MEMORANDUM

SUBJECT: EPA Reg. No.: 279-2862; Carbofuran; miscellaneous data; five acute studies
Caswell #: 160A
Accession #: 256481

TO: Jay Ellenberger
Product Manager (12)
Registration Division (TS-767)

THRU: Robert P. Zendzian, Ph.D.
Acting Head, Review Section IV
Toxicology Branch
Hazard Evaluation Division (TS-769)

FROM: William Dykstra, Ph.D.
Toxicology Branch
Hazard Evaluation Division (TS-769)

Requested Action:

Review acute oral LD₅₀ studies on carbamate and phenolic metabolites of carbofuran to determine relative toxicity.

Conclusions:

1. The acute oral LD₅₀ studies are acceptable and support the registration of carbofuran.

Background:

The registrant, FMC, submitted these additional studies to Agriculture Canada in order that a determination of the toxicological significance of carbamate and phenolic metabolites could be made.

Review:

1. Acute oral LD₅₀ of FMC 18209 (3-hydroxy carbofuran) technical in rats (FMC # A83-1136; 4/12/84).

Groups of 10 male and 10 female Sprague-Dawley rats were orally gavaged with graded doses of test material in corn oil.

Observation was 14 days.
Results:

Mortality data are shown below:

<table>
<thead>
<tr>
<th>Dosage (mg/kg)</th>
<th>Male % mortality</th>
<th>Dosage (mg/kg)</th>
<th>Female % mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>80</td>
<td>18</td>
<td>100</td>
</tr>
<tr>
<td>20</td>
<td>30</td>
<td>15</td>
<td>70</td>
</tr>
<tr>
<td>18</td>
<td>10</td>
<td>10</td>
<td>60</td>
</tr>
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<td></td>
<td></td>
<td>8</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.5</td>
<td>55</td>
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<tr>
<td></td>
<td></td>
<td>7.0</td>
<td>45</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.0</td>
<td>0</td>
</tr>
</tbody>
</table>

Male LD₅₀ = 21.9 mg/kg (19.9 - 23.8)

Female LD₅₀ = 8.3 mg/kg (6.8 - 9.9)

Toxic Signs: Tremors, oral discharge, stained fur.

Body Weight: All but two surviving animals gained weight.

Necropsy: No gross lesions except for blood in intestine of one rat.

Toxicity Category I: Danger.

Classification: Core minimum data.

2. Acute oral LD₅₀ study with FMC 1781 Technical (3-Keto carbofuran) in rats (FMC study #: A83-1137; 4/12/84).

Groups of 10 male and female Sprague-Dawley rats were orally gavaged with graded doses of test material in corn oil.

Observations were for 14 days.

Results: Mortality data are shown below:

<table>
<thead>
<tr>
<th>Dosage (mg/kg)</th>
<th>Male % mortality</th>
<th>Dosage (mg/kg)</th>
<th>Female % mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>200</td>
<td>100</td>
<td>150</td>
<td>100</td>
</tr>
<tr>
<td>120</td>
<td>80</td>
<td>120</td>
<td>80</td>
</tr>
<tr>
<td>110</td>
<td>90</td>
<td>100</td>
<td>40</td>
</tr>
<tr>
<td>100</td>
<td>20</td>
<td>70</td>
<td>30</td>
</tr>
<tr>
<td>70</td>
<td>10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Male  \( LD_{50} = 108 \text{ mg/kg (94.5-121)} \)
Female  \( LD_{50} = 93.1 \text{ mg/kg (76.2-110)} \)
Combined  \( LD_{50} = 107 \text{ mg/kg (91.1-123)} \)

**Toxic Signs:** Tremors, oral discharge, stained fur and decreased locomotion.

**Body Weight:** Survivors gained weight.

**Necropsy:** No gross lesions.

**Toxicity Category II:** Warning.

**Classification:** Core minimum data.

3. Acute oral \( LD_{50} \) study with FMC 1649\% technical (3-hydroxy-7-phenol) in rats (FMC A83-1134; 3/29/84).

Groups of 10 males and 10 females Sprague Dawley rats received oral gavage graded doses of test material in corn oil.

Observation was for 14 days.

**Results:**

Mortality data are shown below:

<table>
<thead>
<tr>
<th>Dosage mg/kg</th>
<th>Male % mortality</th>
<th>Female Dosage mg/kg</th>
<th>Female % mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>2400</td>
<td>80</td>
<td>2000</td>
<td>90</td>
</tr>
<tr>
<td>2000</td>
<td>60</td>
<td>1700</td>
<td>50</td>
</tr>
<tr>
<td>1400</td>
<td>10</td>
<td>1400</td>
<td>20</td>
</tr>
</tbody>
</table>

Male  \( LD_{50} \)  = 1916 mg/kg (1656-2175)
Female  \( LD_{50} \)  = 1654 mg/kg (1500-1807)
Toxic signs: Prostration, decreased locomotion, nasal, ocular and oral discharge.

Body weight: Survivors gained weight.

Necropsy: Blood in intestines of decedents.

Toxicity Category III: Caution.

Classification: Core minimum data.

4. Acute oral LD_{50} study with FMC 16490 technical (3-keto-7-phenol) in rats (FMC # A83-1135; 3/28/84).

Groups of 10 males and 10 females Sprague-Dawley rats were orally gavaged with graded dosages of test material in corn oil. Observations was for 14 days.

Results:

No deaths at 300 and 800 mg/kg of test material.

LD_{50} > 800 mg/kg (both sexes)

Toxic Signs: Lacrimation and decreased locomotion in the 800 mg/kg.

Body Weight: All rats gained weight.

Necropsy: No gross lesions.

Toxicity Category III: Caution.

Classification: Core minimum data.

5. Acute oral LD_{50} study with FMC 10272 technical (7-phenol) in rats (FMC # A83-1133; 3/28/84).

Groups of 10 males and 10 females Sprague-Dawley rats were orally gavaged with graded dosages of test material undiluted. Observations was for 14 days.
Results:

Mortality data are shown below:

<table>
<thead>
<tr>
<th>Dosage (mg/kg)</th>
<th>Male % mortality</th>
<th>Female Dosage (mg/kg)</th>
<th>Female % mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>3000</td>
<td>80</td>
<td>2300</td>
<td>70</td>
</tr>
<tr>
<td>2300</td>
<td>40</td>
<td>1800</td>
<td>50</td>
</tr>
<tr>
<td>1800</td>
<td>10</td>
<td>1400</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1000</td>
<td>10</td>
</tr>
</tbody>
</table>

Male LD₅₀ = 2450 mg/kg (2137-2764)

Female LD₅₀ = 1743 mg/kg (1362-2124)

Toxic Signs: Prostration, tremors, discharge, decreased locomotion.

Body Weight: Survivors gained weight.

Necropsy: Blood in intestine of decedents.

Toxicity Category III: Caution.

Classification: Core minimum data.