4-26-91

MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 524-ULE

Roundup Quik Stik Grass and Weed Killer

FROM: Mark J. Perry MJP 4.15.91
Precautionary Review Section
Registration Support Branch
Registration Division (H75-05C)

E 4/26/91

TO: Robert Taylor (PM 25)
Edward Allen
Registration Division (H75-05C)

APPLICANT: Monsanto Company
700 14th Street, N.W., #1100
Washington, D.C. 20005

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Glyphosate N-(phosphanomethyl)-glycine	60.0%
Inert Ingredient(s):	40.0%
Total	100.0%

BACKGROUND: The Monsanto Company has submitted acute oral toxicity, acute dermal toxicity, primary eye irritation, dermal irritation, and dermal sensitization studies for review. All studies were conducted by WIL Research Laboratories, Inc. The product name is Roundup Quik Stik Grass and Weed Killer and the active ingredient is Glyphosate, N-(phosphonomethyl)-glycine. The MRID numbers are 417627-01 to 417627-05. The requirement for an inhalation study has been waived by Van Seabaugh on 8-9-90, due to the products packaging, usage, and formulation.

RECOMMENDATION: All five studies were found acceptable as core guideline data.

Acute Toxicity Profile:

study	Tox Cat	Grade
Acute Oral Tox	IV	Guideline
Acute Dermal Tox	IV	Guideline
Eye Irritation	IV	Guideline
Dermal Irritation	IV	Guideline
Dermal Sensitization	not a sensitizer	Guideline

Label:

1) The appropriate signal word is "CAUTION"

2) The precautionary statements have been found acceptable.

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

Product Manager: (25)
MRID No.: 417627-01
Testing Facility: WIL Research Labs., Inc.
Author(s): G.R. Kiplinger
Species: Rat, albino
Age: Young Adult
Weight: 234-288g
Source: Charles River Portage, Mich
Test Material: MON 35035 (Lot No. PIT-9009-2499F) 60% glyphosate
Quality Assurance (40 CFR §160.12): Yes

Reviewer: M. Perry
Report Date: 4-12-91
Report No. WI-90-483/WIL-50191

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

Conclusion:

1. LD_{50} (mg/kg): Males = > 5,000 mg/Kg ; Females = > 5,000 mg/kg ; Combined =
2. The estimated LD_{50} is > 5,000 mg/Kg
3. Tox. Category: IV. Classification: Core Guideline

Procedure (~~Deviations From §81-1~~): The animals were fasted 18-20 hours prior to dosing of test material at a volume of 10ml/Kg bodyweight. The test material was administered by

Results:

Reported Mortality

DOSAGE (mg /kg)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
5,000	0/5	0/5	0/10

~~Symptomology & Gross Necropsy Findings~~:

gastric intubation. The animals were observed at 1, 3, and 4 hours post-dose on day 0 and twice per day thereafter for 14 days. Body weights were recorded on study days 0, 7, and 14. All animals gained weight during the study. Clinical finding included abnormal defecation, urogenital staining and hypo-activity. No abnormalities were revealed upon necropsy.

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

Product Manager: (25)
MRID No.: 417627-02
Testing Laboratory: W.I.L. Research Labs., Inc.
Author(s): G.R. Kiplinger
Species: Rat
Sex: 5 ♂, 5 ♀ Wt.: 264-298g
Test Material: MON 35035 (Lot No.: PIT 9009-2499F) 60% glyphosate
Quality Assurance (40 CFR §160.12): Yes

Reviewer:- M. Perry
Report Date: 4-12-91
Report No. WI-90-483/WIL-50192

Summary:

1. LD_{50} (mg/kg): Males = >5,000mg/Kg; Females = >5,000mg/kg; Combined = ____
2. The estimated LD_{50} is >5,000 mg/Kg
3. Tox. Category: IV. Classification: Core Guideline

Procedure ~~(Deviations From §81-2)~~: The moistened test material was applied to the clipped backs of the test animals. The application sites were wrapped with semi-occlusive material and the animals were placed in collars during the 24 hour exposure period.

Results:

Reported Mortality

DOSAGE (mg /kg)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
5,000	0/5	0/5	0/10

~~Symptomology & Gross Necropsy Findings:~~

After the exposure period the application sites were wiped clean with towels. The animals were observed at 1, 3, and 4 hours post dosing (exposure) and twice per day thereafter for 14 days. Body weights were recorded on days 0, 7, and 14. All animals gained weight during the study. Clinical findings included dried red material around the eyes and ears, and urogenital

staining. Necropsy revealed reddened cortico-medullary junction in both kidneys of one female test animal. No other significant changes were observed during necropsy.

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

Product Manager: (25)
MRID No.: 417627-03
Testing Laboratory: WIL Research Labs., Inc.
Author(s): GR Kiplinger
Species: Rabbit, albino
Sex: 3♀, 3♂ Weight: 2740-3213g
Source: Hazleton Res. Prod., Inc.
Dosage: 46mg
Test Material: MON 35035 (Lot No. PIT 9009-2499F) 60% glyphosate
Quality Assurance (40 CFR §160.12): yes

Reviewer: M. Perry
Report Date: 4-12-91
Report No. WI-90-483/WIL-50194

Summary:

Tox. Category: IV Classification: Core Guideline

Procedure ~~(Deviation From §81-4)~~: Doses of 46mg of test material was placed into the right conjunctival sacs of the six test animals. Following instillation the eyes were held closed for approximately one second. The eyes were examined

Results:

	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	1/6	0/6	0/6	0/6				
Conjunctivae Redness	2/6	0/6	0/6	0/6				
Chemosis	2/6	0/6	0/6	0/6				
Discharge	3/6	0/6	0/6	0/6				

~~Comments~~: for reactions at 1, 24, 48, 72, and 96* hours after dosing. Observations were made with the aid of a penlight and fluorescein (at 72 hrs).

* If irritation persisted

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

Product Manager: (25)
MRID No.: 417627-04
Testing Laboratory: WIL Res. Labs., Inc.
Author(s): G.R. Kiplinger
Species: Rabbit, albino
Age: Young Adult
Sex: 4♂, 2♀
Weight: 2112-2328g
Dosage: 0.5g
Test Material: MON 35035 (Lot No. PIT 9009-2499F) 60% glyphosate
Quality Assurance (40 CFR §160.12): yes

Reviewer: M. Perry
Report Date: 4-12-91
Report No. WI-90-483/WIL-50193

Summary:

The Primary Irritation Index = 0

Toxicity Category: IV

Classification: Core Guideline

Procedure ~~(Deviations From §81-5)~~: Doses of 0.5g of test material were moistened and applied to the clipped backs of the test animals. The application sites were covered with semi-occlusive material and the animals were placed in collars during the 4th hour exposure period. After the exposure period the sites were wiped with moist paper towels. The exposure sites were examined at 0.5-1, 24, 48, and 72 hours after semi-occlusive wrap removal. No dermal irritation was observed upon exposure site examinations.

~~Results:~~

Special Comments:

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

Product Manager: (25)
MRID No.: 417627-05
Testing Laboratory: WIL Research Labs., Inc.
Author(s): G.R. Kiplinger
Species: Guinea Pigs, albino
Sex: 5♀, 5♂ (test)/5♀, 5♂ (control) Weight: 326-398g
Source: Murphy Breeding Labs., Inc.
Test Material: MON 35035 (Lot No. PIT-9009-2499F) 60% glyphosate
Positive Control Material: [redacted] DNCB
Quality Assurance (40 CFR §160.12): Yes

Reviewer: M. Perry
Report Date: 4-12-91
Report No. WI-90-483/WIL-50195

Method: Buehler

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

Procedure (~~Deviation From §81-6~~): A primary irritation screen resulted in the selection of a 100% concentration of test material for both induction and challenge exposures. The induction exposures consisted of the application of 0.4g

~~Results:~~ of test material (moistened) to a clipped area on the left flanks of 10 test animals (5 male, 5 female). All doses were occluded with plastic wrap and secured with 75 mm of tape. After a 6 hour exposure period all occlusive material was removed and the application sites were washed. This procedure was performed on one day each week for 3 successive weeks. Two weeks after the final induction exposure, 0.4g of moistened test material was applied to a previously unexposed site on the right flanks of the 10 test (induced) animals and 10 naive control animals. All doses were occluded with plastic wrap and secured with 75 mm of tape. After a six hour exposure period all occlusive material was removed and the application sites were washed. Dermal observations were made 24 and 48 hours following the induction and challenge exposures. One dermal

reaction (±) was observed 24 hours following the first induction exposure. No other reactions were detected during the induction phase. No reactions were detected in the test animals (induced) or in the naive control animals during the 24 and 48 hour evaluations of the challenge exposure. The positive control test successfully demonstrated the reliability of the test system.

Tox Chem No: 471 AAB File Last Updated _____ Current Date 4-15-91

Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LD_{50}, LC_{50}, PIS, NOEL, LEL	TOX. Cat.	CORE Grade/ Doc. No.
WIL Research Labs, Inc. Ashland, Ohio 44805-9281					
Acute Oral Toxicity LD50 1-2-91 Rat WI-90-483/WIL-50191	Glyphosate, N-(phosphonomethyl)-glycine (60%)	417627-01	LD50 > 5,000mg/Kg	IV	Guideline
Acute Dermal Toxicity LD50 1-2-91 Rat WI-90-483/WIL-50192	"	417627-02	LD50 > 5,000mg/Kg	IV	Guideline
Primary eye Irritation 1-2-91 Rabbit WI-90-483/WIL-50194	"	417627-03	Very slight irritation clearing in less than 24hrs	IV	Guideline
Primary Dermal Irritation 1-2-91 Rabbit WI-90-483/WIL-50193	"	417627-04	Primary Irritation Index = 0	IV	Guideline
Dermal Sensitization 1-2-91 WI-90-483/WIL-50195 Guinea Pig	"	417627-05	Not a sensitizer		Guideline