2-7-90

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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

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

FROM: William S. Woodrow WSW 2-7-90 E 2/7/90
Precautionary Review Section
Registration Support Branch
Registration Division (H7505C)

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

APPLICANT: BASF Corp. Chemicals Division
100 Cherry Hill Road
Parsippany, New Jersey 07054

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
(±)-(R)-2-(2-methyl-4-Chlorophenoxy) Propionic Acid	93.0
Inert Ingredient(s):	7.0
Total	100.0%

BACKGROUND

The BASF Corp. submitted acute oral, dermal, inhalation, primary skin and dermal irritation, dermal sensitization, and acute intraperitoneal toxicity studies in support of BASF MCI technical. MRID NOS. used were 410139-02 through 410139-07, and 410269-01.

RECOMMENDATION

1) The acute toxicity studies submitted by BASF are acceptable to RSB/PRS.
2) No additional acute toxicity studies are required.

LABELING

1) Change the CAUTION signal word to read, "DANGER".
2) Begin Precautionary Statements as follows, Harmful if swallowed, absorbed through skin. Causes irreversible eye damage.
3) Add a precautionary labeling section entitled "Statements of Practical Treatment".

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If Swallowed: 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.

If On Skin: Wash with plenty of soap and water. Get medical attention.

If In Eyes: Flush with plenty of water. Call a physician. 11

DATA REVIEW FOR ACUTE ~~RAL~~ TOXICITY TESTING (§81-

Product Manager: (23)
MRID No.: 410839-02
Testing Facility: BASF Aktiengesellschaft
Author(s): P. Kirsch
Species: Rat, Wister
Age: not given
Weight: not given
Source: Dr. Thomae
Test Material: CMPP (Mecoprop) D-Form
Quality Assurance (40 CFR §160.12): None

Reviewer: Woodrow ~~M. Walter~~
Report Date: 2-6-90
Report No. 84/0028

Observation Days (Post Exposure): (14); other ( )

Conclusion:

1. LD_{50} (mg/kg): Males = approx. 1327 mg/kg; Females = >681, <1000 mg/kg; Combined =
2. The estimated LD_{50} is 1050 mg/kg (890–1230)
3. Tox. Category: III. Classification: Guidelines

Procedure (~~Deviations From §81-1~~): Groups of 5M+5F rats administered test material dose mixed with 0.5% aqueous CMC by gavage. Treated animals observed for toxic signs and mortality daily to 14 days - All animals subjected to necropsy examinations.

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	0/5	5/5	5/10
1420 mg/kg	4/5	5/5	9/10
2150 mg/kg	5/5	5/5	10/10

Symptomology & Gross Necropsy Findings:

Clinical: In-life symptoms included: dyspnea, apathy, staggering, paresis, tremor, twitching, spastic gait, pelvic erection, lacrimation, blood in urine.

Necropsy: Sacrificed animals (no gross abnormalities). Dead animals – Showed congestive hyperemia, 2 (1000 mg/kg) bloody stomach ulcerations. Slightly atonic stomachs. Bladders filled to striking degree.

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (1-2)

Product Manager: (23)
Reviewer:- ~~H. Wallis~~ Woodrow
MRID No.: 410139-03
Report Date: 2-6-90
Testing Laboratory: BASF Aktiengesellschaft
Report No. 84/0152
Author(s): P. Kitsch
Species: Rat, Wistar
Sex: M & F
Wt.:
Test Material: EMPP (Meccaprop) D-Form
Quality Assurance (40 CFR §160.12):

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 5 M & 5 female rats each dosed to bodies (clipped) of animals (dorsal & flanks). Sites covered with semi-occlusive dressing - 24 hours contact. Sites rinsed. Animals observed for mortality & toxic signs to 14 days.

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 abnormal clinical signs.
Necropsy: One animal showed moderate erythema and edema at test mat. site.

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

Product Manager: (23)
MRID No.: 410139-05
Testing Laboratory: BASF Aktiengesellschaft
Author(s): H. J. Klimisch
Species: Rat, Wistar
Sex: 5M/5F
Source: Dr. Theimmer
Test Material: CMPP (mecoprop) D-Form granulate
Quality Assurance (40 CFR §160.12): adequate

Reviewer: W. Woodrow
Report Date: 2-6-90
Report No. 86/a379
Weight: M 270-280, F 179-241 g.

Summary:

1. LC_{50} (mg/kg): Males = —; Females = —; Combined = —
2. The estimated LC_{50} is > 5.6 mg/L
3. Mean Concentration:
4. Tox. Category: IV. Classification: Guideline

Procedure (~~Deviations From §81-2~~): 5M+5F rats exposed for 4 hours in 55 liter head/nose exposure tubes. Generation of test material dust by means of BASF rotating dust pan feeding equipment. Test material mixed with 2% wt. of Aerosil to achieve a more

Results:

Reported Mortality

Exposure Concentration (mg/L)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
5.6 mg/L	0/5	0/5	0/10

~~Symptomology & Gross Necropsy Findings~~:

~~respiratory~~ aerosol concentration: Air flow: 1500 L/hr compressed air by injector + 1500 L/hr conditioned air (dilution air). Exhaust air system about 10% lower pressure to adjust system.

Gravimetric sampling: samples of chamber air through millipore (pre-weighed) filters = nominal concentration of exposure aerosol. Gravimetric: wt. collected ÷ by vol. sampled → mg/L. Particle size analysis using Anderson Stack Sampler Model III. Samples equipped = pre-weighed glass fiber collecting discs + back up particle filter. Animals observed 14 days for toxic signs + mortality. All animals necropsied.

Results:

1) Actual chamber (exposure) concentration:
   Gravimetric = (4 samples AV.) = 5.6 mg/L (2% aerosil subtracted)
   Nominal: 11.5 mg/L (2% Aerosil subtracted).

2) Particle size analysis:
   impactor disc #6: 2.8μ (5.58mg), 16.4% distribution
   #7: 1.2μ (1.93mg), 5.7% "

3) All animals gained weight.

4) Animals: Post exposure, day 7 some animals ruffled appearance around nose, edges. Necropsies: no gross abnormalities.

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

Product Manager: (23)
MRID No.: 410269-01
Testing Laboratory: BASF Aktiengesellschaft
Author(s): P. Kitsch
Species: Rabbit, White Vienna
Sex: 3M+3F Weight: not given
Source: Gaulkler, Main, FRG
Dosage: 0.1ml (approx. 39 mg)
Test Material: CMPP (mecoprop) D-Form
Quality Assurance (40 CFR §160.12): none

Reviewer: ~~M. Waller~~ Woodrow
Report Date: 2-6-90
Report No. 84/0031

Summary:

Tox. Category: I Classification: Guidelines

Procedure ~~(Deviation From §81-4):~~ 0.1ml test material placed in conjunctival sac of one eye of each of 3M+3 female rabbits. Animals examined and scored for irritation using the Draize system @ 1, 24, 48 + 72hrs

Results:

Observations (number "positive"/number tested)

	Hour	Days						scores
	1	1	2	3	4	7	14	21	
Cornea Opacity	6/6	6/6	6/6	6/6					1-2-1 ended 3.0
Iris	6/6	6/6	6/6	6/6					1 - ended on 2.0
Conjunctivae Redness	6/6	6/6	6/6	6/6					1-2-ended on 3.0
Chemosis	6/6	6/6	6/6	6/6					2-ended on 3.0
Discharge	6/6	6/6	6/6	6/6					2-ended on 3.0

Comments: Study discontinued after 72 hours due to severe irritation/suppuration

Draize scoring index

1 hr	38
24 hr	62
48 hr	66
72 hr	89

Note: 110 possible score

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

Product Manager: (23)
MRID No.: 410139-04
Testing Laboratory: BASF Aktiengesellschaft
Author(s): P. Kitsch
Species: Rabbit, White Vienna
Age: not stated
Sex: 4M + 2F
Weight: not given
Dosage: 0.5 g.
Test Material: CMPP (Mecoprop) D-Form
Quality Assurance (40 CFR §160.12): none

Reviewer: Goodlow
Report Date: 2-6-90
Report No.: 84/0030

Summary:

The Primary Irritation Index = P.I. index: 3.03 (moderate irritation)

Toxicity Category: III

Classification: Guidelines

Procedure ~~(Deviations From §81-5):~~ Test patches (2.5 cm^2) covered with 0.5 mm layer of 50% aqueous suspension of test material (0.5 g); patches applied to clipped backs of 4M + 2F rabbits. Patches secured to Depa. Treated site/patches covered w occlusive dressing for 24 hr exposure. Wiped sites examined & scored for irritation according to

Results: Draize @ 30-60 min, 48, 72 hrs, and 8 & 15 days after beginning of application.

Time	Av. individual irritation index
24 hr	3.5
48 hr	2.8
72 hr	2.8
8 days	1.0
15 days	0.0

Special Comments:

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

Product Manager: (23) Reviewer: ~~M. Waller~~ Woodrow
MRID No.: 410139-07 Report Date: 2-6-90
Testing Laboratory: BASF Aktiengesellschaft Report No. 85/0392
Author(s): Dr. Kleczka
Species: guinea pig, Pirbright white) Dunkin Hartley
Sex: Female Weight: 236-288g.
Source: Lippische Versuchstierzucht.
Test Material: CMPP (mecoprop) - D-Form, granules
Positive Control Material:
Quality Assurance (40 CFR §160.12): adequate

Method: Maximization Test of Magnusson + Kligman

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

Procedure (~~Deviation From §81-6~~): Pre testing determined maximum, non irritating concentrations:
Intradermal injection: 10% in paraffin oil/aqua dest. (1:1) or in Freund's adjuvant/aqua dest. (1:1).

Results: Percutaneous induction: 50% in aqua dest.
1st. challenge: in aqua dest.
2nd challenge: in aqua dest.
No. of animals/control group = 10, no. animals/test group = 20.
Induction: 6 intradermal injections in groups of 2/animal:
Test group - front row - 2 injections each of 0.1 ml Freund's adjuvant without test substance emulsified ± (water @ 1:1)
middle row - 2 injections each of 0.1 ml of test substance formulation.
back row - 2 injections each of 0.1 ml Freund's adjuvant/water (1:1) with test substance.
Control groups 1 + 2 - 1. The animals were given the same injections described above, without test substance, only ± formulating agent.
Readings 24hrs after begining of injections.

Percutaneous induction: Using same sites as for intradermal injections. 2×4 cm filter paper strips applied to same sites; in case of solid material, paper strip coated ± 0.5mm thick layer of test material (about 0.3 g test material). Control animals not treated (by percutaneous route).
48 hour exposure. Readings 48 hrs after beginning exposure.
Challenge: 1st challenge 14 days after percutaneous, 2nd challenge, 1 week later.
2 cm² filter paper applied to skin of flank under occlusive dressing. In the case of liquids, filter paper soaked in test substance formulation; exposure about 0.15 g of test material.
1st challenge - test group and control group 1 c. test substance formulation (2nd control group untreated.
2nd challenge - treatment of test group and of control groups 1+2 with test substance formulation. (percutaneous), for 24 hours - Readings 24, 48 & 72 hrs.

Results: The test group gave sporadic 1.0 erythema scores at both 1st and 2nd challenge, when challenged either at induction sites, or at virgin test sites. Control animals (1st and 2nd group) showed similar sporadic 1.0 scores, when challenged with test material.

Conclusion: Cmpd (inecoptop) - D-form, did not sensitize guinea pigs.

Acute Intraperitoneal Toxicity in Rats of CMPP (Mecoprop)

Product Manager: (23) Reviewer: Woodrow
MRID NO.: 41039-06 Report Date: (2-6-90)
Testing Laboratory: BASF Aktiengesellschaft
Author: P. Klisch Report NO.: 84/0029
Species: Rat, Wistar
Source: Dr. Thamae
Test Material: CMPP (Mecoprop) D-Form
Animal Sex: 5M+5F/dose Weight: M-Av 180, F 177

Summary: M LD_{50} = >316, <464 mg/kg
F LD_{50} = 383 mg/kg (282-520)
M+F LD_{50} = 383 mg/kg (334-439)

Classification: Guidelines

Procedure: Formulation: Test material mixed with 0.5% aqueous CMC, for single abdominal (I.P.) injection. 5M+5F rats/dose injected I.P. with test material/0.5% CMC. Tested animals observed daily for 14 days for toxic signs + mortality. All animals subjected to necropsy. Body weights.

Results:

mg/kg Dosage	NO. killed / NO. tested Males	Females	Combined
215	0/5	0/5	0/10
316	0/5	1/5	1/10
464	5/5	4/5	9/10
681	5/5	5/5	10/10

Clinical symptoms: Included: dyspnea, apathy, abnormal posture, staggering, ataxia, paresis, tremors, twitching, prostration, cyanoses, poor general state. Animals generally lost weight, or maintained weight.

Necropsy: Dead animals (spontaneous), showed general congestive hyperemia, very fine focal febrin coatings on livers, adipose tissue necrosis, in some cases serous bladder after full of white contents.

Tox Chem No. 559 Mecoprop | File Last Updated _____ | Current Date 2-7-90

Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LD_{50}, LC_{50}, PIS, NOEL, LEL	TOX. Cat.	CORE Grade/ Doc. No.
Acute oral LD50, Rat BASF # 84/0028 12-29-83	Mecoprop	410139 -02	LD_{50} = 1050 mg/kg (890-1230)	III	Guide-lines
Acute dermal LD50, Rat BASF # 84/0152 5-25-84	"	410139 -03	LD_{50} = > 40.00 mg/kg	III	Guide-lines
Acute inhalation LC_{50}, Rat. BASF # 86/0379 12-5-86	"	410139 -05	LC_{50} > 5.6 mg/L	IV	Guide-lines
Primary eye irrit., Rabbit BASF # 84/0031 12-29-83	"	410269 -01	Ocular score @ 72 hrs = 89; study discontinued after 72 hrs due to severe irritation/suppuration	I	Guide-lines
Primary skin irritation, Rabbit. BASF # 84/0030 12-29-83	"	410139 -04	P.I. Irritant 3.03; a moderate irritant (dermal).	III	Guide-lines

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Tox Chem No. 559 Mecoprop File Last Updated _____ Current Date 2-7-90

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 pig. BASF # 85/0392 11-29-85	Mecoprop	410139 -07	Mecoprop did not sensitize guinea pigs	-	Guide-lines
Acute intraperitoneal toxicity, Rat. BASF # 84/0029 12-29-83	"	410139 -06	Intraperitoneal LD_{50} = 383 mg/kg (334-439)	-	Guide-lines

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