CUMULATIVE AND AGGREGATED EXPOSURE TO PESTICIDES (ACROPOLIS PROJECT)

Partners: RIVM, FERA, University of Milan, CRD, IRAS, INRAN, NIPH, DLO, NFA, Freshfel Europe and University of Ghent

Associated partners: DTU (Denmark), CSL (Cyprus), ANSES (France), FVC (Latvia), NIPH (Slovenia), BPI (Greece) AGES (Austria)

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Aims of EU project ACROPOLIS

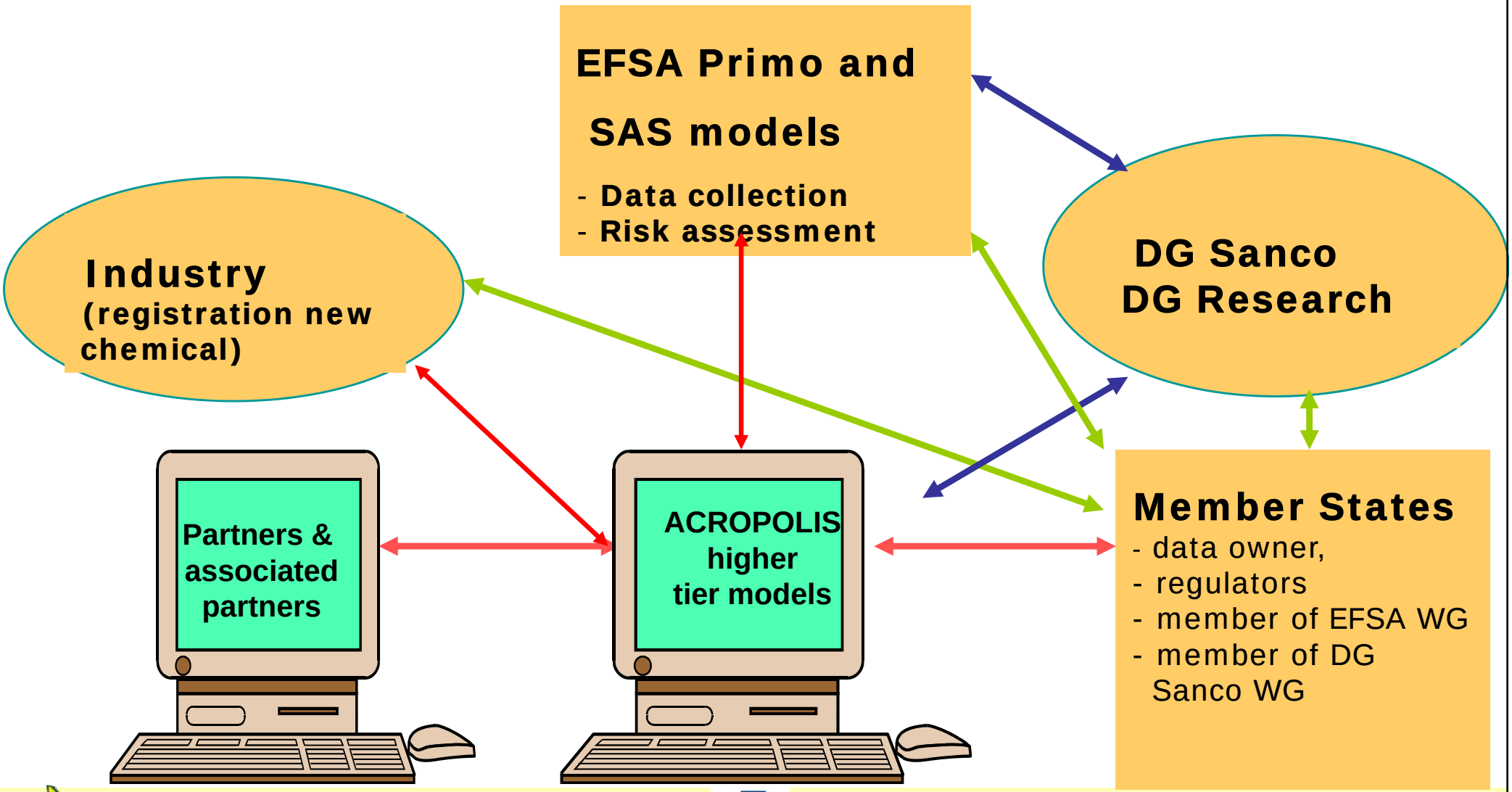
- Improved cumulative **exposure** assessment and cumulative hazard assessment;
- To integrate **cumulative and aggregate risk models** in a web-based tool, including accessible data for all stakeholders;
- **Improving the understanding** of cumulative risk assessment methodology of different **stakeholders**.

GREENPEACE

HSE

efsa
European Food Safety Authority

Internet exchange of models and results



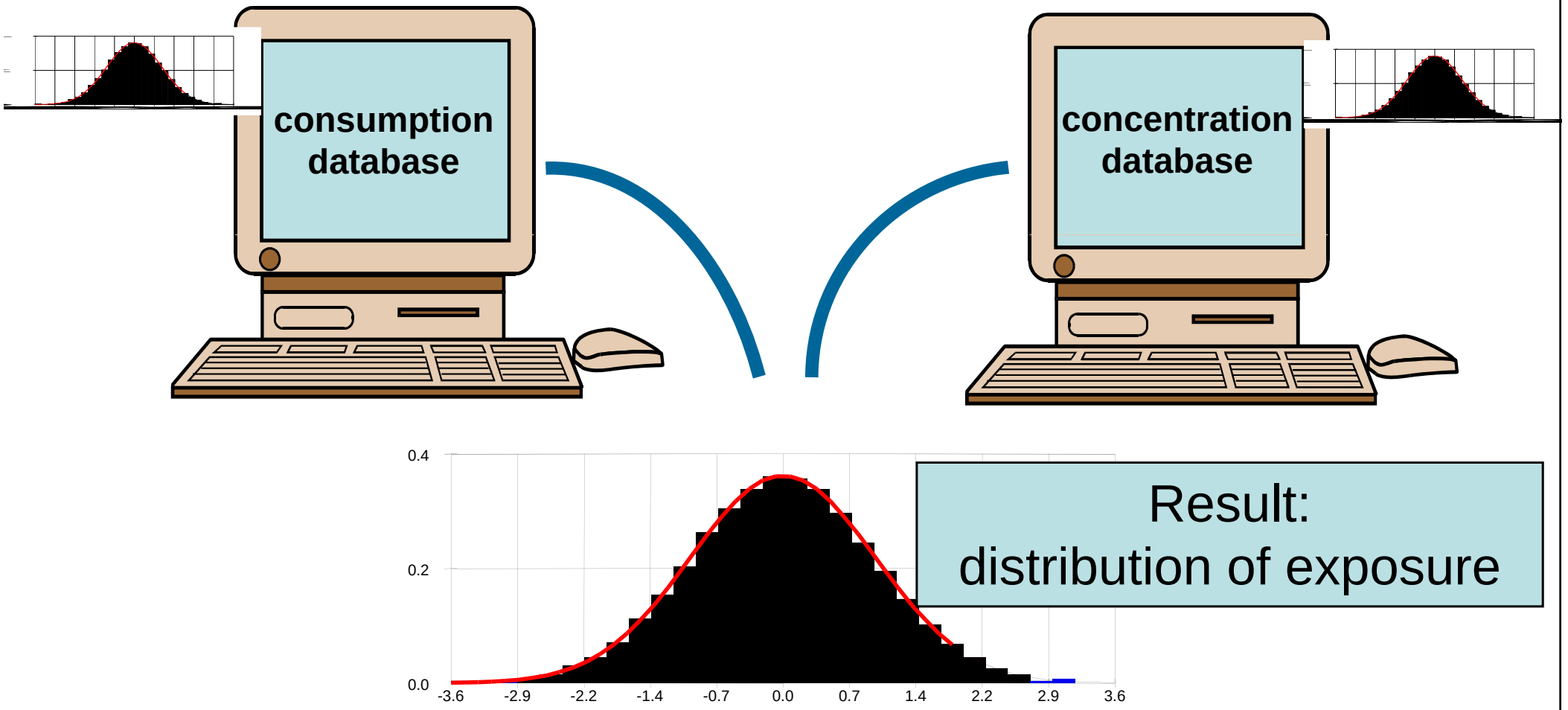
Stakeholder involvement

- is concept understandable?
- usefulness?
- attitudes

First stakeholders conference

- DG SANCO expectation from ACROPOLIS
  - call for cooperation EFSA and ACROPOLIS
  - IT tool accessible to all stakeholders
- Carl Schlyter (European Parliament)
  - difficult to explain that it has not been regulated since 2005 Go for it, and fix the hole!
- Trust in ACROPOLIS from (nearly) all stakeholders

MCRA: How it works acute



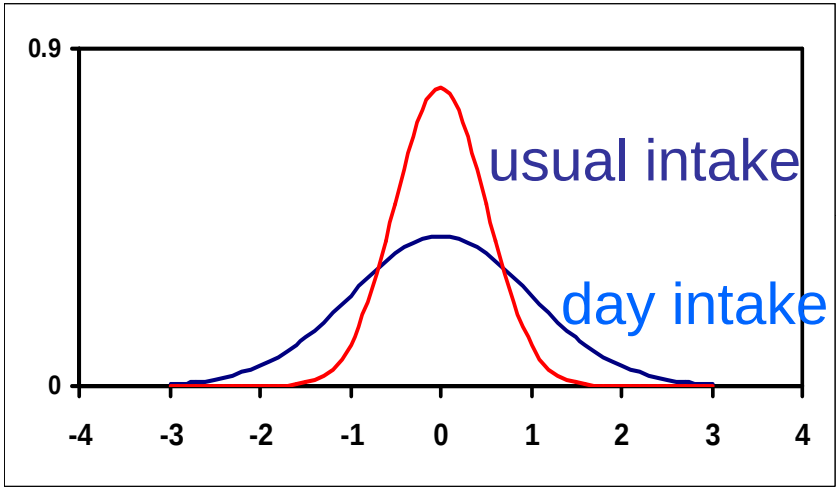
Result:
distribution of exposure

Random sampling from a concentration and a consumption database

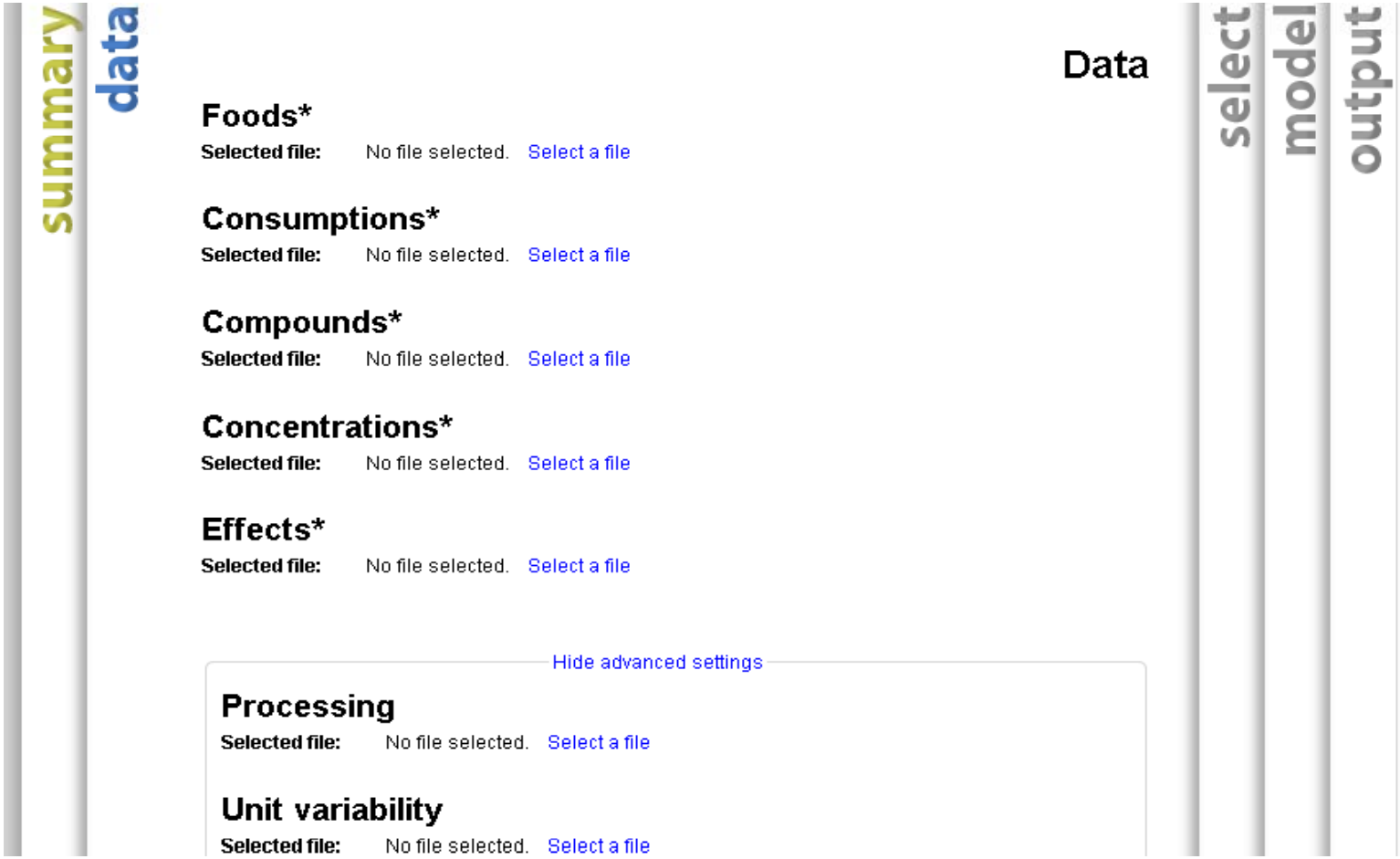
How it works chronic (ETUI project)

- Observed individual Mean
  EFSA Guidance

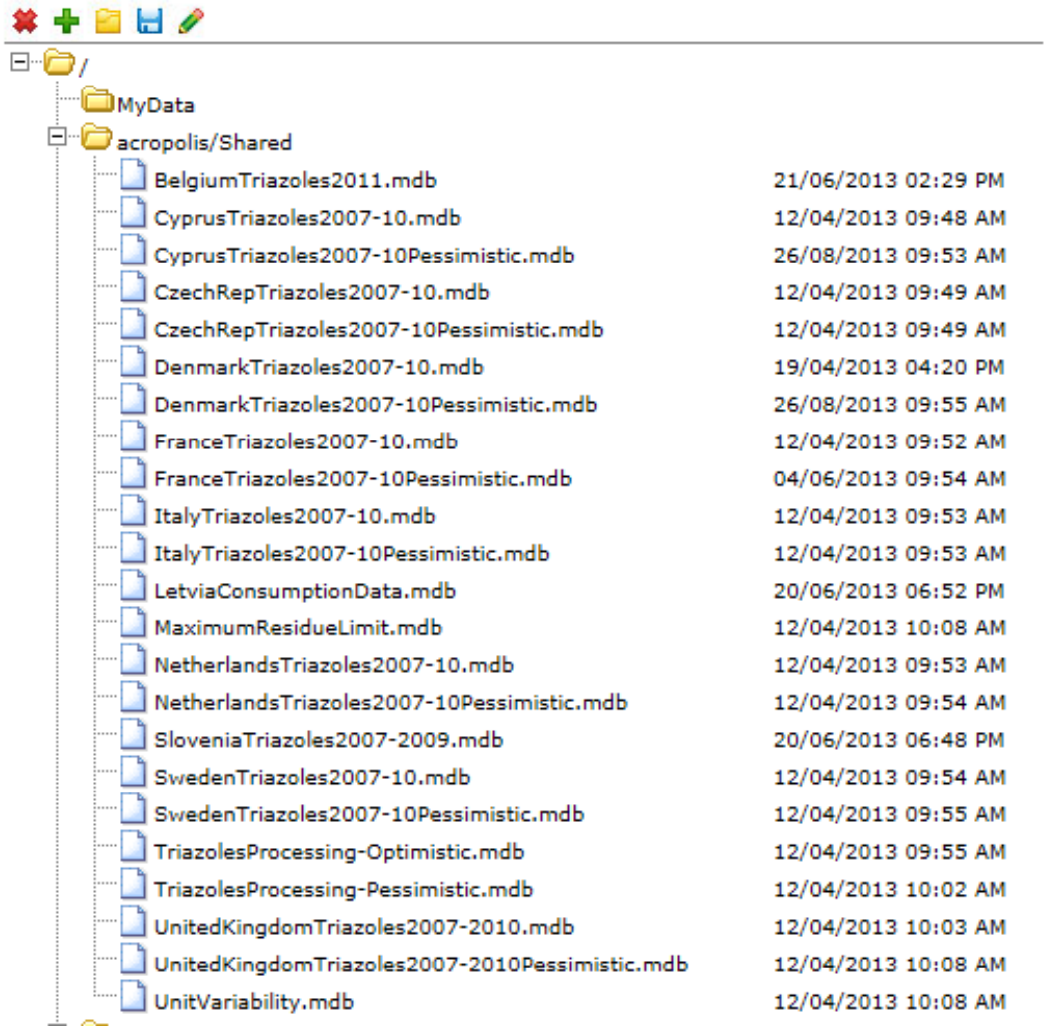
- variance components model
  - between individuals
  - days within individuals
  - transformation to a log or power (Box-Cox) scale
  - remove within persons variation



MCRA: Data


summary
data
Data
select
model
output
Foods*
Selected file: No file selected. Select a file
Consumptions*
Selected file: No file selected. Select a file
Compounds*
Selected file: No file selected. Select a file
Concentrations*
Selected file: No file selected. Select a file
Effects*
Selected file: No file selected. Select a file
Hide advanced settings
Processing
Selected file: No file selected. Select a file
Unit variability
Selected file: No file selected. Select a file

E-Platform and get data connected

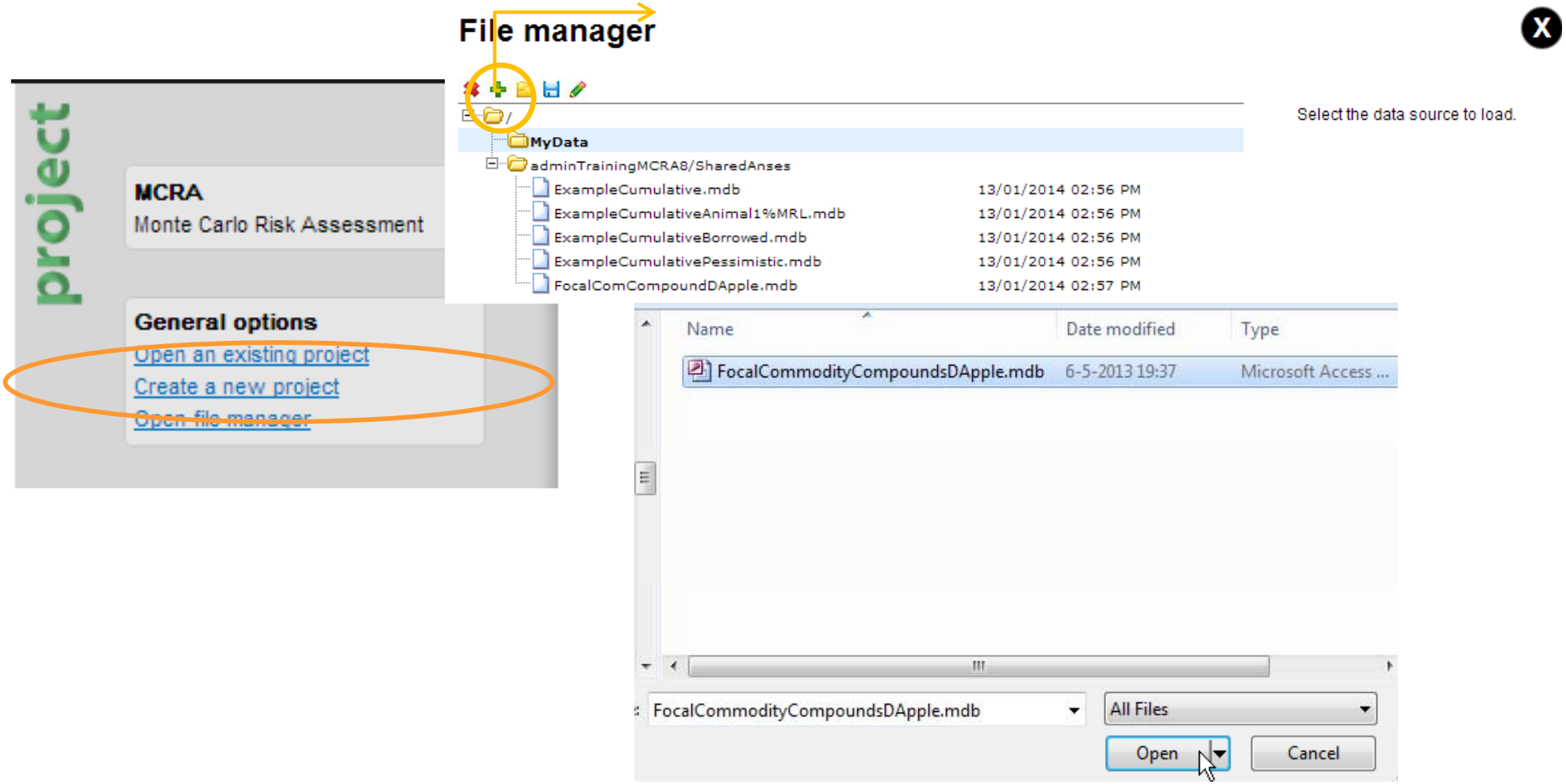


New or adjusted information

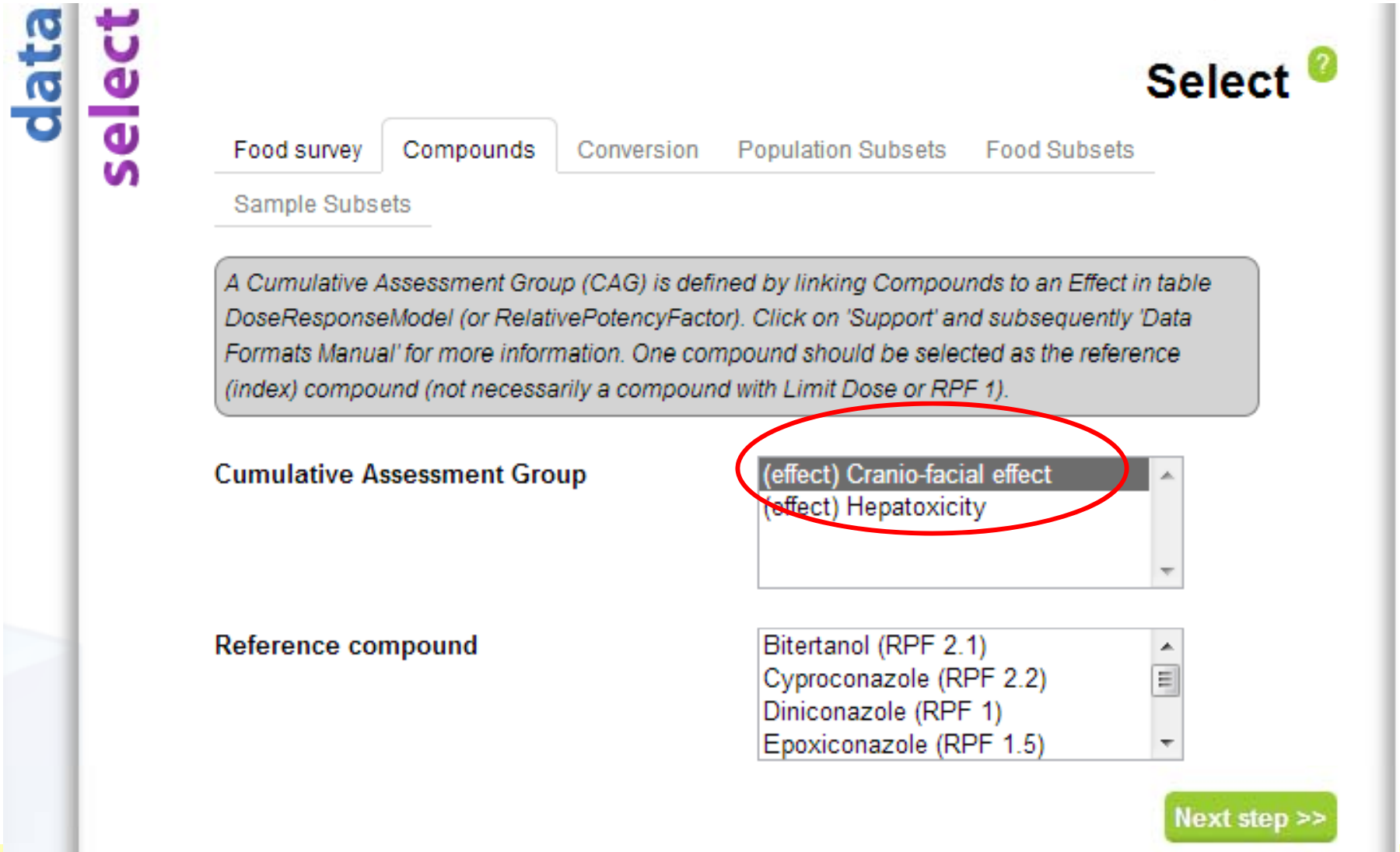
Data to add/modify for MCRA 8.0 simulations.

- [ ] Supervised trial data
- [ ] Adjust toxicological information
- [ ] View and update unit variability information
- [ ] Adjust variability factors
- [ ] Adjust unit variability usage
- [ ] Prepare processing factors
- [ ] Exit

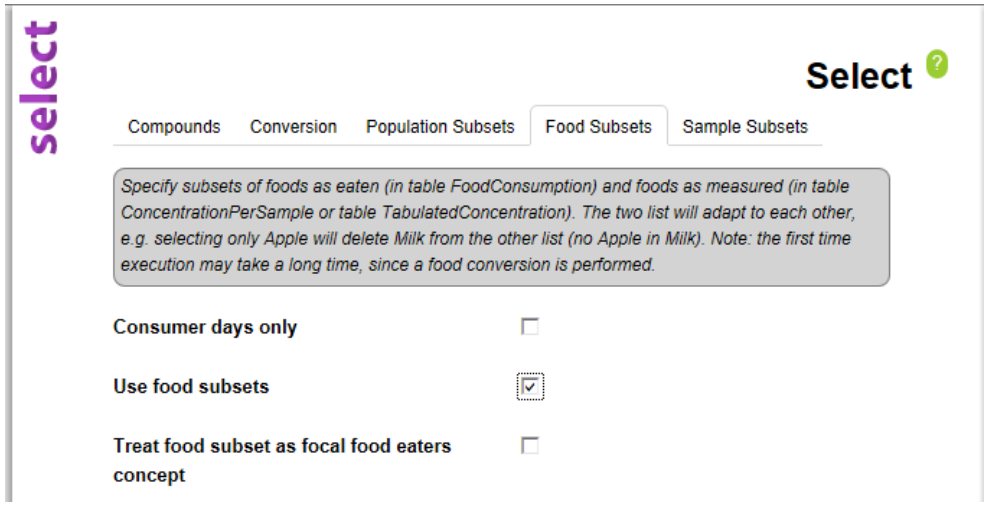
MCRA: upload focal commodity database

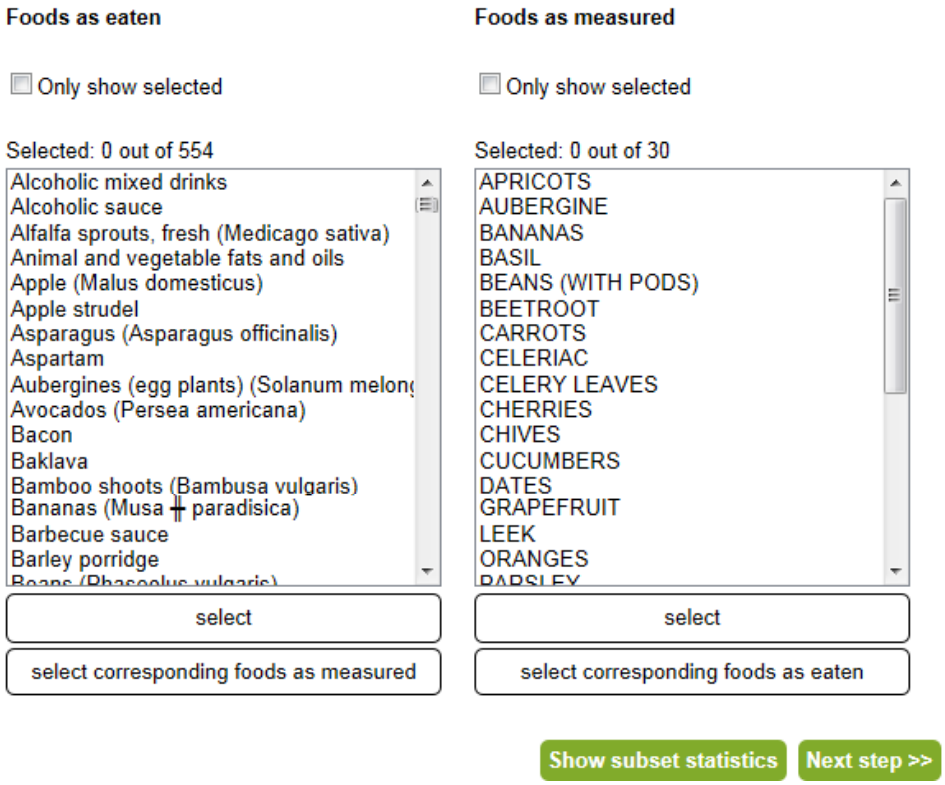


MCRA: common assessment group

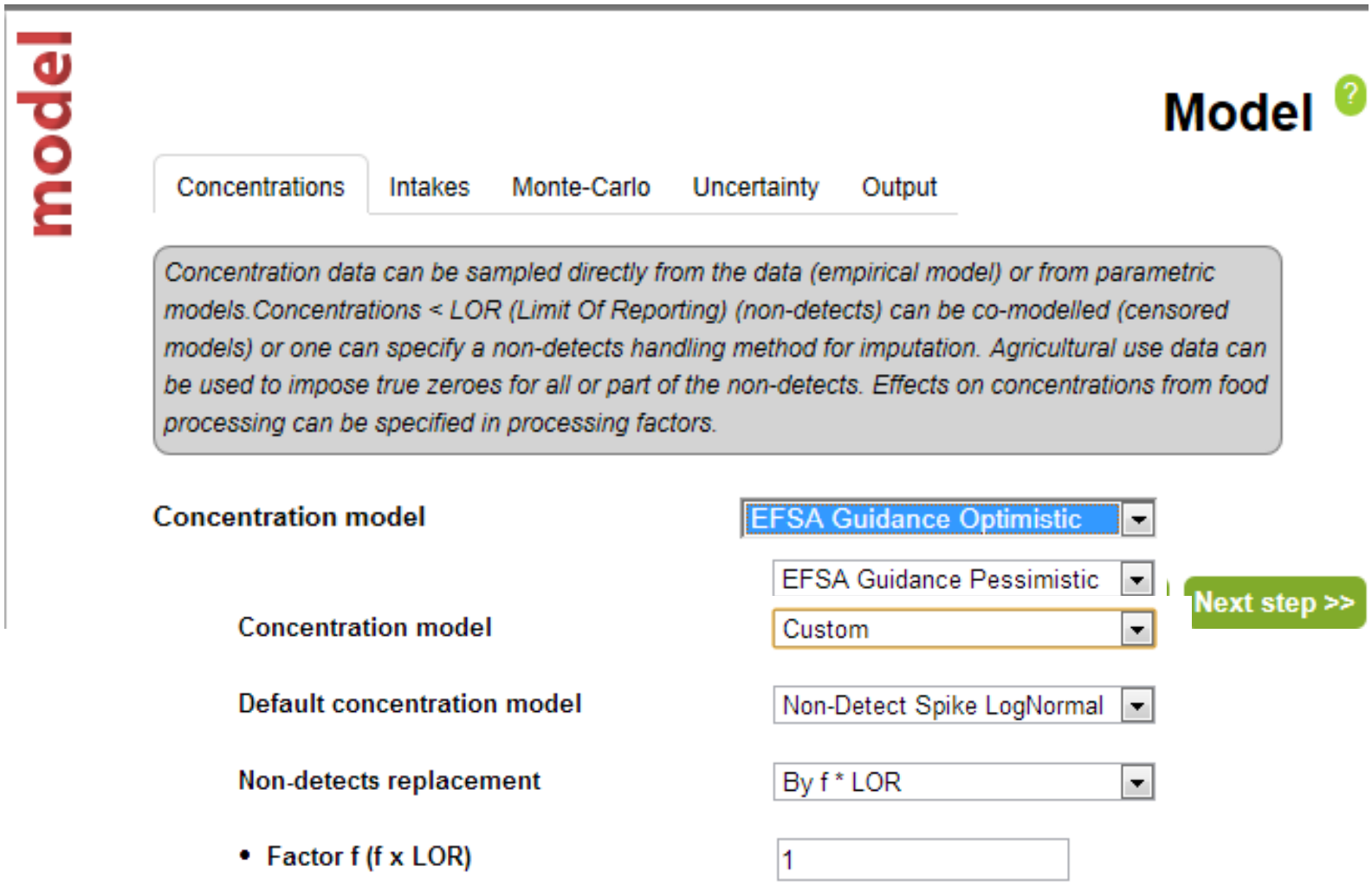


MCRA: consumer only approach

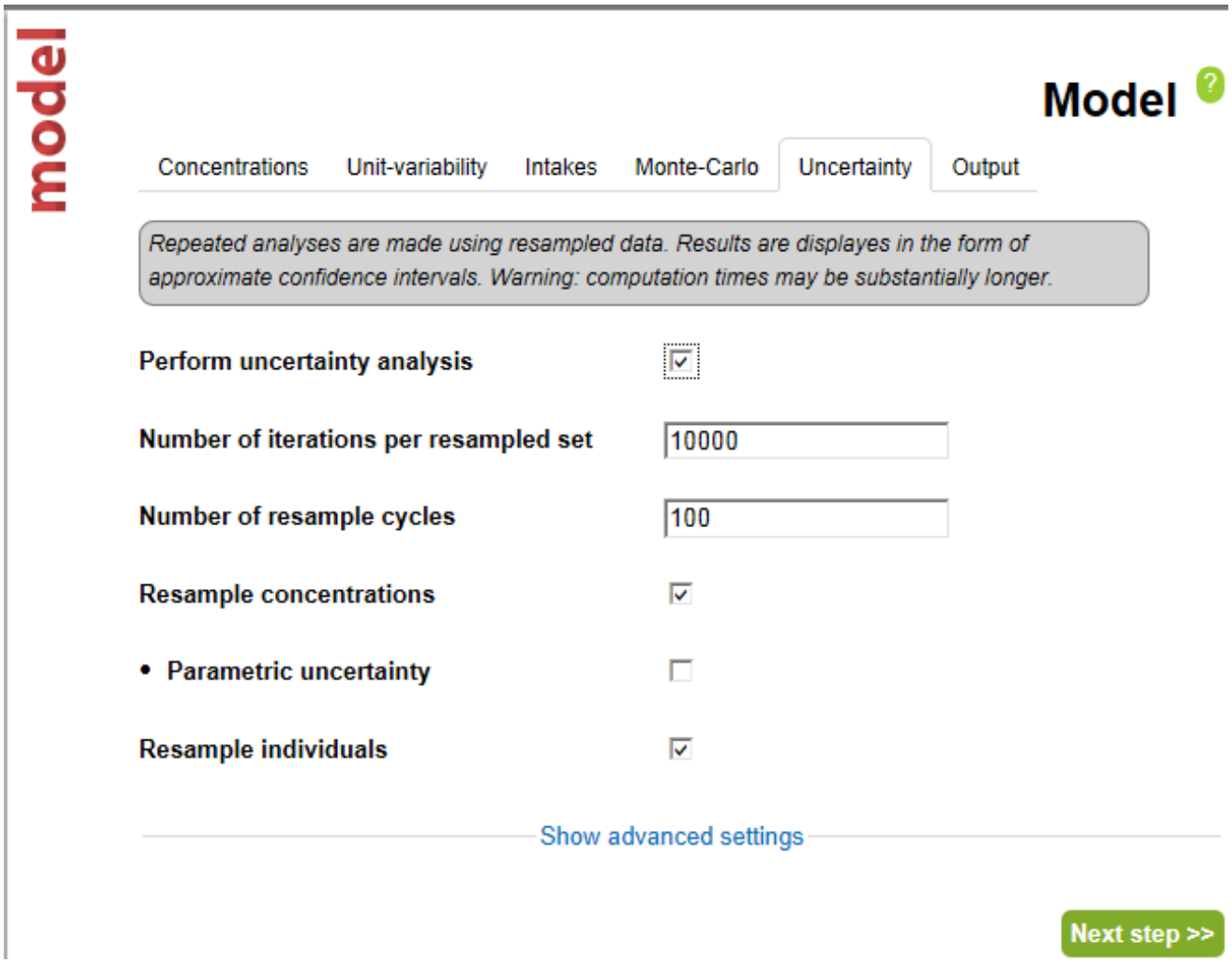




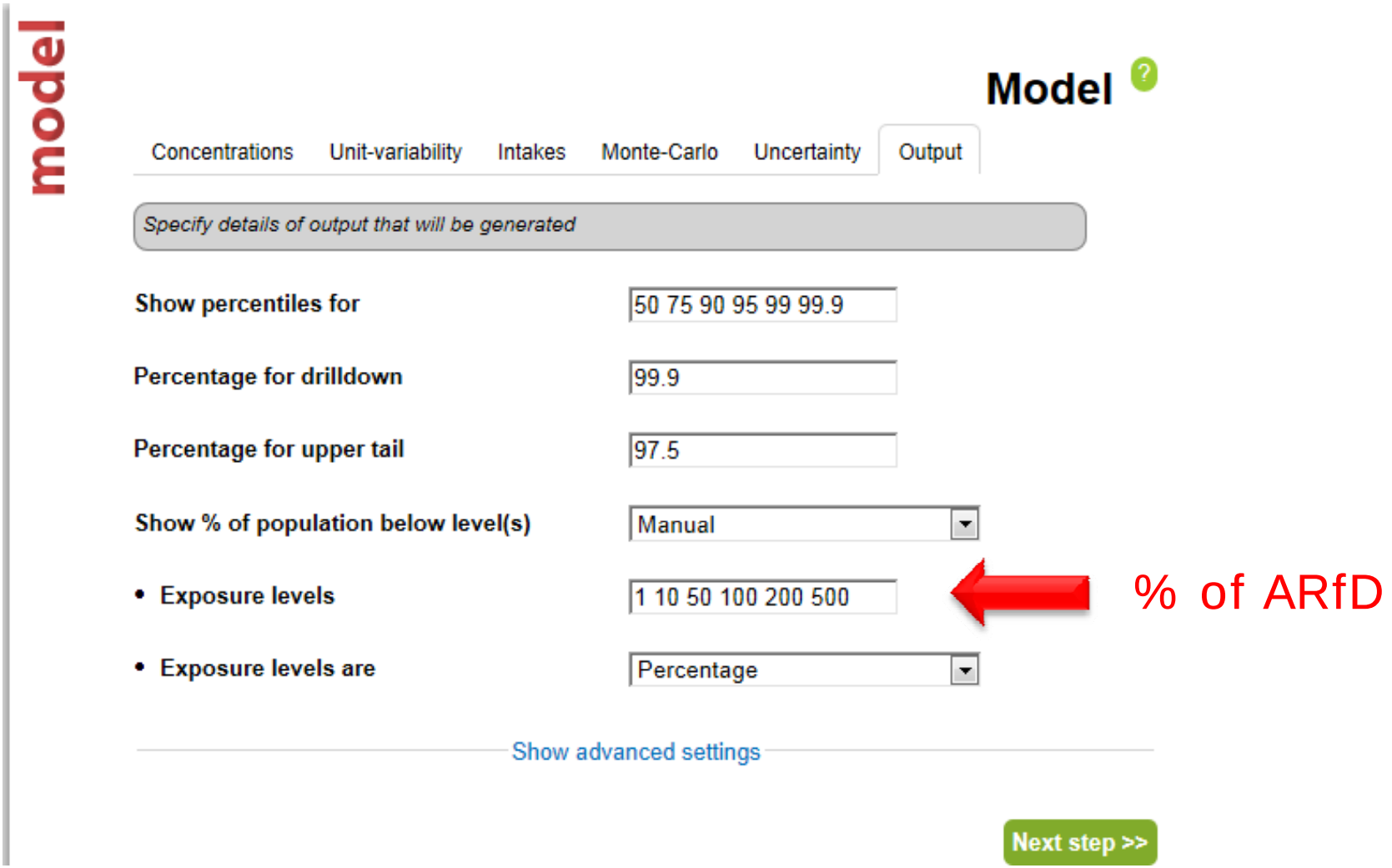
MCRA: Model (1)


model
Model
Concentrations
Intakes
Monte-Carlo
Uncertainty
Output
Concentration data can be sampled directly from the data (empirical model) or from parametric models.Concentrations < LOR (Limit Of Reporting) (non-detects) can be co-modelled (censored models) or one can specify a non-detects handling method for imputation. Agricultural use data can be used to impose true zeroes for all or part of the non-detects. Effects on concentrations from food processing can be specified in processing factors.
Concentration model
EFSA Guidance Optimistic
EFSA Guidance Pessimistic
Next step >>
Concentration model
Custom
Default concentration model
Non-Detect Spike LogNormal
Non-detects replacement
By f * LOR
• Factor f (f x LOR)
1

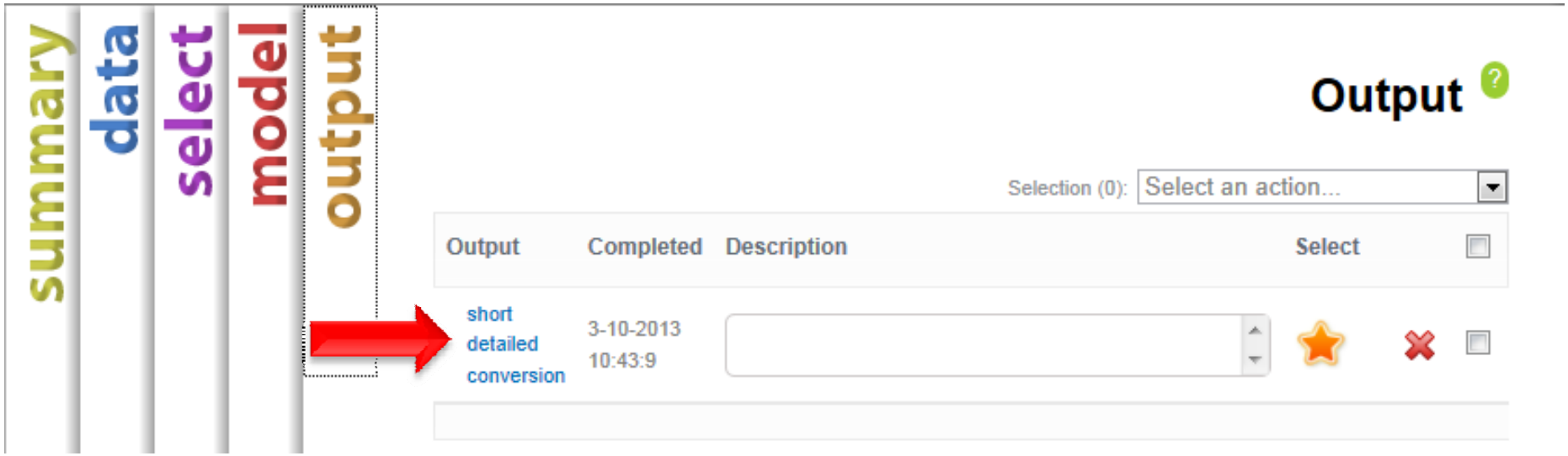
MCRA: Model (2)


model
Model
Concentrations
Unit-variability
Intakes
Monte-Carlo
Uncertainty
Output
Repeated analyses are made using resampled data. Results are displayes in the form of approximate confidence intervals. Warning: computation times may be substantially longer.
Perform uncertainty analysis
Number of iterations per resampled set
10000
Number of resample cycles
100
Resample concentrations
• Parametric uncertainty
Resample individuals
Show advanced settings
Next step >>

MCRA: output requirements

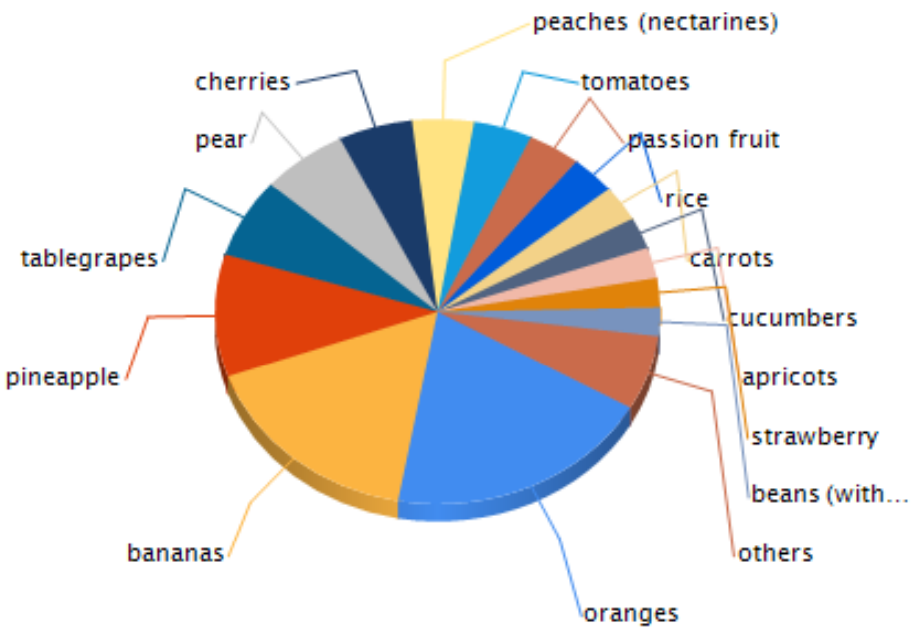


MCRA: Output (1)

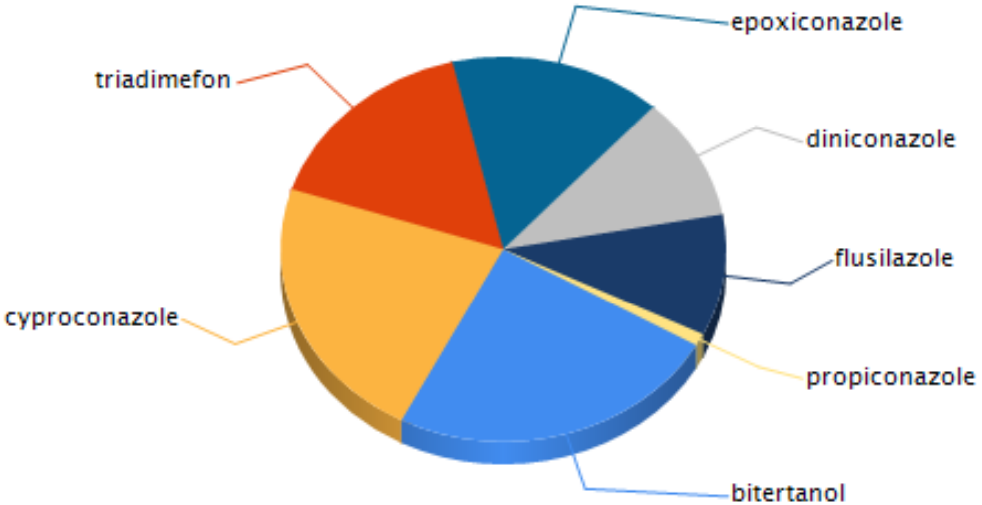


Output (2): Contribution foods and compounds

Contribution to total exposure distribution for foods as measured



Contribution to the total exposure distribution



Output (3): Number of person-days per million

Exposure percentages

Reference: Flusilazole , ARfD = 500 (µg/kg bw/day), Safety factor = 100

Exposure (µg/kg bw/day)	Percentage of reference dose	Margin of Exposure	Percentage	Lower Bound (p2.5)	Upper Bound (p97.5)	Number of people per million exceeding individual days
5	1.00 %	1E+04	79.51 %	77.91 %	80.85 %	204,873
50	10.00 %	1000	99.98 %	99.91 %	100.00 %	199
250	50.00 %	200	100.00 %	100.00 %	100.00 %	0
500	100.00 %	100	100.00 %	100.00 %	100.00 %	0
1000	200.00 %	50	100.00 %	100.00 %	100.00 %	0
2500	500.00 %	20	100.00 %	100.00 %	100.00 %	0

Output (4): Number of person-days per million (example)

Exposure (µg/kg bw/day)	Percentage of reference dose	Margin of Exposure	Percentage	Lower Bound (p2.5)	Upper Bound (p97.5)	Number of people per million exceeding individual days
5	1.00 %	1E+04	2.33 %	0.2748	5.321	976,750
50	10.00 %	1000	83.05 %	74.97	91.22	169,460
250	50.00 %	200	99.24 %	98.38	99.79	7,620
500	100.00 %	100	99.96 %	99.86	100	440
1000	200.00 %	50	100.00 %	99.99	100	0
2500	500.00 %	20	100.00 %	100	100	0

Validation

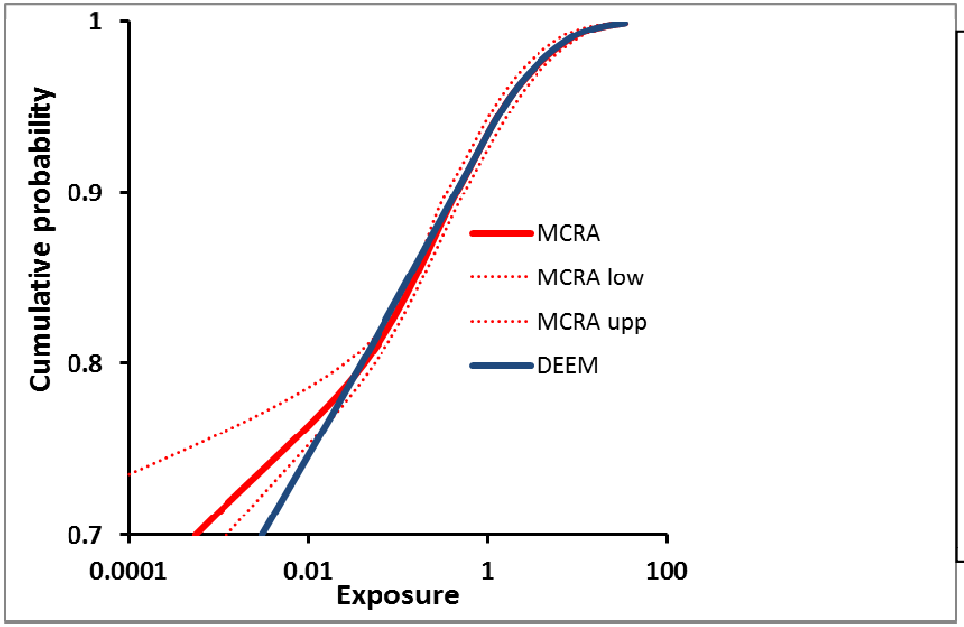
- DEEM-FCID is standard of US-EPA

DEEM-FCID Ver. 3.16, 03-08-d

Food translations based on EPA/USDA FCID recipe set as of February 2012

Dietary Exposure Evaluation Model

Based on NHANES 2-day food consumption data for 2003-2008



- Validation result: Good agreement MCRA and DEEM
- DEEM less precise at low exposures due to binning
- Not a problem because upper tail is relevant

Documentation and help

- In-line documentation of software, using strict protocols for naming classes, methods and properties
- User manual, data format manual, reference manual
- Help function

ACROPOLIS EXERSICE

- Use of the IT tool and data to calculate **cumulative exposure** to pesticides
  - Triazole pesticides
- **Practicality** of performing a cumulative dietary exposure assessment according to the requirements of the EFSA guidance on probabilistic modelling
- Training and user groups

Experience 1 ACROPOLIS partners

- Acute and chronic cumulative exposure modelling is possible
- Application of the optimistic model is feasible
- Performance of the pessimistic model run is very laborious:
  1. Determination authorised uses
  2. Supplementation or replacement of RACs with insufficient data
     - Borrowing data from other countries
     - MRLs or field trial data

Experience 2 ACROPOLIS partners

- Inclusion of MRLs of animal commodities resulted in
  - Unrealistic conclusions regarding the contribution of animal commodities to the dietary exposure.

- Which number of person-days exceeding the ARfD/ADI is associated with an unacceptable health risk is an open issue
  - should be decided by risk managers
  - ACROPOLIS IT tool is open for all stakeholders
  - there is not any decision taken by the tool, it just follows the EFSA guidance

Experience 3 user group regulators

- More experience is needed with the EFSA guidance and the model with other (larger) CAGs
  - Proof of principle, plan to upscale performance
- Need for ‘realistic’ scenario that combines the optimistic and pessimistic model run
  - still be argued to be conservative (precautionary principle) but not over-conservative

Experience 4 user group food authorities

- Pessimistic scenario: replacement LoR
  - Look at historical use
    - If not detected in the past nd (or < LoR) = 0
    - If detected in certain percentage uses insert 1/2/ LoD or fraction of LoD (or LoR)
- SSD data easy to use
- Animal products are measured and can be made available

Experience 5 user group industry (a)

- Scenario 1: existing situation → run with monitoring data
- Scenario 2: 100% of use on food A is replaced by new agricultural use
  - Measure 1 or more chemicals in FT of new agricultural use
  - Implication is that monitoring data for food A are no longer relevant
  - → Run with FT data instead of monitoring data for food A **Exposure can be higher, equal or lower**

    e.g. high conc. Tebuconazole may still be lower than RPF*low conc. Flusilazole when RPF=40

Experience 5 user group industry (b)

- Scenario 3: p% of use on food A is replaced → run where in p% of Monte Carlo draws FT data are sampled, and in (100-p)% the monitoring data
- Scenario 4: the new agricultural use is additional to all existing uses
- Scenario 5: the new agricultural use with compound C is additional to all existing uses without compound C, and replaces existing uses with compound C

(replacement scenarios not in EFSA guidance)

Second stakeholders conference

- Training was well-received by nearly all stakeholders (NGO did not attend training, although they were invited)
- Pesticide industry was able to connect focal commodity to monitoring and consumption data
- More transparent use of data through the use of the ACROPOLIS IT tool
- Easy-to-use software
- One uniform tool for discussing the level op protection, but no direction or decision has been taken (objective tool)

DG SANCO and ACROPOLIS

- The European Commission sets the level of protection

- all member states are trained
- European investment should be used
- involvement of stakeholders responsible for pesticide risk assessment
- linking innovation with practical needs of DG SANCO

Current and future organization

- New concept requires time to digest
- ACROPOLIS follow-up initiative
- Agreement to share data and to use it
- DG SANCO and EFSA cooperation
  - Form ‘proof of principle’ to a full production server
  - Still a lot of issues to be solved
- Open debate also with NGOs

Thanks to all the people involved