MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 9779-GNT
        Malathion R.T.U.

FROM: Sheila A. Moats 3/15/90 E 3/16/90
Precautionary Review Section
Registration Support Branch
Registration Division (H75-05C)

TO: Miller/Loehman (PM 16)
Insecticide/rodenticide Branch
Registration Division (H75-05C)

APPLICANT: Riverside/Terra Corporation
P.O. Box 171376
Memphis, Tennessee 38187-1376

FORMULATION FROM LABEL:

Active Ingredient(s):
Malathion (O,O-dimethyl phosphorodithioate of diethyl mercaptosuccinate) 46.2

Inert Ingredient(s): ........................................ 53.8

Total 100.0%
Background

The Riverside/Terra Corporation submitted acute oral, dermal, inhalation, primary eye, and skin irritation and dermal sensitization studies to support registration of Malathion RTU. MRID nos used were: 409551-02-07.

Recommendations

1. The acute toxicity studies submitted by Riverside/Terra Corporation are acceptable to RSP/PRF.

2. No further acute toxicity tests are required.

Labeling

1. The CAUTION signal word is acceptable.

2. Precautionary Statements are acceptable.

3. The Statement of Practical Treatment is acceptable, except as explained below. According to agency guidelines, the toxic category for the acute dermal test is III. Therefore, the Statement of Practical Treatment "IF ON SKIN" should also include "get medical attention".
DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (§81-1)

Product Manager: (16) Reviewer: S. N. Oats
RID No.: 40 9551 - 02 Report Date: 3/13/80
Testing Facility: Stillmeadows Inc. Report No. 5621-88
Author(s): Kubin, Tanrice O.
Species: Harlan Sprague Dawley - rats.
Age: Young adults Observation Days (Post
Weight: 184 - 277 g. Exposure: (14); other ( )
Source: Harlan Sprague Dawley Inc. Houston Texas.
Test Material: Malathion.
Quality Assurance (40 CFR §160.12): Adequate

Conclusion: \[ \% = 95\% \text{ confidence limits (mg/kg)} \]

1. LD50 (mg/kg): Males = 5150 \text{mg/kg} * 4940 - 5380, Females = 4380 \text{mg/kg} * 4210 - 4580, Combined =
2. The estimated LD50 is 4910 \text{mg/kg} * 4550 - 5080.
3. Tox. Category: III. Classification: Guideline

Procedure (Deviations From §81-1): Young adult \text{♂ + ♀} rats were administered undiluted doses of the test material. Observations for toxicity and mortality were made 3 times on the day of treatment plus once daily thereafter for 14 days.

Results:

<table>
<thead>
<tr>
<th>DOSAGE \text{(mg/kg)}</th>
<th>(NUMBER KILLED/NUMBER TESTED)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
</tr>
<tr>
<td>4000</td>
<td>0/5</td>
</tr>
<tr>
<td>5400</td>
<td>0/5</td>
</tr>
<tr>
<td>8400</td>
<td>0/5</td>
</tr>
<tr>
<td>5050</td>
<td>3/5</td>
</tr>
<tr>
<td>5200</td>
<td>2/5</td>
</tr>
</tbody>
</table>

Symptomology & Gross Necropsy Findings:

Toxicological signs included, decreased activity, ataxia, tremors, chromatocytosis, diarrhea, epistaxis, gasping, nasal discharge, pilo-erection etc.

Gross necropsy findings included, signs of chromatocytosis, diarrhea, lacrimation, nasal discharge, polyuria, and salivation and distended gastrointestinal tract.
DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§81-2)

Product Manager: (16)  Reviewer: S. Yacots
MRID No.: 409551-03  Report Date: 3/14/90
Testing Laboratory: Stillmeadow Inc.  Report No. 5622-88
Author(s): Kuhn, Janice C.
Species: New Zealand Whites - rabbits
Sex: Males + females  Wt.: 2.800 - 3.675 kg
Test Material: [Blank]
Quality Assurance (40 CFR §160.12): Adequate

Summary:

1. LD50 (mg/kg): Males = [Blank]; Females = [Blank]; Combined = > 2020 mg/kg
2. The estimated LD50 is > 2020 mg/kg.
3. Tox. Category: III. Classification: Guidelines

Procedure (Deviations From §81-2): 5 males + 5 females were used for the study. Fur was clipped and undiluted test article was applied over the clipped area. Gauze 10 × 10 cm 2 layers thick was applied to the trunk of the animal held in place with non-irritating tape. The entire trunk of each animal was next wrapped with semi-permeable stockinet. After 24-hr exposure to the test material, the wrappings were removed. Exposure sites were cleaned to remove residues. Animals were observed at 1/2, 3 + 6 hrs after treatment, once daily thereafter for 14 days.

<table>
<thead>
<tr>
<th>DOSAGE (mg/kg)</th>
<th>(NUMBER KILLED/NUMBER TESTED)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2020 mg.</td>
<td>Males</td>
</tr>
<tr>
<td>0/5</td>
<td>0/5</td>
</tr>
</tbody>
</table>

Results: Reported Mortality

Symptomology & Gross Necropsy Findings:

Clinical signs were minimal, limited to decreased defecation, no defecation + diarrhea. No animals died during the study. All animals were sacrificed and necropsied. Necropsy examinations revealed signs of diarrhea, discoloration of the gastrointestinal tract, and empty large intestine.
DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (§81-4)

Product Manager: [Redacted]  Reviewer: S. Moats
MRID No.: 409557-04  Report Date: 3/14/90
Testing Laboratory: Stillmeadow Inc. Report No. 5623-88
Author(s): Kuhn, Janice C.
Species: New Zealand White - rabbits
Sex: males & females  Weight:
Source: Ray Nichols Rabbitry, Lumberton, Texas
Dosage: 0.1 mL
Test Material: Male Khan
Quality Assurance (40 CFR §160.12): Adequate

Summary:
Tox. Category: III  Classification: Guidelines

Procedure (Deviation From §81-4): A dose of 0.1 mL of undiluted test material was instilled into the conjunctival sac of the left eye of each of 9 rabbits. The right eye served as the untreated control. The lids were held open for 1 sec. Then the 9 treated eyes were washed for 1 min beginning 30 secs after treatment. The eyes were examined 4 times and results recorded at 1, 24, 48, and 72 hrs after treatment.

Results:

<table>
<thead>
<tr>
<th>Observations</th>
<th>Hour</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Cornea Opacity</td>
<td>0/6</td>
<td>0/6</td>
</tr>
<tr>
<td>Iris</td>
<td>0/6</td>
<td>0/6</td>
</tr>
<tr>
<td>Conjunctivae Redness</td>
<td>6/6</td>
<td>6/6</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>6/6</td>
<td>3/6</td>
</tr>
<tr>
<td>Discharge</td>
<td>6/6</td>
<td>3/6</td>
</tr>
</tbody>
</table>

Comments: All eye involvement +/− irritation cleared in 7 days or less (3 days in this case)
Product Manager: 16  
MRID No.: 409551-05  
Testing Laboratory: Stillmeadow  
Author(s): Kuhn, Janice, O.  
Species: New Zealand white - rabbits  
Age: Young adults  
Sex: ♂  
Weight:  
Dosage: 0.5 ml, Malathion F/P 1A-115  
Test Material: Malathion  
Quality Assurance (40 CFR $160.12): Adequate

Summary:

The Primary Irritation Index = 10.8

Toxicity Category: IV

Classification: Guidelines

Procedure (Deviations From §81-5):

Each test site of Six rabbits were dosed with 0.5 ml of the test material introduced beneath a gauze patch 2 layers in thickness. Each patch was secured in place with non-irritating tape. The entire trunk loosely wrapped with a semi-permeable stockinette. The wraps were removed after 4 hrs. The sites were washed to remove residues. The animals were examined for irritation as follows: 1, 24, 48 + 72 hrs + on days 7, 10 + 14.

Results

The mean irritation score at 72 hrs is 1.3. The test material causes mild or slight irritation to rabbits.

Special Comments:

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DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (§81-3)

Product Manager: (16)  
Reviewer: S. Moats  
MRID No.: 409551-06  
Report Date: 3/14/90  
Testing Laboratory: Stillmeadow Inc  
Report No. 5626-88  
Author(s): Holbert  
Species: Harlan Sprague Dawley - Rats  
Sex: Males & Females  
Weight:  
Source: Harlan Sprague Dawley Inc.  
Quality Assurance (40 CFR §160.12): Adequate

Summary:

1. LC50 (mg/kg): Males =  
   Females =  
   Combined = 7.792 mg/l
2. The estimated LC50 is 7.292 mg/l
3. Mean Concentration: 7.918 mg/l
4. Tox. Category: IV  
   Classification: Guidelines

Procedure (Deviations From §81-2): The test animals were housed individually in cages within a 200 L stainless steel dynamic inhalation chamber, during the exposure period. The animals were exposed to an aerosol generated undiluted test material. Observations were made on the day of exposure and once daily for 14 days. The aerosol was generated by pumping the test material through a pressure operated spray nozzle. The concentrated aerosol was diluted with dried filtered air drawn from the exposure chamber. Air flow was monitored and recorded every 5 minutes. Andersen's Collostral impactor was used to determine particle size.

<table>
<thead>
<tr>
<th>Exposure Concentration (mg/L)</th>
<th>(NUMBER KILLED/NUMBER TESTED)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.92 mg/L</td>
<td>Males 0/5, Females 0/5, Combined 0/10</td>
</tr>
</tbody>
</table>

Symptomology & Gross Necropsy Findings:

Clinical signs included activity decrease, dilated pupils, lacrimation, nasal discharge, piloerection, polyuria, ptosis & satiety. No animals died during the study. Gross necropsy examination at the end of the study revealed no observable abnormalities.

MMAD + Geometric std deviation at 1½ hour distribution = 2.406 µm + 1.988 respectively +

MMAD at 3½ hrs = 2.418 µm

Geometric std dev = 2.155
DATA REVIEW FOR SKIN SENSITIZATION TESTING (§81-6)

Product Manager: [Redacted] Reviewer: S. Moats
MRID No.: 405151-0-7 Report Date: 3/11/90
Testing Laboratory: Stillmeadow Inc Report No. 5623-58
Author(s): Kuhn Janice C
Species: Hartley's strain albino guinea pigs
Sex: male
Weight: 295-375 g
Source: Hartley Sprague Dawley Inc. Houston, Texas
Test Material: Malathion
Positive Control Material: Dichloroethane (DNCB)
Quality Assurance (40 CFR §160.12): Adequate

Method: Open Epicutaneous

Summary:
1. This product is not a dermal sensitizer.
2. Classification: Guidelines

Procedure (Deviation From §81-6): Gp I, 10 animals were treated with 0.05% w/v soln of DNCB (Positive Control). Gp II, animals were treated with the test material, 1.0% w/v malathion, for both the induction + challenge phases. Prior to dosing, back trunk of each animal was clipped to expose a 5 x 10 cm area. The test material was applied approximately under a gauze pad. Results: 4 secured with adhesive dressing. The entire trunk was next wrapped in clean plastic. The animals were restrained for 6 hrs. At the end of the exposure period the patches were removed + the animals returned to their cages. Same test location was used on each animal on all treatment days. On Day 36, all animals were treated in an identical manner as on the previous 10 treatment days. In addition, a 2nd test site was chosen in the right rear of the animal. Observations for skin reactions were made 24 hrs after each treatment for each test site + 48 hrs after treatments 1 + 10 + the challenge treatment on Day 36.

Results: 1.0% v/v soln of the test material did not produce a sensitizing reaction, whereas 0.05% w/v soln of DNCB produced a sensitizing reaction in guinea pigs.