UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

14/JUN/2011

**MEMORANDUM**

| | | |
|---|---|---|
| Subject: | Name of Pesticide Product: | Chlorothalonil Technical |
| | EPA File Symbol: | 88058-R |
| | DP Barcode: | D385901 |
| | Decision No.: | 443314 |
| | Action Code: | R310 |
| | PC Code: | 081901 (chlorothalonil) |

From: Eugenia McAndrew, Biologist
Technical Review Branch
Registration Division (7505P)

E. McAndrew

M. Hasler
Toxicologist

To: Rosemary Kearns, RM Team 22
Fungicide Branch
Registration Division (7505P)

Applicant: Orion ATO, LLC
P.O. Box 21720
Mesa, AZ 85277

FORMULATION FROM LABEL:

| Active Ingredient(s): | % by wt. |
|---|---|
| Chlorothalonil | 98.5 |
| Other Ingredient(s): | 1.5 |
| Total: | 100.0% |

**ACTION REQUESTED:** The Risk Manager requests review of acute toxicity data for EPA File Symbol 88058-R.

**BACKGROUND**: Orion ATO, LLC has submitted a six pack of acute toxicity studies to support the proposed manufacturing use product, Chlorothalonil Technical, EPA File Symbol 88058-R. The studies were conducted at Stillmeadow, Inc., Sugar Land, Texas with assigned MRID numbers 483266-06 to -11. A basic CSF dated December 10, 2010, label and company letter are included in the submission. An Agency contractor, Summitec Corporation, conducted the primary review of the studies. TRB performed the secondary review and made changes as necessary.

**RECOMMENDATIONS**:

1. The six studies have been reviewed and are classified as acceptable.

2. The acute toxicity profile for Chlorothalonil Technical, EPA File Symbol 88058-R, is as follows:

| | | | |
|---|---|---|---|
| Acute oral toxicity | IV | Acceptable | MRID 48326606 |
| Acute dermal toxicity | IV | Acceptable | MRID 48326607 |
| Acute inhalation toxicity | III | Acceptable | MRID 48326608 |
| Primary eye irritation | II | Acceptable | MRID 48326609 |
| Primary skin irritation | IV | Acceptable | MRID 48326610 |
| Dermal sensitization | Negative | Acceptable | MRID 48326611 |

3.The basic CSF must be accepted by the TRB Product Chemistry Team.

**LABELING**: Based on the toxicity profile above, the following are the precautionary and first aid statements for the proposed product as obtained from the Label Review System:

**PRODUCT ID #:** 088058-00001

**PRODUCT NAME:** Chlorothalonil Technical

**PRECAUTIONARY STATEMENTS**

**SIGNAL WORD:** WARNING

**Hazards to Humans and Domestic Animals:**

Causes substantial but temporary eye injury. Harmful if inhaled. Avoid breathing dust. Do not get in eyes or on clothing. Wear protective eyewear (goggles, face shield, or safety glasses). Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco or using the toilet. Remove and wash contaminated clothing before reuse.

**First Aid:**

If in eyes:
-Hold eye open and rinse slowly and gently with water for 15-20 minutes.
-Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
-Call a poison control center or doctor for treatment advice.

If inhaled:
-Move the person to fresh air.
-If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably mouth-to-mouth if possible.
-Call a poison control center or doctor for further treatment advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

**DATA EVALUATION RECORD**

**CHLOROTHALONIL TC**
**(CHLOROTHALONIL)**

**STUDY TYPE: ACUTE ORAL TOXICITY - RAT [OPPTS 870.1100; OECD 425]**
**ACUTE DERMAL TOXICITY - RABBIT [OPPTS 870.1200; OECD 402]**
**ACUTE INHALATION TOXICITY - RAT [OPPTS 870.1300; OECD 403]**
**ACUTE EYE IRRITATION - RABBIT [OPPTS 870.2400; OECD 405]**
**ACUTE DERMAL IRRITATION - RABBIT [OPPTS 870.2500; OECD 404]**
**DERMAL SENSITIZATION - GUINEA PIG [OPPTS 870.2600; OECD 406]**

**MRID 48326606, 48326607, 48326608, 48326609, 48326610, and 48326611**

Prepared for
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Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard
2777 South Crystal Drive
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Prepared by
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Task Order No. 3-B-03

Primary Reviewer:
Susan Chang, M.S.
Signature: Susan Chang
Date: MAY 25 2011

Secondary Reviewers:
Robert Ross, M.S.
Signature: Robert H. Ross
Date: MAY 25 2011

Kowetha Mack, Ph.D., D.A.B.T., Program Manager
Signature: KMack
Date: MAY 25 2011

Quality Assurance:
Angie Edmonds, B.S.
Signature: RAR for Angie Edmonds
Date: MAY 25 2011

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

**Reviewer:** Eugenia McAndrew
**Risk Manager (EPA):** RM 22

**Date:** June 14, 2011

**STUDY TYPE:** Acute Oral Toxicity – Rat; OCSPP 870.1100; OECD 425

**TEST MATERIAL:** Chlorothalonil TC (99.3% Chlorothalonil; Lot No. JXA09092202; white crystals according to the study text and yellowish powder according to the certificate of analysis)

**CITATION:** Kuhn, J. (2007) Chlorothalonil TC – Acute Oral Toxicity (UDP) Study in Rats. Study Number 14089-10. Stillmeadow, Inc., 12852 Park One Drive, Sugar Land, TX 77478. September 16, 2010. MRID 48326606.

**SPONSOR:** Jiangsu Xinhe Agrochemical Co., Ltd., No. 19 Xingang Road, Economic Development Zone, Xinyi, Jiangsu Province, 221400, P.R. China

**EXECUTIVE SUMMARY:** In an acute oral toxicity study (MRID 48326606), three fasted, young adult female Sprague-Dawley rats (age: approximately 9 weeks; body weight: 175-193 g; source: Texas Animal Specialties, Humble, TX) were given a single dose of Chlorothalonil TC (99.3% Chlorothalonil; Lot No. JXA09092202). The test substance was mixed with deionized water to produce a 40% w/v concentration. Three females received a dose of 5000 mg/kg bw by gavage and were observed for 14 days.

All animals survived the study. All animals appeared normal throughout the study. No observable abnormalities were noted from any animal at necropsy.

$LD_{50}$ Females > 5000 mg/kg bw

**Based on the observed $LD_{50}$ in females, Chlorothalonil TC is classified as EPA Toxicity Category IV.**

This study is classified as acceptable. It does satisfy the guideline requirements for an acute oral study (OCSPP 870.1100; OECD 425) in the rat.

**COMPLIANCE:** Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

## RESULTS AND DISCUSSION:

Individual animals were dosed as follows:

| Animal Number | Sex | Dose Level (mg/kg) | Short-Term Outcome | Long-Term Outcome |
|---|---|---|---|---|
| 181 | F | 5000 | S | S |
| 182 | F | 5000 | S | S |
| 183 | F | 5000 | S | S |

S = Survival, D = Death

**Statistics:** Acute Oral Toxicity (Guideline 425) Statistical Program (Westat, version 1.0, May 2001) was used for all data analyses including: dose progression selections, stopping criteria determinations and/or $LD_{50}$ and confidence limit calculations.

AOT425statpgm (Version: 1.0) Test Results and Recommendations
Acute Oral Toxicity (OECD Test Guideline 425) Statistical Program

Date/Time: Friday, May 06, 2011, 10:27:05 PM
Data file name: work.dat
Last modified: 5/6/2011 10:27:03 PM

Test/Substance: Chlorothalonil TC
Test type: Limit Test
Limit dose (mg/kg): 5000
Assumed $LD_{50}$ (mg/kg): Default
Assumed sigma (mg/kg): 0.5

DATA:

| Test Seq. | Animal ID | Dose (mg/kg) | Short-term Result | Long-term Result |
|---|---|---|---|---|
| 1 | 181 | 5000 | O | O |
| 2 | 182 | 5000 | O | O |
| 3 | 183 | 5000 | O | O |

(X = Died, O = Survived)

Dose Recommendation: The limit test is complete.

SUMMARY OF LONG-TERM RESULTS:

| Dose | O | X | Total |
|---|---|---|---|
| 5000 | 3 | 0 | 3 |
| All Doses | 3 | 0 | 3 |

Statistical Estimates:

The $LD_{50}$ is greater than 5000 mg/kg.

**A. Mortality:** All animals survived the study.

**B. Clinical observations:** All animals appeared normal throughout the study.

**C. Gross necropsy:** No observable abnormalities were noted from any animal at necropsy.

**D. Reviewer's conclusions:** This reviewer agrees with the study author's conclusions. Based on the observed $LD_{50}$ in females, Chlorothalonil TC is classified as EPA Toxicity Category IV.

**E. Deficiencies:** None

**Reviewer:** Eugenia McAndrew **Date:** June 14, 2011
**Risk Manager (EPA):** RM 22

**STUDY TYPE:** Acute Dermal Toxicity – Rat; OCSPP 870.1200; OECD 402

**TEST MATERIAL:** Chlorothalonil TC (99.3% Chlorothalonil; Lot No. JXA09092202; white crystals according to the study text and yellowish powder according to the certificate of analysis)

**CITATION:** Kuhn, J. (2010) Chlorothalonil TC – Acute Dermal Toxicity in Rats. Study Number 14090-10. Stillmeadow, Inc., 12852 Park One Drive, Sugar Land, TX 77478. September 22, 2011. MRID 48326607.

**SPONSOR:** Jiangsu Xinhe Agrochemical Co., Ltd., No. 19 Xingang Road, Economic Development Zone, Xinyi, Jiangsu Province, 221400, P.R. China

**EXECUTIVE SUMMARY:** In an acute dermal toxicity study (MRID 48326607), young adult Sprague-Dawley rats (5/sex; age: approximately 9 weeks; body weight: males: 241-292 g and females: 189-208 g; source: Texas Animal Specialties, Humble, TX) were dermally exposed for 24 hours on an area of approximately 10% of the total body surface area on the clipped dorsal trunk to 5050 mg/kg bw Chlorothalonil TC (99.3% Chlorothalonil; Lot No. JXA09092202) moistened with a sufficient amount of deionized water (1.0 m/L/g of test substance). The test material was applied evenly over the dose area and covered with a gauze patch and secured with non-irritating adhesive tape. The gauze and the trunk were wrapped with vet wrap and secured with non-irritating adhesive tape. The animals were then observed for 14 days.

All animals survived and appeared normal throughout the study. One male and three females that lost weight during the second week; all other animals gained weight during the study. Very slight erythema was noted at one site on day 1 only. At necropsy, two females were emaciated and the stomach and/or small intestines were empty. No observable abnormalities were noted from the other animals at necropsy.

$LD_{50}$ Males > 5050 mg/kg bw
$LD_{50}$ Females > 5050 mg/kg bw
$LD_{50}$ Combined > 5050 mg/kg bw

**Based on the observed $LD_{50}$, Chlorothalonil TC is classified as EPA Toxicity Category IV.**

This study is classified as acceptable. It does satisfy the guideline requirements for an acute dermal study (OCSPP 870.1200; OECD 402) in the rat.

**COMPLIANCE:** Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

## RESULTS AND DISCUSSION:

| Dose (mg/kg bw) | Mortality/Number Tested | | |
|---|---|---|---|
| | Males | Females | Combined |
| 5050 | 0/5 | 0/5 | 0/10 |

**Statistics:** No statistical analysis was required since all animals survived at the limit dose. The dermal $LD_{50}$ was observed as being > 5050 mg/kg.

A. **Mortality:** All animals survived the study.

B. **Clinical observations:** One male and three females that lost weight during the second week; all other animals gained weight during the study. Very slight erythema was noted at one site on day 1 only.

C. **Gross necropsy:** Two females were emaciated and the stomach and/or small intestines were empty. No observable abnormalities were noted from the other animals at necropsy.

D. **Reviewer's conclusions:** This reviewer agrees with the study author's conclusions. Based on the observed $LD_{50}$, Chlorothalonil TC is classified as EPA Toxicity Category IV.

E. **Deficiencies:** None

**Reviewer:** Eugenia McAndrew
**Risk Manager (EPA):** RM 22

**Date:** June 14, 2011

**STUDY TYPE:** Acute Inhalation Toxicity – Rat; OCSPP 870.1300; OECD 403

**TEST MATERIAL:** Chlorothalonil TC (99.3% Chlorothalonil; Lot No. JXA09092202; white crystals according to the study text and yellowish powder according to the certificate of analysis)

**CITATION:** Doig, A. (2010) Chlorothalonil TC – Acute Inhalation Toxicity Study in Rats. Study Number 14091-10. Stillmeadow, Inc., 12852 Park One Drive, Sugar Land, TX 77478. October 6, 2010. MRID 48326608.

**SPONSOR:** Jiangsu Xinhe Agrochemical Co., Ltd., No. 19 Xingang Road, Economic Development Zone, Xinyi, Jiangsu Province, 221400, P.R. China

**EXECUTIVE SUMMARY:** In an acute inhalation toxicity study (MRID 48326608), three groups of young adult Sprague-Dawley rats (5/sex/group; age: approximately 9 weeks; body weight: males: 253-314 g and females: 169-223 g; source: Texas Animal Specialties, Humble, TX) were exposed by nose-only inhalation to Chlorothalonil TC (99.3% Chlorothalonil; Lot No. JXA09092202) for 4 hours at concentrations of 0.57, 1.14, or 2.20 mg/L. The animals were observed for 14 days. The MMADs of 0.57 mg/L concentration were 3.8 and 4.0 µm and the GSD 5.6 and 6.6 at 1 and 2 hours, respectively. The MMADs of the 1.14 mg/L concentration were 2.8 and 2.6 µm and the GSD 6.1 and 5.8 at 1 and 2 hours, respectively. The MMADs of the 2.20 mg/L concentration were 2.1 and 2.3 µm and the GSD 6.3 and 6.6 at 1 and 2 hours, respectively.

One male exposed at 1.14 mg/L and one male exposed at 2.20 mg/L were found dead on day 1. One male exposed at 2.20 mg/L was found dead on day 2. One female exposed at 1.14 mg/L was found dead on day 3. One female exposed at 0.57 mg/L and one female exposed at 2.20 mg/L were found dead on day 4. All other animals survived the study. Piloerection and decreased activity were noted from all animals exposed at 0.57 mg/L upon removal from the chamber through day 1 with recovery by day 2. Piloerection, decreased activity, respiratory gurgle, and/or red liquid on muzzle were noted from the animals exposed at 1.14 or 2.20 mg/L. No individual animal data were provided, however, all survivors recovered by day 7. Three females in the 0.57 mg/L group lost weight during the first week, but all gained weight by the end of the study. All other survivors gained weight throughout the study. The decedents had red liquid on muzzle, dark red swollen lungs, stomach/intestines full of gas, empty intestines, and/or red crust around mouth. Stomachs full of gas were noted from two females in the 0.57 mg/L group. No observable abnormalities were noted in the other surviving animal at necropsy.

$LC_{50}$ Males = 4.68 mg/L (95% confidence Limits 2.59-6.73 mg/L)
$LC_{50}$ Females = 1.88 mg/L (95% confidence Limits 1.59-2.12 mg/L)
$LC_{50}$ Combined = 2.32 mg/L (95% confidence Limits 1.86-2.75 mg/L)

**Based on the observed $LD_{50}$ in females, Chlorothalonil TC is classified as EPA Toxicity Category III.**

This study is classified as acceptable. It does satisfy the guideline requirements for an acute inhalation study (OCSPP 870.1300; OECD 403) in the rat.

**COMPLIANCE:** Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

**RESULTS AND DISCUSSION:**

| Nominal Conc. (mg/L) | Gravimetric Conc. (mg/L) | MMAD µm | GSD | Mortality/Number Tested | | |
|---|---|---|---|---|---|---|
| | | | | Males | Females | Combined |
| 4.86 | 0.57 | 3.8, 4.0 | 5.6, 6.6 | 1/5 | 0/5 | 1/10 |
| 11.9 | 1.14 | 2.8, 2.6 | 6.1, 5.8 | 1/5 | 1/5 | 2/10 |
| 30.5 | 2.20 | 2.1, 2.3 | 6.3, 6.6 | 2/5 | 3/5 | 5/10 |

$LC_{50}$ calculation based on Rosiello, Essignmann, and Wogan, Rapid and Accurate Determination of the Median Lethal Dose and its Error with a Small Computer. Journal Toxic Environ Health 797-809 (1977).

**Test Atmosphere / Chamber Description:** The exposure atmosphere (aerosol) was generated by a Venturi Aspirator which aspirated the ground and sifted test material from a coupled motorized revolving disc delivery system and then spraying the resulting aerosol directly into the exposure chamber. Air flow was maintained at a rate of 29.3 air changes per hour and was sufficient to ensure an oxygen content of at least 19% of the exposure atmosphere. A 500 L nose-only stainless steel, dynamic flow inhalation chamber was utilized in the study. Polycarbonate tubes were inserted into individual ports. The animals were held in the capped tubes. The test material was introduced through the opening in the top of the chamber and air flow exited the chamber to the bottom.

| **Gravimetric Conc. (mg/L):** | **0.57** | **1.14** | **2.20** |
|---|---|---|---|
| **Chamber Volume (L):** | **500** | **500** | **500** |
| **Total Airflow (L/min):** | **244** | **244** | **244** |
| **Temperature** | **23.7-25.3°C** | **22.8-24.5°C** | **23.1-25.9°C** |
| **Relative Humidity** | **58.1-65.6%** | **50.5-58.1%** | **58.4-66.2%** |
| **Time to equilibrium:** | **9 minutes** | **9 minutes** | **9 minutes** |

**Test atmosphere concentration:** During exposure, samples were collected from the breathing zone of the animals twice per hour during exposure and nominally at the end of the exposure. The gravimetric concentration was determined by passing a known volume of exposure air through a pre-weighed filter and dividing the amount of test material deposited on the filter by the volume of air that passed through the filter. The nominal concentration was determined by dividing the loss in weight of the test material after the exposure by the total volume of air that passed through the chamber.

**Particle size determination:** Particle size for each exposure concentration was determined twice using a cascade impactor, at a rate of 13.2 L/minute for 26-60 seconds. The mass median aerodynamic diameter and particle size distributions were calculated by a computer program using probit analysis.

A. **Mortality:** One male exposed at 1.14 mg/L and one male exposed at 2.20 mg/L were found dead on day 1. One male exposed at 2.20 mg/L was found dead on day 2. One female exposed at 1.14 mg/L was found dead on day 3. One female exposed at 0.57 mg/L and one female exposed at 2.20 mg/L were found dead on day 4. All other animals survived the study.

B. **Clinical observations:** Piloerection and decreased activity were noted from all animals exposed at 0.57 mg/L upon removal from the chamber through day 1 with recovery by day 2. Piloerection, decreased activity, respiratory gurgle, and/or red liquid on muzzle were noted from the animals exposed at 1.14 or 2.20 mg/L. No individual animal data were provided, however, all survivors recovered by day 7. Three females in the 0.57 mg/L group lost weight during the first week, but all gained weight by the end of the study. All other survivors gained weight throughout the study.

C. **Gross necropsy:** The decedents had red liquid on muzzle, dark red swollen lungs, stomach/intestines full of gas, empty intestines, and/or red crust around mouth. Stomach full of gas was noted from two females in the 0.57 mg/L group. No observable abnormalities were noted in the other surviving animal at necropsy.

D. **Reviewer's conclusions**: This reviewer agrees with the study author's conclusion. Based on the observed $LD_{50}$ in females, Chlorothalonil TC is classified as EPA Toxicity Category III.

E. **Deficiencies:** None

**Reviewer:** Eugenia McAndrew
**Risk Manager (EPA):** RM 22

**Date:** June 14, 2011

**STUDY TYPE:** Primary Eye Irritation – Rabbit; OCSPP 870.2400; OECD 405

**TEST MATERIAL:** Chlorothalonil TC (99.3% Chlorothalonil; Lot No. JXA09092202; white crystals according to the study text and yellowish powder according to the certificate of analysis)

**CITATION:** Kuhn, J. (2010) Chlorothalonil TC – Acute Eye Irritation Study in Rabbits. Study Number 14092-10. Stillmeadow, Inc., 12852 Park One Drive, Sugar Land, TX 77478. October 4, 2010. MRID 48326609.

**SPONSOR:** Jiangsu Xinhe Agrochemical Co., Ltd., No. 19 Xingang Road, Economic Development Zone, Xinyi, Jiangsu Province, 221400, P.R. China

**EXECUTIVE SUMMARY:** In a primary eye irritation study (MRID 48326609), 100 mg of Chlorothalonil TC (99.3% Chlorothalonil; Lot No. JXA09092202; yellowish powder) was instilled as received into the conjunctival sac of the right eye of three female young adult New Zealand White albino rabbits (age: 13 weeks; source: Myrtle Rabbitry, Thompsons Station, TN). The untreated eye served as a control. The animals were observed for 72 hours and at 4, 7, and 10 days after treatment.

One of the original three animals dosed was found dead during the study. The death was not considered related to the test substance administration, and that animal was replaced. Corneal opacity was noted on one rabbit 24 and 48 hours after test material instillation with clearance by 72 hours. Iritis was not noted on any rabbit. Positive conjunctival irritation was noted on 1/3 rabbits one hour after test material instillation with clearance by day 10. Positive conjunctival irritation was noted on 2/3 rabbits 24 hours after test material instillation with clearance on one rabbit by 72 hours and on the other rabbit by day 7. The highest maximum mean total score was 19.3, recorded 24 and 48 hours after test material instillation.

**Based on the corneal involvement and irritation clearing in 8-21 days, Chlorothalonil TC is is classified as EPA Toxicity Category II for primary eye irritation.**

This study is classified as acceptable. It does satisfy the guideline requirements for a primary eye irritation study (OCSPP 870.2400; OECD 405) in the rabbit.

**COMPLIANCE:** Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

## RESULTS AND DISCUSSION:

| | Number "positive"/Number treated | | | | | | |
|---|---|---|---|---|---|---|---|
| | Hours | | | | Days | | |
| **Observations** | **1** | **24** | **48** | **72** | **4** | **7** | **10** |
| Corneal Opacity | 0/3 | 1/3 | 1/3 | 0/3 | 0/3 | 0/3 | 0/3 |
| Iritis | 0/3 | 0/3 | 0/3 | 0/3 | 0/3 | 0/3 | 0/3 |
| Conjunctivae: | | | | | | | |
| Redness* | 1/3 | 3/3 | 3/3 | 2/3 | 2/3 | 1/3 | 0/3 |
| Chemosis* | 1/3 | 2/3 | 2/3 | 1/3 | 0/3 | 0/3 | 0/3 |
| Discharge** | 1/3 | 1/3 | 1/3 | 0/3 | 0/3 | 0/3 | 0/3 |

* Score of 2 or more required to be considered "positive"
** Discharge is not a positive effect according to the grading scale

A. **Observations:** Corneal opacity was noted on one rabbit 24 and 48 hours after test material instillation with clearance by 72 hours. Iritis was not noted on any rabbit. Positive conjunctival irritation was noted on 1/3 rabbits one hour after test material instillation with clearance by day 10. Positive conjunctival irritation was noted on 2/3 rabbits 24 hours after test material instillation with clearance on one rabbit by 72 hours and on the other rabbit by day 7.

B. **Results:** The highest maximum mean total score was 19.3, recorded 24 and 48 hours after test material instillation.

C. **Reviewer's conclusions:** This reviewer agrees with the study author's conclusion. Chlorothalonil TC is classified as EPA Toxicity Category II.

D. **Deficiencies:** None

**Note:** This reviewer verified with the study author, Dr. Janice Kuhn of Stillmeadow, Inc., that the test substance was a powder (phone call on June 13, 2011).

**Reviewer:** Eugenia McAndrew
**Risk Manager (EPA):** RM 22

**Date:** June 14, 2011

**STUDY TYPE:** Primary Dermal Irritation – Rabbit; OCSPP 870.2500; OECD 404

**TEST MATERIAL:** Chlorothalonil TC (99.3% Chlorothalonil; Lot No. JXA09092202; white crystals according to the study text and yellowish powder according to the certificate of analysis)

**CITATION:** Kuhn, J. (2010) Chlorothalonil TC – Acute Dermal Irritation Study in Rabbits. Study Number 14093-10. Stillmeadow, Inc., 12852 Park One Drive, Sugar Land, TX 77478. August 19, 2010. MRID 48326610.

**SPONSOR:** Jiangsu Xinhe Agrochemical Co., Ltd., No. 19 Xingang Road, Economic Development Zone, Xinyi, Jiangsu Province, 221400, P.R. China

**EXECUTIVE SUMMARY:** In a primary dermal irritation study (MRID 48326610), two male and one female young adult New Zealand White albino rabbits (age: 14 weeks; source: Myrtle's Rabbitry, Thompsons Station, TN) were dermally exposed to 500 mg of Chlorothalonil TC (99.3% Chlorothalonil; Lot No. JXA09092202) moistened with 0.4 mL of deionized water for 4 hours on an area of the clipped dorsal skin (8 x 8 cm) that was covered with a 2.5 x 2.5 cm gauze patch. The patch and trunk were loosely wrapped with semi-permeable dressing and secured with strips of tape. The animals were observed and irritation was scored at 1, 24, 48, and 72 hours after patch removal.

No irritation was noted on any rabbit during the study.

**In this study, the formulation was non-irritating based on the Primary Irritation Index (PII) of 0.0. Chlorothalonil TC is classified as EPA Toxicity Category IV for primary dermal irritation.**

This study is classified as acceptable. It does satisfy the guideline requirements for a primary dermal irritation study (OCSPP 870.2500; OECD 404) in the rabbit.

**COMPLIANCE:** Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

## RESULTS AND DISCUSSION:

| Animal Number | Sex | Hours | | | |
|---|---|---|---|---|---|
| | | 1 | 24 | 48 | 72 |
| 5138 | M | 0/0[a] | 0/0 | 0/0 | 0/0 |
| 5140 | M | 0/0 | 0/0 | 0/0 | 0/0 |
| 5139 | F | 0/0 | 0/0 | 0/0 | 0/0 |
| **Severity of Irritation – Mean Score** | | 0.0 | 0.0 | 0.0 | 0.0 |

[a] Erythema/edema

**A. Observations:** No irritation was noted on any rabbit during the study.

**B. Results:** Chlorothalonil TC was not irritating. The Primary Irritation Index (PII) is 0.0.

**C. Reviewer's conclusions:** This reviewer agrees with the study author's conclusion. Chlorothalonil TC is classified as EPA Toxicity Category IV for primary skin irritation.

**D. Deficiencies:** None

**Reviewer:** Eugenia McAndrew
**Risk Manager (EPA):** RM 22

**Date:** June 14, 2011

**STUDY TYPE:** Dermal Sensitization – guinea pig; OCSPP 870.2600; OECD 406

**TEST MATERIAL:** Chlorothalonil TC (99.3% Chlorothalonil; Lot No. JXA09092202; white crystals according to the study text and yellowish powder according to the certificate of analysis)

**CITATION:** Kuhn, J. (2010) Chlorothalonil TC – Skin Sensitization Study in Guinea pigs. Study Number 14049-10. Stillmeadow, Inc., 12852 Park One Drive, Sugar Land, TX 77478. October 8, 2010. MRID 48326611.

**SPONSOR:** Jiangsu Xinhe Agrochemical Co., Ltd., No. 19 Xingang Road, Economic Development Zone, Xinyi, Jiangsu Province, 221400, P.R. China

**EXECUTIVE SUMMARY:** In a dermal sensitization study (MRID 48326611) with Chlorothalonil TC (99.3% Chlorothalonil; Lot No. JXA09092202), 15 male and 15 female young adult Hartley albino guinea pigs (age: approximately 8 weeks; body weight: males: 386-484 g; females: 346-424 g; source: Charles River Laboratories, Wilmington, MA) were tested using the Buehler Method. The test animals were induced with 400 mg test material moistened with 0.5 mL deionized water applied beneath a surgical gauze patch to the clipped back at the left front quadrant for six hours. The procedure was repeated once each week for three consecutive weeks. After a two week rest period, the animals were challenged with 400 mg test material moistened with 0.5 mL deionized water at a naive site. The naive control animals were treated with 400 mg of test material moistened with 0.5 mL deionized water under occlusion at challenge. Reactions were scored 24 and 48 hours after test material applications.

After three consecutive weekly inductions, no dermal reactions were noted from any animal after challenge.

**Based on the results of this study, Chlorothalonil TC was not a dermal sensitizer. The mean challenge scores were 0.0 for naive control and test animals at 24 and 48 hours.**

This study is classified as acceptable. It does satisfy the guideline requirements for a dermal sensitization study (OCSPP 870.2600; OECD 406) in the guinea pigs.

**COMPLIANCE:** Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

**PROCEDURE:**

A. **Induction**: The animals were induced and challenged according to the Buehler method. The backs of the animals were clipped one day prior to each treatment. For the induction, the 20 test animals (10 males and 10 females) were induced with 400 mg test material moistened with 0.5 mL deionized water applied beneath a 4 ply, 2.5 x 2.5 cm surgical gauze patch to the clipped back at the left front quadrant and secured with non-irritating adhesive tape. A strip of clear polyethylene film was placed over the patch and securely taped. After approximately six hours, the animals were removed from the restrainer and the coverings were removed. The induction was performed once each week for three weeks. Reactions were scored 24 and 48 hours after the first induction and 24 hours after the second and third inductions.

B. **Challenge**: After a two week rest period, the animals were challenged. The backs of the animals were clipped one day prior to challenge. The test animals were challenged with 400 mg test material moistened with 0.5 mL deionized water at a naive site (right rear quadrant) and secured with non-irritating adhesive tape. After six hours of exposure, reactions were scored 24 and 48 hours after exposure.

C. **Naive control:** The naive control animals were not treated during the induction phase. The backs of the animals were clipped one day prior to challenge. The naive control animals were challenged with 400 mg test material moistened with 0.5 mL deionized water. After six hour of exposure, reactions were scored 24 and 48 hours after exposure.

**RESULTS AND DISCUSSION:**

A. **Reactions and durations**: No dermal irritation was noted on any animal after the first induction. Very faint usually nonconfluent erythema and faint usually confluent erythema were noted on 9/20 and 5/20 test animals, respectively, 24 hours after the second induction. Very faint usually nonconfluent erythema, faint usually confluent erythema, and moderate erythema were noted on 1/20, 13/20, and 6/20 test animals, respectively, 24 hours after the third induction. No dermal irritation was noted on any test or naive control animal after challenge. The test material was not a dermal sensitizer.

B. **Positive control**: The report included the results of a positive control (alpha-hexylcinnamaldehyde) study conducted within six months of the current study; the results were appropriate.

C. **Reviewer's conclusion**: This reviewer agrees with the study author's conclusion and Chlorothalonil TC is not a dermal sensitizer.

D. **Deficiencies:** None

## ACUTE TOX ONE-LINERS:

1. **DP BARCODE:** DP385901
2. **PC CODE:** 081901
3. **CCURRENT DATE:** June 14, 2011
4. **TEST MATERIAL:** Chlorothalonil TC (99.3% Chlorothalonil; Lot No. JXA09092202; white crystals according to the study text and yellowish powder according to the certificate of analysis)

| Study/Species/Lab<br>Study # / Date | MRID | Results | Tox. Cat. | Core Grade |
|---|---|---|---|---|
| Acute oral toxicity/rat<br>Stillmeadow, Inc.<br>30510 / September 16, 2010 | 48326606 | $LD_{50}$ Females > 5000 mg/kg bw | IV | A |
| Acute dermal toxicity/rat<br>Stillmeadow, Inc.<br>14090-10/September 22, 2010 | 48326607 | $LD_{50}$ Males > 5050 mg/kg bw<br>$LD_{50}$ Females > 5050 mg/kg bw<br>$LD_{50}$ Combined > 5050 mg/kg bw | IV | A |
| Acute inhalation toxicity/rat<br>Stillmeadow, Inc.<br>14091-10/October 6, 2010 | 48326608 | $LC_{50}$ Males = 4.68 mg/L (95% confidence Limits 2.59-6.73 mg/L)<br>$LC_{50}$ Females = 1.88 mg/L (95% confidence Limits 1.59-2.12 mg/L)<br>$LC_{50}$ Combined = 2.32 mg/L (95% confidence Limits 1.86-2.75 mg/L) | III | A |
| Primary eye irritation/rabbit<br>Stillmeadow, Inc.<br>14092-10/October 4, 2010 | 48326609 | Corneal opacity was noted on one rabbit 24 and 48 hours after test material instillation with clearance by 72 hours. Iritis was not noted on any rabbit. Positive conjunctival irritation was noted on 1/3 rabbits one hour after test material instillation with clearance by day 10. Positive conjunctival irritation was noted on 2/3 rabbits 24 hours after test material instillation with clearance on one rabbit by 72 hours and on the other rabbit by day 7. The highest maximum mean total score was 19.3, recorded 24 and 48 hours after test material instillation. | II | A |
| Primary dermal irritation/rabbit<br>Stillmeadow, Inc.<br>14093-10/August 19, 2010 | 48326610 | Non-irritating; No irritation was noted on any rabbit during the study. The Primary Irritation Index (PII) is 0.0. | IV | A |
| Dermal sensitization/Guinea pig<br>Stillmeadow, Inc.<br>14094-10/October 8, 2010 | 48326611 | Not sensitizing | - | A |

Core Grade Key: A = Acceptable, S = Supplementary, U = Unacceptable, W = Waived