EU MRLs procedures

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Global Minor Uses Summit
7 December 2007
FAO - Rome
Outline presentation

- DG SANCO
- Overall regulatory framework for pesticides
- Regulation (EC) N. 396/2005
  - On-going implementation
  - MRL setting
  - Minor uses
- Future challenges
Unit E3
Chemicals, contaminants, pesticides
Pesticides
EU Regulatory Framework

Placing of plant protection products on the market
Directive 91/414/EEC

Pesticide residues: EU MRL settings
Directives
76/895/EEC
86/362/EEC
86/363/EEC
90/642/EEC

Replaced by
Regulation (EC) No 396/2005
Basic objective

- Establishment of a Community Positive List of Active Substances (Annex I)
- Once a substance is on the Community list, Member State may grant authorisations for plant protection products which contain a listed active substance.
Directive 91/414/EEC
Approval of active substances

1. **Industry**: submit dossier (data requirements: Annexes II and III)
2. **Rapporteur Member State**: evaluate dossier
3. **European Food Safety Authority (EFSA)**: co-ordinate peer review
4. **EU Commission**: decision for inclusion in Annex I

“New” substances:
- 75 evaluated and approved

Review programme of “old” substances:
- More than 600 eliminated
- 92 approved
- Review to be finalised by the end of 2008 (ca. 230 substances)
Pesticide Residues
MRLs setting

Legislation partially harmonised

EU- MRLs
\[\pm 250 \text{ pesticides}\]

- Dir. 76/895/EEC (selected fruits and vegetables)
- Dir. 86/362/EEC (cereals)
- Dir. 86/363/EEC (animal products)
- Dir. 90/642/EEC (fruits and vegetables)

National MRLs
\[\pm 850 \text{ pesticides}\]

- No harmonised risk assessment for EU consumers
- Trade problems

4 Directives \(\rightarrow\) 1 Regulation 396/2005
completing process of harmonisation
Regulation (EC) N. 396/2005

of the European Parliament and of the Council of 23 February 2005

on maximum residue levels of pesticides in or on food and feed of plant and animal origin

Key points

• High and consistent level of consumer protection across EU
  – Community harmonised MRLs
  – Consumer risk assessment reviewed by EFSA
• No authorisation of a PPP without an established EU MRL
Reg. 396/2005 will be fully applicable as from 6 months from the publication of the last of the Annexes I, II, III and IV.


Annex II → Existing EU MRLs

Annex III → Temporary MRLs

Annex IV → Substances for which no MRLs are required

Reg. (EC) N. 396/2005 → application date foreseen: July 2008
ANNEX I: List of commodities

Regulation (EC) N. 178/2006

- **315 commodities** – 10 main groups.
- **190 existing** entries from current Directives.
- **125 new entries.**
  - Mainly minor crops (e.g. cassava, thyme, lupins), but also cocoa, coffee, sugar plants.
- **Fish** and **plants used in animal feed** listed, but for the time being exempted from MRL setting (not enough information).
ANNEX II: EU-MRLs

First establishment

- **238 pesticides** from current MRLs Directives.
  - ± 45000 MRLs
  - only existing crops under current Directives
  - combinations new crops/238 pesticides in Annex III B

- Mostly pesticides for which EU risk assessment has been completed under Dir. 91/414/EEC.

- Voted in the Standing Committee on the Food Chain and Animal Health (October 2007). Publication expected **January 2008**.
ANNEX III: temporary EU-MRLs

First establishment

- **National MRLs** collected until May 2006 on all the non-harmonised substances.
- EFSA asked for an opinion (September 2006).
- **EFSA** delivered a *reasoned opinion* (March 2007).
- COM-EFSA-MS: refinement risk assessment (March-September 2007).
- SPS notification (July 2007)
EFSA developed a model to perform the risk assessment:

- **Harmonised food consumption database:**
  - Data collected from Member States: 22 chronic diets, 19 acute diets
  - Data from WHO (GEMS Food) also considered: 3 cluster, 1 regional
  - Consumption data organised by sub-groups of population
## Active substance

**Status of the active substance:** non-registered  
**Code no.:** 14  
**Proposed LOD (mg/kg bw):** 0.05

### Toxicological endpoints

<table>
<thead>
<tr>
<th>ADI (mg/kg bw/day)</th>
<th>Source of ADI:</th>
<th>Source of ARID:</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.008</td>
<td>JMPR 1989, BD 1991, BC</td>
<td></td>
</tr>
</tbody>
</table>

### Chronic risk assessment

**TMDI (range) in % of ADI**  
minimum - maximum  
7 - 262

<table>
<thead>
<tr>
<th>Highest calculated TMDI values in % of ADI</th>
<th>MS Diet</th>
<th>Highest contributor to MS diet (in % of ADI)</th>
<th>Commodity / group of commodities</th>
<th>2nd contributor to MS diet (in % of ADI)</th>
<th>Commodity / group of commodities</th>
<th>3rd contributor to MS diet (in % of ADI)</th>
<th>Commodity / group of commodities</th>
</tr>
</thead>
<tbody>
<tr>
<td>91.0</td>
<td>WHO Cluster diet B</td>
<td>87.5 Citrus fruit</td>
<td></td>
<td>1.0 CEREALS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>82.6</td>
<td>ES adult</td>
<td>81.1 Citrus fruit</td>
<td></td>
<td>0.6 PRODUCTS OF ANIMAL ORIGIN-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>80.8</td>
<td>UK Infant</td>
<td>75.3 Citrus fruit</td>
<td></td>
<td>2.7 CEREALS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>80.7</td>
<td>SE general population 90th percentile</td>
<td>77.7 Citrus fruit</td>
<td></td>
<td>1.4 PRODUCTS OF ANIMAL ORIGIN-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65.3</td>
<td>WHO Cluster diet F</td>
<td>63.4 Citrus fruit</td>
<td></td>
<td>0.6 PRODUCTS OF ANIMAL ORIGIN-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>64.4</td>
<td>Fi adult</td>
<td>63.3 Citrus fruit</td>
<td></td>
<td>0.6 PRODUCTS OF ANIMAL ORIGIN-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>62.7</td>
<td>FR infant</td>
<td>59.2 Citrus fruit</td>
<td></td>
<td>2.2 PRODUCTS OF ANIMAL ORIGIN-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60.1</td>
<td>UK vegetarian</td>
<td>58.8 Citrus fruit</td>
<td></td>
<td>0.3 Sugar beet (root)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>49.0</td>
<td>WHO cluster diet E</td>
<td>46.7 Citrus fruit</td>
<td></td>
<td>0.5 PRODUCTS OF ANIMAL ORIGIN-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>47.8</td>
<td>WHO regional European diet</td>
<td>45.7 Citrus fruit</td>
<td></td>
<td>0.8 PRODUCTS OF ANIMAL ORIGIN-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>44.3</td>
<td>PT General population</td>
<td>42.9 Citrus fruit</td>
<td></td>
<td>0.4 CEREALS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>42.8</td>
<td>IT toddler</td>
<td>41.3 Citrus fruit</td>
<td></td>
<td>0.7 CEREALS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40.4</td>
<td>UK Adult</td>
<td>39.0 Citrus fruit</td>
<td></td>
<td>0.4 PRODUCTS OF ANIMAL ORIGIN-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>37.9</td>
<td>FR all coconut</td>
<td>38.5 Citrus fruit</td>
<td></td>
<td>0.4 PRODUCTS OF ANIMAL ORIGIN-</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The acute risk assessment is based on the ADI as no ARID was available.
For each commodity the calculation is based on the highest reported MS consumption per kg bw and the corresponding unit weight from the MS with the critical consumption. If no data on the unit weight is available, the variability factors were 10.7 or 5 (according to JMPR manual 2002), for lettuce a variability factor of 5 was used.

Threshold MRL is the calculated residue level which would lead to an exposure equivalent to 100% of the ARID.

<table>
<thead>
<tr>
<th>Unprocessed commodities</th>
<th>No of commodities for which ARID/ADI is exceeded (ESTI 1): 12</th>
<th>No of commodities for which ARID/ADI is exceeded (ESTI 2): 8</th>
<th>No of commodities for which ARID/ADI is exceeded (ESTI 1): ---</th>
<th>No of commodities for which ARID/ADI is exceeded (ESTI 2): ---</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highest % of ARID/ADI</td>
<td>Commodities</td>
<td>pTMRL/ threshold MRL (mg/kg)</td>
<td>Highest % of ARID/ADI</td>
<td>Commodities</td>
</tr>
<tr>
<td>223.1</td>
<td>Melons</td>
<td>0.5 / 0.22</td>
<td>223.1</td>
<td>Melons</td>
</tr>
<tr>
<td>208.0</td>
<td>Watermelons</td>
<td>0.5 / 0.23</td>
<td>208.0</td>
<td>Watermelons</td>
</tr>
<tr>
<td>195.0</td>
<td>Oranges</td>
<td>0.5 / 0.25</td>
<td>148.8</td>
<td>Pineapples</td>
</tr>
<tr>
<td>148.8</td>
<td>Pineapples</td>
<td>0.5 / 0.33</td>
<td>140.6</td>
<td>Oranges</td>
</tr>
<tr>
<td>144.1</td>
<td>Apples</td>
<td>0.5 / 0.24</td>
<td>131.2</td>
<td>Grapefruit</td>
</tr>
<tr>
<td>139.0</td>
<td>Pears</td>
<td>0.5 / 0.37</td>
<td>129.6</td>
<td>Scario (broad-leaf)</td>
</tr>
<tr>
<td>131.2</td>
<td>Grapefruit</td>
<td>0.5 / 0.38</td>
<td>125.3</td>
<td>Table grapes</td>
</tr>
<tr>
<td>128.6</td>
<td>Scario (broad-leaf)</td>
<td>0.5 / 0.38</td>
<td>100.2</td>
<td>Apples</td>
</tr>
<tr>
<td>125.3</td>
<td>Table grapes</td>
<td>0.5 / 0.39</td>
<td>97.2</td>
<td>Cauliflower</td>
</tr>
<tr>
<td>120.0</td>
<td>Bananas</td>
<td>0.5 / 0.4</td>
<td>98.3</td>
<td>Pears</td>
</tr>
<tr>
<td>115.7</td>
<td>Mangoes</td>
<td>0.5 / 0.43</td>
<td></td>
<td></td>
</tr>
<tr>
<td>108.0</td>
<td>Sweet corn</td>
<td>0.5 / 0.46</td>
<td></td>
<td></td>
</tr>
<tr>
<td>99.4</td>
<td>Kale</td>
<td>0.5 / -</td>
<td></td>
<td></td>
</tr>
<tr>
<td>97.2</td>
<td>Cauliflower</td>
<td>0.5 / -</td>
<td></td>
<td></td>
</tr>
<tr>
<td>95.2</td>
<td>Carrots</td>
<td>0.5 / -</td>
<td></td>
<td></td>
</tr>
<tr>
<td>92.6</td>
<td>Peppers</td>
<td>0.5 / -</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

No of critical MRLs (ESTI 1): 12
No of critical MRLs (ESTI 2): 8

<table>
<thead>
<tr>
<th>Processed commodities</th>
<th>No of commodities for which ARID/ADI is exceeded: ---</th>
<th>No of commodities for which ARID/ADI is exceeded: ---</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highest % of ARID/ADI</td>
<td>Processed commodities</td>
<td>pTMRL/ threshold MRL (mg/kg)</td>
</tr>
<tr>
<td>74.0</td>
<td>Apple juice</td>
<td>0.5 / -</td>
</tr>
<tr>
<td>79.8</td>
<td>Orange juice</td>
<td>0.5 / -</td>
</tr>
</tbody>
</table>
ANNEX III: temporary EU-MRLs

Structure

- **Part A**
  - MRLs Harmonisation for 167 pesticides
  - ± 50000 MRLs
  - Mostly pesticides not yet evaluated under Dir. 91/414/EEC

- **Part B**
  - combinations new crops/238 pesticides in Annex II
  - ± 30000 MRLs
Harmonisation = Simplification

National MRLs
500,000

EU-harmonised MRLs
Annex III - Part A
50,000
Annex III
Forthcoming update

Need for an update:
- National MRLs set after May 2006
- Comments received from non-EU Countries (SPS)


On-going update:
- Data collected from the Member States
- Changes requested for 112 substances:
  - 51 new entries (not covered by current Annex III – part A)
  - 61 already covered by first establishment Annex III – part A
- EFSA asked for an opinion
- Vote: March 2008
ANNEX IV: substances for which an MRL is not necessary

First establishment

- EFSA asked for an opinion on the risk to consumers.
- Only substances already evaluated under Directive 91/414/EEC
  - 3 Chemicals
  - 5 Micro-organisms
- Many substances candidate for Annex IV still under evaluation under Dir. 91/414/EEC.
- Update possible before July 2008.
Complete list of Annexes Reg. 396/2005

- **Annex II**: Existing EU MRLs
- **Annex III**: Temporary EU MRLs
- **Annex IV**: List of active substances for which no MRLs are required
- **Annex V**: Substances for which a default MRL applies
- **Annex VI**: Processed products
- **Annex VII**: Fumigants → Under development

Adoption and publication expected January 2008
Compliance with MRLs

Pesticides not covered by any of the Annexes

Default MRL
0,01 mg/kg
Regulation 396/2005
MRL setting

Applicant → Application for MRL

Member State → Evaluation report

EFSA → Reasoned opinion

Commission → Proposal for a Regulation/Decision

Standing Committee → Opinion

Parliament and Council → Right of scrutiny

Commission → Adoption and publication

Δt = 1 year

Art. 6-16
EU-MRL setting

1. Risk assessment
   - Evaluate short-term and long-term consumer health risks
   - Based on WHO methodology
   - Use EU-agreed VF
   - Member State
   - EFSA

2. Risk management
   - European Commission
   - MRL cannot be set if ADI or ARfD exceeded
Regulation 396/2005
MRL setting – Import tolerances

- When the request comes from outside the EU: Import tolerance.
- The requirements are the same as for applicants in the EU.
- A request for an import tolerance has to be submitted to the Rapporteur Member State (RMS).
- If a RMS does not exist, a Member State is designated by the Commission.
Regulation 396/2005
MRL setting – data requirements

- Toxicology data to derive ADI/ARfD (only for substances not yet evaluated in the EU).
- Information on authorised use and Good Agricultural Practice.
- Supervised residue trials 8 for major crops 4 for minor crops (for minor crops, extrapolations may be possible). Plant metabolism data; processing studies; peel/pulp distribution.
- Animal feeding studies (if crop used for animal feed).
Current Directives
Minors crops and very minor crops

Minor and very minor crops not always listed

<table>
<thead>
<tr>
<th>Groups of products</th>
<th>Products included in the groups</th>
<th>Part of product to which maximum residue levels apply</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Fruit, fresh, dried or uncooked, preserved by freezing, not containing added sugar; nuts</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(i) CITRUS FRUIT</td>
<td>Grapefruit</td>
<td>Whole product</td>
</tr>
<tr>
<td></td>
<td>Lemons</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Limes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mandarins (including clementines and similar hybrids)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Oranges</td>
<td></td>
</tr>
</tbody>
</table>
### Reg. 396/2005
**Simplification for (very) minor crops**

#### Clearer classification in Annex I

<table>
<thead>
<tr>
<th>Code number (1)</th>
<th>Groups to which the MRLs apply</th>
<th>Examples of individual products within the groups to which the MRLs apply</th>
<th>Scientific Name (2)</th>
<th>Examples of related varieties or other products included in the definition to which the same MRL applies</th>
</tr>
</thead>
<tbody>
<tr>
<td>0100000</td>
<td>1. FRUIT FRESH OR FROZEN; NUTS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0110000</td>
<td>(i) Citrus fruit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0110010</td>
<td></td>
<td>Grapefruit</td>
<td>Citrus paradisi</td>
<td>Shaddocks, pomelos, sweeties, tangelo, ugli and other hybrids</td>
</tr>
<tr>
<td>0110020</td>
<td></td>
<td>Oranges</td>
<td>Citrus sinensis</td>
<td>Bergamot, bitter orange, chinotto and other hybrids</td>
</tr>
</tbody>
</table>

All crops covered by one code ➔ same MRL
Next challenges

- **Annex I**: add fish and animal feed
- **Annex VI**: processed products
- **Database** on MRLs (DG SANCO website)
- **Database** on toxicological reference values, GAPs, dietary intake assessment (EFSA)
- Variables **IESTI equation** (EFSA opinion)
- Consider **cumulative and synergistic effects** (EFSA)
Timeframe entering into force Reg. 396/2005

- First publication Annexes II, III, IV: January '08
- Vote on update Annexes II, III, IV: March '08
- Publication update Annexes II, III, IV: June '08
- Implementation Reg. 396/2005: July '08
Conclusions

1. **Pesticide legislation in the EU**
   - Approval active substances, autorisation PPP
   - Setting MRLs

2. **MRL legislation**
   - Full harmonisation on-going
   - Reg. 396/2005 applicable as from July 2008

3. **MRL setting**
   - EFSA involved in the risk assessment
   - Increased transparency

4. **Minor uses**
   - Benefits from new legal framework
DG SANCO webpage
http://ec.europa.eu/dgs/health_consumer/index_en.htm

Pesticide Residue Legislation

Annexes II, III and IV (voted texts to be published in January 2008)
http://ec.europa.eu/food/plant/protection/pesticides/index_en.htm

Approval of active substances

EFSA model
Thank you for your attention