2-6-90

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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 7969-OR
BASF MCPP technical

FROM: William S. Woodrow WSW 2-5-90
Precautionary Review Section
Registration Support Branch E 2/6/90
Registration Division (H7505C)

TO: Joann Miller / Jesse Maines (PM 23)
Fungicide - Herbicide Branch
Registration Division (H7505C)

APPLICANT: BASF
Parsippany, N.J. 07054

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
2-(2-Methyl-4-Chlorophenoxy) Propionic Acid	95.0
Inert Ingredient(s):	5.0
Total	100.0%

BACKGROUND

The BASF Co. submitted acute oral, dermal, inhalation, primary eye and skin irritation, and 3 dermal sensitization studies to support registration of MCPP. MRID NOS. used were 410134-02 through 410134-09.

RECOMMENDATION

1) The acute oral, dermal, inhalation, primary eye and skin irritation, and two of the dermal sensitization studies are acceptable to RSB/PRS. One of the dermal sensitization studies (MRID NO 410134-07) was graded Supplementary Data; however, ~~Summary Data may not independently support registration (Summary data not acceptable); need all raw data.~~

2) No additional acute toxicity studies are necessary to support Mecoprop (MCPP) #7969-OR ~~excepting the~~ LABELING (One of the dermal sensitization studies was fully exceptable - thus no further data needed)

1) Change the signal word from CAUTION, to read "DANGER".

2) Add the following to the Precautionary Statements, "Harmful if swallowed,

absorbed throughskin, and causes eye irritation.

3) Add a precautionary labeling section entitled "STatement of Practical treatment

<u>If Swallowed</u>: Call a physician or Poison Control Center. Drink 1 or 2 glasses of water and induce vomiting by touching back of throat with finger. Do not induce vomiting or give anything by mouth to an unconscious person.

<u>If on Skin</u>: Wash with plenty of soap and water. Get medical attention.

<u>If in eyes</u>: Flush with plenty of water. Call a physician.

DATA REVIEW FOR ACUT ORAL TOXICITY TESTING (§81)

Product Manager: (23)
MRID No.: 410134-02
Testing Facility: BASF Aktiengesellschaft
Author(s): P. Kitsch
Species: Rat, Wistar
Age: not given
Weight: M172-187, F170-177 g.
Source: Dr. Thomae GMBH
Test Material: CMPP (MECOPROP)
Quality Assurance (40 CFR §160.12): none

Reviewer: ~~M. Weller~~ Woodrow
Report Date: 2-2-90
Report No. 83/0074
Observation Days (Post Exposure): (14); other ( )

Conclusion:

1. LD50 (mg/kg): Males = 1240 mg/kg (890-1750); Females = 1210 mg/kg (890-1640); Combined = —
2. The estimated LD50 is 1166mg/kg (1004-1367)
3. Tox. Category: III. Classification: Guidelines

Procedure (~~Deviations From §81-1~~): ~~Groups of 5M+5F treated by~~ gavage with test material. Animals examined daily for toxic signs and mortality.

Results:

Reported Mortality

DOSAGE (mg/kg)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
681 mg/kg	0/5	0/5	0/10
1000 mg/kg	1/5	1/5	2/10
1470 mg/kg	5/5	4/5	9/10
2150 mg/kg	4/5	5/5	9/10

Symptomology & Gross Necropsy Findings:

Clinical: Symptoms included - Dyspnea, apathy, abnormal position, staggering, ataxia, paresis, twitching, piloerection, poor general state.

Necropsy: Bloody ulcerations in stomach, some stomachs c injected vessels. Intestines slightly atonic + contents striped with blood - some animals. Urinary bladder strikingly filled in some animals.

DATA REVIEW FOR AC[illegible]E DERMAL TOXICITY TESTING (81-2)

Product Manager: (23) Reviewer: ~~M. Waller~~ Woodrow
MRID No.: 410134-03 Report Date: 2-5-90
Testing Laboratory: BASF Aktiengesellschaft Report No. 83/0116
Author(s): P. Kitsch
Species: Rat, Wistar
Sex: 5M+5F Wt.: 200-300g
Test Material: MCPP technical (mecoprop)
Quality Assurance (40 CFR §160.12): none

Summary:

1. LD_{50} (mg/kg): Males = —; Females = —; Combined = —;
2. The estimated LD_{50} is > 4000 mg/kg
3. Tox. Category: III. Classification: Guidelines

Procedure (~~Deviations from §81-2~~): 2 groups of 5M+5F each dosed separately with test material; single dermal applications to 6 cm² clipped dorsal areas. Treated sites covered with semi-occlusive dressing for 24 hours. T. mat. formulation in 0.5% aqueous carr. Animals checked for mortality and topic signs daily to 14 days. Necropsies.

Results:

Reported Mortality

DOSAGE (mg/kg)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
2000 mg/kg	0/5	0/5	0/10
4000 mg/kg	0/5	0/5	0/10

Symptomology & Gross Necropsy Findings:

Clinical: No general symptoms; 1 male + 1 female showed lacrimation at each of the 4000 + 2000 mg/kg dose levels.
Necropsy: No gross abnormalities.

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

Product Manager: (23) Reviewer: W. Woodrow
MRID No.: 410134-04 Report Date: 2-5-90
Testing Laboratory: BASF Aktiengesellschaft Report No. 86/0630
Author(s): H. J. Klimisch
Species: Rat, Wistar
Sex: 30M+30F Weight: 284-9 M, 189 g F
Source: K. Thomae GmbH
Test Material: CMPP Mecoprop, powder
Quality Assurance (40 CFR §160.12): adequate

Summary:

1. LC_{50} (mg/kg): Males = —; Females = —; Combined = —
2. The estimated LC_{50} is > 12.5 mg/L
3. Mean Concentration: —
4. Tox. Category: IV. Classification: Guidelines

Procedure ~~(Deviations From §81-2)~~: Groups of m+f rats dposed in 55 L head/nose exposure chambers. Test material milled + injet with 1 % wt % of Aerosil to make more uniform. 1500 L/hr Compressed air through injector + 1500 L/hr conditioned air as dilution.

Results:

Reported Mortality

Exposure Concentration (mg/L)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
5.4 mg/L	2/10	1/10	3/20
9.5 mg/L	2/10	2/10	4/20
12.5 mg/L	5/10	2/10	7/20

Symptomology & Gross Necropsy Findings:

4 hour exposures. Pre-weighed filters used to collect Chamber aerosol samples of known volume. Nominal concentrations also determined. Particle size analyses conducted using Anderson Stack (cascade) Sampler Mark III, impactor equipped + glassfiber collecting discs + back up particle

filter (all filters pre-weighed). Animals observed (4 days for toxic symptoms and mortality. Necropsies performed on all animals. Body weight @ 0, 7 & 14 days.

Results:

Particle size distribution:

Group 1 – 27.3% of particles 2.8 μ
MMAD 50% = 5.6 μ
GSD = 2.3

Group 2 – 21.6% of particles 2.8 μ
MMAD of 6.2 μ
GSD = 2.3

Group 3 – 46.4% = 2.8 μ
MMAD of 4.1 μ
GSD = 2.3

Chamber Concentration: (Gravimetric measurements)

Group 1 – 12.5 mg/L
Group 2 – 9.5 mg/L
Group 3 – 5.4 mg/L

All animals lost weight.

Necropsy: Dead animals; 5.4 mg/L, lungs slight edematization; 9.5 mg/L, severe congestion; 12.5 mg/L, lungs showed slightly number dark areas irregular in regions.

DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (§81-4)

Product Manager: (23)
Reviewer: ~~M. Waller~~ Woodrow
MRID No.: 410134-05
Report Date: 2-5-90
Testing Laboratory: BASF Aktiengesellschaft
Report No. 83/0184
Author(s): P. Kirsch
Species: Rabbit, White Vienna
Sex: 3M+3F
Weight: not given
Source: Gaukler, Main FRG
Dosage: 0.1ml (54mg)
Test Material: CMPP (mecoprop)
Quality Assurance (40 CFR §160.12): none

Summary:

Tox. Category: I
Classification: Guidelines

Procedure ~~(Deviation From §81-4):~~ 0.1ml bulk volume (54mg) placed in conjunctival sac of 3M+3F rabbits. Eyes examined and scored for irritation according to the Draize system at 1, 24, 48 & 72 hours post treatment.

Results:

Observations
(number "positive"/number tested)

	Hour	Days						
	1	1	2	3	4	7	14	21
Cornea Opacity	6/6	6/6	6/6	6/6				
Iris	6/6	6/6	6/6	6/6				
Conjunctivae Redness	6/6	6/6	6/6	6/6				
Chemosis	6/6	6/6	6/6	6/6				
Discharge	6/6	6/6	6/6	6/6				

2/3.0 scores thru 72 hrs.
1/2.0, 2.0 scores thru 72 hrs
3.0 scores → 72 hrs
3.0 scores → 72 hrs
3.0 scores → 72 hrs

Comments: Study discontinued after 72 hours because of severe irritation; some detachment of corneas, margins vessel. of cornea. Irritation index could not be used because of suppuration

DATA REVIEW FOR SKIN IRRITATION TESTING (§81-5)

Product Manager: (23)
MRID No.: 410134-06
Testing Laboratory: BASF Aktiengellschaft
Author(s): P. Kirsch
Species: Rabbit
Age: not given
Sex: 3 m + 3 f
Weight: not given
Dosage: 0.5 g
Test Material: Empp (mecoprop)
Quality Assurance (40 CFR §160.12): none

Reviewer: Woodrow
Report Date: 2-5-90
Report No.: 83/0182

Summary:

The Primary Irritation Index = 3.5 (moderate irritant)

Toxicity Category: III

Classification: Guidelines

Procedure ~~(Deviations from §81-5):~~ A 50% aqueous formulation used (W/W). Test patches covered c (2.5 cm²) 0.5 mm 50% suspension of test material; about 0.5 g test material, at dorsal, clipped sites on 3 m + 3 f rabbits. Patches applied/taped - 24 hours contact; sites scored for irritation according to Draize @ 30-60 min after patch removal, and at 48 & 72 hours, and at 8 & 15 days.
Results:

Time	All-irritation index (6 animals)
24 hr	3.8
48 hr	3.3
72 hr	3.3
8 days	0.7
15 days	0.0

Special Comments:

DATA REVIEW FOR SKIN SENSITIZATION TESTING (§81-6)

Product Manager: (23)
MRID No.: 410134-07
Testing Laboratory: BASF Aktiengesellschaft
Author(s): P. Kirsch
Species: guinea pig
Sex : _____ Weight: _____
Source: _____
Test Material: CMPP (mecoprop)
Positive Control Material: _____
Quality Assurance (40 CFR §160.12): _____

Reviewer: ~~M. Waller~~ Woodrow
Report Date: 2-6-90
Report No. 84/0238

Method: Summary data only — cannot use alone.

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

Procedure (~~Deviation From §81-6~~): This report is a summary of skin sensitizing effect of mecoprop in the Maximization Test, and in the Open Epicutaneous Test.

~~Results~~: Summary (main tests reported separately):
"On the basis of the result from a Maximization Test and an Open Epicutaneous test, no skin sensitizing effect of CMPP on guinea pigs is detectable".

DATA REVIEW FOR SKIN SENSITIZATION TESTING (§81-6)

Product Manager: (23)
MRID No.: 410134-08
Testing Laboratory: BASF Aktiengesellschaft
Author(s): P. Kirsch
Species: guinea pig, Dunkin Hartley
Sex: Female Weight: 264-329g
Source: Lippische Versuchtierzucht
Test Material: CMPD (mecoprop) powder (0.5mm mesh)
Positive Control Material: none
Quality Assurance (40 CFR §160.12): adequate

Reviewer: ~~M. Waller~~ Woodrow
Report Date: 2-5-90
Report No. 84/0239

Method: Maximization test (Magnusson & Kligman)

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

Procedure ~~(Deviation From §81-6):~~ Pre-test screening for maximum (percutaneous), non-irritating concentration resulted in a 10% aqueous concentration use in the main study. The following test material preparations were used:

~~Results~~: intradermal induction - 10% in paraffin oil/aqua dest. (1:1) or in Freund's adjuvant/aqua dest. (1:1).
percutaneous induction - 50% in aqua dest.
1st challenge - 10% in aqua dest.
2nd challenge - 10% in aqua dest.

Induction - intradermal - 6 injections - groups of two:
front row: 2 inj. each of 0.1ml Freund adjuvant - emulsified to water 1:1.
middle row: 2 inj. of 0.1ml test substance - alone.
back row: 2 inj. of 0.1ml Freund's adjuvant/water (1:1) + test material. (10 animals)
10 additional animals given same injections - without the test material (controls). Injection skin site read 24hrs post injection.

Percutaneous induction - performed 1 week after intradermal induction.
Exposure (topical) to about 0.3g test material by means of 2x4 cm filter paper strip. Control animals not treated.
This is repeated percutaneous occluded - exposure for 48 hours.
Same shoulder site as for intradermal induction
Site covered appox. 48 hours after beginning application.
Challenge: First challenge 14 days after percutaneous application, second challenge 1 week later.
About 0.15g test material - 2x2 cm paper strip
1st challenge: test and control group 1 with test substance. (Control group 2 remained untreated.
2nd Challenge: treatment of test group and of control groups 1 & 2 with test material.
24 hour exposures - Readings about 24, 48 & 72 hrs after beginning of application.

Results:
Induction 1st control, also second control & test group. all 2.2
2/2 = 2.0 for both erythema & edema
1st control & 2nd control: 0 wounds adj., paraffin oil + aqua dest., 0 wounds + aqua dest. test: 0 wounds, aqua dest. + test material.
Challenge: (test.) 1.0 scores
1st challenge: 24 hrs 0/0, 48 hrs 3/10, 72 hrs 4/10
2nd challenge: 24 hrs 3/10 wounds, 48 hrs 5/10 wounds, 72 hrs 2/10 wounds (1.0 scores)
Conclusion: Test material is not a weak sensitizer.

DATA REVIEW FOR SKIN SENSITIZATION TESTING (§81-6)

Product Manager: (23)
Reviewer: ~~M. Waller~~ Woodrow
MRID No.: 410134-09
Report Date: 2-8-90
Testing Laboratory: BASF Aktiengellschaft
Report No. 84/0240
Author(s): Grundler
Species: guinea pig, Dunkin Hartley
Sex: Female
Weight: 292-353g
Source: Lippische Versuchstierzucht
Test Material: CMPP (mecoprop)
Positive Control Material:
Quality Assurance (40 CFR §160.12): adequate

Method: Open Cutaneous test

Summary:
1. This product is / ~~is not a dermal sensitizer~~
2. Classification: guidelines

Procedure ~~(Deviation From §81-6):~~ 2 groups of 8 guinea pigs were clipped before applying 0.1ml / 8 cm^2 20 applications (1 concentration) / test group animal to clipped right flanks, over 4 week period. Sites graded @ ~~Results:~~ 48 & 72 hours (Induction applications)
Challenge: 0.025 ml / 2 cm^2 challenge applications to left flanks. 4 concentrations per animal, applied 3 and 13 days after last induction (1st and 2nd challenge). The readings were 24, 48 and 72 hours after application.

The test results are presented on page 2:

quote

31H19/83	Induction	Concentrations of 1st challenge 50% in a	15% in a	5% in a	1.5% in a	2nd challenge 50% in a	15% in a	5% in a	1.5% in a	
Control group 1	untreated	5/8 7/8	2/8 4/8	0/8	0/8	8/8	8/8	1/8	0/8	48 h 72 h
Control group 2	untreated	untreated				8/8	4/8 6/8	0/8 1/8	0/8	48 h 72 h
Test group 4	50% in a	8/8	8/8	0/8	0/8	8/8	8/8	0/8 2/8	0/8	48 h 72 h
Test group 5	15% in a	8/8	7/8	0/8	0/8	8/8	5/8 7/8	0/8	0/8	48 h 72 h
Test group 6	5% in a	8/8	8/8	0/8	0/8	8/8	5/8 7/8	0/8	0/8	48 h 72 h
Test group 7	1.5% in a	8/8	8/8	0/8	0/8	8/8	7/8 8/8	0/8	0/8	48 h 72 h

a: aqua dest.
x/y: number of skin changes/number of application sites in each case 48 and 72 hours after the challenge (72 hours only if there were deviations from 48 hours)

unquote From table above:

a. Controls: 5% and 1% gave no skin reactions (no irritation)

b. Groups 4, 5, 6 & 7: 50% & 15% test mat. gave + (irritation reactions); at 1st & at the 2nd challenge.

c: 5% and 1.5% test material (aqua dest. present in all preparations) resulted in only 2 of 8 animals showing reactions @ 5% test material at 72 hours.

d. It seems clear that all 50% & 15% test material reactions were due to irritation (too concentrated material)

Conclusions: Test material did not sensitize guinea pigs.

Tox Chem No. 559 mecoprop File Last Updated _____ Current Date 2-5-90

Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LD_{50}, LC_{50}, PIS, NOEL, LEL	TOX. Cat.	CORE Grade/ Doc. No.
Acute oral LD_{50}, Rat BASF # 83/0074 3-83	mecoprop	410134 -02	LD_{50} M-1240 mg/kg (890-1750) F-1210 mg/kg (590-1640) overall = 166 mg/kg (1004-1362)	III	Guide-lines
Acute dermal LD_{50}, Rat BASF # 83/0116 6-83	"	410134 -03	LD_{50} > 4000 mg/kg	III	Guide-lines
Acute inhalation, Rat BASF # 86/0630 11-14-86	"	410134 -04	> 12.5 mg/L	IV	Guide-lines
Primary eye irritation, Rabbit. BASF # 83/0184 9-19-83	"	410134 -05	Study discontinued after 72 hrs because of severe irritation. (Irritation index could not be read because of suppuration	I	Guide-lines
Primary skin irritation, Rabbit. BASF # 83/0182 9-83	"	410134 -06	P.I. Index = 3.5 (moderate irritant).	III	Guide-lines

Tox Chem No. 559 mecoprop File Last Updated _____ Current Date 2-5-90

Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LD_{50}, LC_{50}, PIS, NOEL, LEL	TOX. Cat.	CORE Grade/ Doc. No.
Dermal sensitization, guinea pigs. BASF # 84/0238 10-1984	Mecoprop	410134 -07	Summary only - Co. says on basis of Maximization and open epicutaneous tests, test material not a sensitizer	-	Supplementary
Dermal sensitization, guinea pig. BASF # 84/0239 (Maximization study) 10-84	"	410134 -08	Test material did not sensitize guinea pigs.	-	Guidelines
Dermal sensitization, guinea pigs. BASF # 84/0240	"	410134 -09	Test material did not sensitize guinea pigs	-	Guidelines

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