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

OFFICE OF
PREVENTION, PESTICIDES
AND
TOXIC SUBSTANCES

25/SEPT/2003

MEMORANDUM

Subject:	Name of Pesticide Product:	SIERRA™
	EPA Reg. No. /File Symbol:	75802-R
	DP Barcode:	D290892
	Decision No:	327134
	PC Code:	121301
From:	Rick J. Whiting, Biologist Technical Review Branch Registration Division (7505C)	RJW
To:	Linda DeLuise, PM Team 03 Insecticide-Rodenticide Branch Registration Division (7505C)	
Applicant:	Triad Specialty Products LLC 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410	

FORMULATION FROM LABEL:

	Active Ingredient(s):	% by wt.
121301	Cyromazine	2.12%
	Inert Ingredient(s):	97.88%
	Total:	100.0%

ACTION REQUESTED: PM requests review of acute toxicity data for Sierra™, EPA File Symbol 75802-R.

BACKGROUND: Triad Specialty Products LLC has submitted a six pack of acute toxicity studies in support of registration of Sierra™, EPA File Symbol 75802-R. The studies were assigned MRID Numbers 459367-03 to -08. The product is referred to as "Cy-Equi Pellet" or "Cy-Equi Pre-pellet Mix" in the study reports.

All the studies were conducted at Stillmeadow, Inc., Sugar Land, TX. The acute oral (45936703), acute inhalation and primary eye irritation (45936706) studies used "Cy-Equi Pellet" as the test material. The acute dermal (45936704), primary dermal irritation (45936707) and dermal sensitization (45936708) studies used "Cy-Equi Pre-pellet Mix."

RECOMMENDATIONS: The six studies have been reviewed and are classified as acceptable. The acute toxicity profile for Sierra™, EPA File Symbol 75802-R, is as follows:

Acute oral toxicity	IV	Acceptable	MRID 45936703
Acute dermal toxicity	IV	Acceptable	MRID 45936704
Acute inhalation toxicity	IV	Waived	MRID 45936705
Primary eye irritation	IV	Acceptable	MRID 45936706
Primary skin irritation	IV	Acceptable	MRID 45936707
Dermal sensitization	Negative	Acceptable	MRID 45936708

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 #: 075802-00001

PRODUCT NAME: Sierra™

Hazards to Humans and Domestic Animals:

SIGNAL WORD: (Optional)

First Aid: None required. Registrant may use Category III statements.

2

DATA EVALUATION RECORD

STUDY TYPE: ACUTE ORAL TOXICITY TESTING (870.1100 formerly §81-1)

Product Manager: 03 **Reviewer:** Rick J. Whiting

TEST MATERIAL PURITY: Cy-Equi Pellet (Cyromazine 2.12% Pellet, Lot No. 297:92)

CITATION: Kuhn, J. (2002) Acute Oral Toxicity Study in Rats: Cyromazine 2.12% Pellet. Stillmeadow Inc. Laboratory Project Number: 7302-02. December 18, 2002. MRID No. 45936703. Unpublished study.

SPONSOR: Triad Specialty Products LLC, 204 Muirs Chapel Road, Suite 200, Greensboro, NC 27410

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID No. 45936703), five young adult Sprague-Dawley rats/sex (Age: 8-9 weeks; Weight: 241-286 g males; 162-182 g females; Source: Texas Animal Specialties, Humble, TX) were give a single oral dose of Cy-Equi Pellet (Cyromazine 2.12% Pellet, Lot No. 297:92) at 5050 mg/kg. The test material was mixed with corn oil to produce a 40% w/v concentration. Body weights were obtained just prior to dosing and on days 7 and 14. Animals were observed for clinical signs of toxicity and mortality at least three times on the day of dosing (Day 0) and at least once daily thereafter for 14 days. A gross necropsy examination was performed on all animals at scheduled euthanasia.

Oral LD_{50} Males => 5050 mg/kg (observed); Oral LD_{50} Females => 5050 mg/kg (observed)

Cy-Equi Pellet is classified as Toxicity Category IV based on the observed LD_{50} value in males and females.

All animals survived the study. Body weight gain was unaffected except for one male which lost 11 g between Days 7 and 14. The only clinical sign observed was slight piloerection in one female on Day 2. No gross abnormalities were noted a necropsy.

This study is classified as Acceptable (870.1100) and satisfies the guideline requirement for an acute oral study in the rat.

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

RESULTS:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
5050	0/5	0/5	0/10

OBSERVATIONS: All animals survived the study. Body weight gain was unaffected except for one male which lost 11 g between Days 7 and 14. The only clinical sign observed was slight piloerection in one female on Day 2.

GROSS NECROPSY: No gross abnormalities were noted a necropsy.

4

DATA EVALUATION RECORD

STUDY TYPE: ACUTE DERMAL TOXICITY TESTING (870.1200 formerly §81-2)

Product Manager: 03 **Reviewer:** Rick J. Whiting

TEST MATERIAL PURITY: Cy-Equi Pre-pellet Mix (Cyromazine Pellet Mix, Lot No. 297:92)

CITATION: Kuhn, J. (2002) Acute Dermal Toxicity Study in Rabbits: Cyromazine 2.12% Pellet. Stillmeadow, Inc., Laboratory Project Number: 7299-02. December 19, 2002. MRID No. 45936704. Unpublished study.

SPONSOR: Triad Specialty Products LLC, 204 Muirs Chapel Road, Suite 200, Greensboro, NC 27410

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID No. 45936704), five adult young New Zealand White rabbits/sex (Age: 11-12 weeks; Weight: 2.0-2.6 kg males; 2.2-3.1 kg females; Source: Ray Nichols Rabbitry, Lumberton, TX) were dermally exposed to a single application of Cy-Equi Pre-pellet Mix (Cyromazine Pellet Mix, Lot No. 297:92) at 5050 mg/kg for 24 hours. Each dose of the test material was moistened with deionized water (1.9 mL/g of test material) and was evenly applied to the exposure area of each animal. Body weights were recorded just prior to dosing and on Days 7 and 14. Observations for evidence of dermal irritation were made at approximately 60 minute intervals after removal of wrappings and on Days 4, 7, 11 and 14. All animals were observed for clinical signs of toxicity and mortality at least three times on the day of dosing (Day 0) and at least once daily thereafter for 14 days. A gross necropsy examination was performed on all animals at the time of scheduled euthanasia.

Dermal LD_{50} Males => 5050 mg/kg (observed); Dermal LD_{50} Females => 5050 mg/kg (observed)

Cy-Equi Pre-pellet is classified as Toxicity Category IV based on the observed LD_{50} value in both sexes.

All animals survived the study. Body weight gain was unaffected with the exception of one male that failed to gain weight and two females that lost weight between Days 0 and 7. Another male failed to gain weight between Days 7 and 14. Very slight erythema was observed in 4/5 males and 5/5 females on Day 1 but was resolved by Day 4. No gross abnormalities were noted a necropsy.

This study is classified as Acceptable (870.1200) and satisfies the guideline requirement for an acute dermal study in the rat.

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

RESULTS:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
5050	0/5	0/5	0/10

OBSERVATIONS: All animals survived the study. Body weight gain was unaffected with the exception of one male that failed to gain weight and two females that lost weight between Days 0 and 7. Another male failed to gain weight between Days 7 and 14. Very slight erythema was observed in 4/5 males and 5/5 females on Day 1 but was resolved by Day 4. No gross abnormalities were noted a necropsy.

GROSS NECROPSY: No gross abnormalities were noted at necropsy.

DATA EVALUATION RECORD

STUDY TYPE: ACUTE INHALATION TOXICITY TESTING (870.1300 formerly §81-3)

Product Manager: 03 **Reviewer:** Rick J. Whiting

TEST MATERIAL PURITY: Cy-Equi Pellet (Cyromazine 2.12% Pellet, Lot No. 297:92)

CITATION: Carter, L. (2002) Acute Inhalation Toxicity Study in Rats: Cyromazine 2.12% Pellet. Stillmeadow, Inc., Laboratory Project Number: 7303-02. December 19, 2002. MRID No. 45936705. Unpublished study.

SPONSOR: Triad Specialty Products LLC, 204 Muirs Chapel Road, Suite 200, Greensboro, NC 27410

EXECUTIVE SUMMARY: "The test substance, Cy-Equi Pellet, was evaluated for its acute inhalation toxicity potential in albino rats. A pre-study test for resistance to attrition was conducted. A known weight of test substance that had been ground for 24 hours was combined with steel balls in a sieve-bottom receiver pan. After a specified period of mechanical agitation, the steel balls were removed and the weight of the granular substance that passed through the specified limiting sieve was measured. The measurement was used to calculate the resistance to attrition. The procedure resulted in less than 0.1 mg (weight) of test substance; therefore, this test substance is not considered suitable to provide meaningful acute inhalation toxicity data."

Cy-Equi Pellet is classified as Toxicity Category IV.

This study cannot be classified and a waiver is granted for Acute Inhalation Toxicity Study (870.1300).

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

DATA EVALUATION RECORD

STUDY TYPE: PRIMARY EYE IRRITATION TESTING (870.2400 formerly §81-4)

Product Manager: 03 **Reviewer:** Rick J. Whiting

TEST MATERIAL PURITY: Cy-Equi Pre-pellet Mix (Cyromazine Pellet Mix, Lot No. 297:92)

CITATION: Kuhn, J. (2002) Acute Eye Irritation Study in Rabbits: Cyromazine 2.12% Pellet. Stillmeadow, Inc., Laboratory Project Number: 7304-02. December 19, 2002. MRID No. 45936706. Unpublished study.

SPONSOR: Triad Specialty Products LLC, 204 Muirs Chapel Road, Suite 200, Greensboro, NC 27410

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID No. 4593670), 0.1 ml by volume (0.051 g) of Cy-Equi Pre-pellet Mix (Cyromazine Pellet Mix, Lot No. 297:92) was placed into the conjunctival sac of one eye of each of adult New Zealand White rabbits (1 male and 2 females) (Source: Ray Nichols Rabbitry, Lumberton, TX.). All animals were observed for ocular irritation and lesions at 1, 24, 48 and 72 hours. "The corneas of all treated eyes were examined immediately after the 24 hour observation with a fluorescein sodium ophthalmic solution. Any of the corneas which exhibited fluorescein staining at the 24 hour observation were re-examined with the fluorescein sodium ophthalmic solution at each consecutive observation until fluorescein staining of the cornea no longer occurred. All treated eyes were washed with room temperature deionized water for one minute immediately after recording the the 24 hour observation."

Cy-Equi Pre-pellet Mix is classified as Toxicity Category IV based on the observations in this study.

There were no "positive" effects observed in any eyes during the study. At 1 hour, all animals showed grade "1" conjunctival redness, chemosis and discharge. The conjunctival effects were resolved by 48 hours.

This study is classified as Acceptable (870.2400) and satisfies the guideline requirement for a primary eye irritation study in the rabbit.

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

RESULTS:

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

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

OBSERVATIONS: There were no "positive" effects observed in any eyes during the study. At 1 hour, all animals showed grade "1" conjunctival redness, chemosis and discharge. The conjunctival effects were resolved by 48 hours.

DATA EVALUATION RECORD

STUDY TYPE: PRIMARY DERMAL IRRITATION TESTING (870.2500 formerly §81-5)

Product Manager: 03 **Reviewer:** Rick J. Whiting

TEST MATERIAL PURITY: Cy-Equi Pre-pellet Mix (Cyromazine Pellet Mix, Lot No. 297:92)

CITATION: Kuhn, J. (2002) Acute Dermal Irritation Study in Rabbits: Cyromazine 2.12% Pellet. Stillmeadow, Inc., Laboratory Project Number: 7300-02. December 19, 2002. MRID No. 45936707. Unpublished study.

SPONSOR: Triad Specialty Products LLC, 204 Muirs Chapel Road, Suite 200, Greensboro, NC 27410

EXECUTIVE SUMMARY: In a primary skin irritation study (MRID No. 45936707), Cy-Equi Pre-pellet Mix (Cyromazine Pellet Mix, Lot No. 297:92) was applied the test site on three New Zealand White rabbits (2 males and 1 female) (Age: 11-12 weeks; Weight: 2.425-2.550 kg males; 2.450 kg females; Source: Ray Nichols Rabbitry, Lumberton, TX). On Day 0, 500 mg of the test material with 0.5 ml of deionized water was applied to each test site. The duration of the single dermal application was for 4 hours. Animals were examined for signs of erythema and edema and the responses scored at 1, 24, 48 and 72 hours after patch removal.

Cy-Equi Pre-pellet Mix is classified as Toxicity Category IV based on the observations in this study.

Primary Dermal Irritation Index (PDII) = 0.25 Very slight erythema was observed in all animals at 1 hour but was resolved by 24 hours. Edema was not observed at any time during the study. The test material was considered to be slightly irritating.

This study is classified as Acceptable (870.2500) and satisfies the guideline requirement for a primary skin irritation study in the rabbit.

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

(0

RESULTS: Primary Dermal Irritation Index (PDII) = 0.25

OBSERVATIONS: Very slight erythema was observed in all animals at 1 hour but was resolved by 24 hours. Edema was not observed at any time during the study. The test material was considered to be slightly irritating.

11

DATA EVALUATION RECORD

STUDY TYPE: DERMAL SENSITIZATION TESTING (870.2600 formerly §81-6)

Product Manager: 03 **Reviewer:** Rick J. Whiting

TEST MATERIAL PURITY: Cy-Equi Pre-pellet Mix (Cyromazine Pellet Mix, Lot No. 297:92)

CITATION: Kuhn, J. (2002) Skin Sensitization Study in Guinea Pigs: Cyromazine 2.12% Pellet. Stillmeadow, Inc., Laboratory Project Number: 7301-02: 6934-02. MRID No. 45936708. Unpublished study.

SPONSOR: Triad Specialty Products LLC, 204 Muirs Chapel Road, Suite 200, Greensboro, NC 27410

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID No. 45936708) conducted with Cy-Equi Pre-pellet Mix (Cyromazine Pellet Mix, Lot No. 297:92), 15 male and 15 female Hartley-Albino guine pigs (Age: not reported; Source: Charles River Laboratories, Wilimington, MA) were tested using a modified Buehler design. Preliminary testing was conducted to determine the correct concentrations for induction and challenge. Group I animals (5/sex) served as a naive control and Group II animals (10/sex) were designated as the test group. Based on the results of the preliminary screening study, the test material was administered by application of 400 mg of test material moistened with 4.0 mL of deionized water. Group II animals were treated once a week for a three induction phase (six hours/exposure). Group I animals remained untreated. After a two-week rest period (Day 29), all animals in Groups I and II were each challenged at a new test site with an application of 400 mg of test material moistened with 4.0 mL of deionized water. Test sites were graded for irritation at 24 and 48 hours after each induction and after the challenge. A positive control study using 1-Chloro-2,4-dinitrobenzene (DNCB) was conducted within six months of the main study to validate the test system.

Cy-Equi Pre-pellet Mix is classified as a non-sensitizer based on the results of this study.

No dermal irritation was observed at any of the test animal sites during the induction phase. Following the challenge, no dermal irritation was observed at any of the test animal sites or at the naive control animal sites. Based on these results, the test substance is not considered to be a contact sensitizer. The positive response observed in the 1-Chloro-2,4-dinitrobenzene (DNCB) study validates the test system used in this study.

This study is classified as Acceptable (870.2600) and satisfies the guideline requirement for an dermal sensitization study in the guinea pig.

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

PROCEDURE: In a dermal sensitization study (MRID No. 45936708) conducted with Cy-Equi Pre-pellet Mix (Cyromazine Pellet Mix, Lot No. 297:92), 15 male and 15 female Hartley-Albino guine pigs (Age: not reported; Source: Charles River Laboratories, Wilimington, MA) were tested using a modified Buehler design. Preliminary testing was conducted to determine the correct concentrations for induction and challenge. Group I animals (5/sex) served as a naive control and Group II animals (10/sex) were designated as the test group. Based on the results of the preliminary screening study, the test material was administered by application of 400 mg of test material moistened with 4.0 mL of deionized water. Group II animals were treated once a week for a three induction phase (six hours/exposure). Group I animals remained untreated. After a two-week rest period (Day 29), all animals in Groups I and II were each challenged at a new test site with an application of 400 mg of test material moistened with 4.0 mL of deionized water. Test sites were graded for irritation at 24 and 48 hours after each induction and after the challenge. A positive control study using 1-Chloro-2,4-dinitrobenzene (DNCB) was conducted within six months of the main study to validate the test system.

RESULTS: No dermal irritation was observed at any of the test animal sites during the induction phase. Following the challenge, no dermal irritation was observed at any of the test animal sites or at the naive control animal sites. Based on these results, the test substance is not considered to be a contact sensitizer. The positive response observed in the 1-Chloro-2,4-dinitrobenzene (DNCB) study validates the test system used in this study.

ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D290892
2. **PC CODE:** 121301
3. **CURRENT DATE:** 25/SEPT/2003
4. **TEST MATERIAL:** * Cy-Equi Pellet (Cyromazine 2.12% Pellet, Lot No. 297:92)

** Cy-Equi Pre-Pellet Mix (Cyromazine 2.12% Pellet, Lot No. 297:92)

Study/Species/Lab Study # /Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity / rat * Stillmeadow Inc. 7302-02 / 12-18-2002	45936703	LD_{50} => 5050 mg/kg (males and females)	IV	A
Acute dermal toxicity / rat ** Stillmeadow Inc. 7299-02 / 12-19-02	45936704	LD_{50} => 5050 mg/kg (males and females)	IV	A
Acute inhalation toxicity / rat * Stillmeadow Inc. 7303-02 / 12-19-2002	45936705	Waived	IV	W
Primary eye irritation/rabbit * Stillmeadow Inc. 7304-02 / 12-19-2002	45936706	No positive results	IV	A
Primary dermal irritation/rabbit ** Stillmeadow Inc. 7300-02 / 12-19-2002	45936707	Slightly irritating	IV	A
Dermal sensitization/guinea pig ** Stillmeadow Inc. 7301-02: 6934-02 / 12-18-2002	45936708	Non-sensitizer		A

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

14