2/8/90

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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol DP AMINE 60 (Dichloroprop 2,4-DP), Duplosan-DP (2,4-DP-D Form)

FROM: William S. Woodrow WSW 2-7-90
Precautionary Review Section E 2/8/90
Registration Support Branch
Registration Division (H7505C)

TO: Joanne Miller/Jesse Mays (PM 23)
Fungicides-Herbicides Branch
Registration Division (H7505C)

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

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
600 grams / liter dichloroprop	
(see Notes to PM in review)	
Inert Ingredient(s):	
Total	100.0%

BACKGROUND

The BASF Corp. submitted acute oral, dermal, inhalation, primary eye and skin irritation, and dermal sensitization studies to support registration of two products, both (at present) under EPA Reg. NO. 7969-ON; "Duplosan-DP" - 600g/liter of the optically active isomer of dichloroprop, and "DP AMINE 60", which contains 600 g/liter of dichloroprop as a racemic mixture of D and L forms.

RECOMMENDATION

1) The acute studies submitted by BASF are acceptable to RSB/PRS.

2) The PM should note what appear to be items that need clarification, or are missing:

a. An ingredients list should appear on both labels.

b. Were the acute toxicity studies conducted using the "D" form of dichloroprop, as stated for the acute studies?

c. Does BASF know from previous experience that toxicologically, the D form and the racemic mixture are identical?

3) Provided the questions raised under 2) above are satisfactorily answered, no additional acute toxicity studies are required.

4) LABEL NEEDS A THOROUGH EFFICACY REVIEW OF CLAIMS AND COMPARISONS TO LABELING

1) A "DANGER" signal word must appear on both the Duplosan-DP, and DP-AMINE-60 labels.

2) Add the following to the Precautionary Statements, This material may be harmful if swallowed, inhaled, absorbed through skin, and causes irreversible eye damage.

3) Add the following statements under "Statement of Practical Treatment (to both labels)

If Swallowed: Call a physician or poison control center.

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

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

4) The label must state the following, or similar wording "Frequent use of this product may cause allergic contact dermatitis".

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (§81-1)

Product Manager: (23)
Reviewer: ~~M. Waller~~ (Woodrow)
MRID No.: 409556-02
Report Date: 10-16-89
Testing Facility: BASF Aktiengesellschaft
Report No. 84/0032
Author(s): P. Klisch
Species: Rat, Wistar
Age: not given
Weight: M208-, F178
Observation Days (Post Exposure): ~~(14)~~; other (15)
Source: K. Thomae GMBH
Test Material: 2,4-DP (Dichlorprop) (D-Form)
Quality Assurance (40 CFR §160.12): none

Conclusion:

1. LD_{50} (mg/kg): Males = Approx. 962 mg/kg; Females = >825, <1470 mg/kg; Combined = —
2. The estimated LD_{50} is > 825; < 1470 mg/kg
3. Tox. Category: III. Classification: Guidelines

Procedure (~~Deviations From §81-1~~): Groups of 5M & 5F each received graded doses by gavage of the test material. Animals observed for toxic signs and mortality 1x/day. All animals necropsied.

Results:

Reported Mortality

DOSAGE (mg/kg)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
464 mg/kg	0/5	0/5	0/10
825 mg/kg	0/5	1/5	1/10
1470 mg/kg	5/5	5/5	10/10
2150 mg/kg	5/5	5/5	10/10

Symptomology & Gross Necropsy Findings:

Clinical toxs: Dyspnea, apathy, abnormal position, staggering, ataxia, paresis, piloerection, twitching, salivation, lactimation, imbalance.

N. exam: Decreases no abnormalities. Dead - congestive hyperemia, foam colored liver, stomachs bloody, ulcerated. Hemat. intestinal contents, Urinary bladder very full.

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (81-2)

Product Manager: (23)
Reviewer: ~~[illegible] Weller~~ Woodrow
MRID No.: 409556-03
Report Date: 10-16-89
Testing Laboratory: BASF Aktiengesellschaft
Report No. 84/0153
Author(s): P. Kitsch
Species: Rat, Wistar
Sex: M+F
Wt.: M(AV) 233, F 214
Test Material: 2,4-DP (Dichloroprop) (D-Form)
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: Guideline.

Procedure ~~(Deviations From §81-2)~~: 2 groups of 5M+5F each were treated with test material & applied to clipped dorsal area (50 cm^2). Area covered w semi-occlusive dressing for 24 hrs. Subsequently animals observed for toxic signs & mortality for 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 toxic symptoms.
Necropsy: No abnormalities detected at site of application.

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

Product Manager: (23) Reviewer: W. Woodrow
MRID No.: 412312-01 Report Date: 10-16-89
Testing Laboratory: BASF Aktiengesellschaft Report No. 87/0357
Author(s): H. V. Klimisch
Species: Rat, Wistar
Sex: M & F Weight: M 268 ± 20.8 g, F 191 ± 16.0 g
Source: K. Thomae GmbH
Test Material: 2,4-DP; D Form
Quality Assurance (40 CFR §160.12): acceptable

Summary:

1. LC_{50} (mg/kg): Males = —; Females = —; Combined = —
2. The estimated LC_{50} is > 7.5 mg/L
3. Mean Concentration: —
4. Tox. Category: IV. Classification: Guidelines

Procedure ~~(Deviations From §81-2)~~: Groups of 5M & 5F rats exposed (head/nose) to test material dust, in 55 l chamber. Dust/air mixture generated using vibration dust partitioning device (BASF). Test substance milled ± 1% of Sipernat 50 in order to achieve more uniform dust concentration. Dust concen. adjusted by varying aperture width of dust reservoir & varying amplitude of oscillations of metering feeder. 4 hour exposure. Nominal conc. Determined: amt. expended ÷ L air through exposure chamber. Exposure sampled @ ½ hr intervals

Results:

Reported Mortality

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

~~Symptomology & Gross Necropsy Findings~~:

through pre-weighed filters - adjacent to animal noses. ∴ air sampled.
Particle size: Stack sampler (Mark III Andersen): All impactor pre-weighed glass-fiber discs + backup particle filter contents weighed.
Animals observed 14 days for mortality & toxic symptoms.
Results:
Group 1 5.6 mg/L cloud conc., MMAD = 4.5 μ, geometric S. dev. = 2.9. 27.7 % of particles = 2.8 μ
Group 2 7.5 mg/L cloud conc., MMAD = 4.25 μ, G.S. Dev. = 3.1, 34.9 % of particles = 2.8 μ.
Clinical symptoms: During exposure - dyspnea, after exposure - irregular or intermittent breathing, nasal area c̄ B reddish crust, anal and genital area smeared c̄ urine, apathy, unsteady gait. By day 6 - no abnormalities.
Autopsies - no gross abnormalities.

The dust aerosols were respirable.

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

Product Manager: (23)
Reviewer: ~~M. Waller~~ Woodrow
MRID No.: 409556-05
Report Date: 10-16-89
Testing Laboratory: BASF Aktiengesellschaft
Report No. 84/00235
Author(s): P. Kitsch
Species: Rabbit, White Vienna
Sex: 2M + 4F
Weight: (AV) = M 2.88, F 2.66 KG
Source: Gaulker, Main, FRG
Dosage: 0.1ml (62 mg)
Test Material: 2,4-DP (Dichlorprop) - D Form
Quality Assurance (40 CFR §160.12): none

Summary:

Tox. Category: I Classification: Core Guidelines

Procedure ~~(Deviation From §81-4)~~: 0.1ml placed in conjunctival sac of 2M+4F rabbits. Animals were scored for irritation @ 1H, 24H, 48H, & 72HR, post treatment, according to the Draize scale.

Results:

Observations (number "positive"/number tested)

	Hour	Days					
	1	1	2	3	4	7	14	21
Cornea Opacity	1.0 6/6	2.0 6/6	2.0 6/6	3.0 6/6				
Iris	6/1.0 6/6	2.0 6/6	6/2.0 6/6	2.0 6/6				
Conjunctivae Redness	2.0 6/6	2-3 6/6	3.0 6/6	3.0 6/6				
Chemosis	2.0 6/6	2.0 6/6	2-4 6/6	3-4 6/6				
Discharge	2-3 6/6	2-3 6/6	2-3 6/6	2-3 6/6				

Comments: Cornea (6/6) @ 3.0 score, @ 72 hrs - 3/6 = detached cornea, suppuration. All animals - study descontinued after 72 hrs, because of severe irritation

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

Product Manager: (23)
MRID No.: 409556-04
Testing Laboratory: BASF Aktiengellschaft
Author(s): P. Kitsch
Species: Rabbit; White Vienna
Age: not given
Sex: 3M ♂3F
Weight: Av: M 2.91, F 3.25
Dosage: 0.5 mg (used a 50% suspension over 2.5 cm^2)
Test Material: 2,4-DP (Dichlorprop) (D-Form)
Quality Assurance (40 CFR §160.12): none

Reviewer: Woodrow
Report Date: 10-16-89
Report No.: 84/0024

Summary:

The Primary Irritation Index = 2.93 (slight irritant)

Toxicity Category: III

Classification: Guidelines

Procedure (Deviations From §81-5): About 0.5g of test substance (total) - 50% suspension spread over 2.5 cm^2 area (clipped) - to 3M ♂3F. Sites wiped after 24 hour exposure. Animals observed/scored 30-60 min, 48 hr, 72 hr, 8 days, 15 days after patch removal.

Results:

Average Irritation Indexes:

24 hr 3.3
48 hr 2.7
72 hr 2.8
8 Days 1.3
15 Days 0.0

Special Comments:

Note to PM: Tester needed to have continued test through 72 hours - 24 hour exposure not necessary - guideline prescribe a 4 hr exposure.

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

Product Manager: (23) Reviewer: ~~M. Waller~~ Woodrow
MRID No.: 410517-01 Report Date: 10-16-89
Testing Laboratory: BASF Aktiengesellschaft Report No. 87/0217
Author(s): Dr. Kleczka
Species: guinea pig) Pirbright Dunkin Hartley
Sex: female Weight: 247-296 g.
Source: Lippische Versuchtierzucht GmbH FRG
Test Material: 2,4-DP (Dichlorprop) D-Form, granules
Positive Control Material: none tried
Quality Assurance (40 CFR §160.12): acceptable

Method: Maximization Test in Guinea Pigs (Magnusson & Kligman)

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

Procedure ~~(Deviation From §81-6):~~ 10 animals used/control group, 20 animals used for test group.
Induction: 6 intradermal injections in groups of 2/animal:
test group: front row - 2 injections each of 0.1ml Freund's adjuvant without test substance emulsified c water (1:1).
middle row: 2 injections each of 0.1ml of the test material preparation.
back row: 2 injections each of 0.1ml Freund's adjuvant/water (1:1) with test substance.
Control groups 1 & 2: Animals given same injections shown above, but without test substance, only with the formulating agent.
All injections to the shoulder, read for irritation 24 hrs.
~~Results:~~
Percutaneous Induction: Performed 1 week after intradermal induction, using same sites:
2 x 4 cm filter paper strips applied to skin of shoulder under occlusive dressing. Filter paper strips coated with approx. 0.5 mm layer of test substance; animals then

exposed to approx 0.3 g of test substance. 48 hours exposure. Readings about 48 hours after beginning of application.

Challenge: 1st challenge 14 days after last percutaneous induction, 2nd challenge one week later. 2 x 4 cm filter paper applied to shoulder under occlusive dressing - same as for induction. 48 hour exposure. Applications made in same areas used for induction. Amount for challenge was 0.15 g test material. Readings about 24, 48 & 72 hours.

Results:

1st challenge: 4/20 test animals showed 1.0 erythema scores (2 @ 1.0 for edema)

1st challenge controls: 0/10 animals

2nd challenge: 6/20 test animals showed 1.0 for erythema, 5/20 1.0 scores for edema

2nd challenge controls: 2/10 1.0 scores for erythema

Conclusions: The test material displayed a weak sensitizing potential in guinea pigs.

Tox Chem No. 320 dichloroptop 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 LD_{50}, Rat BASF # 84/0032 12-83	Dichloroptop	409556 -02	LD_{50} > 825, < 1470 mg/kg	III	Guidelines
Acute dermal LD_{50}, Rat BASF # 84/0163 5-84	"	409556 -03	LD_{50} > 4000 mg/kg	III	Guidelines
Acute inhalation LC_{50}, RAT. BASF # 87/0359	"	412312 -01	LC_{50} > 7.5 mg/L	IV	Guidelines
Primary eye irritation, Rabbit. BASF # 84/0035 12-83	"	409556 -05	Study discontinued after 72 hrs because of severe irritation, detached retinas, suppuration	I	Guidelines
Primary skin irritation, Rabbit. BASF # 84/0034. 12-83	"	409556 -04	P.I. Index = 2.93 (slight irritant) 24 hr reponse (only needed 4 hrs)	III	Guidelines
Dermal sensitization, guinea pig. BASF # 87/0217. 6-11-85	"	410517 -01	test material did (weakly) sensitize guinea pigs.	—	Guidelines

Page __ of __