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

OFFICE OF
PREVENTION, PESTICIDES
AND
TOXIC SUBSTANCES

30/JULY/2004

MEMORANDUM

| | | |
|---|---|---|
| Subject: | Name of Pesticide Product: | Roundup Weed & Grass Killer Ready-to-Use Plus |
| | EPA Reg. No. /File Symbol: | 71995-33 |
| | DP Barcode: | D305209 |
| | Decision No: | 344064 |
| | PC Codes: | 103601, 217500 |
| From: | Eugenia McAndrew, Biologist<br>Technical Review Branch<br>Registration Division (7505C) | EM<br>SCR |
| To: | Vickie Walters, RM Team 25<br>Herbicide Branch<br>Registration Division (7505C) | |
| Applicant: | Monsanto Company<br>800 N. Lindbergh Blvd.<br>St. Louis, MO 63141 | |

FORMULATION FROM LABEL:

| | Active Ingredient(s): | % by wt. |
|---|---|---|
| 103601 | Glyphosate, isopropylamine salt | 2.0 |
| 217500 | Pelargonic acid and related fatty acids | 2.0 |
| | Inert Ingredient(s): | 96.0 |
| | Total: | 100.0% |

**ACTION REQUESTED:** "Please review enclosed information to determine if registration of proposed alternate formulation is supported."

**BACKGROUND:** Monsanto Company has submitted a six pack of acute toxicity studies to support the registration of an alternate formulation for Roundup Weed & Grass Killer Ready-to-Use Plus, EPA Reg. No. 71995-33 (CSF Alternate B dated 29 April 2004). The studies were conducted at Springborn Laboratories, Inc., Spencerville, Ohio with assigned MRID numbers 462847-02 to -07. In a previous similarity action (Hashim; D282511; EPA File Symbol 71995-GG; 31/MAY/2002), TRB requested that the Registrant submit the six acute toxicity studies.

**RECOMMENDATIONS**: The six studies have been reviewed and are classified as acceptable. They do support registration of the basic and alternate A and B formulations.

The acute toxicity profile for Roundup Weed & Grass Killer Ready-to-Use Plus, EPA Reg. No. 71995-33, is as follows:

| | | | |
|---|---|---|---|
| acute oral toxicity | IV | Acceptable | MRID 46284702 |
| acute dermal toxicity | IV | Acceptable | MRID 46284703 |
| acute inhalation toxicity | IV | Acceptable | MRID 46284704 |
| primary eye irritation | III | Acceptable | MRID 46284705 |
| primary skin irritation | IV | Acceptable | MRID 46284706 |
| dermal sensitization | Negative | Acceptable | MRID 46284707 |

**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 #:** 071995-00033

**PRODUCT NAME:** Roundup Weed & Grass Killer Ready-to-Use 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 July 30, 2004
**Product Manager:** 25

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

**TEST MATERIAL:** MON 79458 (Lot No. GLP-0305-14056-F; 1.47% glyphosate acid (a.e.)[2.0% isopropylamine salt of glyphosate] and 2.0% pelargonic acid; clear colorless liquid)

**CITATION:** Bonnette, K. An Acute Oral Toxicity Study in Rats with MON 79458 (Up/Down Study Design). Springborn Laboratories, Inc. Laboratory Report Number 3044.959. September 12, 2003. MRID 46284702. Unpublished.

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

**EXECUTIVE SUMMARY:** In an acute oral toxicity study (MRID 46284702), three female young adult Hsd: Sprague-Dawley SD rats (Age: 11 weeks; Source: Harlan Sprague Dawley, Inc., Indianapolis, IN; 207-223 g) were given a single oral dose of MON 79458 (Lot No. GLP-0305-14056-F; 1.47% glyphosate acid (a.e.)[2.0% isopropylamine salt of glyphosate] and 2.0% pelargonic acid; clear colorless liquid) 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, soft stools and dark material around the nose in one female on day 0 only. No gross internal findings were noted at necropsy.

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** - as noted in table.

**B. Clinical observations** - All animals gained weight during the study. Clinical signs noted included congested breathing, soft stools and dark material around the nose in one female on day 0 only.

**C. Gross Necropsy** - No gross internal findings were noted at necropsy.

**D. Reviewer's Conclusions:** Agree with the study author

**Reviewer:** Eugenia McAndrew July 30, 2004
**Product Manager:** 25

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

**TEST MATERIAL:** MON 79458 (Lot No. GLP-0305-14056-F; 1.47% glyphosate acid (a.e.)[2.0% isopropylamine salt of glyphosate] and 2.0% pelargonic acid; clear colorless liquid)

**CITATION:** Bonnette, K. An Acute Dermal Toxicity Study in Rats with MON 79458. Springborn Laboratories, Inc. Laboratory Report Number 3044.960. October 7, 2003. MRID 46284703. Unpublished.

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

**EXECUTIVE SUMMARY:** In an acute dermal toxicity study (MRID 46284703), 5/sex of young adult Hsd: Sprague-Dawley SD rats (Age: 10 weeks; Source: Harlan Sprague Dawley, Inc., Indianapolis, IN; 288-318 g males and 209-226 g females) were dermally exposed to MON 79458 (Lot No. GLP-0305-14056-F; 1.47% glyphosate acid (a.e.)[2.0% isopropylamine salt of glyphosate] and 2.0% pelargonic acid; clear colorless liquid) 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. 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. Clinical signs noted included transient incidences of urine staining, soft stools and dark material around the facial area. Dermal irritation was present at the site of test substance application. All animals except one female gained weight. No gross internal findings were noted at necropsy.

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** - as noted in table.

**B. Clinical observations** - Clinical signs noted included transient incidences of urine staining, soft stools and dark material around the facial area. Dermal irritation was present at the site of test substance application. All animals except one female gained weight.

**C. Gross Necropsy** - No gross internal findings were noted at necropsy.

**D. Reviewer's Conclusions:** Agree with the study author

**Reviewer:** Eugenia McAndrew July 30, 2004
**Product Manager:** 25

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

**TEST MATERIAL:** MON 79458 (Lot No. GLP-0305-14056-F; 1.47% glyphosate acid (a.e.)[2.0% isopropylamine salt of glyphosate] and 2.0% pelargonic acid; clear colorless liquid)

**CITATION:** Bonnette, K. An Acute Nose-Only Inhalation Toxicity Study in Rats with MON 79458. Springborn Laboratories, Inc. Laboratory Report Number 3044.961. October 9, 2003. MRID 46284704. 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: 8 weeks; Source: Harlan Sprague Dawley, Inc., Indianapolis, IN; 217-227 g males and 164-169 g females) were exposed nose only via the inhalation route to MON 79458 (Lot No. GLP-0305-14056-F; 1.47% glyphosate acid (a.e.)[2.0% isopropylamine salt of glyphosate] and 2.0% pelargonic acid; clear colorless liquid) for 4 hours at a concentration of 2.87 mg/L. Animals were then observed for 14 days.

$LC_{50}$ Males = 2.87 mg/L
$LC_{50}$ Females = 2.87 mg/L
$LC_{50}$ Combined = 2.87 mg/L

All animals survived and gained weight during the study. Clinical signs noted included transient incidences of congested breathing, labored breathing, rales, few feces, dark material around the facial area, rough coat and decreased food consumption until day 10. No gross internal findings were noted at necropsy. The gravimetric chamber concentration was 2.87 mg/L and the mass median aerodynamic diameter was estimated to be 3.4µm with a geometric standard deviation of 2.31.

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 |
| 314.57 | 2.87 | 3.4 | 2.31 | 0/5 | 0/5 | 0/10 |

**Test Atmosphere / Chamber Description:**

| | |
|---|---|
| **Chamber Volume:** | **10 L** |
| **Airflow:** | **26 LPM** |
| **Temperature:** | **70-72°F** |
| **Relative Humidity:** | **79-83%** |
| **Time to Equilibrium:** | **3 min.** |

**A.** **Mortality** - as noted in table.

**B.** **Clinical observations** - All animals survived and gained weight during the study. Clinical signs noted included transient incidences of congested breathing, labored breathing, rales, few feces, dark material around the facial area, rough coat and decreased food consumption until day 10.

**C.** **Gross Necropsy** - No gross internal findings were noted.

**D.** **Reviewer's Conclusions:** Agree with the study author

**Reviewer:** Eugenia McAndrew July 30, 2004
**Product Manager:** 25

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

**TEST MATERIAL:** MON 79458 (Lot No. GLP-0305-14056-F; 1.47% glyphosate acid (a.e.)[2.0% isopropylamine salt of glyphosate] and 2.0% pelargonic acid; clear colorless liquid)

**CITATION:** Bonnette, K. A Primary Eye Irritation Study in Rabbits with MON 7 9458. Springborn Laboratories, Inc. Laboratory Report Number 3044.962. September 8, 2003. MRID 46284705. Unpublished.

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

**EXECUTIVE SUMMARY:** In a primary eye irritation study (MRID 46284705), 0.1 mL of MON 79458 (Lot No. GLP-0305-14056-F; 1.47% glyphosate acid (a.e.)[2.0% isopropylamine salt of glyphosate] and 2.0% pelargonic acid; clear colorless liquid) was instilled into the conjunctival sac of the right eye of three adult New Zealand White rabbits (2 male and 1 female; Source: Myrtle's Rabbitry, Thompson Station, Tennessee). The left eye served as the control. Animals were then observed at 1, 24, 48, 72 hours and at 7 days post-instillation. Irritation was scored by the method of Draize.

All three eyes exhibited iritis and conjunctivitis at the one hour observation. By 24 hours, one eye exhibited corneal opacity. The irritation decreased with time. No positive scores were noted at 72 hours and all eyes were free of irritation by day 7.

In this study, formulation is mildly 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 | | | | Days |
| | 1 | 24 | 48 | 72 | 7 |
| | | | | | |
| Corneal Opacity | 0/3 | 1/3 | 0/3 | 0/3 | 0/3 |
| Iritis | 3/3 | 0/3 | 0/3 | 0/3 | 0/3 |
| Conjunctivae: | | | | | |
| Redness* | 3/3 | 2/3 | 1/3 | 0/3 | 0/3 |
| Chemosis* | 3/3 | 0/3 | 0/3 | 0/3 | 0/3 |
| Discharge* | 3/3 | 0/3 | 0/3 | 0/3 | 0/3 |

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

**A. Observations** - All three eyes exhibited iritis and conjunctivitis at the one hour observation. By 24 hours, one eye exhibited corneal opacity. The irritation decreased with time. No positive scores were noted at 72 hours and all eyes were free of irritation by day 7.

**B. Reviewer's Conclusions:** Agree with study author

**Reviewer:** Eugenia McAndrew July 30, 2004
**Product Manager:** 25

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

**TEST MATERIAL:** MON 79458 (Lot No. GLP-0305-14056-F; 1.47% glyphosate acid (a.e.)[2.0% isopropylamine salt of glyphosate] and 2.0% pelargonic acid; clear colorless liquid)

**CITATION:** Bonnette, K. A Primary Skin Irritation Study in Rabbits with MON 79458. Springborn Laboratories, Inc. Laboratory Report Number 3044.963. September 9, 2003. MRID 46284706. Unpublished.

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

**EXECUTIVE SUMMARY:** In a primary dermal irritation study (MRID 46284706), three adult New Zealand White male rabbits (Source: Myrtle's Rabbitry, Thompson Station, Tennessee) were dermally exposed to 0.5 mL of MON 79458 (Lot No. GLP-0305-14056-F; 1.47% glyphosate acid (a.e.)[2.0% isopropylamine salt of glyphosate] and 2.0% pelargonic acid; clear colorless liquid) . 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. 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 minimally irritating. EPA Toxicity Category IV.

Primary Dermal Irritation Index (PDII) = 0.08 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 one test site. The irritation resolved by 24 hours and no other irritation was noted.

**B. Results** - PDII - 0.08

**C. Reviewer's Conclusions** - Agree with study author

**Reviewer:** Eugenia McAndrew
**Product Manager:** 25 July 30, 2004

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

**TEST MATERIAL:** MON 79458 (Lot No. GLP-0305-14056-F; 1.47% glyphosate acid (a.e.)[2.0% isopropylamine salt of glyphosate] and 2.0% pelargonic acid; clear colorless liquid)

**CITATION:** Bonnette, K. A Dermal Sensitization Study in Guinea Pigs with MON 79458 (Modified Buehler Design). Springborn Laboratories, Inc. Laboratory Report Number 3044.964. October 10, 2003. MRID 46284707. Unpublished.

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

**EXECUTIVE SUMMARY:** In a dermal sensitization study (MRID 46284707) with MON 79458 (Lot No. GLP-0305-14056-F; 1.47% glyphosate acid (a.e.)[2.0% isopropylamine salt of glyphosate] and 2.0% pelargonic acid; clear colorless liquid), 30 young adult male Hartley-derived albino guinea pigs (Age 6-8 weeks; Source: Hilltop Lab Animals, Inc., Scotttdale, PA; 334-379 g males and 320-378 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-eight 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 7/20 test animal sites during the induction phase. Following the challenge, erythema was noted at 1/20 test animal sites at 24 hours only. No dermal irritation was noted at the naive control animal sites. No positive scores were observed in any of the animals at the challenge. 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-eight 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 7/20 test animal sites during the induction phase. Following the challenge, erythema was noted at 1/20 test animal sites at 24 hours only. No dermal irritation was noted at the naive control animal sites.

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

**C. Reviewer's Conclusions:** Agree with study author

**ACUTE TOX ONE-LINERS**

**1. DP BARCODE:** D305209
**2. PC CODES:** 103601, 217500
**3. CURRENT DATE:** 30/JULY/2004
**4. TEST MATERIAL:** MON 79458 (Lot No. GLP-0305-14056-F; 1.47% glyphosate acid (a.e.)[2.0% isopropylamine salt of glyphosate] and 2.0% pelargonic acid; clear colorless liquid)

| Study/Species/Lab<br><br>Study # /Date | MRID | Results | Tox. Cat. | Core Grade |
|---|---|---|---|---|
| Acute oral toxicity/rat<br>Springborn Laboratories, Inc.<br>3044.959/9-12-03 | 46284702 | $LD_{50}$ females > 5000 mg/kg | IV | A |
| Acute dermal toxicity/rat<br>Springborn Laboratories, Inc.<br>3044.960/10-7-03 | 46284703 | $LD_{50}$ > 5000 mg/kg<br>(males, females combined) | IV | A |
| Acute inhalation toxicity/rat<br>Springborn Laboratories, Inc.<br>3044.961/10-9-03 | 46284704 | $LC_{50}$ > 2.87 mg/L (males females combined) | IV | A |
| Primary eye irritation/rabbit<br>Springborn Laboratories, Inc.<br>3044.962/9-8-03 | 46284705 | Corneal opacity, iritis and conjunctivitis resolving by day 7. | III | A |
| Primary dermal irritation/rabbit<br>Springborn Laboratories, Inc.<br>3044.963/9-9-03 | 46284706 | PDII = 0.08<br>Minimal irritant | IV | A |
| Dermal sensitization/guinea pig<br>Springborn Laboratories, Inc.<br>3044.964/10-10-03 | 46284707 | Not a sensitizer | – | A |

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