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

OFFICE OF
PREVENTION, PESTICIDES
AND
TOXIC SUBSTANCES

17/MAY/2005

MEMORANDUM

Subject:	Name of Pesticide Product:	Roundup Ready-to-Use Poison Ivy & Tough Brush Killer Plus
	EPA Reg. No.:	71995-36
	DP Barcode:	D316639
	Decision No:	355827
	PC Codes:	103601, 116002

From: Eugenia McAndrew, Biologist EM
Technical Review Branch
Registration Division (7505C) RJW

To: Vickie Walters, RM Team 25
Herbicide Branch
Registration Division (7505C)

Applicant: Monsanto Company
800 N. Lindbergh Blvd.
St. Louis, MO 63141

FORMULATION FROM LABEL:

	Active Ingredient(s):	% by wt.
103601	Glyphosate, isopropylamine salt	1.0
116002	Triclopyr, triethylamine salt	0.1
	Inert Ingredient(s):	98.9
	Total:	100.0%

ACTION REQUESTED: "Please review enclosed information to determine if proposed revised basic CSF is supported."

BACKGROUND: Monsanto Company has submitted a six pack of acute toxicity studies to support the registration of a revised basic formulation for Roundup Ready-to-Use Poison Ivy & Tough Brush Killer Plus, EPA Reg. No. 71995-36 (Basic CSF dated 08 March 2005). The studies were conducted at Charles River Laboratories, Inc., Discovery and Development Services, Ohio Division, Spencerville, Ohio with assigned MRID numbers 465176-02 to -07.

The Registrant states that the new formulation will replace the existing basic formulation, "MON 78783." The name of the new formulation is "MON 79244" but one point of confusion is that the new basic CSF (08 March 2005) still lists the name of the product as "MON 78783." The acute toxicity studies submitted were not conducted on "MON 79244" but on a similar formulation, "MON 79799," which contains a greater amount of one inert ingredient and two additional ingredients.

RECOMMENDATIONS: The six studies have been reviewed and are classified as acceptable. They do support registration of the revised basic formulation.

The acute toxicity profile for Roundup Ready-to-Use Poison Ivy & Tough Brush Killer Plus, EPA Reg. No. 71995-36, is as follows:

acute oral toxicity	IV	Acceptable	MRID 46517602
acute dermal toxicity	IV	Acceptable	MRID 46517603
acute inhalation toxicity	IV	Acceptable	MRID 46517604
primary eye irritation	III	Acceptable	MRID 46517605
primary skin irritation	IV	Acceptable	MRID 46517606
dermal sensitization	Negative	Acceptable	MRID 46517607

LABELING: Based on the toxicity profile above, the following are the precautionary and first aid statements for this product as obtained from the Label Review System.

PRODUCT ID #: 071995-00036

PRODUCT NAME: Roundup Ready-To-Use Poison Ivy & Tough Brush Killer Plus

PRECAUTIONARY STATEMENTS

Hazards to Humans and Domestic Animals:

SIGNAL WORD: CAUTION

Causes moderate eye irritation. Avoid contact with eyes or clothing. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco.

First Aid:

If in eyes:
-Hold eye open and rinse slowly and gently with water for 15-20 minutes.
-Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
-Call a poison control center or doctor for treatment advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

Reviewer: Eugenia McAndrew May 17, 2005
Risk Manager: 25

STUDY TYPE: Acute Oral Toxicity - S-D Rat; OPPTS 870.1100; OECD 425

TEST MATERIAL: MON 79799 (Lot No. GLP-0409-1587-F; 1.48% glyphosate acid (a.e.)[2.00% isopropylamine salt of glyphosate] and 0.071% triclopyr acid; clear colorless liquid in pipet, light yellow liquid in bulk)

CITATION: Smedley, J. An Acute Oral Toxicity Study in Rats with MON 79799 (Up/Down Study Design). Charles River Laboratories, Inc. Laboratory Report Number EUF00037. March 3, 2005. MRID 46517602. Unpublished.

SPONSOR: Monsanto Company, 800 N. Lindbergh Blvd., St. Louis, MO 63141

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 46517602), three female young adult Hsd: Sprague-Dawley SD rats (Age: 8-10 weeks; Source: Harlan Sprague Dawley, Inc., Indianapolis, IN; 181-185 g) were given a single oral dose of MON 79799 (Lot No. GLP-0409-1587-F; 1.48% glyphosate acid (a.e.)[2.00% isopropylamine salt of glyphosate] and 0.071% triclopyr acid; clear colorless liquid in pipet, light yellow liquid in bulk) using the Up and Down Procedure. A limit dose of 5000 mg/kg of the test substance was administered to one healthy female rat by oral gavage. Due to the absence of mortality in this animal, two additional female rats were tested at the same level. Animals were then observed for 14 days.

Oral LD_{50} Females > 5000 mg/kg

All animals survived and gained weight during the study. Clinical signs noted included congested breathing in one female on day 0 only. One incidence of foci present on the thymus was noted at gross necropsy. No other gross internal findings were noted.

Toxicity based on the lack of deaths at the limit dose. EPA Toxicity Category IV.

This acute oral study is classified as acceptable. It does satisfy the guideline requirement for an acute oral study (OPPTS 870.1100; OECD 425) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

Individual animals were dosed as follows:

Limit Test

Dosing Sequence	Animal No.	Dose level (mg/kg)	Short Term Outcome	14 Day Outcome
1	A7458	5000	O	O
2	A7510	5000	O	O
3	A7524	5000	O	O

O = survival X = death

Statistics - OECD 425 Acute Oral Toxicity Statistical Program was used for all data analyses

A. Mortality - None

B. Clinical observations - All animals gained weight. Clinical signs noted included congested breathing in one female on day 0 only.

C. Gross Necropsy - One incidence of foci present on the thymus was noted at gross necropsy. No other gross internal findings were noted.

D. Reviewer's Conclusions: We agree with the study author that the acute oral LD_{50} of MON 79799 was determined to be greater than 5000 mg/kg.

Reviewer: Eugenia McAndrew May 17, 2005
Risk Manager: 25

STUDY TYPE: Acute Dermal Toxicity - S-D Rat; OPPTS 870.1200; OECD 402

TEST MATERIAL: MON 79799 (Lot No. GLP-0409-1587-F; 1.48% glyphosate acid (a.e.)[2.00% isopropylamine salt of glyphosate] and 0.071% triclopyr acid; clear colorless liquid in pipet, light yellow liquid in bulk)

CITATION: Smedley, J. An Acute Dermal Toxicity Study in Rats with MON 79799. Charles River Laboratories, Inc. Laboratory Report Number EUF00038. March 3, 2005. MRID 46517603. Unpublished.

SPONSOR: Monsanto Company, 800 N. Lindbergh Blvd., St. Louis, MO 63141

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 46517603), 5/sex of young adult Hsd: Sprague-Dawley SD rats (Age: 10 weeks; Source: Harlan Sprague Dawley, Inc., Indianapolis, IN; 289-312 g males and 211-239 g females) were dermally exposed to MON 79799 (Lot No. GLP-0409-1587-F; 1.48% glyphosate acid (a.e.)[2.00% isopropylamine salt of glyphosate] and 0.071% triclopyr acid; clear colorless liquid in pipet, light yellow liquid in bulk) applied to approximately 10% of body surface area at a dose of 5000 mg/kg. Test sites were covered with a gauze pad and wrapped with an occlusive binding for a 24 hour period. The bindings were then removed and the residual test article was removed. Animals were then observed for 14 days.

Dermal LD_{50} Males > 5000 mg/kg
Dermal LD_{50} Females > 5000 mg/kg
Dermal LD_{50} Combined > 5000 mg/kg

All animals survived the study. Body weight loss was noted in one male and two females during the first week but all animals exceeded initial body weight by the end of the study. Clinical signs noted included transient incidences of few feces and dark material around the facial area. Dermal irritation was present at the site of test substance application. At necropsy, one animal had foci present in the thymus and left lung lobe adhered to the body wall and one animal has cysts present on the uterus. No other gross internal findings were noted.

Toxicity based on the lack of deaths at the limit dose. EPA Toxicity Category IV.

This acute dermal study is classified acceptable. It does satisfy the guideline requirement for an acute dermal study (OPPTS 870.1200; OECD 402) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

Dose (mg/kg bw)	Mortality/Number Tested		
	Males	Females	Combined
5000	0/5	0/5	0/10

A. Mortality - None

B. Clinical observations - Body weight loss was noted in one male and two females during the first week but all animals exceeded initial body weight by the end of the study. Clinical signs noted included transient incidences of few feces and dark material around the facial area. Dermal irritation was present at the site of test substance application.

C. Gross Necropsy - At necropsy, one animal had foci present in the thymus and left lung lobe adhered to the body wall and one animal has cysts present on the uterus. No other gross internal findings were noted.

D. Reviewer's Conclusions: We agree with the study author that the acute dermal LD_{50} of MON 79799 was estimated to be greater than 5000 mg/kg in the rat.

Reviewer: Eugenia McAndrew May 17, 2005
Risk Manager: 25

STUDY TYPE: Acute Inhalation Toxicity -S-D rat; OPPTS 870.1300; OECD 403

TEST MATERIAL: MON 79799 (Lot No. GLP-0409-1587-F; 1.48% glyphosate acid (a.e.)[2.00% isopropylamine salt of glyphosate] and 0.071% triclopyr acid; clear colorless liquid in pipet, light yellow liquid in bulk)

CITATION: Smedley, J. An Acute Nose-Only Inhalation Toxicity Study in Rats with MON 79799. Charles River Laboratories, Inc. Laboratory Report Number EUF00039. February 15, 2005. MRID 46517604. Unpublished.

SPONSOR: Monsanto Company, 800 N. Lindbergh Blvd., St. Louis, MO 63141

EXECUTIVE SUMMARY: In an acute inhalation toxicity study (MRID 46284704), 5/sex of young adult Hsd: Sprague-Dawley SD rats (Age: 11 weeks; Source: Harlan Sprague Dawley, Inc., Indianapolis, IN; 307-336 g males and 216-232 g females) were exposed nose only via the inhalation route to MON 79799 (Lot No. GLP-0409-1587-F; 1.48% glyphosate acid (a.e.) [2.00% isopropylamine salt of glyphosate] and 0.071% triclopyr acid; clear colorless liquid in pipet, light yellow liquid in bulk) for 4 hours at a concentration of 5.20 mg/L. Animals were then observed for 14 days.

LC_{50} Males > 5.20 mg/L
LC_{50} Females > 5.20 mg/L
LC_{50} Combined > 5.20 mg/L

All animals survived. Clinical signs noted included congested breathing in all animals from the day of exposure to day 3. Slight body weight loss was noted in two males and one female during the first week but all animals exceeded initial body weight by the end of the study. At necropsy, one female was noted to have a cyst present on the uterus; no other gross internal findings were noted. The gravimetric chamber concentration was 5.20 mg/L and the mass median aerodynamic diameter was estimated to be 2.2μm with a geometric standard deviation of 1.95.

Toxicity based on lack of deaths at the limit dose. EPA Toxicity Category IV.

This acute inhalation study is classified as acceptable. It does satisfy the guideline requirement for an acute inhalation study (OPPTS 870.1300; OECD 403) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

Nominal Concentration (mg/L)	Gravimetric Concentration (mg/L)	MMAD µm	GSD µm	Mortality/Number Tested		
				Males	Females	Combined
133.40	5.20	2.2	1.95	0/5	0/5	0/10

Test Atmosphere / Chamber Description:

Chamber Volume:	**10 L**
Airflow:	**24 LPM**
Temperature:	**72-73°F**
Relative Humidity:	**71-74%**
Time to Equilibrium:	**3 min.**

A. Mortality - None

B. Clinical observations - Clinical signs noted included congested breathing in all animals from the day of exposure to day 3. Slight body weight loss was noted in two males and one female during the first week but all animals exceeded initial body weight by the end of the study.

C. Gross Necropsy - One female was noted to have a cyst present on the uterus; no other gross internal findings were noted.

D. Reviewer's Conclusions: We agree with the study author that the acute inhalation LD_{50} of MON 79799 was estimated to be greater than 5.20 mg/L in the rat.

Reviewer: Eugenia McAndrew May 17, 2005
Risk Manager: 25

STUDY TYPE: Primary Eye Irritation - NW Rabbit; OPPTS 870.2400; OECD 405

TEST MATERIAL: MON 79799 (Lot No. GLP-0409-1587-F; 1.48% glyphosate acid (a.e.)[2.00% isopropylamine salt of glyphosate] and 0.071% triclopyr acid; clear colorless liquid in pipet, light yellow liquid in bulk)

CITATION: Smedley, J. A Primary Eye Irritation Study in Rabbits with MON 79799. Charles River Laboratories, Inc. Laboratory Report Number EUF00040. March 3, 2005. MRID 46517605. Unpublished.

SPONSOR: Monsanto Company, 800 N. Lindbergh Blvd., St. Louis, MO 63141

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 46517605), 0.1 mL of MON 79799 (Lot No. GLP-0409-1587-F; 1.48% glyphosate acid (a.e.)[2.00% isopropylamine salt of glyphosate] and 0.071% triclopyr acid; clear colorless liquid in pipet, light yellow liquid in bulk) was instilled into the conjunctival sac of the right eye of three adult male New Zealand White rabbits (Source: Myrtle's Rabbitry, Thompson Station, Tennessee). The left eye served as the control. Animals were then observed at 1, 24, 48, 72 hours post-instillation. Irritation was scored by the method of Draize.

Two eyes exhibited iritis and conjunctivitis at the one hour observation. By 24 hours, one eye exhibited corneal opacity. The irritation decreased with time. All eyes were free of irritation by 72 houes.

In this study, formulation is moderately irritating to the eye. EPA Toxicity Category III.

This study is classified as acceptable. It does satisfy the guideline requirement for a primary eye irritation study (OPPTS 870.2400; OECD 405) in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS AND DISCUSSION:

Observations	Number "positive"/number tested			
	Hours			
	1	24	48	72
Corneal Opacity	0/3	1/3	1/3	0/3
Iritis	2/3	1/3	0/3	0/3
Conjunctivae:				
Redness*	0/3	1/3	0/3	0/3
Chemosis*	2/3	1/3	0/3	0/3
Discharge*	0/3	0/3	0/3	0/3

*Score of 2 or more required to be considered "positive."

A. Observations - Two eyes exhibited iritis and conjunctivitis at the one hour observation. By 24 hours, one eye exhibited corneal opacity. The irritation decreased with time. All eyes were free of irritation by 72 hours.

B. Reviewer's Conclusions: We agree with the study author that MON 79799 is considered to be moderately irritating to the ocular tissue of the rabbit.

Reviewer: Eugenia McAndrew May 17, 2005
Risk Manager: 25

STUDY TYPE: Primary Dermal Irritation - NW Rabbit; OPPTS 870.2500; OECD 404

TEST MATERIAL: MON 79799 (Lot No. GLP-0409-1587-F; 1.48% glyphosate acid (a.e.)[2.00% isopropylamine salt of glyphosate] and 0.071% triclopyr acid; clear colorless liquid in pipet, light yellow liquid in bulk)

CITATION: Smedley, J. A Primary Skin Irritation Study in Rabbits with MON 79799. Charles River Laboratories, Inc. Laboratory Report Number EUF00041. March 3, 2005. MRID 46517606. Unpublished.

SPONSOR: Monsanto Company, 800 N. Lindbergh Blvd., St. Louis, MO 63141

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 46517606), three adult New Zealand White male rabbits (Source: Myrtle's Rabbitry, Thompson Station, Tennessee) were dermally exposed to 0.5 mL of MON 79799 (Lot No. GLP-0409-1587-F; 1.48% glyphosate acid (a.e.)[2.00% isopropylamine salt of glyphosate] and 0.071% triclopyr acid; clear colorless liquid in pipet, light yellow liquid in bulk). The test substance was applied to a 1 inch by 1 inch dose site on the dorsal area of each animal. Test sites were covered with a gauze pad, secured with tape and wrapped with a semi-occlusive binding for a 4 hour period. The binding materials were then removed and the residual test article was removed. Animals were then observed at 1, 24, 48 and 72 hours after patch removal. Irritation was scored by the method of Draize.

In this study, formulation is essentially nonirritating. EPA Toxicity Category IV.

Primary Dermal Irritation Index (PDII) = 0.17 One hour after patch removal, very slight erythema was noted at one test site. The irritation resolved by 24 hours and no other irritation was noted.

This study is classified as acceptable. It does satisfy the guideline requirement for a primary dermal irritation study (OPPTS 870.2500; OECD 404) in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

A. Observations - One hour after patch removal, very slight erythema was noted at 2/3 test sites. The irritation resolved by 24 hours and no other irritation was noted.

B. Results - PDII - 0.17

C. Reviewer's Conclusions - We agree with the study author that MON 79799 is considered to be essentially nonirritating to the skin of the rabbit.

Reviewer: Eugenia McAndrew May 17, 2005
Risk Manager: 25

STUDY TYPE: Dermal Sensitization - Guinea Pig; OPPTS 870.2600; OECD 406

TEST MATERIAL: MON 79799 (Lot No. GLP-0409-1587-F; 1.48% glyphosate acid (a.e.)[2.00% isopropylamine salt of glyphosate] and 0.071% triclopyr acid; clear colorless liquid in pipet, light yellow liquid in bulk)

CITATION: Smedley, J. A Dermal Sensitization Study in Guinea Pigs with MON 79799 (Modified Buehler Design). Charles River Laboratories, Inc. Laboratory Report Number EUF00042. March 3, 2005. MRID 46517607. Unpublished.

SPONSOR: Monsanto Company, 800 N. Lindbergh Blvd., St. Louis, MO 63141

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 46517607) with MON 79799 (Lot No. GLP-0409-1587-F; 1.48% glyphosate acid (a.e.)[2.00% isopropylamine salt of glyphosate] and 0.071% triclopyr acid; clear colorless liquid in pipet, light yellow liquid in bulk), 30 young adult male Hartley-derived albino guinea pigs (Age 6-8 weeks; Source: Hilltop Lab Animals, Inc., Scotttdale, PA; 310-372 g males and 337-400 g females) were tested using a modified Buehler design. The procedures were validated using alpha-Hexylcinnamaldehyde, technical grade (85% HCA) as the positive control substance.

Once each week for three weeks, 0.3 mL of undiluted test substance was applied to the left side of 20 test animals for a 6-hour exposure period for a total of three exposures. Twenty-seven days after the first induction, 0.3 mL of undiluted test substance (the highest non-irritating concentration) was applied to a naive site on each test animal for a 6-hour challenge exposure. Ten naive control guinea pigs were also treated with the undiluted test substance at challenge only. Readings were made 24 and 48 hours after each induction application and after the challenge application.

In this study, the formulation is not a dermal sensitizer.

Slight patchy erythema (±) was noted at 8/20 test animal sites during the induction phase. Following the challenge, no dermal irritation was noted at either the test or naive control animal sites. The results of the HCA positive control study were appropriate to validate test procedures.

This study is classified as acceptable. It does satisfy the guideline requirement for a dermal sensitization study (OPPTS 870.2600; OECD 406) in the Guinea pig .

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. PROCEDURE

A. Induction - Once each week for three weeks, 0.3 mL of undiluted test substance was applied to the left side of 20 test animals for a 6-hour exposure period for a total of three exposures. The animals rested for two weeks. Readings were made 24 and 48 hours after each induction application.

B. Challenge - Twenty-seven days after the first induction, 0.3 mL of undiluted test substance (the highest non-irritating concentration) was applied to a naive site on each test animal for a 6-hour challenge exposure. Readings were made 24 and 48 hours after the challenge application.

C. Naive Controls - Ten naive control guinea pigs were also treated with the undiluted test substance at challenge only.

II. RESULTS and DISCUSSION:

A. Reactions and duration - Slight patchy erythema (±) was noted at 8/20 test animal sites during the induction phase. Following the challenge, no dermal irritation was noted at either the test or naive control animal sites.

B. Positive control - Results were appropriate to validate test procedures.

C. Reviewer's Conclusions: We agree with the study author that MON 79799 is not considered to be a contact sensitizer in guinea pigs.

ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D316639
2. **PC CODES:** 103601, 116002
3. **CURRENT DATE:** 17/MAY/2005
4. **TEST MATERIAL:** MON 79799 (Lot No. GLP-0409-1587-F; 1.48% glyphosate acid (a.e.)[2.00% isopropylamine salt of glyphosate] and 0.071% triclopyr acid; clear colorless liquid in pipet, light yellow liquid in bulk)

Study/Species/Lab Study # /Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat Charles River Laboratories, Inc. EUF00037/3-3-05	46517602	LD_{50} females > 5000 mg/kg	IV	A
Acute dermal toxicity/rat Charles River Laboratories, Inc. EUF00038/3-3-05	46517603	LD_{50} > 5000 mg/kg (males, females combined)	IV	A
Acute inhalation toxicity/rat Charles River Laboratories, Inc. EUF00039/2-15-05	46517604	LC_{50} > 5.20 mg/L (males females combined)	IV	A
Primary eye irritation/rabbit Charles River Laboratories, Inc. EUF00040/3-3-05	46517605	Corneal opacity, iritis and conjunctivitis resolving by 72 hours.	III	A
Primary dermal irritation/rabbit Charles River Laboratories, Inc. EUF00041/3-3-05	46517606	PDII = 0.17 Minimal irritant	IV	A
Dermal sensitization/guinea pig Charles River Laboratories, Inc. EUF00042/3-3-05	46517607	Not a sensitizer	–	A

Core Grade Key: **A =Acceptable, S = Supplementary, U = Unacceptable, W = Waived**