UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, DC 20460

APR _ 9 1990

OFFICE OF
PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM:

SUBJECT: CLEAN CROP LOW VOLATILE 2D-2DP

2-Ethylhexyl Ester of Dichlorophenoxyacetic acid and 2 Ethylhexyl Ester of 2-(2,4-dichlorophenoxy) Propionic Acid

007857

TO: JoAnn Miller
Mary Erumsele
Project Manager (23)
Pesticide Registration

FROM: Velma Charles-Shannon, Ph.D. V. Charles-Shannon 3/27/90
Toxicology Branch II, Section II
Health Effects Division (H7509C)

THRU: K. Clark Swentzel K. Clark Swentzel 3/27/90
Section II Head, Toxicology Branch II
Health Effects Division (H7509C)
and
Marcia Van Gemert, Ph.D. Marcia Van Gemert 3/27/90
Chief, Toxicology Branch/HFAS/HED (H7509C)

EPA ID NO.: 34704-607

PROJECT NO.: 0-0244

CASWELL NO.: 315

REGISTRANT: Platte Chemical Company

Data Evaluation Reports (DER) for the following acute toxicity studies are attached.

STUDY TITLES AND CONCLUSION

1. Acute Oral LD_{50} Study of DPD Ester in Male and Female Sprague-Dawley Rats

   LD_{50}=1578 mg/kg (combined sexes)
   LD_{50}=1434 mg/kg (males)
   LD_{50}=1732 mg/kg (females)

   Core-Classification-Guideline
   This study satisfies the guideline requirements (81-1) for an acute oral LD_{50} study

   Toxicity Category III

2. Acute Dermal LD_{50} of DPD Ester in New Zealand White Rabbits

   LD_{50} > 2000 mg/kg

   Core-Classification-Minimum
   This study satisfies the guideline requirements (81-2) for and acute dermal LD_{50} study

   Toxicity Category III

3. Acute Inhalation Limit Test of DPD Ester in Sprague-Dawley Rats

   Four-hour whole body inhalation exposure to a liquid droplet aerosol of DPD Ester at an average actual concentration of 2.3 mg/l based of 2,4-dichlorophenoxyacetic acid, produced mortality in 40% of the males and 60% of the females. Because of the mortality associated with this limit test, a lower level of 1.3 mg/l was run. No mortality in five male and five female Sprague-Dawley rats was noted at this lower concentration. The inhalation limit test protocol was amended to include one additional exposure level. The LC_{50} was not determined. The Agency does not recognize 2.3 mg/l as a limit test. The Registrant should conduct an acute LC_{50} inhalation study.

   Core-Classification-Supplementary
   This study does not satisfy the guideline requirements (81-3) for an acute inhalation study

   Toxicity Category-II

4. Acute Ocular Irritation in New Zealand Rabbits

Ocular administration of 0.1 ml of the DPD Ester resulted in conjunctival irritation in all New Zealand rabbits, one hour after administration of the test article. Conjunctival redness was exhibited by one rabbit 24 hours after exposure. At 48 hours, no ocular irritation was apparent. The maximum average score was 5.7 at one hour following dose administration.

Core-Classification-Minimum
This study satisfies the guideline requirements (81-4) for an acute ocular irritation study

Toxicity Category-III

5. Primary Dermal Irritation Study of DPD Ester in New Zealand White Rabbits

Following the test application, very slight to well defined erythema and very slight edema were indicated. Dermal irritation was not noted on days 7 or 10 of study . The dermal irritation score was determined to be 1.0 based on 2, 4, 48 and 72 hour reading.

Core-Classification-Minimum
This study satisfies the guideline requirements for (81-5) a primary dermal irritation study

Toxicity Category -III

6. Skin Sensitization Study in Guinea Pigs with DPD Ester

The results from a comparison between the incidence and severity indices for the first challenge test using 100% undiluted DPD Ester, were equivocal. A rechallenge test was deemed necessary due to dermal irritation folowing the 24 hour exposure period. The results of the rechallenge test at 0.5% (w/v) DPD Ester, did not reveal any meaningful differences between the incidence and severity indices for the test article and the naive control group. The results of the study indicate that the DPD Ester is not a sensitizer. The study is considered supplementary until recent results of a positive control for Hartley derived guinea pigs are submitted.

Core-Classification-Supplementary

This study does not satisfy the guideline requirements for (81-6) a skin sensitization study

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Toxicology Branch II, Section II (H7059C)
Secondary Reviewer: K. Clark Swentzel K Clark Swentzel 3/21/90
Head Section II, Toxicology Branch II (H7059C)

DATA EVALUATION REPORT

TOX CHEM NO. 315

007857

STUDY TYPE : Acute Inhalation LD_{50}

MRID NO. : 412090-03

TEST MATERIAL : 2-Ethylhexyl Ester of 2,4-Dichlorophenoxyacetic acid and 2-Ethylhexyl Ester of 2-(2,4-Dichlorophenoxy) Propionic Acid

SYNONYMS : DPD Ester

STUDY NUMBER : 89-19A

SPONSOR : Platte Chemical Company

PRODUCT NAME : Clean Crop Low Volatile 2D-2DP Herbicide

TESTING FACILITY: Food and Drug Research Laboratories
P. O. Box 107, Route 17C
Waverly, NY

TITLE OF REPORT: Acute Inhalation Limit test of DPD Ester in Sprague-Dawley Rats

AUTHORS: William M. Mahlburg

REPORT ISSUED: June 16, 1988

QUALITY ASSURANCE: A Quality Assurance statement was provided and signed by the QAU

CONCLUSIONS: A four-hour whole body inhalation exposure to a liquid droplet aerosol of DPD Ester at an average actual concentration of 2.3 mg/l based on 2,4-Dichlorophenoxyacetic acid produced mortality in 40% of males and in 60% of the

females. An additional level at an average actual concentration of 1.3 mg/l produced no mortality in five male and five female Sprague-Dawley Rats. The LC_{50} was not determined. The Agency does not recognize 2.3 mg/l as a limit test. This study is unacceptable and the Registrant should repeat the Acute Inhalation LC_{50} Test.

CLASSIFICATION: Supplementary

TOXICITY CATEGORY: II

A. MATERIALS:

1. TEST COMPOUND: 2-Ethylhexyl Ester of 2,4-Dichlorophenoxyacetic Acid and 2-Ethylhexyl Ester of 2-(2,4-Dichlorophenoxy) Propionic Acid

BATCH: Not reported

DESCRIPTION: The identity of the test material for this study was Clean Crop DPD Ester, EPA Reg. No. 39335-24-34704. The formula of DPD Ester and DPD Ester Brush Killer (EPA Reg. No. 34704-607) as stated are virtually identical, the only difference being the active ingredient as defined below:

Active Ingredient 34704-607	
2-Ethylhexyl Ester of 2,4-Dichlorophenoxyacetic acid	33.18%
2-Ethylhexyl Ester of 2-(2,4-Dichlorophenoxy) Propionic Acid	32.52%

Active Ingredient 39335-24-34704	
2-Ethylhexyl Ester of 2,4-Dichlorophenoxyacetic acid	33.2%
2-Ethylhexyl Ester of 2-(2,4-Dichlorophenoxy Propionic Acid	32.1%

PURITY: Refer to the above statement

2. **TEST ANIMALS:**

SPECIES: Rat

STRAIN: Sprague-Dawley Rats

AGE: 8 weeks

WEIGHT: Not reported

SOURCE: Charles-River Breeding Laboratories Inc., Wilmington, Massachusetts

STUDY DESIGN: An acute inhalation test was conducted consisting of twenty male and female (two groups of five male and female) rats. The test animals were exposed, whole body, to liquid droplet aerosol generated from DPD Ester. The average actual concentration was based on the active component 2,4-Dichlorophenoxyacetic acid (2,4-D). An exposure period consisted of 260 minutes of average actual concentration of 2.3 mg/l (Group 1), or 1.3 mg/l (Group 2) of active the component of 2,4-D. At 260 minutes, the test system reached 99% equilibrium. The animals were allowed to remain in the chamber for twenty minutes following exposure at the designated air flow rate of 31.2 liters/minute using clean ambient air only.

Food and water were not made available during the whole body exposure period. Food and fresh water were supplied ad libitum during the acclimation and post-exposure phase of this study.

Animals were observed frequently during the exposure period, three times on day 1, after exposure, and twice daily following this period for the 14-day-post exposure period. Animals were sacrificed with CO_2 gas on day 15 of the study. Animals were subjected to a gross necropsy and major visceral organs, body cavities and carcass were examined for lesions and abnormalities. Periodically during exposure, animal observations were made for pharmacotoxic signs and mortality subsequent to exposure on day one, and twice daily thereafter for 14 post-exposure days. Animal body weights were recorded on days 1 prior to exposure and on days 4, 8, 15 or at death.

The test article was atomized by means of a pressure spray set-up (1/4JSS atomizer

with 2050SS fluid cap and 67-6-20-70-316SS air cap, spraying stystem) attached to a Harvard Syringe Pump. Delivery was made into the exposure chamber using an air inlet port, allowing the test article and incoming air to mix evenly within the chamber at the top before being drawn down over the animals.

In the analysis procedure for particle size, the mass median aerodynamic diameter (MMAD), geometric standard deviation, and percent of the sample (by weight) comprised of particles ≤ 12um in size, were determined. For Group 1 (2.3 mg/l) the mass median aerodynamic diameter (MMAD, um) was 7.6 micons, the geometric standard deviation was 2.9, and the estimated percent of collected particle ≤ 12 um was 66.0. For Group 2, (1.3 mg/l) the mass media aerodynamic diameter (MMAD, um) was 6.4 microns, the geometric standard deviation was 3.0 and the estimated percent of collected particles ≤ 12 um was 72.0.

RESULTS:

The report states that the most frequent observations noted among surviving animals were labored breathing, decreased activity, ataxia, wet coat and salivation. Rales, hair loss, nasal discharge, wet abdomen due to incontinence, animal prostrate, and swollen eyelids were also observed.

More animals in both test groups had a greater body weight loss between study day 8 and 4 than between study day 4 and 1. It is noted that this observation in conjunction with the time of mortality could be an indicator of delayed toxicity. Since the surviving animals exhibited a final body weight greater than their initial body weight, the weight loss was considered transient.

Gross Pathology, Group 1 (2.3 mg/L)

Nasal Passages-Two males and three females were noted as having red nasal passages.

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Lungs-Two males and three females were noted as having bright red lungs

Liver-Pale areas on the liver were noted in one male and three females

Stomach-Glandular mucosa dark red in two males and three females. One male and one female were noted to have the absence of rugae. One male was noted as having a thin fore-stomach wall

Intestine-One female was noted as having a red substance in the intestines

Kidneys-Fluid filled right kidney and dilated pelvis was noted in one female

Gross Pathology, Group 2, (1.3 mg/L)

No abnormalities or lesions were noted for Group 2

Total mortality for the two exposure consentrations is summarized below:

MORTALITY %

Exposure Concentration mg/L	Mortality % Males	Females	Combined
2.3	40	60	50
1.3	0	0	0

CONCLUSIONS:

An average actual concentration of 2.3 mg/L based on the active component of 2,4-Dicholorophenoxyacetic acid (2,4-D) for four consecutive hours produced mortality in 40% of the males and 60% of the females in Sprague-Dawley rats. Because of the occurance of mortality during this test, one lower level concentration was run. Five male and five female Sprague-Dawley rats exposed to an average actual concentration of 1.3 mg/l for four (4)

consecutive hours. There were no indications of mortality at this lower doses

To facillitate the reduced use of animals during toxicity testing, the Agency has suggested the use of a limit test (when such a test seems appropriate). However, if deaths are seen during the limit test, a full LC_{50} test as described in the Guidelines is still required.

The acute inhalation test protocol, which was used by this testing facility, was ammended. The protocol for the limit test at 2 mg/l states that if the LC_{50} is expected to be between 2 and 5 mg/l, a single exposure of 2 mg/l will be administered to 10 rats; 5 males and 5 females. If no test compound-related deaths occur during the 14-day post exposure observation period, additional testing will not be performed. If any deaths occur which are considered related to the test compound, at least 2 additional appropriately spaced dose levels will be administered. This study included only one additional exposure level and therefore does not fulfill the requirements. The Agency does not recognize 2.3 mg/l as a limit test. The Registrant should conduct an acute inhalation LC_{50} study on the test material.

The study also fails to state the percent of particles which are less than 1 micron. If the mass median aerodynamic diameter reported in a study is larger than 1 um, the study can be accepted if at least 25% of the particles are 1 um or less. (Stan Gross memo, Comments on Standard Evaluation Procedure, Inhalation Toxicology Testing, SEP/Inhalation, 4/18/89). Data should be submitted specifying the percentage of particles which are less than 1 um.

CORE-CLASSIFICATION: Supplementary

TOXICITY CATEGORY: II

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FDRL Study No. 88.3505.013

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Acute Inhalation Limit Test of "DPD Ester" in Sprague-Dawley Rats

Summary of Body Weight Data[a]

Sex and Exposure Level (mg/L)	Body Weight (g) on Day 1	4	8	15	Body Weight Gain 1-4	4-8	8-15
Males							
2.3	240 ±4	246 ±26 (4)	250 ±8 (3)	282 ±12 (3)	+6 23 (4)	-9 ±11 (3)	+31 ±6 (3)
1.3	243 ±2	248 ±6	262 ±16	306 ±17	+5 ±6	+13 ±15	+44 ±5
Females							
2.3	217 ±2	220 ±11 (3)	217 -- (2)	228 -- (2)	+2 ±10 (3)	-9 -- (2)	+11 -- (2)
1.3	218 ±2	222 ±7	218 ±5	223 ±2	+4 ±6	-4 ±6	+5 ±5

[a] Values are group mean ± standard deviation for five observations per sex unless otherwise noted in ( ).
-- Standard deviation not calculated; insufficient number of observations.

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Head Section II, Toxicology Branch II (H7059C)

DATA EVALUATION REPORT

TOX CHEM NO. 315

STUDY TYPE:	Aute Oral LD50 Rat
MRID NO. :	412090-01
TEST MATERIAL :	2-Ethylhexyl Ester of Dichlorophenoxyacetic acid and 2-Ethylhexyl Ester of 2-(2,4-Dichlorophenoxy) Propionic Acid
SYNONYMS :	DPD Ester
STUDY NUMBER :	89-19A
SPONSOR :	Platte Chemical Company
PRODUCT NAME :	Clean Crop Low Volatile 2D-EDP Herbicide
TESTING FACILITY:	Food and Drug Research Laboratories P.O. Box 107, Route 17C Waverly, New York
TITLE OF REPORT:	Acute Oral Toxicity of DPD Ester in Sprague-Dawley Rats
AUTHORS:	William Mahlbury
REPORT ISSUED:	March 30, 1988
QUALITY ASSURANCE:	Quality Assurance statement provided and signed by QAU

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CONCLUSIONS: The oral LD_{50} for the combined sexes of the Sprague-Dawley Rat was determined to be 1578 mg/kg body weight with a 95% confidence interval of 1324 to 1823 mg/kg.

CORE-CLASSIFICATION: Guideline

TOXICITY CATEGORY: III

A. MATERIALS:

1. TEST COMPOUND: 2-Ethylhexyl Ester of Dichlorophenoxyacetic acid and 2-Ethylhexyl Ester of 2-(2,4-Dichlorophenoxyl) Propionic Acid

BATCH: 04LG88567

ID No: 88-0121

DESCRIPTION: The identity of the test material for this study was Clean Crop DPD Ester, EPA Reg. No. 39335-24-34704. The formula of DPD Ester and DPD Brush Killer (EPA Reg. N. 34704-607) as stated, are virtually identical, the only difference being the active ingredient declaration as defined below:

Active Ingredient	34704-607
2-Ethylhexyl Ester of 2,4-Dichlorophenoxyacetic Acid	33.18%
2-Ethylhexyl Ester of 2-(2,4-Dichlorophenoxy) Propionic Acid	32.52%

Active Ingredient	39335-24-34704
2-Ethylhexyl Ester of 2,4-Dichlorophenoxyacetic Acid	33.2%
2-Ethylhexyl Ester of 2-(2,4-Dichlorophenoxy) Propionic Acid	32.1%

PURITY: Refer to above statement

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2. TEST ANIMALS:

SPECIES: Rat

STRAIN: Sprague-Dawley

AGE: Not provided

WEIGHT: 216-319 grams

SOURCE: Charles River Breeding Laboratories, Inc., Wilmington, Ma.

STUDY DESIGN: Twenty male and 20 female Sprague-Dawley rats per dose group were, by gavage, administered single doses of 1000, 1500, 2000, and 3000 mg/kg body weight. Animals were observed three times on the day of dose administration and twice daily following this period for pharmacotoxic signs and mortality. Body weights were recorded prior to dose administration and on study days, 1, 4, 8, and at the termination of study on day 15, or at the death of the animal. All animals were subjected to gross necropsy. External body surfaces, orifices, major visceral organs and body cavities were examined.

RESULTS: One male exhibited ataxia on day one in the 1000 mg/kg group. Other pharmacotoxic signs observed in animals were ataxia, bloated appearance, blood in the stools, dark material around the eyes, decreased activity, diarrhea, labored and shallow breathing, rigid limbs and apparent urinary incontinence. At 1000 mg/kg dose level, male mean weights increased at all time intervals. Female mean body weights increased from days 1 to 4, remained the same from day 4 to 8 and increased from day 8 to 15. At 1500 mg/kg dose level, the surviving male and female had increased body weight throughout the study. At 2000 mg/kg, the male exhibiting weight loss, died while the remaining male gained weight throughout the study. The one female which survived gained weight from day 1 to 4, lost from day 4 to 8 and gained from day 8 to 15.

At necropsy, macroscopic findings included the follcwing:

gastrointestinal tract-presence of red/black substance

lungs-dark bright red in coloration

forestomach-thin walled

mucosa-glandular in appearance, red and black and black areas present, and the absence of rugae

Under the conditions of this study, the LD_{50} for the DPD Ester in Sprague-Dawley is 1578 mg/kg body weight with a 95% confidence interval of 1324 to 1823 mg/kg. The LD50 for male rats was calculated to be 1434 mg/kg with a 95% confidence interval of 929 to 1816 mg/kg and the LD50 for female was calculated to be 1732 mg/kg body weight with a 95% confidence interval of 1066 to 2817 mg/kg.

Mortality and Results of LD_{50} Calculations

	Number of Deaths		
Dose Level (mg/kg	Male	Female	Combined
1000	0	0	0
1500	4	1	5
2000	4	4	8
3000	5	5	10

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Acute Oral Toxicity Study
DPD Ester
In Sprague-Dawley Rats

Results of LD_{50} calculations were as follows:

	Males	Females	Combined
LD50 (mg/kg)	1434	1732	1578
95% Confidence Interval	929-1816	1065-2817	1324-1823
Slope	9.3	13.7	10.1

CONCLUSION: The oral LD_{50} for the DPD Ester in Sprague-Dawley rats was determined to be 1578 mg/kg body weight with a 95% confidence interval of 1324 to 1823 mg/kg.

CORE CLASSIFICATION: Guideline

TOXICITY CATEGORY: III

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Head Section II, Toxicology Branch II (H7059C)

DATA EVALUATION REPORT

TOX CHEM NO. 315

STUDY TYPE :	Acute Dermal LD50
MRID NO. :	412090-02
TEST MATERIAL :	2-Ethylhexyl Ester of Dichlorophenoxyacetic acid and 2-Ethylhexyl Ester of 2-(2,4-Dichlorophenoxy) Propionic Acid
SYNONYMS :	DPD Ester
STUDY NUMBER :	89-19A
SPONSOR :	Platte Chemical Company
PRODUCT NAME :	Clean Crop Low Volatile 2D-2DP Herbicide
TESTING FACILITY:	Food Research Laboratories P. O. Box 107, Route 17C Waverly, NY
TITLE OF REPORT:	Acute Dermal Toxicity Study of DPD Ester in New Zealand White Rabbits
AUTHORS:	William Mahlbury
REPORT ISSUED:	March 31, 1988
QUALITY ASSURANCE:	Quality Assurance statement was issued and signed by QAU
CONCLUSIONS:	Under the conditions of this study, the acute dermal LD50 of DPD Ester is considered to be greater than 2000 mg/kg body weight.

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CORE-CLASSIFICATION: Minimum

TOXICITY CATEGORY: III

A. MATERIALS:

1. **TEST COMPOUND:** 2-Ethylhexyl Ester of 2,4-Dichlorophenoxy acetic acid and 2-Ethylhexyl of 2-(2,4-Dichlorophenoxy) Propionic acid

BATCH: Lot # 04LG88567

I.D. No.: 88-0121

DESCRIPTION: The identity of the test material for this study was Clean Crop DPD Ester, EPA Reg. No. 39335-24-34704. The formula of DPD Ester and DPD Ester Brush Killer (EPA Reg. No. 34704-607 as stated are viturally identical, the only difference being the active ingredient declaration as defined below:

Active Ingredient	
2-Ethylhexyl Ester of 2,4-Dichlorophenoxyacetic Acid	33.18%
2-Ethylhexyl Ester of 2-(2,4-Dichlorophenoxy) Propionic Acid	32.52

Active Ingredient	39335-24-34704
2-Ethylhexyl Ester of 2,4-Dichlorophenoxyacetic Acid	33.2%
2-Ethylhexyl Ester of 2-(2,4-Dichlorophenoxy) Propionic Acid	32.1%

PURITY: Refer to above statement

2. **TEST ANIMALS:**

SPECIES: Rabbits

STRAIN: New Zealand White

AGE: Not reported

WEIGHT: 2.0-3.0 kilograms

SOURCE: Ace Animals Inc., Boyertown, Pa.

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STUDY DESIGN: The backs of five male and five female rabbits were clipped the day prior to dose administration. The applied dose level was 2000 mg/kg b.w. Gauze was used to cover the test site and which was also occluded with a layer of plastic wrap and a stockinette sleeve. Following a period of 24 hours, the binders were removed and gauze used to remove non-absorbed test article. The appropriate amount of test material applied per unit of exposed skin was calculated to be 33.4 mg/cm^2. Pharmacotoxic signs as well as mortality were monitored for three times on day one of administration, and twice daily following this time period. Body weights were recorded on days 4, 8 at the termination of the study on day 15. Following euthanasia by intracardiac injection of sodium pentobarbital, gross necropsy was performed on all animals. External body surfaces, orifices, major visceral organs and body cavities as well as the carcass were examined.

RESULTS: All animals survived the duration of the study. Anorexia was observed in 3 female rabbits. Soft stools were found in females and diarrhea was observed in some male and female rabbits. All other rabbits appeared normal. Mean body weight increase were noted for both male and female at all time intervals. No abnormalities were noted in the male rabbit at necropsy. Green fluid was found in the stomach of two female rabbits while another female rabbit exhibited a gel-like substance in the large intestine.

Under the conditions of this study, the LD_{50} was determined to be greater than 2000 mg/kg for the test material.

Acute Dermal Toxicity Study of DPD Ester In New Zealand White Rabbits

Sex	Group Mean Body Weight (kg) ± Standard Deviation on Study Day 1	4	8	15	Body Wt. Change 4	8	15
Males	2.17 ±0.09	2.28 ±0.10	2.35 ±0.12	2.51 ±0.12	+.11 ±.08	+.07 ±.08	+.16 ±.09
Females	2.18 ±0.12	2.19 ±0.09	2.32 ±0.08	2.33 ±0.13	+.01 ±.04	+.14 ±.03	+.01 ±.12

CONCLUSIONS: The dermal LD50 for the DPD Ester in New Zealand White Rabbits was determined to be >2000 mg/kg. All test animals, male and female survived until day 15 of study.

CORE CLASSIFICATION: Minimum

TOXICITY CATEGORY: III

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Head Section II, Toxicology Branch II (H7059C)

DATA EVALUATION REPORT

TOX CHEM NO.: 315

STUDY TYPE :	Acute Ocular Irritation
MRID NO. :	412090-04
TEST MATERIAL :	2-Ethylhexyl Ester of Dichlorophenoxyacetic acid and 2-Ethylhexyl Ester of 2-(2,4-Dichlorophenoxy) Propionic Acid
SYNONYMS :	DPD Ester
STUDY NUMBER :	89-19A
SPONSOR :	Platte Chemical Company
PRODUCT NAME :	Clean Crop Low Volatile 2D-2DP Herbicide
TESTING FACILITY:	Food and Drug Research Laboratories P.O. Box 107, Route 17C Waverly, NY
TITLE OF REPORT:	Primary Eye Irritation Study of DPD Ester in New Zealand White Rabbits
AUTHORS:	William M. Mahlburg
REPORT ISSUED:	March 20, 1988
QUALITY ASSURANCE:	Quality assurance statement provided and signed by QAU
CONCLUSIONS:	Results of the primary eye irritation study of DPD Ester in New Zealand White Rabbits indicate conjunctival irritation in all rabbits one hour after instillation. Ocular irritation was not present at 48 hours. Only one rabbit exhibited conjunctival redness 24 hours

after the dose was administrated. One hour after dose administration, a maximum average score of 5.7 was obtained.

CORE-CLASSIFICATION: Minimum

TOXICITY CATEGORY: III

A. MATERIALS:

1. **TEST COMPOUND:** 2-Ethylhexyl Ester of 2,4-Dichlorophenoxyacetic Acid and 2-Ethylhexyl Ester of 2-(2,4-Dichlorophenoxy) Propionic Acid

BATCH: 04LG88567

ID. NO. 88-0121

DESCRIPTION: The identity of the test material for this study was Clean Crop DPD Ester, EPA Reg. No 39335-24-3470. The formula of DPD and DPD Ester Brush Killer (EPA Reg. No. 34704-607) are virtually identical, the only difference being the active ingredient declaration as defined below:

Active Ingredient	34704-607
2-Ethylhexyl Ester of 2,4-Dichlorophenoxyacetic Acid	33.18%
2-Ethylhexyl Ester of 2-(2,4-Dichlorophenoxy) Propionic Acid	32.52%

Active Ingredient	39335-24-34704
2-Ethylhexyl Ester of 2,4-Dichlorophenoxyacetic Acid	33.2%
2-Ethylhexyl Ester of 2-(2,4-Dichlorophenoxy) Propicnic Acid	32.1%

PURITY: Refer to the above statement

2. **TEST ANIMALS:**

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SPECIES:	Rabbits
STRAIN:	New Zealand White Rabbits
AGE:	Young adults
WEIGHT:	2.0-3.0 kilograms
SOURCE:	Ace Animals Inc. Boyertown, Pa.

STUDY DESIGN: The eyes of the animals were examined prior to treatment to determine preexisting corneal damage of conjunctival inflammation. Rabbit ration and fresh tap water was supplied ad. libitum. Instilled into the conjunctival sac of one eye of each rabbit was 0.1 ml of the test article. The lids were held together for a second and then released. Primary eye irritation was evaluated at 1, 24, 48 and 72 hours after dose administration. Scoring was done by the Draize method with separate scoring of the cornea, iris and conjunctiva.

RESULTS: The test article caused conjunctival irritation in all rabbits (6 of 6) one hour after instillation of the test article. At 24 hours after administration, only one rabbit exhibited conjunctival redness. Ocular irritation was not noted 48 hours after examination. After one hour of dose administration, the maximum average score was 5.7.

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Primary Eye Irritation Study of
DPD Ester
In New Zeland White Rabbits

Summary of Primary Eye Irritation Scores

Number of Animals Dosed	Mean Score ± Standard Deviation After Test Article Instillation			
	1hr	24hr	48hr	72hr
6	5.7 ± 2.3	0.3 ± 0.8	0	0

CONCLUSIONS: The results of the primary eye irritation study indicated that the DPD Ester caused conjunctival irritation in all rabbits (6 of 6) one hour after dose administration. No ocular irritation was noted at the 48 hour examination. The maximum average score was 5.7 one hour after the dose was administered.

CORE CLASSIFICATION: Minimum

TOXICITY CATEGORY: III

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Head Section II, Toxicology Branch II (H7059C)

DATA EVALUATION REPORT

TOX CHEM NO. 315

007857

STUDY TYPE :	Acute Dermal Irritation
MRID NO. :	412090-05
TEST MATERIAL :	2-Ethylhexyl Ester Dichlorophenoxyacetic and 2-Ethylhexyl Ester of 2-(2,4-Dichlorophenoxy) Propionic Acid
SYNONYMS :	DPD Ester
STUDY NUMBER :	89-19A
SPONSOR :	Platte Chemical Company
PRODUCT NAME :	Clean Crop Low Volatile 2D-2EP Herbicide
TESTING FACILITY:	Food and Drug Research Laboratories P.O. Box 107, Route 17C Waverly, NY
TITLE OF REPORT:	Primary Dermal Irritation Study of DPD Ester in New Zealand White Rabbits
AUTHORS:	William Mahlburg
REPORT ISSUED:	March 27, 1988
QUALITY ASSURANCE:	Quality Assurance statement was provided and signed by QAU
CONCLUSIONS:	Following the test application, very slight to well defined erythema and very slight edema were indicated. Dermal irritation was not noted on days 7 or 10 of study following application of test article. The dermal irritation score was determined to be 1.0 based on 3, 4, 48 and 72 hours reading.

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CORE-CLASSIFICATION: Minimum

TOXICITY CATEGORY: III

TOXICITY CATEGORY:

A. MATERIALS:

1. TEST COMPOUND:

BATCH: 04LG88567

ID. No.: 88-0121

DESCRIPTION: The identity of the test material for this was Clean Crop DPD Ester, EPA Reg. No 3935-24-34704. The formula of DPD Ester and DPD Ester Brush Killer (EPA Reg. No. 34704-607) as stated, are virtually identical, the only difference being the active ingredient declaration as defined below:

Active Ingredient	34704-607
2-Ethylhexyl Ester of 2,4-Dichlorophenoxyacetic Acid	33.18%
2-Ethylhexyl Ester of 2-(2,4-Dichlorophenoxy) Propionic Acid	32.52%

Active Ingredient	39335-24-34704
2-Ethylhexyl Ester of 2,4-Dichlorophenoxyacetic Acid	33.2%
2-Ethylhexyl Ester of 2-(2,4-Dichlorophenoxy) Propionic Acid	32.1%

PURITY: Refer to the above statement

2. **TEST ANIMALS:**

SPECIES: Rabbits

STRAIN: New Zealand White

AGE: Not reported

WEIGHT: 2.0-3.0 kilograms

SOURCE: Ace Animal Inc., Boyertown, Pa.

after the dose was administrated. One hour after dose administration, a maximum average score of 5.7 was obtained.

CORE-CLASSIFICATION: Minimum

TOXICITY CATEGORY: III

A. MATERIALS:

1. **TEST COMPOUND:** 2-Ethylhexyl Ester of 2,4-Dichlorophenoxyacetic Acid and 2-Ethylhexyl Ester of 2-(2,4-Dichlorophenoxy) Propionic Acid

BATCH: 04LG88567

ID. NO. 88-0121

DESCRIPTION: The identity of the test material for this study was Clean Crop DPD Ester, EPA Reg. No 39335-24-3470. The formula of DPD and DPD Ester Brush Killer (EPA Reg. No. 34704-607) are virtually identical, the only difference being the active ingredient declaration as defined below:

Active Ingredient	34704-607
2-Ethylhexyl Ester of 2,4-Dichlorophenoxyacetic Acid	33.18%
2-Ethylhexyl Ester of 2-(2,4-Dichlorophenoxy) Propionic Acid	32.52%

Active Ingredient	39335-24-34704
2-Ethylhexyl Ester of 2,4-Dichlorophenoxyacetic Acid	33.2%
2-Ethylhexyl Ester of 2-(2,4-Dichlorophenoxy) Propionic Acid	32.1%

PURITY: Refer to the above statement

2. **TEST ANIMALS:**

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SPECIES:	Rabbits
STRAIN:	New Zealand White Rabbits
AGE:	Young adults
WEIGHT:	2.0-3.0 kilograms
SOURCE:	Ace Animals Inc. Boyertown, Pa.

STUDY DESIGN: The eyes of the animals were examined prior to treatment to determine preexisting corneal damage of conjunctival inflammation. Rabbit ration and fresh tap water was supplied ad. libitum. Instilled into the conjunctival sac of one eye of each rabbit was 0.1 ml of the test article. The lids were held together for a second and then released. Primary eye irritation was evaluated at 1, 24, 48 and 72 hours after dose administration. Scoring was done by the Draize method with separate scoring of the cornea, iris and conjunctiva.

RESULTS: The test article caused conjunctival irritation in all rabbits (6 of 6) one hour after instillation of the test article. At 24 hours after administration, only one rabbit exhibited conjunctival redness. Ocular irritation was not noted 48 hours after examination. After one hour of dose administration, the maximum average score was 5.7.

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Primary Eye Irritation Study of
DPD Ester
In New Zeland White Rabbits

Summary of Primary Eye Irritation Scores

Number of Animals Dosed	Mean Score ± Standard Deviation After Test Article Instillation			
	1hr	24hr	48hr	72hr
6	5.7 ± 2.3	0.3 ± 0.8	0	0

CONCLUSIONS: The results of the primary eye irritation study indicated that the DPD Ester caused conjunctival irritation in all rabbits (6 of 6) one hour after dose administration. No ocular irritation was noted at the 48 hour examination. The maximum average score was 5.7 one hour after the dose was administered.

CORE CLASSIFICATION: Minimum

TOXICITY CATEGORY: III

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Reviewed By: Velma Charles-Shannon, Ph.D. Velma Charles-Shannon 3/27/9.
Toxicology Branch II, Section II (H7059C)
Secondary Reviewer: K. Clark Swentzel K Clark Swentzel 3/27/90
Head Section II, Toxicology Branch II (H7059C)

DATA EVALUATION REPORT

TOX CHEM NO. 315

STUDY TYPE :	Skin Sensitization
MRID NO. :	412090-06
TEST MATERIAL :	2-Ethylhexyl Ester of 2,4-Dichlorophenoxyacetic Acid and 2-Ethylhexyl Ester of 2-(2,4-Dichlorophenoxy) Propionic Acid
SYNONYMS :	DPD Ester
STUDY NUMBER :	89-19A
SPONSOR :	Platte Chemical Company
PRODUCT NAME :	Clean Crop Low Volatile 2D-2DP Herbicide
TESTING FACILITY:	Food and Drug Research Laboratories
TITLE OF REPORT:	Dermal Sensitization Study in Guinea Pigs with DPD Ester
AUTHORS:	William Mahlbury
REPORT ISSUED:	April 20, 1988
QUALITY ASSURANCE:	Quality Assurance statement provided and signed by QAU

CONCLUSIONS: The results from a comparison between the incidence and severity indices for the first challenge test were equivocal. A rechallenge test was necessary due to dermal irritation following the 24 hour exposure period. The results of the rechallenge test at 0.5% (w/v) DPD Ester, did not reveal any meaningful differences between the incidence and severity indices for the test article and the naive control group. The study is considered

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supplementary until recent results of positive control for the Hartley derived guinea pig are submitted.

The results of the dermal sensitization study indicate that the DPD Ester is not a sensitizer when exposed to 0.5% (w/v) of DPD Ester in distilled water.

CORE-CLASSIFICATION: Supplementary

A. MATERIALS:

1. TEST CCMPOUND: 2-Ethylhexyl Ester of 2,4-Dichlorophenoxyacetic Acid and 2-Ethylhexyl Ester of 2-(2,4-Dichlorophenoxy) Propionic Acid

BATCH: Lot# 04LG88567

DESCRIPTION: The identity of the test material for this study was Clean Crop DPD Ester, EPA Reg. No. 39995-24-34704. The formula of DPD Ester and DPD Brush Killer (EPA Reg. No. 34704-607) as stated, are virtually identical, the only difference being the active ingredient declaration as defined below:

Active Ingredient	34704-607
2-Ethylhexyl Ester of 2,4-Dichlorophenoxyacetic Acid	33.18%
2-Ethylhexyl Ester of 2-(2,4-Dichlorophenoxy) Propionic Acid	32.52%

Active Ingredient	39335-24-34704
2-Ethylhexyl Ester of 2,4-Dichlorophenoxyacetic Acid	33.2%
2-Ethylhexyl Ester of 2-(2,4-Dichlorophenoxy) Propionic Acid	32.1%

PURITY: Refer to the above statement

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2. TEST ANIMALS:

SPECIES: Guinea Pig

STRAIN: Hartley derived albino

AGE:
4-12 weeks

WEIGHT: 300-500 grams

SOURCE: Charles River Breeding Laboratories, Inc, Wilmington, Ma.

STUDY DESIGN: Dermal contact sensitization was evaluated using the modified Buehler (Buehler, E.V., 1975) test method. Three times a week, five male and five female guinea pigs were exposed topically for six hours to 0.5 ml of test material. Following a period of 4 weeks rest, the induced test animals and 4 naive control animals were challenged to 0.5 ml of test material. The DPD Ester was applied undiluted, 100% for challenge application I and applied as 0.5% (w/v) solution of DPD Ester in distilled water for challenge application II. A vehicle control of distilled water was administered for challenge application II to test animals and to naive controls. The backs of the animals were shaved and 0.5 ml of the test article was applied. The backs were then covered with gauze patch on days 1, 3, 6, 8, 10, 13, 15, and 17 and 20.

The challenge dose application was made on days 34 and 41 for the undiluted test article of (100%) and on days 34 and 41 for the 0.5% (w/v) in distilled water. The topical inductions were performed three times a week for three weeks for a total of 9 applications. Three different sites were used for the first week and the same sites were used for weeks 2 and 3. The test article and vehicle control were administered for the challenge application(s) on separate dorsal virgin skin sites. These sites were shaved on day one, prior to application. The application sites were evaluated for irritation following each application.

For the induction phase, patches were secured in place for six hours and 24 hours for the challenge phase. After the removal of the patches, clear gauze was used to remove any remaining material following the exposure period. At 24 and 48 hours, post induction, application sites were examined for erythema. Following the challenge, application sites were examined for erythema at 26 and 48 hours.

The Buehler grading scale was used to determine the dermal irritation score. Animals were observed daily for pharmacotoxic signs and mortality. Mortality checks were done daily at least five hours apart. Body weights were taken before exposure on day 1 of the study and at the termination of the study, prior to sacrifice. Animals were sacrificed with CO_2 gas and the results of the challenge application was reported in terms of the incidence and severity of the reactions.

RESULTS:

Throughout the study, all animals appeared normal and showed weight gain. During induction, dermal irritation scores of individual animals were 0 (no reactions) to 1 (faint erythema) following the test article application. Dryness characterized one test site following induction at application 9.

The incidence and severity indices data for the first test article challenge resulted in an incidence index of .80 at 26 hours for the test group and .50 for the control. The incidence index for the test group was .70 at 40 hours as compared to .25 for the naive control group.

The severity index for the test group at 26 hours was 1.6 as compared to .75 for the control. At 48 hours, the severity index was 1.3 for the test group and 0.5 for the naive controls.

A rechallenge was considered necessary due to dermal irritation following the 24 hour exposure period. For challenge II, both incidence and severity indices were 0 for the test and the naive control at 26 and

48 hours. At the lower concentration, comparison of the incidence and severity indices indicated no difference between the test and naive control group.

Challenge I and II: Incidence and severity indices for each group following Challenge I were as follows:

Incidence Index

	26 hrs	48 hrs
Test Group	0.80	0.70
Naive Control Group	0.50	0.25

Severity Index

	26 hrs	48 hrs
Test Group	1.6	1.3
Naive Control Group	0.75	0.5

Incidence and severity indices for the test and naive control groups following Challenge II were as follows:

Incidence Index

	26 hrs	48 hrs
Test Group	0	0
Naive Control Group	0	0

Severity Index

	26 hrs	48 hrs
Test Group	0	0
Naive Control Group	0	0

CONCLUSION: The DPD Ester is not considered to be a sensitizer under the conditions of this study. This study is considered supplementary until recent results of a positive control for the Hartley derived guinea pigs are submitted.

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CORE-CLASSIFICATION: Supplementary

The study is to be considered supplementary until recent results of a positive control study from the Hartley derived guinea pigs are submitted.

Buehler, E.V. and Griffith, F., 1975, Experimental Skin Sensitization in the Guinea Pig and Man. In: Animal Models in Dermatology, ed. H.I. Maibach (ed.) pp. 56-66, Edinburgh: Churchill Livingstone.

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