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

OFFICE OF
PREVENTION, PESTICIDES
AND
TOXIC SUBSTANCES

December 30, 2002

MEMORANDUM

Product Name: NATIONS AG II ABAMECTIN 0.15 EC
EPA File Symbol: 72167-EE
DP Barcode: D285189
Case No: 072417
Submission: S621027
Chemical: 122804 Abamectin

From: Byron T. Backus, Ph.D., Toxicologist
Technical Review Branch
Registration Division (7505C)

Byron T. Backus
12/30/2002

To: Thomas Harris/Meredith Laws, PM 04
Insecticide-Rodenticide Branch
Registration Division (7505C)

Registrant: NATIONS AG II, LLC

ACTION REQUESTED: "AVERMECTIN (new source)

"Please review product tox. Claims to be similar to 100-897, 100-898. MRIDs 45708003, 45708004, 45708005, 45708006, 45712807, 45708007..."

BACKGROUND: According to the label received by TRB, this product [NATIONS AG II ABAMECTIN 0.15 EC] has the following ingredient declaration:

Active Ingredient:
Abamectin (CAS No. 65195-55-3 and CAS No. 65195-56-4):.....1.9%
Inert Ingredients:.....98.1%

As part of this package, TRB has received the following acute toxicity studies: acute oral LD50 in rats (MRID 45708003); acute dermal LD50 in rats (MRID 45708004); acute inhalation LC50 in rats (MRID 45708005); primary eye irritation in rabbits (MRID 45708006); primary dermal irritation in rabbits (MRID 45712801), and dermal sensitization in guinea pigs (MRID 45708007).

COMMENTS AND RECOMMENDATIONS:

1. The six submitted acute toxicity studies (MRIDs 45708003 through 45708007 and 45712801) have been reviewed and have been classified as acceptable.
2. Based on the results of the reviewed acute toxicity studies, the following is the acute toxicity profile for EPA File Symbol 72167-EE, NATIONS AG II ABAMECTIN 0.15 EC:

Acute Oral LD50	Acceptable	Tox. Cat. II (MRID 45708003)
Acute Dermal LD50	Acceptable	Tox. Cat. III (MRID 45708004)
Acute Inhalation LC50	Acceptable	Tox. Cat. IV (MRID 45708005)
Primary Eye Irritation	Acceptable	Tox. Cat. II (MRID 45708006)
Primary Dermal Irritation	Acceptable	Tox. Cat. IV (MRID 45712801)
Dermal Sensitization	Acceptable	Negative (MRID 45708007)

3. From the toxicity studies indicated above, the tentative signal word is WARNING, as the product is in toxicity category II in terms of the acute oral toxicity and the eye irritation potential. Also, note that according to the memorandum dated September 5, 2002 (copy attached), from Kathleen C. Raffaele of RAB3 of HED additional studies are required on the technical active, and the findings from these may impact on the final precautionary labeling of this product.
4. Based on the acute toxicity profile given above and based on the proposed label use directions (no label was received for this proposed product, but according to a letter dated June 26 2002 from the registrant: "This product is substantially similar to the currently registered products...EPA Reg. No. 100-898 and...EPA Reg. No. 100-897. Our label combines the uses of these products onto one label." Labels for these two products are supplied. TRB notes that the question of similarity would have to be supported by the additional studies required by HED on the technical). The following is then a tentative precautionary labeling for this product, as obtained from the Label Review System:

PRODUCT ID #: 072167-00022

PRODUCT NAME: NATIONS AG II ABAMECTIN 0.15 EC

PRECAUTIONARY STATEMENTS

SIGNAL WORD: WARNING

SPANISH SIGNAL WORD: AVISO

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle.
(If you do not understand the label, find someone to explain it to you in detail.)

Hazards to Humans and Domestic Animals:

May be fatal if swallowed. Causes substantial but temporary eye injury. Harmful if absorbed through skin. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco. Do not get in eyes or on clothing. Avoid contact with skin. Wear protective eyewear (goggles, face shield, or safety glasses). Remove and wash contaminated clothing before reuse. Wear long-sleeved shirt and long pants, socks, shoes, and chemical-resistant gloves (such as Barrier Laminate, Nitrile Rubber, Neoprene Rubber, Viton, Selection Category E).

First Aid:

If swallowed:

- Call a poison control center or doctor immediately for treatment advice.
- Have person sip a glass of water if able to swallow.
- Do not induce vomiting unless told to by a poison control center or doctor.
- Do not give anything to an unconscious person.

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.

If on skin:

- Take off contaminated clothing.
- Rinse skin immediately with plenty of water for 15-20 minutes.
- Call a poison control center or doctor for treatment advice.

NOTE TO PHYSICIAN: Note to PM/CRM/Registrant: The proposed label should contain a "Note to Physician". The following statements are suggested types of information that may be included, if applicable: - technical information on symptomatology; - use of supportive treatments to maintain life functions; - medicine that will counteract the specific physiological effects of the pesticide; - company telephone number to specific medical personnel who can provide specialized medical 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.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (870.1100, formerly §81-1)

Product Manager: 04
MRID No.: 45708003

Reviewer: Byron T. Backus, Ph.D.

CITATION: Merkel, D.J. Abamectin 0.15 EC Acute Oral Toxicity Study in Rats - Defined LD₅₀ Laboratory Study No. 11285. Unpublished study prepared by Product Safety Labs, East Brunswick, NJ 08816. Study Completion Date: January 2, 2002. MRID 45708003.

SUBMITTER & SPONSOR: NATIONS AG II, LLC, Williamsburg, VA

TEST MATERIAL: Abamectin 0.15 EC, Batch #1081701. A straw-amber liquid. Composition: Abamectin - 0.15 lb./gallon, pH 5-6. If the product density is 0.99 g/mL, then this would be approximately 1.82% Abamectin [=0.15/(8.34 x 0.99)], but from information on the bean sheet the product claim is 1.9% Abamectin, and the 1.9% is consistent with information in the CFS. (Certificate of analysis of the material tested was not provided by sponsor).

SPECIES: Rat, albino, Sprague-Dawley derived
AGE(at dosing): young adult, 8-12 weeks
WEIGHT (fasted): Males: 200-300 g; Females: 160-183 g
SOURCE: Ace Animals, Inc., Boyertown, PA

EXECUTIVE SUMMARY: *In an acute oral toxicity study (MRID 45708003), fasted (approximately 17-21 hrs) young adult (8-12 week old) albino Sprague-Dawley derived rats (5 males and 5 females/dose level) were orally gavaged with Abamectin 0.15 EC, Batch #1081701, a straw-amber liquid containing 0.15 lb. Abamectin/gallon. Doses were 50, 500 and 5000 mg/kg. The test material was administered undiluted to rats in the 500 and 5000 mg/kg groups, and as a 1% w/w solution in distilled water to rats in the 50 mg/kg group.*

At 50 mg/kg there were no mortalities; at 500 mg/kg 4/5 males and 3/5 females died; and at 5000 mg/kg 5/5 males and 5/5 females died.

At 50 mg/kg one female had reduced fecal volume, with recovery by Day 2. At 500 mg/kg, 4/5 males and 3/5 females died by Day 2. Symptoms in rats which died included abnormal posture, hypoactivity and/or tremors. The 3 survivors had similar signs along with ocular discharge, facial staining and/or reduced fecal volume, with recovery by Day 6. At 5000 mg/kg 5/5 males and 5/5 females died within one day of dosing; symptoms included hypoactivity, a prone posture and/or tremors.

At 50 mg/kg, no gross abnormalities were observed at post-sacrifice necropsy. At 500 mg/kg, gross necropsy of rats which died showed discoloration of the lungs and intestines. No gross abnormalities were observed in rats which survived to termination. At 5000 mg/kg gross necropsy of rats which died showed edema of the lungs and discoloration of the lungs and intestines.

*Oral LD50 Males = 271 mg/kg with 95% C.L. of 158 to 429 mg/kg
Oral LD50 Females = 455 mg/kg with 95% C.L. of 236 - 1013 mg/kg*

Abamectin 0.15 EC, Batch #1081701, a straw-amber liquid containing 0.15 lb Abamectin/gallon, is in toxicity category II for oral toxicity based on the oral LD50 >50 mg but less than 500 mg/kg.

Study Classification: Acceptable

COMPLIANCE: Signed and dated GLP Compliance (p. 3), Quality Assurance (p. 22), and [No] Data Confidentiality (p. 2) statements were provided.

Procedure (including deviations from 870.1100): The sample was administered as received for the 500 and 5000 mg/kg dose groups. For the 50 mg/kg group it was diluted to a 1% w/w solution in distilled water that was administered to these rats. "Each animal received the appropriate amount of the test substance (50, 500 or 5,000 mg/kg) by intubation using a stainless steel ball-tipped gavage needle attached to an appropriate syringe...The day of administration was considered Day zero of the study."

Results:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Total
50	0/5	0/5	0/10
500	4/5	3/5	7/10
5000	5/5	5/5	10/10

Observations: At 50 mg/kg "All animals survived and gained weight over the 14-day observation period...one female exhibited reduced fecal volume, but recovered by Day 2..." All other rats were normal.

At 500 mg/kg, 4/5 males and 3/5 females died within 2 days of test substance administration. "Toxic signs noted prior to death included an abnormal posture, hypoactivity and/or tremors. The three surviving rats exhibited similar signs along with ocular discharge, facial staining and/or reduced fecal volume, but recovered by Day 6 and appeared active and healthy for the remainder of the study, gaining bodyweight over the 14-day observation period..."

At 5000 mg/kg: "All animals died within one day of test substance administration. Toxic signs prior to death included hypoactivity, a prone posture and/or tremors."

Gross Necropsy: At 50 mg/kg, no gross abnormalities were observed at post-sacrifice necropsy. At 500 mg/kg, gross necropsy of rats which died showed discoloration of the lungs and intestines. No gross abnormalities were observed in rats which survived to termination. At 5000 mg/kg gross necropsy of rats which died showed edema of the lungs and discoloration of the lungs and intestines.

Comment: The calculated oral LD50 value for males is reported as 271 mg/kg with 95% C.L. of 158 to 429 mg/kg; and for females, it is reported as 455 mg/kg with 95% C.L. of 236 to 1013 mg/kg. However, the combined value is reported as 416 mg/kg with 95% C.L. of 265 to 690 mg/kg. This reviewer believes that the combined LC50 value should be in the range of 350-363 mg/kg. However, this does not impact on the toxicity category (II) assigned to this product by the oral exposure route.

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (870.1200, formerly §81-2)

Product Manager: 04
MRID No.: 45708004

Reviewer: Byron T. Backus, Ph.D.

CITATION: Merkel, D.J. Abamectin 0.15 EC Acute Dermal Toxicity Study in Rats. Laboratory Study No. 11286. Unpublished study prepared by Product Safety Labs, East Brunswick, NJ 08816. Study Completion Date: January 2, 2002. MRID 45708004.

SUBMITTER & SPONSOR: NATIONS AG II, LLC, Williamsburg, VA 23185

TEST MATERIAL: Abamectin 0.15 EC, Batch #1081701. A straw-amber liquid. Composition: Abamectin - 0.15 lb./gallon, pH 5-6. If the product has a density of 0.99 g/mL, then this would be approximately 1.82% Abamectin [=0.15/(8.34 x 0.99)], but from information on the bean sheet the product claim is 1.9% Abamectin, and the 1.9% is consistent with information in the CFS. (Certificate of analysis for the test material was not provided by sponsor).

SPECIES: Rat, albino, Sprague-Dawley derived
AGE(at dosing): young adult, 9-10 weeks
WEIGHT: Males: 210-251 g; Females: 190-226 g
SOURCE: Ace Animals, Inc., Boyertown, PA

EXECUTIVE SUMMARY: *In an acute dermal toxicity study (MRID 45708004), groups of 5M & and/or 5F young adult (9-10 weeks old) albino Sprague-Dawley derived rats were dermally exposed for 24 hrs (occluded exposure) to doses of 2000 (females only) or 5000 mg/kg Abamectin 0.15 EC, Batch #1081701, a straw-amber liquid containing 0.15 lb. Abamectin/gallon. The test material was applied undiluted.*

At 2000 mg/kg 0/5 females died; there were no symptoms. At 5000 mg/kg 0/5 males and 4/5 females died (females died on Days 2-4); none of the males showed any symptoms but symptoms (hunched posture, hypoactivity, prone position, tremors) were observed in several females, although two females died without any symptoms being noted. All survivors at both dose levels gained weight in the period from Day 0 to Day 7 and again from Day 7 to 14.

No gross abnormalities were found on post-sacrifice necropsy in rats which survived to termination. Females which died following dosing at 5000 mg/kg had yellow and/or red intestines, and, in some animals, slightly mottled red or slightly red lungs, discolored liver, and ano-genital staining.

*Dermal LD50 Males > 5000 mg/kg (0/5 died at this dose level)
Dermal LD50 Females > 2000 mg/kg (0/5 died at this dose level); < 5000 mg/kg (4/5 died)
Combined = not stated*

Abamectin 0.15 EC, Batch #1081701, a straw-amber liquid containing 0.15 lb Abamectin /gallon is in toxicity category III in terms of dermal toxicity, based on the dermal LD50 of between 2000 and 5000 mg/kg in females.

Study Classification: Acceptable

COMPLIANCE: Signed and dated GLP Compliance (p. 3), Quality Assurance (p. 19), and [No] Data Confidentiality (p. 2) statements were provided.

Procedure (including deviations from 870.1200): "On the day before application, each group of animals was prepared by clipping the dorsal area and the trunk... The appropriate amount of test substance (2,000 or 5,000 mg/kg) was applied evenly over a dose area of approximately 2 inches x 3 inches (approximately 10% of the body surface) and covered with a 2 inch x 3 inch, 4-ply gauze pad. The gauze pad and entire trunk of each animal were then wrapped with 3 inch Durapore tape to avoid dislocation of the pad and to minimize loss of the test substance... The day of application was considered Day zero of the study. After 24 hours of exposure to the test substance, the pads were removed and the test sites gently wiped with water and a clean towel to remove any residual test substance..."

Results:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
2000	-	0/5	0/5
5000	0/5	4/5	4/10

Observations: None of the 5 females dosed at 2000 mg/kg died or showed any evidence of toxicity. At 5000 mg/kg none of the 5 males died or showed any symptoms; 4/5 females died within 4 days of exposure; signs noted prior to death included a prone posture, tremors and/or hypoactivity. The one female survivor showed similar signs and reduced fecal volume but had recovered by Day 4. All survivors at both dose levels gained weight in the period from Day 0 to Day 7 and again from Day 7 to 14.

Gross Necropsy: 2000 mg/kg: "No gross abnormalities were noted for the animals necropsied at the conclusion of the 14-day observation period."

DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (870.1300, formerly §81-3)

Product Manager: 04
MRID No.: 45708005

Reviewer: Byron T. Backus, Ph.D.

CITATION: Merkel, D.J. Abamectin 0.15 EC Acute Inhalation Toxicity Study in Rats - Limit Test. Laboratory Study No. 11287. Unpublished study prepared by Product Safety Labs, East Brunswick, NJ 08816. Study Completion Date: January 2, 2002. MRID 45708005.

SUBMITTER & SPONSOR: NATIONS AG II, LLC, Williamsburg, VA 23185

TEST MATERIAL: Abamectin 0.15 EC, Batch #1081701. A straw-amber liquid. Composition: Abamectin - 0.15 lb./gallon, pH 5-6. If the product has a density of 0.99 g/mL, then this would be approximately 1.82% Abamectin [=0.15/(8.34 x 0.99)], but from information on the bean sheet the product claim is 1.9% Abamectin, and the 1.9% is consistent with information in the CFS. (Certificate of analysis for the test material was not provided by sponsor).

SPECIES: Rat, albino, Sprague-Dawley derived
AGE(at exposure): young adult, 9-10 weeks
WEIGHT (at exposure): Males: 247-269 g; Females: 184-212 g
SOURCE: Ace Animals, Inc., Boyertown, PA

EXECUTIVE SUMMARY: *In an acute inhalation toxicity study (MRID 45708005), a group of 5 male and 5 female young adult (9-10 weeks old) Sprague-Dawley rats received a 4-hour nose-only exposure to a mean concentration of 2.13 mg/L (gravimetrically determined) Abamectin 0.15 EC, a straw amber liquid with 0.15 lb Abamectin/gallon. The MMAD was 2.15 µm, and the GSD was 2.00.*

There were no mortalities (0/5 males & 0/5 females died), although 4/5 males and 3/5 females showed symptoms of toxicity (hypoactivity was seen in all rats which showed signs; in addition, irregular respiration, hunched posture, and tremors were also observed in some of these rats). All rats had recovered by Day 2. All had bodyweight gains in the period from Day 0 to Day 7 and again from Day 7 to Day 14.

No gross abnormalities were found following post-sacrifice necropsy.

*Inhalation LC50 Males > 2.13 mg/L (0/5 died with nose-only exposure)
Inhalation LC50 Females > 2.13 mg/L (0/5 died with nose-only exposure)
Combined LC50 > 2.13 mg/L (0/10 rats died)*

Abamectin 0.15 EC, a straw amber liquid with 0.15 lb Abamectin/gallon, is in toxicity category IV in terms of acute inhalation toxicity, based on the LC50 > 2.13 mg/L under nose-only exposure conditions.

Study Classification: *Acceptable*

COMPLIANCE: Signed and dated GLP (p. 3), Quality Assurance (p. 22) and [No] Data Confidentiality (p. 2) statements are provided.

Procedure (including deviations from 870.1300): "The test substance was a straw-amber liquid... The sample was aerosolized as received... The exposure procedures and atomization equipment used were based on the results of [a] pre-test trial... which provided a gravimetric concentration of 2.06 mg/L and a mass median aerodynamic diameter of 2.1 µm."

Results:

Mean Exposure Concentration mg/L ± S.D. (Gravimetrically Determined)	Number of Deaths/Number Tested		
	Males	Females	Combined
2.13 ± 0.15 (nose-only exposure)	0/5	0/5	0/10

The nominal concentration was 14.93 mg/L.

Clinical Observations: There was no mortality. "Clinical signs noted in the test animals [symptoms were observed in 4/5 males and 3/5 females] following exposure included irregular respiration, hunched posture and hypoactivity. In addition, one female exhibited tremors one hour after the termination of the exposure period. However, all animals recovered from these symptoms by Day 2 and appeared active and healthy for the remainder of the study..." All animals gained bodyweight in the period from Day 0 to Day 7 and again in the period from Day 7 to Day 14.

Gross Necropsy: No gross abnormalities were observed on post-sacrifice necropsy.

Chamber Atmosphere		
Grav. Conc. (mg/L)	MMAD (µm)	Mean GSD
2.13	2.15	2.00

Particle Size Distribution: >70% of the particles by weight had an effective cut-off diameter of 3.3 µm or smaller.

Chamber Environment	
Internal Chamber Volume	6.7 L
Mean Airflow	25.6 LPM
Mean Temperature	21°C
Relative Humidity Range	46-52%

DATA REVIEW FOR PRIMARY EYE IRRITATION TESTING (870.2400, formerly §81-4)

Product Manager: 04
MRID No.: 45708006

Reviewer: Byron T. Backus, Ph.D.

CITATION: Merkel, D.J. Abamectin 0.15 EC Primary Eye Irritation Study in Rabbits. Laboratory Study Number 11288. Unpublished study prepared by Product Safety Labs, East Brunswick, NJ 08816. Study Completion Date: January 2, 2002. MRID 45708006.

SUBMITTER & SPONSOR: NATIONS AG II, LLC, Williamsburg, VA 23185

TEST MATERIAL: Abamectin 0.15 EC, Batch #1081701. A straw-amber liquid. Composition: Abamectin: 0.15 lb/gallon, pH 5-6. If the product has a density of 0.99 g/mL, then this would be approximately 1.82% Abamectin [$=0.15/(8.34 \times 0.99)$], but from information on the bean sheet the product claim is 1.9% Abamectin, and the 1.9% is consistent with information in the CFS. (Certificate of analysis for the test material was not provided by sponsor).

SPECIES: Rabbit, New Zealand White (2 males and 1 female used)

AGE: "young adult"

WEIGHT: not stated

SOURCE: Davidson's Mill Farm, South Brunswick, NJ

EXECUTIVE SUMMARY: *In a primary eye irritation study (MRID 45708006), 0.1 mL of Abamectin 0.15 EC, Batch #1081701, a straw-amber liquid containing 0.15 lb./gallon Abamectin, was instilled into one eye of each of 3 young adult New Zealand white rabbits.*

All 3 eyes showed corneal opacity from 24 hrs through Day 4, and 2/3 eyes still showed corneal opacity on Day 10. One eye had corneal opacity on Day 14 but this had cleared by Day 17. In addition, all three eyes were positive for conjunctival irritation at 48 hours, but this had cleared by Day 7.

The test material, Abamectin 0.15 EC, Batch #1081701, a straw-amber liquid containing 0.15 lb./gallon Abamectin, is in toxicity category II in terms of primary eye irritation potential, based on the occurrence of corneal opacity in 2/3 eyes on Day 10 which had completely cleared by Day 17.

Study Classification: *Acceptable*

COMPLIANCE: Signed and dated GLP (p. 3), Quality Assurance (p. 17) and [No] Data Confidentiality (p. 2) statements are provided.

Procedure (including deviations from 870.2400): "One-tenth of a milliliter of the test substance, as received, was instilled into the conjunctival sac of the right eye of each rabbit by pulling the lower lid away from the eyeball. The upper and lower lids were then gently held together for about one second before releasing to minimize loss of the test substance..."

Results:

Observations	Number scoring positive/total number						
	1 hr	24 hrs	72 hrs	7 days	10 days	14 days	17 days
Corneal Opacity	0/3	3/3	3/3	2/3	2/3	1/3	0/3
Iritis	0/3	0/3	0/3	0/3	0/3	0/3	0/3
Conjunctivae:							
Redness ^a	3/3	3/3	1/3	0/3	0/3	0/3	0/3
Chemosis ^a	3/3	0/3	0/3	0/3	0/3	0/3	0/3
Discharge ^a	3/3	3/3	0/3	0/3	0/3	0/3	0/3

^aScore of 2 or more considered positive.

A fluorescein dye evaluation procedure (one drop of 2% ophthalmic fluorescein sodium installed into the eye) was used at 24 hours and, as needed, at subsequent scoring intervals to evaluate the extent of corneal damage or to verify reversal of effects.

All 3 eyes scored "2" for conjunctival redness at 1, 24 and 48 hours, and 1/3 scored "2" for conjunctival redness at 72 hours, and this was the maximum conjunctival redness observed (all eyes scored zero for conjunctival effects on Day 7). All eyes scored "1" for corneal opacity at 24, 48 and 72 hours and on Day 4. One eye had cleared by Day 7, an additional one had cleared by Day 14 and the last one had cleared by Day 17.

DATA REVIEW FOR PRIMARY DERMAL IRRITATION TESTING (870.2500, formerly §81-5)

Product Manager: 04
MRID No.: 45712801

Reviewer: Byron T. Backus, Ph.D.

CITATION: Merkel, D.J. Abamectin 0.15 EC Primary Skin Irritation Study in Rabbits. Laboratory Study Identification No. 11289. Unpublished study prepared by Product Safety Labs, East Brunswick, NJ 08816. Study Completion Date: January 2, 2002. MRID 45712801.

SUBMITTER & SPONSOR: NATIONS AG II, LLC, Williamsburg, VA 23185

TEST MATERIAL: Abamectin 0.15 EC, Batch #1081701. A straw-amber liquid. Composition: Abamectin: 0.15 lb/gallon, pH 5-6. If the product has a density of 0.99 g/mL, then this would be approximately 1.82% Abamectin [$=0.15/(8.34 \times 0.99)$], but from information on the bean sheet the product claim is 1.9% Abamectin, and the 1.9% is consistent with information in the CFS. (Certificate of analysis for the test material was not provided by sponsor).

SPECIES: Rabbit, albino, New Zealand White (2 males and 1 female used)

AGE: "young adult"

WEIGHT: not stated

SOURCE: Davidson's Mill Farm, South Brunswick, NJ

EXECUTIVE SUMMARY: *In a dermal irritation study (MRID 45712801), 0.5 mL of Abamectin 0.15 EC, a straw-amber liquid containing 0.15 lb Abamectin/gallon, pH 5-6 was applied to an intact skin site on the back of each of 3 New Zealand white rabbits, with 4-hr semi-occluded exposure.*

At 1 and 24 hours all scores for erythema were "1," at 48 hrs 1/3 sites scored "1" for erythema and the remaining sites scored zero. At 72 hours all sites scored zero for erythema. All scores for edema (at 1, 24, 48 and 72 hours) were zero. The Primary Irritation Index (average of 1, 24, 48 and 72 hour scores) = 0.58. The test material, Abamectin 0.15 EC, a straw-amber liquid containing 0.15 lb Abamectin/gallon, is in toxicity category IV in terms of primary skin irritation potential.

Study Classification: *Acceptable*

COMPLIANCE: Signed and dated GLP (p. 3), Quality Assurance (p. 15) and [No] Data Confidentiality (p. 2) statements were provided.

Procedure (including deviations from 870.2500): "On the day before application, a group of animals was prepared by clipping...the dorsal area and the trunk... Five-tenths of a milliliter of the test substance was applied to one 6 cm² intact dose site on each animal and covered with a 1 inch . The pad and entire trunk of each animal were then wrapped with semi-occlusive 3 inch Micropore tape to avoid dislocation of the pad. Elizabethan collars were placed on each rabbit... After 4 hours of exposure to the test substance, the pads and collars were removed and the test sites gently wiped with water and a clean towel to remove any residual test substance."

Results: At 1 and 24 hours all scores for erythema were "1," at 48 hrs 1/3 sites scored "1" for erythema and the remaining sites scored zero. At 72 hours all sites scored zero for erythema. All scores for edema (at 1, 24, 48 and 72 hours) were zero. The Primary Irritation Index (average of 1, 24, 48 and 72 hour scores) = 0.58.

DATA REVIEW FOR DERMAL SENSITIZATION TESTING (870.2600, formerly §81-6)

Product Manager: 04
MRID No.: 45708007

Reviewer: Byron T. Backus, Ph.D.

CITATION: Merkel, D.J. Abamectin 0.15 EC Dermal Sensitization Study in Guinea Pigs (Buehler Method). Laboratory Study Identification No. 11290. Unpublished study prepared by Product Safety Labs, East Brunswick, NJ 08816. Study Completion Date: January 2, 2002. MRID 45708007.

SUBMITTER & SPONSOR: NATIONS AG II, LLC, Williamsburg, VA 23185

TEST MATERIAL: Abamectin 0.15 EC, Batch #1081701. A straw-amber liquid. Composition: Abamectin: 0.15 lb/gallon, pH 5-6. If the product has a density of 0.99 g/mL, then this would be approximately 1.82% Abamectin [$=0.15/(8.34 \times 0.99)$], but from information on the bean sheet the product claim is 1.9% Abamectin, and the 1.9% is consistent with information in the CFS. (Certificate of analysis for the test material was not provided by sponsor).

SPECIES: Guinea Pig, albino, Hartley, Females only (test group)

AGE(at initiation of induction): "Young adult"

WEIGHT(at initiation of induction): Females: 334-396 g

SOURCE: Elm Hill Breeding Labs, Chelmsford, MA

EXECUTIVE SUMMARY: *In a dermal sensitization study (MRID 45708007) using a Buehler protocol, 20 young adult Hartley albino female guinea pigs each received a total of three six-hour occluded induction exposures, once a week for three weeks, to 0.4 mL of undiluted Abamectin 0.15 EC (identified as containing 0.15 lb Abamectin/gallon, or 1.9% Abamectin).*

Twenty-seven days after the first induction dose, previously induced guinea pigs were challenged (at a previously unexposed dermal site), along with a previously unexposed control group of 10 female guinea pigs, to a 6-hr exposure to 0.4 mL of undiluted Abamectin 0.15 EC (identified as containing 0.15 lb Abamectin/gallon). A naive control group of 10 females was exposed at challenge only.

During induction, the maximum irritation following each of the first two exposures was 0.5. Following the third induction treatment 11/20 of the guinea pigs scored 1.0 at 24 hours (the remaining 9 scored 0.5) and 20/20 scored 0.5 at 48 hours. At challenge 13/20 scored 0.5 at 24 hours and 6/20 scored 0.5 at 48 hours (0.5 was the maximum score); the corresponding incidences for the naive controls were 3/10 and 1/10. As "0.5" is not a positive response, it is concluded that the test material did not elicit a dermal sensitization reaction.

The report includes a positive control study which used 1-Chloro-2,4-Dinitrobenzene (DNCB) as the test material (with 0.08% w/w DNCB in 80% aqueous alcohol used for inductions, and 0.04% w/w DNCB in acetone used for challenge). The results were appropriate. This study was completed on August 17, 2001; it is noted that the first induction treatment with Abamectin technical was on or shortly after October 3, 2001.

Study Classification: *Acceptable. The findings of this study are consistent with a lack of dermal sensitization activity for the test material, Abamectin 0.15 EC, a straw-amber liquid containing 0.15 lb Abamectin/gallon.*

COMPLIANCE: Signed and dated GLP (p. 3), Quality Assurance (p. 24) and [No] Data Confidentiality (p. 2) statements are provided.

Procedure: The dosages used for induction and challenge were based on a preliminary irritation study. For induction: "Once each week for three weeks, four-tenths of a milliliter of the undiluted test substance was applied to the left side of each test animal using an occlusive 25 mm Hill Top Chamber[®]. The chambers were secured in place and wrapped with non-allergenic Durapore adhesive tape to avoid dislocation of the chambers and to minimize loss of the test substance. After the 6-hour exposure period, the chambers were removed and the test sites were gently wiped with water and a clean towel to remove any residual test substance. Approximately 24 and 48 hours after each induction application, readings were made of local reactions (erythema)..."

For challenge: "Twenty-seven days after the first induction dose, four-tenths of a milliliter of the HNIC of the test substance (100%) was applied to a naive site on the right side of each animal as a challenge dose... These sites were evaluated for a sensitization response (erythema) approximately 24 and 48 hours after the challenge application... In addition to the [previously induced] test animals, 10 guinea pigs from the same shipment were maintained under identical environmental conditions and were treated with the HNIC of the test substance at challenge only. These animals constituted the "naive" group."

Results: During induction, the maximum irritation following each of the first two exposures was 0.5. Following the third induction treatment 11/20 of the guinea pigs scored 1.0 at 24 hours (the remaining 9 scored 0.5) and 20/20 scored 0.5 at 48 hours. At challenge 13/20 scored 0.5 at 24 hours and 6/20 scored 0.5 at 48 hours (0.5 was the maximum score); the corresponding incidences for the naive controls were 3/10 and 1/10. As "0.5" is not a positive response, it is concluded that the test material did not elicit a dermal sensitization reaction.

The report includes a positive control study which used 1-Chloro-2,4-Dinitrobenzene (DNCB) as the test material (with 0.08% w/w DNCB in 80% aqueous alcohol used for inductions, and 0.04% w/w DNCB in acetone used for challenge). The results were appropriate. This study was completed on August 17, 2001; the first induction treatment with Abamectin technical was on or shortly after October 3, 2001.

ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D285189
2. **PC CODE:** 122804 Abamectin
3. **CURRENT DATE:** December 30, 2002
4. **TEST MATERIAL:** Abamectin 0.15 EC, Batch #1081701. A straw-amber liquid. Composition: Abamectin: 0.15 lb/gallon, pH 5-6. If the product has a density of 0.99 g/mL, then this would be approximately 1.82% Abamectin [=0.15/(8.34 x 0.99)], but from information on the bean sheet the product claim is 1.9% Abamectin, and the 1.9% is consistent with information in the CFS. (Certificate of analysis for the test material was not provided by sponsor).

Study/Species/Lab Study #/Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat/ Product Safety Labs/Lab Study No. 11285/JAN-2-2002	45708003	LD ₅₀ (M) = 271 (95% C.L. 158-429) mg/kg; LD ₅₀ (F) = 455 (95% C.L. 236-1013) mg/kg. 0/5M & 0/5F died at 50 mg/kg; 4/5M & 3/5F died at 500 mg/kg; and 5/5M and 5/5F died at 5000 mg/kg. At 50 mg/kg 1F had reduced fecal volume with recovery by Day 2; at 500 mg/kg symptoms included abnormal posture, tremors, hypoactivity, facial staining and/or reduced fecal volume with recovery by Day 6. At 500 mg/kg animals which died had discoloration of lungs and intestines.	II	A
Acute dermal toxicity/rat/ Product Safety Labs/Lab Study No. 11286/JAN-2-2002	45708004	LD ₅₀ (M) > 5000 mg/kg (0/5 died at this dose level; no symptoms). LD ₅₀ (F) > 2000 mg/kg (0/5 died at this dose level; no symptoms). 4/5 females died at 5000 mg/kg so LD ₅₀ (F) < 5000 mg/kg. Symptoms in females at 5000 mg/kg included hunched position, hypoactivity, prone position and tremors, although 2 animals which died did so without any symptoms being noted. Necropsy findings in females which died at 5000 mg/kg: yellow and/or red intestines and in some, slightly mottled red or slightly red lungs, discolored liver and anogenital staining.	III	A
Acute inhalation toxicity/ rat/ Product Safety Labs/ Lab Study No. 11287/ JAN-2-2002	45708005	LC ₅₀ > 2.13 mg/L by nose-only exposure (no mortalities among 5 M, 5 F); hypoactivity was observed in 4/5M & 3/5F; in addition, some of the rats with hypoactivity also showed other signs (irregular respiration, hunched posture and tremors) with symptoms clearing by Day 2. MMAD = 2.15 µm; GSD = 2.00	IV	A
Primary eye irritation/ rabbit/Product Safety Labs /Lab Study No. 11288/ JAN-2-2002	45708006	3 NZ white rabbit eyes exposed. 0.1 mL test material) instilled. All 3 eyes showed corneal opacity from 24 hrs through Day 4, and 2/3 eyes still showed corneal opacity on Day 10. All eyes had cleared by Day 17.	II	A

Primary dermal irritation/ rabbit/Product Safety Labs /Lab Study No. 11289/ JAN-2-2002	45712801	PII (av. of 1, 24, 48 & 72 hr scores) = 0.58; at 1 & 24 hrs all scores for erythema were 1, at 48 hrs 1/3 sites scored 1 for erythema and 2/3 scored zero; at 72 hrs all sites scored 0 for erythema. All scores (1, 24, 48 & 72 hrs) for edema were zero.	IV	A
Dermal sensitization/ guinea pig/Product Safety Labs/Lab Study No. 11290/ JAN-2-2002	45708007	Buehler protocol: 20 Hartley albino female guinea pigs each received a total of 3 6-hr occluded exposures to 0.4 mL undiluted test material, then were challenged (along with 10 naive guinea pigs) to 0.4 mL undiluted test material 27 days after first induction dose. Maximum score seen on challenge was 0.5 (not a positive response), consistent with a lack of dermal sensitization activity for test material.	Not a sen sitiz er	A

Core Grade Key: **A** =Acceptable, **S** = Supplementary, **U** = Unacceptable, **V** = Self Validated