



WEBINAR ON THE OPEN MCRA TOOL FOR PROSPECTIVE CUMULATIVE RISK ASSESSMENT

STARTING AT 09:30 (CEST)

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



This event is **being recorded** and the recording will be published on EFSA's website



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



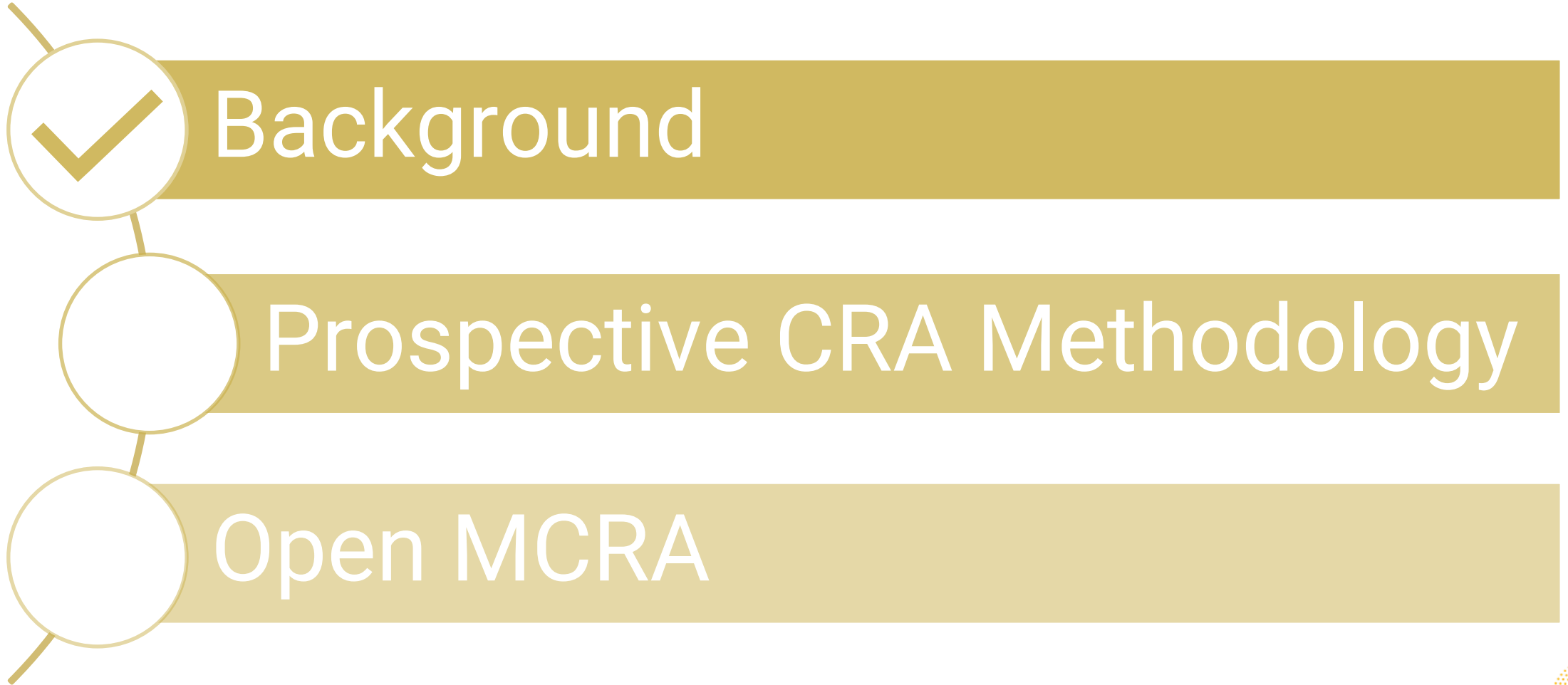


Cumulative risk assessment of pesticide residues: An Overview

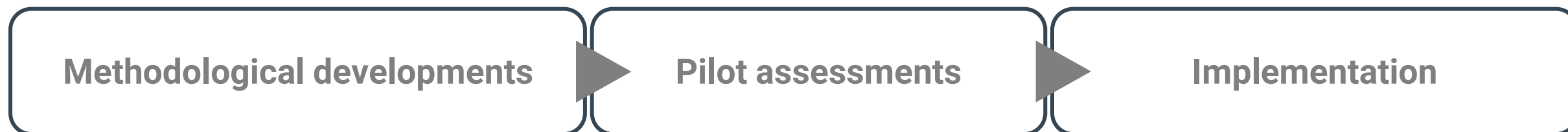
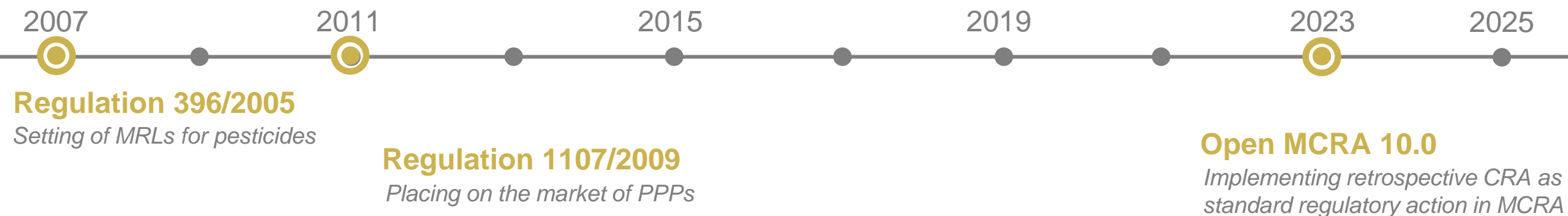
Angelo Cafaro, EFSA



OVERVIEW



BACKGROUND

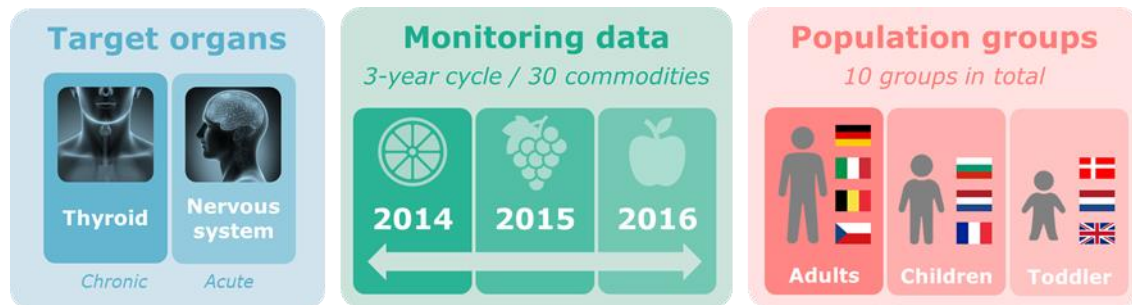


"...take into account known cumulative and synergistic effects of pesticides when the methods are available..."



RETROSPECTIVE CRA, SO FAR...

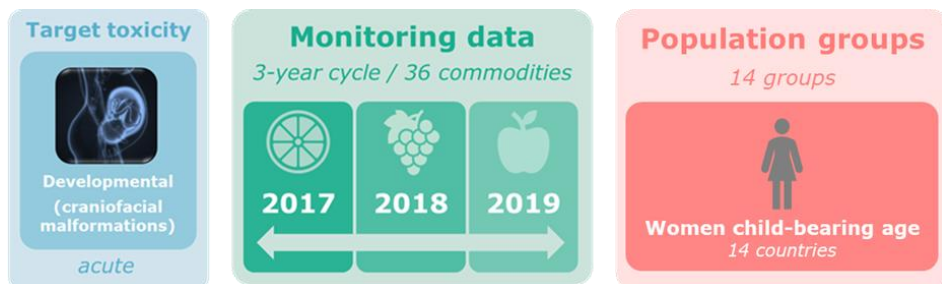
Pilot assessment



2019

2020

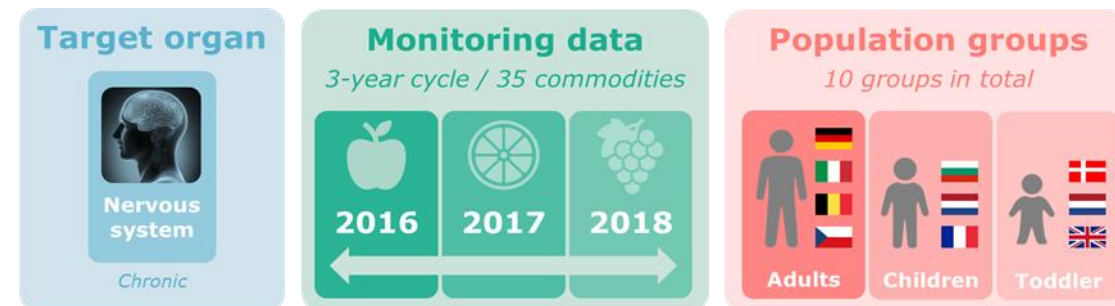
Cranio-facial malformations



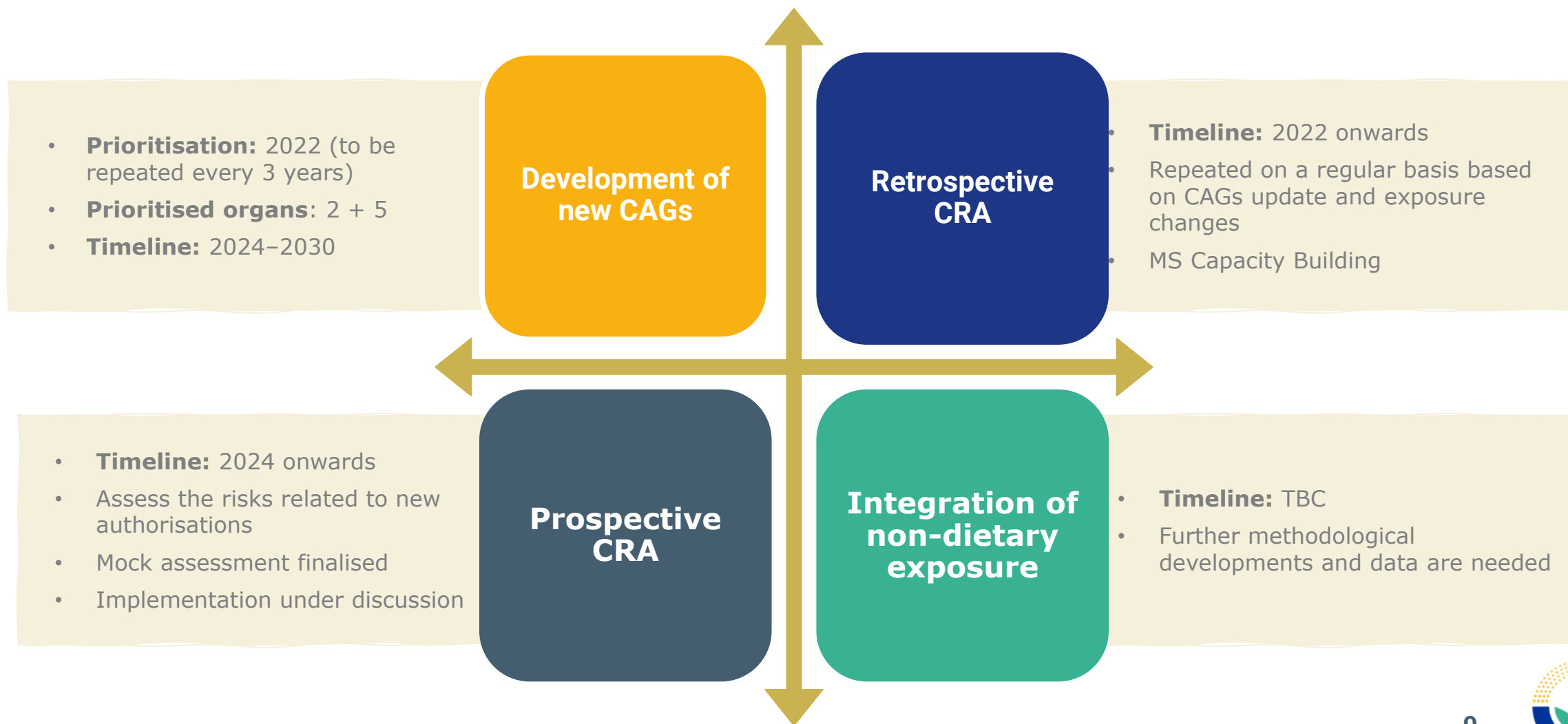
2021

2022

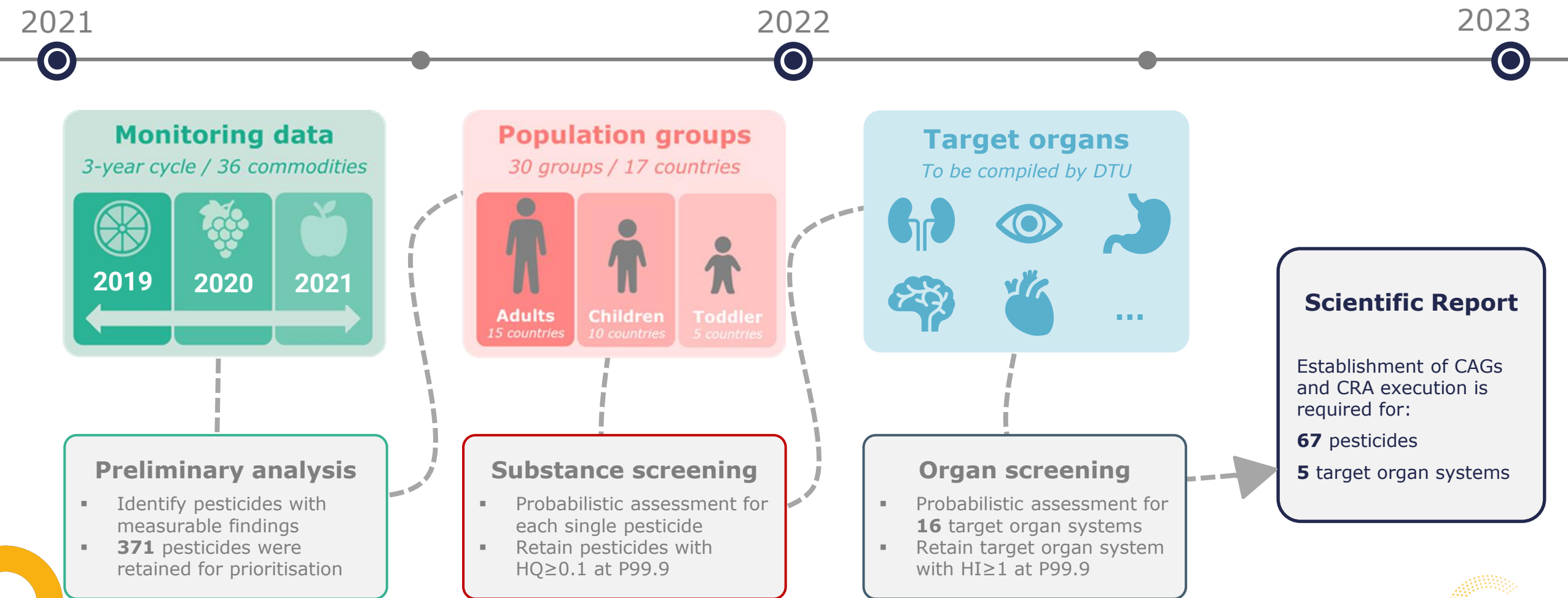
Chronic AChE inhibition



EFSA-SANTE ACTION PLAN



CRA PRIORITISATION



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)

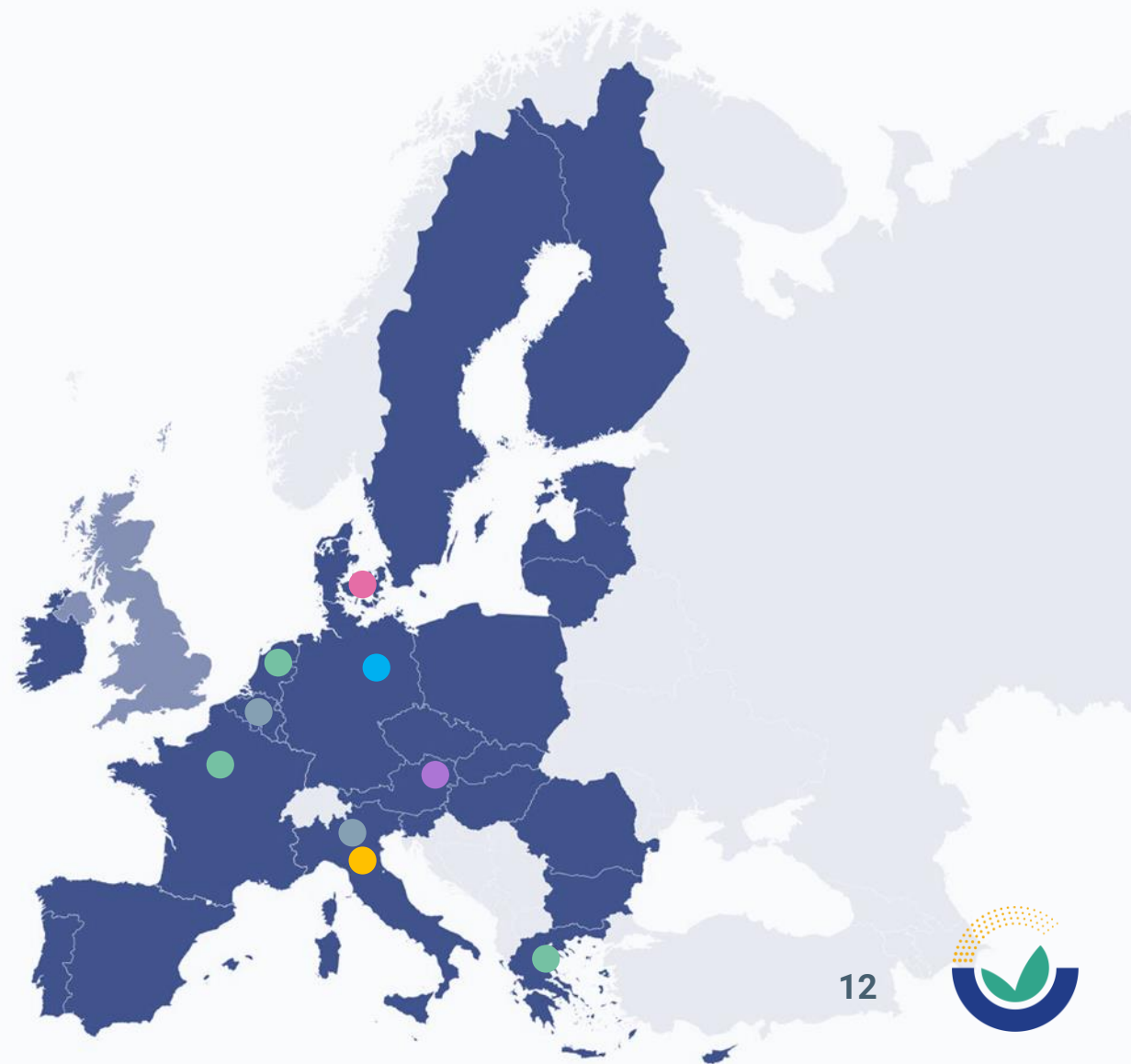


Developmental toxicity and haematopoietic system toxicity: Ongoing (WG identification of specific effects)

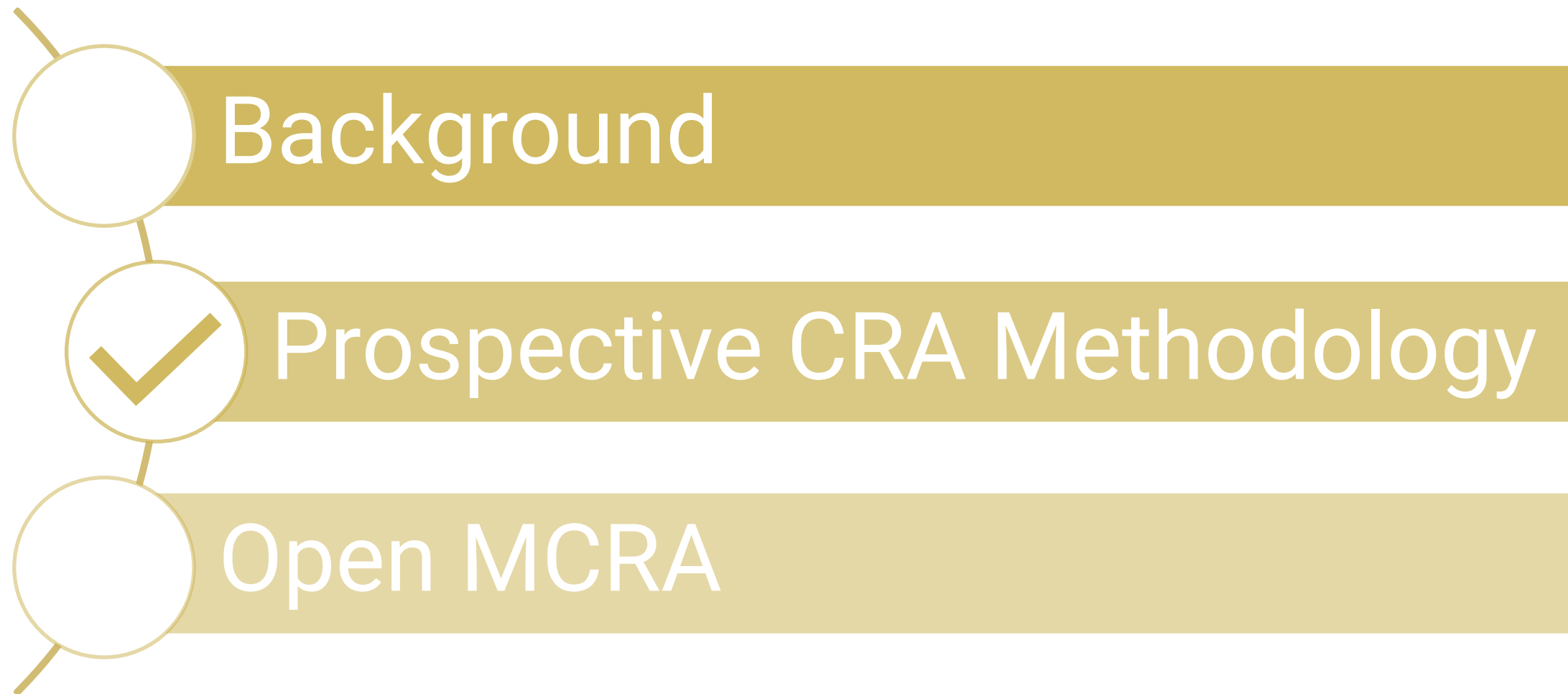
+ CRA update every 3 years for organs already assessed



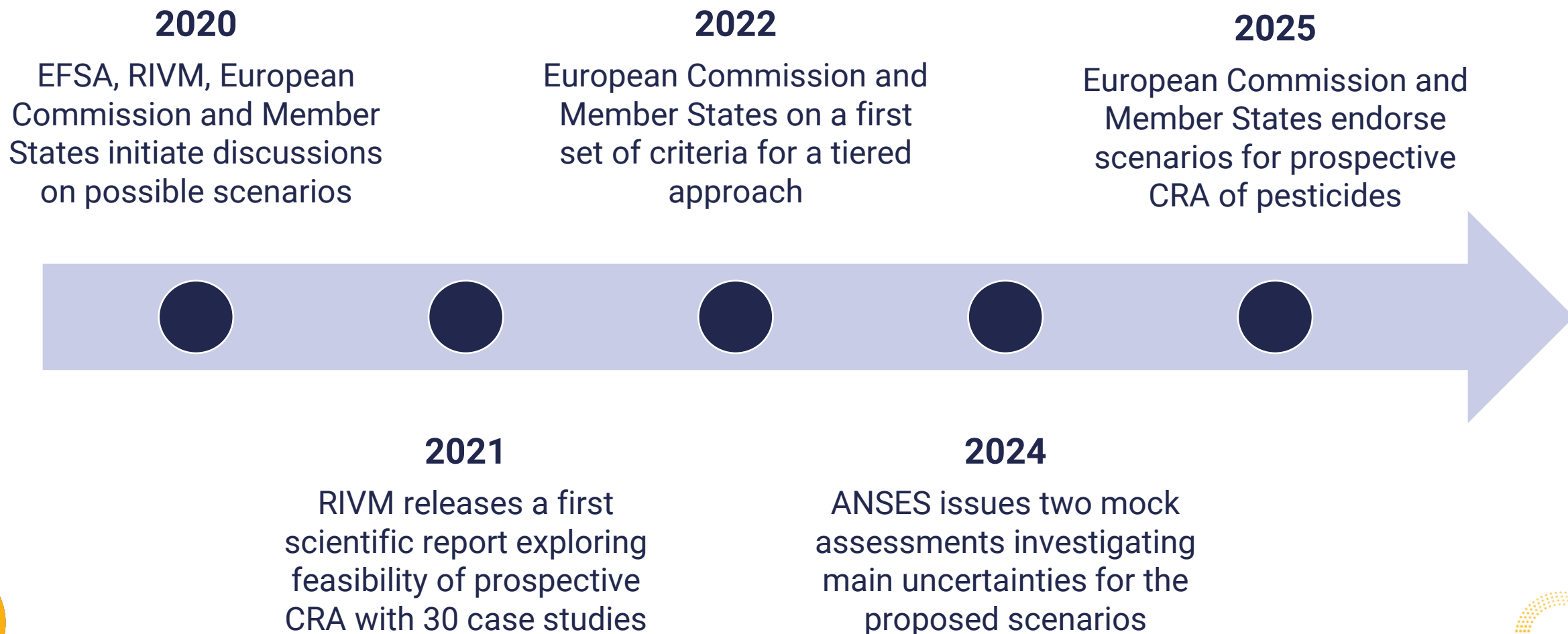
EU CAPACITY BUILDING ON CRA OF PESTICIDES



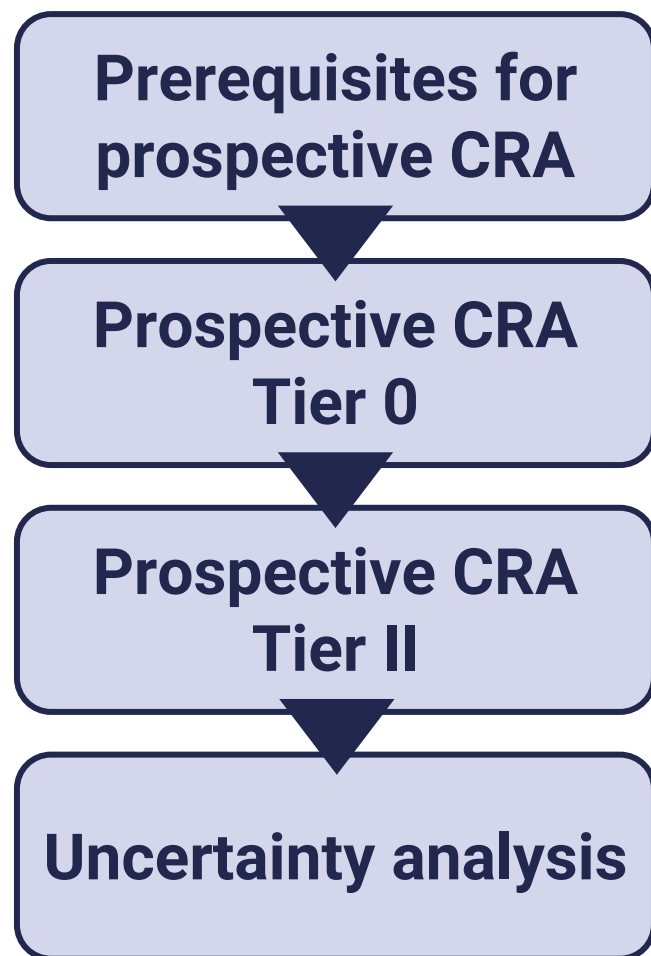
OVERVIEW



PROSPECTIVE CRA - TIMELINES



PROSPECTIVE CRA – TIERED APPROACH



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

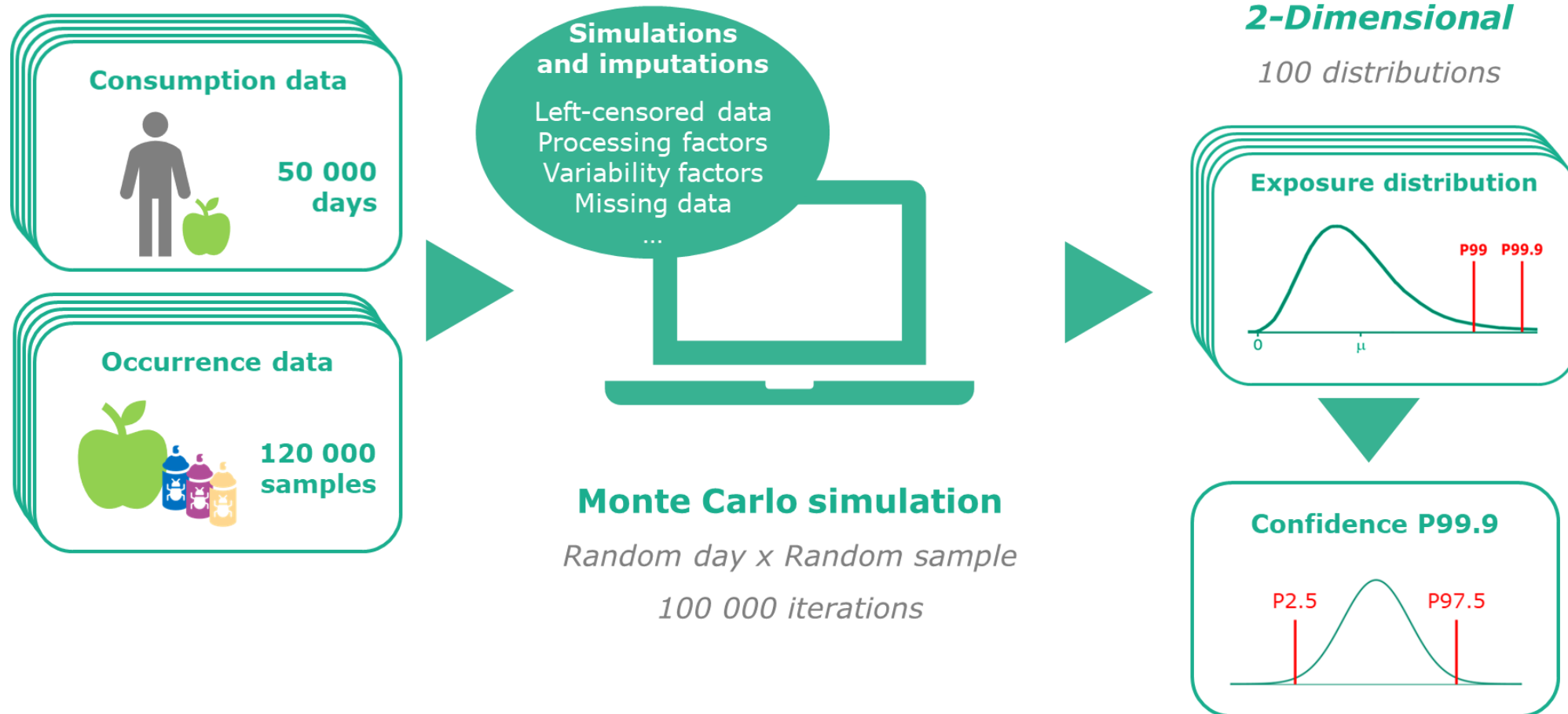
Important notes:

- 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., $IESTI \leq 100\%$ ARfD or $IEDI \leq 100\%$ ADI).
- Tier I scenario was removed during the elaboration process as it was not demonstrated to be effective.



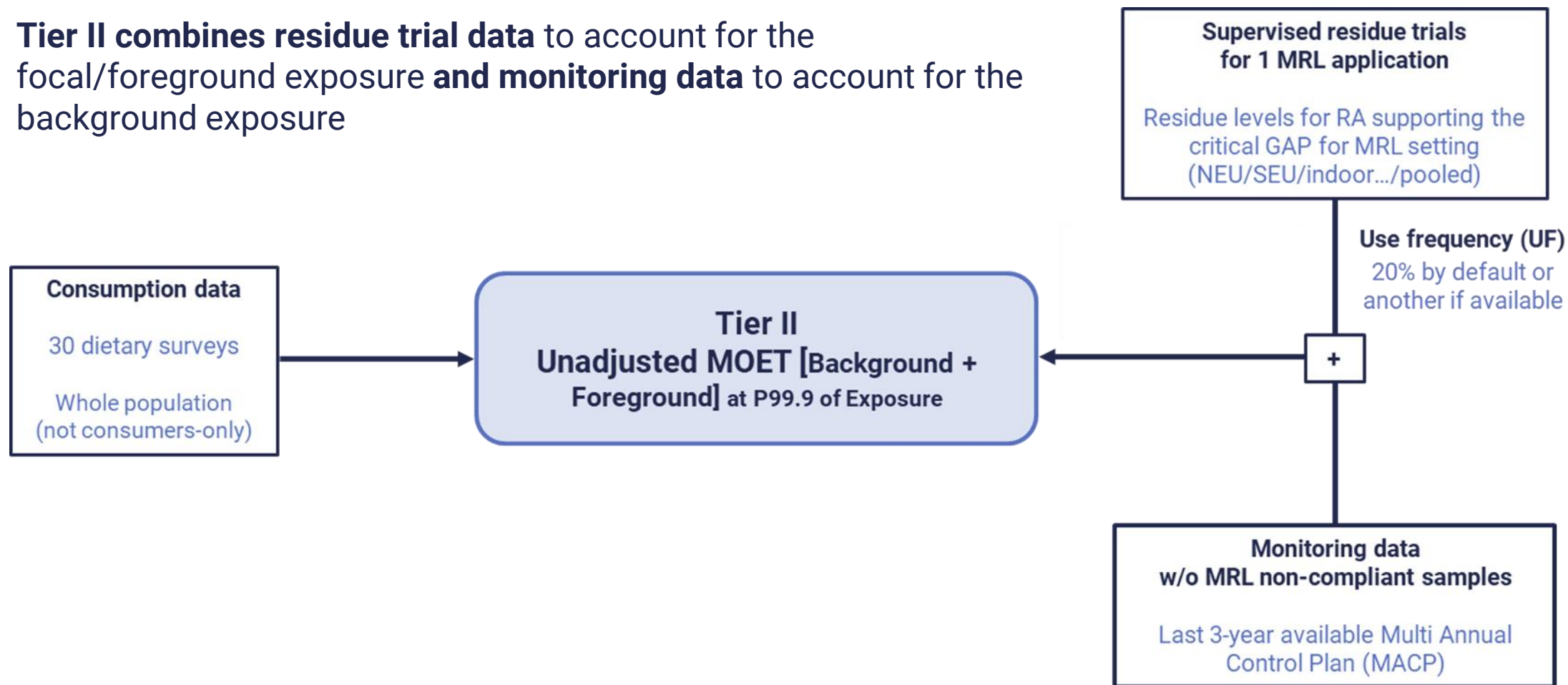
TIER II – BASIC PRINCIPLES

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

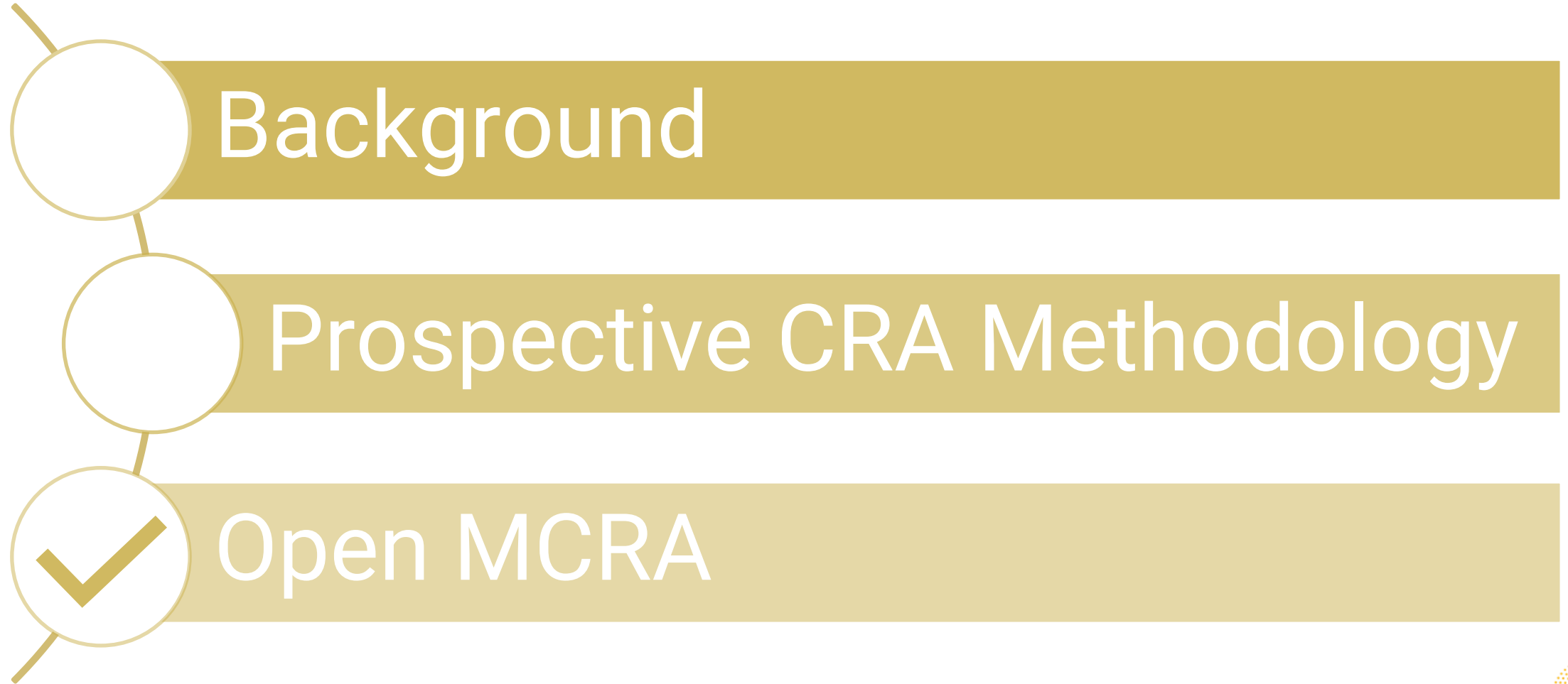


TIER II - FINAL SCENARIO

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



OVERVIEW

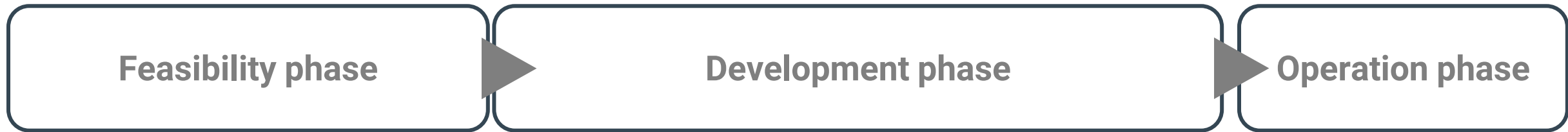
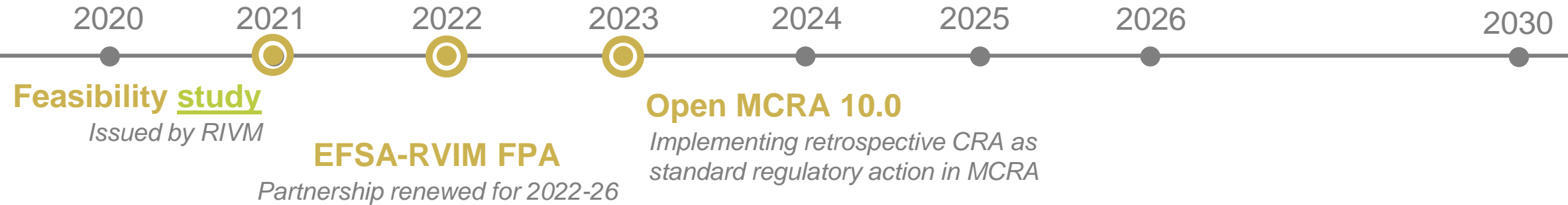


MONTE-CARLO RISK ASSESSMENT (MCRA) PLATFORM



- 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)

Standard regulatory actions

1. Regulatory method (RM)

- Uniquely identifiable by name and defining article
- Detailed definition of methodology and structure of inputs and outputs
- One or more validation test cases

Implementation RM EFSA 2022 dietary CRA

- Implementation in SAS
- Implementation in MCRA

2. SRA definition

- Defined for specific RM with specification of the fixed inputs (data, settings) and which inputs can be freely chosen by the user
- Depending on governance choices there will be few or many SRAs per RM

3. SRA implementation

- Implemented in MCRA for specific SRA definition
- Specification of the presentation of the results, extra outputs possible
- Linked to a corresponding MCRA full action
- Used for validation of the MCRA implementation for the RM tests cases

Implementation/application SRA acute dietary CRA craniofacial alterations


- Running with SAS
- Running with MCRA
 - Core
 - Web
 - SA



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:

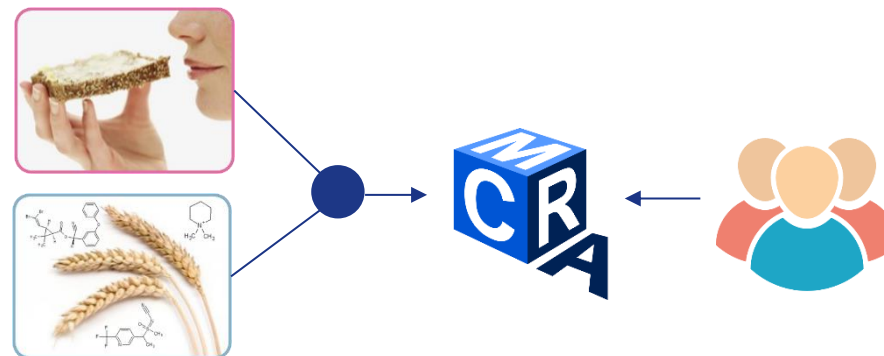
- Relevant EFSA networks (2023, 2024 and 2025).
- DG SANTE staff, e-working group, SCoPAFF member and/or appointed experts (May 2023).



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



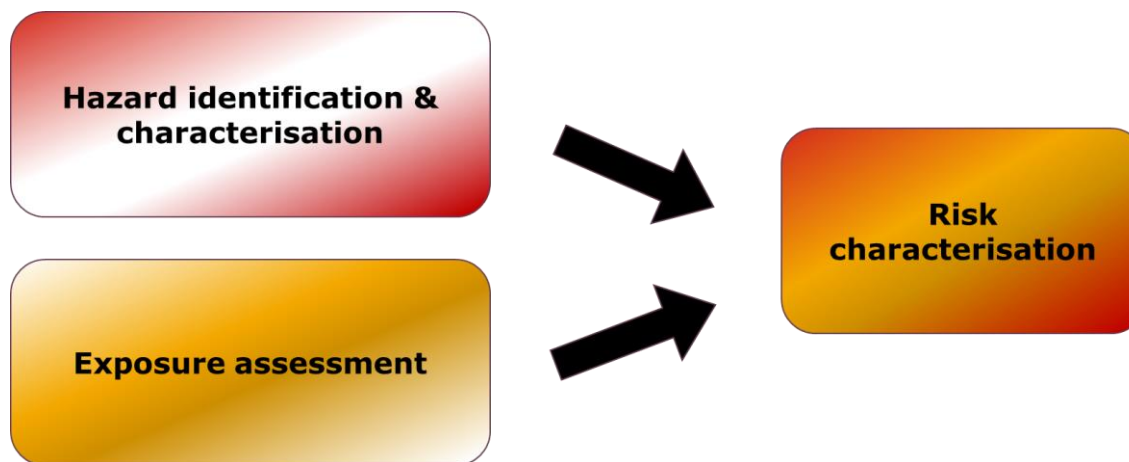
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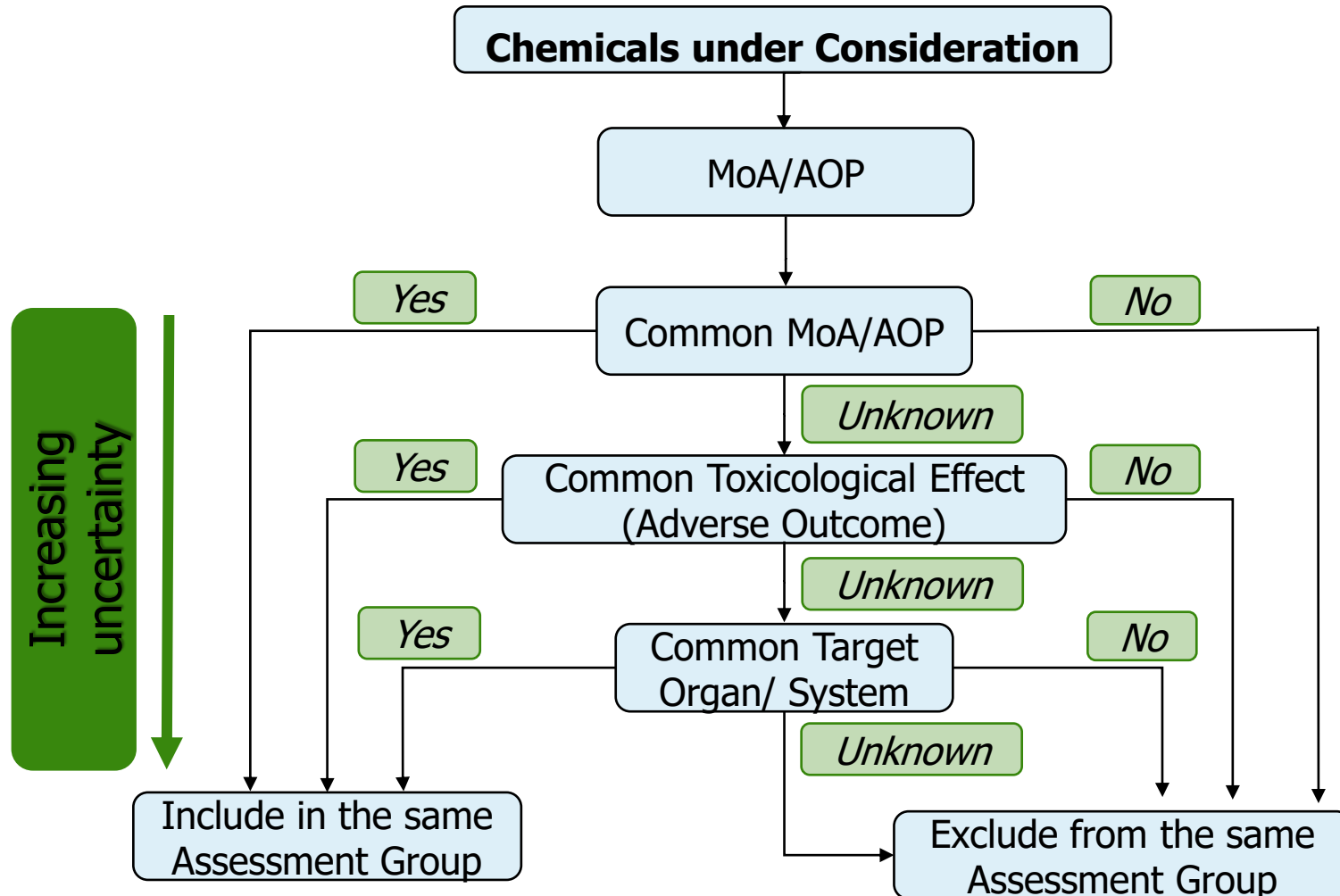


Retrospective CRA method in short

- 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)

Retrospective CRA – exposure assessment (1/3)

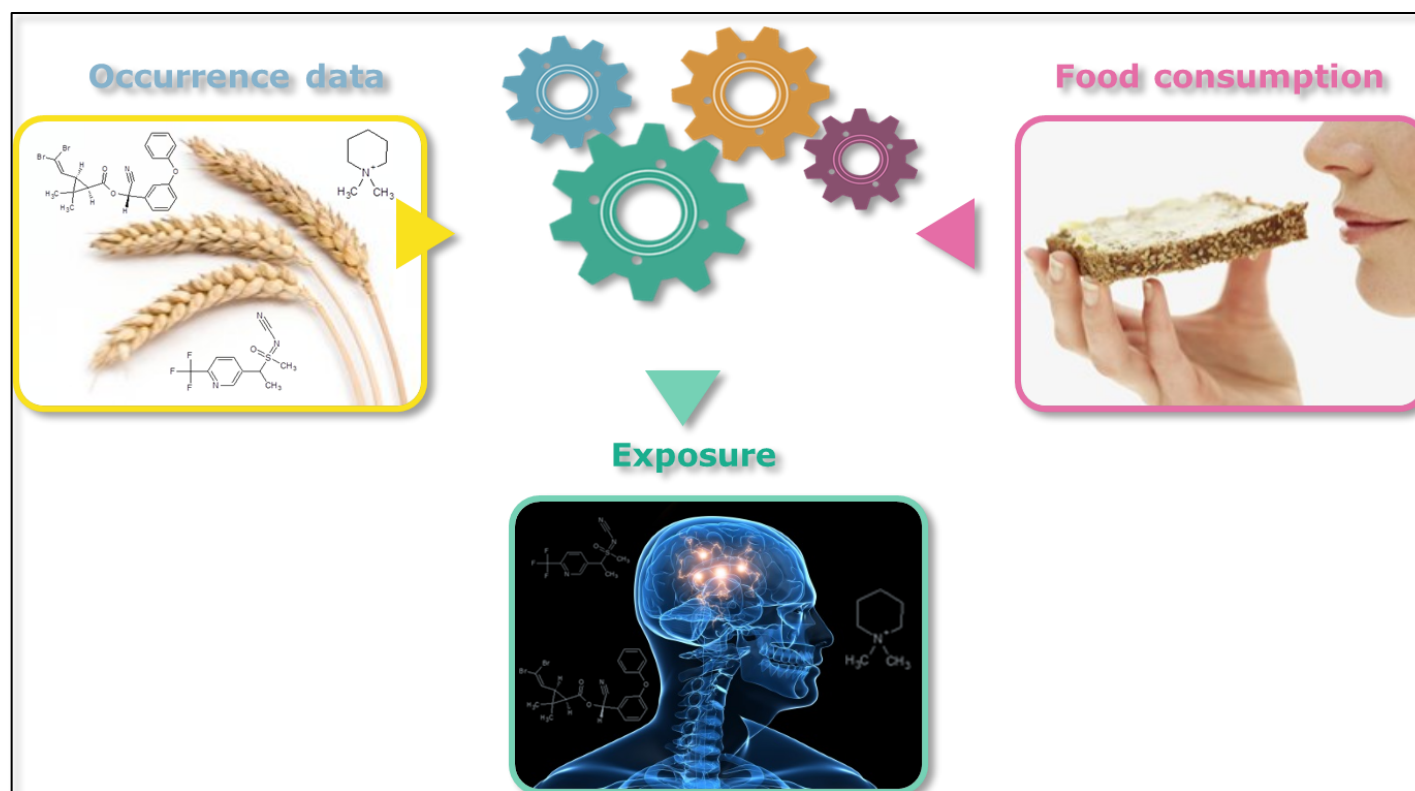
Food consumption data

- Food consumption data
 - 16 countries
 - 30 populations

NETWORK ON FOOD CONSUMPTION DATA

AGENDA OF THE 14th MEETING

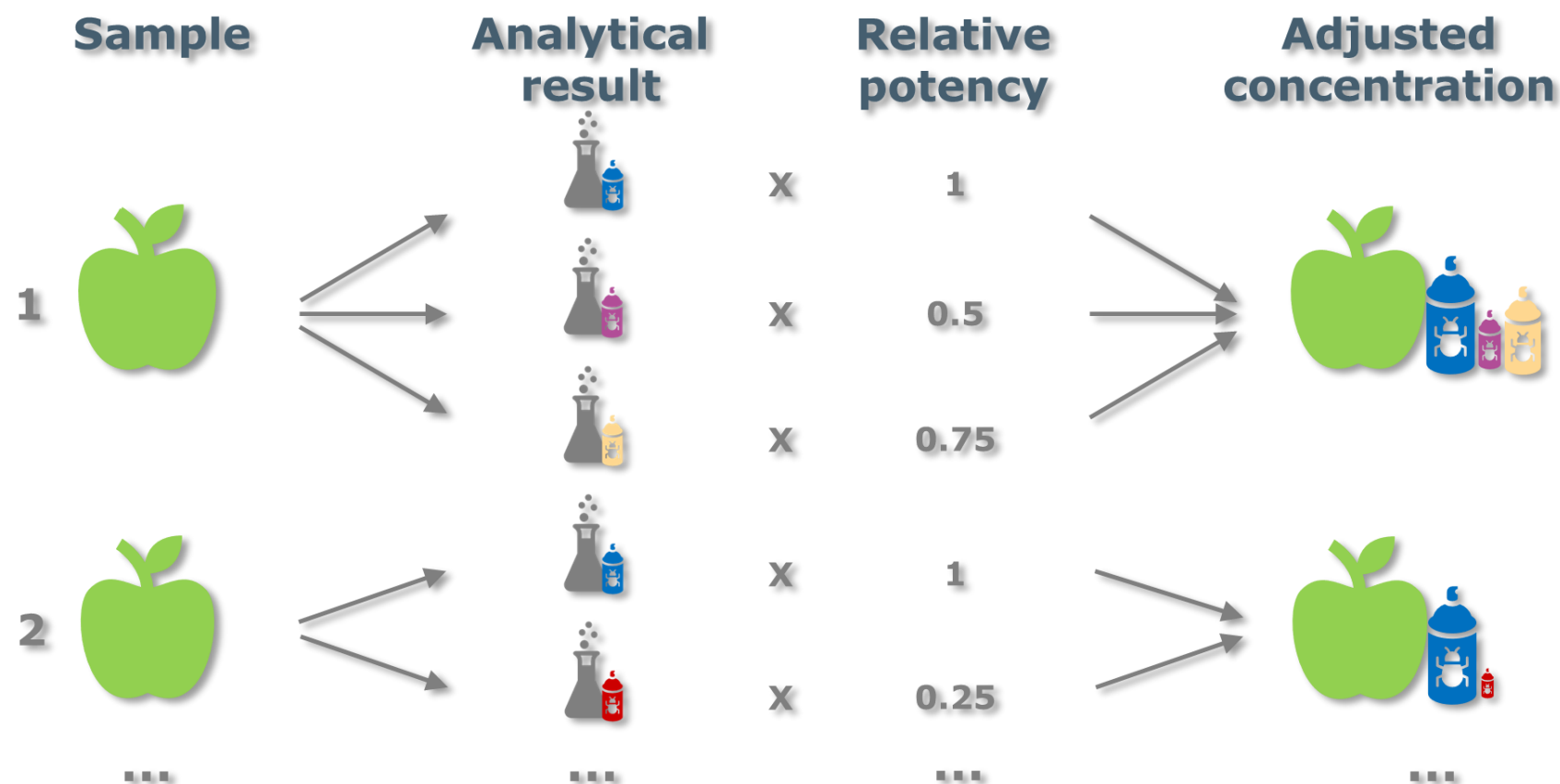
Meeting date:	06 April 2022
Meeting hours:	09:30 – 17:30
Meeting venue:	Online (MS Teams)
Chair:	Sofia Ioannidou



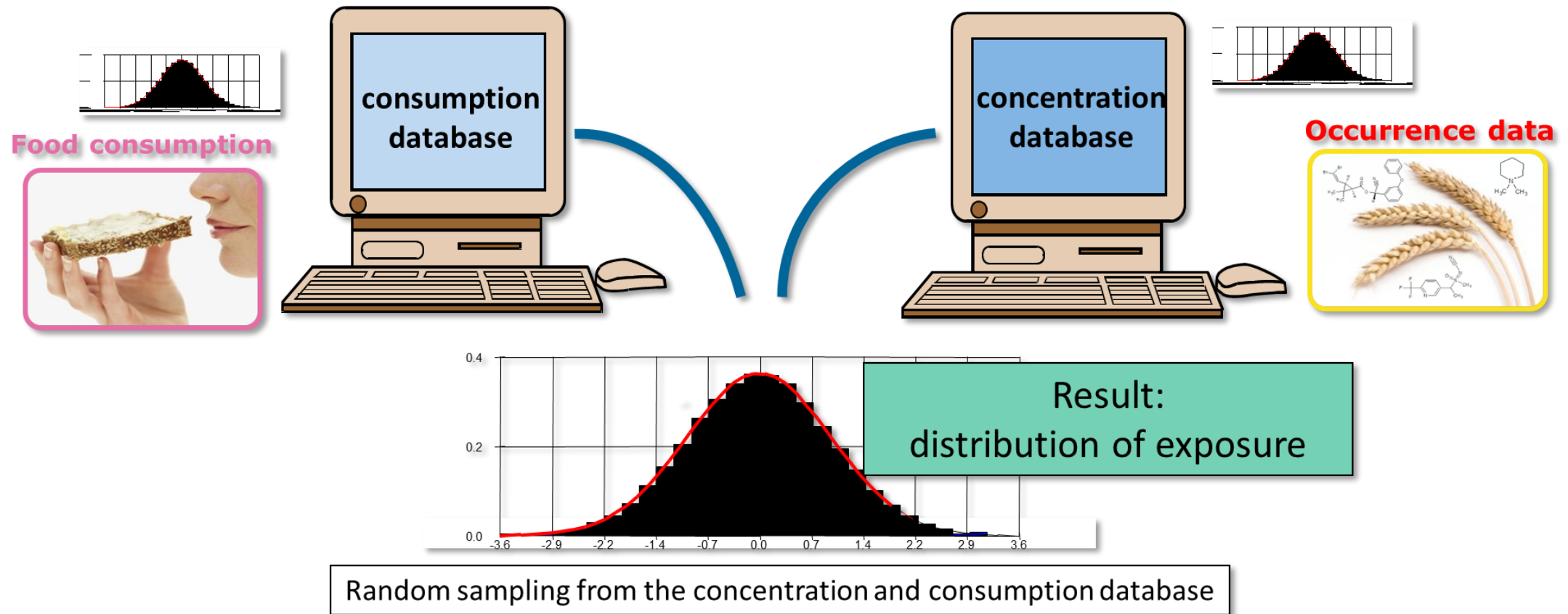
Retrospective CRA – exposure assessment (2/3)

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



Retrospective CRA – exposure assessment (3/3)



Retrospective CRA – Risk characterisation

Risk matrix: **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

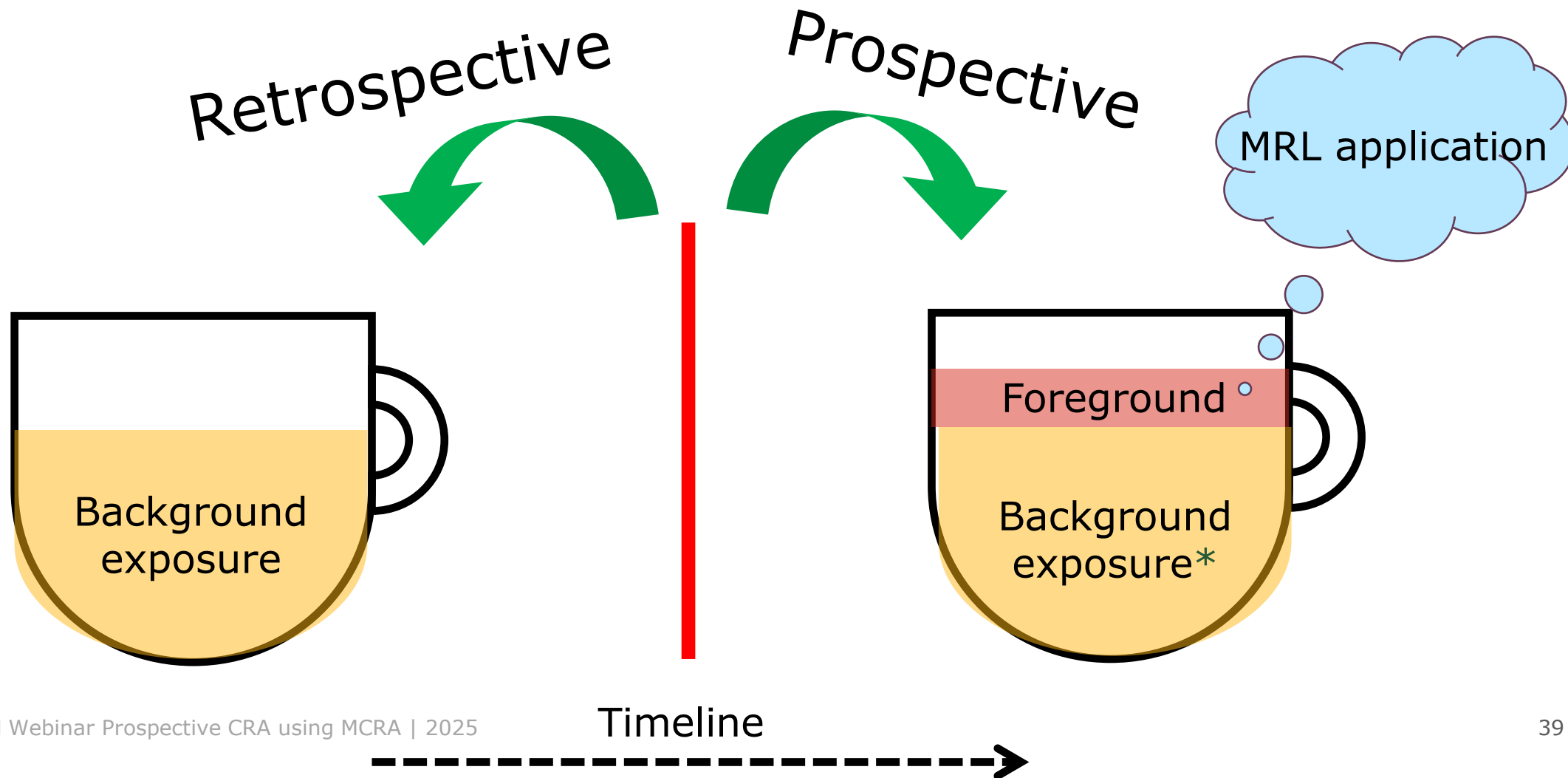


Content

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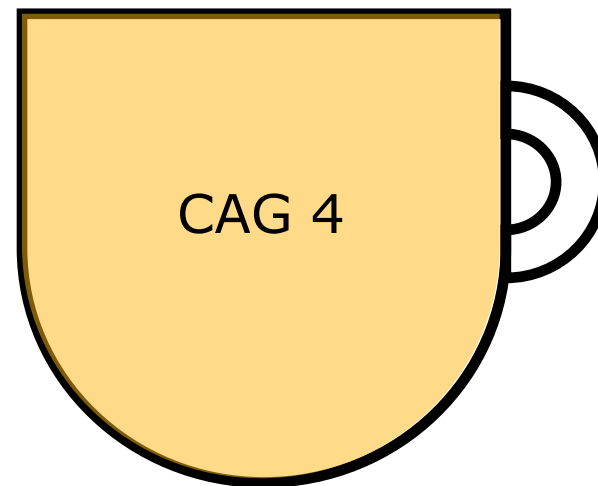
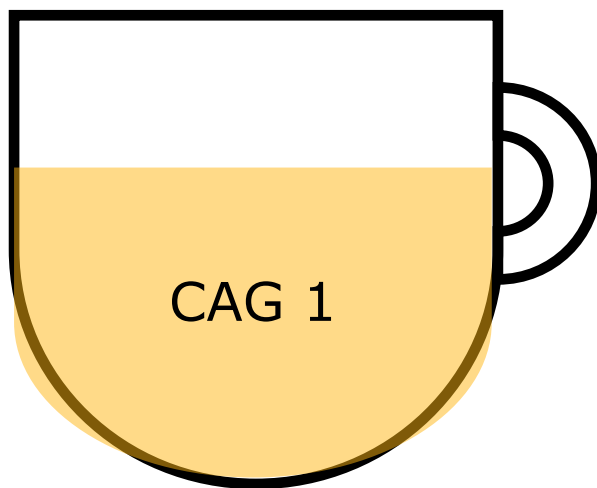
Retrospective vs. prospective CRA





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



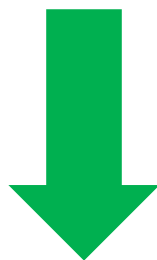


When is CRA using MCRA needed?

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

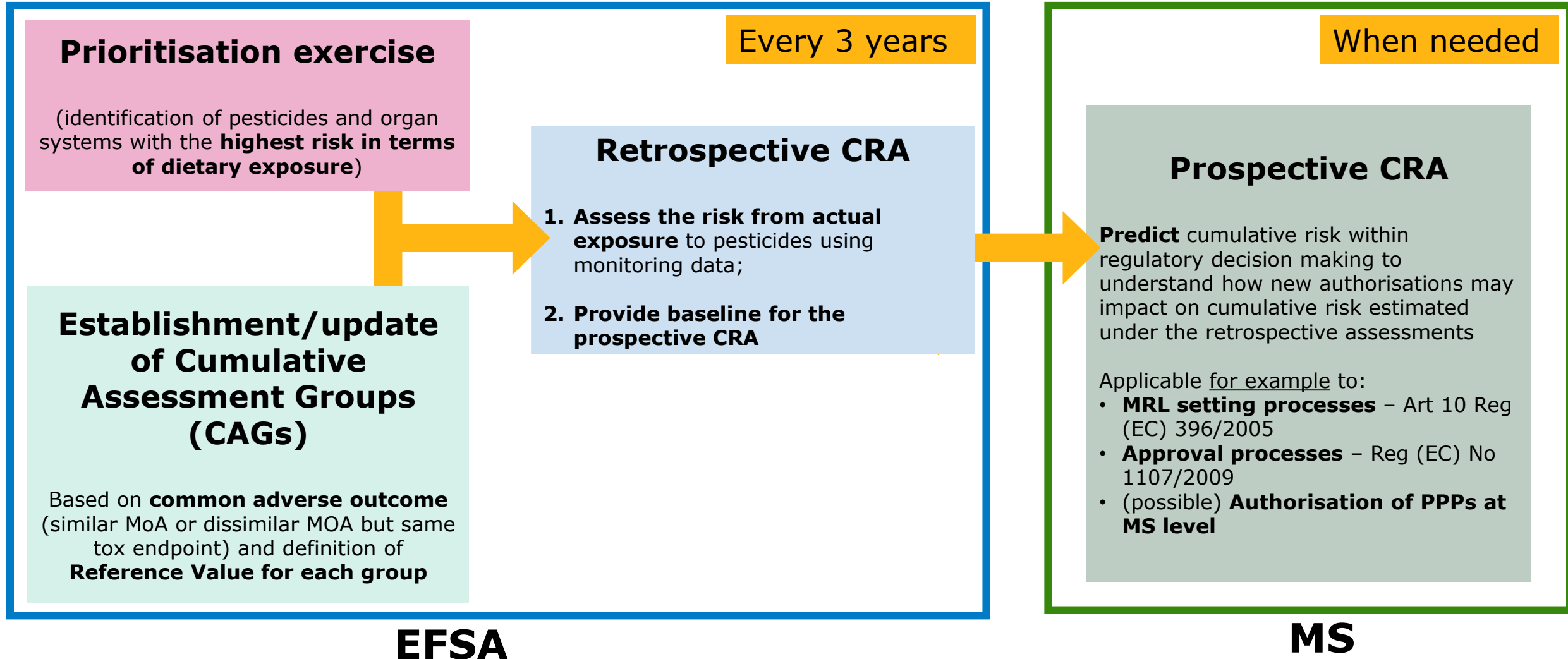
However, CRA can only be performed when:

- ✓ 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?



EFSA

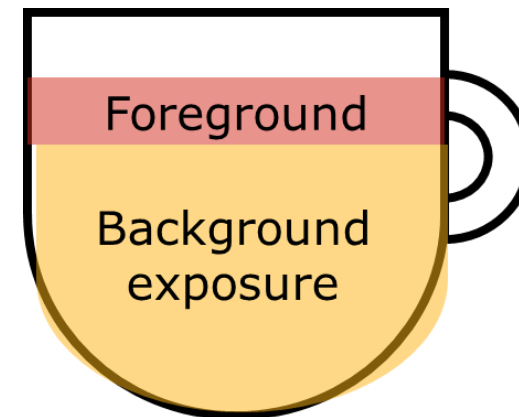
MS



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											
14											

	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							



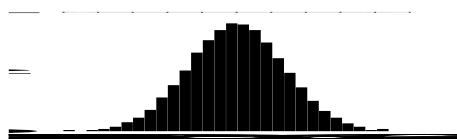
Content

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



Uncertainties already addressed

Food consumption

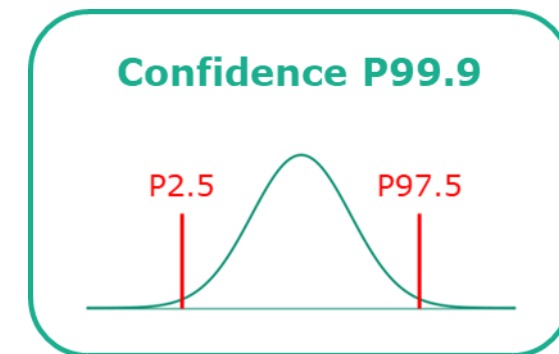
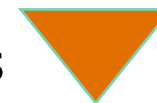
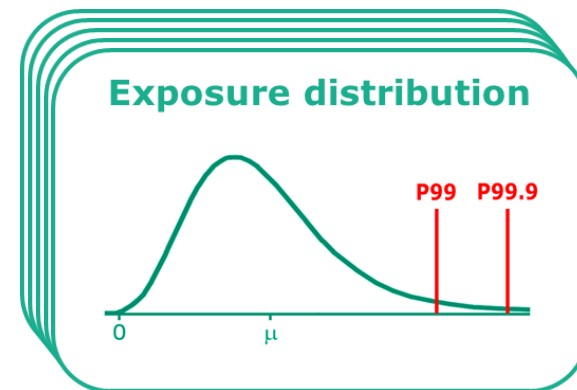
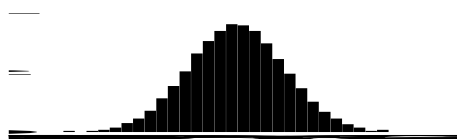
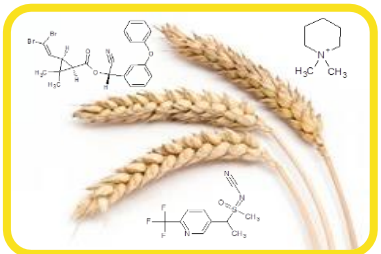


Random day x
random sample
(100.000 iterations)



100 bootstraps

Occurrence data



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

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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)

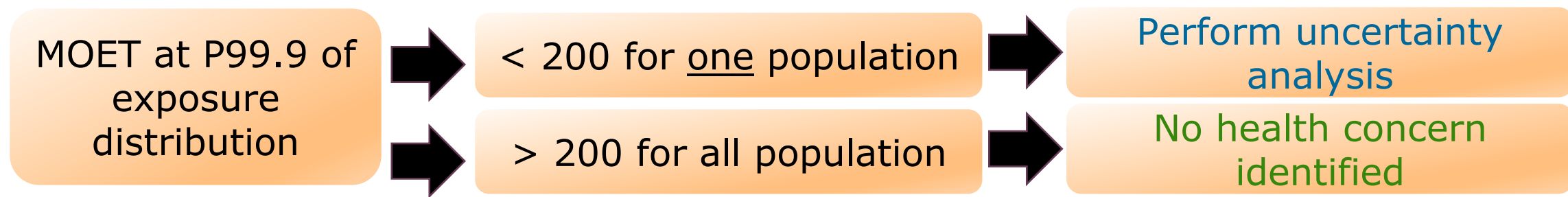
~5-6 of 11 will probably
be automated

Impact of each individual uncertainty on the MOET for the 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

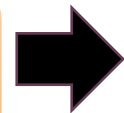




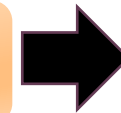
Additional uncertainty analysis needed?

> Remember:

MOET at P99.9 of exposure distribution



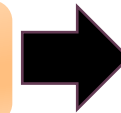
> 200 for all populations



No health concern identified



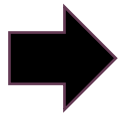
< 200 for one population



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:

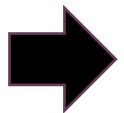
Adjusted MOET at P99.9 of exposure distribution with specific or reference population MF



> 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](#)





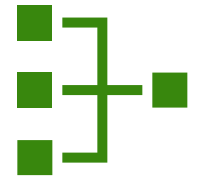
Implementation into MCRA

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



 **MCRA**
Exposure, Hazard & Risk Assessment




Welcome to MCRA


Chemical exposure, hazard and risk assessment

On a daily basis, people are exposed to multiple chemicals via food intake, inhalation and dermal contact. The risk to human health resulting from this exposure depends on the effects of the different chemicals in the mixture and how they combine. MCRA stands for **Monte Carlo Risk Assessment**. It is a web-based platform containing various models that users can use to assess these health risks for specific populations in various scenarios.

In MCRA, more than 50 **modules** are available to address hazard characterisation, exposure assessment and risk regulatory methodologies of the European Commission. MCRA includes novel scientific models that could improve or replace existing models.


MCRA was and is being developed in multiple projects, including (2010-2013), EuroMix (2015-2019), FNS Cloud (2019-2020) and 2021-2025.

 MCRA documentation

 Publications

MCRA account

Use of the MCRA web-platform requires an active account.

 Register for an account

Do you already have an account? [Log in here.](#)

Contact: **MCRA Support**, National Institute for Public Health and the Environment (RIVM).

MCRA is developed by Wageningen University & Research, Biometris for the National Institute for Public Health and the Environment (RIVM) (2007 - 2025).

Current version: **MCRA 10.1.9**.

Welcome page of MCRA

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

Using MCRA

You can specify your models, such as a dietary exposure assessment, within **actions** that are organised in **workspaces**. Each action is of a **module type** and contains selected data and settings. After specifying data and settings, the modelling task can be started. The output report contains concise sections of main results and detailed drilldown information.

The data used in the actions is organised in the **data repository**. Users have their own private data repository for uploading data. In addition, shared repository folders are available used for sharing data among user groups.

For more information on using MCRA consult the **documentation pages**.



Workspaces



Data



Create a workspace

Workspaces can be used to separate dossiers/assessments

The screenshot shows the MCRA (Exposure, Hazard & Risk Assessment) interface. The top bar displays the MCRA logo and the user 'TrainingCRA15'. The main area shows a table titled 'Workspaces' with columns: Name, Created, Last modified, and Tags. The table is currently empty. A dialog box titled 'Create new workspace' is open, prompting the user to 'Create a new workspace, please provide a descriptive name.' The dialog box contains a text input field labeled 'workspace name *' with the text 'Training' entered. The 'OK' button is highlighted. A large 'CRA' watermark is visible in the background.

2 Create new workspace

Create a new workspace, please provide a descriptive name.

workspace name *
Training

3 OK Cancel

1 +



Create a standard action

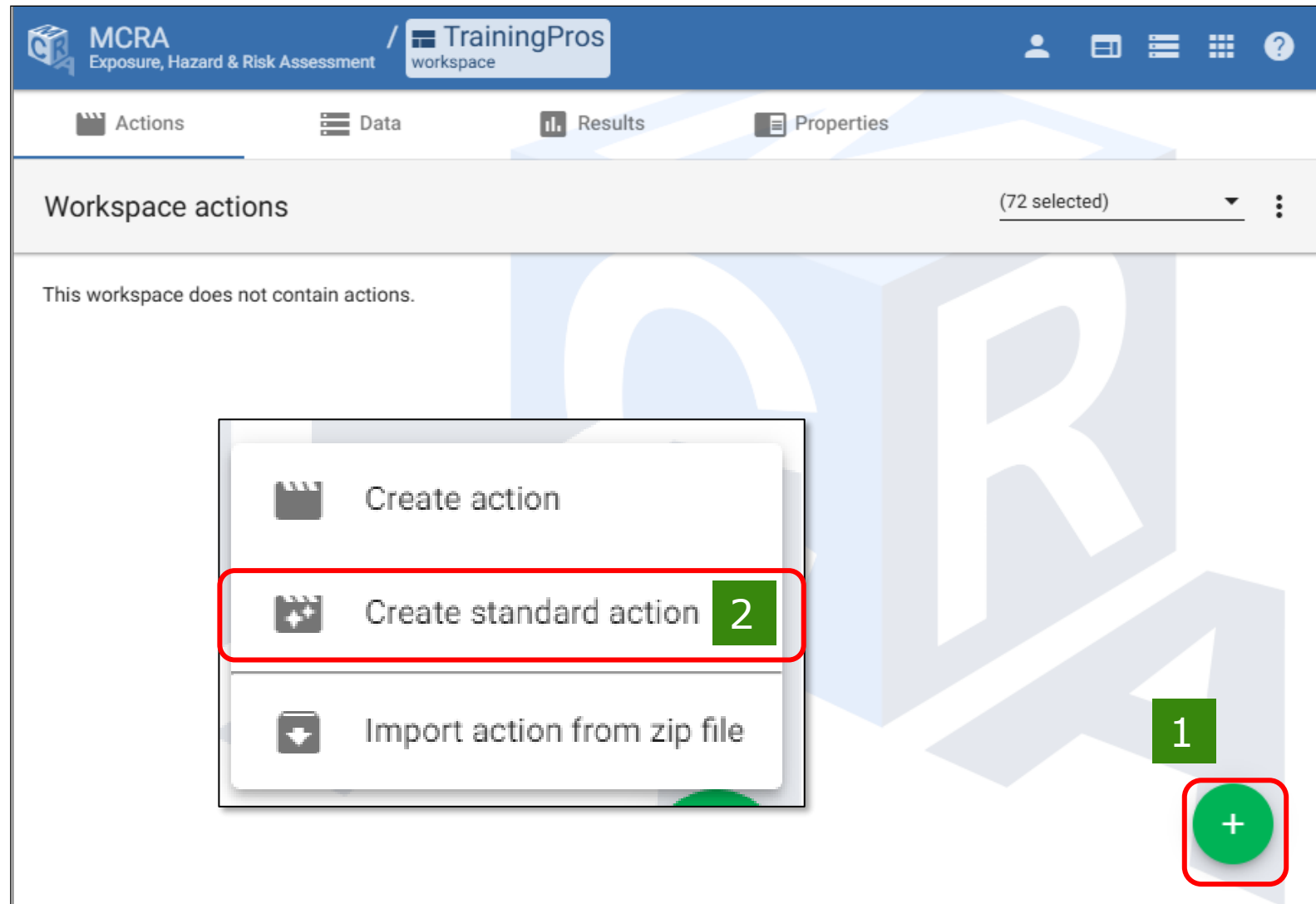
Actions can be used to separate different calculations within an assessment

Standard Regulatory Actions (SRAs) 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

Create new standard action

Select standard action type

Type filter text here

Demo acute cumulative risk assessment

In this demo with fictitious data, acute cumulative risk assessments can be performed following various calculation methods (EFSA 2012 Optimistic and Pessimistic, EC 2018 Tier 1 and Tier 2). Here, also the effect of applying processing factors can be assessed.

EU Prospective Dietary Cumulative Risk Assessment (2024)

This standard action allows you to run and compare the background and Tier II scenarios to probabilistic prospective risk assessment for a newly proposed use (focal substance/food) as defined by the EC working group. This is a risk assessment for four acute effects (NAN, NAM, DAC, DAH) and for three chronic effects (NCN, TCF and TCP) for different consumption surveys/populations. Occurrence datasets for the background are different 3-year cycle datasets containing occurrence data of all member states in the 3-year cycle, or it can be omitted (for comparison) so that only the background exposure is calculated. MRL exceedances can be removed taking into account measurement uncertainty. As an advanced option it is possible to adjust the 99.9th percentile of the exposure using uncertain adjustment factors from the EFSA cumulative risk assessment report 2020. The exposure is calculated probabilistically and the risk is expressed as margin of exposure (MOE) and is compared to a threshold value of 100. You can upload your own focal commodity/focal substance data (+ processing factors/conversion factors).



Give action a name

Create new standard action

×

Specify name/description

General

Name *

EU Prospective Dietary Cumulative Risk Assessment (2024)

Tags

Description

Back

Create



Note: These are example settings

Settings of the prospective SRA

1

2

3

4

5

6

7

8

9

Cumulative risk assessment

☐ Show advanced options

Focal food *

Mandarins (P0110050A) →

Lettuce (P0251020A)

Mandarins (P0110050A)

Melons (P0233010A)

Focal substance *

Dithiocarbamates (Dithiocarbamates expressed as CS2, including Maneb, Mancozeb, Metiram, Propineb, T (RF-0151-001-PPP) →

Disulfoton (sum of disulfoton)

Dithianon (RF-0150-001-PPP)

Dithiocarbamates (Dithiocarbamates)

Diuron (RF-0152-002-PPP)

Effect *

NAM-Acute: Functional effects on Motor division (acute) →

DAH-Acute: Head abnormalities not due to abnormal skeletal development

NAM-Acute: Functional effects on Motor division (acute)

NAN-Acute: Neurochemical end-points (acute)

Scenario *

Safety of GAP - 20% use frequency →

Safety of MRL

Safety of GAP - 100% use frequency

Safety of GAP - 20% use frequency

Consumptions data source *

NL - Toddlers (2) →

NL - Other children (3-6)

NL - Toddlers (2)

RO - Adults (19-64)

☐ Restrict population to

Monitoring period *

Concentration data (2020-2022) →

Concentration data (2019-2021)

Concentration data (2020-2022)

Concentrations data source *

Netherlands (NL) (2020 - 2022) →

Malta (MT) (2020 - 2022)

Netherlands (NL) (2020 - 2022)

Norway (NO) (2020 - 2022)

Uncertainty analysis *

Full uncertainty analysis: 100 bootstrap cycles →

No uncertainty analysis

Limited uncertainty analysis (demo/testing): 10 bootstrap cycles with restricted Monte Carlo iterations

Full uncertainty analysis: 100 bootstrap cycles with full Monte Carlo iterations

☐ Run sensitivity analysis scenario



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

EU Prospective Dietary Cumulative Risk Assessment (2024)

This standard action allows you to run and compare the background and Tier II scenarios to probabilistic prospective risk assessment for a newly proposed use (focal substance/food) as defined by the EC working group. This is a risk assessment for four acute effects (NAN, NAM, DAC, DAH) and for three chronic effects (NCN, TCF and TCP) for different consumption surveys/populations. Occurrence datasets for the background are different 3-year cycle datasets containing occurrence data of all member states in the 3-year cycle, or it can be omitted (for comparison) so that only the background exposure is calculated. MRL exceedances can be removed taking into account measurement uncertainty. As an advanced option it is possible to adjust the 99.9th percentile of the exposure using uncertain adjustment factors from the EFSA cumulative risk assessment report 2020. The exposure is calculated probabilistically and the risk is expressed as margin of exposure (MOE) and is compared to a threshold value of 100. You can upload your own focal commodity/focal substance data (+ processing factors/conversion factors).

[Download data template](#) [Go to documentation](#)

Data sources

Deterministic substance conversion factors	No data source selected	<div><div>+</div><div>+</div></div>
Focal food concentrations	No data source selected	<div><div>+</div><div>+</div></div>

Cumulative risk assessment settings

☐ Show advanced options [Save changes](#)

Focal food *

Mandarins (P0110050A)

Focal substance *

Dithiocarbamates (Dithiocarbamates expressed as CS2, including Maneb, Mancozeb, Metiram, Propineb, T (RF-0151-001-PPP))



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	4: DeterministicConversionFactors: Factor (MW) to calculate Measured Substance to Active Substance. 5: Delete all ActiveSubstances other than the one of interest						
10							
11							
12							
13							
14							
15							
	ConcentrationsS	3	DeterministicConversionFactors				



Note: These are example settings

Run the action

MCRA
Exposure, Hazard & Risk Assessment

TrainingPros
workspace

EU Prospective Die...
action

TrainingPros3

EU Prospective Dietary Cumulative Risk Assessment (2024)
Standard action - EU Prospective Dietary Cumulative Risk Assessment (2024)

Settings

EU Prospective Dietary Cumulative Risk Assessment (2024)

This standard action allows you to run and compare the background and Tier II scenarios to probabilistic prospective risk assessment for a newly proposed use (focal substance/food) as defined by the EC working group. This is a risk assessment for four acute effects (NAN, NAM, DAC, DAH) and for three chronic effects (NCN, TCF and TCP) for different consumption surveys/populations. Occurrence datasets for the background are different 3-year cycle datasets containing occurrence data of all member states in the 3-year cycle, or it can be omitted (for comparison) so that only the background exposure is calculated. MRL exceedances can be removed taking into account measurement uncertainty. As an advanced option it is possible to adjust the 99.9th percentile of the exposure using uncertain adjustment factors from the EFSA cumulative risk assessment report 2020. The exposure is calculated probabilistically and the risk is expressed as margin of exposure (MOE) and is compared to a threshold value of 100. You can upload your own focal commodity/focal substance data (+ processing factors/conversion factors).

Download data template

Go to documentation

Data sources

Deterministic substance conversion factors	FT-ZiramMandarin-Fictitious.xlsx	<div></div> <div></div>
Focal food concentrations	FT-ZiramMandarin-Fictitious.xlsx	<div></div> <div></div>

Cumulative risk assessment settings

☐ Show advanced options

Save changes

Focal food *

Mandarins (P0110050A)

Focal substance *

Dithiocarbamates (Dithiocarbamates expressed as CS2, including Maneb, Mancozeb, Metiram, Propineb, T (RF-0151-001-PPP)



Note: These are example settings

Rename and wait for the calculation to finish

The screenshot displays the MCRA (Exposure, Hazard & Risk Assessment) software interface. The top navigation bar includes the MCRA logo, the current workspace 'TrainingPros', and the active action 'EU Prospective Die...'. The main header shows the task name 'EU Prospective Dietary Cumulative Risk Assessment (2024)' and its standard action. A 'Results' section is visible, containing a table with columns for 'Output', 'Status', 'Message', 'Date', and 'Running time'. A task named 'Prospective CRA 2024 NAM-Acute - NL-Toddlers (2020-2022) No UNC' is listed with a status of 'Running'. A red box highlights the edit icon (pencil) next to this task. A 'Rename task' dialog box is open, showing the current task name 'Pros-2024-NAM-NLTod-NLconc20-22' and a red box around the 'OK' button. The background interface also shows a search bar and a 'Running' status indicator.



Results pages

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

The screenshot displays the MCRA (Exposure, Hazard & Risk Assessment) software interface. The top navigation bar includes the MCRA logo, the user 'TrainingPros3', and a workspace titled 'EU Prospective Die...'. Below this, a header for the current assessment reads 'EU Prospective Dietary Cumulative Risk Assessment (2024) - ZiramMandarin-fict'. A green bar indicates the current results file: 'Results / Pros-2024-NAM-NLTod-NLconc20-22-Use20', with a 'Show detailed report' button. The main content area features two tabs: 'Results' (highlighted with a red box) and 'Settings'. Under the 'Results' tab, a list of assessment components is shown with expandable arrows: 'EU Prospective Dietary Cumulative Risk Assessment (2024)', 'Settings', 'Focal exposure scenario', 'Distribution margin of exposure total (MOET)', and 'Contributions of foods and substances to upper exposure distribution'. A large, semi-transparent 'QR' watermark is visible on the right side of the interface.

MCRA / TrainingPros / EU Prospective
Exposure, Hazard & Risk Assessment / workspace / action

EU Prospective Dietary Cumulative Risk Assessment (2024) -
Standard action - EU Prospective Dietary Cumulative Risk Assessment (2024)

Results / Pros-2024-NAM-NLToD-NLconc20-22-Use20

Results Settings

- ✓ Action inputs
- > Data sources
- > Single value risks
- > Effects
- > Substances
- > Populations
- > Risks
- > Dietary exposures
- > Concentration models
- > Occurrence frequencies
- > Occurrence patterns
- > Consumptions by model
- > Food conversions
- > Modelled foods
- > Concentrations
- > Relative potency factors

✓ 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-Fictitious.xlsx\FT-ZiramMandarin-Fictitious.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-Fictitious.xlsx\FT-ZiramMandarin-Fictitious.xlsx	1	-
Consumptions	12784-EFSA-CRA-2024-Consumptions NL-Toddlers.zip\EFSA-CRA-2024-Consumptions NL-Toddlers.zip	1	-

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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

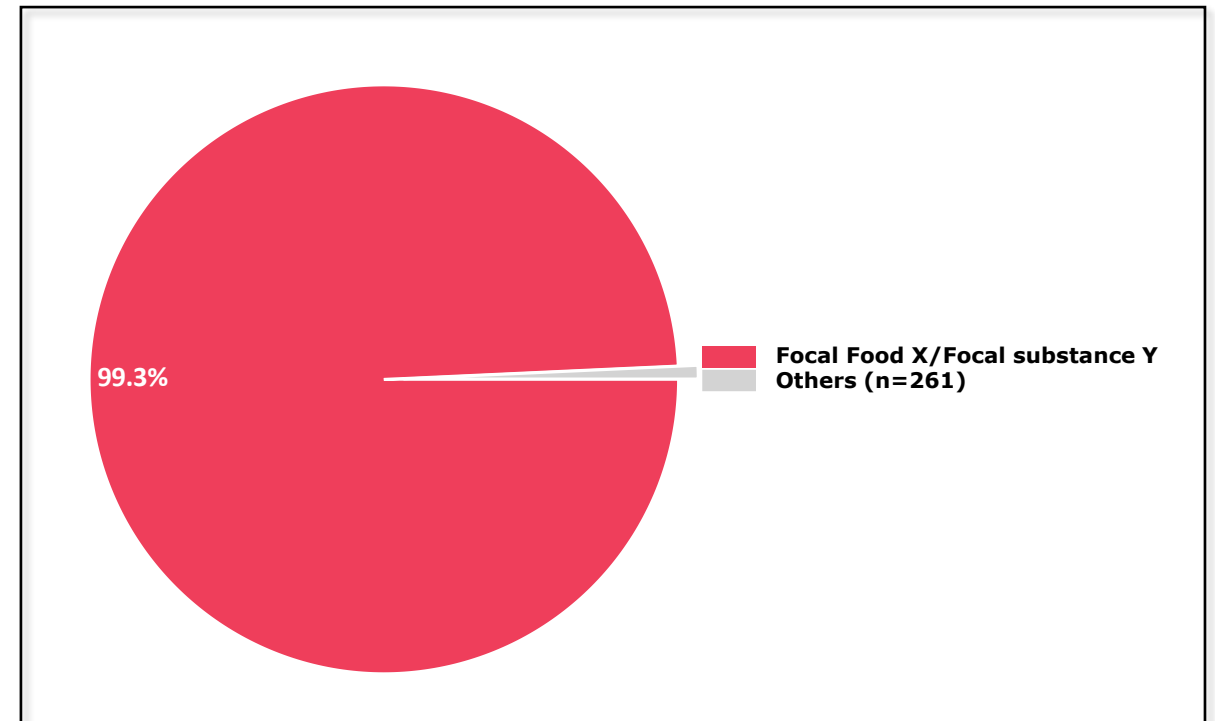
Risk characterisation ratio (H/E) = MOET

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 consideration =
MOET at 99.9th percentile < 100

Food/substance combinations contributing most to the risk



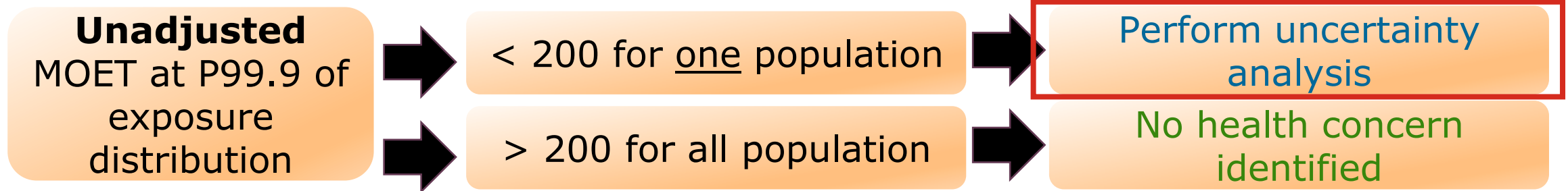


Conclusions of this **fictive** assessment

- 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)

MCRA Exposure, Hazard & Risk Assessment / TrainingPros workspace / EU Prospective Die... action

TrainingPros2

EU Prospective Dietary Cumulative Risk Assessment (2024)
Standard action - EU Prospective Dietary Cumulative Risk Assessment (2024)

Settings

Consumptions data source *
NL - Toddlers (2)

☐ Restrict population to consumers or consumer days only

Monitoring period *
Concentration data (2020-2022)

Concentrations data source *
Netherlands (NL) (2020 - 2022)

Uncertainty analysis *
Full uncertainty analysis: 100 bootstrap cycles with full Monte Carlo iterations

☒ Run sensitivity analysis scenario

Sensitivity analysis scenario *
U09: Missing processing factors

Save changes



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



Conclusions of these **fictive assessments**

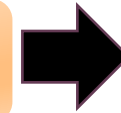
- > Results (fictive): **Unadjusted** MOET at P99.9 for one population (NL toddlers) = 26, but **adjusted** MOET for missing PF at P99.9 for the same population = 821

- > Please recall:

Adjusted MOET at P99.9
of exposure distribution
with reference population
MF



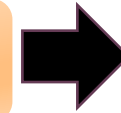
> 200 for all populations



No additional analysis needed



< 200 for one population

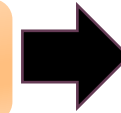


Perform uncertainty analysis for
specific population

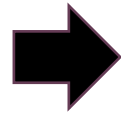
Adjusted MOET at P99.9
of exposure distribution
with specific or reference
population MF



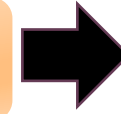
> 100 for all populations



No health concern identified



< 100 for one population



Health risk cannot be excluded

- > 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



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

Regulatory users are being trained

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	

An official EU website How do you know? ▾

European Union

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Performing retrospective cumulative risk assessment using Open MCRA

One day Beginner



National Institute for Public Health and the Environment
Vlaamse Landbouwkampioenschap



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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