Version 18 Updated 2/99

MEMORANDUM

DATE: 18 - MAY - 1999

SUBJECT: ID#99OK0008. SECTION 18 EXEMPTION FOR THE USE OF EMAMECTIN ON COTTON IN OKLAHOMA.

DP Barcode:	D255356	PRAT Case:	291856
Submission No.:	S560659	Caswell No.:	999
Chemical No.:	122806	Class:	Insecticide
Trade Name:	Denim 0.16EC	EPA Reg No.:	N/A
40 CFR:	180.505	MRID No.	N/A

TO: Robert Forrest/Andrea Beard, PM Team 41
MUIERB/RD (7505C)

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INTRODUCTION

The Oklahoma Department of Agriculture is proposing an emergency exemption for the use of emamectin (product name Denim) on cotton for control of the beet armyworm. This is the first Section 18 request for this use. The proposed program will entail application of 28,125 gallons of Denim (4500 lbs active ingredient) on 150,000 acres throughout the state during the period from June 1 to October 31, 1999.

SUMMARY

Occupational exposure and aggregate risk estimates do not exceed HED's level of concern. This Section 18 exemption should not pose an unacceptable aggregate risk to infants, children, or adults. Therefore, HED has no objection to the issuance of this Section 18 exemption for the use of emamectin on cotton in the State of Oklahoma. A time-limited tolerance for residues of emamectin and its regulated metabolites at the following levels should be established to support this Section 18 exemption.

Cottonseed	0.002 ppm
Cottonseed oil	0.006 ppm
Cotton meal	0.002 ppm
Cotton hulls	0.004 ppm
Cotton gin trash	0.025 ppm

Also, time-limited tolerances in milk, meat, fat, kidney and liver of cattle, goats, sheep, and swine should be established at 0.002 ppm. Poultry tolerances are not needed since exposure to chickens would be negligible.

It should be noted that, according to the Worker Protection Standard, **a 48-hour restricted-entry interval (REI) is required on emamectin product labels** based upon the chemical's classification as a Toxicity Category 1 eye irritant. Recently, HED was asked to comment on Novartis' request to reduce the restricted-entry interval (REI) for the products with the trade name Proclaim (active ingredient emamectin) to 12 hours (see memo dated 5/10/99, Barcode D254469). This request from the registrant is associated with the use of emamectin on various leafy vegetables and cole crops, for which HED recently completed a human health risk assessment (4/6/99, Barcode D241907). In that document it was concluded that a 48-hour REI is needed to comply with the Worker Protection Standard (WPS).

A. TOXICOLOGICAL ENDPOINTS

The FQPA Safety Factor Committee (4/13/98), determined that the ten-fold Safety Factor for enhanced sensitivity of infants and children as required by the Food Quality Protection Act of 1996 should be reduced to 3X for this active ingredient. A copy of the report of the FQPA Safety Factor Committee for emamectin is included as an attachment to this assessment.

The following information was reported in the Hazard Identification Assessment Review Committee report dated March 19, 1998 and the FQPA Safety Factor Committee report dated April 23, 1998. Both of these reports are provided as attachments to this memorandum.

Toxicological Endpoints Selected for Emamectin Risk Assessments

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY, MRID
Acute Dietary	NOAEL=0.075	Tremors observed on day 3 of dosing.	15-day mouse; 42851503
	U.S. Population: Acute RfD[1] = 0.00075 mg/kg/day (Uncertainty Factor=100)		
	Infants, Children and Females 13+: Acute PAD[2] = 0.00025 (Uncertainty Factor=300)		
Chronic Dietary (non-cancer)	NOAEL=0.075	Moribund sacrifices, clinical signs of neurotoxicity, decreased body weight and food consumption and histopathological lesions in the sciatic nerve.	15-day mouse; 42851503
	U.S. Population: Chronic RfD = 0.00025 mg/kg/day (Uncertainty Factor=300)		
	Infants, Children and Females 13+: Chronic PAD = 0.000083 mg/kg/day (Uncertainty Factor=900)		
Chronic Dietary (Cancer)	No evidence of carcinogenicity.		
Short-Term (Dermal)	Oral NOAEL=0.075	Tremors observed on day 3 of dosing.	15-day mouse; 42851503
Intermediate-Term (Dermal)	Oral NOAEL=0.075	Moribund sacrifices, clinical signs of neurotoxicity, decreased body weight and food consumption and histopathological lesions in the sciatic nerve.	15-day mouse; 42851503
Long-Term (Dermal)[a] (Non-cancer)	Based on the use pattern, long-term dermal exposure is not a concern; risk assessment not required.		
Inhalation (Any Time Period)	Oral NOAEL=0.075	Moribund sacrifices, clinical signs of neurotoxicity, decreased body weight and food consumption and histopathological lesions in the sciatic nerve.	15-day mouse; 42851503
Dermal Absorption	Rate: 1.8%		26-day Rhesus monkey; 43850113

1. RfD=Reference Dose. Used to determine dietary risk to general (i.e. non-susceptible) populations.
2. PAD=Population Adjusted Dose. Used to determine dietary risk to susceptible populations (i.e., infants, children and females 13+).

OPP's FQPA Safety Factor Committee met on April 13, 1998 and determined that the ten-fold FQPA Safety Factor for the protection of infants and children should be reduced to three. The Committee's decision was based on the following rationale:

- No increased susceptibility was demonstrated in rats or rabbits following *in utero* exposure to emamectin, although increased susceptibility was demonstrated in a developmental neurotoxicity study in rats;
- Although increased susceptibility was demonstrated in a developmental neurotoxicity study in rats, the Committee determined that the 10x factor should be reduced to 3x based on the following weight-of-the-evidence considerations in the developmental neurotoxicity study: 1) the LOAEL was based on a single effect/end point (i.e., decrease in open field motor activity); 2) the effect at the LOAEL was seen only on postnatal day 17 and was not seen either on earlier (Day 13) or later (Day 21) evaluations whereas at the high dose (3.6/2.5 mg/kg/day), this effect was seen on postnatal days 13 and 17; 3) the effect at the LOAEL was not accompanied with other toxicity whereas at the high dose tremors and hindlimb splay were also seen; 4) the decreased performance was lower only when compared to the concurrent control; and 5) there was limited (only 2 studies) historical control data available for comparison.
- Exposure assessments do not indicate a concern for potential risk to infants and children because: 1) the dietary exposure estimates are based on field study data assuming 100% percent crop treated resulting in an overestimate of dietary exposure; 2) modeling data

1. Acute Dietary Toxicity. **Acute RfD = 0.00075** EPA has established the acute Reference dose (RfD) for emamectin at 0.00075 milligrams/kilogram/day (mg/kg/day). This acute RfD was established based on a maternal no observable adverse effect level (NOAEL) of 0.075 mg/kg/day from a 15-day neurotoxicity study in mice. Tremors were observed on the third day of dosing at the lowest observable adverse effect level (LOAEL) of 0.10 mg/kg/day. The population subgroups of concern for this endpoint are: infants, children and females 13 years and older. An uncertainty factor of 100 to account for inter-species extrapolation and intra-species variability was applied to the NOAEL of 0.075 mg/kg/day to calculate the acute RfD of 0.00075 mg/kg/day. EPA has determined that the 10-fold safety factor to account for enhanced susceptibility of infants and children (as required by FQPA) be reduced to 3X. This determination is based on the results of reproductive and developmental toxicity studies.

This risk assessment will evaluate acute dietary risk for infants, children and females 13 years and older ("13+"), the population subgroups of concern. Due to the reduction of the FQPA safety factor (3X), acute dietary exposures for the subgroups of concern will be compared to the acute population-adjusted dose (acute PAD). In this case, the acute PAD was calculated as follows:

$$\frac{\text{Acute RfD}=0.00075\ \text{mg/kg/day}}{\text{FQPA Safety Factor of 3}} = \text{Acute PAD} = 0.00025\ \text{mg/kg/day}$$

For acute dietary exposure, EPA determined that the 10X safety factor is applicable to the subpopulations females (13+ years), as well as infants and children.

2. *Short- and Intermediate-Term Dermal and Inhalation Toxicity.* **The NOAEL of 0.075 mg/kg/day** from the neurotoxicity study in mice (discussed above in 1. *Acute Dietary Toxicity*) was also identified as the toxicological endpoints for short- and intermediate-term dermal and inhalation toxicity. A dermal absorption rate of 1.8%, based on a dermal absorption study in Rhesus monkeys. 100% absorption is assumed for inhalation risk assessments. Generally, margins of exposure (MOEs) of 100 or greater are acceptable.

2. Chronic Dietary Toxicity. **Chronic RfD = 0.00025 mg/kg/day** EPA has established the chronic RfD for emamectin at 0.00025 mg/kg/day. This RfD is based on the no observable adverse effect level (NOAEL) of 0.075 mg/kg/day from a neurotoxicity study in mice. Moribund sacrifices, clinical signs of neurotoxicity, decreased body weight and food consumption and histopathological lesions in the sciatic nerve were observed at the lowest observable adverse effect level (LOAEL) of 0.1 mg/kg/day. An uncertainty factor of 100 to account for inter-species extrapolation and intra-species variability was applied to the NOAEL. EPA has determined that the 10X factor to account for enhanced susceptibility of infants and children (as required by FQPA) be reduced to 3X. This determination is based on the results of reproductive and developmental toxicity studies.

This risk assessment will evaluate acute dietary risk for infants, children and females 13 years and older ("13+"), the population subgroups of concern. Due to the reduction of the FQPA safety factor (3X), chronic dietary exposures for the subgroups of concern will be compared to the chronic population-adjusted dose (chronic PAD). In this case, the chronic PAD was calculated as follows:

$$\frac{\text{Chronic RfD}=0.00025\ \text{mg/kg/day}}{\text{FQPA Safety Factor of 3}} = \text{Chronic PAD} = 0.000083\ \text{mg/kg/day}$$

4. *Carcinogenicity.* Emamectin is classified as a "not likely" human carcinogen. This classification was based on the lack of evidence of carcinogenicity in male and female rats or male and female mice at doses that were judged to be adequate to assess the carcinogenic potential of the chemical.

B. EXPOSURES AND RISKS

1. From Food and Feed Uses: Tolerances have been established (40 CFR 180.505) for emamectin and its metabolites, in or on a variety of raw agricultural commodities. Secondary residues are expected in animal commodities as gin trash containing measurable residues is among the feed items associated with this Section 18 use. Poultry tolerances are not needed since exposure to chickens would be negligible. Risk assessments were conducted by EPA to assess dietary exposures and risks from emamectin as follows:

i. *Acute Dietary Exposure and Risk*: Acute dietary risk assessments are performed for a food-use pesticide if a toxicological study has indicated the possibility of an effect of concern occurring as a result of a one day or single exposure. An acute dietary (food) risk assessment was submitted by the petitioner where the DEEM (Dietary Exposure Evaluation Model) system Tier 3 (Monte Carlo) approach was used. This methodology incorporates distributions of residues and refined percent of crop treated estimates for some crops, and thus results in refined risk estimates. This acute dietary exposure analysis from food sources was conducted using the Acute PAD of 0.00025 mg/kg/day. The acute analysis was conducted using half of LOQ values in a probabilistic analysis. The analysis evaluated individual food consumption as reported by respondents in the USDA Continuing Surveys of Food Intake by Individuals conducted in 1989 through 1992. The model accumulated exposure to emamectin for each commodity and expresses risk as a function of dietary exposure. For the most highly exposed population subgroup, Children 1-6 years old, the resulting high-end exposure (at the 99.9th percentile) occupies 65% of the acute PAD. For the overall U.S. Population, the high-end exposure (99.9th percentile) occupies 29% of the acute PAD.

Acute Dietary Exposure Estimates at the 99.9th Percentile

Populations Subgroup	Exposure (mg/kg/day)	% Acute PAD[1]
US Population	0.000074	29
All Infants	0.000023	9.2
Nursing Infants	0.000016	6.5
Non-Nursing Infants	0.000024	9.6
Children 1-6 years	0.00016	65
Children 7-12 years	0.000086	34
Females (13+ years/nursing)	0.000067	27

1. PAD=Population-adjusted dose: The acute RfD/FQPA safety factor = 0.00075/3 = 0.00025 mg/kg/day.

ii. *Chronic Dietary Exposure and Risk:* The Agency conducted a chronic dietary exposure analysis and risk assessment. The chronic analysis for emamectin used the Chronic PAD of 0.000083 mg/kg/day. The analysis evaluated individual food consumption as reported by respondents in the USDA 1989-92 Continuing Surveys of Food Intake by Individuals and accumulates exposure to the chemical for each commodity. The chronic analysis was conducted using tolerance-level residues and 25% percent of crop treated information for broccoli, Brussels sprouts, cabbage, cauliflower, lettuce and celery. For the most highly exposed population subgroup, Children 1-6 years old, the resulting exposure occupies 21% of the chronic PAD. For the overall U.S. Population, the exposure occupies 15% of the chronic PAD.

Chronic Dietary Exposure Estimates

Populations Subgroup	Exposure (mg/kg/day)	%Chronic PAD[1]
US Population	0.000013	15
All Infants	0.000001	1.6
Nursing Infants	0.000001	1
Non-Nursing Infants	0.000002	1.8
Children 1-6 years	0.000018	21
Children 7-12 years	0.000013	16
Females (13+years/nursing)	0.000017	20

1. PAD=Population-adjusted dose: The chronic RfD/FQPA safety factor = 0.000025 / 3 = 0.000083 mg/kg/day.

iii. *Cancer Risk.* Emamectin was classified as a "not likely" human carcinogen. Therefore, a dietary cancer risk assessment was not conducted.

2. *From Drinking Water:* There are no established Maximum Contaminant Levels or health advisory levels for residues of emamectin in drinking water. HED does not have monitoring data available to perform a quantitative drinking water risk assessment for emamectin at this time. The Environmental Fate and Effects Division (EFED) provided ground and surface water exposure estimates for use of emamectin on cabbage (12/2/98) as well as information about emamectin environmental fate.

In the environment, emamectin and its primary degradates are expected to be relatively immobile due to the high degree of sorption to soil particles. Concentrations for surface water exceeded those for ground water; therefore, HED used surface water values for risk calculations. The estimated environmental concentration (EEC) for acute drinking water exposure is 0.107 ppb, from the PRZM/EXAMS model (surface water). The highest EEC for chronic drinking water exposure is 0.0203 ppb from the PRZM/EXAMS model. The drinking water values provided by EFED can be considered to include both emamectin and its metabolites AB1a, MFB1a, and FAB1a. In calculating aggregate dietary risk, these estimates were compared to back-calculated Drinking Water Levels of Comparison (DWLOCs) for emamectin.

Drinking water levels of comparison (DWLOCs) are calculated and compared to the models' estimates for both surface and ground water. DWLOCs are theoretical upper limits on a pesticide's concentration in drinking water in light of total aggregate exposure to a pesticide in food, drinking water, and through residential uses. A DWLOC will vary depending on the toxic endpoint, with drinking water consumption, and body weights. Different populations will have different DWLOCs. Since DWLOCs address total aggregate exposure to emamectin they are further discussed in the aggregate risk sections below.

HED has calculated DWLOCs for acute exposure to emamectin and its metabolites for the U.S. population and selected subgroups. Values for acute and chronic DWLOCs are presented in the tables below.

Summary of Acute Drinking Water Levels of Comparison Calculations.

Population Subgroup[1]	Acute Scenario					
	Acute PAD (mg/kg/day)	Acute Food Exposure (mg/kg/day)	Maximum Water Exposure (mg/kg/day)[2]	SCI-GROW (μg/L)	PRZM/ EXAMS (ppb)	Acute DWLOC (μg/L)
U.S. Population	0.00025	0.000074	0.00018	0.006	0.107	6.2
Children (1-6 years)	0.00025	0.00016	0.00009	0.006	0.107	1
Females 13+ years/nursing	0.00025	0.000067	0.00018	0.006	0.107	5.5

[1]Population subgroups chosen were U.S. population (70 kg. body weight assumed), and the two children subgroups with the highest food exposure (10 kg. body weight assumed).
[2]Maximum Water Exposure (mg/kg/day) = Acute PAD (mg/kg/day) - ARC from DEEM (mg/kg/day)

Summary of Chronic Drinking Water Levels of Comparison Calculations.

Population Subgroup[1]	Chronic Scenario					
	Chronic PAD (mg/kg/day)	Chronic Food Exposure (mg/kg/day)	Maximum Water Exposure (mg/kg/day)[2]	SCI-GROW (μg/L)[3]	PRZM/EXAMS (ppb)	Chronic DWLOC (μg/L)
U.S. Population	0.000083	0.000013	0.00007	0.0006	0.0203	2.5
Children (1-6 years)	0.000083	0.000018	0.000065	0.0006	0.0203	0.65
Females (13+ years)	0.000083	0.000017	0.000066	0.0006	0.0203	2.0

[1]Population subgroups chosen were U.S. population (70 kg. body weight assumed), the infant or children subgroup with the highest food exposure (10 kg. body weight assumed), and females 13+ (60 kg body weight assumed).
[2]Maximum Water Exposure (mg/kg/day) = Chronic RfD (mg/kg/day) - ARC from DEEM (mg/kg/day)
[3]The crop producing the highest level was used.

3. From Non-Dietary Uses: Emamectin is currently not registered for use on any residential non-food sites. The proposed and existing uses of emamectin are not expected to result in residential exposure. Therefore, HED did not calculate residential risk estimates.

4. From Cumulative Exposure to Substances with a Common Mechanism of Toxicity: Emamectin is synthetically derived avermectin, which is a member of the actinomycetes, antibiotic-producing chemicals, which are the source of all antibiotic pesticides. *Streptomyces avermitilus* produces the insecticide abamectin, which is a mixture of two homologues which

have equal biological activity. Currently, members of this class which are registered for agricultural uses include abamectin and emamectin. Avermectin and ivermectin are structurally similar to emamectin. For the purposes of this tolerance action, therefore, HED has not assumed that emamectin has a common mechanism of toxicity with other substances.

C. AGGREGATE RISK AND DETERMINATION OF SAFETY FOR U.S. POPULATION

1. Acute Aggregate Risk: There are currently no registered residential uses of emamectin or uses which may expose residents. Therefore, acute aggregate risk consists of exposure from food and drinking water sources only. Food-source acute dietary risk results in 29% of the acute PAD for the US population including infants and children.

The estimated maximum concentrations of emamectin and its metabolites in surface and ground water are less than HED's DWLOCs as a contribution to acute aggregate exposure. The estimated concentrations of emamectin and its metabolites in ground and surface water are conservative estimates. Therefore, HED concludes with reasonable certainty that residues of emamectin in food and drinking water would not result in an unacceptable estimate of acute or chronic (non-cancer) aggregate human health at this time.

As discussed earlier, exposure to emamectin residues in food will occupy no more than 29% of the acute PAD for adult population subgroups and no more than 65% of the acute PAD for infant/children subgroups. Residue levels used for food-source dietary risk assessments were partially refined and did incorporate percent of crop treated information. Acute dietary exposure estimates were for the 99.9th percentile. As discussed earlier, estimated concentrations of emamectin residues in surface and ground water are lower than HED's DWLOCs. Estimated drinking water levels were calculated using EFEDs drinking water models, and the values are considered conservative. Therefore, HED does not expect chronic aggregate risk to emamectin residues from food and water sources to exceed HED's level of concern for chronic aggregate risk.

2. Short- and intermediate-term risk: Not applicable. There are no registered residential uses of emamectin.

3. Chronic Aggregate Risk: As discussed earlier, exposure to emamectin residues in food will occupy no more than 15% of the chronic PAD for the U.S. population and no more than 21% of the chronic PAD for infant, children and females 13+ subgroups. Residue levels used for food-source dietary risk assessments were partially refined and did incorporate percent of crop treated information. Estimated concentrations of emamectin residues in surface and ground water are lower than HED's DWLOCs. Estimated drinking water levels were calculated using EFEDs drinking water models, and the values are considered conservative. Therefore, HED does not expect chronic aggregate risk to emamectin residues from food and water sources to exceed HED's level of concern for chronic aggregate risk.

4. *Aggregate cancer risk for U.S. population.* Not applicable. There is no evidence of carcinogenicity.

5. *Determination of safety.* Based on these risk assessments, EPA concludes that there is a reasonable certainty that no harm will result from aggregate exposure to emamectin residues.

D. AGGREGATE RISKS AND DETERMINATION OF SAFETY FOR INFANTS AND CHILDREN

1. *Safety factor for infants and children.* In assessing the potential for additional sensitivity of infants and children to residues of emamectin, HED considered data from prenatal developmental toxicity studies in rats and rabbits and a two-generation reproduction study in rats. The developmental toxicity studies are designed to evaluate adverse effects on the developing organism resulting from maternal pesticide exposure during gestation. Reproduction studies provide information relating to effects from exposure to the pesticide on the reproductive capability of mating animals and data on systemic toxicity.

On April 13, 1998, the FQPA Safety Factor Committee determined the 10x safety factor for the protection of infants and children should be **reduced to 3x**. The Committee's rationale for reducing the FQPA Safety Factor is as follows:

- No increased susceptibility was demonstrated in rats or rabbits following *in utero* and/or postnatal exposure to emamectin. However, increased susceptibility was demonstrated in a developmental neurotoxicity study in rats (MRID 42851508).

- Although increased susceptibility was demonstrated in a developmental neurotoxicity study in rats, the Committee determined that the 10x factor should be reduced to 3x based on the following weight-of-the-evidence considerations in the developmental neurotoxicity study: 1) the LOAEL was based on a single effect/end point (i.e., decrease in open field motor activity); 2) the effect at the LOAEL was seen only on postnatal day 17 and was not seen either on earlier (Day 13) or later (Day 21) evaluations whereas at the high dose (3.6/2.5 mg/kg/day), this effect was seen on postnatal days 13 and 17; 3) the effect at the LOAEL was not accompanied with other toxicity whereas at the high dose tremors and hindlimb splay were also seen; 4) the decreased performance was lower only when compared to the concurrent control; and 5) there was limited (only 2 studies) historical control data available for comparison.

- Exposure assessments do not indicate a concern for potential risk to infants and children because: 1) the dietary exposure estimates are based on field study data assuming 100% percent crop treated resulting in an overestimate of dietary exposure; 2) modeling data were used for the ground and surface source drinking water exposure assessments; the resulting estimates are considered to be reasonable upper-bound concentrations; 3) there are no registered residential uses.

The FQPA Safety Factor Committee also determined that the FQPA Safety Factor (3x) is applicable for acute dietary risk assessments for the general population including infants and children because the endpoint for this risk assessment is neurotoxicity (tremors), and to chronic dietary because the endpoint for this risk assessment is based on clinical signs of neurotoxicity histopathological lesions in the sciatic nerve following oral exposure.

It should be noted that the rationale stated in the FQPA Safety Factor Committee's report was written in April, 1998, and at that time, 100% crop treated was expected to be assumed for the dietary risk assessment. However, for this action, residues were highly refined: 25% crop treated was assumed, along with residue levels at ½ the limit of quantitation. Since emamectin is a new chemical, it is unlikely that it would be used on 25% of crops. Although dietary risk was not calculated based on the assumption of 100% crop treated (as stated in the FQPA SFC report rationale), HED is confident that the estimate of percent of crop treated which was used, 25%, is an over estimate, and HED does not expect more than 25% of any crop to be treated with emamectin. The DEEM exposure assessment, although refined, confirms the Committee's assertion that the exposure potential for infants and children is low.

2. *Acute risk.* Using the exposure assumptions described above, EPA has concluded that aggregate exposure to emamectin from food will utilize no more than 9.6% of the acute PAD for infants and no more than 65% of the acute PAD for children. EPA generally is not concerned for exposures below 100% of the RfD or PAD. Including drinking water sources, EPA does not expect the aggregate exposure to exceed 100% of the acute RfD or PAD.

3. *Short- or intermediate-term risk.* Emamectin is not currently registered for use on residential non-food sites. Therefore no short- and intermediate-term aggregate risk assessments are required.

4. *Chronic risk.* Using the exposure assumptions described above, EPA has concluded that aggregate exposure to emamectin from food will utilize no more than 1.8% of the Chronic PAD for infants and no more than 21% of the Chronic PAD for children. EPA generally has no concern for exposures below 100% of the Chronic RfD or PAD. Including drinking water sources, EPA does not expect the aggregate exposure to exceed 100% of the Chronic RfD or PAD.

5. *Determination of safety.* Based on these risk assessments, EPA concludes that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to emamectin residues.

DETERMINATION OF SAFETY TO OCCUPATIONALLY EXPOSED WORKERS

Workers may be exposed to emamectin during mixing, loading, application, and postapplication activities. Based on the proposed application rates, short and intermediate-term exposures may occur. Chronic exposures (≥6 months of continuous exposure) are not expected.

The highest rate for a single application of emamectin on cotton is 0.015 pounds of active ingredient per acre (lb ai/A). This rate was used for assessing risk to workers.

1. *Handler Exposure and Risk.* No chemical-specific handler exposure data were submitted in support of this Section 3 registration. In accordance with HED's Exposure Science Advisory Council (SAC) policy, exposure data from the Pesticide Handlers Exposure Database (PHED) Version 1.1 as presented in PHED Surrogate Exposure Guide (8/98) was used with other HED default values for acres treated per day, body weight, and the level of personal protective equipment to assess handler exposures. Dermal and inhalation absorption rates used for this assessment were 1.8% and 100%, respectively. Daily dermal and inhalation exposures were summed and then compared to the short- and intermediate- term oral NOAEL of 0.075 mg/kg/day. The MOEs calculated for mixer/loaders (liquid) for aerial application and for groundboom application are 620 and 2,700, respectively. For groundboom and aerial applicators, MOEs were 6,400 and 4,400, respectively. For workers, MOEs of 100 or greater do not exceed HED's level of concern. See Table 1 below for specific exposure data.

2. *Post-Application Exposure and Risk.* No chemical-specific postapplication exposure data were submitted in support of this Section 3 registration. Therefore, HED default assumptions for dermal transfer coefficient, exposure time, and residue dissipation were selected in accordance with current HED Exposure SAC policy. It was assumed that on the day of application, 20% of the application rate is retained on the foliage. Dermal transfer coefficients of 2,500 cm^2/hr for hand harvest and 1,000 cm^2/hr for scouting/ irrigation were also assumed. Using estimated residue levels for the initial day of application, short- and intermediate-term MOEs are above 100. See Table 2 below for details on the postapplication exposure assessment.

The proposed label for Denim 0.16EC has a 12-hour restricted entry interval (REI). The technical material is in Acute Toxicity Category 1 for primary eye irritation. **Therefore, a 48-hour REI is required to comply with the Agency's Worker Protection Standard.**

OTHER CONSIDERATIONS

1. *Metabolism in Plants and Animals.* The nature of the residue in plants is adequately understood. The residue of concern is emamectin, Δ-8,9 isomer of B_{1a} and B_{1b}, AB_{1a} (N-desmethyl B_{1a}), MFB_{1a} (N-formyl B_{1a}), and FAB_{1a} (N-formyl AB_{1a}) (emamectin and its metabolites and photo degradates). HED's Metabolism Assessment Review Committee concluded that these residues should be included in the tolerance expression and in the dietary exposure assessment in plants. It should be noted that B_{1a} and its Δ-8,9 isomer account for >50% of the residue in lettuce, cabbage and corn (Briefing memo to MARC, 9/2/97, J. Stokes). No

metabolism data in livestock and poultry have been provided. For the purposes of this Section 18 request, the residue of concern in livestock is emamectin, and Δ-8,9 isomer of B_{1a} and B_{1b}.

2. Analytical Enforcement Methodology. Adequate enforcement methodology is available; it is a HPLC method using fluorescence as the means of detection for both plant and livestock commodities. The methods described in MRID 44795001 are adequate to enforce the tolerance expression.

3. Magnitude of the Residues. Residues of emamectin and its metabolites and photo degradates are not expected to exceed 0.002 ppm in/on cottonseed, 0.006 ppm in cottonseed oil, 0.002 ppm cotton meal,0.004 ppm in cotton hulls, and 0.025 ppm in gin trash as a result of this Section 18 use. Time-limited tolerances should be established at these levels.

Secondary residues are expected in animal commodities as gin trash containing measurable residues is among the feed items associated with this Section 18 use. Time-limited tolerances in milk, meat, fat, kidney and liver of cattle, goats, sheep, and swine should be established at 0.002 ppm. Poultry tolerances are not needed since exposure to chickens would be negligible.

4. Rotational Crop Restrictions. According to the petition review (PP#6F4628, M. Rust et al, 6-April-99), the confined rotational crop database is adequate and no plantback restrictions are needed on labels.

5. International Residue Limits. There are no CODEX, Canadian, or Mexican MRLs for emamectin.

SUPPLEMENTAL INFORMATION
OCCUPATIONAL EXPOSURE

Table 1. Exposure and Risk Assessment for Occupational Handlers

PHED Scenario Selected from PSEG (8/98)	Personal Protective Equipment	Exposure Route	App-lication Rate (lb ai/acre)	Acres Treated (acres/ day)	PHED Unit Exposure (mg/lb ai)	PHED Data Confidence Level	Abs-orption Factor	Body Wt (kg)	Daily Dose[1] (mg/kg/day)		Short- and Intermediate-Term Dermal	
											NOAEL (mg/kg/day)	MOE[2]
Mix/load : Open Mixing Liquid for ground appl.	Long Sleeves, Long Pants, Gloves	Dermal	0.015	80	0.023	High	0.018	70	7E-6	Total = 2.8E-5	0.075	2,700
		Inhalation	0.015	80	0.0012	High	1.0	70	2.1E-5			
Mix/Load: Open Mixing Liquid for aerial appl.	Long Sleeves, Long Pants, Gloves	Dermal	0.015	350	0.023	High	0.018	70	3.1E-5	Total = 1.2E-4		620
		Inhalation	0.015	350	0.0012	High	1.0	70	9E-5			
Groundboom Application: Open Cab	Long Sleeves, Long Pants, Gloves	Dermal	0.015	80	0.014	Medium	0.018	70	4.3E-06	Total = 1.7E-5		4,400
		Inhalation	0.015	80	0.00074	High	1.0	70	1.3E-5			
Aerial Application: Closed Cab	Long Sleeves, Long Pants, No Gloves	Dermal	0.015	350	0.005	Low	0.018	70	6.7E-6	Total = 1.2E-5		6,400
		Inhalation	0.015	350	0.000068	Medium	1.0	70	5.1E-6			

[1] Daily Dose =[Application Rate (lb ai/A) x Acres Treated (A/day) x Unit Exposure(mg/lb ai handled) x Absorption Factor]/Body Weight

[2] MOE = NOAEL/Daily Dose

Table 2. Exposure and Risk Assessment for Occupational Postapplication Activities

Work Activity	Application Rate (lb ai/A)	Post-application Day (t)	Fraction of ai Retained on the Foliage	Fraction of Residue That Dissipates Daily	Dislodgeable Foliar Residue (ug/cm^2)	Dermal Transfer Coefficient (cm^2/hr)	Exposure Time (hrs/day)	Dermal Absorption Factor	Body Wt (kg)	Daily Dose[2] (mg/kg/day)	Short- and Intermediate- Term Dermal	
											NOAEL (mg/kg/day)	MOE[3]
Scouting, early season	0.015	0	0.2	0.1	0.034	**1,000**	8	0.018	70	7E-5	0.075	1,100
Scouting late season	0.015	0	0.2	0.1	0.034	**4,000**	8	0.018	70	2.8E-4		270

[1] Dislodgeable Foliar Residue $_{\text{Postapplication day}}$ (ug/cm^2) = Application rate (lb ai/A) x Fraction of ai Retained on the Foliage x (1- Fraction of Residue That Dissipates Daily) $_{\text{Postapplication day}}$ x 4.54E+8 ug/lb x 24.7E-9 A/cm^2

[2] Daily Dose = (Dislodgeable Foliar Residue x Absorption Factor x 0.001 mg/ug x Dermal Transfer Coefficient x Exposure Time)/Body weight

[3] MOE = NOAEL/Daily Dose

DIETARY EXPOSURE

Table 3. Residue Consideration Summary Table		
PARAMETER	**PROPOSED USE**	**RESIDUE DATA**
CHEMICAL	Emamectin	Emamectin
FORMULATION	Emulsifiable Concentrate	Soluble Granular
CROP	Cotton	Cotton
TYPE APPLICATION	Ground and Aerial	Ground
# APPLICATIONS	3 per season	
TIMING	> 5 day intervals between treatments	
RATE/APPLICATION	0.015 lbs ai/A	lbs ai/A
RATE/YEAR or SEASON	lbs ai/A/[ ]	lbs ai/A/[ ]
MAXIMUM RESIDUE	N/A	RAC AND PROC ITEMS ppm
RESTRICTIONS	21-day preharvest interval (PHI)	
RESIDUE DATA SOURCE	N/A	
PERFORMING LAB	N/A	

cc: with Attachments: M.Rust, L.Cheng,

cc without Attachments: RAB3 File, RAB2