Use of pesticide urinary metabolites from residents living near agricultural land to validate exposure models

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Background

- Currently a lack of information on pesticide exposure for residents and bystanders in Britain
- Previous study by Sleeuwenhoek *et al*
  - regulatory methods appropriate for farm workers.
  - methods may underestimate bystander exposure
  - no measurements collected for residents
  - need to check current tools sufficiently conservative
- DEFRA funded new study
  - Started 1st Oct 2010, due for completion end Jan 2014
  - Led by IOM, in collaboration with Health and Safety Laboratory (HSL) and Glasgow Caledonian University
Aims

• Determine if spray events lead to increased exposure in residents
  • Statistical analyses of urinary metabolites, comparing levels
    • Following spray events
    • Background within and out with season
  • Compare urinary metabolite concentration with internal exposure estimates provided by regulatory risk assessment (RRA)
Survey strategy

- 3 agricultural regions: East Lothian, Kent, Norfolk
- Recruit farmers - Obtain info on pesticide usage
- Recruit residents living within 100m of fields
- Collect urine samples
  - Weekly samples during and out with spraying season
  - Reactive samples (1 and 2 days after spray) if receive sufficient notice from the farmer
- Urine sample analysis
  - Urine samples collected 1 and 2 days after spraying event
  - Background within the spraying season (n=3)
  - Background outside the spraying season (n=3)
Pesticides of interest

- Not selected on basis of any health concern, but
  - Availability of urinary marker
  - Likelihood of application

- In 2011 and 2012 collected urine samples relevant to spray events involving:
  - Captan
  - Chlormequat
  - Chlorpyrifos
  - Penconazole
  - Cypermethrin (2012 only)
Population and urine samples

- 909 urine samples collected during 2011, with 2,384 urine samples collected in 2012

<table>
<thead>
<tr>
<th>Farms</th>
<th>Residents</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>2012</td>
</tr>
<tr>
<td>Farms</td>
<td>Residents</td>
</tr>
<tr>
<td>2011</td>
<td>2012</td>
</tr>
<tr>
<td>Adult : Child</td>
<td>Adult : Child</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Spray event samples</th>
<th>2011</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlormequat</td>
<td>31</td>
<td>250</td>
</tr>
<tr>
<td>Captan</td>
<td>28</td>
<td>244</td>
</tr>
<tr>
<td>Penconazole</td>
<td>13</td>
<td>83</td>
</tr>
<tr>
<td>Chlorpyrifos</td>
<td>6</td>
<td>54</td>
</tr>
<tr>
<td>Z-Cypermethrin</td>
<td>0</td>
<td>50</td>
</tr>
</tbody>
</table>
Information collected inc.

- **Background questionnaire**
  - Weight, height, date of birth
  - Pesticide exposure - occupational / para-occ. / home usage

- **Questionnaire for each urine sample**
  - Activities (and where)
  - Pesticide exposure - occupational / para-occ. / home usage
  - Consumption of home grown product

- **Spray records**
  - Start / finish time
  - Weather conditions
  - Product sprayed, quantities applied and spray method
Regulatory Risk Assessments

• RRA completed for each relevant spray event where urine samples were collected

• Current approach
  • Spray drift on adults, breathing zone at 8 metres
  • Adults and children 24h vapour exposure
  • Children dermal, hand-to-mouth, object-to-mouth, from average drift fallout in adjacent area
Regulatory Risk Assessments

• Also two modified approaches used

<table>
<thead>
<tr>
<th>Modified approach</th>
<th>Bystanders (single exposure)</th>
<th>Residents (repeated exposure)</th>
</tr>
</thead>
<tbody>
<tr>
<td>spray drift from low crops for adults and children at 2m</td>
<td>Yes, based on BREAM P95</td>
<td>Yes, based on BREAM P75</td>
</tr>
<tr>
<td>spray drift from high crops for adults at 8 metres</td>
<td>Yes, based on P95 current data</td>
<td>Yes, based on P75 current data</td>
</tr>
<tr>
<td>adults and children 24h vapour</td>
<td>Yes (as before)</td>
<td>Yes (as before)</td>
</tr>
<tr>
<td>children dermal, hand-to-mouth, etc, from higher level of drift fallout in adjacent area</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Pharmacokinetic (PK) model

- PK model used to estimate the amount of metabolite of interest excreted in urine

- Starting with the estimated internal dose of active ingredient

- Uses information such as
  - MW of active ingredient and metabolite
  - Volume of distribution
  - Half-life of metabolite
How will this be used?

• RRA completed for specific exposure scenarios to obtain an estimate of the internal dose

• PK model then used to estimate amount excreted in urine given this internal dose

• Estimated urinary levels compared to that obtained from the urine samples

• Allows for some evaluation of whether the RRA over or under estimates the levels actually found in urine for the residents in the study
Statistical analysis will...

- Summarise urinary metabolite levels obtained during spray season and investigate whether any recorded factors have an effect on the levels.

- Differences in levels obtained within and outwith spray season.

- Estimate exposure based on urinary levels.

- Determine estimates of long-term exposure by combining exposure from spray events, within season and outwith season backgrounds.
Current status of project

- Sample and data collection completed
- RRA completed and being reviewed
- Urine sample analysis on-going
- Project end date Jan 2014
- Publication and other dissemination activities will follow
Further information

- **Project website**
  - [www.pesticidebiomonitoring.org](http://www.pesticidebiomonitoring.org)

- **Published study protocol**

- **Dr. Karen Galea**
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