Body burden modeling for bird and mammal risk assessment of pesticides: findings from the SETAC MODELINK workshop case study

Agnieszka J. Bednarska(1,2), Virginie Ducrot(3), Silvia Hinarejos(4), Gabe Weyman(5), Pernille Thorbek(1)

(1) Syngenta, Jealott’s Hill International Research Centre, Bracknell, RG42 6EY, UK
(2) Institute of Nature Conservation, Polish Academy of Sciences, Mickiewicza 33, 31-120 Kraków, Poland
(3) INRA, UMR985 Ecologie et Santé des Ecosystèmes, INRA-Agrocampus Ouest, 65 rue de Saint Brieuc, 35000 Rennes, France
(4) Sumitomo Chemical Agro Europe, 2 rue Claude Chappe, 69771 Saint Didier au Mont d’Or, France
(5) Makhteshim Agan (UK) Ltd, Unit 15, Thatcham Business Village, Colthrop Way, Thatcham, Berkshire, RG19 4LW, UK

Introduction

The current risk assessment for birds and mammals is based on measurements of external exposure, but it is normally the internal concentration which drives the toxicological effect. Internal concentration is the net result of absorption, distribution, metabolism and excretion (ADME), and toxicokinetic (TK) models are mathematical descriptions of these processes. To improve our understanding of the relationship between the external and internal concentrations of pesticides, we need TK models which translate an external concentration of toxicant, which may change over time, to an internal concentration at target site. Within the registration process of plant protection products, often ADME data within rat, live-stock or hen are available. Based on the ADME data, a simple body burden (BB) model was developed and then applied to a variety of feeding scenarios, including one tested in a standard laboratory test on rats.

Methods

Body Burden model – TK concept

A one-compartment first-order model gave the best fit to the measured blood concentration over time. The residues in different tissues were highly correlated with each other which suggest that the insecticide was rapidly perfused throughout the body. Therefore, all tissues and blood were treated as one compartment. The gastro-intestinal tract was treated separately as its content is not strictly ‘in’ the organism. The body burden model equations were implemented in an excel spreadsheet and the model was applied to a variety of feeding scenarios (Table 2).

BB models are considered as a tool for higher-tier risk assessment for birds and mammals (EFSA, 2009). However, currently BB-type models are a research area rather than an established methodology in environmental risk assessment. The applicability of the BB approach as a refinement option in bird and mammal risk assessment was discussed during the SETAC MODELINK workshop. A case study for a hypothetical insecticide applied as seed treatment served as an example to explain the main assumptions behind the model, its advantages and limitations, and to indicate where and how it should be extended or adapted. This case study was also used to illustrate the consequences of different feeding scenarios on internal concentration of pesticide. Participants from academia, industry and regulators have worked together to consider the critical properties needed during the development of a BB model, such as species (indicator, generic focal or focal species) and their feeding behavior.

Results

Table 1. Results of standard Tier 1 risk assessment for generic focal species

<table>
<thead>
<tr>
<th>Generic focal species</th>
<th>FIR/bw</th>
<th>NAR [mg a.i/kg seed]</th>
<th>Daily Dietary Dose [mg a.i/kg bw]</th>
<th>LD50 [mg a.i/kg bw]</th>
<th>TER , value</th>
<th>Acceptable vs TER trigger 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small granivorous bird</td>
<td>0.3</td>
<td>150</td>
<td>45</td>
<td>262</td>
<td>5.8</td>
<td>no</td>
</tr>
<tr>
<td>Small omnivorous mammal</td>
<td>0.24</td>
<td>150</td>
<td>35</td>
<td>280</td>
<td>7.8</td>
<td>no</td>
</tr>
</tbody>
</table>

NAR = normal feeding/application rate of active ingredient (a.i.); TER=TER(max) / NAR x FIR(bw).

Table 2. Results of refined risk assessment by using metabolism (ADME) and BB modeling

Focal species | FIR | Daily dietary dose [mg a.i/kg bw] | Total feeding time [min] | Feeding pattern | Max C , [mg a.i/kg bw] | TER(max) |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Skylark</td>
<td>10.03</td>
<td>40.14</td>
<td>56</td>
<td>4 x 14 min feeding + 40 min breaks between feeding occasions</td>
<td>15.7</td>
<td>11</td>
</tr>
<tr>
<td>Wood mouse</td>
<td>4.71</td>
<td>32.59</td>
<td>120</td>
<td>4 th feeding + 1 h break + 1 h feeding</td>
<td>14.0</td>
<td>12.3</td>
</tr>
</tbody>
</table>

Safety threshold (i.e., Max C, for LD50/10) for skylark is 11.2 and for wood mouse 18.4 mg a.i./kg bw.

Conclusions

Feeding pattern greatly influenced the exposure pattern, which cannot be taken into account in the current acute risk assessment approach based upon gavage with a bolus dose. Using a safety factor of 10, values for the threshold (i.e., Max C , for LD50/10) were 17.2 and 18.4 mg a.i./kg bw for skylark and wood mouse, respectively. These thresholds were exceeded in none of studied realistic exposure scenarios. BB model provides more realism for risk refinement. It can be extended to different types of pesticide application and feeding scenarios as well as include the full range of values for TK parameters and/or ingestion rates (probabilistic approach).