



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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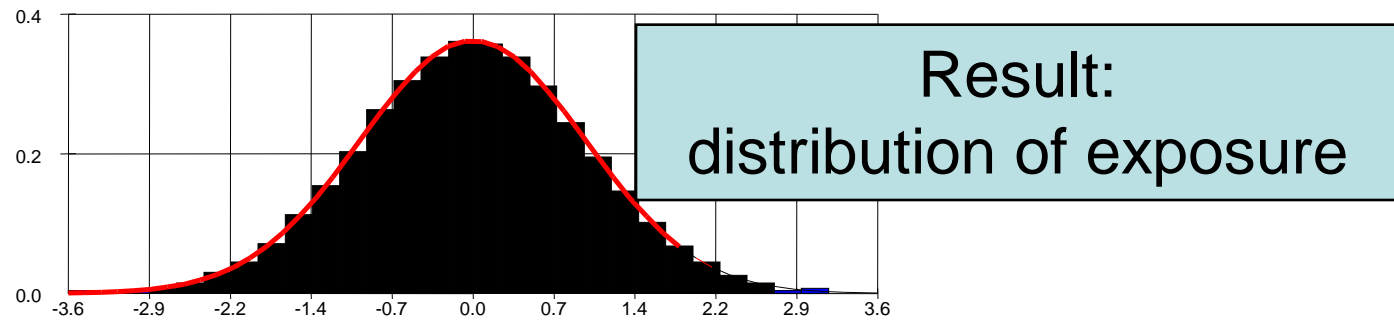
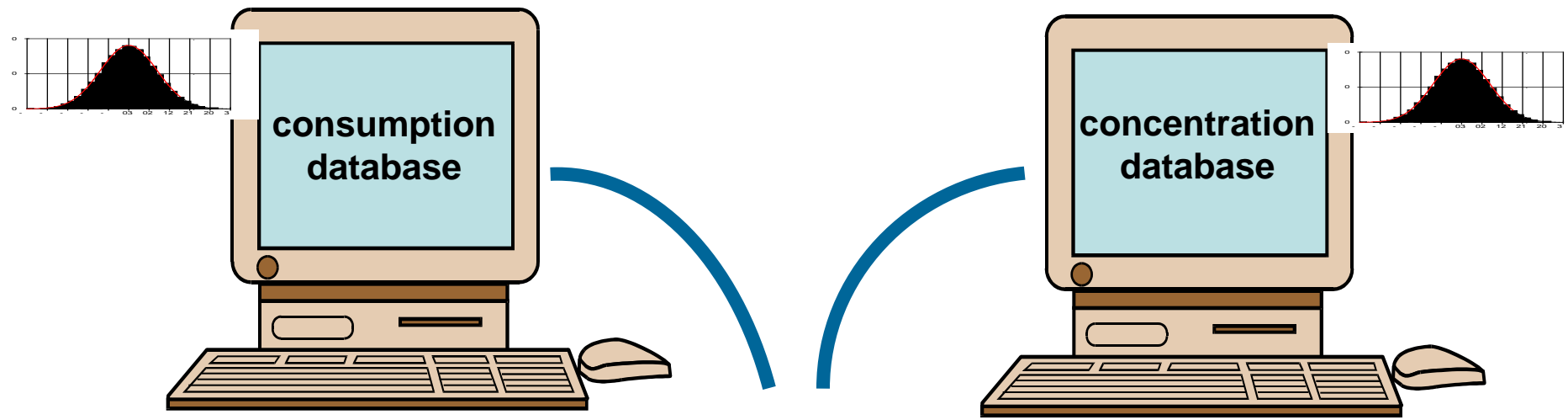
Aims of EU project ACROPOLIS

- 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**.





ACROPOLIS IT tool: How it works



Random sampling from a concentration and a consumption database



Conclusions first stakeholders

- DG SANCO's expectation from ACROPOLIS
 - IT tool risk assessment, management and communication
 - call for cooperation EFSA and ACROPOLIS
- 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
- NGO made an exception (different attitude)





EFSA Opinion guidance probabilistic methodology

- Different scenarios
 - acute and chronic
 - new registrations (industry)
 - actual exposure (Food Authorities and EFSA)

- Type of modelling
 - optimistic and pessimistic
 - basic and refined
 - empirical and parametric

- Uncertainties



The screenshot shows the EFSA website interface. At the top, there is the EFSA logo (European Food Safety Authority) with the tagline "Committed to ensuring that Europe's food is safe". Below the logo is a navigation menu with items: "About EFSA", "News & events", "Topics A-Z", "Publications", "Panels & units", "Cooperation", "Applications helpdesk", and "Calls & consultations". A search bar is visible on the right. The main content area displays a public consultation titled "Public consultation on a Guidance on the Use of Probabilistic Methodology for Modelling Dietary Exposure to Pesticide Residues". A sidebar on the left lists categories: "Procurement", "Article 36 grants", "Calls for data", "Public consultations", and "Closed consultations". A "Deadline: 7 March 2012" is noted at the bottom right of the consultation area.



Common Assessment Group: developmental

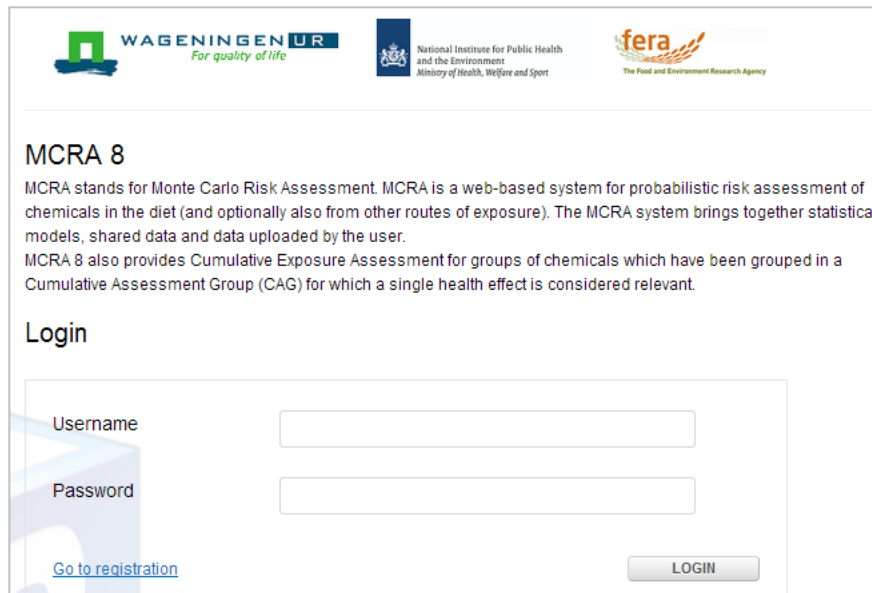
- Effect: developmental, craniofacial

Compound	Acute	
	BMD	NOAEL
Flusilazole	1.0	1.0
Bitertanol	2.1	1.7
Cyproconazole	2.2	4.2
Diniconazole	1.0	0.6
Epoxiconazole	1.5	0.8
Propiconazole	0.1	1.7
Triadimefon	1.2	1

EFSA has not decided yet on common assessment groups



ACROPOLIS IT tool (or MCRA software)



WAGENINGEN UR For quality of life

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

fera The Food and Environment Research Agency

MCRA 8

MCRA stands for Monte Carlo Risk Assessment. MCRA is a web-based system for probabilistic risk assessment of chemicals in the diet (and optionally also from other routes of exposure). The MCRA system brings together statistical models, shared data and data uploaded by the user.

MCRA 8 also provides Cumulative Exposure Assessment for groups of chemicals which have been grouped in a Cumulative Assessment Group (CAG) for which a single health effect is considered relevant.

Login

Username

Password

[Go to registration](#)

- currently available for user groups within the ACROPOLIS project
- users has to sign confidentiality agreements
 - data owned by member states

Logged in as: vandervoet | Logout | Support

project

[Open an existing project](#)
[Create a new project](#)

summary

Summary

Overview

data

select

model

output



MCRA: Select (1)

summary

data

select

Select ?

- Compounds
- Conversion
- Population Subsets
- Food Subsets
- Sample Subsets

A Cumulative Assessment Group (CAG) is defined by linking Compounds to an Effect in table RelativePotencyFactor. One compound should be selected as the reference (index) compound (not necessarily a compound with RPF 1).

Cumulative Assessment Group

(effect) Example Common effect

Reference compound

CompoundD (RPF 1.5)

CompoundE (RPF 0.1)

CompoundF (RPF 1.2)

IndexCompound (RPF 1)

Next step >>

model

output

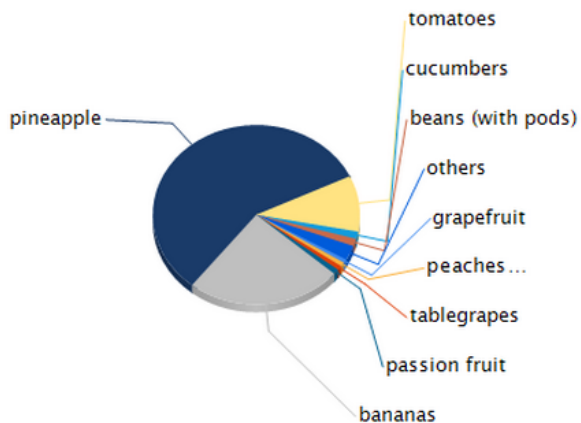


MCRA – Output: sources of exposure

Exposure by food

Foods as measured total distribution

Contribution to total intake distribution



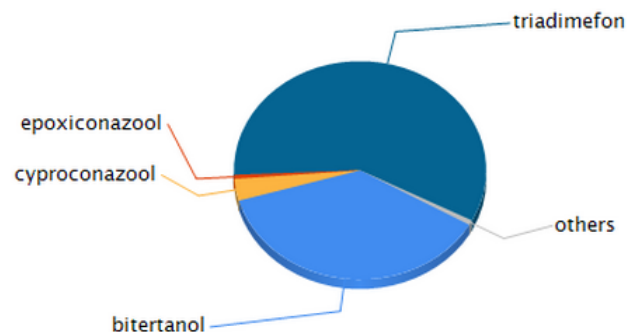
statistics

Food code	Food name	Contribution (%)	Median	Mean	Range	Percentage zero's (%)
P0110010A	GRAPEFRUIT	0.62	0.00	0.00	(0.00 - 0.00)	96.6
P0110020A	ORANGES	0.27	0.00	0.00	(0.00 - 0.00)	99.8
P0110040A	LIMES	0.01	0.00	0.00	(0.00 - 0.00)	100.0
P0130010A	APPLE	0.37	0.00	0.00	(0.00 - 0.00)	99.6
P0130020A	PEAR	0.14	0.00	0.00	(0.00 - 0.00)	99.7
P0140010A	APRICOTS	0.41	0.00	0.00	(0.00 - 0.00)	94.9
P0140020A	CHERRIES	0.07	0.00	0.00	(0.00 - 0.00)	98.3

Exposure by compound

Compounds total distribution

Contribution to the total intake distribution



statistics

Compound code	Compound name	Contribution (%)	Mean	Relative potency factor
RF-0048-001-PPP	BITERTANOL	37.2	0.00	2.1
RF-0113-001-PPP	CYPROCONAZOOL	3.2	0.00	2.2
RF-0142-001-PPP	DINICONAZOOL	0.3	0.00	1.0
RF-0157-001-PPP	EPOXICONAZOOL	0.6	0.00	1.5
RF-0218-001-PPP	FLUSILAZOL	0.4	0.00	1.0
RF-0358-001-PPP	PROPICONAZOOL	0.0	0.00	0.1
RF-0428-003-PPP	TRIADIMEFON	58.3	0.00	1.2



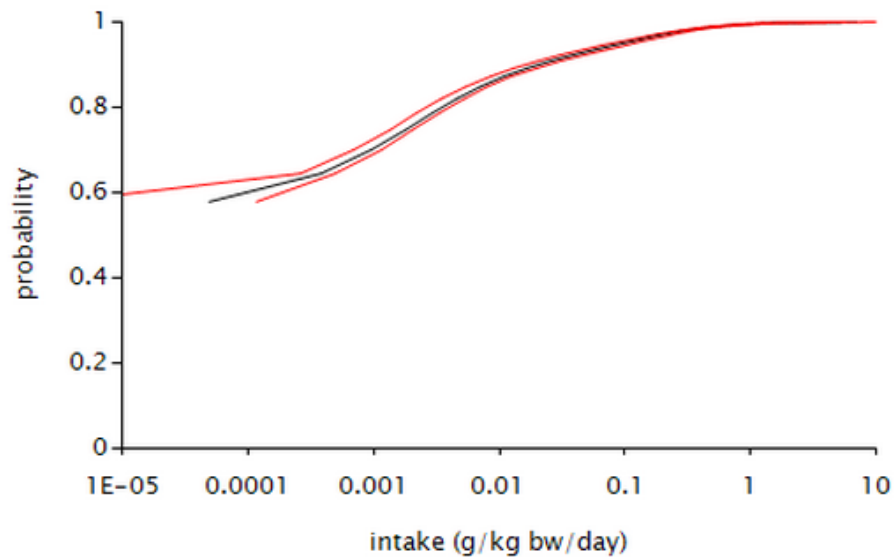
MCRA - uncertainties

- Graphical and tabular output

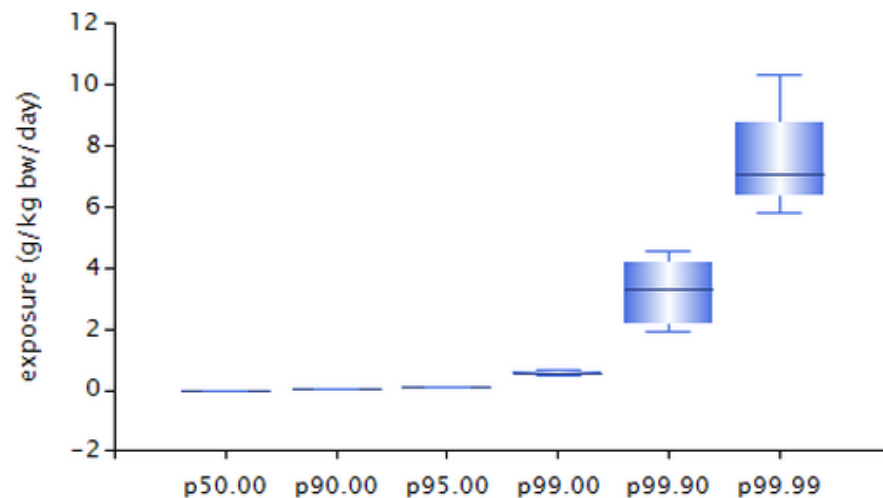
Percentiles

Percentage (%)	Reference (g/kg bw/day)	Lower Bound	Upper Bound
50.00	0.00	0.00	0.00
90.00	0.02	0.02	0.02
95.00	0.09	0.08	0.11
99.00	0.56	0.48	0.66
99.90	3.30	1.91	4.52
99.99	7.06	5.77	10.31

Cumulative intake distribution



Uncertainty of percentiles





Experience with EFSA guidance

- More experience is needed with the EFSA guidance and the model with other (larger) CAGs
- EFSA pessimistic guideline is not practical
- Need for some kind of intermediate 'realistic' scenario that combines the optimistic and pessimistic model run
 - More realistic exposures that can still be argued to be conservative (precautionary principle) but not over-conservative
 - A model run that is more practical
- Decision on level of risk that is acceptable



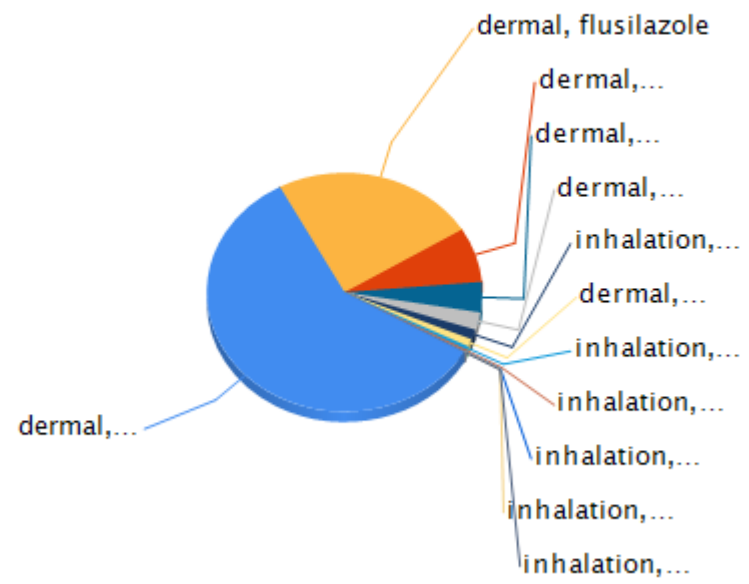
Proof of principle aggregated exposure

UK operator or resident

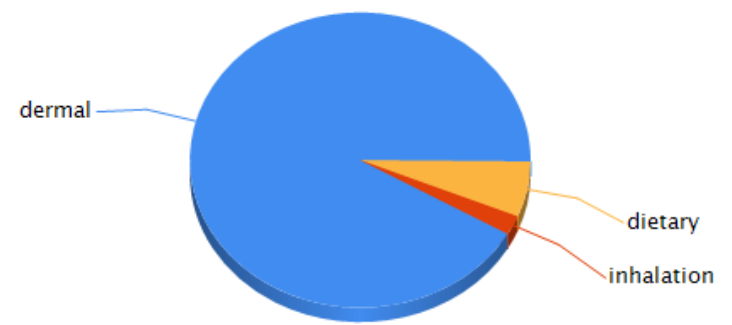
- UK males (19-64) to represent arable spray operators
 - Dietary data for 766 individuals in MCRA databases
 - EUROPOEM data for (dermal, inhalation) exposure per kg a.s. applied
 - PUS data for variation in kg a.s. applied/day
 - Empirical simulation, usage & exposure rate, to represent variability in conditions

UK operator

Contribution to the total non-dietary intake distribution

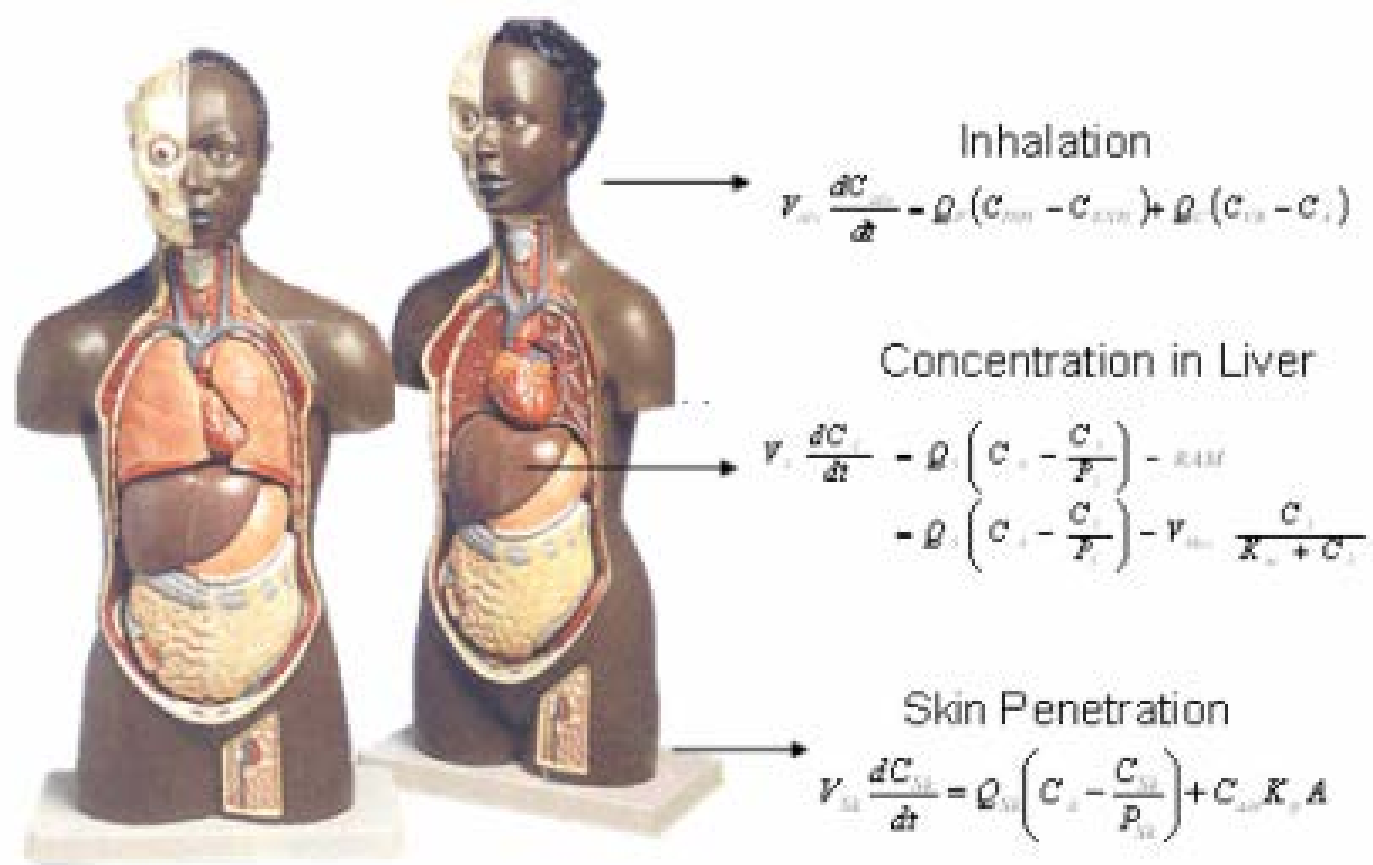


Contribution to the total intake distribution





PB-PK modeling internal dose

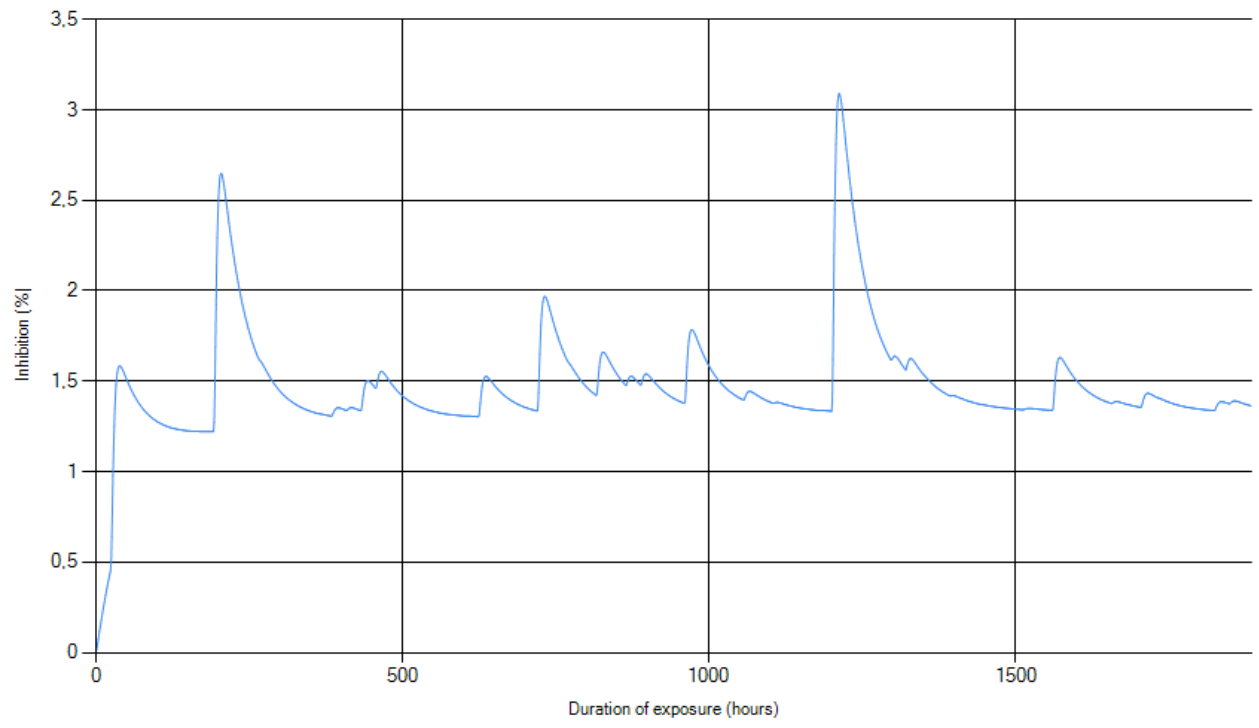




PB-PK output (internal dose of mixtures)

Run simulation

Inhibition of active Acetylcholinesterase in Plasma



Duration of the simulation (hours): 1884; Iteration interval (hours): 0.1; Discontinuous daily random dose CPF ($\mu\text{g}/\text{kg}$ body weight): 100; Continuous daily background CPF ($\mu\text{g}/\text{kg}$ body weight): 10; Continuous daily background DZN ($\mu\text{g}/\text{kg}$ body weight): 10



Validation

- DEEM-FCID is standard of US-EPA



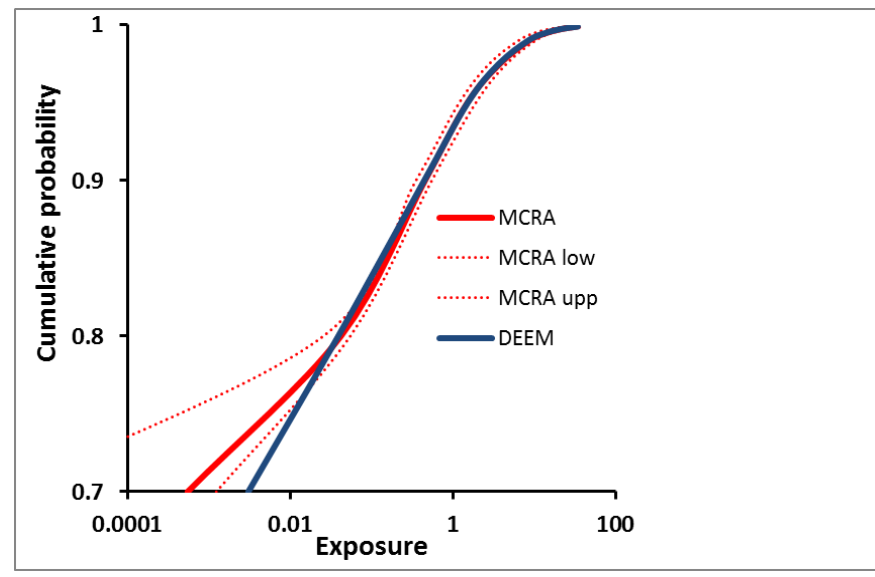
Ver. 3.16, 03-08-d

DEEM-FCID

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

Experiences and path forward

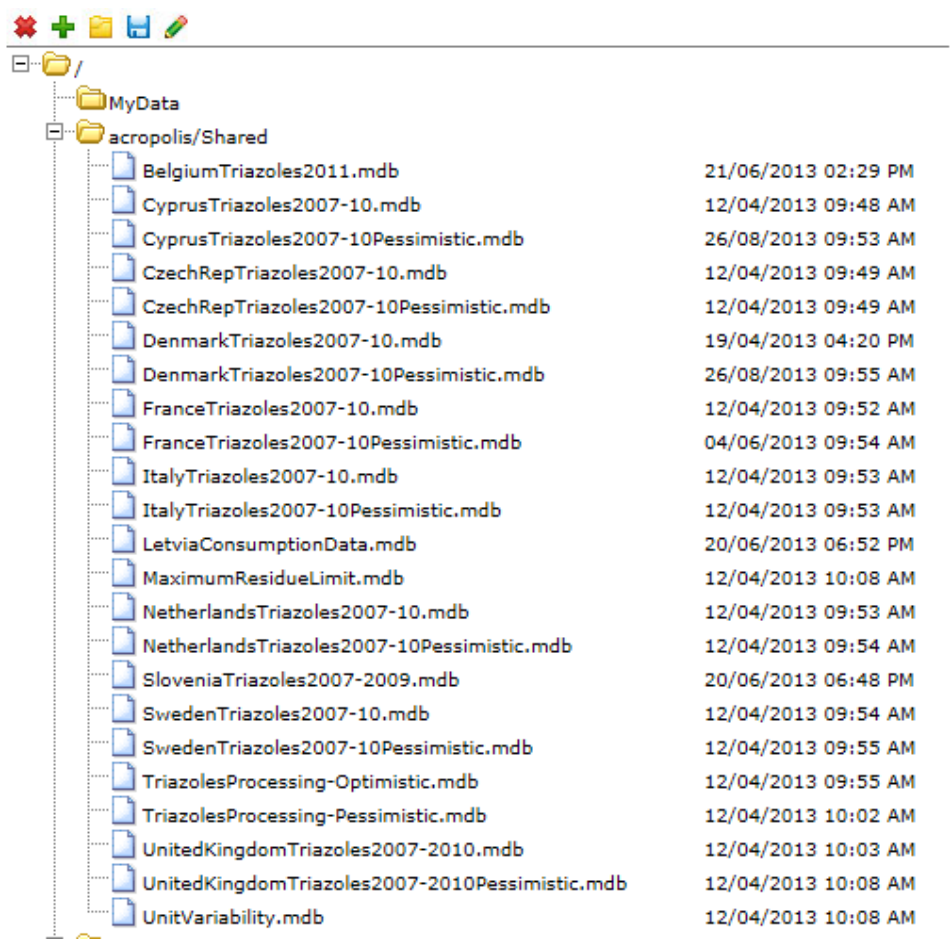
“Tool”:

- Status “Today” in MCRA version 8
 - Single platform with access to consumption / monitoring data
 - Easy to use
 - Sufficiently supported by RIVM and RIKILT
 - **BUT:** Still blackbox (calculation steps not understood)
- Path forward:
 - Transparency considerably improved (including calculation methodologies)
 - Further development increased / maintenance of MCRA ensured
 - User support also guaranteed in future

→ Proposed next step: Preparation of a “detailed cook book” (updated manual) explaining calculation steps to “non-expert” users



In kind contributions of food authorities



File Name	Modification Date
BelgiumTriazoles2011.mdb	21/06/2013 02:29 PM
CyprusTriazoles2007-10.mdb	12/04/2013 09:48 AM
CyprusTriazoles2007-10Pessimistic.mdb	26/08/2013 09:53 AM
CzechRepTriazoles2007-10.mdb	12/04/2013 09:49 AM
CzechRepTriazoles2007-10Pessimistic.mdb	12/04/2013 09:49 AM
DenmarkTriazoles2007-10.mdb	19/04/2013 04:20 PM
DenmarkTriazoles2007-10Pessimistic.mdb	26/08/2013 09:55 AM
FranceTriazoles2007-10.mdb	12/04/2013 09:52 AM
FranceTriazoles2007-10Pessimistic.mdb	04/06/2013 09:54 AM
ItalyTriazoles2007-10.mdb	12/04/2013 09:53 AM
ItalyTriazoles2007-10Pessimistic.mdb	12/04/2013 09:53 AM
LetviaConsumptionData.mdb	20/06/2013 06:52 PM
MaximumResidueLimit.mdb	12/04/2013 10:08 AM
NetherlandsTriazoles2007-10.mdb	12/04/2013 09:53 AM
NetherlandsTriazoles2007-10Pessimistic.mdb	12/04/2013 09:54 AM
SloveniaTriazoles2007-2009.mdb	20/06/2013 06:48 PM
SwedenTriazoles2007-10.mdb	12/04/2013 09:54 AM
SwedenTriazoles2007-10Pessimistic.mdb	12/04/2013 09:55 AM
TriazolesProcessing-Optimistic.mdb	12/04/2013 09:55 AM
TriazolesProcessing-Pessimistic.mdb	12/04/2013 10:02 AM
UnitedKingdomTriazoles2007-2010.mdb	12/04/2013 10:03 AM
UnitedKingdomTriazoles2007-2010Pessimistic.mdb	12/04/2013 10:08 AM
UnitVariability.mdb	12/04/2013 10:08 AM



Comments DG SANCO

- An EFSA guidance is not an EU guideline
 - theory and practice
- The European Commission sets the level of protection



- all member states are trained
- involvement of stakeholders
- best practice in cooperation
- links innovation to the practical needs of DG SANCO
- DG SANCO supports continuation of ACROPOLIS



Welcome to ACROPOLIS

Project summary

Current risk assessment of pesticides, and MRL setting does not sufficiently account for cumulative and aggregate exposure (Regulation (EC) 396/2005). The central aim of the project is to improve risk assessment strategies in Europe. The project will develop a framework for cumulative and aggregate risk assessment of pesticides that is scientifically sound and accessible for all actors involved in the European risk assessment and risk management.

This work consists of: 1) studying the data needs, data availability and organization including uncertainties for cumulative exposure and effect assessment in a probabilistic risk assessment framework; 2) integrating models describing various routes of exposure into an aggregate exposure model; 3) setting up new toxicological testing for identifying possible additive or synergistic effects and developing a strategy for refinement of cumulative assessment groups; 4) integrating cumulative and aggregate risk models including uncertainty analyses in a web-based tool, including accessible data for all stakeholders; 5) improving risk assessment strategies in Europe by analysing stakeholders attitudes, by training and by discussing the new methodology in several stakeholder conferences.

FP7-KBBE-2009-3

Quicklinks

- Report 2nd Stakeholder conference meeting-October 15th, 2013
- Recommendations from the ACROPOLIS project
- Summary of the ACROPOLIS project
- 2nd Stakeholder conference Agenda -October 15th, 2013
- Stakeholder conference meeting-February 1st, 2012
- Stakeholder conference Agenda-February 1st, 2012
- Training stakeholders cumulative pesticide exposure-January 16-17 and 19, 2012
- MCRA

Web address: acropolis-eu.com



Thanks to all the people involved

