Development of methodologies to be used for assessing exposure to multiple pesticides

Hermine Reich
Senior Scientific Officer

Chemical mixtures: challenges for research and risk assessment
10/11 December 2013
EFSA outputs on Cumulative Risk Assessment

2006  **EFSA's 7th Scientific Colloquium** - Cumulative Risk Assessment of Pesticides to Human Health: The Way Forward

2008  **Scientific Opinion to evaluate the suitability of existing methodologies** and, if appropriate, the identification of new approaches to assess cumulative and synergistic risks from pesticides to human health with a view to set MRLs for those pesticides in the frame of Regulation (EC) 396/2005

2009  **Scientific Opinion for a selected group of pesticides from the triazole group** to test possible methodologies to assess cumulative effects from exposure through food from these pesticides on human health
EFSA outputs on Cumulative Risk Assessment

2012  Guidance on the use of **probabilistic methodology for modelling dietary exposure** to pesticide residues

2013  Scientific Opinion on the identification of **pesticides to be included in cumulative assessment groups** on the basis of their toxicological profile

(Published on EFSA Website for public consultation – closed on 30 September)
Ongoing activities and next steps

- Evaluation of **comments** received during the **public consultation** on the Scientific Opinion on cumulative assessment groups (CAGs)
- Preparation of Scientific Opinion on the relevance of **dissimilar mode of action** and its appropriate application for cumulative risk assessment of pesticides residues in food
- Outsourced project on collection of data relevant for cumulative risk assessment (until end of 2015)
- Technical Meeting with stakeholders on cumulative risk assessment, 11 February 2014, EFSA, Parma
  - aiming at information of and exchange with stakeholders
Other activities of EFSA related to Cumulative Risk Assessment

- Development of **new format for reporting monitoring data** on pesticide residues (SSD – Standard Sample Descriptor)
- Increased quantity and **quality of monitoring data**
- Establishment of the **comprehensive food consumption data**
- Development of **EFSA PROFile** (Pesticide Residue Overview File) to collect data in the framework of the MRL review in a structured format
- Development of **EFSA PRIMo** (Pesticide Residue Intake Model)
- **Indicative cumulative risk assessment for OP pesticides and carbamates** using PRIMo (deterministic approach) (see 2010 EU Report on Pesticide Residues)
Dietary risk assessment

Chemical Occurrence

Exposure Assessment

Toxicological reference value

Food consumption
Cumulative risk assessment: work packages

1. Development of Guidance
   - Establishment of CAG
   - Potency factors
2. Collection of data
   - Residue data
   - Consumption
   - Other data
3. Development of a tool
4. Implementation
Toxicological data
Where are we today?

287 active substances were screened

Cumulative assessment groups (CAGs)

CAG level 1

- Nervous system (68 substances)
- Thyroid system (113 substances)
  - Liver
  - Kidney
  - Adrenal gland
  - Eyes
  - Developmental/reproductive toxicity
CAG level 1 – Nervous system

Cumulative assessment groups (CAGs)

CAG level 2: Common specific phenomenological effect *(acute effects)*

- Functional effects on motor division:
  - 45 pesticides

- Functional effects on sensory division:
  - 21 pesticides

- Functional effects on autonomic division:
  - 29 pesticides

- Neurochemical endpoints:
  - 15 pesticides
Cumulative assessment groups (CAGs)

CAG level 2: Common specific phenomenological effect (chronic effects)

- Functional effects on motor division:
  - 53 pesticides
- Functional effects on sensory division:
  - 22 pesticides
- Functional effects on autonomic division:
  - 24 pesticides
- Neurochemical endpoints:
  - 15 pesticides
- Neuropathological effects:
  - 21 pesticides
CAG level 1 – Thyroid system

Cumulative assessment groups (CAGs)

CAG level 2: Common specific phenomenological effect (chronic effects)

- Effects on parafollicular cells or the calcitonin system:
  - 25 pesticides

- Substances affecting follicular cells and/or thyroïd hormone (T3/T4) system
  - 98 pesticides
Future work

- Assessment of the remaining 5 CAGs (level 1)

- Assessment of non-approved substances? (check first their relevance in terms of exposure, based on occurrence data)

- Assessment of metabolites? (check first the relevance – metabolism studies)
Monitoring data

- Since 2009 the monitoring results are reported at detailed level (individual determinations) using the SSD format, including a lot of background information
- Residue definition for enforcement
- 27 EU MS + NO, IC
- ca. 70,000 samples/year
- ca. 15 to 20 Mio determinations/year
### National Monitoring Programmes

- **Ca. 300 different commodities**
  - (range from 12-170)
- **Less representative**
  - (geographical distribution)
- **Many commodities less than 10 samples**
- **More than 900 different pesticides**
  - (range from 60-840)

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**EU-coordinated Monitoring Programme**

- **Ca. 12,000 samples**
- In 3 yr. cycle covers 30-40 food commodities
- **Ca. 180 pesticides**

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**Monitoring data**

- Ca. 5 % Enforcement samples
Monitoring data – pesticides covered

- Monitoring data – pesticides covered
- EU-coordinated programme
- Ca. 180 pesticides
- 15/24 Chronic autonomic division
- 34/45 Acute motor division
- 17/21 Acute sensory division
- 11/25 Thyroid group 2A
- 40/98 pesticides classified in thyroid group 2B

Need to adapt scope of EU coordinated monitoring programme, considering the potency of the active substance and the likelihoods to find measurable residues (“significant contributors”)
## Occurrence data – Food types

### Cumulative exposure

<table>
<thead>
<tr>
<th>Monitoring data</th>
<th>Supervised field trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>EU coordinated programme</td>
<td>reflecting realistic worst case situation for critical GAPs</td>
</tr>
<tr>
<td>National control programmes</td>
<td>STMRs / HRs for RAC, sometimes for edible portion</td>
</tr>
</tbody>
</table>

Data reflecting residue definition for risk assessment and enforcement (parent compound and metabolites where relevant)

- Outdoor NEU / SEU / Third countries
- Indoor conditions
### Monitoring data – Food types

#### Number of samples per commodity
(EU coord. + national programmes)

<table>
<thead>
<tr>
<th>Commodity</th>
<th>Number of Samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apples</td>
<td>Table grapes</td>
</tr>
<tr>
<td>Tomatoes</td>
<td>Oranges</td>
</tr>
<tr>
<td>Potatoes</td>
<td>Peaches</td>
</tr>
<tr>
<td>Wheat</td>
<td>Peppers</td>
</tr>
<tr>
<td>Table Grapes</td>
<td>Strawberries</td>
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<tr>
<td>Lettuce</td>
<td>Wine grapes</td>
</tr>
<tr>
<td>Mandarin</td>
<td>Peaches</td>
</tr>
<tr>
<td>Spinach</td>
<td>Limes</td>
</tr>
<tr>
<td>Cattle Milk</td>
<td>Courgettes</td>
</tr>
<tr>
<td>Baby Food</td>
<td>Onions</td>
</tr>
<tr>
<td>Bananas</td>
<td>Aubergines</td>
</tr>
<tr>
<td>Plums</td>
<td>Head cabbage</td>
</tr>
<tr>
<td>Cereal b.</td>
<td>Asparagus</td>
</tr>
<tr>
<td>Fish</td>
<td>Melon</td>
</tr>
<tr>
<td>Olive</td>
<td>Swine fat</td>
</tr>
<tr>
<td>Egg</td>
<td>Cultivated</td>
</tr>
<tr>
<td>Milk</td>
<td>Spring onion</td>
</tr>
<tr>
<td>Bovine</td>
<td>Raspberry</td>
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<tr>
<td>Sheep</td>
<td>Rye</td>
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<tr>
<td>Sheep</td>
<td>Mango</td>
</tr>
<tr>
<td>Lamb</td>
<td>Lamb's milk</td>
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<tr>
<td>Tea</td>
<td>Tea leaves</td>
</tr>
<tr>
<td>Beef</td>
<td>Broccoli</td>
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<tr>
<td>Pork</td>
<td>Celery</td>
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<tr>
<td>Pork</td>
<td>Maize</td>
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<tr>
<td>Veal</td>
<td>Peas</td>
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<tr>
<td>Lamb</td>
<td>Garlic</td>
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<tr>
<td>Veal</td>
<td>Pumpkin</td>
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<tr>
<td>Liver</td>
<td>Beef</td>
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<tr>
<td>Chicken</td>
<td>Rainbow</td>
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<tr>
<td>Pork</td>
<td>Strawberry</td>
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<tr>
<td>Poultry</td>
<td>Kale</td>
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<tr>
<td>Poultry</td>
<td>Oats</td>
</tr>
<tr>
<td>Poultry</td>
<td>Basil</td>
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<tr>
<td>Poultry</td>
<td>Wild rice</td>
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<tr>
<td>Poultry</td>
<td>Oregano</td>
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<tr>
<td>Chicken</td>
<td>Cumin</td>
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<tr>
<td>Turkey</td>
<td>Thyme</td>
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<td>Turkey</td>
<td>Dill</td>
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<tr>
<td>Turkey</td>
<td>Lovage</td>
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<td>Turkey</td>
<td>Tarragon</td>
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<tr>
<td>Turkey</td>
<td>Sage</td>
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<tr>
<td>Turkey</td>
<td>Marjoram</td>
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<td>Turkey</td>
<td>Fennel</td>
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<td>Turkey</td>
<td>Bay leaf</td>
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<td>Pimento</td>
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<td>Rosemary</td>
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<td>Blue cheese</td>
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<td>Turkey</td>
<td>Rosemary</td>
</tr>
</tbody>
</table>
Monitoring data – Food types

Food intake: relevance of food in the diet
Monitoring data results: determination level

- EU-coordinated programme
- Ca. 1.2 Mio determinations per year

- >LOQ
- >MRL
- <LOQ
Monitoring data results: sample level

All commodities covered by EU coordinated programme
Monitoring data results: sample level

How to handle results exceeding the MRL? Illegal uses?

How to handle non-detects?

Strawberries
Monitoring data results: MS/sample level

Strawberries from Member State A

What to do for cases where approval has changed?

Refinement

Is the product authorised in MS A for this crop?
Percentage crop treated?

How to handle non-detects?

Refinement

>LOQ
>MRL
<LOQ
Monitoring data: Contribution of individual commodities to total exposure
Occurrence data

- Which food commodities need to be considered?
- Which occurrence data should be used?
  - Monitoring data
    - *EU coordinated programme*
    - *National monitoring programmes*
  - Supervised field trials
- How to fill the gaps for pesticides not sufficiently covered by the monitoring programmes
- How to trim the data?
  - Non-detects?
  - MRL exceedences?
  - Conversion factors for risk assessment?
Monitoring data

- Data trimming – replacement/complement occurrence data
- Identify need for further data collection
  - Authorisation status
  - % crop treatment
  - Processing data
- Transparent handling of data, documentation of manipulation
- Identify limitations of available data, uncertainty of estimations
### EFSA comprehensive food consumption database

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<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Dietary surveys</td>
<td>32</td>
</tr>
<tr>
<td>Member States</td>
<td>22</td>
</tr>
<tr>
<td>Number of subjects</td>
<td>66,492</td>
</tr>
<tr>
<td>Number of different foods</td>
<td>63,495</td>
</tr>
<tr>
<td>Number of different FoodEx codes</td>
<td>1,504</td>
</tr>
<tr>
<td>Number of consumption records</td>
<td>6,309,489</td>
</tr>
</tbody>
</table>

The Comprehensive Database will be updated in 2014 with the addition of 10 new surveys. A Call for proposals is currently out for the 2014 update.
Comprehensive food consumption data

Examples of differences in survey methodology:

- **24 h dietary recall vs. food record**
- **broad survey period, from 1997 (Estonia) to 2009 (Spain)**
- **from 1 to 7 days per subject**
- **individual vs. household sample unit**
- **from 28% to 98% response rate**
- **week end days not evenly represented in 6 surveys**
- **seasonality not fully covered in 10 surveys (only one season represented in 4 surveys)**
- **body weight and height measured or estimated**
- **food classification**
## Comprehensive food consumption data: Age classes

<table>
<thead>
<tr>
<th>Age class</th>
<th>Age range</th>
<th>Number of surveys</th>
<th>Number of countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants</td>
<td>0 - 12 months</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Toddlers</td>
<td>12 - 36 months</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Children</td>
<td>3 - 10 years</td>
<td>16</td>
<td>14</td>
</tr>
<tr>
<td>Adolescents</td>
<td>10 - 18 years</td>
<td>14</td>
<td>12</td>
</tr>
<tr>
<td>Adults</td>
<td>18 - 65 years</td>
<td>21</td>
<td>20</td>
</tr>
<tr>
<td>Elderly</td>
<td>65 - 75 years</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Very elderly</td>
<td>&gt; 75 years</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>78 diets</strong></td>
<td><strong>22 MS</strong></td>
</tr>
</tbody>
</table>
Do the consumption data match with the occurrence data?

**Number of different FoodEx codes: 1,504**
- Unprocessed food
- Processed food
- Composite food

**Number of commodities for which monitoring data are available: ca. 300**
- Mainly unprocessed food
- Results reported for commodity as described in Annex I of Regulation (EC) No 396/2005 (e.g. orange with peel)
Food as consumed vs. RACs

Raw Agricultural Commodity (RACs)
edible portion

Food as consumed

List of ingredients and proportions

Conversion factors

Individual ingredient
Conditions of use

- EFSA has the right to use raw individual food consumption data for carrying out risk assessments and other scientific analyses within the activities related to EFSA’s mandate.

- A formal authorization from the data provider must be requested for any other use of the data.
Comprehensive food consumption data

- Which are the representative diets to perform cumulative exposure assessments?
  - Which age groups?
  - Which geographic regions?
  - Specific groups (e.g. vegetarians, breastfeeding women)?
- Which recipe data to use for calculation of ingredients?
- Can we use a standard conversion model to derive food consumption expressed in edible portion of raw agricultural commodity for aggregation of the consumption data?
- How to do refined calculations for processed food?
- Legal questions: permission to use consumption data
Which tool should be used for the calculation?

Which methodology?

Which data to use?

Which tool can be used?
Which tool should be used for the calculation?

Criteria

- Performance of the tool:
  - Number of pesticides in CAG
  - Number of CAG
  - Number of diets
  - Number of commodities

- Are the available tools capable to perform these calculations?
- Tool should be accessible for risk assessors and stakeholders
- Flexibility: possibility to adapt the tool for needs
- Clarity: documentation how the calculations are performed
- Costs
Concluding remarks

- Implementation of cumulative risk assessment is an iterative process
- Need to gain experience
- Identify the relevant questions that have to be solved
- Close dialogue with risk managers to address their needs
  - Protection goal
  - Level of uncertainty
- Need to be transparent how the calculations are performed; uncertainties and limitations of calculation
- Regular evaluation of guidance implementation is needed
Development of Guidance

Collection of data

Establishment of CAG

Potency factors

Residue data

Consumption

Other data

Coordination

Development of a tool

Implementation
Too many cooks spoil the broth

Thanks for your attention!