Status of harmonization of dose expression in 3 D crops for the zonal efficacy evaluation of PPP (Plant Protection Product) in Europe

Suprofruit, Hasselt, 10th May 2017

Schlotter, Peter & Toews, Ralph-Burkhardt
on behalf of ECPA (European Crop Protection Association),
Sub-team 3 D crops
Outline

• EU Zonal regulation process 1107/2009
• Why harmonization of dose rate expression?
• (treated) Leaf Wall Area = tLWA
• Recommendations EPPO workshop, Oct. 2016
• Conversion models of dose expression
• Summary
Why is a common dose expression so important?

EC 1107/2009 Zonal evaluation and registration process, started June 2011

3 Regulatory zones

1 Zonal Rapporteur per Zone (zRMS)
Several Concerned member state (cRMS)

and 4 EPPO climatic zones

How can one zRMS evaluate the efficacy for all countries in the zone if the dose expressions in efficacy trials are different?
Europe

4 EPPO Climatic Zones, 3 EU Administration Zones

According to Regulation EC 1107/2009

Agreement on grouping of biological data across zones (e.g. EPPO climatic zones)
Farmer Instructions

Mutual recognition
National assessment, dose expression for registration+labelling

Reference units/parameter in trial reports

Zonal efficacy evaluation based on
A harmonized dose expression

RR & final conclusion dRR/BAD

Trial reports

Responsibility of
• National registration authorities
Influenced by:
• National legislation
• Local practice

National task

hardly to be harmonized

National registration authorities

Influenced by:
• National legislation
• Local practice

Zonal task

OUR FOCUS
harmonization
targeted

Why harmonization? Dose rate expressions used in European countries

<table>
<thead>
<tr>
<th></th>
<th>Top fruits</th>
<th>Grapevine</th>
<th>High-growing vegetables</th>
<th>Citrus / Olives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria and Germany</td>
<td>Kg/ha/m CH, max. kg/ha</td>
<td>% accord. Eichhorn, max. kg/ha BBCH</td>
<td>Kg/ha/m CH, max. kg/ha</td>
<td>---</td>
</tr>
<tr>
<td>Belgium</td>
<td>Kg or L/10’000m² LWA, max.kg or l/ha</td>
<td>---</td>
<td>Kg or L/10’000m² LWA, max.kg or l/ha</td>
<td>---</td>
</tr>
<tr>
<td>France</td>
<td>Kg/hl</td>
<td>Kg/ha</td>
<td>Kg/ha</td>
<td>---</td>
</tr>
<tr>
<td>Greece</td>
<td>%, max. spray vol / ha</td>
<td>%, max. spray vol / ha</td>
<td>%, max. spray vol / ha</td>
<td>%, max. spray vol / ha</td>
</tr>
<tr>
<td>Italy</td>
<td>%, min. to max. spray vol / ha</td>
<td>%, max. spray vol / ha</td>
<td>%, max. spray vol / ha</td>
<td>%, max. spray vol / ha</td>
</tr>
<tr>
<td>Netherlands</td>
<td>%, max. spray vol / ha</td>
<td>---</td>
<td>%, max. spray vol / ha</td>
<td>---</td>
</tr>
<tr>
<td>Norway</td>
<td>Kg/100m row length</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Portugal</td>
<td>%, max. spray vol / ha</td>
<td>%, max. spray vol / ha</td>
<td>%, max. spray vol / ha</td>
<td>%, max. spray vol / ha</td>
</tr>
<tr>
<td>Spain</td>
<td>%, max. spray vol / ha</td>
<td>%, max. spray vol / ha</td>
<td>%, max. spray vol / ha</td>
<td>%, max. spray vol / ha</td>
</tr>
<tr>
<td>Switzerland</td>
<td>Kg/10’000 m³ TRV</td>
<td>%, max. spray vol / ha</td>
<td>%, max. spray vol / ha</td>
<td>---</td>
</tr>
</tbody>
</table>

6 different dose expression units for top fruits! 3 different expression units in grapevine!

Reference: Tree Fruits Dose Expression Discussion Group Meeting – Wageningen, the Netherlands, September 29, 2009
We need a better description than ha ground or hL concentration!
Pharmaceuticals:
dose rate adapted to the body weight

Logical - Accepted by everybody

- 15 kg child
- 55 kg lady - teacher
- 100 kg worker
Need for harmonization

• Definition of minimum effective dose
  – cannot be seriously justified

• Efficacy
  – risk of low control values in crops with high LWA

• Phytoxicity
  – risk of phytotoxic effects in crops with low LWA

• Resistance
  – Risk of resistance development in crops with high LWA

• Validity of results for all member states

• Conversion of zonal conclusion to national dose expressions
Agriculture: dose rate adapted to the size of the crop

Treated Leaf Wall Area kg or L / 10,000 m²

<table>
<thead>
<tr>
<th>Formula</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>[ \text{treated LWA} = 2 \times \frac{\text{Spray band height (m)} \times 10,000 \text{ m}^2}{\text{Spacing between rows (m)}} ]</td>
<td>Treated Leaf Wall Area</td>
</tr>
</tbody>
</table>

\[ \text{treated LWA} = 2 \times \text{Spray band height (m)} \times \text{Row Length (m)} \]
SWOT Analysis of treated Leaf Wall Area (tLWA)

**Strength**

- **Simple** system - easy measured parameters
- Considers **seasonal vertical development** of the crop and crop parameters
- Already **implemented** in BE, about to be implemented in AT, support in NL and DE
- Reliability, **consistent** results, good dose response
- Allowing better and faster comparison and **understanding** of trial data across different member states; a must for EU Zonal evaluation and registration process
- tLWA rate can be easily **converted** to national label rate expressions
  - trial by trial individually
  - the resulting target rate generally using assumptions
SWOT Analysis of treated Leaf Wall Area (tLWA)

Weakness

• **Simple** system – tLWA model may not to be the best model for crop adapted spraying, but it is far better than dose expressions not considering the crop structure
• Not a good fit for **globular** trees
• Additional information reflecting **regulatory limitations** (dose/ha ground) is needed for the critical GAP and for the farmers’ guidance and labels, but not for dose definition trials
SWOT Analysis of treated Leaf Wall Area (tLWA)

Opportunities

• Can be used as **platform** for dose adjustment
• Helping to cope with **increasing requirements** from regulatory bodies, food chain and trade.
• Applicable to **reduce variability** in other registration sections (residues)
• Facilitating **communication** with and between regulatory bodies.
• Allows **targeted** sprays, e.g. *Botrytis* in grapes or insects cluster in crops
• In line with the **Sustainable Use Directive** and the National Action Plans.
Industry Data –
LWA PER EPPO ZONE and BBCH (apple & pear)

One data point per application, 18,867 data from 2009 to 2015

Majority of apple & pear in EU 28: LWA/ha < 17,000 m², median 10,000-15,000 m²
Industry Data – cherry & plum 
LWA PER EPPO ZONE and BBCH 

One data point per application, 523 data from 2009 to 2016

Majority of cherry & plum in EU 28: LWA/ha < 15.000 m², median 9.500-15.000 m²
Industry Data – grape
LWA per EPPO ZONE and BBCH Central Reg.Zone

One data point per application, data 1.689 from 2013 to 2015

<table>
<thead>
<tr>
<th>Median of LWA by Zone, Training / Country / Growth period</th>
<th>00-08 Shooting</th>
<th>09-60 Bud &amp; leaf growth</th>
<th>61-70 Flowering</th>
<th>71-74 Fruit set</th>
<th>75-99 Berries</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median</td>
<td>Count</td>
<td>Median</td>
<td>Count</td>
<td>Median</td>
</tr>
<tr>
<td>Austria</td>
<td></td>
<td></td>
<td>5714</td>
<td>23</td>
<td>7333</td>
</tr>
<tr>
<td>Czech Republic</td>
<td></td>
<td></td>
<td>8000</td>
<td>28</td>
<td>8000</td>
</tr>
<tr>
<td>Germany</td>
<td>15000</td>
<td>1</td>
<td>10000</td>
<td>228</td>
<td>12657</td>
</tr>
<tr>
<td>Hungary</td>
<td>8800</td>
<td>3</td>
<td>6400</td>
<td>30</td>
<td>10000</td>
</tr>
<tr>
<td>Slovakia</td>
<td></td>
<td></td>
<td>7333</td>
<td>18</td>
<td>7333</td>
</tr>
<tr>
<td>Slovenia</td>
<td></td>
<td></td>
<td>4249</td>
<td>7</td>
<td>6080</td>
</tr>
<tr>
<td>Switzerland</td>
<td></td>
<td></td>
<td>7222</td>
<td>47</td>
<td>10500</td>
</tr>
<tr>
<td>ALL countries</td>
<td>8800</td>
<td>4</td>
<td>8240</td>
<td>381</td>
<td>11000</td>
</tr>
</tbody>
</table>

Grapes in CZ: LWA/ha median 8.000-15.000 m², depends on development stage
### Industry Data – grape

LWA per EPPO ZONE and BBCH, Southern Reg. Zone

One data point per application, 5,569 data from 2013 to 2015

<table>
<thead>
<tr>
<th>Median of LWA by Zone, Training / Country / Growth period</th>
<th>00-08 Shooting</th>
<th>09-60 Bud &amp; leaf growth</th>
<th>61-70 Flowering</th>
<th>71-74 Fruit set</th>
<th>75-99 Berries</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median</td>
<td>Count</td>
<td>Median</td>
<td>Count</td>
<td>Median</td>
</tr>
<tr>
<td>Bulgaria</td>
<td></td>
<td></td>
<td>7900</td>
<td>4</td>
<td>9100</td>
</tr>
<tr>
<td>Croatia</td>
<td></td>
<td></td>
<td>9750</td>
<td>2</td>
<td>12500</td>
</tr>
<tr>
<td>France</td>
<td>12982</td>
<td>4</td>
<td>7200</td>
<td>662</td>
<td>9630</td>
</tr>
<tr>
<td>Greece</td>
<td></td>
<td></td>
<td>12982</td>
<td>28</td>
<td>14042</td>
</tr>
<tr>
<td>Italy</td>
<td>667</td>
<td>3</td>
<td>6000</td>
<td>347</td>
<td>7857</td>
</tr>
<tr>
<td>Portugal</td>
<td>741</td>
<td>3</td>
<td>5714</td>
<td>111</td>
<td>7208</td>
</tr>
<tr>
<td>Romania</td>
<td></td>
<td></td>
<td>9800</td>
<td>10</td>
<td>10400</td>
</tr>
<tr>
<td>Spain</td>
<td>417</td>
<td>3</td>
<td>6762</td>
<td>202</td>
<td>9000</td>
</tr>
<tr>
<td>ALL countries</td>
<td>741</td>
<td>13</td>
<td>6667</td>
<td>1366</td>
<td>8839</td>
</tr>
</tbody>
</table>

Grapes in SZ: LWA/ha median all countries 7,000-15,000 m², depends on development stage, differences within countries and regions.
Recommendaons

• Agreement to use tLWA as dose expression for efficacy trials of PPP for Zonal evaluation in pome fruit, grapevine and high growing vegetables for new registrations

• Kg or L/ha ground is not to be used in the zonal efficacy evaluation as it is not linked to any crop structure. However, the dose/ha ground is to be given in the GAP table

• Expert Working Group (EWG) established
  – on dose conversion
  – on glossary of terms and on measurement of crop parameters

• Citrus and olives (and globular trees) are still under review and evaluators in Europe should discuss any proposal and validate it
Conversion between models of dose expression for new product developments

- **treated Tree Row Volume TRV m³**
- **treated Leaf Wall Area tLWA L/10,000 m² (spray volume)**
- **critical GAP (max rate/ha)**
- **‘Fix’ rate (rate/ha)**
- **Canopy height (kg ha⁻¹ m⁻¹)**
- **Concentration (%) (spray volume)**

**Protocols**
- Dev field trials
- Dossier (efficacy)
- Zonal Evaluation
- Product Authorisation

➢ Agreed on Conversion factors and tLWA/EPPO Zone

Conversion between models of dose expression

When is a conversion factor needed?

1) from tLWA rate to critical GAP* rate/ha (used for tox, fate, ecotox risk assessment)

2) to convert the proposed target dose rate/tLWA into national expressions on labels

3) to keep old trials that did not follow the tLWA approach valid

GAP = Good agriculture practice: document describing all intended uses
Transfer from Zonal efficacy evaluation to label rates

Simplest approach – if legally accepted:

- Labels display the rate per tLWA (as validated in Zonal efficacy evaluation) plus a max. ha ground rate (as validated in other sections and GAP)

- Plus national expressions (converted from tLWA using agreed parameters)
Summary

• In view of the new zonal evaluation and registration system in the EU, the dose expression harmonisation in **efficacy assessments** will be a help for zonal rapporteur regulators who need to assess and to register on behalf of several countries.

• A dose unit which expresses the product quantity in relation to the **treated area** would be consistent with any kind of spray application (field crops, spray band, 3D crops).

• **Agreement to use tLWA** as dose expression for **efficacy trials** of PPP for Zonal evaluation in **pome fruit, grapevine and high growing vegetables** for new registrations (EPPO workshop, Oct. 2016). A transition period is needed for all registered PPP.

• Other crops (citrus, olives, globular trees) are under evaluation.

• Continue harmonization effort in close cooperation is needed.

86 participants from 18 EPPO countries, 35 from National Regulatory Authorities, Research Institutes and Universities, 29 from Crop Protection Industry, 20 from Consultants.

http://archives.eppo.int/MEETINGS/2016_conferences/dose_expression.htm
Questions and comments?
Thank you!

On behalf of ECPA (European Crop Protection Association), sub team 3 D crops
Richard Massie, Adama
Martin Teichmann, BASF
Ralph Burkhard Toews, Bayer Crop Science
Xavier Van Waetermeulen, Bayer Crop Science
Jean-Pierre Huby, DuPont
Robert Matysiak, DuPont
Juan Miguel Cantus, Syngenta
Frank Meier-Runge, Syngenta
Peter Schlotter, Dow AgroSciences