MEMORANDUM

SUBJECT: Dietary Exposure Analysis for Imidacloprid (NTN) through the Use on Mango (PP#4F4285).

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Science Analysis Branch/HED (7509C)

TO: Dennis Edwards, PM Team 19  
Insecticide-Rodenticide Branch  
Registration Division (7505C)

THROUGH: Elizabeth A. Doyle, Ph.D., Section Head  
Dietary Risk Evaluation Section  
SAB/Health Effects Division

Action Requested

Provide a Dietary Risk Evaluation System (DRES) analysis of the dietary exposure for imidacloprid through the proposed use on mango.

Discussion

Toxicological Endpoint:

The chronic analysis used a Reference Dose (Rfd) of 0.057 mg/kg body weight/day, based on a no observed effect level (NOEL) of 5.7 mg/kg bwt/day and an uncertainty factor of 100. The NOEL is based on a chronic toxicity study in rats that demonstrated increased thyroid lesions in males as an endpoint effect. The HED Rfd Peer Review Committee also classified imidacloprid as a Group E carcinogen (G. Ghali memo, 11/10/93).

An acute dietary assessment is required by the Toxicology Endpoint Selection Document for Imidacloprid (Karl Baetcke memo, 4/18/94). The endpoint for acute dietary risk assessment is 24 mg/kg/day from the rabbit developmental study. The LEL (72 mg/kg/day) was based upon decreased body weight, and increased resorptions, abortion and increased skeletal abnormalities.

Residue Information:

Food uses evaluated in this analysis were the published interim tolerance on hops listed in the Tolerance Index System (TIS) and 40 CFR §180.472. Hops is included in this analysis as a published commodity with an expiration date of 6/28/95. Meat and
milk tolerances, 0.2 and 0.05 ppm, respectively, are also published as interim tolerances along with hops.

CBTS recommends for a tolerance on mango at 0.2 ppm in a F.
Griffith memo dated 7/22/94. Mango is included in the analysis as
a new tolerance.

No information has been provided for refinement of percent of
crop treated or anticipated residues for either chronic or acute
analyses. A summary of the residue information used in the analysis
is attached as Table 1.

Results:

Chronic Exposure

A DRES chronic exposure analysis was performed using tolerance
level residues and 100 percent crop treated information to estimate
the Theoretical Maximum Residue Contribution (TMRC) for the general
population and 22 subgroups.

Summaries of the TMRCs and their representations as
percentages of the RfD for imidacloprid are attached as Table 2.

The following table provides exposure information for the U.S.
population and the most highly exposed subgroup, children 1-6 years
old. The exposure and percent of the Reference Dose for each
proposed commodity is given in the table as well.

<table>
<thead>
<tr>
<th>Commodity Type</th>
<th>U.S. Population (TMRC) (µg/kg/day)</th>
<th>Non-Nursing Infants (TMRC) (µg/kg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Published Uses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>hops, meat &amp; milk</td>
<td>0.000985</td>
<td>0.003693</td>
</tr>
<tr>
<td>Proposed New Use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>mango</td>
<td>&lt;0.000001</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>0.000985</td>
<td>0.003693</td>
</tr>
</tbody>
</table>

Acute Exposure

The DRES detailed acute exposure analysis evaluates individual
food consumption as reported by respondents in the USDA 77-78
Nationwide Food Consumption Survey (NFCS) and estimates the
distribution of single day exposures through the diet for the U.S.
population and certain subgroups. The analysis assumes uniform
distribution of imidacloprid in the commodity supply. Since the
toxicological effect to which high end exposure is being compared
to in this analysis is developmental toxicity, the DRES subgroup of
concern is females (13+ years) which approximates women of child-
bearing age.

The Margin of Exposure (MOE) is a measure of how closely the
high end exposure comes to the NOEL (the highest dose at which no
effects were observed in the laboratory study), and is calculated
as the ratio of the NOEL to the exposure (NOEL/exposure = MOE). For
substances whose acute NOEL is based on animal studies, the Agency
is not generally concerned unless the MOE is below 100.
In the analysis, tolerance level residues for hops, meat, milk and mango were used to calculate the high-end exposure for the females (13+ years) subgroup. High end exposure was compared to the NOEL of 24 mg/kg bwt/day from the rabbit developmental study to get a high end Margin of Exposure. The MOE for females was calculated in the attached table and the results are as follows:

Females (13+ years) High End Exposure = 0.00288 mg/kg/day
NOEL/Exposure = 24 mg/kg/day ÷ 0.00288 mg/kg/day = 8333

Using the given endpoints, the MOE is not of concern for the subgroup females (13+ years) with an estimated MOE considerably above 100.

Discussion
To the extent that this analysis used tolerance level residues and 100 percent-crop-treated assumptions, it is considered a "worst-case" picture of the dietary risk from imidacloprid. The chronic dietary risk from exposure of imidacloprid appears to be of minimal concern, with all DRES subgroups having TMRC values well below the Reference Dose.

The acute dietary analysis of imidacloprid is not of concern for females of child-bearing age considering the proposed tolerances.

There appears to be no excessive dietary risk from the proposed new tolerance for imidacloprid on mango at 0.2 ppm.

Attachments

cc: DRES, Caswell #497E, Tox I, CBTS
### Table 2: Limited Data on Mann

<table>
<thead>
<tr>
<th>Reference Doses</th>
<th>Chemical Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Type</td>
<td></td>
</tr>
<tr>
<td>Status</td>
<td></td>
</tr>
<tr>
<td>Data Gaps</td>
<td></td>
</tr>
<tr>
<td>Dose</td>
<td></td>
</tr>
</tbody>
</table>

#### Dose

- **Oncode (NIH/NIH)**: 200.00 ppm
- **Indicated**: 100.00 ppm
- **No increases of occupational, environmental or non-human exposures**: 0.0000
- **No data gaps**: 0.0000

#### Reference Doses

- **Oral**: 0.0024
- **Parenteral**: 0.0000

#### Chemical Information

- **CAS NO.**: 103507-79-9
- **Density**: 1.109 g/mL
- **Molecular formula**: OT
- **Molecular weight**: 108.994
- **Molar volume**: 151.25 mL/mol

#### Data Gaps

- **No data gaps**: 0.0000
- **No increases of occupational, environmental or non-human exposures**: 0.0000

#### Study Type

- **Single exposure to a dose of 200.00 ppm over 2 days**
<table>
<thead>
<tr>
<th>% of the ADI</th>
<th>mg/kg/day</th>
<th>% of the RDI</th>
<th>mg/kg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.000</td>
<td>0</td>
<td>0.000</td>
<td>0</td>
</tr>
<tr>
<td>0.074</td>
<td>0.0099</td>
<td>0.074</td>
<td>0.0099</td>
</tr>
<tr>
<td>0.172</td>
<td>0.0600</td>
<td>0.172</td>
<td>0.0600</td>
</tr>
<tr>
<td>0.327</td>
<td>0.1000</td>
<td>0.327</td>
<td>0.1000</td>
</tr>
<tr>
<td>0.500</td>
<td>0.1667</td>
<td>0.500</td>
<td>0.1667</td>
</tr>
<tr>
<td>0.749</td>
<td>0.2500</td>
<td>0.749</td>
<td>0.2500</td>
</tr>
<tr>
<td>1.000</td>
<td>0.3333</td>
<td>1.000</td>
<td>0.3333</td>
</tr>
</tbody>
</table>

ANALYSIS FOR POPULATION AGE GROUP: NON-NURSING INFANTS (< 1 YEAR OLD)

ANALYSIS FOR POPULATION AGE GROUP: 1-6 YEARS OLD

ANALYSIS FOR POPULATION AGE GROUP: 7-12 YEARS OLD

ANALYSIS FOR POPULATION AGE GROUP: 13-18 YEARS OLD

DATE: 11/09/94