EuroMix

Introduction to the EuroMix model and data platform

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

www.euromixproject.eu

Training materials, 11 February 2019
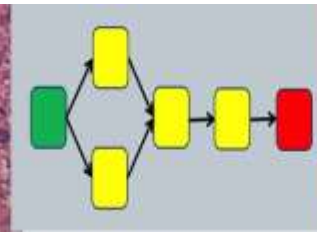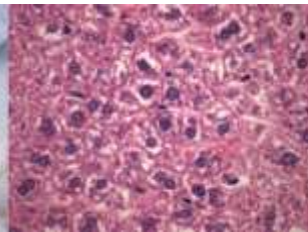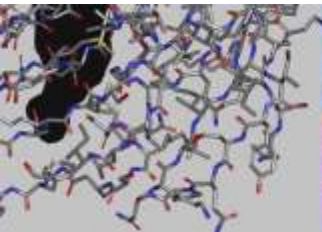
Content

1. **How to login**

2. **Support and help function**

3. **How to get connected to data needed to perform exposure or hazard assessment**

4. **How to perform an action in a workspace (example dietary exposure assessment)**

5. **Short overview of other actions**

Login via MCRA 9 beta

EuroMix

1. <u>Make sure you are using Google Chrome</u>
2. <u>Copy https://mcra-test.rivm.nl</u> in Google Chrome
3. Click on EuroMix toolbox to get access to the EuroMix model test toolbox

National Institute for Public Health and the Environment, Ministry of Health, Welfare and Sport — WAGENINGEN UNIVERSITY & RESEARCH — efsa European Food Safety Authority — fera

MCRA 9.0 Beta

MCRA stands for **Monte Carlo Risk Assessment**.

MCRA is a web-based system for probabilistic exposure and risk assessment of chemicals in the diet.

The MCRA system brings together statistical models, shared data and data uploaded by the user.

MCRA also provides **Cumulative Exposure Assessment** for chemicals grouped in a Cumulative Assessment Group for which a single health effect is considered relevant.

Optionally exposure from other routes can be added in an **Aggregate Exposure Assessment**.

MCRA was developed in EU project ACROPOLIS and is further developed in actions for EFSA and in EU project EuroMix

Publications and reports using MCRA

Login

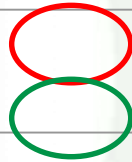| Username | |
| Password | |

Go to registration   LOGIN

Go to the **EuroMix** Test Toolbox

Contact: Prof. J.D. van Klaveren National Institute for Public Health and the Environment (RIVM)
MCRA is developed by Wageningen University & Research, Biometris for RIVM (2007 - 2019)

Login EuroMix toolbox
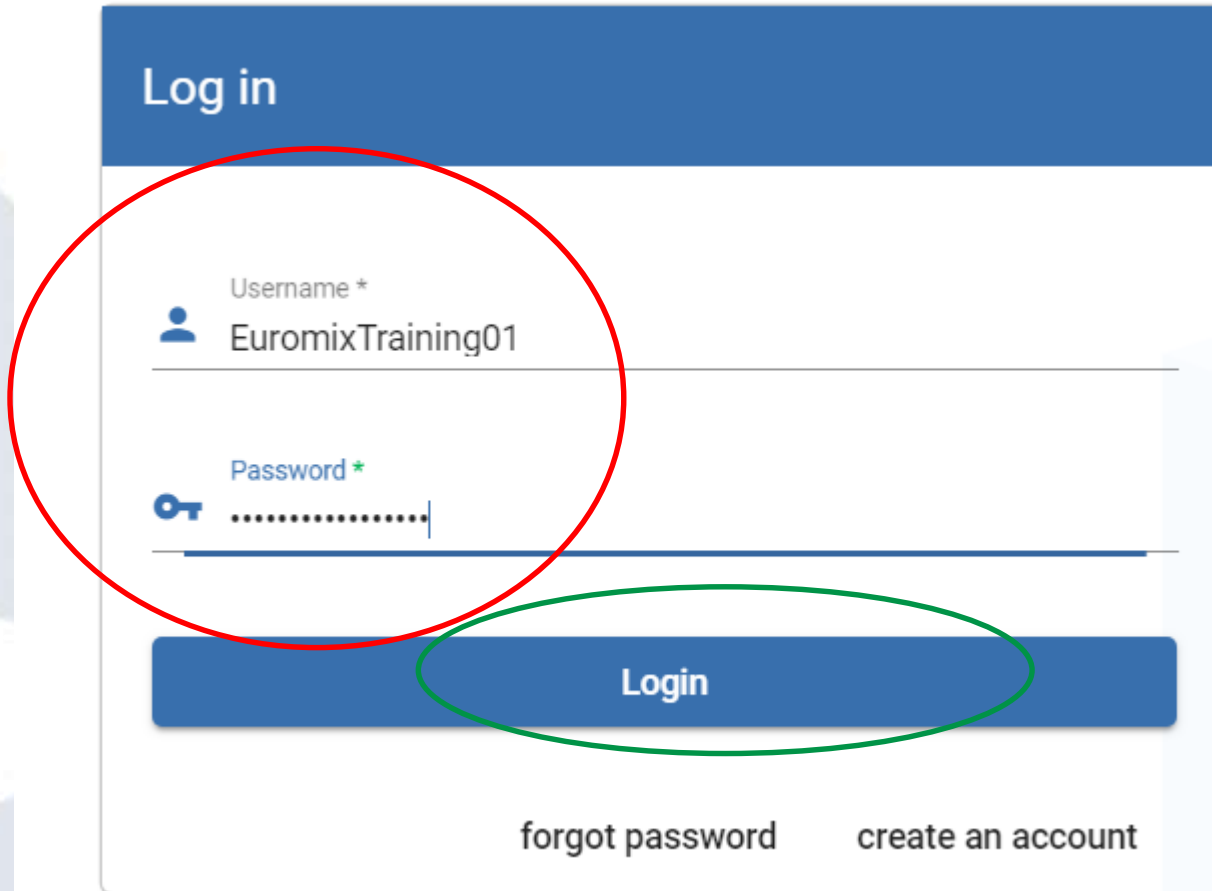
1. Log in: click on
2. Then log in

This project is funded by the Horizon 2020 Framework Programme of the European Union

Insert username password

EuroMix

Log in

Username *
EuromixTraining01

Password *
················

Login

forgot password   create an account

1. Login with the username and password provided by the tutor

2. Login

Content

Data folders

Basic input for dietary exposure assessment

- **Description of food, substances, recipes etc. (secondary data)**
- **Food consumption data**
- **Concentration data**
- **For multiple chemicals also effect data**
- **Hazard data translated to Relative Potency Factors (RPFs)**

Optional

- **Processing factors (e.g. peeling, cooking, juicing)**
- **Variability factors (correction composite samples)**
- **Expected or known percentage agricultural use (occurrence patterns)**

Data folders

1. Click on data

2. The data folder will be unfolded (see second screenshot)
   You will see EuroMix Training01 which is your own folder. You can upload your own files on this folder. For the training you click on EuroMix Training

MCRA 9 - EuroMix toolbox
Exposure, Hazard & Risk Assessment

≡ Data / EuromixTraining01

Name ▾	Version
↑ (Data)	

MCRA 9 - EuroMix toolbox
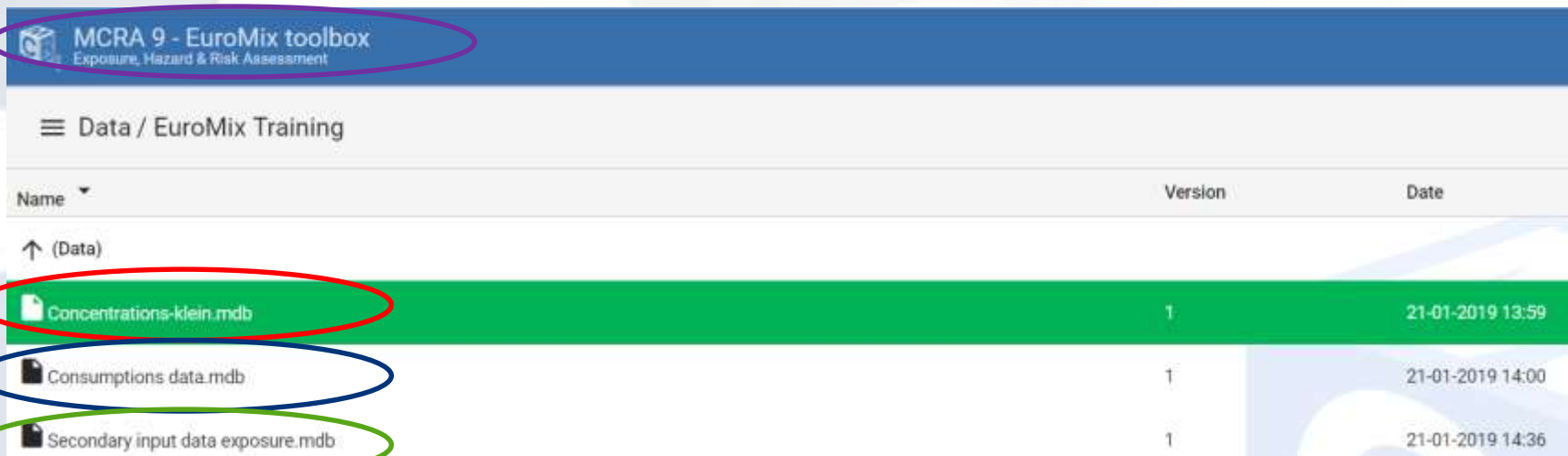Exposure, Hazard & Risk Assessment

≡ Data

Name ▾
📁 EuroMix Training
📁 EuromixTraining01

Data folders

1. The shared folder contains Concentration data

2. Consumption data

3. Secondary input data needed for the exposure assessment (e.g. codes and names of foods, substances, relative potency factors or hazard doses etc.)

4. When the input data is understood, go to EuroMix toolbox main page by clicking on MCRA 9 – EuroMix toolbox

MCRA 9 - EuroMix toolbox
Exposure, Hazard & Risk Assessment

≡ Data / EuroMix Training

Name ▼	Version	Date
↑ (Data)		
Concentrations-klein.mdb	1	21-01-2019 13:59
Consumptions data.mdb	1	21-01-2019 14:00
Secondary input data exposure.mdb	1	21-01-2019 14:36

Actions needs to be done in workspaces

1. Click on workspaces and create a new workspace

Welcome to MCRA 9 (beta), the EuroMix toolbox

Chemical exposure, hazard and risk assessment

Typical **action types** which this system can perform are: dietary exposure assessment, hazard dose assessment and risk assessment. Actions are structured in a network of modular calculators [see Overview].

You have to organize your work in one or more **workspaces**. The work consists of specifying **tasks** of a specific action type. Tasks may need subtasks of other action types.

After running a task, **outputs** are available. Outputs are in the form of screen reports and print reports, and may also include data that may be useful as input in other tasks.

All tasks need input data, and some tasks produce output data. Data, but also saved tasks and outputs, are organised in a data repository, which includes shared items from other users and user groups.

Start by clicking **Workspaces** or **Data**, or use wizard options

WORKSPACES   **DATA**

Create a new workspace

1. Click on + and a new window pops up

MCRA 9 - EuroMix toolbox
Exposure, Hazard & Risk Assessment

Workspaces

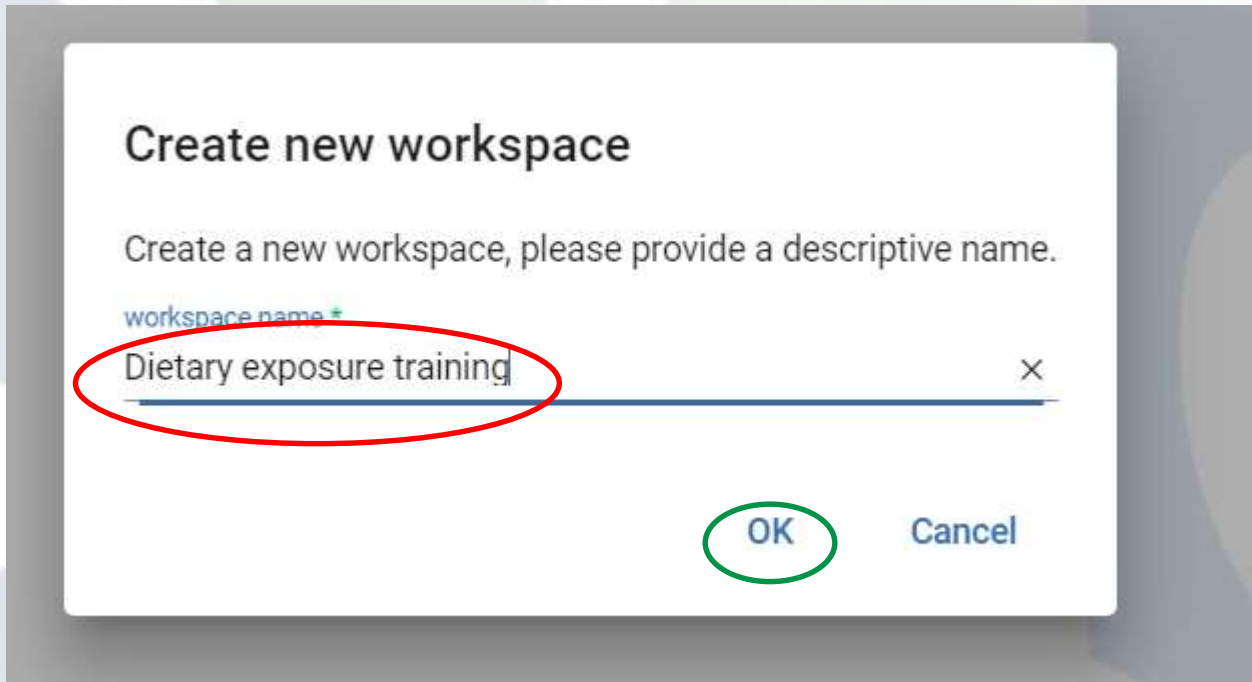Name ▾   Tags

Create a new workspace (2)

EuroMix

1. Insert a name for the new workspace

2. Click on ok

Create new workspace

Create a new workspace, please provide a descriptive name.

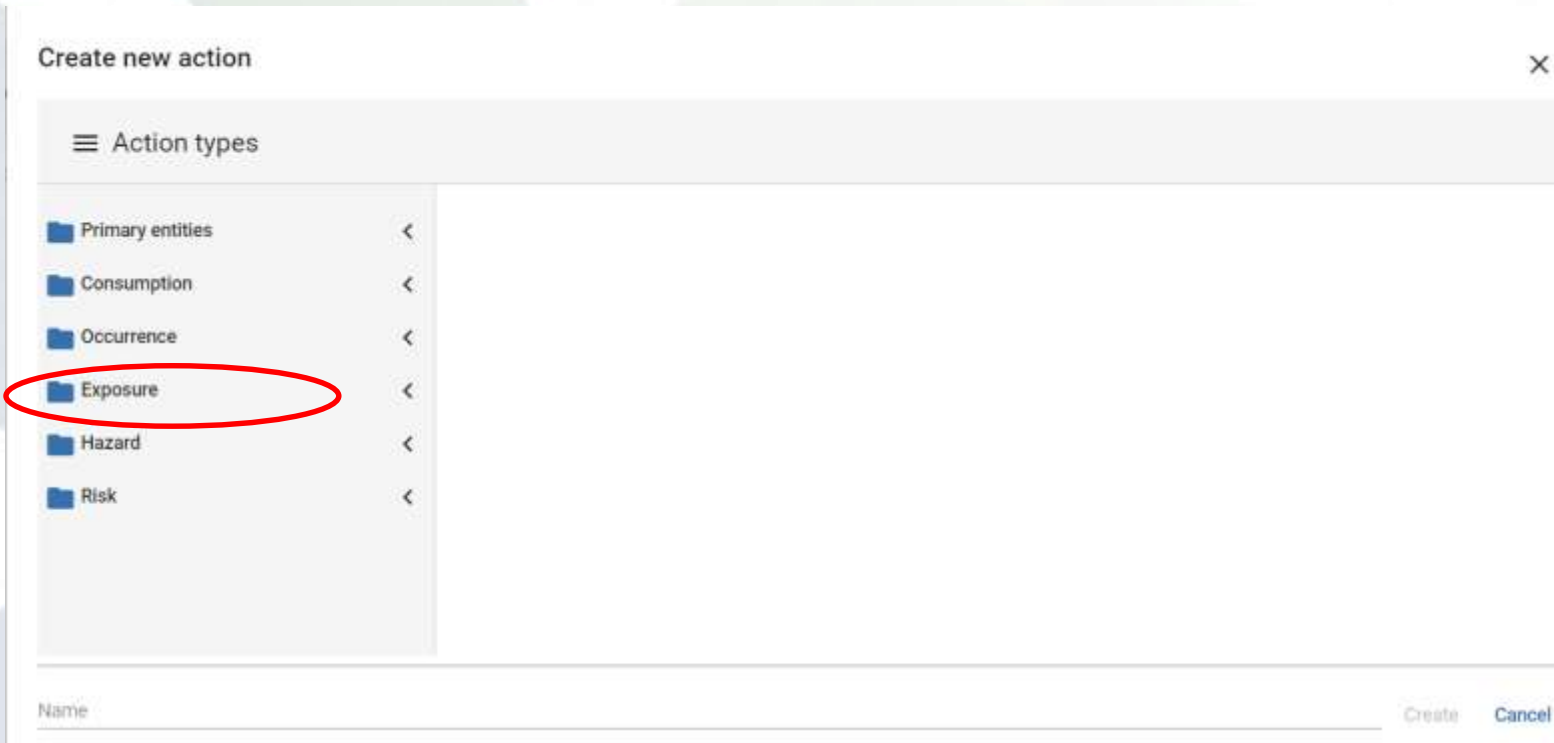workspace name *

Dietary exposure training ✕

OK   Cancel

Create an action in the workspace

EuroMix

1. Click on + and a new window pops up

Create an action in the workspace (2)

EuroMix

1. Create a new action Exposure

Create new action   ✕

≡ Action types

📁 Primary entities   ‹
📁 Consumption   ‹
📁 Occurrence   ‹
📁 Exposure   ‹
📁 Hazard   ‹
📁 Risk   ‹

Name   Create   Cancel

Create an action in the workspace (2)

1. Create a new action type Dietary exposure

Create an action in the workspace (3)

EuroMix

1. Insert a name for the action 'Dietary exposure training'

2. Click on create

Create new action   ✕

☰ Action type: Dietary exposures

| General | Calculation | Uncertainty sources | Output settings |

Primary entities	‹
Consumption	‹
Occurrence	‹
Exposure	‹
Hazard	‹
Risk	‹

Dietary exposures module
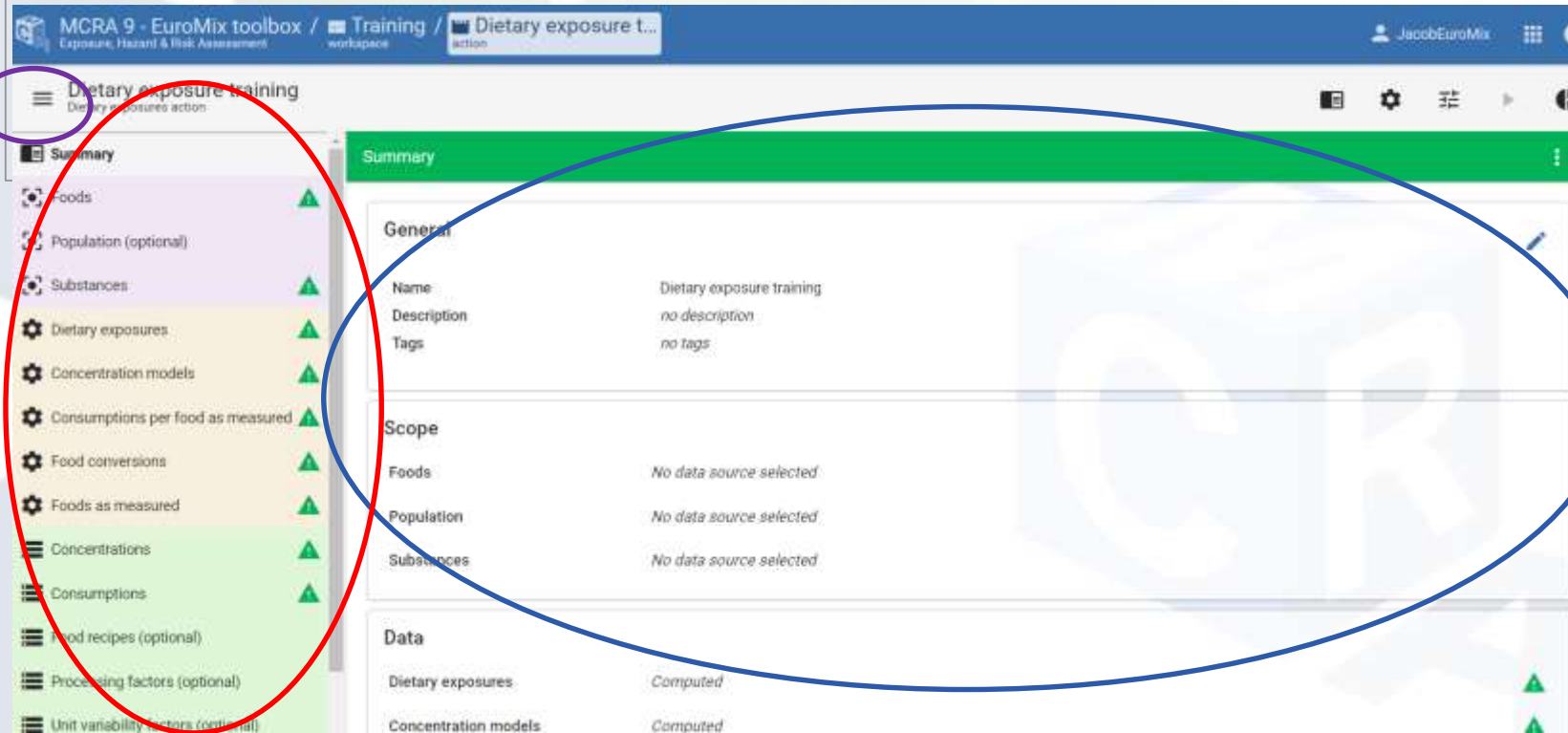
Scope: **Populations** **Foods** **Substances** **Effects**

Calculation module. Dietary exposures are calculated from Consumptions per food-as-measured and from Concentration models. Optionally, also Processing factors and Food unit concentration models are applied.

Name
Dietary exposures training

Create   Cancel

Create dietary exposure action type

EuroMix

1. Provide a name to the new action e.g. 'dietary exposure training'

2. Create the new action type

Create new action ×

≡ Action type: Dietary exposures

Primary entities	‹
Consumption	‹
Occurrence	‹
Exposure	‹
Hazard	‹
Risk	‹

General · Calculation · Uncertainty sources · Output settings

Dietary exposures module

Scope: Population Foods Substances Effects

Calculation module. Dietary exposures are calculated from Consumptions per food-as-measured and from Concentration models. Optionally, also Processing factors and Food unit concentration models are applied.

Name
Dietary exposures

Create   Cancel

Start dietary exposure assessment

1. You see a panel at the left for navigation

2. The panel on the right is for selecting input data needed for the scope of your assessment and selecting settings for the model run

3. The left panel is sometimes confusing, you can close it down

Overview of work to be done

EuroMix

1. You entered the summary overview. Click on the pencil and you can insert a name for your exposure assessment output

Insert name, description and tags

EuroMix

1. Insert or adjust name

2. Insert description 'EFSA optimistic scenario'

3. Insert tags 'VCP" is the consumption data used and 'optimistic' is the calculation method. You can insert more tags

4. Save

Edit general settings   ×

Dietary exposures training

EFSA optimistic scenario

VCP ⊗   optimistic ⊗

Save   Cancel

Navigate via the icons on top of your screen

EuroMix

1. Go to action section

Start adjusting the settings

1. Decide whether you will perform an acute or chronic assessment, which depends on the toxicity of your substances. Change to chronic, you will perform an exposure assessment addressing liver steatosis, which is a chronic effect.
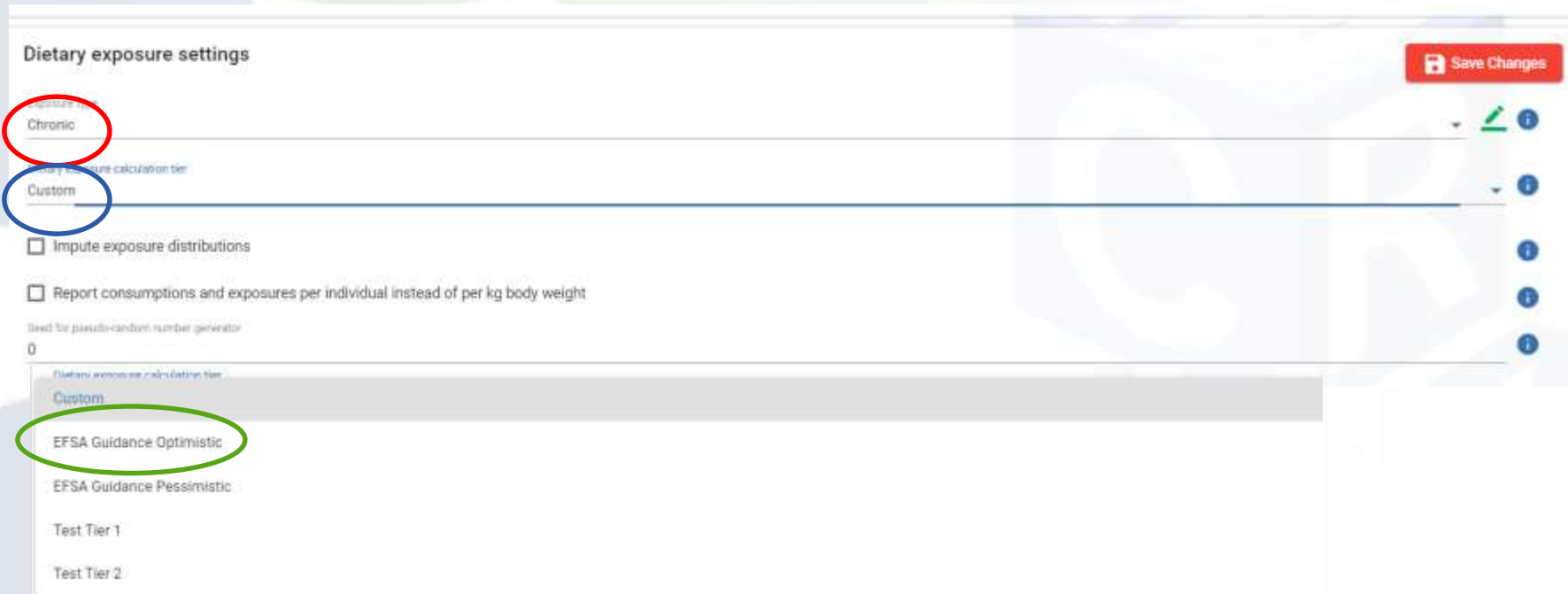2. Change acute to chronic

Adjust more settings

EuroMix

1. Scroll down to dietary settings

2. Make sure you selected chronic

3. Click on custom

4. A pop-up window appears on your screen. Select EFSA optimistic

Dietary exposure settings

Save Changes

Chronic

Custom

☐ Impute exposure distributions

☐ Report consumptions and exposures per individual instead of per kg body weight

Seed for pseudo-random number generator
0

Dietary exposure calculation tier

Custom

EFSA Guidance Optimistic

EFSA Guidance Pessimistic

Test Tier 1

Test Tier 2

Check and save settings

1. Check the settings

2. Save the settings

Dietary exposure settings

Save Changes

Exposure type
Chronic

Dietary exposure calculation tier
EFSA Guidance Optimistic

☐ Impute exposure distributions

☐ Report consumptions and exposures per individual instead of per kg body weight

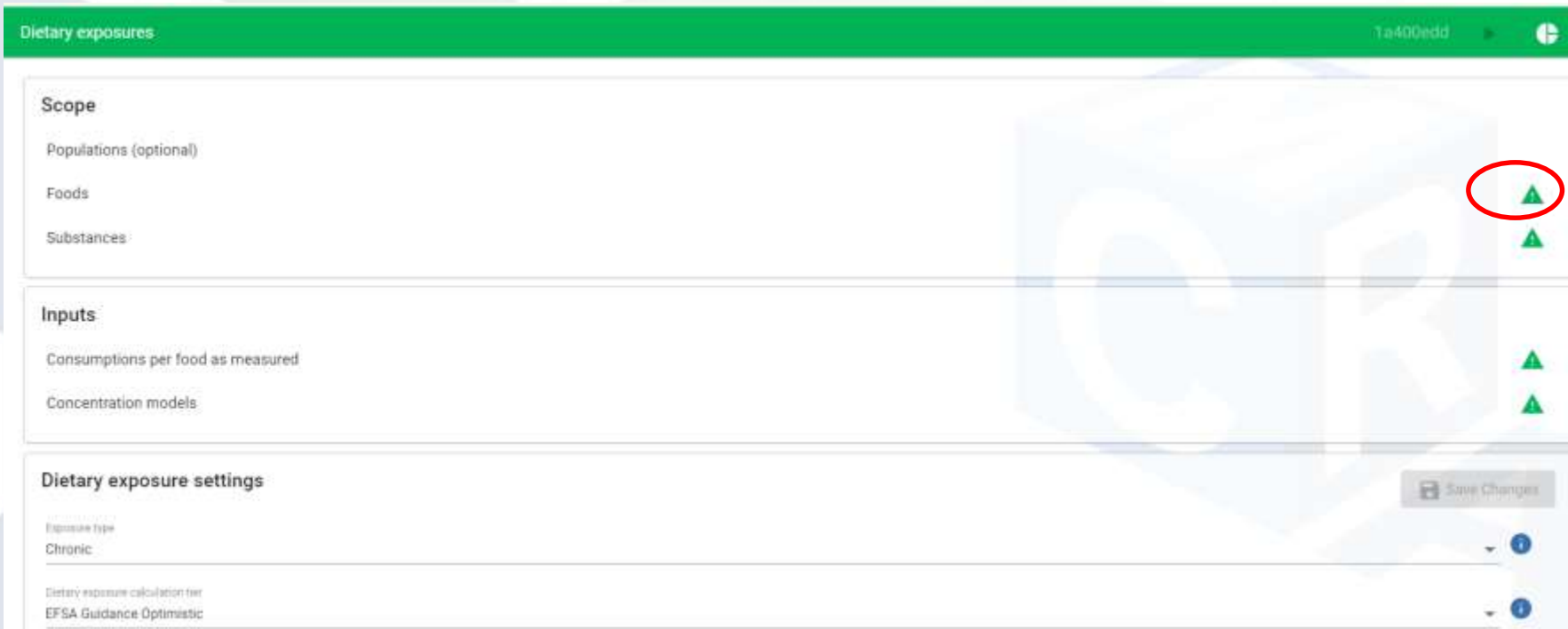Seed for pseudo-random number generator
0

Go back to the scope and insert data

EuroMix

1. A ⚠ indicates that something needs to be done

2. If you are using the toolbox for the first time, we advise you to work from top of the screen. Start with inserting data for foods
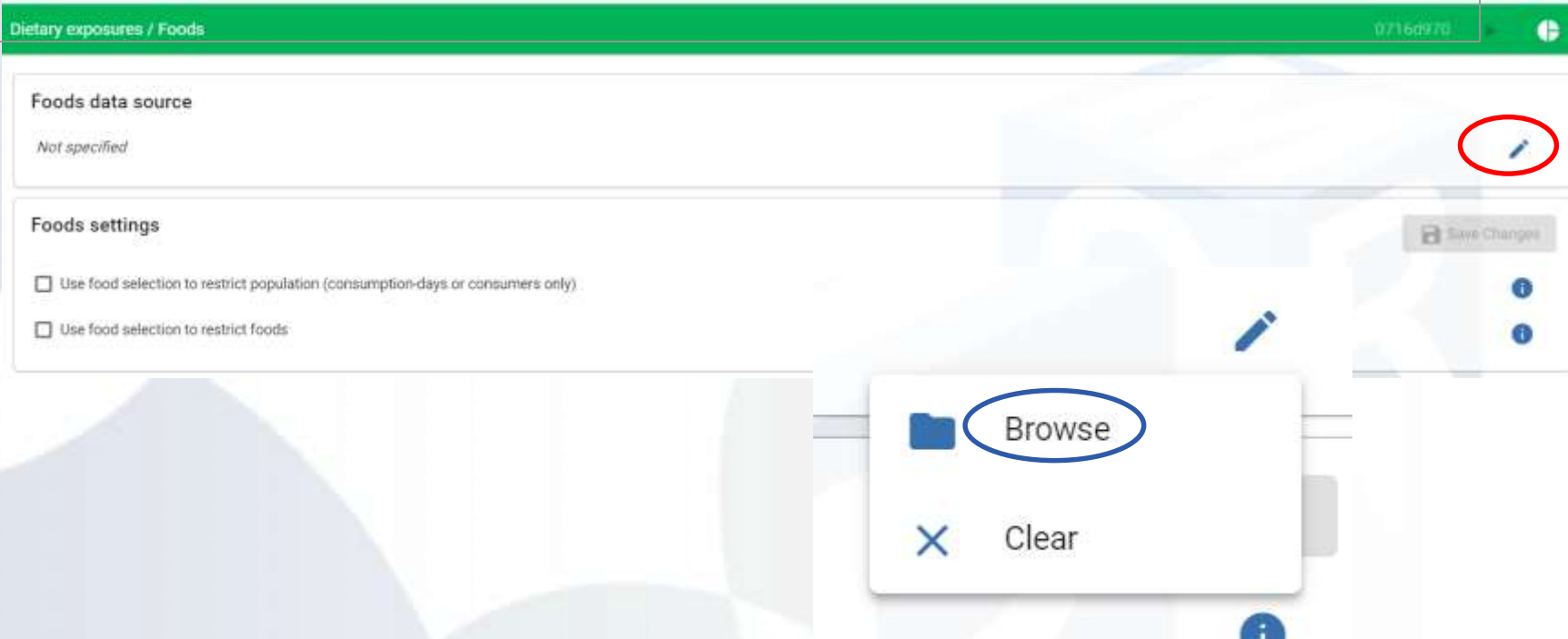
Specify data sources

EuroMix

1. A ✏️ indicates that you can insert data or names

2. Click on pencil

3. After you clicked on pencil a window pop-up, select Browse and you will be connected to your data folders

Dietary exposures / Foods   0716d970

Foods data source

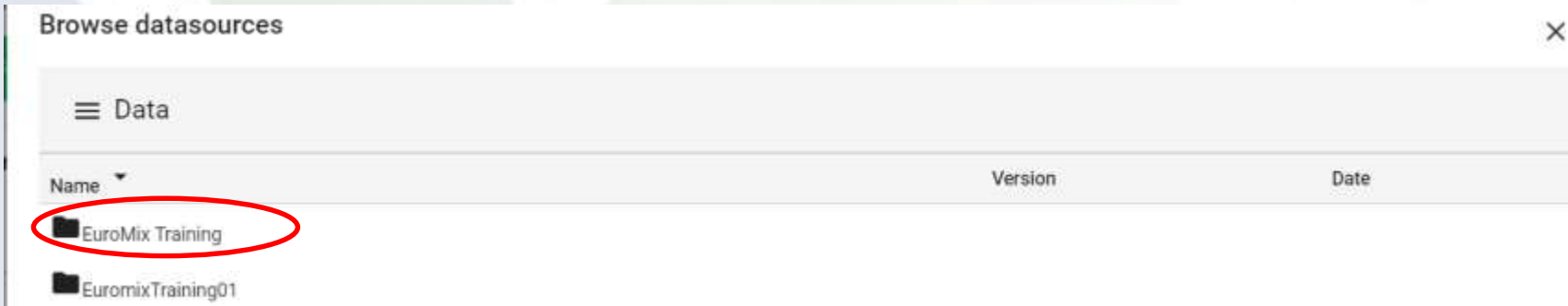Not specified   ✏️

Foods settings   💾 Save Changes

☐ Use food selection to restrict population (consumption-days or consumers only)   ℹ️

☐ Use food selection to restrict foods   ✏️   ℹ️

📁 Browse

✕ Clear

ℹ️

Specify data sources

1. Click on EuroMix training

2. A second window will open and select secondary data

Browse datasources   ✕

≡ Data

Name ▼	Version	Date
📁 EuroMix Training		
📁 EuromixTraining01		

Browse datasources

≡ Data / EuroMix Training

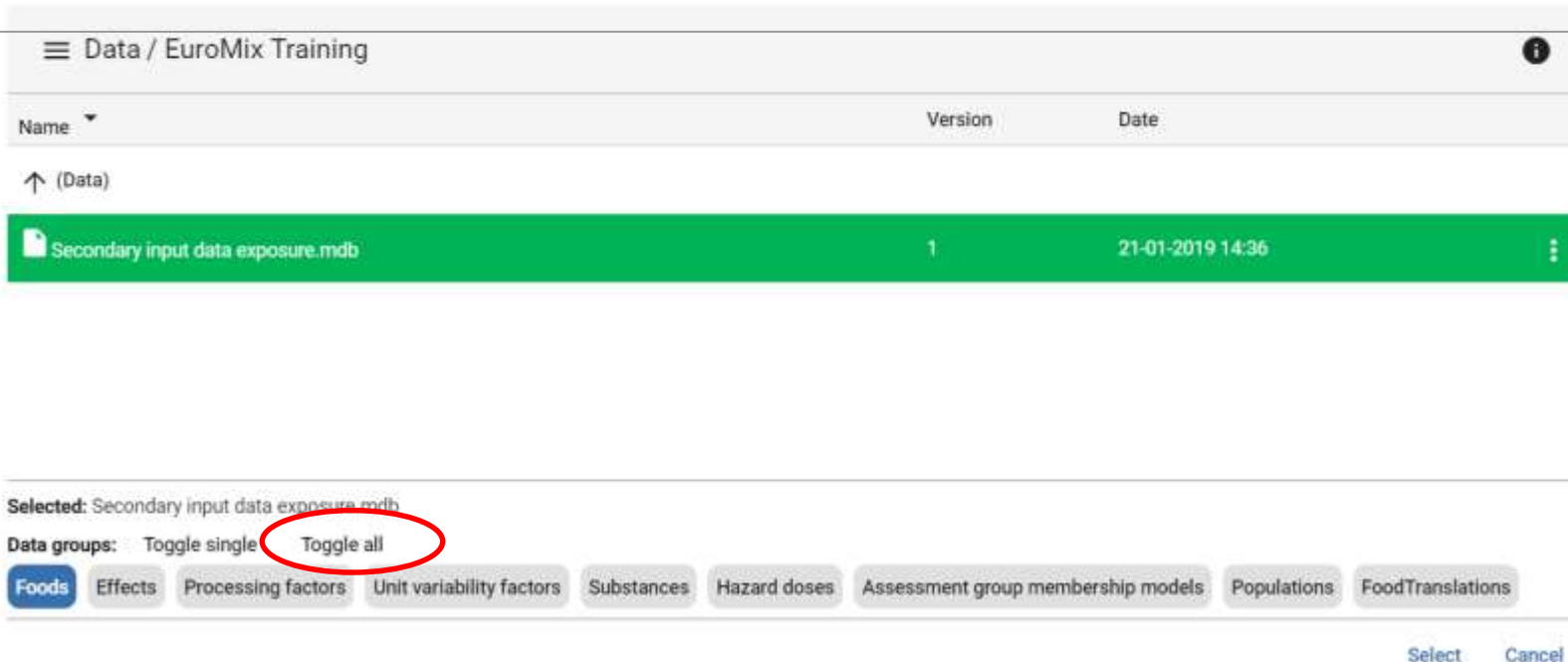| Name ▼	Version	Date
↑ (Data)		
📄 Secondary input data exposure.mdb	1	21-01-2019 14:36

Specify data sources

EuroMix
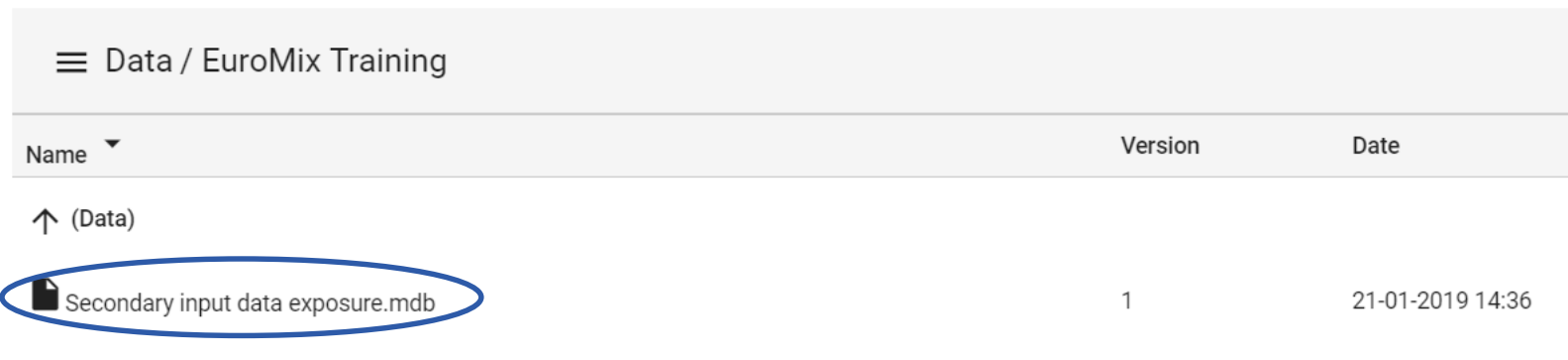
1. The secondary input data exposure.mdb (database)contains a food table, but it includes more information also on effects, processing factors etc. Toggle all to get all data connected in one step

3.

Browse datasources ✕

≡ Data / EuroMix Training ⓘ

Name ▾	Version	Date
↑ (Data)		
📄 Secondary input data exposure.mdb	1	21-01-2019 14:36 ⋮

Selected: Secondary input data exposure.mdb

Data groups: Toggle single   Toggle all

| Foods | Effects | Processing factors | Unit variability factors | Substances | Hazard doses | Assessment group membership models | Populations | FoodTranslations |

Select   Cancel

Select all database at once

EuroMix

1. Select all data by clicking on select
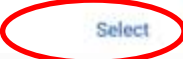
Browse datasources   ×

≡ Data / EuroMix Training   ⓘ

Name ▾	Version	Date	
↑ (Data)			
📄 Secondary input data exposure.mdb	1	21-01-2019 14:36	⋮

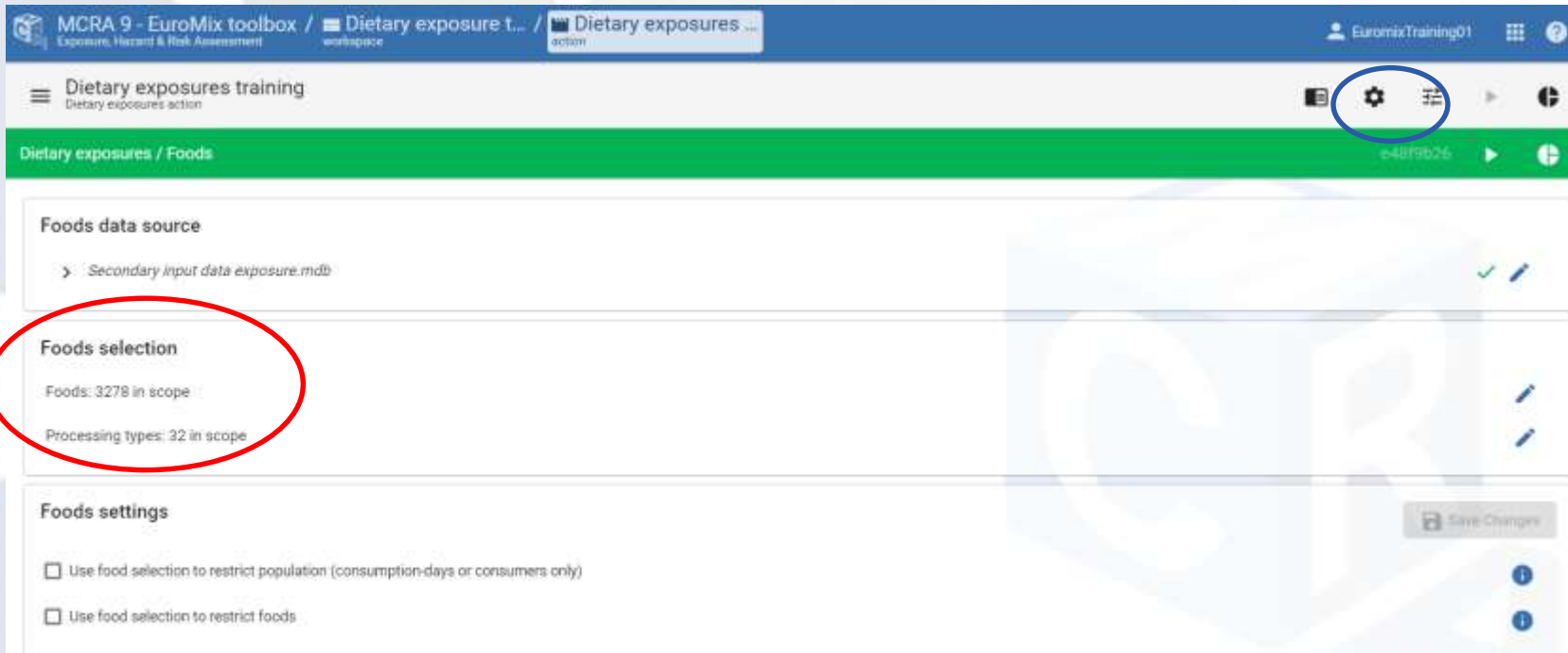**Selected:** Secondary input data exposure.mdb

Data groups: Toggle single   Toggle all

Foods   Effects   Processing factors   Unit variability factors   Substances   Hazard doses   Assessment group membership models   Populations   FoodTranslations

Select   Cancel

Select all database at once

 EuroMix

1. A ✓ means that the data connection is ok

2. Foods 3278 in scope means that your database contains 3278 food items and 32 processing types (e.g. juicing) no action required
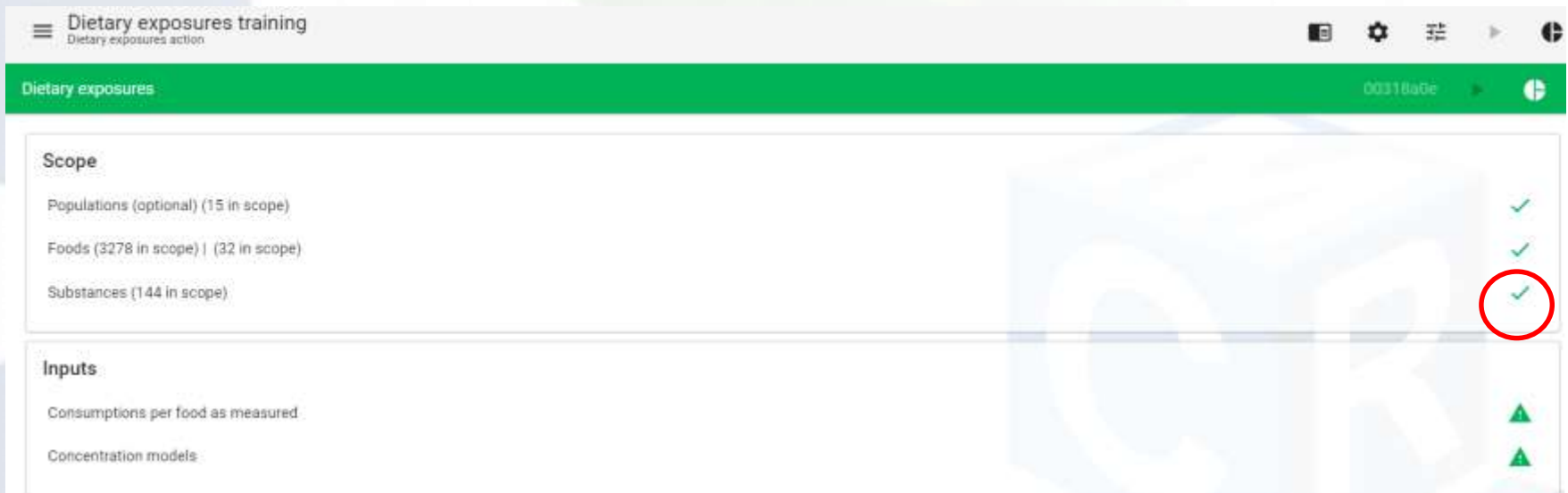
3. Go back to action in the navigation

Which substances should be in the scope of your assessment

1. A ✓ **does not** mean that all settings are ok

2. The user can either chose to do a single chemical (substance) exposure assessment or a exposure assessment for multiple substances. This selection can be made under substances.
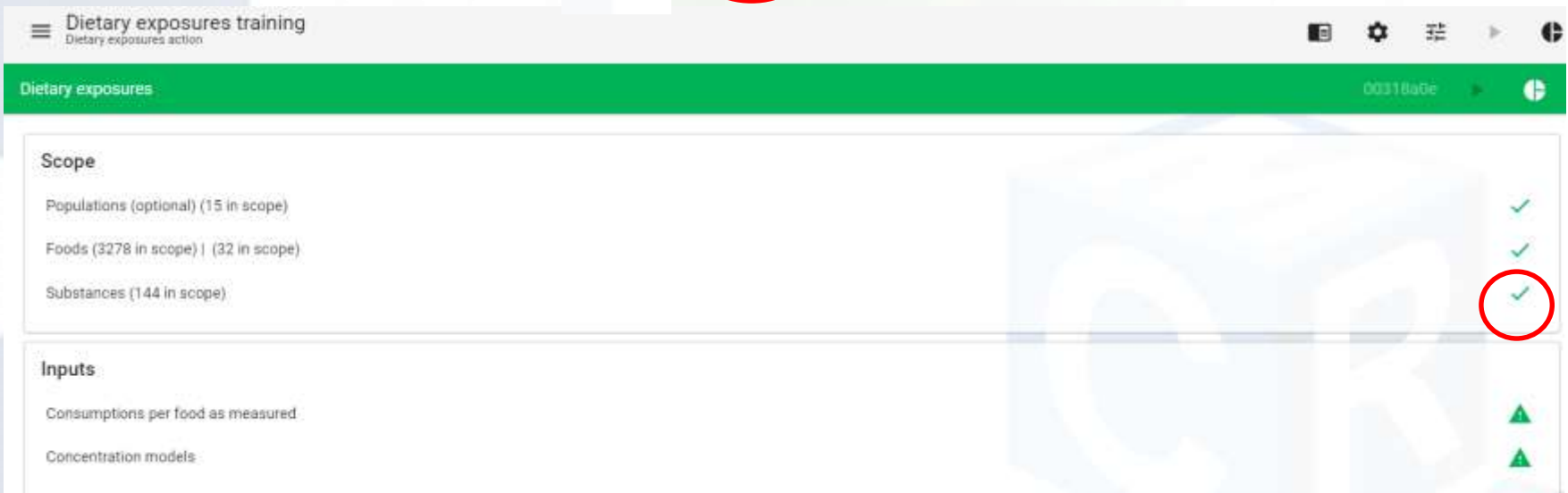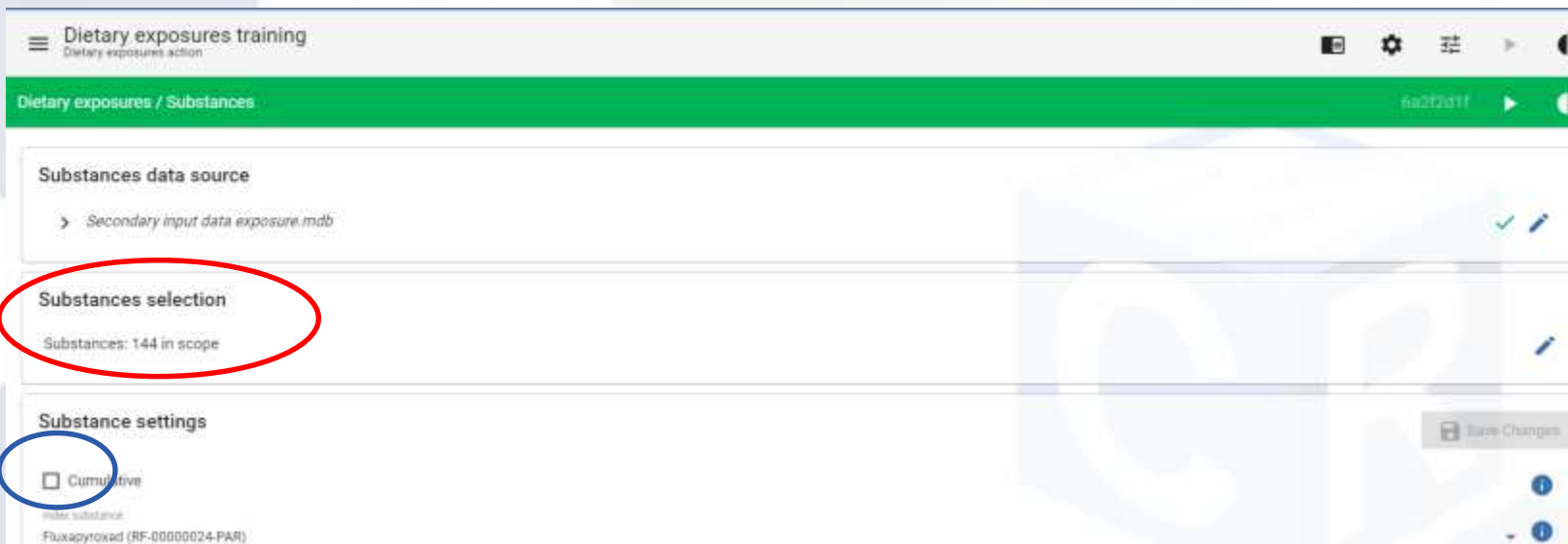
3. Click on substances ✓

Which substances should be in the scope of your assessment

EuroMix

1. A ✓ means that data are ok, but it **does not** mean that all settings are ok

2. The user can either chose to do a single chemical (substance) exposure assessment or a exposure assessment for multiple substances. This selection can be made under substances.

3. Click on substances ✓ ⭕

Which substances should be in the scope of your assessment

1. Please not that you have 144 substances in your scope. In this examples these are 144 pesticides grouped together in the cumulative assessment group liver steatosis. No action required

2. In this exercise you are going to include 144 substances in a cumulative exposure assessment. Click on cumulative

Identify a index chemical

EuroMix

1. Select and index substance by clicking on fluxapyroxqad

2. A new window pop-up with a list of all substances grouped in the cumulative assessment group liver steatosis. You now have to select an index substance..

Substance settings

Save Changes

☑ Cumulative

index substance
Fluxapyroxad (RF-00000024-PAR)

Dietary exposures / Substances

Filter text

Fluxapyroxad (RF-00000024-PAR)

Isopyrazam (RF-00000025-PAR)

Penthiopyrad (RF-00002609-PAR)

Fenpyrazamine (RF-00002610-PAR)

the Horizon
nme of the

Which substances should be in the scope of your assessment

EuroMix

1. Type in flusilazole

2. Save changes

Flusilazole

Flusilazole (RF-0218-001-PPP)

Substance settings   Save Changes

☑ Cumulative

index substance
Flusilazole (RF-0218-001-PPP)

Substance settings   Save Changes

☑ Cumulative

index substance
Flusilazole (RF-0218-001-PPP)

Identify an index chemical

EuroMix

1. Type in flusilazole

2. Save changes

Flusilazole

Flusilazole (RF-0218-001-PPP)

Substance settings

Save Changes

☑ Cumulative

Index substance
Flusilazole (RF-0218-001-PPP)
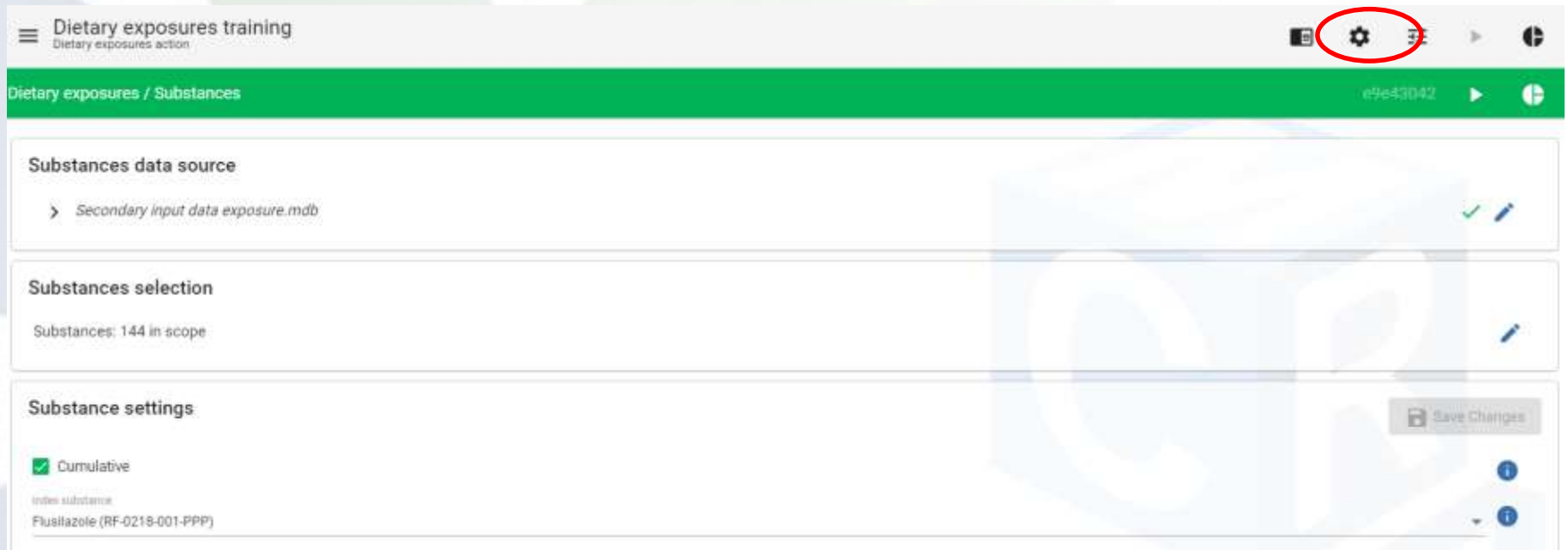
Substance settings

Save Changes

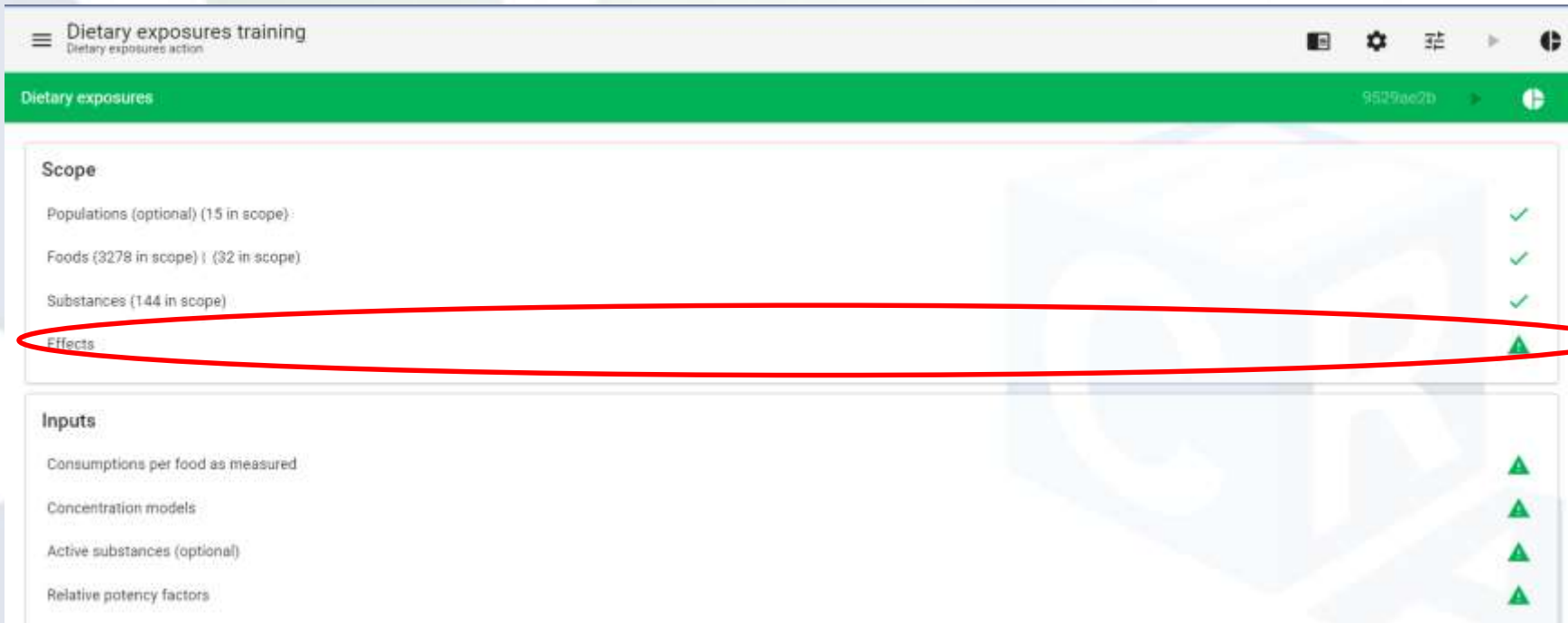☑ Cumulative

Index substance
Flusilazole (RF-0218-001-PPP)

Go back to action

1. Go back to action to select more data and settings

Select an effect

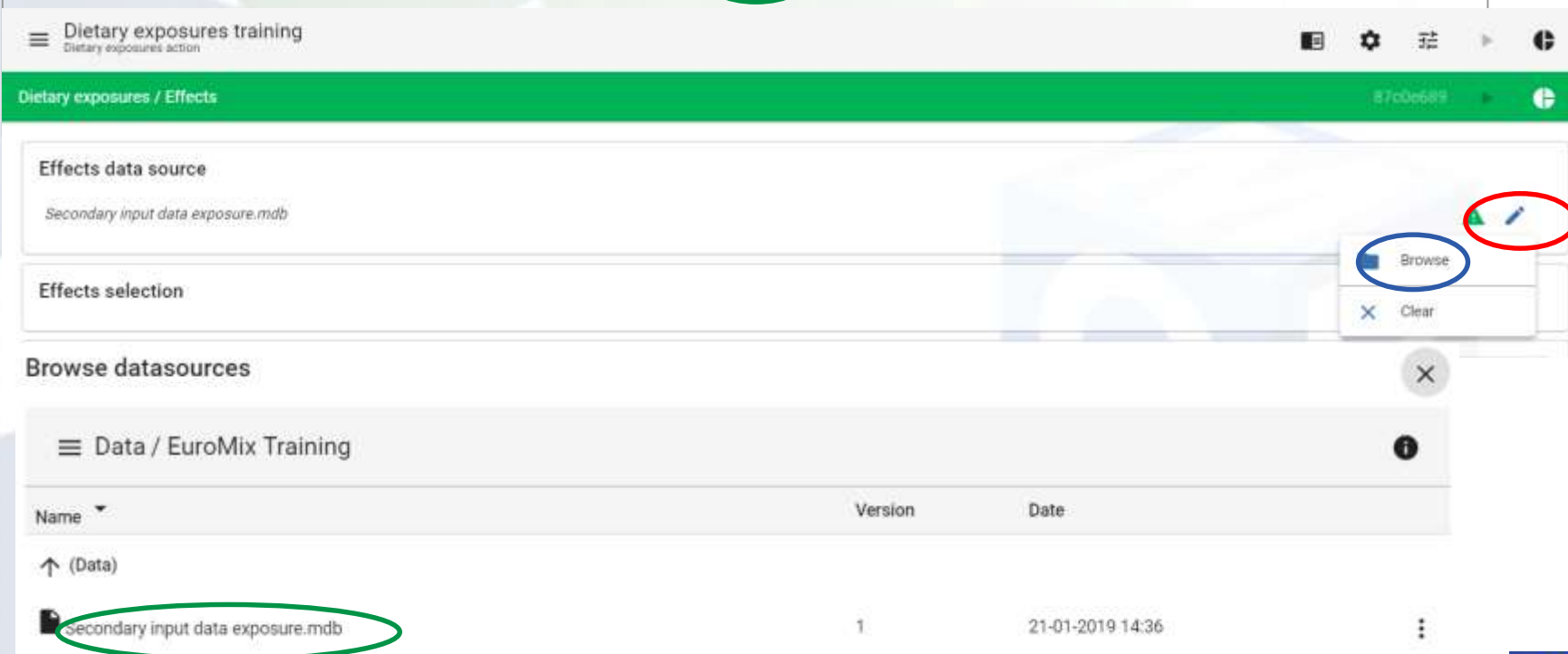1. Because you selected multiple substances you need to select an effect. Click on ⚠️

Select an effect

EuroMix

1. Click on pencil

2. A new window appears on your screen. Click on Browse

3. You are then connected to your data repository. Select secondary input data exposure.mdb

---

≡ Dietary exposures training
Dietary exposures action

Dietary exposures / Effects   87c0e689

Effects data source

Secondary input data exposure.mdb

                                                   ▣ Browse

Effects selection

                                                   ✕ Clear

Browse datasources   ✕

≡ Data / EuroMix Training   ℹ

Name	Version	Date
↑ (Data)		
Secondary input data exposure.mdb	1	21-01-2019 14:36

Select effect

1. Select effect database

Select effect

EuroMix

1. Click on pencil ✏ and see there is one effect in scope ⭕

2. Click on focal effect ⭕

3. Select Steatosis-liver ⭕

Dietary exposures / Effects   87c0e689 ▶ ⬤

Effects data source

⌄ *Secondary input data exposure.mdb*   ✓ ✏

    Effects: 1 in scope   ✓ ☰

Effects selection

Effects: 1 in scope   ✏

Effect settings   🖫 Save Changes

Focal effect   ▾ ⓘ

Please select a health effect

☐ Include key events (effects) of AOP network   ⓘ

☐ Include key events (effects) of AOP network   ⓘ

Please select a health effect

Steatosis-liver (Steatosis-liver)   ⓘ
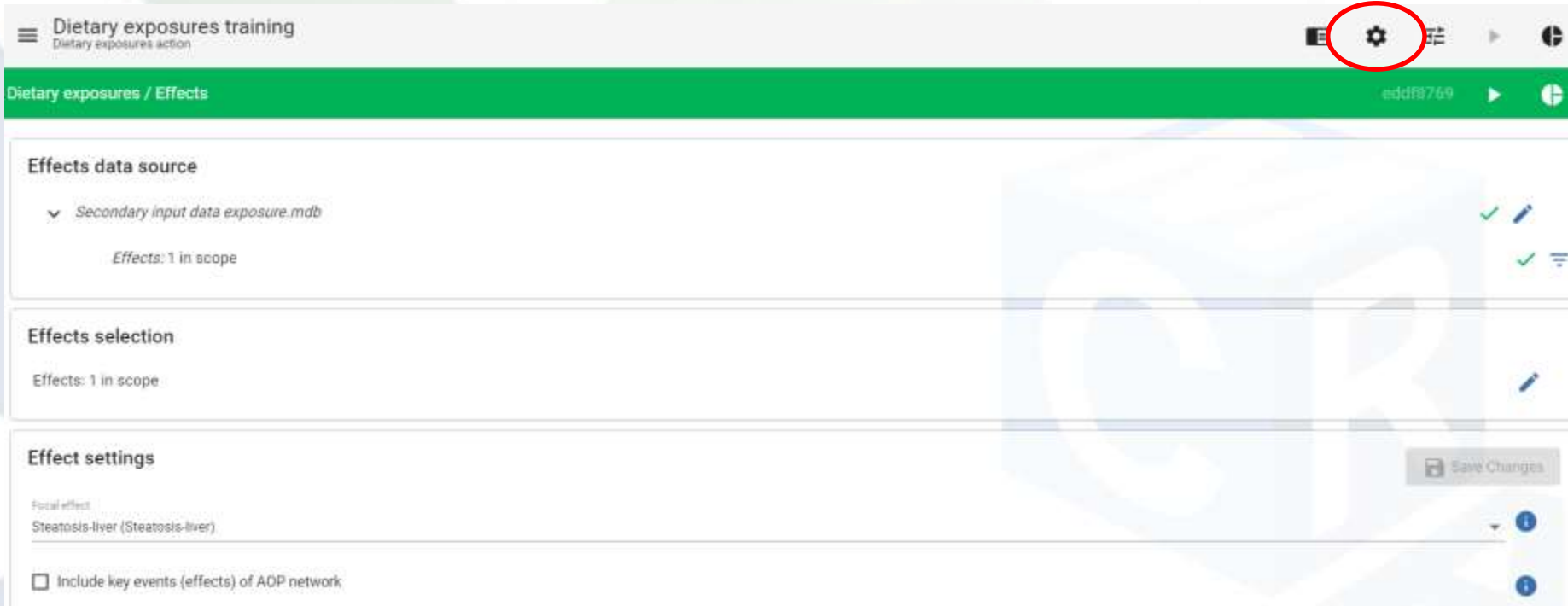
Save changes

Go back to actions

EuroMix

1. Go back to actions

Select more input

EuroMix

1. Go Consumptions per food as measured and click on

Dietary exposures	a2ac5477
Scope	
Populations (optional) (15 in scope)	✓
Foods (3278 in scope) | (32 in scope)	✓
Substances (144 in scope)	✓
Effects (1 in scope)	✓
Inputs	
Consumptions per food as measured	▲
Concentration models	▲
Active substances (optional) (1 assessment group membership models selected)	✓
Relative potency factors	▲

Select consumption data

EuroMix

1. Go to consumptions and click on

Select consumption data

1. Select Consumption data source by clicking on ⭕

Select consumption data

EuroMix

1. Select Consumption data source by clicking on

2. Click on Browse to get connected to your data repository

Select consumption data

1. Select EuroMix training

2. A new window pop-up. Select Consumptions data mdb

Browse datasources

☰ Data

Name ▼
📁 EuroMix Training
📁 EuromixTraining01

Browse datasources

☰ Data / EuroMix Training

Name ▼	Version	Date
↑ (Data)		
📄 Consumptions data.mdb	1	21-01-2019 14:00

by the Horizon
2020 Framework Programme of the
European Union

Select consumption data

1. Click on select

Browse datasources   ×

≡ Data / EuroMix Training   ℹ

Name ▼	Version	Date
↑ (Data)		
📄 Consumptions data.mdb	1	21-01-2019 14:00

Selected: Consumptions data.mdb

Data groups: Toggle single   Toggle all

Consumptions

Select   Cancel

Select consumption data

EuroMix

1. Click on Food Consumption survey

2. Select VCP-basis

Dietary exposures / Consumptions per food as measured / Consumptions   3ab63c7d

Scope

Populations (optional) (15 in scope)   ✓

Foods (3278 in scope) | (32 in scope)   ✓

Consumptions data source

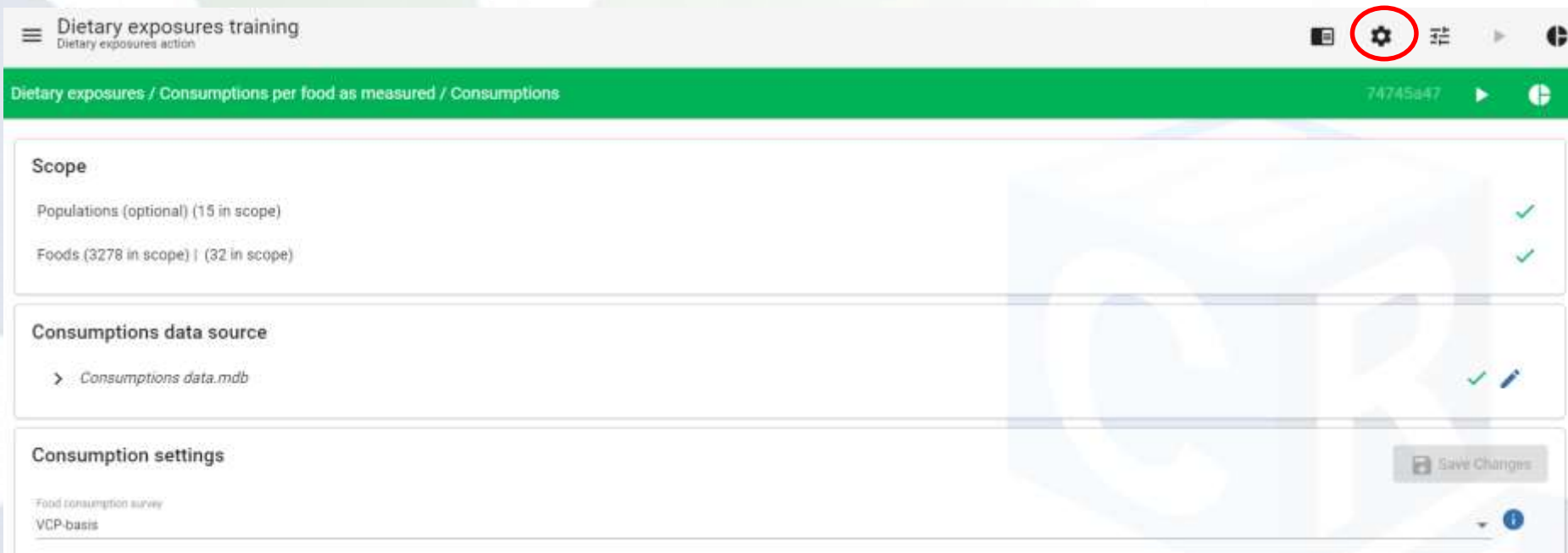> *Consumptions data.mdb*   ✓ ✏

Consumption settings   💾 Save Changes

Food consumption survey   ▾ ℹ

Please select a food consumption survey from the list

Filter text

VCP-basis

Please select a food consumption survey from the list

Select consumption data

1. Click on Food Consumption survey

2. Select VCP-basis

Select consumption data

1. Save settings

Select consumption data

1. Go back to actions

Select consumption data

1. Select Consumption per food as measured

2. Select food conversion in the new window

Select consumption data

1. Go to food as measured

Select concentration data

EuroMix

1. Select concentrations

Select concentration data

Select concentration data

EuroMix

1. Click on pencil

2. A new window pops-up. Click on Browse

Dietary exposures / Consumptions per food as measured / Food conversions / Foods as measured / Concentrations   2514da11   ▶   ◑

Scope

Foods (3278 in scope) | (32 in scope)   ✓

Substances (144 in scope)   ✓

Concentrations data source

Not specified   🖊

Concentrations data source

Not specified   🖊

Concentration settings

🔲 Browse

✕ Clear

Select concentration data

1. Select EuroMix training

2. A new window pop-up. Select Concentration-klein data mdb

Browse datasources

≡ Data

Name ▼

📁 EuroMix Training

📁 EuromixTraining01

Browse datasources

≡ Data / EuroMix Training

Name ▼	Version	Date
↑ (Data)		
📁 Concentrations-klein.mdb	1	21-01-2019 13:59

Select concentration data

EuroMix

1. Click on select

Browse datasources   ✕

≡ Data / EuroMix Training   ⓘ

Name ▾	Version	Date
↑ (Data)		
▣ Concentrations-klein.mdb	1	21-01-2019 13:59	⋮

Selected: Concentrations-klein.mdb

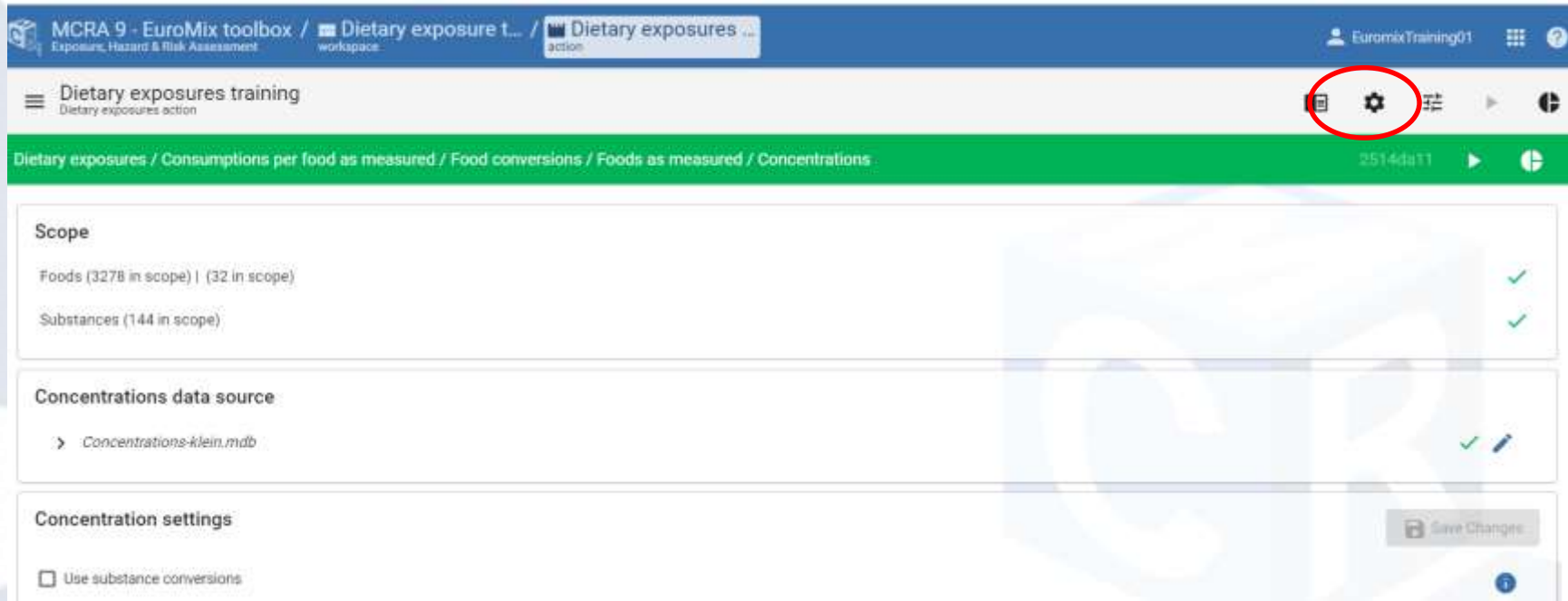**Data groups:** Toggle single   Toggle all

[Concentrations] [Substances]

Select   Cancel

Select concentration data

1. The consumption and concentration data (primary data) are selected. Go back to actions

Select hazard data

1. Click on Concentration model

Dietary exposures	e4a4cabe	
Scope		
Populations (optional) (15 in scope)		✓
Foods (3278 in scope) | (32 in scope)		✓
Substances (144 in scope)		✓
Effects (1 in scope)		✓
Inputs		
Consumptions per food as measured		✓
Concentration models		⚠
Active substances (optional) (1 assessment group membership models selected)		✓
Relative potency factors		⚠

Select hazard data

EuroMix

1. Get connected to a database with hazard information (relative potency factors) by clicking on
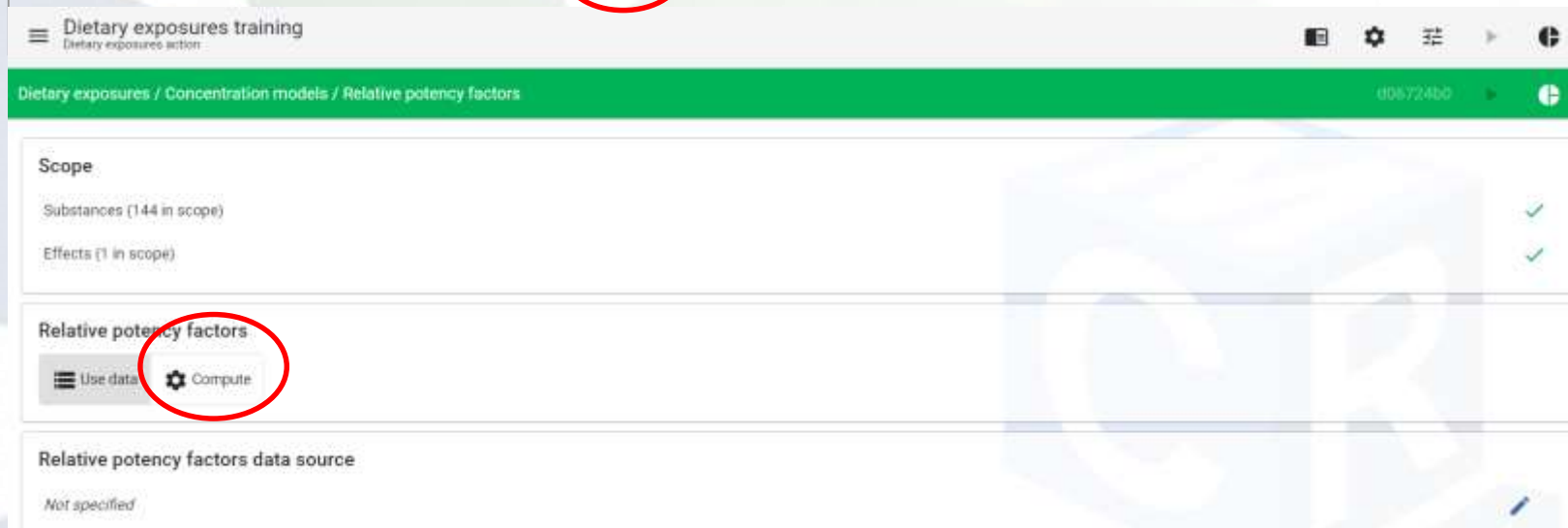
Use or compute hazard data

1. Sometime you have a table with Relative Potency Factors (RPFs), but usually a table with No-Effect-Level (NO(A)EL) or BMDLs information is provided. Such information needs to be transferred to a table with RPFs by using the Compute function.
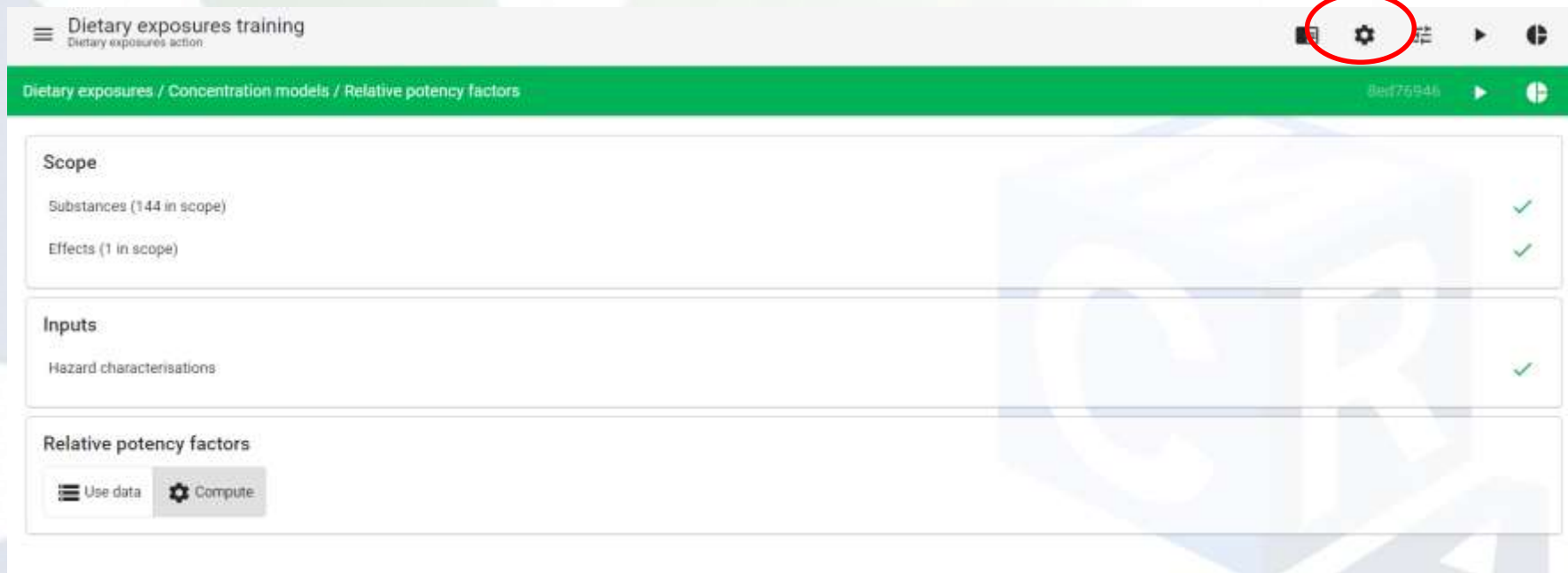
2. Click on compute

Go back to action

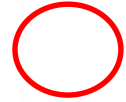**EuroMix**

1. Go back to action

Overview of inputs

1. At this stage all relevant secondary, consumption, concentration and hazard data are correctly linked to the model.

2. However, a ✓ **does not mean** that all settings are correct.

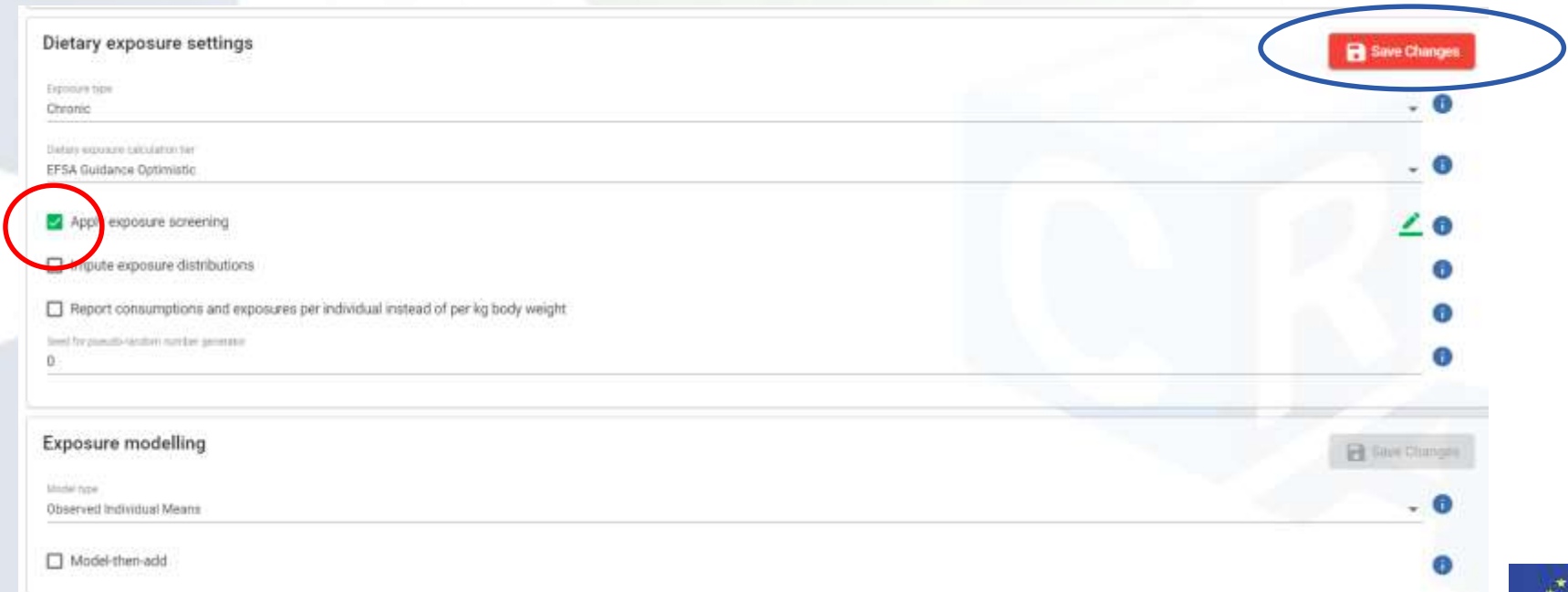3. Scroll down to see more settings

Change setting

1. At this stage all relevant secondary, consumption, concentration and hazard data are correctly linked to the model.

2. However, a ✓ **does not mean** that all settings are correct.

3. Scroll down to see more settings. Click on apply screening

4. Save Changes

Dietary exposure settings

Save Changes

Exposure type
Chronic

Dietary exposure calculation tier
EFSA Guidance Optimistic

☑ Apply exposure screening

☐ Impute exposure distributions

☐ Report consumptions and exposures per individual instead of per kg body weight

Seed for pseudo-random number generator
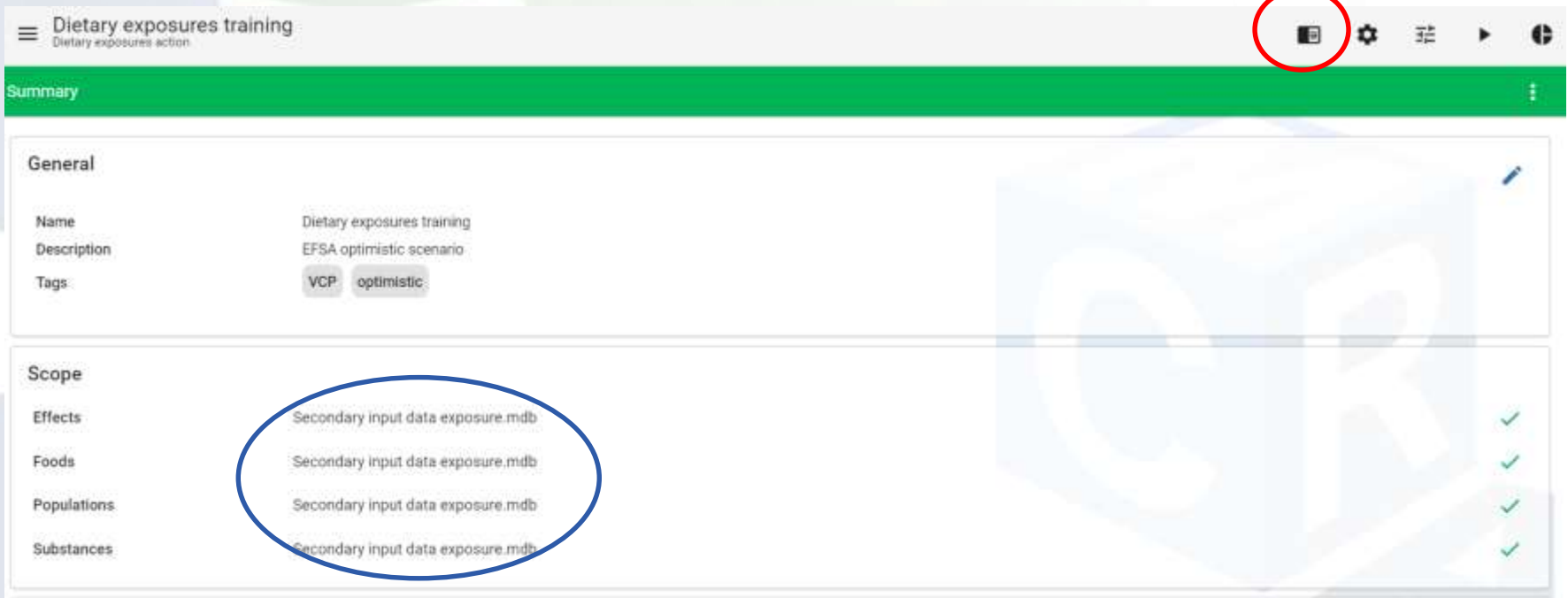0

Exposure modelling

Save Changes

Model type
Observed Individual Means

☐ Model-then-add

Summary overview

1. Click on summary symbol to overview the data and settings before you start running the simulation

2. Check if your data selection corresponds with the information on these slides

3. Scroll down to see more (see next slide)
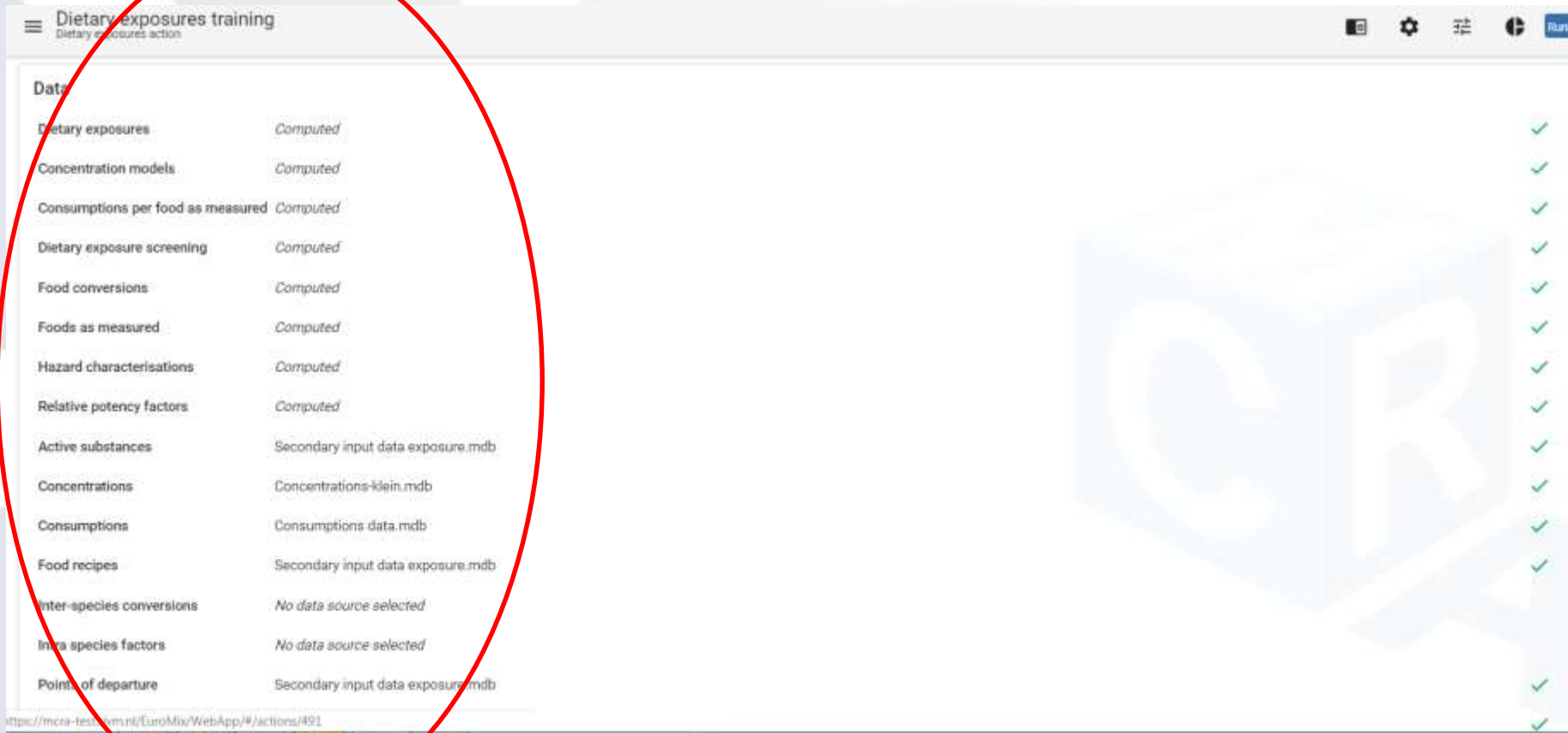
Summary overview

1. Check data and input settings

2. Scroll down

Summary overview

EuroMix

1. Check data and input settings

2. If all data and settings are ok, then go up and start running the simulation

Settings

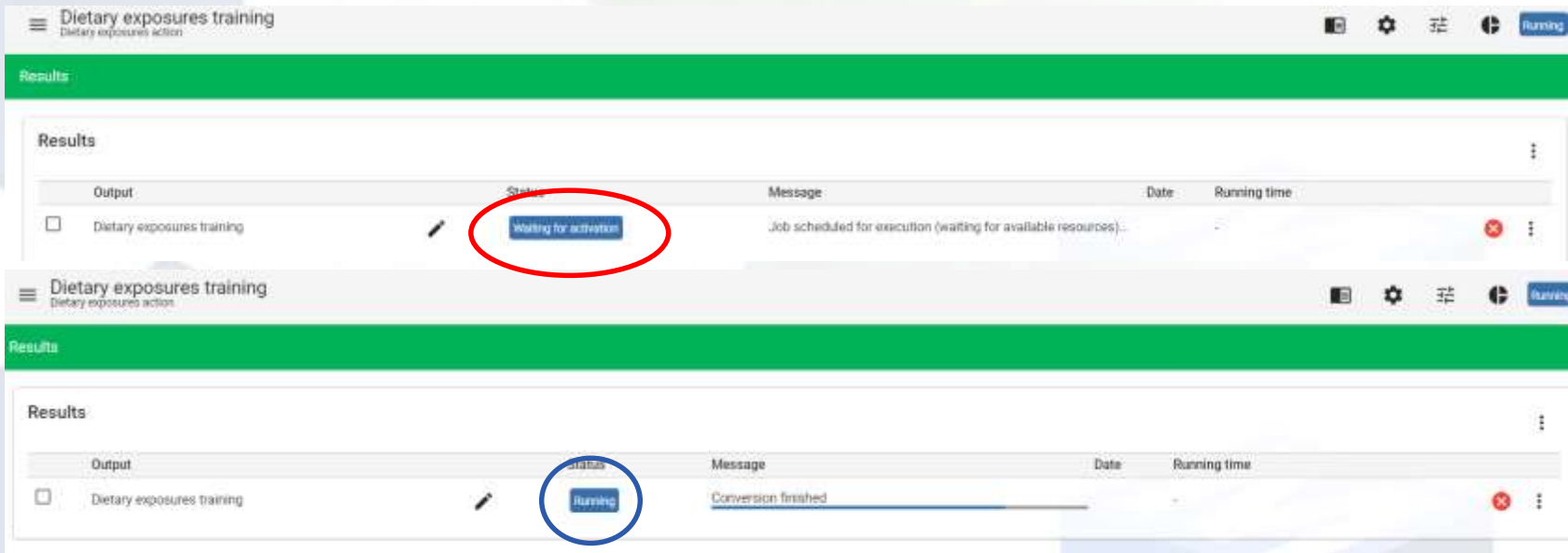|	
Exposure type	Chronic
Dietary exposure calculation tier	EFSA Guidance Optimistic
Apply processing factors	Yes
Processing factor model	Fixed
Apply exposure screening	Yes
Report consumptions and exposures per individual instead of per kg body weight	No
Covariate modelling	No
Model type	Observed individual Means

Summary

Dietary exposures action
Dietary exposures training

Run the simulation

EuroMix

1. After you start running the simulation, you see a screen with waiting for resources. This takes 10-20 seconds

2. Then waiting for resources changes into running (second screenshot)

3. This might take 3-4 minutes. If it takes longer than 10 minutes abort the job

Run the simulation

EuroMix
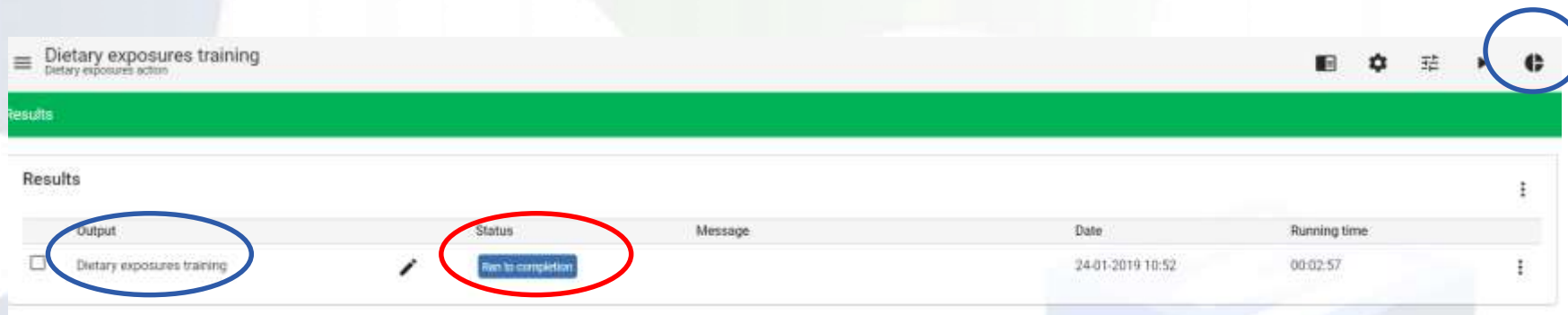
1. After 3-4 minutes you see Run to completion

2. Navigate to view the output results or click on Dietary exposure training
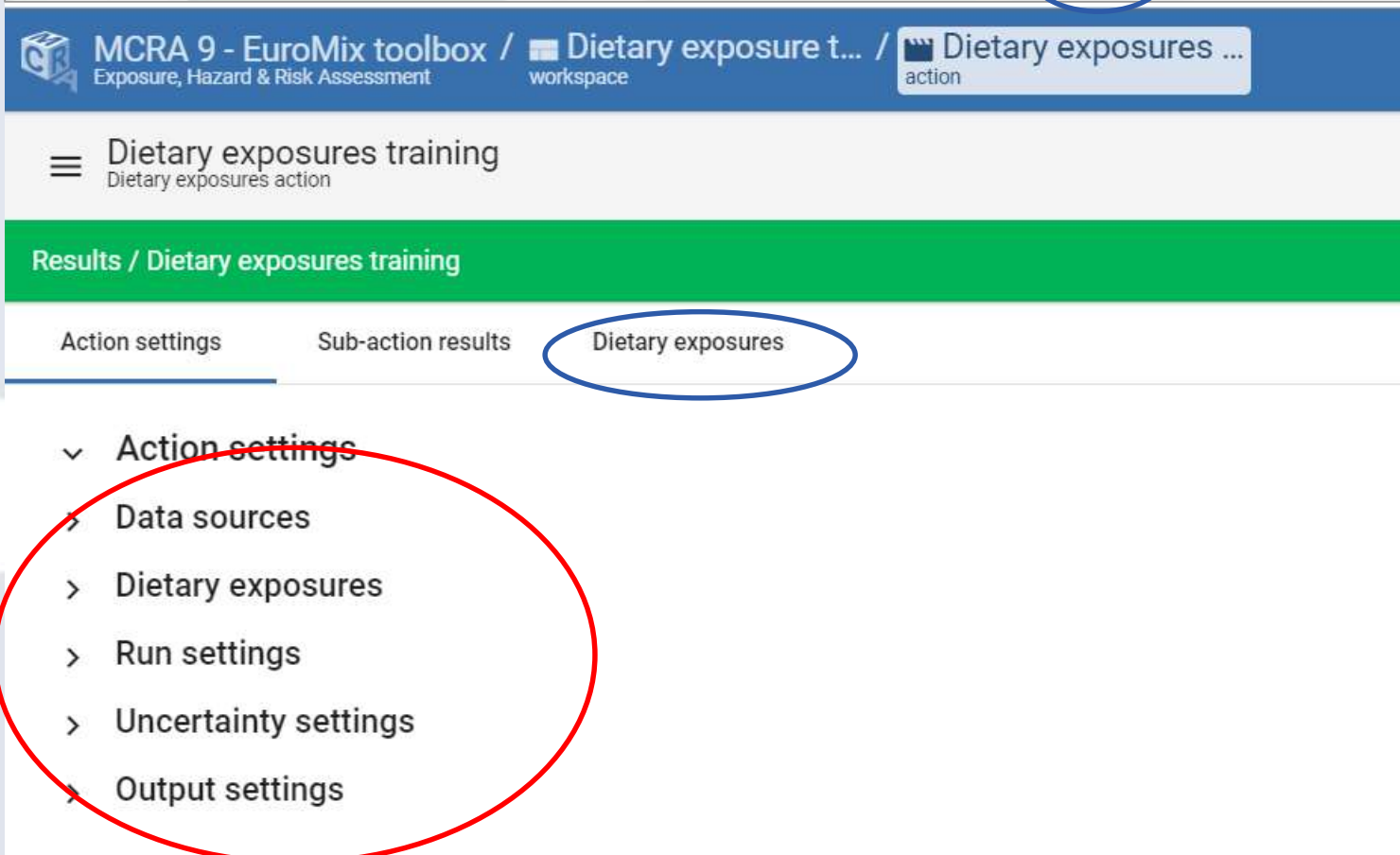
View the output

1. Your can check, and store the settings of your simulation. You can click on the options one by one

2. Go to dietary exposure to view the results

by the Horizon
gramme of the
European Union

View the output

EuroMix

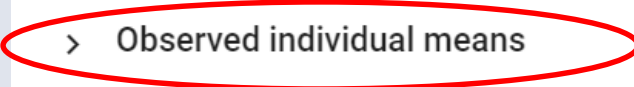1. Click on Observed individual means

---

≡ **Dietary exposures training**
Dietary exposures action

Results / Dietary exposures training

Action settings	Sub-action results	Dietary exposures

∨ Dietary exposures

› Dietary exposure distribution (daily intakes)

› Exposures by food

› Exposures by substance

› Exposures by food and substance

› Observed individual means

View the output

EuroMix

1. Click on percentile

- ⌄ Dietary exposures
- ﹥ Dietary exposure distribution (daily intakes)
- ﹥ Exposures by food
- ﹥ Exposures by substance
- ﹥ Exposures by food and substance
- ⌄ Observed individual means
- ﹥ Graph total
- ﹥ Graph upper tail
- ﹥ Percentiles
- ﹥ Percentages

View the output

EuroMix

1. Look at Margin of Exposure at the 99.9 percentile

2. Study the other percentile

Percentiles

Reference: Flusilazole, PoD = 530 µg/kg bw/day

Mean exposure: 0,2789 (µg/kg bw/day)

Percentage	Exposure (µg/kg bw/day)	Percentage of PoD (%)	Margin of exposure
50.00	0.1067	0.02	4968
90.00	0.7635	0.14	694.2
95.00	1.073	0.20	493.8
99.00	1.88	0.35	281.9
99.90	3.058	0.58	173.3
99.99	4.403	0.83	120.4

View the output

EuroMix

1. Check Exposure by substance

2. Chose total distribution or upper tail

3. Study the results and conclude that Imazalil is a very important contributor
4. What if you didn't had hazard data for Imazalil?
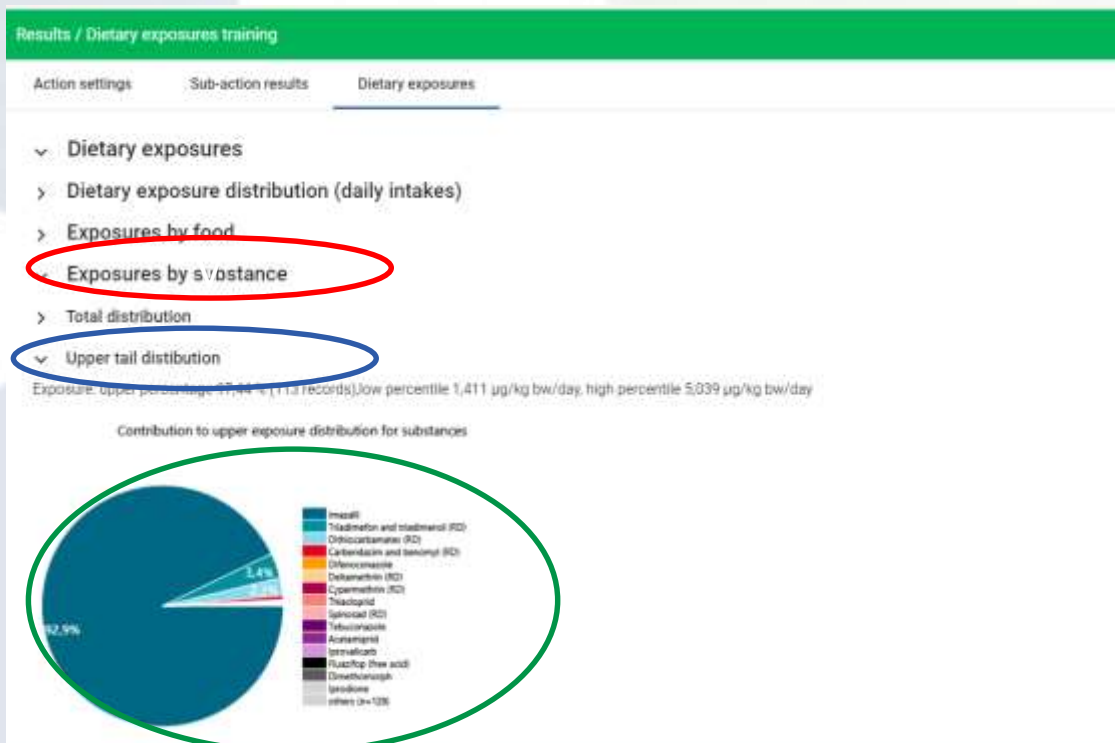
EuroMix participants

22 beneficiaries from 16 countries linked to international organisations including WHO, FAO and EFSA.
EuroMix is coordinated by RIVM.