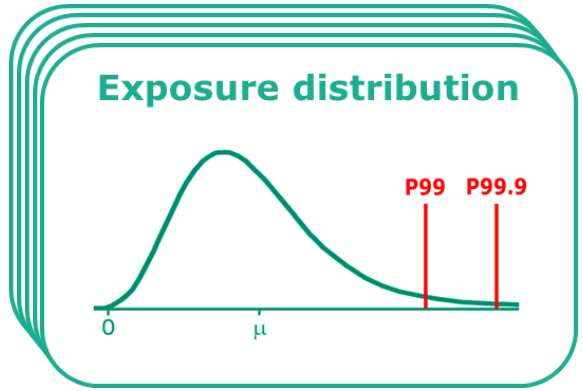
Occurrence data

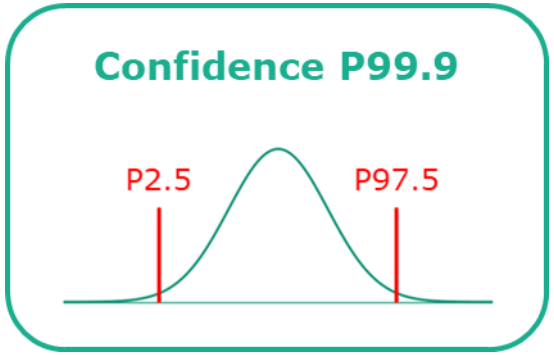






100 bootstraps





Sampling uncertainty in consumption data and occurrence data is helpful for a reliable estimate of the median exposure at the P99.9

Uncertainties were explored in previous EFSA opinions

Pesticides: first cumulative risk reports published

Published: 29 April 2020 | 2 minutes read

Share:

EFSA has published the results of its two pilot assessments on the risks posed to humans by residues of multiple pesticides in food.

- Some uncertainties do not impact the results
- Relevant uncertainties are covered in the methodology established in 2025

Relevant sources of uncertainty

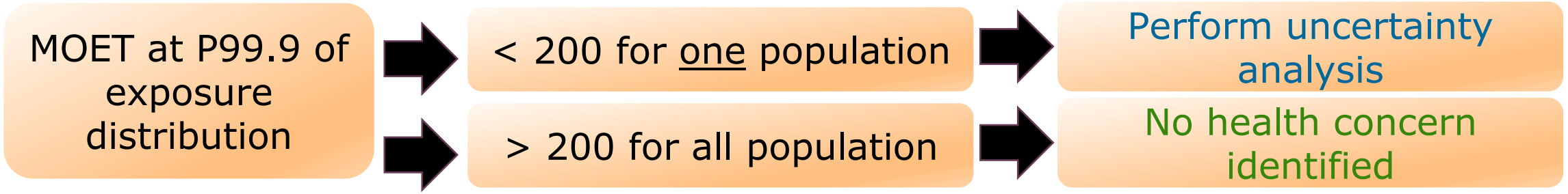
U01: Substances not included in the CAG (TOX)
U02: Risk drivers included in the CAG with low CAG-membership probability (TOX)
U03: Toxicological characterisation of risk drivers (TOX)
U04: Dose-addition model (TOX)
U05: Sampling uncertainty of occurrence and consumption data (EXP)
U06: Commodities not included (EXP)
U07: Metabolites not included (EXP)
U08: Unspecific residue definitions (EXP)
U09: Missing processing factors (EXP)
U10: Washing of commodities and peeling of edible peels (EXP)
U11: Exposure calculation model (TOX and EXP)

~5-6 of 11 will probably be automated

Impact of each individual uncertainty on the MOET for de reference population will be determined – using either expert judgement or sensitivity analysis

This leads to 11 multiplicative factors (MF) → 2 combined MF (TOX/EXPO) → **1 overall MF**

When to perform additional uncertainty analysis?



MF example based on sensitivity analysis

- Uncertainty on impact of **missing processing factors (PF)**
- Monitoring is focused on raw primary commodities e.g. apples
- Apples can also be processed e.g. apple juice, apple pie
- Pesticide concentration may change during processing
- Many processing factors are still missing
- When missing → a conservative assumption → no loss of pesticide residues in processed commodity

Sensitivity analysis assumes no residues transferred to processed food when no PF is available → implemented in MCRA

Additional uncertainty analysis needed?

- Remember:

MOET at P99.9 of exposure distribution	> 200 for all populations	No health concern identified
	< 200 for one population	Perform uncertainty analysis

- Now:

Adjusted MOET at P99.9 of exposure distribution with reference population MF	> 200 for all populations	No additional analysis needed
	< 200 for one population	Perform uncertainty analysis for specific population

- Then:

Adjusted MOET at P99.9 of exposure distribution with specific or reference population MF	> 100 for all populations	No health concern identified
	< 100 for one population	Health risk cannot be excluded

No health concern identified when:

Tier 0:

- MOE > 1000
- CAG is not flagged

Tier II (safety of GAP with 20% use frequency):

- **Unadjusted** median MOET at P99.9 for all populations ≥ 200
- **Adjusted** median MOET at P99.9 of all populations ≥ 100 (previous slide)

National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

Demonstration of prospective CRA using MCRA

Webinar on the open MCRA Tool for prospective cumulative risk assessment

26-05-2025, Online

Anne Zwartsen

Department of Chemical Food Safety, RIVM

Content

- EFSA – RIVM partnership and alignment with DG SANTE
- Demonstration of the prospective standard regulatory action
- Foreseen developments

Content

- EFSA – RIVM partnership and alignment with DG SANTE
- Demonstration of the prospective standard regulatory action
- Foreseen developments

Monte Carlo Risk Assessment **(MCRA)** Platform

- The MCRA platform is a web-based data and model platform to assess exposure and health risks of single chemicals and chemical mixtures
- Need for a common EU efficient, transparent, accessible, harmonized and user-friendly software tool for supporting human health risk assessments for combined exposure to multiple chemicals
- EFSA and the Dutch government have provided funding for the development of MCRA in three EFSA-RIVM framework partnership agreements from 2015 until 2029 (most likely beyond)
- Resources:
  - MCRA Web
  - MCRA page on RIVM's website

Implementation into MCRA

Outcomes of the EFSA-DG SANTE action plan are implemented in MCRA in the EFSA-RIVM partnership on Open MCRA

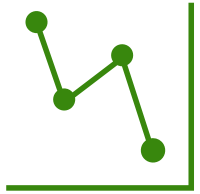
- Available CAGs are included
  - When new CAGs become available, they will be included
- Newest available data is available for use
  - (yearly) Data updates will continuously be included
- Retrospective CRA is implemented
- Prospective CRA is (partly) implemented
  - Coming months will focus on the implementation of the uncertainty analysis

Users of MCRA can perform CRA for agreed cumulative assessment groups

- Acute
  - Developmental:
    - Cranio-facial alterations due to abnormal skeletal development (DAC) – Women 15-45 years
    - Head abnormalities not due to abnormal skeletal development (DAH) – Women 15-45 years
  - Neurochemical:
    - Functional effects on motor division (NAM)
    - Neurochemical end-points (NAN)

- Chronic:
  - Neurochemical:
    - Neurochemical endpoints (NCN)
  - Thyroid:
    - Substances affecting follicular cells and/or thyroid hormone (T3/T4) system (TCF)
    - Effects on the parafollicular (C-) cells of the calcitonin system (TCP)

MCRA offers access to concentration and consumption data needed for cumulative risk assessment



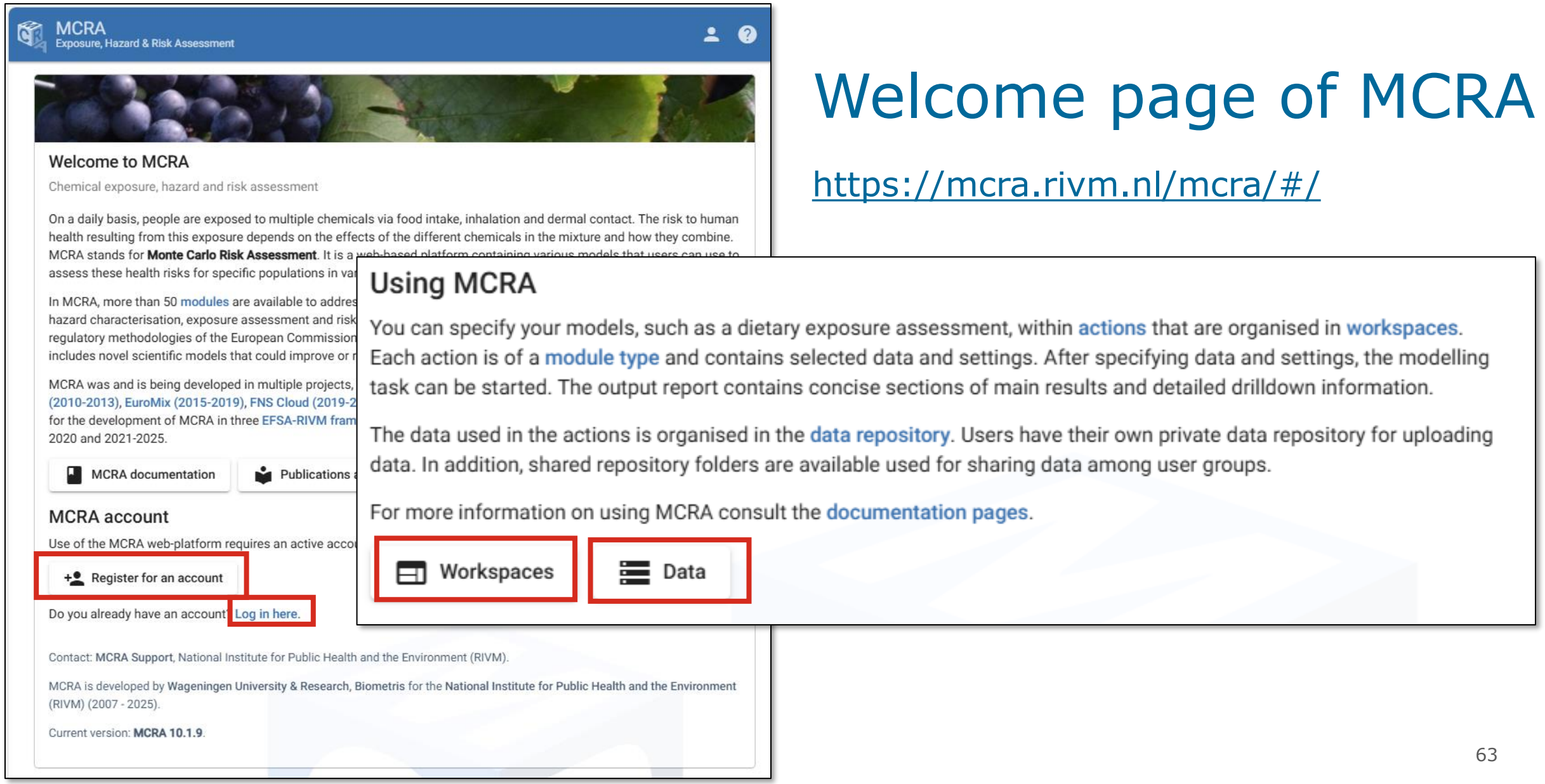
- Concentration data from MS pesticide monitoring programmes
  - 30 different countries
  - 36 different commodities
  - Will be updated, and new 3-year cycles will become available over time
- Consumption data
  - 16 countries
  - 30 populations
- Privacy sensitive consumption and human biomonitoring data is safe within MCRA (tests are performed according to the European Privacy Regulation (GDPR))

Content

- EFSA – RIVM partnership and alignment with DG SANTE
- Demonstration of the prospective standard regulatory action
- Foreseen developments

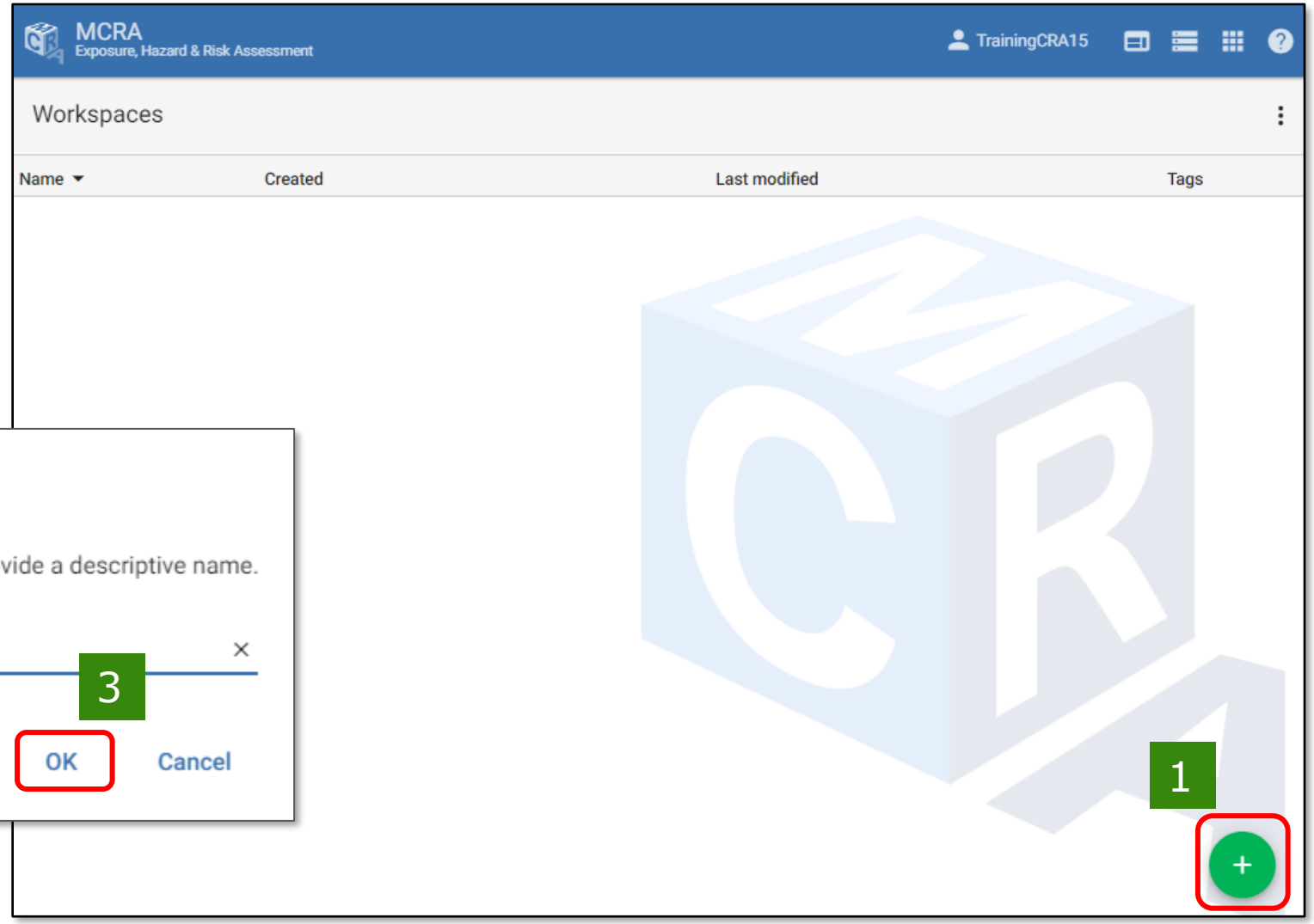
Welcome page of MCRA

https://mcra.rivm.nl/mcra/#/



Create a workspace

Workspaces can be used to separate dossiers/assessments



Create a standard action

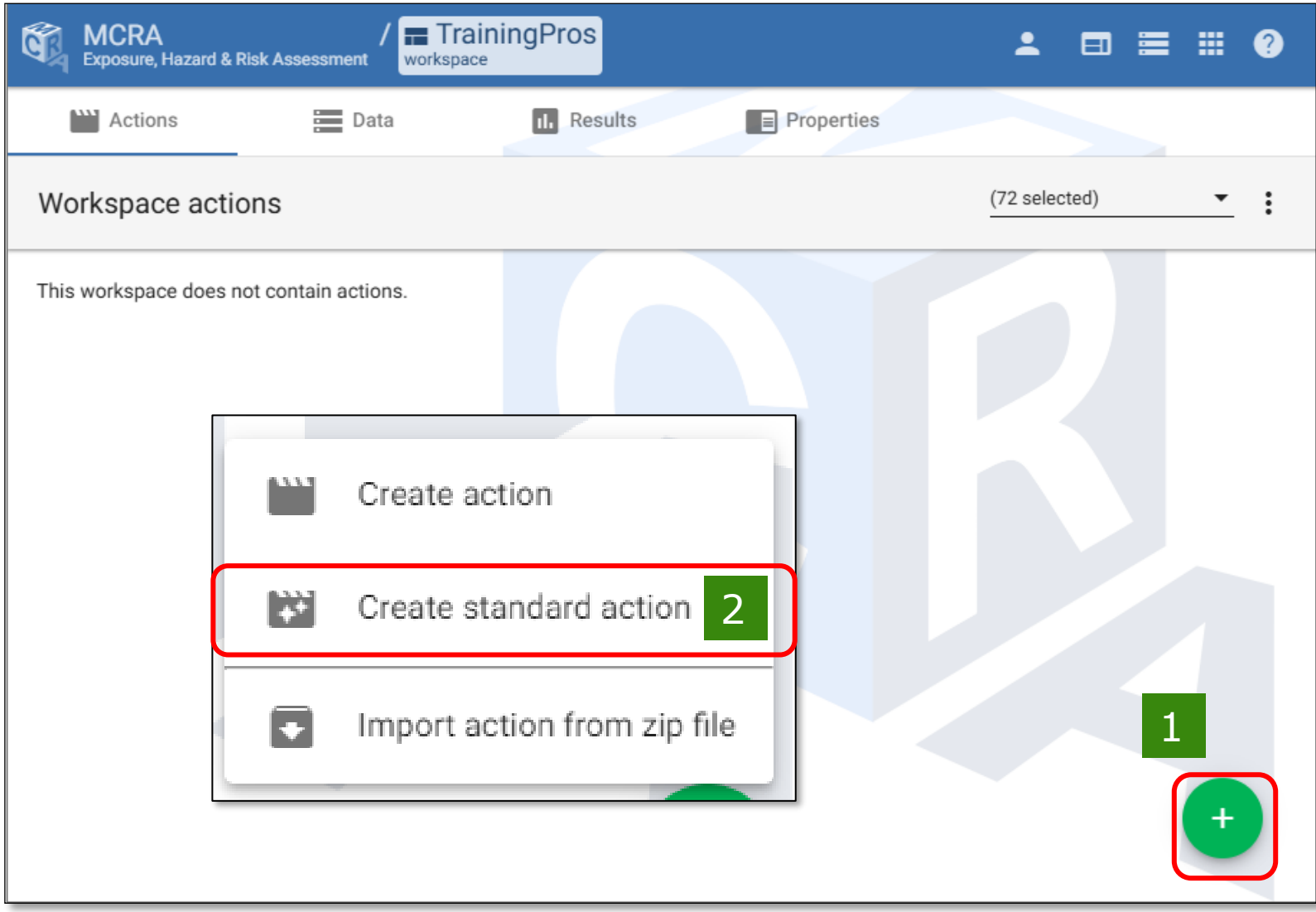
Actions can be used to separate different calculations within an assessment

Standard Regulatory Actions (SRA's) include the regulatory accepted methodology and are developed to:

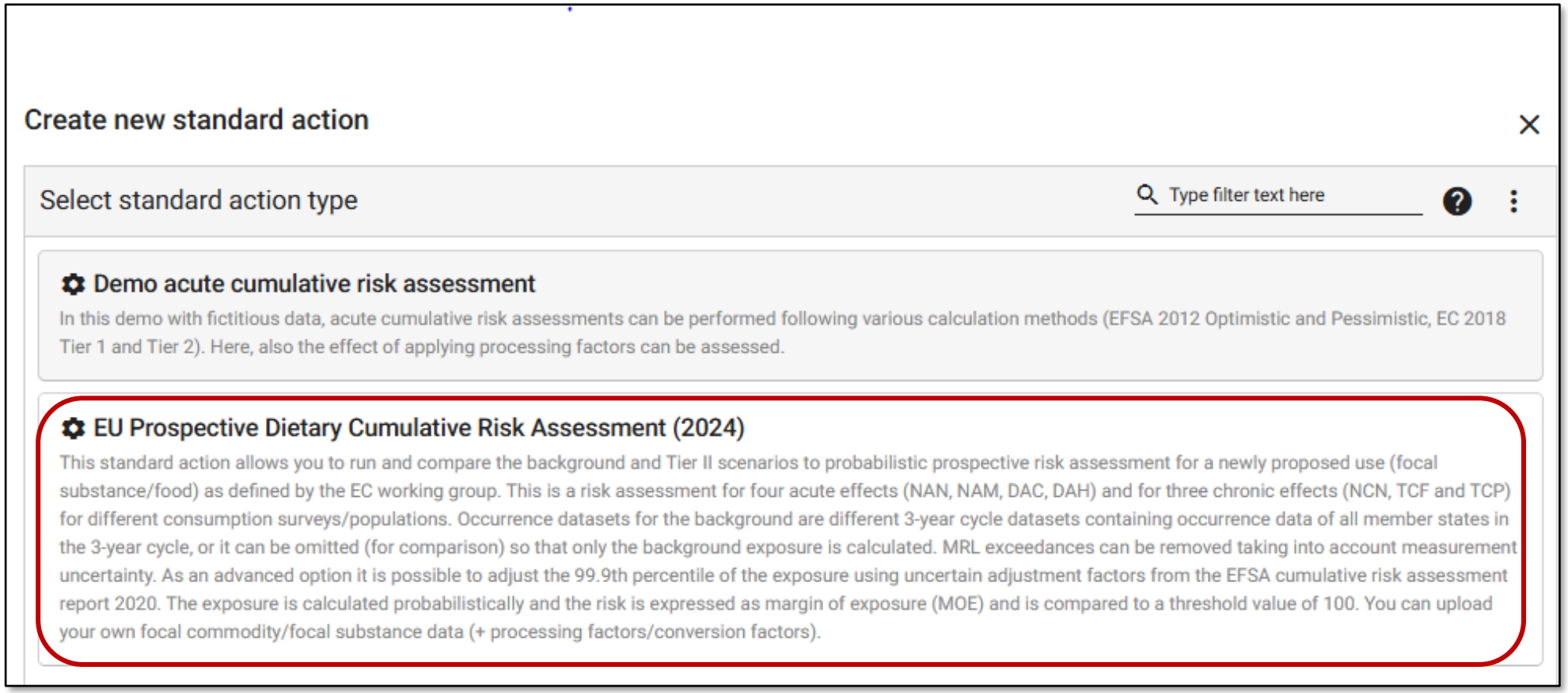
- Harmonize the assessment
- More user friendly
- Ease of assessment
- Automate assessments

SRAs are developed for:

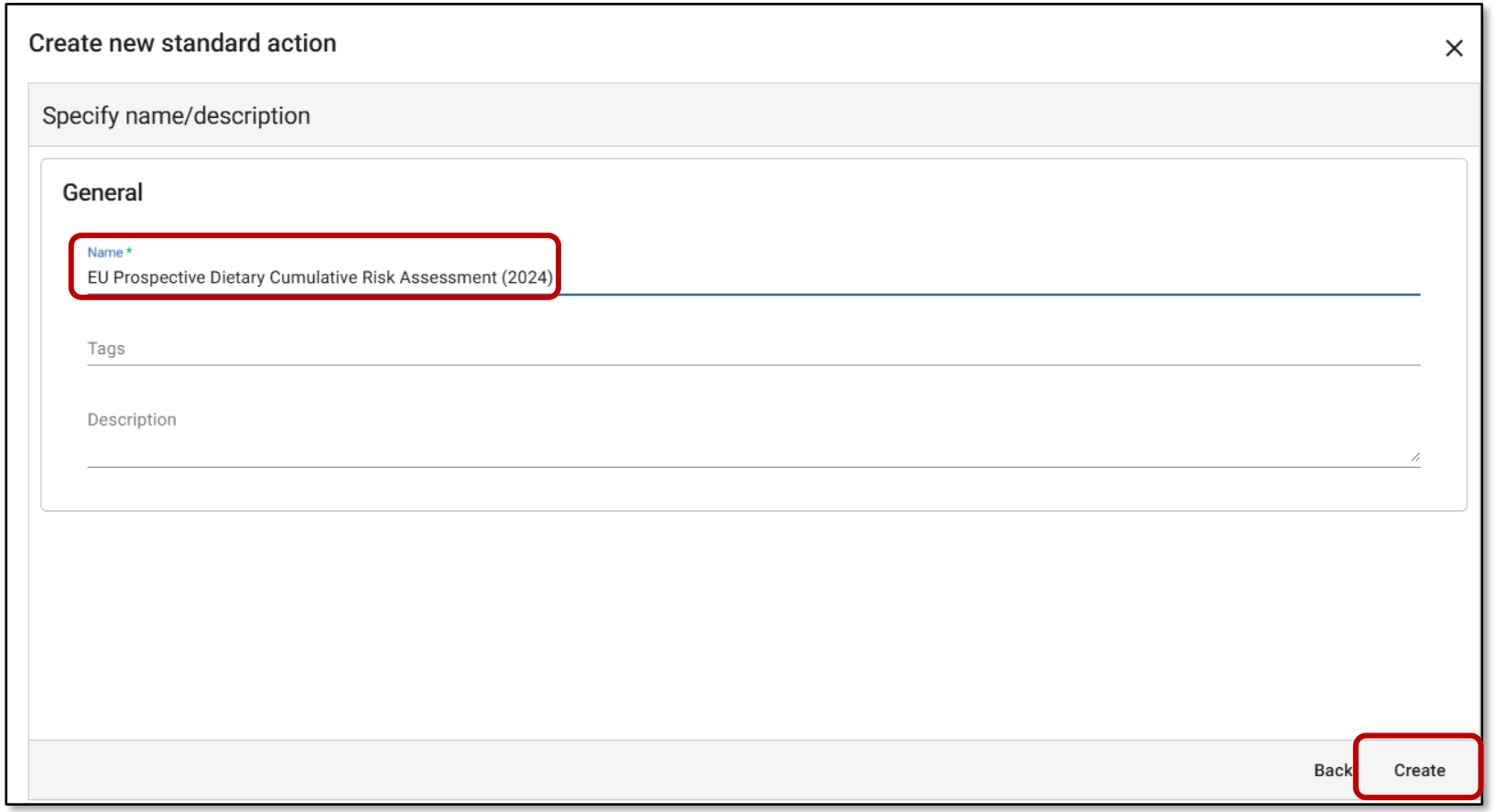
- Retrospective Cumulative Risk Assessments
- Prospective Cumulative Risk Assessments (under development)



Select methodology

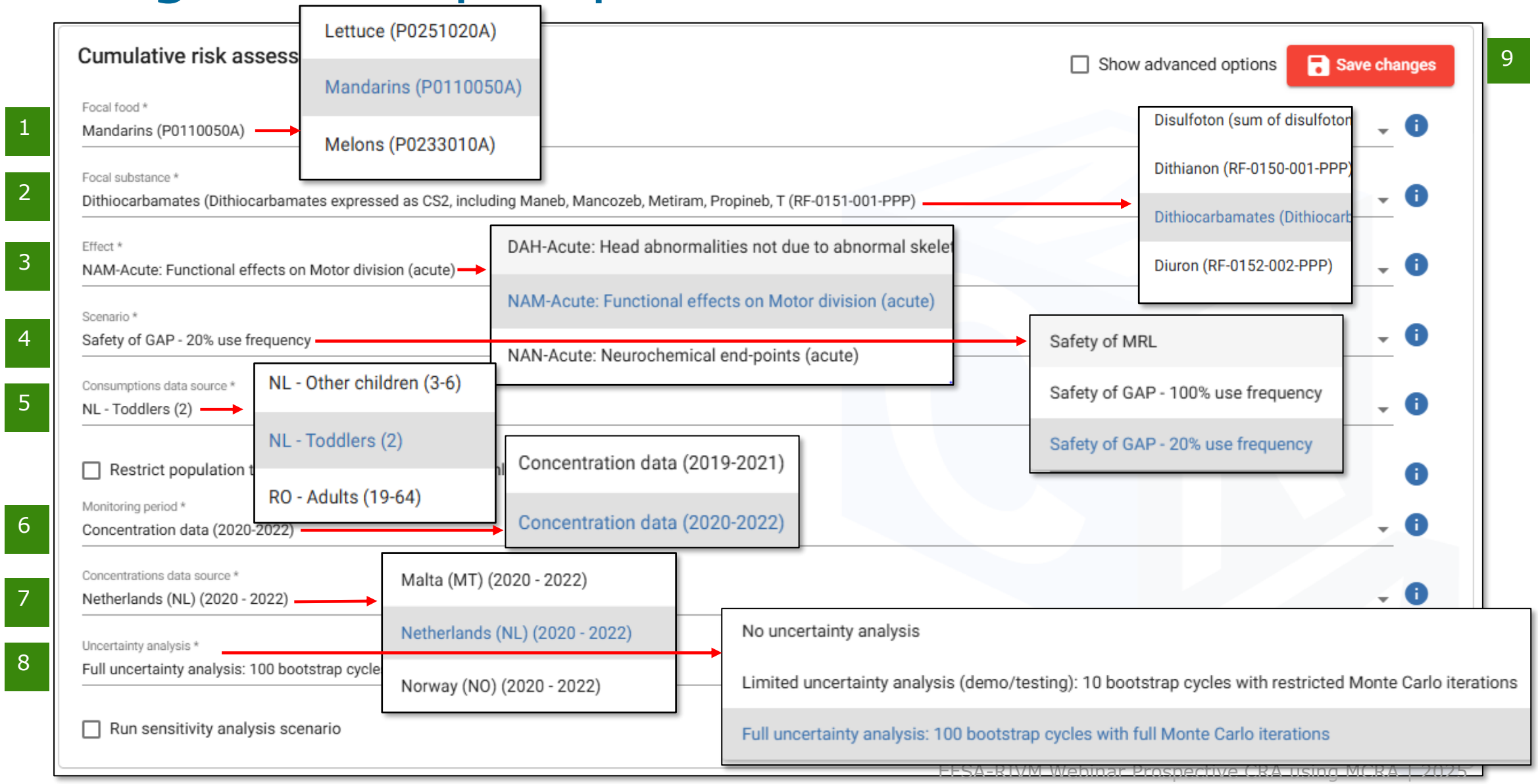


Give action a name



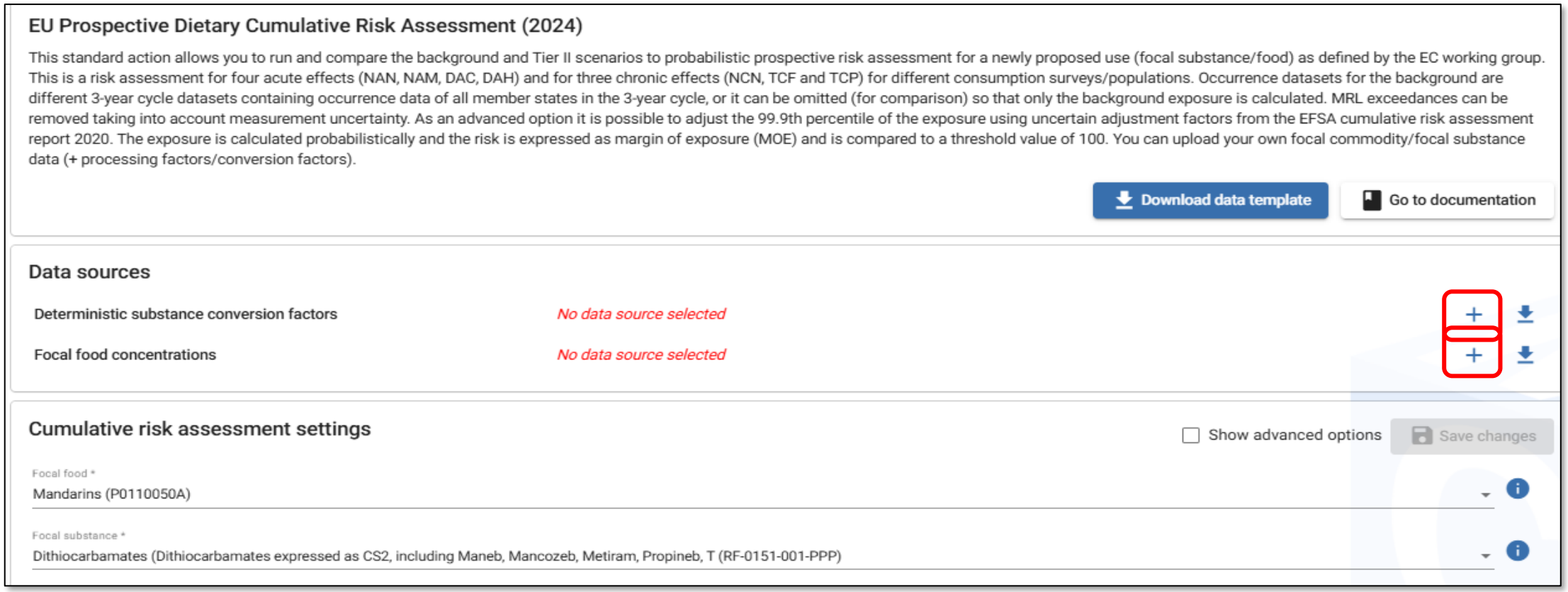
Note: These are example settings

Settings of the prospective SRA



Deterministic substance conversion factors are used to convert a RD to an active substance based on MW

Link the field trail data and deterministic substance conversion factors to the action



Data template after download

2

	A	B	C	D	E	F	G	H	I	J	K	L
1	labSampCode	prodCode	prodName	paramCode	paramName	sampY	resUnit	resLOD	resLOQ	resVal	resType	
2	Sample-01	prod X code	prod X	chemical Y code	chemical Y	2024	mg/kg		0.01		LOQ	
3	Sample-02	prod X code	prod X	chemical Y code	chemical Y	2024	mg/kg		0.01		LOQ	
4	Sample-03	prod X code	prod X	chemical Y code	chemical Y	2024	mg/kg		0.01		LOQ	
5	Sample-04	prod X code	prod X	chemical Y code	chemical Y	2024	mg/kg		0.01		LOQ	
6	Sample-05	prod X code	prod X	chemical Y code	chemical Y	2024	mg/kg		0.01		LOQ	
7	Sample-06	prod X code	prod X	chemical Y code	chemical Y	2024	mg/kg		0.01		LOQ	
8	Sample-07	prod X code	prod X	chemical Y code	chemical Y	2024	mg/kg		0.01		LOQ	
9	Sample-08	prod X code	prod X	chemical Y code	chemical Y	2024	mg/kg		0.01		LOQ	
10	Sample-09	prod X code	prod X	chemical Y code	chemical Y	2024	mg/kg		0.01		LOQ	
11	Sample-10	prod X code	prod X	chemical Y code	chemical Y	2024	mg/kg		0.01		LOQ	
12												
13												
14												
15												

1 ConcentrationsSSD DeterministicConversionFactors

2: Enter the results:
<loq : leave resVal empty, resType=LOQ,
>= loq : enter value is resVal, resType=VAL

1: ConcentrationsSSD: Worksheet were you enter results from field trial studies

Data template after download

	A	B	C	D	E	F	G
1	ParamCodeMeasuredSubstance	MeasuredSubstanceName	ParamCodeActiveSubstance	ActiveSubstanceName	idFood	FoodName	ConversionFactor
2	Residue definition of MeasuredSubstance code	Residue definition of MeasuredSubstance	ActiveSubstance 1 code	ActiveSubstance 1	idProd X	prod X	a
4	Residue definition of MeasuredSubstance code	Residue definition of MeasuredSubstance	ActiveSubstance 2 code	ActiveSubstance 2	idProd X	prod X	b
4	Residue definition of MeasuredSubstance code	Residue definition of MeasuredSubstance	ActiveSubstance 3 code	ActiveSubstance 3	idProd X	prod X	c
5	Residue definition of MeasuredSubstance code	Residue definition of MeasuredSubstance	ActiveSubstance 4 code	ActiveSubstance 4	idProd X	prod X	d
6	Residue definition of MeasuredSubstance code	Residue definition of MeasuredSubstance	ActiveSubstance 5 code	ActiveSubstance 5	idProd X	prod X	e
7	Residue definition of MeasuredSubstance code	Residue definition of MeasuredSubstance	ActiveSubstance 6 code	ActiveSubstance 6	idProd X	prod X	f
8							
9							
10							
11							
12							
13							
14							
15							

4

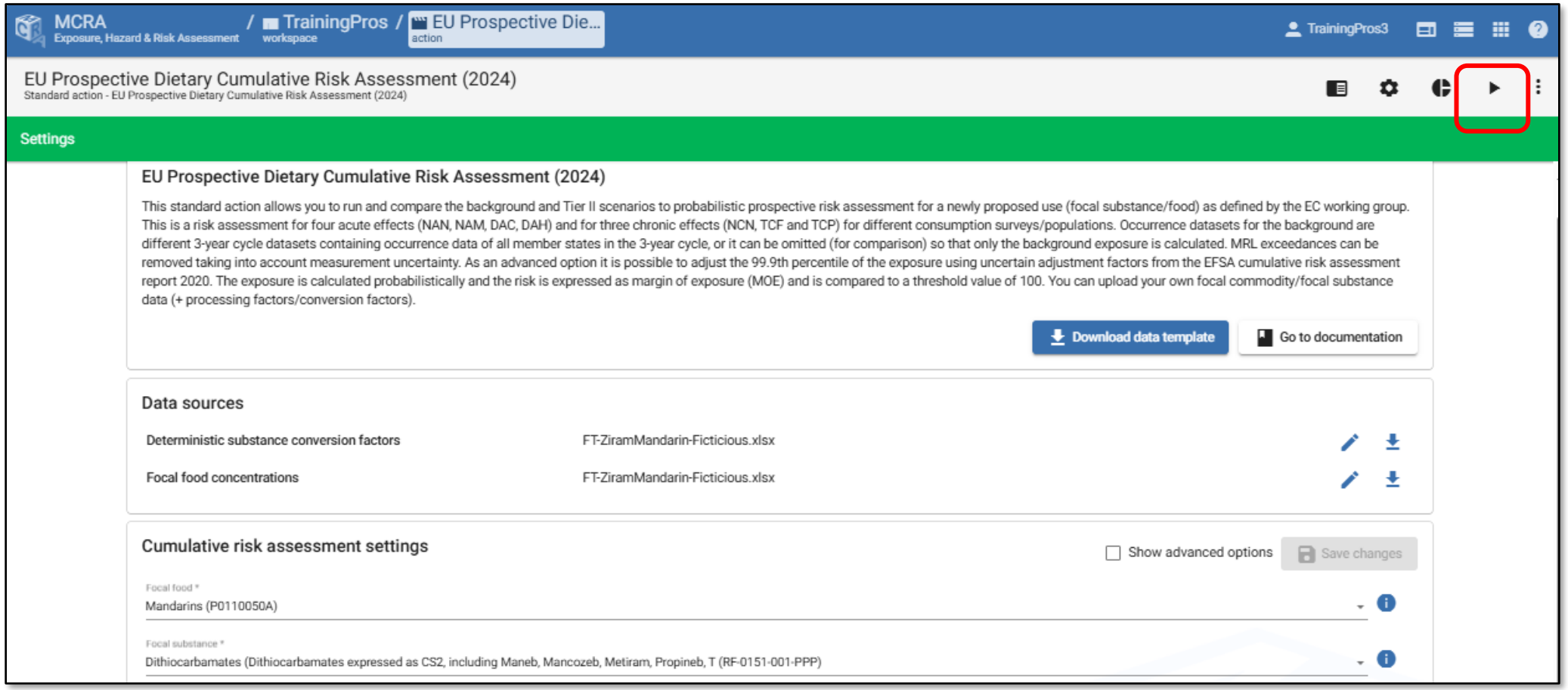
4: DeterministicConversionFactors: Factor (MW) to calculate Measured Substance to Active Substance.

5: Delete all ActiveSubstances other than the one of interest

ConcentrationsS 3 DeterministicConversionFactors

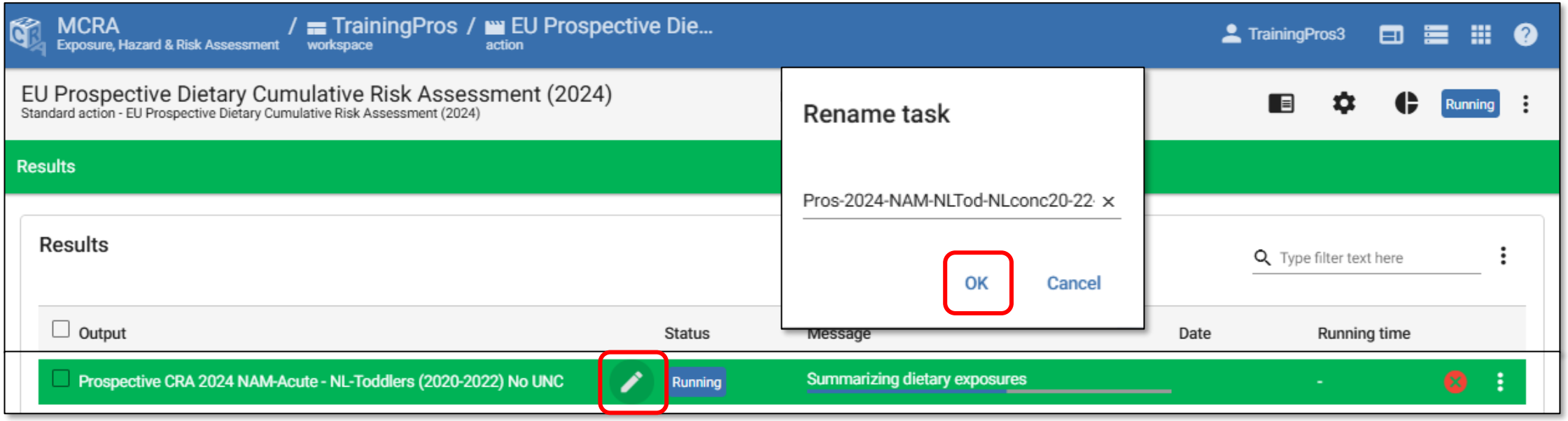
Note: These are example settings

Run the action



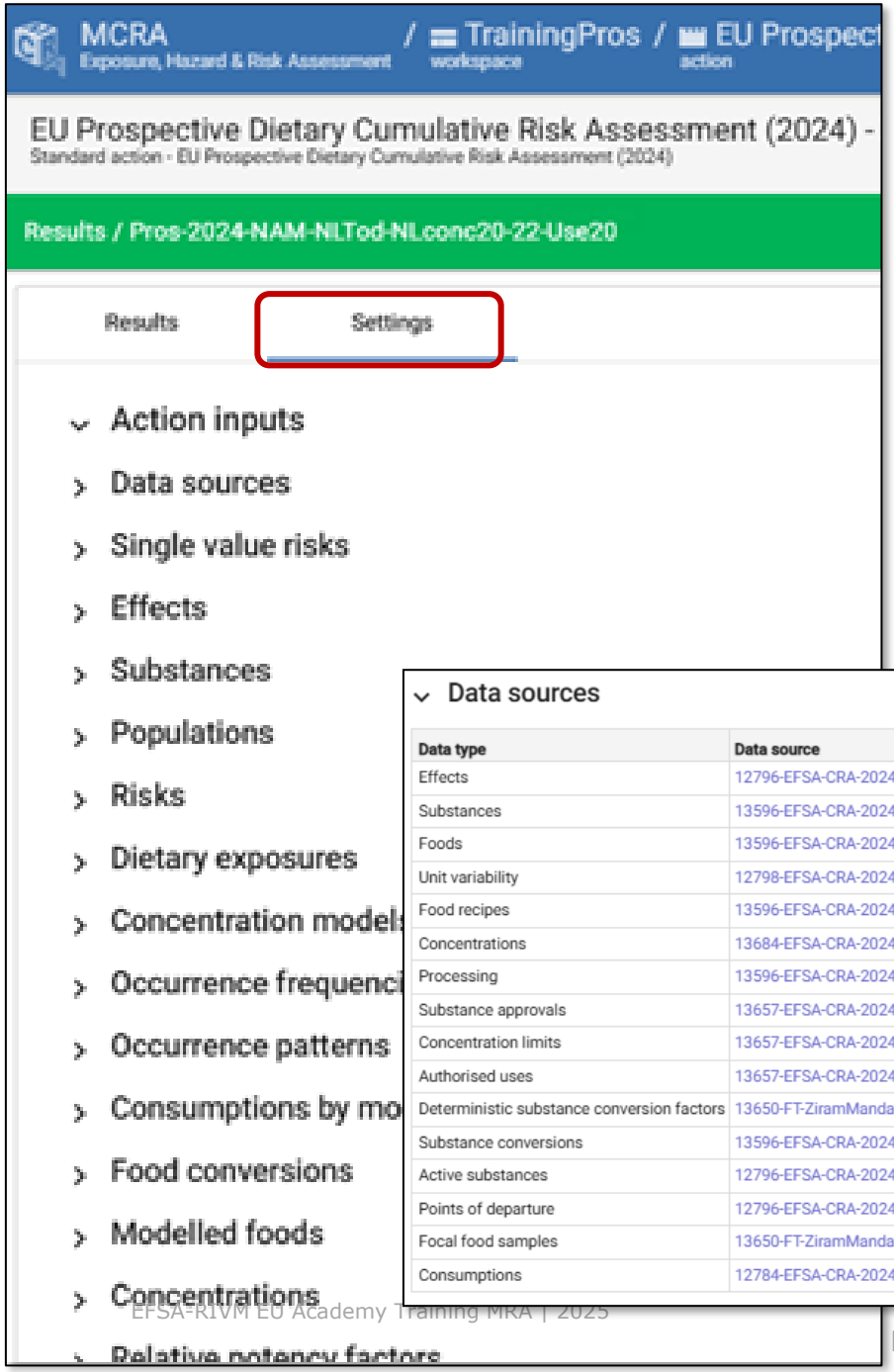
Note: These are example settings

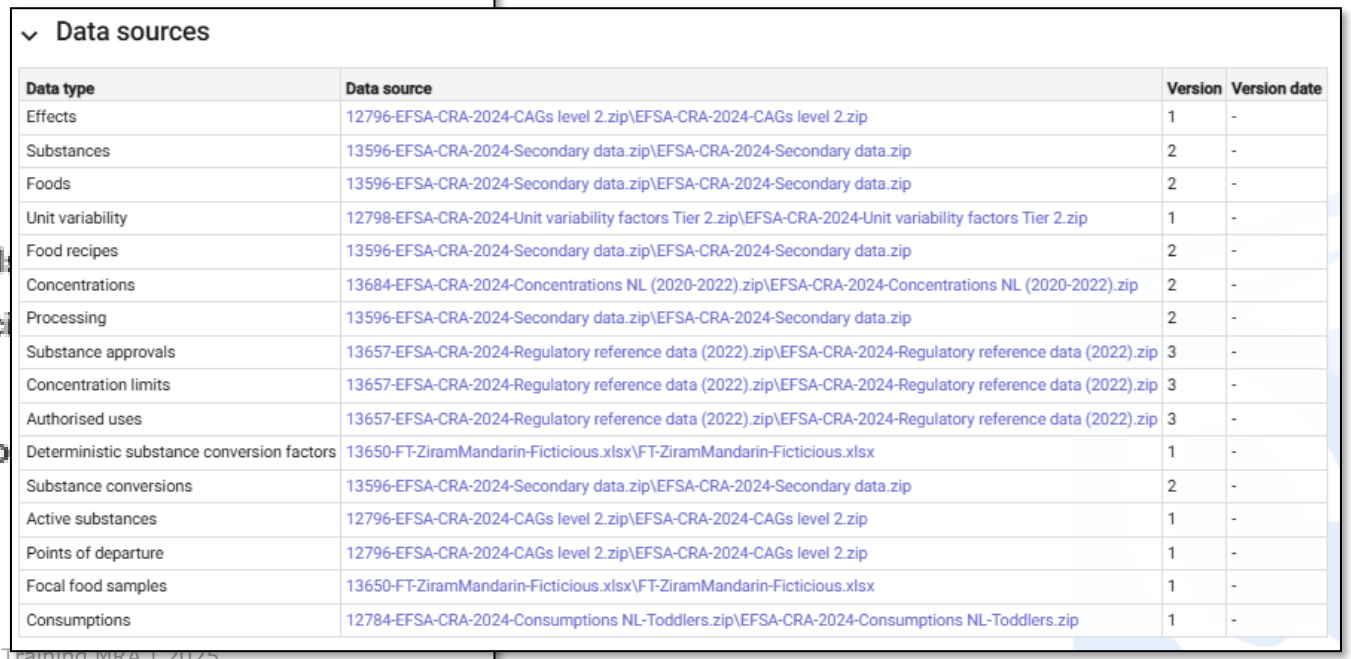
Rename and wait for the calculation to finish



Results pages

- Tabs for *Results* and *Settings*
  - *The Results tab provides output on →*





Data sources

Data type	Data source	Version	Version date
Effects	12796-EFSA-CRA-2024-CAGs level 2.zip\EFSA-CRA-2024-CAGs level 2.zip	1	-
Substances	13596-EFSA-CRA-2024-Secondary data.zip\EFSA-CRA-2024-Secondary data.zip	2	-
Foods	13596-EFSA-CRA-2024-Secondary data.zip\EFSA-CRA-2024-Secondary data.zip	2	-
Unit variability	12798-EFSA-CRA-2024-Unit variability factors Tier 2.zip\EFSA-CRA-2024-Unit variability factors Tier 2.zip	1	-
Food recipes	13596-EFSA-CRA-2024-Secondary data.zip\EFSA-CRA-2024-Secondary data.zip	2	-
Concentrations	13684-EFSA-CRA-2024-Concentrations NL (2020-2022).zip\EFSA-CRA-2024-Concentrations NL (2020-2022).zip	2	-
Processing	13596-EFSA-CRA-2024-Secondary data.zip\EFSA-CRA-2024-Secondary data.zip	2	-
Substance approvals	13657-EFSA-CRA-2024-Regulatory reference data (2022).zip\EFSA-CRA-2024-Regulatory reference data (2022).zip	3	-
Concentration limits	13657-EFSA-CRA-2024-Regulatory reference data (2022).zip\EFSA-CRA-2024-Regulatory reference data (2022).zip	3	-
Authorised uses	13657-EFSA-CRA-2024-Regulatory reference data (2022).zip\EFSA-CRA-2024-Regulatory reference data (2022).zip	3	-
Deterministic substance conversion factors	13650-FT-ZiramMandarin-Ficticious.xlsx\FT-ZiramMandarin-Ficticious.xlsx	1	-
Substance conversions	13596-EFSA-CRA-2024-Secondary data.zip\EFSA-CRA-2024-Secondary data.zip	2	-
Active substances	12796-EFSA-CRA-2024-CAGs level 2.zip\EFSA-CRA-2024-CAGs level 2.zip	1	-
Points of departure	12796-EFSA-CRA-2024-CAGs level 2.zip\EFSA-CRA-2024-CAGs level 2.zip	1	-
Focal food samples	13650-FT-ZiramMandarin-Ficticious.xlsx\FT-ZiramMandarin-Ficticious.xlsx	1	-
Consumptions	12784-EFSA-CRA-2024-Consumptions NL-Toddlers.zip\EFSA-CRA-2024-Consumptions NL-Toddlers.zip	1	-

Results pages

- Tabs for *Results* and *Settings*
  - *The Settings tab provides output on →*

- *Settings* info on:
  - Data sources
  - All settings

Note: This is a demo using fake data

Results of a **fictive assessment**

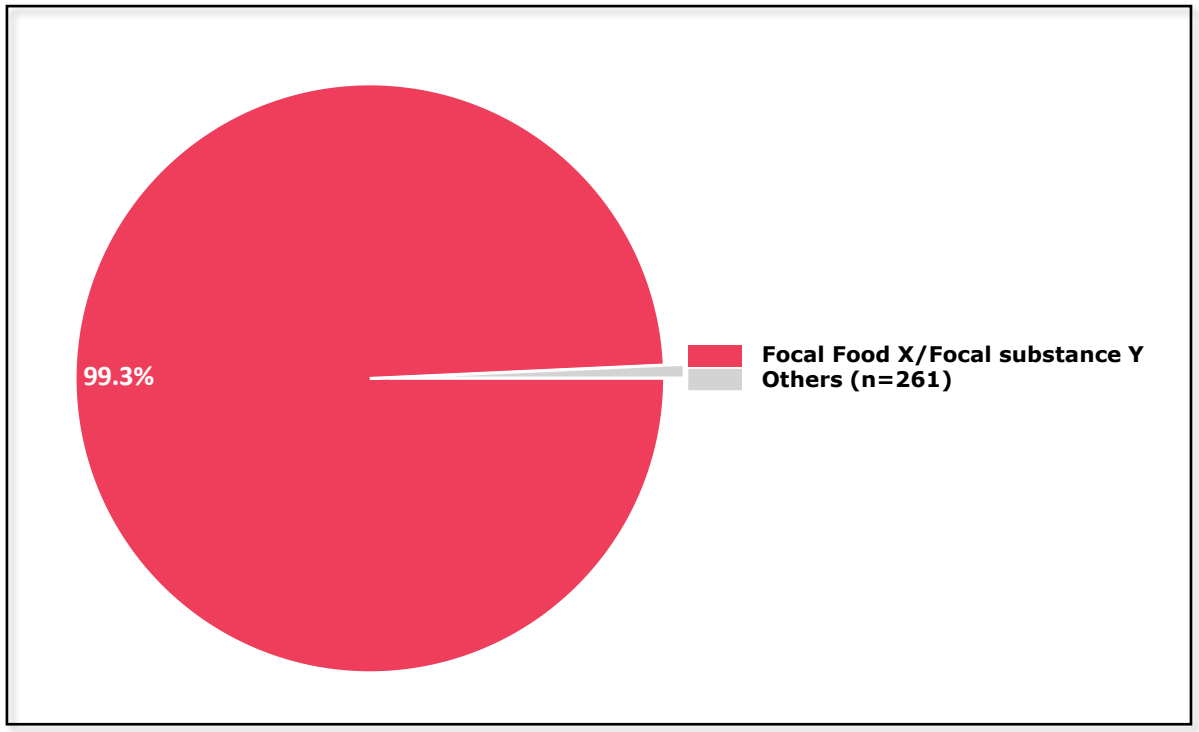
Risk characterisation ratio (H/E) = MOET

Risk characterisation ratio distribution percentiles.

Percentage	Percentage risk distribution	Risk characterisation ratio (H/E)
50.00	50.00	9812
90.00	10.00	973.9
95.00	5.00	264.3
99.00	1.00	74.46
99.90	0.10	25.95
99.99	0.01	18.63

Threshold of regulatory concideration = MOET at 99.9th percentile < 100

Food/substance combinations contributing most to the risk

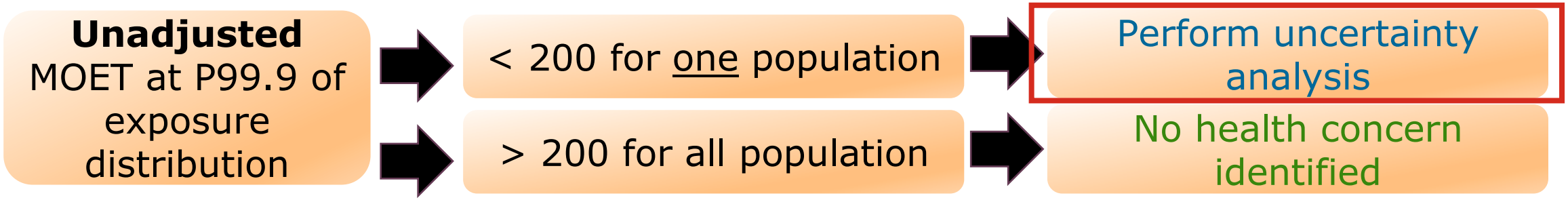


Conclusions of this **fictive assessment**

- Results (fictive):

Unadjusted MOET at P99.9 for one population (NL toddlers) = 26

- Please recall:

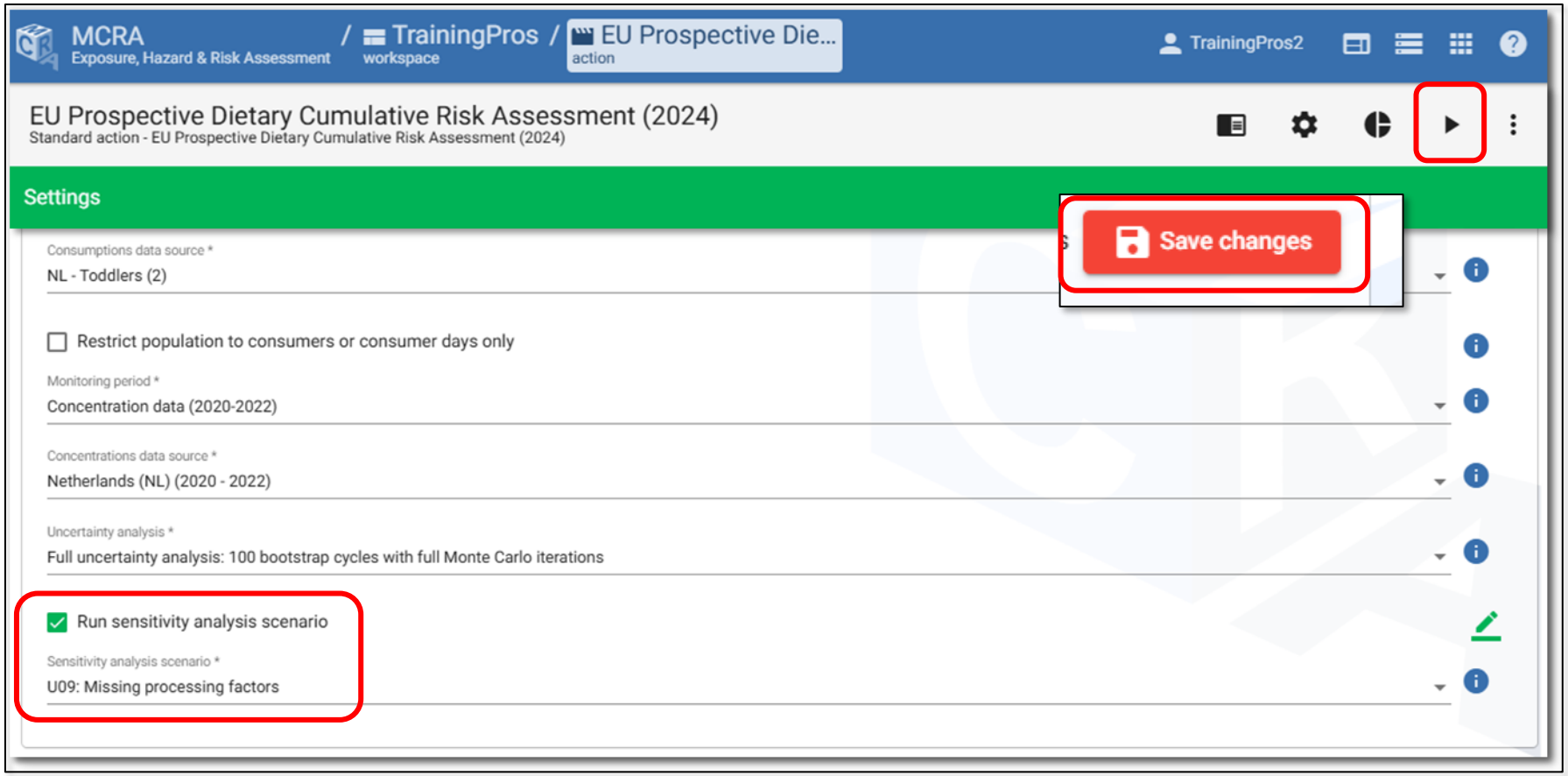


- Conclusion: Uncertainty analysis is needed

Note: These are example settings

Run sensitivity analysis

- Only available for missing processing factors (at the moment)



Reminder: still demo using fictional data

Comparison of these **fictive assessments**

Nominal run

Risk characterisation ratio distribution percentiles.

Percentage	Percentage risk distribution	Risk characterisation ratio (H/E)
50.00	50.00	9784
90.00	10.00	973.8
95.00	5.00	264.3
99.00	1.00	74.46
99.90	0.10	25.95
99.99	0.01	18.63

With PF sensitivity analysis

Risk characterisation ratio distribution percentiles.

Percentage	Percentage risk distribution	Risk characterisation ratio (H/E)
50.00	50.00	1.472E+04
90.00	10.00	6190
95.00	5.00	4328
99.00	1.00	2054
99.90	0.10	821.2
99.99	0.01	353.7

Reminder: still demo using fictional data

Conclusions of these **fictive assessments**

- Results (fictive): **Unadjusted** MOET at P99.9 for one population (NL toddlers) = 26, but **adjusted** MOET for missing PF at P99.9 for the same population = 821

- Please recall:

Adjusted MOET at P99.9 of exposure distribution with reverence population MF	> 200 for <u>all</u> populations	No additional analysis needed
	< 200 for <u>one</u> population	Perform uncertainty analysis for specific population
Adjusted MOET at P99.9 of exposure distribution with specific or reference population MF	> 100 for <u>all</u> populations	No health concern identified
	< 100 for <u>one</u> population	Health risk cannot be excluded

- In this example no health concern is identified
  - When this is the case for all populations – since we only tested 1
  - Only one uncertainty is tested – EFSA's cookbook

Regulatory users are being trained

Training of implemented methodology to SCoPAFF members the 23rd of May

Trainings to facilitate use of MCRA for CRA

- Food safety authorities responsible for enforcing MRLs trained on respective CRA (28 European Countries)
- EC and Competent authorities responsible for the approval of new pesticides trained on prospective CRA (23 European Countries)
- Followed by 132 participants from >22 European Countries
- Yearly EFSA training to discuss further development of methods

Training 2024	Date	No. participants	No. European countries
Beginner - Retrospective CRA	25-03-2024	34	28
	07-06-2024	26	
Advanced - Retrospective CRA	30-04-2024	28	22
Prospective CRA	02-05-2024	23	23
	10-06-2024	21	

Concluding remarks

- Methodology CRA for dietary exposure is nearby regulatory acceptance
- EFSA develops ProsCRA cookbook
- EFSA and RIVM are supporting practical implementation of CRA via the MCRA software
- Regulatory users have been trained using MCRA and will receive follow-up training on prospective CRA
- In the next year, training for 3rd party stakeholders is foreseen

Thank you for your attention

EFSA-RIVM Framework Partnership

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Anne.Zwartsen@rivm.nl

https://mcra.rivm.nl/mcra/#/

Q&A

Bruno Dujardin, EFSA

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The **recording** and **presentations** from this webinar will be made available on EFSA's website in the coming days

Please take a few minutes to complete the **satisfaction survey** that you will receive by email

Replies to **unanswered questions** will be available on EFSA's website in the coming days

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