Results from the EFSA/FAO/WHO workshop on the evaluation of the IESTI equation – plus preliminary impact analysis

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Chongqing, 25 April 2016

HISTORY OF IESTI

- 1997 FAO/WHO Geneva Consultation
- 1998 York International Conference on Pesticide Residues Variability and Acute Dietary Risk Assessment (PSD, UK)
- ad hoc Expert Meeting held before the 1999 CCPR (Annex V in JMPR 1999 report)
- changes consolidated at FAO/WHO ‘Annapolis’ workshop (WHO, 2008 = EHC 240)
HOW IESTI EQUATIONS ARE USED

In the process of MRL setting:

- Revisiting IESTI
- IESTI = International Estimate of Short-Term dietary Intake

Short-term = 24 hours (for comparison with ARfD)

HOW IESTI EQUATIONS ARE USED; EU SPECIFIC

- In the pre-authorisation risk assessment
- In the EU annual reports on the monitoring programme for pesticide residues
- In the process of enforcement:
  - EU Rapid Alert System for Food and Feed (RASFF)
  - PSTI = Predicted short term intake from sampling result
  - Uses 'OR' = observed residue in equation instead of HR, but is essentially identical to IESTI. OR refers to residue definition for monitoring!
Please check the condition in the right bottom corner:

Intake > ADI; ARfD
REICH Hermine; 25-2-2016
**IESTI EQUATIONS**

Select case 1, 2a, 2b or 3:

- **Case 1**
  Unit weight \((U_{RAC}) < 25\) g
  (e.g. green beans)

- **Case 2a**
  Unit weight \((U_{RAC}) \geq 25\) g
  edible portion \((U_e) < \) large portion
  (e.g. potatoes)

- **Case 2b**
  Unit weight \((U_{RAC}) \geq 25\) g
  edible portion \((U_e) \geq \) large portion
  (e.g. red cabbage)

- **Case 3**
  bulked/blended commodity
  (e.g. tea)

**CURRENT IESTI EQUATIONS**

- **Case 1**
  Unit weight \((U_{RAC}) < 25\) g
  (e.g. green beans with pods)

- **Case 2a**
  Unit weight \((U_{RAC}) \geq 25\) g,
  \(v=3, 5, 7, 10\)
  edible portion \((U_e) < \) large portion
  (e.g. potatoes)

- **Case 2b**
  Unit weight \((U_{RAC}) \geq 25\) g,
  \(v=3, 5, 7, 10\)
  edible portion \((U_e) \geq \) large portion
  (e.g. red cabbage)

- **Case 3**
  bulked/blended commodity
  (e.g. tea, cereals)
CURRENT IESTI EQUATIONS

Effect of the unit weight

Initially, MRL instead of HR in IESTI

In 1999, MRL was replaced by HR, because:

- the JMPR practice of recommending MRLs within ‘MRL classes’. This may lead to the IESTI not being sufficiently discriminatory to be used as a screening technique.

- wish to consider total toxicologically relevant residue; use of residue definition for risk assessment (HR) instead of residue definition for enforcement/monitoring (MRL)

- no rounding in the middle of a calculation

<table>
<thead>
<tr>
<th>Spinach-total LP = 420.3 g/p/d, bw = 14.2 kg, South Africa (ZA)</th>
<th>HR = 2.5 mg/kg, ARFD = 0.1 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bunch of spinach</td>
<td>Spinach plant</td>
</tr>
<tr>
<td>$U_{AC}=U_a=300$ g, JPN</td>
<td>$U_{AC}=45$ g, $U_a=33.3$ g, AUS</td>
</tr>
<tr>
<td>Case 2a, $v=3$</td>
<td>Case 2a, $v=3$</td>
</tr>
<tr>
<td>180% ARFD</td>
<td>90% ARFD</td>
</tr>
</tbody>
</table>
HISTORY OF VARIABILITY FACTOR

- Definition for variability factor (v): 97.5th percentile of the residues present in single crop units divided by the mean residue of the lot
- 2002 JMPR: default factors of 3, 5, 7, 10
  2003 JMPR: default factor 3; 2005 JMPR confirmed this (new data)
- Not accepted in EU; EFSA PPR Panel opinion 2005. Variability factor is itself variable, 3 is the mean of the distribution. How conservative do risk managers want to be?
- 2007 EFSA PPR opinion; influence of changing v on Level of Protection

REASONS TO REVISIT IESTI - 1

- Check against current science and practicalities after 15 years of use
- Communicating that the legal standards (MRLs) are assessed may contribute to building trust among the general audience
- Harmonizing the IESTI methodology will increase the acceptability of Codex MRLs and as such contribute to a level playing field in international trade.
REASONS TO REVISIT IESTI - 2

- Use of OECD MRL calculator and harmonised MRL classes:
  - MRLs are derived in the same way everywhere
  - using the MRL instead of the HR will no longer lead to different conclusions in different countries

- HR is based on a small dataset.
  - In reality, residue levels may vary outside the dataset. The ‘OECD – MRL calculation unrounded’ is a statistically more reliable estimate of the highest residue. The OECD – MRL calculation in many cases results in a level at approximately 2x the HR

2006/2007 JMPR RECOMMENDATIONS

for issues to address in a global workshop/consultation on IESTI

- Uncertainty and variability of the parameters
- Investigation of the practicalities of using the MRL
- Ways to improve the consumption, unit weight and bodyweight data
- Identification of additional subgroups of the population for which the assessment should be conducted, e.g. toddlers
- The adequacy of the IESTI/NESTI equations when residues from monitoring/enforcement are used
- How to improve the communication between risk assessors and risk managers and the public on the output of the risk assessment
**IESTI EVENT GENEVA SEPT 2015**

**Stakeholder meeting 7 sept**

- **AIM:** to collect views and contributions of stakeholders in order to use this input in the EFSA/FAO/WHO scientific workshop on 8 + 9 sept
- Attended by representatives of risk management bodies, of producing and exporting countries, of NGOs, of Industry
- Expectations of participants for workshop:
  - Global harmonisation of the equations;
  - Development of a roadmap describing the activities needed to reach that goal.

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**IESTI EVENT GENEVA SEPT 2015**

**Stakeholder meeting 7 sept**

Discussion on purpose of IESTI calculations:

1. evaluation of the dietary risk related to a specific use or

2. evaluation of the dietary risk related to a specific MRL
PAN- Europe (NGO):
‘Priority in the EU is to protect human and environmental health’
‘IESTI being over conservative is a myth’
‘IESTI must be modified according to cumulative risk assessment’

ECPA:
‘Keep current IESTI equation (as applied by JMPR) until full impact is known and further work is completed’
‘Promote international harmonization between JMPR, Japan, Europe and USA / Canada’

European Commission:
- ‘All residue levels entered up to and including the MRL should not result in ARfD exceedance’
- ‘Revised IESTI equation should be acceptable at international level, notably Codex/JMPR’
- ‘Overall LoP should not be lowered’

Exporting country (Thailand):
- Use MRL in IESTI as tier 1 in tiered approach
- Develop guidelines on establishing unit weights
- Consider processing / cooking factors
- Establish a guideline for inspection on pesticide residues based on risk
Conclusions workshop 8 + 9 sept.

Proposal for new IESTI equations

- New IESTI equation replacing case 1 and case 3 of the current IESTI equation:
  \[ IESTI = LP_{bw} \times MRL \times CF \times PF \]

- New IESTI equation replacing case 2a and case 2b of the current IESTI equation:
  \[ IESTI = LP_{bw} \times MRL \times v \times CF \times PF \]
Main recommendations

- Replace the HR and STMR by the MRL in all cases of the IESTI equation
- Use a default variability factor of 3
- Derive the P97.5 large portion from the distribution of consumption values expressed as g/kg body weight
- Proposal to remove the unit weight from the IESTI equations
- Applicable to both MRL setting for individual commodities and enforcement purposes

Future work - 1

- Develop a list of commodities for which the variability factor is not applicable
- Information on bulking and blending practices needs to be gathered.
- Further guidance on the derivation of conversion factors is needed (OECD?)
- Conversion factors and processing factors should be made publicly available by the risk assessors in a database.
Future work - 2

- Develop a harmonized and comprehensive list of commodities and certain pre-defined processed commodities for which large portion data need to be derived.
- Develop a harmonized list or database compiling the large portions for the different diets at global level. Data should comply with agreed quality criteria.
- Further guidance on how to derive a large portion is required.

REFERENCES

- Info on Stakeholder meeting + workshop + presentations given:

- Event Report:
An *ad hoc* working group with members from ANSES (FR), APVMA (AUS), BfR (DE), CRD (UK), EFSA, RIVM (NL) has prepared a preliminary impact assessment on the proposed changes. The assessment includes:
- impact on number of MRLs
- ratio of current versus proposed exposure estimates (case 1, 2a, 2b, 3)
- commodities affected
- influence of the number of trials in the derivation of the MRL

IESTI impact assessment; JMPR vs proposed

- Res def ENF = DRA
- Res def ENF<> DRA
- ARFD not necessary
JMPR method versus proposed, MRLs=466 (total)

Number of MRLs affected in the proposed method

IESTI proposed vs JMPR method (MRL=453)

- `<ARID` N=431 (95%)
- `>ARID case 1` N=2 (0%)
- `>ARID case 2a` N=12 (3%)
- `>ARID case 2b` N=4 (1%)
- `>ARID case 3` N=4 (1%)
Impact of changes in IESTI calculations: use of the residue data from EU Art 12 review
Conclusion for all diets (cumulated)

<table>
<thead>
<tr>
<th></th>
<th>Acute risk not identified anymore</th>
<th>MRL lost</th>
<th>Unchanged conclusion</th>
<th>No comparison possible</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>New IESTI IESTI_pers_EU</td>
<td>29</td>
<td>178</td>
<td>16664</td>
<td>23559</td>
<td>40430</td>
</tr>
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<td>New IESTI IESTI_pers_JMPR</td>
<td>1</td>
<td>268</td>
<td>16602</td>
<td>23559</td>
<td>40430</td>
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<td>New IESTI IESTI_calc_EU</td>
<td>47</td>
<td>203</td>
<td>21072</td>
<td>19108</td>
<td>40430</td>
</tr>
<tr>
<td>New IESTI IESTI_calc_JMPR</td>
<td>0</td>
<td>320</td>
<td>21002</td>
<td>19108</td>
<td>40430</td>
</tr>
</tbody>
</table>

MRL by case for each diet
MRL lost by diet and by case

MRL lost by AS and commodity group
MRL lost by commodity

% of MRL lost by commodity group

New IESTI vs IESTI-calc-JMPR

Total number of MRL for each commodity is indicated above each bar
APVMA: MEAN VERSUS MEDIAN, GEN. POP

Ratios of acute intakes using proposed and current methodologies for six chemicals using Australian consumption data (general population)

APVMA: MEAN VERSUS MEDIAN, 2-6 YEAR OLDS

Ratios of acute intakes using proposed and current methodologies for six chemicals using Australian consumption data (2-6 year olds)
BFR: INFLUENCE OF NO. OF TRIALS

Impact of changing input parameters: HR → MRL (case 1, 2a & 2b)

Ratio HR vs. MRL using the OECD Calculator against synthetic data (log-normal, n=1, σ=0.83)

Impact of changing input parameters: STMR → MRL (case 3)

Ratio STMR vs. MRL using the OECD Calculator against synthetic data (log-normal, n=1, σ=0.83)
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ROADMAP

- EFSA event report by end 2015
- Draft report considered by JMPR 2015
- Side-event at CCPR 2016 (25-30 April)
- Need for further international discussions with JMPR and stakeholders and dissemination of information
- Please refer to CRD3 for background information and proposal for future work
THANK YOU FOR YOUR ATTENTION!