US EPA ARCHIVE DOCUMENT

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

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

31/JAN/2007

MEMORANDUM

Subject: Name of Pesticide Product: RD 1653 Herbicide
EPA File Symbol: 71995-47
DP Barcode: 334573
Decision No: 371313
PC Codes: 103601 Glyphosate, isopropylamine salt
128840 Imazapic, ammonium salt
217500 Pelargonic acid and related fatty acids

From: Tracy Keigwin
Technical Review Branch
Registration Division (7505C)

To: Vickie Walters
Herbicide Branch
Registration Division (7505C)

Applicant: Monsanto Company, Lawn & Garden Products
1300 I (Eye) Street, NW., Suite 450 East
Washington DC 20005

FORMULATION FROM THE LABEL:

Active Ingredient(s):	% by wt.
Glyphosate, isopropylamine salt	1.000
Imazapic, ammonium salt	0.017
Pelargonic acid and related fatty acids	2.000
Inert Ingredient(s):	96.983
Total:	100.000%

ACTION REQUESTED: PM requests review of acute toxicity in support of RD 1653 Herbicide, EPA Reg. No. 71995-47.

BACKGROUND: Monsanto Company, Lawn & Garden Products has developed a new formulation of their product RD 1653, EPA Reg. No. 71995-47. The company has submitted two new Alternate Confidential Statements of Formula (CSFs) which represent this change – these being Alternate Formulations D (dated 13 September 2006) and Alternate Formulation E (dated 9 October 2006), respectively. In support of the formulation change the company has submitted 6 new acute toxicity studies (MRIDs 46960302, 46976001, 46960304, 46960305, 46960306, and 46960307). A letter from the company states that the Alternate formulation "D" CSF is the same as the Alternate formulation "B" CSF (approved on 11/14/05) with the exception of a change in one inert ingredient and an additional source of another inert ingredient. Alternate formulation "E" is identical to Alternate formulation "D" with the exception that one inert ingredient has been removed from the formulation.

The subject product is a residential use herbicide containing the isopropylamine salt of glyphosate, the ammonium salt of imazapic, and "pelargonic acid and related fatty acids" as the active ingredients. The studies were conducted at Charles River Laboratories, Inc., Spencerville, Ohio 45887.

OF NOTE: The test substance used in the 6 submitted studies is not "Alternate formulation D" (MON 79823), but a similar formulation (MON 79851) which contains slightly higher concentrations of glyphosate and one other inert ingredient. TRB agrees that MON 79823 and MON 79851 are similar enough that the test substance used in the submitted studies (MON 79851) will give an indicative acute toxicity profile of "Alternate formulation D" (MON 79823).

RECOMMENDATIONS: The studies submitted by Monsanto Company, Lawn & Garden Products are acceptable. However, use of these studies would result in an acute toxicity profile different from the original acute toxicity profile for this product. When EPA Reg. No. 71995-47 was registered, it relied on the acute toxicity data that was originally submitted in support of EPA Reg. No. 241-425 (MRIDs 45814302 – 45814307). At that time, the registrant stated that EPA Reg. No. 71995-47 was identical to EPA Reg. No. 241-425 with the exception that pelargonic acid was being designated as an active ingredient for EPA Reg. No. 71995-47.

The original acute toxicity profile for EPA Reg. No. 71995-47, based on these cited MRIDs (MRIDs 45814302 – 45814307) is as follows:

acute oral toxicity	IV	Acceptable	MRID 45814302
acute dermal toxicity	IV	Acceptable	MRID 45814303
acute inhalation toxicity	IV	Acceptable	MRID 45814304
primary eye irritation	IV	Acceptable	MRID 45814305
primary skin irritation	IV	Acceptable	MRID 45814306
dermal sensitization	NO	Acceptable	MRID 45814307

The acute toxicity profile for EPA Reg. No. 71995-47, Alternates D and E, based on the submitted data using MON 79851 as the test substance is as follows:

acute oral toxicity	IV	Acceptable	MRID 46960302
acute dermal toxicity	IV	Acceptable	MRID 46976001
acute inhalation toxicity	IV	Acceptable	MRID 46960304
primary eye irritation	III	Acceptable	MRID 46960305
primary skin irritation	IV	Acceptable	MRID 46960306
dermal sensitization	NO	Acceptable	MRID 46960307

TRB will not accept an Alternate formulation that would result in a different acute toxicity profile from the Basic formulation. Additionally, per 40 CFR 152.43 (3), the label text of the alternate formulation product must be identical to that of the basic formulation. The alternate formulation proposed by the registrant would result in different precautionary label language. We understand that the registrant has previously included voluntary primary eye irritation precautionary language on the current product label (stamped January 26, 2006), however, this language is voluntary because the product is category IV for primary eye irritation. It would be mandatory for what the registrant has proposed as alternate formulations.

TRB is recommending that the registrant submit Alternate formulations D and E as a new product for registration. They will not be acceptable as alternate formulations for EPA Reg. No. 71995-47.

NOTE PRODUCT BRANCH REVIEWER: If the registrant chooses to submit the formulations used in Alternates "D" and "E" as a new product please route the

submission to TRB so that we may provide you with the appropriate precautionary labeling and verify what the registrant has proposed.

A NOTE REGARDING THE FOLLOWING ACUTE TOXICITY DATA

The following acute toxicity data was submitted by Monsanto Company, Lawn & Garden Products in support of proposed alternate formulations "D" (dated 13 September 2006) and "E" (dated 9 October 2006) for EPA Reg. No. 71995-47. This data is not acceptable for consideration as an Alternate formulation of the subject product. It would be acceptable to support a new product.

DATA EVALUATION RECORD

Reviewer: Tracy Keigwin January 24, 2007
Product Manager (EPA): 25

STUDY TYPE: Acute Oral Toxicity - Sprague-Dawley rat; OPPTS 870.1100; OECD 425

TEST MATERIAL (% a.i.): MON 79851; Lot No. GLP-0603-16960-F; Purity: 1.46% glyphosate a.e (1.97% isopropylamine salt of glyphosate), 0.016% imazapic acid, 1.87% pelargonic acid; Clear, colorless liquid(via pipette), pale yellow liquid (bulk).

CITATION: Smedley, J. An Acute Oral Toxicity Study in Rats with MON 79851 (Up/Down Study Design). OPPTS 870.1100. Study No. EUF00125; Monsanto Study No. CRO-2006-025. Charles River Laboratories, Spencerville, Ohio. August 10, 2006. MRID 46960302. Unpublished

SPONSOR: Monsanto Company, 800 N. Lindbergh Blvd., St. Louis, MO 63167

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 46960302), 3 female Hsd: Sprague Dawley® SD® rats (Source: Harlan Sprague Dawley, Inc., Indianapolis, Indiana; Age: 9 weeks; Weight: 171-187g) were given a single oral dose of MON 79851; Lot No. GLP-0603-16960-F; Purity: 1.46% glyphosate a.e (1.97% isopropylamine salt of glyphosate), 0.016% imazapic acid, 1.87% pelargonic acid; Clear, colorless liquid(via pipette), pale yellow liquid (bulk) using the Up and Down Procedure. The selected dose was 5000 mg/kg. Animals were inspected for clinical abnormalities at least twice on study day "0" and daily thereafter for 14 days. Bodyweights were obtained prior to fasting (day -1), prior to dosing (day 0), and on days 7 and 14. A necropsy examination was performed on all test animals.

No mortality occurred during the study. A single incidence of congested breathing was noted in one animal. All animals gained weight throughout the observation period.

No gross abnormalities were observed at necropsy.

The Oral LD_{50} is greater than 5000 mg/kg. 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:
Limit Test

Dosing Sequence	Animal ID	Dose level (mg/kg)	Short Term Outcome	Long Term Outcome
1	A5921	5000	S	S
2	A6004	5000	S	S
3	A6005	5000	S	S

S = survival D = death

Statistics - Acute Oral Toxicity (Guideline 425) Statistical Program (Westat, version 1.0, May 2001) was used for all data analyses including: dose progression selections, stopping criteria determinations and/or LD_{50} and confidence limit calculations.

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AOT425statpgm (Version: 1.0) Test Results and Recommendations
Acute Oral Toxicity (OECD Test Guideline 425) Statistical
Program

Test/Substance: MON 79851
Test type: Limit Test
Limit dose (mg/kg): 5000
Assumed LD50 (mg/kg): Default
Assumed sigma (mg/kg): 0.5
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DATA:

Test Seq.	Animal ID	Dose (mg/kg)	Short-term Result	Long-term Result
1	A5921	5000	O	O
2	A6004	5000	O	O
3	A6005	5000	O	O

(X = Died, O = Survived)

Dose Recommendation: The limit test is complete.

SUMMARY OF LONG-TERM RESULTS:

Dose	O	X	Total
5000	3	0	3
All Doses	3	0	3

Statistical Estimates:

The LD50 is greater than 5000 mg/kg.

A. Mortality - As listed above.

B. Clinical observations – No mortality occurred during the study. A single incidence of congested breathing was noted in one animal. All animals gained weight throughout the observation period.

C. Gross Necropsy – No gross abnormalities were observed at necropsy.

D. Reviewers Conclusions: Agree with study author that the acute LD_{50} for this product is greater than 5000 mg/kg.

E. Deficiencies - None.

DATA EVALUATION RECORD

Reviewer: Tracy Keigwin
Product Manager (EPA): 25

January 24, 2007

STUDY TYPE: Acute Dermal Toxicity - Sprague Dawley Rats; OPPTS 870.1200; OECD 402

TEST MATERIAL (% a.i.): MON 79851; Lot No. GLP-0603-16960-F; Purity: 1.46% glyphosate a.e (1.97% isopropylamine salt of glyphosate), 0.016% imazapic acid, 1.87% pelargonic acid; Clear, colorless liquid(via pipette), pale yellow liquid (bulk).

CITATION: Smedley, J. An Acute Dermal Toxicity Study in Rats with MON 79851. OPPTS 870.1200. Study No. EUF00126; Monsanto Study No. CRO-2006-026. Charles River Laboratories, Spencerville, Ohio. August 11, 2006. MRID 46976001. Unpublished

SPONSOR: Monsanto Company, 800 N. Lindbergh Blvd., St. Louis, MO 63167

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 46976001), 5 male and 5 female Hsd: Sprague Dawley® SD® rats (Source: Harlan Sprague Dawley, Inc., Indianapolis, Indiana; Age: 9 weeks; Weight: males 291-316g, females 182-196g) were dermally exposed to MON 79851; Lot No. GLP-0603-16960-F; Purity: 1.46% glyphosate a.e (1.97% isopropylamine salt of glyphosate), 0.016% imazapic acid, 1.87% pelargonic acid; Clear, colorless liquid(via pipette), pale yellow liquid (bulk), at a dose level of 5000 mg/kg bw. On the day prior to study initiation fur was removed from the dorsal trunk area with animal clippers. This test area represented approximately 10% of the animals' body surface area. On study day "0" the test substance was evenly applied to the test area and covered with occlusive dressing. The entire trunk and test area was then wrapped with elastic wrap to prevent removal or ingestion of the test substance. "The elastic wrap was secured with a tape harness on the cranial end of the trunk and then secured with adhesive tape around the trunk at the caudal end." After 24 hours all binding materials were removed. Test areas were wiped with a moistened gauze and then a dry gauze to remove any residual test substance. Animals were observed for erythema and edema after patch removal and daily thereafter. Animals were observed for clinical abnormalities at least twice on study day "0" and daily thereafter until study termination. Animals were checked for mortality twice daily (AM and PM).

Bodyweights were taken prior to test substance administration on day "0" and again on days 7 and 14.

No mortalities were observed during the study. "Clinical abnormalities observed during the study included transient incidences of dark material around the facial area. An additional finding of ocular lesion(s) was noted in one female animal. Dermal irritation was noted at the site of test article application on one male and three female animals. Slight bodyweight loss was noted in one female animal, during the day 0 to 7 body weight interval. Body weight gain/maintenance was noted for all other animals during the test period."

No gross abnormalities were observed at necropsy.

Dermal LD_{50} >5000 mg/kg bw (both sexes)

Toxicity based on the lack of mortality observed at the 5000 mg/kg dose level. 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 - as noted in table.

B. Clinical observations – No mortalities were observed during the study. "Clinical abnormalities observed during the study included transient incidences of dark material around the facial area. An additional finding of ocular lesion(s) was noted in one female animal. Dermal irritation was noted at the site of test article application on one male and three female animals. Slight bodyweight loss was noted in one female animal, during the day 0 to 7 body weight interval. Body weight gain/maintenance was noted for all other animals during the test period."

C. Gross Necropsy – No gross abnormalities were observed at necropsy

D. Reviewers Conclusions: Agree with study author that the dermal LD_{50} for this product is greater than 5000 mg/kg.

E. Deficiencies: None

Reviewer: Tracy Keigwin
Product Manager (EPA): 25

January 24, 2007

STUDY TYPE: Acute Inhalation Toxicity - Rat; OPPTS 870.1300; OECD 403

TEST MATERIAL (% a.i.): MON 79851; Lot No. GLP-0603-16960-F; Purity: 1.46% glyphosate a.e (1.97% isopropylamine salt of glyphosate), 0.016% imazapic acid, 1.87% pelargonic acid; Clear, colorless liquid(via pipette), pale yellow liquid (bulk).

CITATION: Smedley, J. An Acute Nose-Only Inhalation Toxicity Study in Rats with MON 79851. OPPTS 870.1300. Study No. EUF00127; Monsanto Study No. CRO-2006-027. Charles River Laboratories, Spencerville, Ohio. September 7, 2006. MRID 46960304. Unpublished

SPONSOR: Monsanto Company, 800 N. Lindbergh Blvd., St. Louis, MO 63167

EXECUTIVE SUMMARY: In an acute inhalation toxicity study (MRID 46960304), 5 male and 5 female Hsd: Sprague Dawley® SD® rats (Source: Harlan Sprague Dawley, Inc., Indianapolis, Indiana; Age: males 10 weeks, females 9 weeks; Weight: males 314-335g, females 202-219g) were exposed via the inhalation route to MON 79851; Lot No. GLP-0603-16960-F; Purity: 1.46% glyphosate a.e (1.97% isopropylamine salt of glyphosate), 0.016% imazapic acid, 1.87% pelargonic acid; Clear, colorless liquid(via pipette), pale yellow liquid (bulk) at a concentration of 2.43 mg/L (gravimetrically determined). Animals were observed for clinical signs during exposure, at least twice on study day "0" and daily thereafter until study termination. Bodyweights were recorded prior to exposure and again on study days 7 and 14. A necropsy examination was performed on all test animals.

No mortality was observed during the study. Clinical abnormalities observed included dark material around the facial area. All animals gained weight throughout the observation period.

No gross abnormalities were observed at necropsy.

LC_{50} Males => Greater than 2.43 mg/L (0/5 males died)
LC_{50} Females => Greater than 2.43 mg/L (0/5 females died)
LC_{50} Combined => Greater than 2.43 mg/L (0/10 died)

Toxicity based on the lack of mortality in both the male and female rat at the 2.43 mg/L exposure. 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:

Exposure (mg/L)	Mortality/Number Tested		
	Males	Females	Combined
2.43	0 / 5	0 / 5	0 / 10

Nominal Concentration (mg/L)	Gravimetric Concentration (mg/L)	MMAD µm	GSD
400.07	2.43	2.4	2.37

Test Atmosphere / Chamber Description:

Gravimetric Concentration (mg/L)	Chamber Volume (L)	Airflow (LPM)	Temperature (F)	Relative Humidity (%)
2.43	10	23	70.4 - 73.6	72.5-78.6

A. Mortality - as noted in table.

B. Clinical observations - No mortality was observed during the study. Clinical abnormalities observed included dark material around the facial area. All animals gained weight throughout the observation period.

C. Gross Necropsy – No gross abnormalities were observed at necropsy.

D. Reviewers Conclusions: TRB agrees with the study author that the test substance has an LC_{50} greater than 2.43 mg/L.

E. Deficiencies – The study states the following: "The animal room temperature range [65-73 °F (18-23 °C)] exceeded the preferred range [66-77 °F (19-25 °C) during the study. This occurrence was considered to have had no adverse effect on the study outcome."

DATA EVALUATION RECORD

Reviewer: Tracy Keigwin
Product Manager (EPA): 25

January 24, 2007

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

TEST MATERIAL (% a.i.): MON 79851; Lot No. GLP-0603-16960-F; Purity: 1.46% glyphosate a.e (1.97% isopropylamine salt of glyphosate), 0.016% imazapic acid, 1.87% pelargonic acid; Clear, colorless liquid(via pipette), pale yellow liquid (bulk).

CITATION: Smedley, J. A Primary Eye Irritation Study in Rabbits with MON 79851. Study No. EUF00128; Monsanto Study No. CRO-2006-028. Charles River Laboratories, Spencerville, Ohio. August 9, 2006. MRID 46960305. Unpublished

SPONSOR: Monsanto Company, 800 N. Lindbergh Blvd., St. Louis, MO 63167

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 46960305), 0.1 ml of undiluted MON 79851; Lot No. GLP-0603-16960-F; Purity: 1.46% glyphosate a.e (1.97% isopropylamine salt of glyphosate), 0.016% imazapic acid, 1.87% pelargonic acid; Clear, colorless liquid(via pipette), pale yellow liquid (bulk) was instilled into the conjunctival sac of the right eye of 2 males and 1 female New Zealand White rabbits (source: Myrtle's Rabbitry, Thompson Station, Tennessee; Age: 15 weeks; Weight: males 2.9-3.4 kg, female 4.0 kg). Following instillation the eyelids were held together for one second to limit any test substance loss. The left eye remained untreated to serve as a control. Animals were observed at 1, 24, 48 and 72 hours and up to 7 days following instillation for signs of irritation. Following macroscopic observations at the 24 hour scoring interval, a fluorescein examination procedure was conducted and any remaining test substance was rinsed from the eye with physiological saline. Health and mortality checks were taken twice daily (AM and PM). Bodyweights were taken prior to test substance instillation.

No corneal opacity was observed during the study. Iritis was observed in 3/3 animals at the 1 hour observation, clearing within 24 hours. Positive signs of conjunctivitis were observed in 3/3 animals at the 1 hour observation, clearing in 1/3 animals within 24

hours and clearing within 48 hours in the remaining 2/3 animals. 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:

	Hours				Days
Observations	1	24	48	72	7
Corneal Opacity	0/3	0/3	0/3	0/3	0/3
Iritis	3/3	0/3	0/3	0/3	0/3
Conjunctivae:					
Redness [a]	3/3	2/3	0/3	0/3	0/3
Chemosis [a]	3/3	1/3	0/3	0/3	0/3
Discharge [a]	3/3	1/3	0/3	0/3	0/3

[a] Score of 2 or more required to be considered a positive.

A. **Observations** - No corneal opacity was observed during the study. Iritis was observed in 3/3 animals at the 1 hour observation, clearing within 24 hours. Positive signs of conjunctivitis were observed in 3/3 animals at the 1 hour observation, clearing in 1/3 animals within 24 hours and clearing within 48 hours in the remaining 2/3 animals. Please note that the study does record additional signs of conjunctivitis, however the scores (grade 1) are not considered positive per 870.2400.

B. **Reviewers Conclusions:** Agree with the study author that this product is moderately irritating to the eye.

C. **Deficiencies** - None

DATA EVALUATION RECORD

Reviewer: Tracy Keigwin
Product Manager (EPA): 25

January 24, 2007

STUDY TYPE: Primary Dermal Irritation - New Zealand White rabbit; OPPTS 870.2500; OECD 404

TEST MATERIAL (% a.i.): MON 79851; Lot No. GLP-0603-16960-F; Purity: 1.46% glyphosate a.e (1.97% isopropylamine salt of glyphosate), 0.016% imazapic acid, 1.87% pelargonic acid; Clear, colorless liquid(via pipette), pale yellow liquid (bulk).

CITATION: Smedley, J. A Primary Skin Irritation Study in Rabbits with MON 79851. Study No. EUF00129; Monsanto Study No. CRO-2006-029. Charles River Laboratories, Spencerville, Ohio. August 8, 2006. MRID 46960306. Unpublished

SPONSOR: Monsanto Company, 800 N. Lindbergh Blvd., St. Louis, MO 63167

EXECUTIVE SUMMARY: In a primary skin irritation study (MRID 46960306), 3 male New Zealand White Rabbits (Source: Myrtle's Rabbitry, Thompson Station, Tennessee; Age: 12 weeks; Weight: 2.5-2.6 kg) were dermally exposed to MON 79851; Lot No. GLP-0603-16960-F; Purity: 1.46% glyphosate a.e (1.97% isopropylamine salt of glyphosate), 0.016% imazapic acid, 1.87% pelargonic acid; Clear, colorless liquid (via pipette), pale yellow liquid (bulk). On the day prior to study initiation fur was removed from the dorsal trunk area with animal clippers. On study day "0" 0.5 mL of the test substance was applied to a 1 inch by 1 inch area on the test site and covered with a gauze patch. The patch was held in place by non irritating tape. An elastic wrap was placed over the trunk and test area to prevent removal or ingestion of the test substance. The wrap was additionally secured with adhesive tape around the trunk "at the cranial and caudal ends. After dosing, collars were placed on each animal and remained in place until removal on day 3". After 4 hours all binding materials were removed. Test areas were wiped with a moistened gauze and then a dry gauze to remove any residual test substance. Animals were observed for erythema and edema at 1 hour after patch removal and at 24, 48 and 72 hours after patch application. Health and mortality checks were performed twice a day (AM and PM). Bodyweights were taken on day "0" prior to dosing.

Very slight (grade 1) erythema was observed in 2/3 test animals at the 1 hour observation, resolving with 24 hours. Irritation outside of the test area was observed in 1/3 test animals, clearing within 48 hours.

EPA Toxicity Category IV. PDI = 0.17.

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:

		Hours				
		1	24	48	72	7
R4427/Male	Erythema	1	0	0	0	0
	Edema	0	0	0	0	0
R4428/Male	Erythema	1 [IT]	0 [IT]	0	0	0
	Edema	0	0	0	0	0
R4430/Male	Erythema	0	0	0	0	0
	Edema	0	0	0	0	0

[IT] Dermal Irritation outside of test area

A. Observations – Very slight (grade 1) erythema was observed in 2/3 test animals at the 1 hour observation, resolving with 24 hours. Irritation outside of the test area was observed in 1/3 test animals, clearing within 48 hours.

B. Results - PDII – 0.17

C. Reviewers Conclusions - Agree with study author that the test substance is essentially non-irritating and that the PDI for this product is 0.17.

D. Deficiencies – None.

DATA EVALUATION RECORD

Reviewer: Tracy Keigwin
Product Manager (EPA): 25

January 24, 2007

STUDY TYPE: Dermal Sensitization - Guinea Pig; OPPTS 870.2600; OECD 406, 429

TEST MATERIAL (% a.i.): MON 79851; Lot No. GLP-0603-16960-F; Purity: 1.46% glyphosate a.e (1.97% isopropylamine salt of glyphosate), 0.016% imazapic acid, 1.87% pelargonic acid; Clear, colorless liquid(via pipette), pale yellow liquid (bulk).

CITATION: Smedley, J. A Dermal Sensitization Study in Guinea Pigs with MON 79851*Modified Buehler Design*. OPPTS 870.2600. Study No. EUF00130; Monsanto Study No. CRO-2006-030. Charles River Laboratories, Spencerville, Ohio. August 10, 2006. MRID 46960307. Unpublished

SPONSOR: Monsanto Company, 800 N. Lindbergh Blvd., St. Louis, MO 63167

EXECUTIVE SUMMARY: In a dermal sensitization study using a modified Buehler design (MRID 46960307) the sensitization potential of MON79851; Lot No. GLP-0603-16960-F; Purity: 1.46% glyphosate a.e (1.97% isopropylamine salt of glyphosate), 0.016% imazapic acid, 1.87% pelargonic acid; Clear, colorless liquid(via pipette), pale yellow liquid (bulk) in Hartley-derived albino guinea pigs was determined [Source: Charles River Laboratories, Inc., Saint Constant, Quebec; Age: approximately 6 weeks (both sexes); weight: males 343-451g, females 330-404g]. The concentration selected for both the induction and challenge applications was 100%. Bodyweights were taken on the day prior to the first induction and challenge applications. A positive control study using HCA as the test substance was performed within 6 months of this study.

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

This study is classified as acceptable. It does satisfy the guideline requirement for a dermal sensitization study (OPPTS 870.2600; OECD 406, 429) in the Guinea pig .

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

I. PROCEDURE

A. Induction - On the day prior to induction test and control animals were weighed and hair was removed with small animal clippers. On the day of the first induction, 0.3 mL of undiluted MON 79851 was applied to a 25 mm Hilltop chamber backed by adhesive tape (occlusive patch) and placed on the left (clipped) side of the test animals. Elastic wrap secured with adhesive tape was wrapped around the trunk of the animal to prevent removal of the test substance. After 6 hours all binding materials were removed and the test areas wiped with moistened gauze and then a dry gauze to remove any residual test substance. This procedure was repeated on study days 7 and 14 for a total of 3 induction applications. Test sites were observed for signs of dermal irritation at 24 and 48 hours after chamber application.

B. Challenge – On the day prior to the challenge application test and control animals were weighed and hair was removed from the right side of the animals with clippers. On study day 28, 0.3 mL of MON 79851 was applied to both test and control animals in the same manner as the induction applications. After 6 hours all binding materials were removed and the test areas wiped with a moistened gauze and then a dry gauze to remove any residual test substance. Test sites were observed for signs of dermal irritation at 24 and 48 hours after chamber removal.

C. Naive Controls - The study does not indicate how the naive control animals were treated in the induction applications, only that they were weighed. At challenge, naive control animals were treated in the same manner as the test animals as detailed, above.

II. RESULTS and DISCUSSION:

A. Reactions and duration – "Following challenge with 100% (as received) MON 79851, dermal reactions were limited to ± to 0 in the test and the challenge control animals at the 24 and 48 hour scoring intervals. Sensitization study animals gained weight during the test period and generally appeared in good health".

B. Positive control – The results of the positive control were appropriate.

C. Reviewers Conclusions: Agree with study author that the test substance is not a dermal sensitizer.

D. Deficiencies – The study states the following: "The animal room temperature and relative humidity ranges exceeded the preferred ranges during the study. The morning mortality check was inadvertently not performed on day 8; however, the afternoon mortality check was performed and there were no early deaths on study. These occurrences were considered to have had no adverse effect on the out come of the study".

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ACUTE TOX ONE-LINERS
1. DP BARCODE: 334573
2. PC CODES: 103601, 128840, 217500
3. CURRENT DATE: 26/JAN/2007
4. TEST MATERIAL: MON 79851; Lot No. GLP-0603-16960-F; Purity: 1.46% glyphosate a.e (1.97% isopropylamine salt of glyphosate), 0.016% imazapic acid, 1.87% pelargonic acid; Clear, colorless liquid(via pipette), pale yellow liquid (bulk).

Study/Species/Lab Study # /Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat Charles River Laboratories Study. No. EUF00125 August 10, 2006	46960302	Oral LD_{50} greater than 5000 mg/kg	IV	A
Acute dermal toxicity/rabbit Charles River Laboratories Study. No. EUF00126 August 11, 2006	46976001	Dermal LD_{50} greater than 5000 mg/kg (both sexes)	IV	A
Acute inhalation toxicity/rat Charles River Laboratories Study. No. EUF00127 September 7, 2006	46960304	Inhalation LC_{50} greater than 2.43 mg/L (females)	IV	A
Primary eye irritation/rabbit Charles River Laboratories Study. No. EUF00128 August 9, 2006	46960305	Iritis, clearing within 24 hours, conjunctivitis, clearing within 48 hours	III	A
Primary dermal irritation/rabbit Charles River Laboratories Study. No. EUF00129 August 8, 2006	46960306	PDI = 0.17	IV	A
Dermal sensitization/Guinea Pig Charles River Laboratories Study. No. EUF00130 August 10, 2006	46960307	Not a Sensitizer	NO	A

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