

(42-93)

MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 7969-EUP-GN
BASF Facet 75 DF Herbicide

FROM: William S. Woodrow WSW 1-26-93
Precautionary Review Section
Registration Support Branch E 4/2/93
Registration Division (H75-05C)

TO: Robert Taylor / Karen Hicks (PM 25)
Fungicide - Herbicide Branch
Registration Division (H75-05C)

APPLICANT: BASF CORP.
Agricultural Chemicals P.O. Box 13528
Research Triangle Park
North Carolina 27709-3528

FORMULATION FROM LABEL:

<u>Active Ingredient(s):</u>	<u>% by wt.</u>
<u>3,7-dichloro-8-quinolinecarboxylic acid</u>	<u>75.0</u>
_____	_____
_____	_____
<u>Inert Ingredient(s):</u>	<u>25.0</u>
Total	100.0%

BACKGROUND

BASF CORP. submitted six acute toxicity studies to support registration of Facet 75 DF Herbicide (EPA No. 7969-EUP-GN). The MRID NOS. used were 424933-05 through 424933-10. The current application is partial fulfillment of requirements for an EUP.

RECOMMENDATION

1) The acute toxicity studies submitted by BASF are acceptable, and all were graded Guideline studies.

2) Current acute toxicity data profile for Facet 75 DF Herbicide (7969-EUP-GN):

study	Classification	Tox. Category
acute oral LD ₅₀ > 2200 mg/kg	Guideline	III
acute dermal LD ₅₀ > 2000 mg/kg	"	III
acute inhalation LC ₅₀ > 6.06 mg/L	"	IV
eye irritation - irrit. absent by 7 days	"	III
skin irritation - moderate irrit. at 72 hrs	"	III
skin sensitization - not a sensitizer	Guideline	-

3) No additional acute toxicity data are required.

LABELING

- 1) The CAUTION signal word is appropriate.
- 2) Add the following to the Precautionary statements: "Causes moderate eye injury".
- 3) Under Statements of Practical Treatment:

Change the "Get medical attention if irritation persists" (the If on skin statement), to read "Get medical attention".

- 4) DELETE THE STATEMENT "MAY CAUSE ALLERGIC SKIN RESPONSE". STUDY INDICATES THIS PRODUCT IS NOT A DERMAL SENSITIZER. E

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

Product Manager: (25) 1-16-92 Reviewer: M. Woodrow
 MRID No.: 424933-05 Report Date: 1-21-92
 Testing Facility: BASF AG Dept. of Tox. ERG Report No. 92/10035
 Author(s): D. Kirsch
 Species: Rat; Wistar
 Age: young adult Observation Days (Post Exposure): (14); other ()
 Weight: 150-300g
 Source: Dr. K. Thomas GmbH Bielefeld, FRG
 Test Material: BAS 51434 H Facet 75 DF
 Quality Assurance (40 CFR §160.12): both G.L.P. & Q.A.

Conclusion:

- LD50 (mg/kg): Males = _____; Females = _____; Combined = _____
- The estimated LD50 is > 2200 mg/kg
- Tox. Category: III. Classification: Guarded

Procedure (~~Deviation From §81-1~~): Animals acclimated at least 1 week. All animals fasted at least 16 hours pre-test. 5mg SF administered 2200mg/kg by gavage (aqueous). (10ml/kg)
 Results: Animals observed for toxic signs and/or mortality for 14 days. All animals subjected to gross path. exams.
 Reported Mortality

DOSAGE (Mg/kg)	(NUMBER KILLED/NUMBER TESTED)		
	Males	Females	Combined
2200 mg/kg	0/5	0/5	0/10

Symptomology & Gross Necropsy Findings:

All animals gained weight. All animals appeared normal throughout the study. Necropsy examinations revealed no gross abnormalities.

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

Product Manager: (257) 1-28-92 Reviewer: Woodrow M. Waller
 MRID No.: 4214933-06 Report Date: 1-21-93
 Testing Laboratory: BASF AG, Dept. tox ERG Report No. 92/10296
 Author(s): Dr. Kirsch
 Species: Rat, Wistar
 Sex: 5M & 5F Wt.: 200-300g
 Test Material: BAS 514-34 H (Facet 75 DP), water dispersible granule
 Quality Assurance (40 CFR §160.12): both G.L.P. & Q.A.

Summary:

- LD50 (mg/kg): Males = _____; Females = _____; Combined = _____
- The estimated LD50 is > 2000 mg/kg
- Tox. Category: III. Classification: Guardian

Procedure (~~Deviations from §81-2~~): Animals were acclimated to lab

conditions at least 1 week. Fur was clipped from

dorsal and dorsal-lateral parts of trunk one day before test.

Test material (2000 mg/kg) prepared in aqueous "paste",

Results: prep.: 4 ml (50 mg/100 ml) = 200 mg. 50 x 10 = 40 ml / 2000 mg/kg

Reported Mortality

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

Symptomology & Gross Necropsy Findings:

40 ml dose (50 mg/100 ml) spread over 50 x 50 cm²
(approx 19" sq). Applied test mat. Covered 3 pores
brushing + semi-occlusive dressing for 24 hrs. Dressings removed,
sites wiped. Animals observed for toxic signs and mortality
to 14 days. All animals subjected to gross path-exam.
No mortality. All animals gained weight. No clinical
symptoms, no gross pathology.

DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (581-3)

Product Manager: (25-) 2-5-92 Reviewer: W. Woodrow
 MRID No.: 424933-07 Report Date: 1-21-93
 Testing Laboratory: BASF Tox. Dept. AG ERG Report No. 92/10105
 Author(s): D. A. Smet
 Species: Rat, Wistar
 Sex: M + F Weight: Av. wt. M 254, F 248 g
 Source: Dr. K. Thomas GBH
 Test Material: BAS 514 34 H (Facet 75DF) - powder
 Quality Assurance (40 CFR \$160.12): both G.L.P. & Q.A.

Summary:

1. LC50 (mg/kg): Males = _____; Females = _____; Combined = _____
2. The estimated LC50 is 6.06 mg/L
3. Mean Concentration: _____
4. Tox. Category: IV. Classification: Guideline

Procedure (Deviations From 581-2): 5 M & 5 F rats were exposed to an aerosol of test material for 4 hours, which contained in a 55l exposure chamber, snout only. Treated animals were observed for toxic signs and

Results: mortality for 14 days. Body weights recorded

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

Symptomology & Gross Necropsy Findings:

on days 0, 8 & 14. Animals observed daily. All animals subjected to gross pathological examination.

The test material was stirred while creation of the aerosol.

A dosing wheel dust generator was used (Gencke/BASF) and a glass cyclone separator (BASF) - aerosol produced using the dust generator and compressed air. Cyclone separator connected downstream from dust generator. Concentration adjusted by varying rotation of metering discs. Compressed air - 1500 liters/hr. ^{inhalation} system air adjusted to be 10% lower in pressure - to ensure mistiness of test mat. and air not diluted at breathing zone.

Chamber concentration measured by collecting samples on pre-weighed millipore filters - samples collected near animal nose - hourly samples. increased at ≈ 6 air samples = mg/L air.

Particle size distribution determined using Cascade Impactor Stack Sampler Mark III (Andersen). Impactor filled with pre-weighed glass fiber discs. Contents of pre-impactor and amounts of test material adsorbed on sampler walls determined quantitatively.

Results:

- 1) Chamber concentration - average of 4 hourly samples:
6.06 mg/L.
- 2) Particle size distribution:

Particle size distribution cont.:

Record of respirable particles ($\rightarrow 1-3 \mu$):

Impactor stage	EACD 50% [*] (μ)	(EACD 50% [*]) % distribution	cum. % dist.
5	2.8	19.8%	56.5%
7	1.2	17.3%	39.1%

* effective aerodynamic cutoff dia. 50%

Clinical effects: Irregular respiration, piloerection
 All animals gained weight.
 Gross pathology: (No mortality). No
 abnormal findings.

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

Product Manager: (25) 10-29-91 Reviewer: Woodrow M. Waller
 MRID No.: 424933-08 Report Date: 1-26-93
 Testing Laboratory: BASF AG Dept. tox. FRG Report No. 91/11005
 Author(s): Dr. Rossbacher
 Species: Rabbit, White Vienna
 Sex: 2 males, 4 females Weight: M 3.03, F 3.01 kg
 Source: Caulkery D-6050 Offenbach/Mainy FRG
 Dosage: 0.1ml bulk volume (50.0mg)
 Test Material: BASF 514 34 H (75% Quinclorac), Facet 75 DE Methicidide
 Quality Assurance (40 CFR §160.12): both G.C.P. & P.A.

Summary:

Tox. Category: III Classification: Guideline

Procedure (~~Deviation From §81-4~~): Animals acclimated at least 8 days prior to test. 0.1ml (50.0mg) to right conjunctival sac (right eye), each of 6 rabbits. Eyes examined and scored for irritation at 1 Hr, 24, 48 & 72 Hrs, post treatment.
 Results: irritation similar to Ocular System.

Observations

(number "positive"/number tested)

	Observations								
	(number "positive"/number tested)								
	Hour	Days							
	1	1	2	3	4	7	14	21	
Cornea Opacity	0/6	0/6	0/6	0/6					
Iris	0/6	0/6	0/6	0/6					
Conjunctivae Redness	6/6	6/6	5/6	0/6					
Chemosis	6/6	5/6	0/6	0/6					
Discharge	6/6	2/6	0/6	0/6					

Comments: Irritation clearing in 7 days or less.

Product Manager: (25-1) 10-29-91 Reviewer: M. Waller
 MRID No.: 424933-09 Report Date: 1-26-93
 Testing Laboratory: BASF AG Dept. Tox. ERG Report No. 91/11006
 Author(s): Dr. Rossbacher
 Species: Rabbit, White Vienna
 Age: not stated
 Sex: 3M & 3F
 Weight: M. 2.77, F. 2.77 kg
 Dosage: 0.5 g moistened with Lutrol/water
 Test Material: BAS 514 34 H, Facet 75 DF Herbicide
 Quality Assurance (40 CFR §160.12): both G.L.P. & Q.A.

Summary:

The Primary Irritation Index = _____
 Toxicity Category: III
 Classification: Guideline

Procedure (~~Deviations From §81-5~~): Animals acclimated at least 8 days prior to test. Hair clipped from dorsal area of 6 rabbits 15 hrs prior to testing. Test patches were covered (2.5 cm²) with 0.5g moistened test material (moistened with distilled water). Test patches secured with a porous dressing. 4 hour exposure.

Wappings removed, sites wiped with Lutrol/water, spanned and scored for irritation at 30, 60 min, 24, 48, 72 hours, 8 days & 15 days post patch removal.

Results:

Time	AV. irrit scores	
	Eq	Ed
30-60 min	1.67	0
24 hrs	2.0	1
48 hrs	2.2	1
72 hrs	2.0	0
8 days	1	0
15 days	0	0

Special Comments:

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

Product Manager: (25) 1-16-92 Reviewer: M. ^{Wood} ~~Waller~~
 MRID No.: 424 933 -10 Report Date: 1-26-93
 Testing Laboratory: BASF AG Dept. tox. FRG Report No.: 92/10036
 Author(s): Dr. Rassbacher
 Species: Guinea pigs, Piebright white, Dunkm Hartley
 Sex: females Weight: 256-321g
 Source: Lippische Versuchstierzucht Hagmann & Co., FRG
 Test Material:
 Positive Control Material:
 Quality Assurance (40 CFR §160.12): both G.L.P. & Q.A.
 Method: "Buehler"

Summary:

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

Procedure (~~Deviation From §81-6~~): The test material is a water dispersible grey, granule. A preliminary effort was made to prepare the highest concentrations of test material, using aqueous

Results: aqua bidest. A 75% preparation of test material in aqua bidest (w/w basis). "No higher test substance concentrations were technically applicable". 75% test material dispersed in aqua bidest (w/w) was employed for induction, and also for challenge. Animals were acclimated at least 7 days prior to test.

Animals used:

- 4 animals pre-test
- 10 animals challenge only (75% test. in aqua bidest)
- 20 animals Induced and challenged using 75% test mat. in aqua bidest.
- 10 animals vehicle control (did not do this test; stated that knew what to expect based on past experience.

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2.
Main study - 3 induction applications.
Animals were clipped free of hair on dorsal and lateral surfaces at least 3 hours prior to application.

Test material suspensions stored using magnetic stirrer immediately before application. 0.5ml 75% test material in aqua bidest applied to clipped animals (75% test m. in aqua bidest) on left flanks & covered with 2x2 cm gauze patches, which were secured using 4x4cm² subdermal linear patches. Six hour exposure - This procedure repeated at weekly intervals to total 3 applications, using the same induction site. After 3rd induction application, animals rested two weeks.

Induced and naive control animals (20/10 respectively) were challenged 2 weeks after last induction application, using 75% test material in aqua bidest. Challenge applications to right flanks (naive sites). All induction and challenge applications scored 2+ and 4+ hours after application - Challenge exposures for 6 hours.

Results:

1) Ted group, 1st induction - scores 0.0. 2nd induction 1/20 animals 1.0 for Erythema. 3rd induction 4/20 animals 1.0 ER, 2/20 animals 2.0 score, 2/20 ER 2.0, 2/20 - 1.0 for ED. (7/20 animals showed response following 3rd induction.)

Challenge - 1st Control group - 10 animals (challenged at same site on right side) - 0.00 scoring.
 (Challenge only) - 8 animals challenged using 75% t.m. and disposed in aqua bidest. (0.0 24 & 48 hrs)

Challenge - test material - animals inhaled and challenged with 75% t.m. in aqua bidest.
 0.0 scoring for 24 and 48 hour scoring intervals - 20 animals.

A positive control study was conducted using chloroacetophenone: (DNCB)

1st induction using DNCB 1% in ethanol well defined erythema & slight edema in 2/20 animals, 9/20 animals showed very slight erythema & edema. Ethanol vehicle control caused slight erythema in one animal in control. Conc. of test material (DNCB), reduced to 0.5%. 2nd induction, 5/20 animals well defined erythema & slight edema. Conc. of test mat. in 3rd induction reduced to 0.2%. - After 3rd induction 7/20 animals well defined erythema. Very slight erythema in 13 of 20 test an. : 0.2% in EtOH

	0.2% in EtOH	EtOH Cont.
Cont. group 1	0/10	0/10
Cont. group 2		0/10
Test group	16/20	0/20

Conclusions

1. DNFB positive control animals were sensitized.

2) Animals indeed was challenged with test material were not sensitized.

Tox Chem. No.

File Last Updated

Current date

325A - Dichloro-8-guandine Carboxylic acid 1-26-93

Study/Species/Lab/Study# - Date	Material	MRID No.	Results	Tox. Cat.	Core Grade
acute oral LD50, Rat BASF AG Dept. of Tox, FRG 92/10035 1-16-92	Facet 75 DF Methicide	424933 -05	LD50 > 2200 mg/Kg	III	Guide line
acute dermal LD50, Rat BASF 92/10096 1-28-92	"	424933 -06	LD50 > 2000 mg/Kg	III	Guide line
acute inhalation LC50 BASF 92/10105 2-5-92	"	424933 -07	LC50 > 6.06 mg/L	IV	Guide line
eye irritation, Rabbit BASF 91/11005 10-29-91	"	424933 -08	Irritation absent by 7 days	III	Guide line
skin irritation, Rabbit BASF 91/11006 10-29-91	"	424933 -09	Moderate irritation at 22 hrs	III	Guide line
skin sensitization, guinea P BASF 92/10036 1-16-92	"	424933 -10	test mat. did not sensitize guinea pigs	-	Guide line

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