December 12, 1996

MEMORANDUM

EPA File Symbol: 55947-150

DP Barcode: D229670

Chemical: 129051 Dimethenamid
080803 Atrazine

Test Material: SAN 1280 H 600 SE 403DP (Guardsman® Herbicide): Dimethenamid 25.2%, Atrazine 29.3%.

From: Wallace Powell, Biologist
Precautionary Review Section
Registration Support Branch (7505W)
Registration Division

To: Product Manager, Team 22
James Stone, Team Reviewer, Team 22

Applicant: Sandoz Agro, Inc.

Performing Lab: Toxicology and Animal Metabolism
Ricerca, Inc.
7528 Auburn Road
P.O. Box 1000
Painesville, OH 44077-1000

FORMULATION FROM LABEL

Ingredient(s)	% by wt.
Dimethenamid: 2-chloro-N-[(1-methyl-2-methoxy) ethyl]-N-(2,4-dimethyl-thien-3-yl)-acetamide	24.8
Atrazine: 2-chloro-4-ethylamino-6-isopropyl-amino-s-triazine	28.4
Inerts	46.8
Total	100.0

BACKGROUND

After revising the product formulation, Sandoz Agro, Inc. has submitted new acute oral toxicity, acute dermal toxicity, primary eye irritation, and acute skin irritation studies (MRID Numbers 440938-04 through -07, respectively) on Guardsman® Herbicide (SAN

1280 H 600 SE 403DP). No dermal sensitization study was submitted for the new formulation, based on the sensitization response from the study on the old formulation. Acute inhalation toxicity also was not submitted, based on the rationale that the old and new formulations should be similar enough that a similar outcome for the other two systemic studies (acute oral and acute dermal toxicity) would suggest that the inhalation study can be waived. The inhalation study previously submitted for the old formulation demonstrated a Category III response.

RECOMMENDATION

81-1. Acute Oral: Category III. The submitted study is acceptable.

81-2. Acute Dermal: Category III. The submitted study is acceptable.

81-3. Acute Inhalation: Category III. The applicant cited a study on its previous formulation, a study previously reviewed by PRS.

81-4. Eye Irritation: Category II. The submitted study is acceptable.

81-5. Skin Irritation: Category III. The submitted study is acceptable.

81-6. Dermal Sensitization: Sensitizer. Self-validated: the applicant claimed similarity between the new formulation and the old formulation, for which a study indicating a sensitizing response was previously reviewed by PRS.

LABELING RECOMMENDATIONS (Generated by the PRS Label Review System)

AGRICULTURAL USE REQUIREMENTS:

DIRECTIONS FOR USE:

For early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil, or water, wear: coveralls over long-sleeved shirt and long pants, socks and chemical resistant footwear, goggles or face shield, and chemical resistant gloves (such as Nitrile, Butyl, Neoprene, and/or Barrier Laminate).

INGREDIENT LABELING:

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

Product Manager: 22 **Reviewer**: W. Powell
MRID No.: 440938-04 **Report No.**: 6831-96-0082-TX-001
Authors: Steven K. Shults, B.A.; Ann W. Brock, M.S.; David M. Serrone. Ph.D., D.A.B.T.
Report Date: July 25, 1996

Conclusion:

LD_{50}: Males: 5660 mg/kg; Females: 3530 mg/kg;
Combined M and F: 4090 mg/kg
Toxicity Category: III
Classification: Acceptable
Quality Assurance (40 CFR §160.12): Included

Deviations from §81-1: Although relative humidity was generally within the range of 40% to 70%, relative humidities in the ranges of 16% to 39% and 71% to 73% were recorded on seven days during the study period. However, this deficiency alone would not be expected to affect the Toxicity Category.

Testing Facility: Toxicology and Animal Metabolism
Ricerca, Inc.
7528 Auburn Road
P.O. Box 1000
Painesville, OH 44077-1000

Test Material: SAN 1280 H 600 SE 403DP (Guardsman® Herbicide): Dimethenamid 25.2%, Atrazine 29.3%.

Test Animal: Rat; Sprague-Dawley
Age: Young adult
Weight: Males/Females: 204-337 g
Source: Zivic-Miller Laboratories, Inc., Zelienople, PA

Test Conditions: Following a pre-screening, doses of 1250, 2500, and 5000 mg/kg were used in the LD_{50} main study. The test material was administered in single doses to fasted animals by gastric intubation. Body weights were recorded on the day of dosing and on days 7 and 14. Clinical observations were performed at hours 1, 2.5, and 4 on the day of dosing, and daily thereafter during the 14-day observation period. Gross necropsy was performed on all animals that died during this period, and all survivors were sacrificed and were subject to gross necropsy.

Results: Body weight gains generally were noted on days 7 and 14 in surviving rats. No internal necropsy findings were noted in rats which survived through the observation period. Mortality

Contains Petroleum Distillate.

SIGNAL WORD: WARNING AVISO

PRECAUTIONARY STATEMENTS:

Causes substantial but temporary eye injury. Harmful if swallowed or absorbed through skin or inhaled. Do not get in eyes or on clothing. Avoid contact with skin. Avoid breathing spray mist. Wear long-sleeved shirt and long pants, socks and shoes, goggles or face shield and chemical resistant gloves (such as Nitrile, Butyl, Neoprene, and/or Barrier Laminate). Prolonged or frequently repeated skin contact may cause allergic reaction in some individuals. Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash clothing before reuse.

STATEMENT OF PRACTICAL TREATMENT (SOPT):

IF SWALLOWED: Call a physician or Poison Control Center. Do not induce vomiting. Drink promptly a large quantity of water. Do not give anything by mouth to an unconscious person. Avoid alcohol.

IF ON SKIN: Wash with plenty of soap and water. Get medical attention.

IF INHALED: Remove victim to fresh air. If not breathing, give artificial respiration, preferably mouth-to-mouth. Get medical attention.

IF IN EYES: Hold eyelids open and flush with steady, gentle stream of water for 15 minutes. Get medical attention.

NOTE TO PHYSICIAN:

Probable mucosal damage may contraindicate the use of gastric lavage.

May pose an aspiration pneumonia hazard.

data is summarized below.

Dosage (mg/kg)	Number Dead/Tested		
	Males	Females	Combined
1250	0/5	0/5	0/10
2500	1/5	0/5	1/10
5000	2/5	5/5	7/10

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

Product Manager: 22 **Reviewer**: W. Powell
MRID No.: 440938-05 **Report No.**: 6831-96-0083-TX-001
Authors: Steven K. Shults, B.A.; Ann W. Brock, M.S.; David M. Serrone. Ph.D., D.A.B.T.
Report Date: July 25, 1996

Conclusion:

LD_{50} (Males, Females, and Combined): LD_{50} > 2,000 mg/kg;
Toxicity Category: III
Classification: Acceptable
Quality Assurance (40 CFR §160.12): Included

Deviations from §81-2: A compressor failure resulted in a 50% reduction in air flow for three days during the study. Additionally, moderately high relative humidities (in the range of 61% to 79%) were recorded on seven days during the study period. These deficiencies, however, would not be expected to affect the Toxicity Category in this study.

Testing Facility: Toxicology and Animal Metabolism
Ricerca, Inc.
7528 Auburn Road
P.O. Box 1000
Painesville, OH 44077-1000

Test Material: SAN 1280 H 600 SE 403DP (Guardsman® Herbicide): Dimethenamid 25.2%, Atrazine 29.3%.

Test Animal: Rabbit/New Zealand White (albino)
Age: Young adult
Weight: Male and Female: 2275-2754 g.
Source: Mohican Valley Rabbitry, Loudonville, Ohio

Test Conditions: The test material was applied to the back of each animal and occluded for 24 hours. The animals were observed for mortality and signs of toxicity at approximately 1, 2.5, and 4 hours after removal of the dressing from the site of application. Dermal irritation was scored on days 1 (the day following dosing), 3, 7, 10, and 14.

Results: All animals survived 14-day study period. Observations during the study included severe erythema and/or eschar. Soft feces and anogenital staining occurred mainly on the day of dosing. The animals generally otherwise appeared normal during the study period. At day 14 moderate to severe erythema was observed in 4 animals; however, by this time the severity of

erythema was decreasing with most of the animals, and edema had disappeared. Gross necropsy yielded no other noteworthy observations other than enlarged and mottled kidneys in 1 animal. Mortality data is summarized below.

Dosage	Number Dead/Tested		
	Males	Females	Combined
2,000 mg/kg	0/5	0/5	0/10

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

Product Manager: 22 **Reviewer**: W. Powell
MRID No.: 440938-06 **Report No.**: 6831-96-0084-TX-001
Authors: Steven K. Shults, B.A.; Ann W. Brock, M.S.; David M. Serrone. Ph.D., D.A.B.T.
Report Date: July 25, 1996

Conclusion:

Toxicity Category: II
Classification: Acceptable
Quality Assurance (40 CFR §160.12): Included

Deviations from §81-4:

A compressor failure resulted in a 50% reduction in air flow for three days during the study. Additionally, moderately high relative humidities (in the range of 61% to 79%) were recorded on four days during the study period. These deficiencies, however, would not be expected to affect the Toxicity Category for this study.

Body weights for each rabbit were not reported. However, the study report indicated the overall weight range (2351 to 2703 grams), and it stated that the lab conducted a physical examination prior to initiation of the study in order to determine the suitability of the animals for the study.

Testing Facility: Toxicology and Animal Metabolism
Ricerca, Inc.
7528 Auburn Road
P.O. Box 1000
Painesville, OH 44077-1000

Test Material: SAN 1280 H 600 SE 403DP (Guardsman® Herbicide): Dimethenamid 25.2%, Atrazine 29.3%.

Test Animal: Rabbit/ New Zealand White (albino); 3 per sex
Age: Young adult
Weights: 2351 - 2703 g
Source: Mohican Valley Rabbitry, Loudonville, Ohio

Test Conditions: 0.1 gram of undiluted test substance was instilled into one eye of each of six healthy rabbits. The other eye was untreated and served as a control. Ocular irritation was evaluated by the Draize method. Observations were made for 10 days following instillation of the test substance. (The tables summarizing the study results contain a column for day 14, thus

implying that the laboratory observed the rats until day 14 in case of any unexpected mortalities; however, this was not actually stated in the report. In any case, day 14 observations were not necessary under the circumstances of this study.)

Results:

All animals survived the 10-day study period. Observations were recorded for hours 1, 24, 48, and 72, and for days 4, 7, 10, and 14. Corneal opacity persisted in 2 rabbits at day 7, both grade 1 (mild) on the Draize scale. Corneal effects disappeared from all rabbits by day 10. No iridial effects were observed after day 4. Conjunctival redness persisted in 2 rabbits at day 7: one grade 1 and one grade 2 on the Draize scale. No positive conjunctival findings were noted on day 10.

The study results indicate a classification of Toxicity Category II. At day 7, the corneal opacity (grade 1) in 2 rabbits and the conjunctival redness (grade 2) in 1 rabbit are considered "positive" effects.

The observations are summarized below.

Observations	Number positive/tested at						
	1 Hr	24 Hrs	48 Hrs	72 Hrs	4 Days	7 Days	10 Days
Cornea Opacity	0/6	5/6	6/6	5/6	3/5	2/3	0/2
Iris	0/6	0/6	0/6	2/6	2/2	0/2	---
Conjunctivae: Redness	6/6	6/6	6/6	6/6	4/6	1/6	0/2
Chemosis	4/6	3/6	1/6	0/6	0/3	0/2	---
Discharge	6/6	1/6	1/6	0/6	0/6	0/3	---

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

Product Manager: 22 **Reviewer**: W. Powell
MRID No.: 440938-07 **Report No.**: 6831-96-0085-TX-001
Authors: Steven K. Shults, B.A.; Ann W. Brock, M.S.; David M. Serrone. Ph.D., D.A.B.T.
Report Date: July 25, 1996

Conclusion:
Toxicity Category: III
Classification: Acceptable
Quality Assurance (40 CFR §160.12): Included
Deviations from §81-5:

A compressor failure resulted in a 50% reduction in air flow for three days during the study. Additionally, moderately high relative humidities (in the range of 61% to 79%) were recorded on a maximum of 7 days during the study period. These deficiencies, however, would not be expected to affect the Toxicity Category for this study.

Body weights for each rabbit were not reported. However, the study report indicated the overall weight range (2439 to 2691 grams), and it stated that the lab conducted a physical examination prior to initiation of the study in order to determine the suitability of the animals for the study.

Testing Facility: Toxicology and Animal Metabolism
Ricerca, Inc.
7528 Auburn Road
P.O. Box 1000
Painesville, OH 44077-1000

Test Material: SAN 1280 H 600 SE 403DP (Guardsman® Herbicide): Dimethenamid 25.2%, Atrazine 29.3%.

Test Animal: Rabbit/ New Zealand White (albino), 3 per sex
Age: Young adult
Weight: 2439 to 2691 grams
Source: Mohican Valley Rabbitry, Loudonville, Ohio

Test Conditions: A 0.5 ml dose of undiluted test substance was applied to each rabbit on approximately a one square inch area of dorsal skin. The area was then covered with a gauze patch and occluded with hypo-allergenic tape for a 4 hour period. After removal of the bandaging, the skin of each back was wetted and gently wiped. Erythema/eschar and edema were scored according to the Draize system at ½, 1, 24, 48, and 72 (day 3) hours after this time, and on days 4, 7, 10, and 14.

Results:

At 72 hours moderate to severe erythema and/or eschar was observed in 5 out of the 6 test rabbits, and well defined erythema and/or eschar was observed in the other rabbit. Effects at 72 hours did not include desquamation. Desquamation occurred later in all rabbits but disappeared by day 14. Very slight edema was observed in 1 rabbit at 72 hours.

All rabbits survived the 14-day study period. Very slight irritation persisted at day 10 in 4 rabbits, and at day 14 in 2 rabbits.

The high incidence (5 of 6 rabbits) of moderate to severe irritation at 72 hours suggests that the Toxicity Category could be either II or III. The balance of the data weigh in favor of Category III.

ACUTE TOX ONE-LINER

ID No.: 55947-150
DP Barcode: D229670
Chemicals: 129051 Dimethenamid
080803 Atrazine
Applicant: Sandoz Agro, Inc.
Test Material: SAN 1280 H 600 SE 403DP (Guardsman® Herbicide): Dimethenamid 25.2%, Atrazine 29.3%.
Date: December 12, 1996

Study, Animal, Test Laboratory, Study #, Date	MRID No.	Results	Tox. Cat.	Core Grade
Acute Oral, Rat, Ricerca, Inc., 6831-96-0082-TX-001, 7/25/96	440938-04	LD_{50}=4090 mg/kg	III	A
Acute Dermal, Rabbit, Ricerca, Inc., 6831-96-0083-TX-001, 7/25/96	440938-05	LD_{50}>2000 mg/kg	III	A
Acute Inhalation, Rat, Bio/dynamics, Inc., 5102, 12/18/92	426666-14	LC_{50} > 0.75 mg/l	III	C
Eye Irritation, Rabbit, Ricerca, Inc., 6831-96-0084-TX-001, 7/25/96	440938-06	At day 7, redness in 1 of 6 rabbits and corneal opacity in 2 rabbits.	II	A
Skin Irritation, Rabbit, Ricerca, Inc., 6831-96-0085-TX-001, 7/25/96	440938-07	At 72 hours, moderate to severe erythema in 5 of 6 rabbits and slight edema in 1 rabbit.	III	A
Skin Sensitization, Guinea pig, Bio/dynamics, Inc., 0664,	426666-17	Sensitizer	——	SV

12/04/92				

A = Acceptable
SV = Self-Validated
C = Cited (applicant cited a previous study)