P. Hurley

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

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

DATE: 7/2/98

SUBJECT: ID#98ND0007. SECTION 18 EXEMPTION FOR THE USE OF **THE SAFENER, HOE-107892 (PUMA 1EC HERBICIDE)** ON **BARLEY** IN **NORTH DAKOTA**.

DP Barcode: D244654
Submission #: S538202
Chemical #: 999999 (Inert)
Trade Name: Puma 1EC
EPA Reg #: 45639-CAN-001

PRAT Case #: 289672
Caswell #: N/A (Inert)
Class: Safener
40 CFR: No number

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MUIERB/RD (7505C)

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INTRODUCTION

The North Dakota Department of Agriculture is proposing a Section 18 exemption for the use of the safener, HOE-107892 (mefenpyr-diethyl) with the active ingredient, fenoxaprop-ethyl as a postemergence treatment on barley to control foxtail species, especially those resistant to trifluralin. This is the first year that North Dakota has submitted a section §18 request for the use of this safener. The proposed program will entail application of 20,000 gallons of Puma 1EC herbicide (20,000 lbs ai; 5000 lbs safener) on 500,000 acres statewide during the period from May 15, 1998 to August 1, 1998.

SUMMARY

The Registration Division (RD) is advised that the label needs to be revised to state that a 60 day plant back interval will be required for all crops other than wheat or barley.

The acute dietary risk estimate (food only) does not exceed the Health Effects Division's (HED) level of concern. The population subgroup of concern is Females 13+ years. Using the Theoretical Maximum Residue Contribution (TMRC), HED concludes that the high-end exposure estimate of 0.00028 mg/kg/day results in an acceptable acute dietary risk estimate (food only) of < 1% of the Acute Reference Dose (RfD) for the population of concern: Females 13+ years. HED's drinking water level of concern (DWLOC) for acute exposure to HOE-107892 for Females, 13 years and older, is 9900 ppb. The Environmental Fate and Effects Division (EFED)'s peak Estimated Environmental Concentration (EEC) (acute) value of 0.29 ppb is lower than the acute DWLOC for Females 13 years and older (9900 ppb). Therefore, HED concludes with reasonable certainty, that the acute exposure to HOE-107892 in drinking water is less than our level of concern.

Occupational risk estimates do not exceed HED's level of concern. HED has estimated that the dermal Margins of Exposure (MOEs) for mixer/loader and applicators range from 30,000 to 220,000. The acceptable MOE for short- and intermediate-term occupational risks is ≥ 100. There are no residential uses. Therefore, aggregate risk assessments do not need to be conducted for short- and intermediate-term exposures.

The chronic dietary risk estimates (food only) do not exceed HED's level of concern. In conducting the chronic dietary risk assessment, HED has made very conservative assumptions: 100% of all commodities (including barley) which have HOE-107892 tolerances (at the present time, time-limited tolerances) contain mefenpyr-diethyl residues, and these residues are present at the level of the tolerance. HED has calculated that dietary exposure to HOE-107892 from food will utilize less than 1% of the chronic RfD for all population subgroups, including infants and children. HED's DWLOCs for chronic exposure to HOE-107892 range from 5,100 ppb for children ages 1-6 to 18,000 ppb for the general population. The EEC's determined by EFED (0.00006 ppb in ground water and 0.15 ppb in surface water) are substantially lower than the DWLOCs calculated. Therefore, the concentrations of HOE-107892 in the drinking water do not exceed HED's level of concern.

The toxicological data base for evaluating pre- and post-natal toxicity for HOE-107892 is complete with respect to current Food Quality Protection Act (FQPA)-relevant toxicological data requirements. HOE-107892 does not appear to have an extra sensitivity for pre-natal effects. An *ad hoc* FQPA meeting was convened on 6/11/98 (R. Kent, W. Burnam, R. Keigwin, J. Rowland and W. Dykstra). **At the meeting, the FQPA safety factor of 10X was reduced to 3X for the purposes of this Section 18 only until the entire database is completely reviewed. The factor of 3X is only to be applied to the acute dietary endpoint for the Females 13+ years**

population subgroup; the factor of 10X is to be removed for the chronic dietary endpoint for all population subgroups. The rationale was as follows: "There is no increased sensitivity in rats and rabbits in developmental and reproduction studies in rats and rabbits, however, in the absence of [an OPP] toxicologist's review of the rabbit developmental study, the summary description of the rabbit developmental study indicates that there may be an increased severity of effect in the offspring (increased preimplantation loss and abortions) relative to effects in the dams at the same dose (decreases in food consumption, food efficiency and weight gain)."

This Section 18 exemption should not pose an unacceptable aggregate risk to infants, children, or adults. Although there is a question concerning a positive statistical trend in Harderian gland tumors in mice exposed to HOE-107892 in the diet over a lifetime, these tumors were not dose - related and it is unlikely that they will be toxicologically significant when officially reviewed by either the Hazard Identification Assessment Review Committee (HIARC) or the Cancer Peer Review Committee (CPRC). Therefore, for the purposes of this Section 18, which allows for a limited use over a limited period of time, a cancer risk assessment will not be conducted. HED has no objection to the issuance of this Section 18 exemption for the use of fenoxaprop-ethyl with the safener, HOE-107892 on barley in the State of North Dakota. Time-limited tolerances for HOE-107892 and metabolites HOE-113225, HOE-109453, and HOE-094270 in/on barley grain at 0.05 ppm, barley hay at 0.5 ppm, and barley straw at 1.0 ppm, and in processed by-products of barley grain: pearled barley at 0.1 ppm, bran at 0.4 ppm, and flour at 0.1 ppm should be established to support this Section 18 exemption.

TOXICOLOGICAL ENDPOINTS

DIETARY

1) *Acute Toxicity.* Acute RfD = 1 mg/kg/day. For acute dietary risk assessment, a reference dose (RfD) was established for Females, ages 13+, the population subgroup of concern. An *ad hoc* HIARC (W. Dykstra, J. Whalan, P. Hurley and W. Burnam) met on 5/15/98. They recommended the use of the No Observable Effect Level (NOEL) of 100 mg/kg/day, based on increased preimplantation loss (indicative of initiation of dosing too early, which appeared after a single dose) at the Lowest Observable Effect Level (LOEL) of 250 mg/kg/day, from the developmental toxicity study in rabbits (Master Record Identification (MRID) No. not available: Canadian review available). Using an uncertainty factor of 100 for intra- and inter-species differences, the Acute RfD for oral exposure is 100 mg/kg/day ÷ 100 or 1 mg/kg/day. The *ad hoc* FQPA Committee determined that the 10X factor required by FQPA for protection of infants and children from exposure to HOE-107892 should be reduced to 3X for the purposes of this Section 18 only. **Application of the additional 3x safety factor for enhanced susceptibility of infants and children to the acute RfD results in an acceptable acute dietary exposure (food plus water) of 33.3% or less of the acute RfD for the population subgroup, Females, 13+ years.**

2) *Chronic Toxicity.* Chronic RfD = 0.51 mg/kg/day. The Reference Dose (RfD) was established from a chronic feeding study in dogs (MRID # not available: Canadian review) with a NOEL of 51.4 mg/kg/day and an uncertainty factor of 100. An LOEL of 260 mg/kg/day is based on increased alkaline phosphatase and absolute/relative liver weights and grade 1 (minimal) intrahepatic cholestasis in the liver (*ad hoc* HIARC, 5/15/98).

The results from the 2-generation reproduction study in the rat support the NOEL from the chronic feeding study in the dog with a NOEL of 57.3 mg/kg/day and an LOEL of 305.9 mg/kg/day based on decreased mean body weight and mean body weight gain in the parents and offspring.

NON-DIETARY

1) *Short-Term Toxicity.* For short-term dermal Margin of Exposure (MOE) calculations, the *Ad Hoc* HIARC (5/15/98) recommended use of the maternal/developmental NOEL of 100 mg/kg/day from the developmental study in the rabbit (MRID# not available, Canadian review available). At the LOEL of 250 mg/kg/day, there were decreases in body-weight gain during days 6 to 13 accompanied by reduced food efficiency index and food consumption and a higher rate of abortions starting on gestation day 16. An acceptable MOE is ≥ 100.

An endpoint for inhalation exposure was not found. The acute LC_{50} is > 1.32 mg/L for the technical material and the acute LC_{50} for an end-use formulation of which HOE-107892 is 2.6% by weight is > 5.14 mg/L (LC_{50} = concentration lethal to 50% of animals after a 4-hour exposure). It appears unlikely that there will be a significant risk from inhalation.

2) *Intermediate-Term Toxicity.* For intermediate-term dermal MOE calculations, the *Ad Hoc* HIARC (5/15/98) recommended use of the NOEL of 80.5 mg/kg/day from the subchronic feeding study in the dog (MRID# 43972220). At the LOEL of 341.0 mg/kg/day, there were increases in alkaline phosphatase (ALP) activities and absolute/relative liver weights; a focal liver lesion characterized by hemorrhage, necrosis, and inflammation; slight anemia and decreases in food consumption and body weight gains. An acceptable MOE is ≥ 100.

An endpoint for inhalation exposure was not found. The acute LC_{50} is > 1.32 mg/L for the technical material and the acute LC_{50} for an end-use formulation of which HOE-107892 is 2.6% by weight is > 5.14 mg/L. It appears unlikely that there will be a significant risk from inhalation.

3) *Chronic Toxicity.* The the *Ad Hoc* HIARC (5/15/98) determined that the NOEL of 51.4 mg/kg/day selected for the chronic dietary risk assessment may be used for the chronic dermal risk assessment for workers. An acceptable MOE is ≥ 100.

4) *Dermal Penetration.* The default value of 100% is being used for dermal penetration in the absence of actual data.

CANCER

In the rat study, there were no treatment related effects, including tumors. The NOEL is >5000 ppm (Highest Dose Tested: HDT). The doses employed in this study were not sufficient to produce any systemic effects and appeared to be inadequate to test the carcinogenic potential of the test material. This study is classified as **unacceptable** because it appears that the animals could have tolerated a higher dose level.

In the mouse study, there were no treatment related effects in mortality, clinical signs, feed consumption, and gross necropsy findings. Increases in liver weights and hepatocellular hypertrophy were detected at several dose levels. At the terminal sacrifice, Harderian gland adenocarcinoma showed a positive trend in both sexes with the incidences exceeding the maximum percentages for historical controls (2%) at some dose levels. However, although there was a positive trend, the incidences were not dose-related (0/50, 0/50, 2/50, 1/50 and 2/50 in males and 0/50, 1/50, 0/50, 0/50 and 2/50 in females). A complete assessment of the toxicological significance of these tumors will be conducted when this chemical is considered for full registration. The dose levels employed in this study were adequate to characterize the carcinogenic potential of HOE-107892 in NMRI mice.

The mouse and rat cancer studies with the safener have not been reviewed and classified by either the Cancer Peer Review Committee or the HIARC. It is not known at this time whether or not the Harderian gland adenocarcinomas mentioned in the mouse study are toxicologically significant and whether or not a cancer risk assessment is appropriate for this chemical. Therefore, for the purposes of this Section 18, a cancer risk assessment will not be conducted.

EXPOSURES AND RISKS

In examining aggregate exposure, FQPA directs EPA to consider available information concerning exposures from the pesticide residue in food and all other non-occupational exposures. The primary non-food sources of exposure the Agency looks at include drinking water (whether from groundwater or surface water), and exposure through pesticide use in gardens, lawns, or buildings (residential and other indoor and/or outdoor uses). In evaluating food exposures, EPA takes into account varying consumption patterns of major identifiable subgroups of consumers, including infants and children.

1. From Food and Feed Uses:

Permanent tolerances have not been established for the residues of HOE-107892. A Section 18 for HOE-107892 on durum wheat in North Dakota, South Dakota, and Montana was granted in 1996. For the purposes of that Section 18 only, it was assumed that there would be no quantifiable residues of HOE-107892 in wheat grain or straw. It was further assumed that there would be no quantifiable residues in meat, milk, poultry, or eggs resulting from the use.

Acute Risk. The Acute RfD is 1 mg/kg bw/day. Application of the 3X safety factor for enhanced susceptibility of infants and children to the Acute RfD results in an acceptable acute dietary exposure (food plus water) of 33.3% or less of the Acute RfD for the population subgroup of concern, Females, age 13+ years. **For this population subgroup, there is an acceptable acute dietary exposure (food only) of <1% of the Acute RfD.**

This acute dietary (food) risk assessment used the TMRC which assumes tolerance level residues and 100% crop-treated. The Dietary Exposure Evaluation Model (DEEM) software was used for this acute dietary exposure analysis. Resulting exposure values and percent of the Acute RfD utilized are shown below.

Table 1. Acute Dietary (Food Only) Risk for HOE-107892

Population Subgroup	Exposure @ 99.9 Percentile (mg/kg bwt/day)	Percent Acute RfD[1]
Females (13-50 yrs)	0.00028	<1

[1]Acute RfD = NOEL (100 mg/kg/day) ÷ 100 for intra- and inter-species differences = 1 mg/kg/day. % Acute RfD = (Exposure (mg/kg bwt/day) ÷ Acute RfD (1 mg/kg bwt/day)) X 100

These results should be viewed as a very conservative risk estimate; refinement using anticipated residue values and percent crop-treated information in conjunction with Monte Carlo analysis would result in a lower estimate of acute dietary exposure.

Chronic Risk. Chronic RfD = 0.51 mg/kg/day. In conducting this chronic dietary risk assessment, HED has made very conservative assumptions: 100% of all commodities (including barley) which have HOE-107892 tolerances (at the present time, time-limited tolerances) contain mefenpyr-diethyl residues, and these residues are present at the level of the tolerance. By making these assumptions, an overestimation of human dietary exposure results. Thus, in making a safety determination for this tolerance, HED is taking into account this conservative exposure assessment.

The time-limited HOE-107892 tolerances, including the necessary Section 18 tolerance(s), result in a Theoretical Maximum Residue Contribution (TMRC) that is equivalent to the following percentages of the Chronic RfD:

Population Subgroup	TMRC(mg/kg/day)	% Chronic RFD
U.S. Population (48 States)	0.000023	<1%
Nursing Infants (<1 year old)	0.000004	<1%
Non-Nursing Infants (<1 year old)	0.000008	<1%
Children (1-6 years old)	0.000038	<1%
Children (7-12 years old)	0.000027	<1%
Females (13-50 years old)	0.000016	<1%

The subgroups listed above are: (1) U.S. population (48 states); (2) Infants and children (4 subgroups) and (3) Females (13-50 years). There are no other subgroups for which the percentage of the RfD occupied is greater than that occupied by the subgroup U.S. population (48 states).

2. *From Drinking Water:*

Environmental Fate Assessment

Based on an EFED memo from D. Spatz to A. Ertman (HOE-107892 [A Safener used with Fenoxaprop-Ethyl (PUMA)]: Section 18 for use on barley in North Dakota, 4/30/98) HOE-107892 is not persistent and not mobile. Even though sorption to soil is relatively low (median Koc of approximately 600), its short half-life of about one week or less and low use rate imply that it has little potential to leach to ground water or runoff to surface water. Under favorable conditions, there could be runoff into surface water, primarily via dissolution in runoff water, for several days post-application. There are no established Maximum Contaminant Levels for residues of HOE-107892 in drinking water. No health advisory levels for HOE-107892 in drinking water have been established (EPA Safe Drinking Water Hotline, 1(800)426-4791, Date of call: 4-16-98).

Ground Water

EFED used its SCI-GROW (Screening Concentration in Ground Water) screening model and environmental fate data to determine the EECs of HOE-197892 in ground water. SCI-GROW is an empirical model based upon actual ground water monitoring data collected for the registration of a number of pesticides that serve as benchmarks for the model. The current version of SCI-GROW appears to provide realistic estimates of pesticide concentrations in shallow, highly vulnerable ground water sites (i.e., sites with sandy soils and depth to ground water of 10 to 20 feet). The SCI-GROW ground water screening concentration is 0.00006 ppb.

Surface Water

EFED used its GENEEC (Generic Estimated Environmental Concentration) screening model and environmental fate data to determine the EECs of HOE-107892 in surface water. GENEEC

simulates a 1 hectare by 2 meter deep edge-of-the-field farm pond which receives pesticide runoff from a treated 10 hectare field. GENEEC can substantially overestimate (by a ≥ 3 fold factor) true pesticide concentrations in drinking water. It has certain limitations and is not the ideal tool for use in drinking water risk assessments. However, it can be used in screening calculations and does provide an upper bound on the concentration of pesticide that can be found in drinking water. Since GENEEC can substantially overestimate true drinking water concentrations, it will be necessary to refine the GENEEC estimate when the level of concern is exceeded. In those situations where the level of concern is exceeded and the GENEEC value is a substantial part of the total exposure, EFED can use a variety of methods to refine the exposure estimates.

Using the GENEEC model and available environmental fate data, EFED calculated the following Tier 1 Estimated EECs for HOE-107892.

Table 2. GENEEC Modeling Results for HOE-107892 on Barley

Chemical	App. Method	App Rate (lbs ai/acre)	App Freq	App Int days	GENEEC Peak EEC (ppb)	Average 4 day EEC (ppb)	Average 21 day EEC (ppb)	Average 56 day EEC (ppb)
HOE-107892	aerial	0.02	1	--	0.29	0.28	0.23	0.15

a. *Acute Risk.* Based on the acute dietary (food) exposure estimates, acute drinking water levels of concern (DWLOC) for HOE-107892 were calculated and summarized in Table 3. The subpopulation group of concern is Females 13 years and older.

Table 3. Acute Drinking Water Levels of Concern

Population	33.3% of Acute RfD mg/kg/day)[1]	TMRC [Food Exposure] (mg/kg/day)	Max Water Exposure (mg/kg/day)[2]	GENEEC Peak EEC (ppb)	SCI-GROW (ppb)	DWLOC (μg/L)[3,4,5]
Females 13+	0.33[6]	0.00028	0.33	0.29	0.00006	9900

Notes:
1. 33.3% of the Acute RfD is to account for the FQPA Safety Factor of 3X.
2. Max water exposure = 33.3% of Acute RfD - Acute dietary food (from the DRES analysis).
3. DWLOC = Max Water Exposure (mg/kg/day) * (kg body weight) ÷ (10^{-3} mg/μg) * (water consumed (L)/day)
4. HED default body weights are: General US Population = 70kg; Females 13+ = 60 kg; Infants/children = 10 kg
5. HED default daily drinking rates are: 2L/day for adults and 1L/day for infants/children.
6. Expressed to 2 significant figures.

b. *Chronic Risk.* Based on the chronic dietary (food) exposure estimates, chronic drinking water levels of concern (DWLOC) for HOE-107892 were calculated and are summarized in Table 4.

Table 4. Chronic Drinking Water Levels of Concern

Population Category	RfD (mg/kg/day)	TMRC [Food Exposure] (mg/kg/day)	Max Water Exposure[1] (mg/kg/day)	DWLOC [2,3,4] (μg/L)
US Population (48 States)	0.51	0.000023	0.51	18,000
Females 13 + years, nursing	0.51	0.000017	0.51	15,000
Children (1-6 years old)	0.51	0.000038	0.51	5,100

[1] Maximum Water Exposure (mg/kg/day) = RfD (mg/kg/day) - TMRC from DRES (mg/kg/day)
[2] DWLOC(μg/L) = Max water exposure (mg/kg/day) * body wt (kg) /[(10^{-3} mg/μg)*water consumed daily (L/day)]
[3] HED default body wts for the general population, females, and children are 70 kg, 60 kg, and 10 kg, respectively.
[4] HED default daily drinking rates are 2 L/day for adults and 1 L/day for children.

It is current HED policy that the following subpopulations be addressed when calculating drinking water levels of concern: US Population (48 States), any other adult populations whose %RfD is greater than that of the US population, and the Female and Infant/Children subgroups (1 each) with the highest food exposure. The subgroups which are listed in Table 4 are those which fall into these categories.

3. From Non-Dietary Uses:

HOE-107892 currently has no registered residential uses.

4. From Cumulative Exposure To Substances with a Common Mechanism of Toxicity:

HOE-107892 is the sole member of a new class of compounds. It has a unique mode of action (personal communication, Bert Volger, AgrEvo USA Company, 5/8/98).

Section 408(b)(2)(D)(v) of the Food Quality Protection Act requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." The Agency believes that "available information" in this context might include not only toxicity, chemistry, and exposure data, but also scientific policies and methodologies for understanding common mechanisms of toxicity and conducting cumulative risk assessments. For most pesticides, although the Agency has some information in its files that may turn out to be helpful in eventually determining whether a pesticide shares a common mechanism of toxicity with any other substances, EPA does not at this time have the methodologies to resolve the complex scientific issues concerning common mechanism of toxicity in a meaningful way. EPA has begun a pilot process to study this issue further through the examination of particular classes of pesticides. The Agency hopes that the results of this pilot process will increase the Agency's scientific understanding of this question such that EPA will be able to develop and apply scientific principles for better determining which chemicals have a common mechanism of toxicity and

evaluating the cumulative effects of such chemicals. The Agency anticipates, however, that even as its understanding of the science of common mechanisms increases, decisions on specific classes of chemicals will be heavily dependent on chemical-specific data, much of which may not be presently available.

Although at present the Agency does not know how to apply the information in its files concerning common mechanism issues to most risk assessments, there are pesticides as to which the common mechanism issues can be resolved. These pesticides include pesticides that are toxicologically dissimilar to existing chemical substances (in which case the Agency can conclude that it is unlikely that a pesticide shares a common mechanism of activity with other substances) and pesticides that produce a common toxic metabolite (in which case common mechanism of activity will be assumed).

HED does not have, at this time, available data to determine whether HOE-107892 has a common mechanism of toxicity with other substances or how to include this pesticide in a cumulative risk assessment. For the purposes of this tolerance action, therefore, HED has not assumed that HOE-107892 has a common mechanism of toxicity with other substances.

DETERMINATION OF SAFETY FOR U.S. ADULT POPULATION

1. Acute Aggregate Risk.

U.S. Adult Population: Toxicological effects applicable to the general U.S. adult population that could be attributed to a single exposure (dose) were not observed in oral toxicity studies in animal species. Therefore, a dose and endpoint were not identified for acute dietary risk assessment for this population.

Females 13 years and older: The population subgroup of concern is Females 13+ years. Using TMRC, HED concluded that the high-end exposure estimate of 0.00028 mg/kg/day, results in an acceptable acute dietary risk estimate (food only) of <1% of the Acute RfD for the population of concern: Females, 13+ years.

For acute exposure, based on an adult female body weight of 60 kg and 2L consumption of water per day, **HED's DWLOC for acute exposure to HOE-107892 for Females, 13 years and older, is 9900 ppb.** EFED's peak EEC (acute) value of 0.29 ppb is lower than the acute DWLOCs for Females, 13 years and older (ppb). Therefore, HED concludes with reasonable certainty that the acute exposure to mefenpyr-diethyl (HOE-107892) in drinking water is less than our level of concern and that the acute aggregate risk estimate (food and water) is less than our level of concern.

2. Short- and Intermediate-Term Aggregate Risk.

Short- and intermediate-term aggregate exposure takes into account chronic dietary food and water (considered to be a background exposure level) plus indoor and outdoor residential uses. There are

no residential uses. Therefore, short- and intermediate-term aggregate risk assessments are not required.

3. Chronic Aggregate Risk. Using the conservative TMRC exposure assumptions described above, and taking into account the completeness and reliability of the toxicity data, HED has calculated that chronic dietary exposure to HOE-107892 from food will utilize <1% of the RfD for the U.S. population. **HED's DWLOC for chronic exposure to HOE-107892 is 18,000 ppb for the US population and 15,000 for nursing females 13 years and older.** EFED's chronic EED, GENEEC 56-day, value of 0.15 ppb is lower than these chronic DWLOCs. Therefore, HED concludes with reasonable certainty that exposure to HOE-107892 in drinking water is less than our level of concern and that the chronic aggregate risk (food and water) is less than our level of concern.

There are no residential exposures. Under current HED guidelines, the proposed and current uses of HOE-107892 under the existing temporary tolerances do not constitute a chronic dermal or inhalation exposure scenario. HED concludes that there is a reasonable certainty that no harm will result from chronic aggregate exposure to HOE-107892 residues.

DETERMINATION OF CANCER RISK

Although there is a question concerning a positive statistical trend in Harderian gland tumors in mice exposed to HOE-107892 in the diet over a lifetime and the incidences exceed historical control incidences, these tumors were not dose-related and there is no statistically significant increase using a pairwise comparison at any dose level. It is unlikely that they will be toxicologically significant when officially reviewed by either the HIARC or the CPRC. Therefore, for the purposes of this Section 18, which allows for a limited use over a limited period of time, a cancer risk assessment will not be conducted.

ENDOCRINE DISRUPTER EFFECTS

EPA is required to develop a screening program to determine whether certain substances (including all pesticides and inerts) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect..." The Agency is currently working with interested stakeholders, including other government agencies, public interest groups, industry and research scientists in developing a screening and testing program and a priority setting scheme to implement this program. Congress has allowed 3 years from the passage of FQPA (August 3, 1999) to implement this program. At that time, EPA may require further testing of this active ingredient and end use products for endocrine disrupter effects.

DETERMINATION OF SAFETY FOR INFANTS AND CHILDREN

In assessing the potential for additional sensitivity of infants and children to residues of HOE-107892, HED considered data from developmental toxicity studies in the rat and rabbit and a 2-generation reproductive toxicity study in the rat. Developmental toxicity studies are designed to

evaluate adverse effects on the developing fetus resulting from maternal pesticide exposure during gestation. Reproductive toxicity studies provide information relating to pre- and post-natal effects from exposure to the pesticide, information on the reproductive capability of mating animals, and data on systemic toxicity.

FFDCA section 408 provides that EPA shall apply a 10-fold margin of safety for infants and children in the case of threshold effects to account for pre-and post-natal toxicity and the completeness of the data base unless EPA determines that a different margin of safety will be safe for infants and children. Margins of safety are incorporated into EPA risk assessments either directly through use of a margin of exposure analysis or through using uncertainty (safety) factors in calculating a dose level that poses no appreciable risk to humans. In either case, EPA generally defines the level of appreciable risk as exposure that is greater than 1/100 of the no observed effect level in the animal study appropriate to the particular risk assessment. This 100-fold uncertainty (safety) factor/margin of exposure (safety) is designed to account for inter-species extrapolation and intra-species variability. HED believes that reliable data support using the 100-fold margin/factor, rather than the 1000-fold margin/factor, when EPA has a complete data base under existing guidelines, and when the severity of the effect in infants or children, the potency or unusual toxic properties of a compound, or the quality of the exposure data do not raise concerns regarding the adequacy of the standard margin/factor.

1. Developmental Toxicity Studies.

a. Rats. In a developmental toxicity study (MRID 43972221) in rats, the maternal NOEL is the limit dose, 1000 mg/kg/day. There were no treatment-related effects in developmental parameters. The developmental NOEL is also the limit dose, 1000 mg/kg/day.

In an embryotoxicity and post-natal development study (Canadian review, no MRID) HOE-107892 was tested at the limit dose of 1000 mg/kg/day. Mean maternal body-weight gain was significantly lower during treatment and was accompanied by a significant reduction in food efficiency and food consumption. There was also a treatment-related impairment in fetal body weight and body-weight gain. Based on the results of the study, the NOEL for maternal, fetal and neonatal toxicity is < 1000 mg/kg/day.

b. Rabbits. In a developmental toxicity study in rabbits (Canadian review, no MRID #) there was a significant decrease in body-weight gain observed at 250 mg/kg/day during the first week of treatment which was accompanied by significantly reduced food efficiency index and food consumption. There was also a higher rate of abortions and an increased preimplantation loss. The NOEL for teratogenicity was 250 mg/kg/day, the highest dose tested. The NOEL for maternal toxicity is 100 mg/kg/day. Based on the higher rate of abortions observed in the dams at 250 mg/kg/day, the NOEL for fetotoxicity is also 100 mg/kg/day.

2. Reproductive Toxicity Studies.

Rats. In a two-generation reproduction study in rats, the NOEL for general toxicity (i.e., for parents and offspring) was determined to be 57.3 mg/kg bw/day based on decreased mean body weight and mean body weight gain and an increase in the severity (but not in the incidence) of splenic extramedullary hematopoiesis. The reproductive NOEL was set at 305.9 mg/kg/day (HDT), since there were no adverse treatment-related effects on reproductive parameters evident at any dose level tested.

3. Pre- and Post-Natal Sensitivity.

The toxicological data base for evaluating pre- and post-natal toxicity for HOE-107892 is complete with respect to current data requirements. Based on the developmental study data discussed above, HOE-107892 does not appear to have an extra sensitivity for pre-natal effects. An *ad hoc* FQPA meeting was convened on 6/11/98 (R. Kent, W. Burnam, R. Keigwin, J. Rowland and W. Dykstra). **At the meeting, the FQPA safety factor of 10X was reduced to 3X for the purposes of this Section 18 only until the entire database is completely reviewed. The factor of 3X is only to be applied to the acute dietary endpoint for the Females 13+ years population subgroup; the factor of 10X is to be removed for the chronic dietary endpoint for all population subgroups.** The rationale was as follows: "There is no increased sensitivity in rats and rabbits in developmental and reproduction studies in rats and rabbits, however, in the absence of [an OPP] toxicologist's review of the rabbit developmental study, the summary description of the rabbit developmental study indicates that there may an increased severity of effect in the offspring (increased preimplantation loss and abortions) relative to effects in the dams at the same dose (decreases in food consumption, food efficiency and weight gain)."

4. Acute Aggregate Risk.

Toxicological effects applicable to children and/or infants that could be attributed to a single exposure (dose) were not observed in oral toxicity studies in several animal species. Therefore, a dose and endpoint were not identified for acute dietary risk assessment for this population subgroup.

5. Short- and Intermediate-Term Aggregate Risk.

Short- and intermediate-term aggregate exposure takes into account chronic dietary food and water (considered to be a background exposure level) plus indoor and outdoor residential uses. There are no residential uses. Short- and intermediate-term endpoints were not identified for infants and children. Therefore, short- and intermediate-term aggregate risk assessments are not required.

6. Chronic Aggregate Risk.

Using the conservative TMRC exposure assumptions described above, and taking into account the completeness and reliability of the toxicity data, HED has calculated that dietary exposure to HOE-

107892 from food will utilize <1% of the RfD for all infants and children subpopulations. **HED's DWLOC for chronic exposure to HOE-107892 is 5100 ppb for Children, ages 1-6, the subgroup with the highest food exposure of all the infant and children subgroups.** EFED's chronic EED, GENEEC 56-day, value of 0.15 ppb is lower than this chronic DWLOC. Therefore, HED concludes with reasonable certainty that exposure to HOE-107892 in drinking water is less than our level of concern for infants and children and that the chronic aggregate risk (food and water) is less than our level of concern.

There are no residential exposures. Under current HED guidelines, the proposed and current uses of HOE-107892 under the existing temporary tolerances do not constitute a chronic exposure scenario. HED concludes that there is a reasonable certainty that no harm to infants and children will result from chronic aggregate exposure to HOE-107892 residues.

DETERMINATION OF RISK FOR WORKERS

1. Occupational exposure assumptions and estimates are summarized in **Tables 5 and 6,** respectively. HED's worker exposure estimates are based on surrogate data from the Pesticide Handlers Exposure Database (PHED) as presented in the Best Available Surrogate Exposure Table (BASET, 5/97). The proposed use may result in short to intermediate-term exposure. Based on the number of applications per year, chronic exposures are not expected. Using these exposure assumptions, HED has estimated that the dermal MOEs for mixer/loader and applicators by workers range from 30,000 (intermediate-term dermal exposure for aerial mixer/loader) to 220,000 (short-term dermal exposure for ground applicator). These MOEs do not exceed HED's level of concern for occupationally exposed workers.

Table 5. Occupational Exposure Assumptions

PARAMETER	ASSUMPTION
Pesticide Handlers Exposure Database (PHED), Version 1.1, (5/97)	Mixer/Loader **[All liquids/Open Mix]:** PROCLAIM 0.16 EC Dermal = **23** μg/lb ai handled **(High Confidence Data)** PPE: Single Layer of Clothes with gloves
	Applicator - Ground **[Groundboom/Open Cab]:** Dermal = **14** μg/lb ai handled **(Medium Confidence Data)** PPE: Single Layer of Clothes with gloves Applicator - Air **[Fixed Wing, Liquid Formulations Enclosed Cab]**: Dermal = **5.0** μg/lb ai applied **(Medium Confidence Data)** PPE: single layer of clothes without gloves
Percent Absorption	Dermal: **100** % (default)
Application Type	ground and air

Table 5. Occupational Exposure Assumptions	
PARAMETER	**ASSUMPTION**
Maximum Application Rate	**0.02** lb ai/A for safener HOE-107892 on Barley
Acres Treated/Day (HED defaults)	Ground: **80** acres Air: 350 acres
Duration of Occupational Exposure	Short to Intermediate

Table 6. Occupational Exposure and Risk Assessment

WORKER SCENERIO[1]		DERMAL ADD[2,3] (mg/kg/day)	SHORT-TERM DERMAL MOE[4]	INTERMEDIATE-TERM DERMAL MOE[5]
Ground:	Mixer/Loader	6.1×10^{-4}	160,000	130,000
	Applicator	3.7×10^{-4}	270,000	220,000
Air:	Mixer/Loader	2.7×10^{-3}	37,000	30,000
	Applicator	5.8×10^{-4}	170,000	140,000

[1] Body wt = 60 kg
[2] Average Daily Dose (ADD) = PHED unit exposure (mg/lb ai) x % absorption x application rate(lb ai/A) x acres treated/day ÷ body weight (kg)
[3] Dermal absorption = 100%
[4] MOE = NOEL/ADD where Short-term Dermal NOEL = 100 mg/kg/day
[5] MOE = NOEL/ADD where Intermediate-term Dermal NOEL = 80.5 mg/kg/day

2. Per the Worker Protection Standard (WPS), the minimum level of Personal Protective Equipment (PPE) is based on the acute toxicity of the end-use product. RD is responsible for ensuring that PPE listed on the label is in compliance with WPS.

3. Acute data for the technical fenoxaprop-ethyl and HOE 107892 are summarized in **Tables 7a and 7b**. The acute toxicity for the HOE 107892 requires a 12-hour restricted entry interval (REI). However, the active ingredient fenoxaprop-ethyl has a Toxicity Category I for primary eye irritation and therefore requires a 48-hour REI per the WPS. The 24-hour REI that is listed on the proposed label DOES NOT COMPLY with the WPS. **RD must ensure that the appropriate REI appears on the label.**

Table 7a. Acute toxicity for Technical Fenoxaprop-ethyl

Guideline No.	Study Type	MRIDs #	Results	Toxicity Category
81-1	Acute Oral - Rat	00130010 00130011	LD_{50} = 2357 mg/kg (M) 2500 mg/kg (F)	III
81-2	Acute Dermal - Rat - Rabbit	00130018 00130019	LD_{50} = > 2000 mg/kg >1000 mg/kg	IV
81-3	Acute Inhalation	00130040	LC_{50} = > 0.511 mg/L	III
81-4	**Primary Eye Irritation**	**00130639**	**Non-reversible corneal opacity, day 21**	**I**
81-5	Primary Skin Irritation	00130639	Slight irritant	IV
81-6	Dermal Sensitization	00144683	Non-sensitizer	NA

Table 7b. Acute toxicity for HOE 107892

Guideline No.	Study Type	MRIDs #	Results	Toxicity Category
81-1	Acute Oral - Rat	43972211	Oral LD_{50}: Males >5,000 mg/kg Females >5,000 mg/kg	IV
81-2	Acute Dermal	43972213	Dermal LD_{50}: M > 4,000 mg/kg F > 4,000 mg/kg	III
81-3	Acute Inhalation	43972214	**Inhalation LC_{50}** **Males: > 1.32 mg/L** **Females > 1.32 mg/L**	III
81-4	**Primary Eye Irritation**	43972215	Slight ocular irritant. PIS: 12.8.	III
81-5	Primary Skin Irritation	43972216	PII: 0.17. Not a dermal irritant.	IV
81-6	Dermal Sensitization	43972217, 44280001	A slight dermal sensitizer.	N/A

OTHER CONSIDERATIONS

Metabolism in Plants and Animals

1. The nature of the residue in plants is adequately understood (Memo, HED Metabolism Committee, D. Davis, 7/16/96). The residue of concern is parent HOE-107892 and metabolites HOE-113225, HOE-109453, and HOE-094270. The HED Metabolism Committee met on 6/20/96.

2. For the purposes of this Section 18 only, the residues of concern in poultry and ruminants are HOE-107892 and metabolites HOE-113225, HOE-109453, and HOE-094270 (MRID #s 443029-06 and 443029-07). **RAB2 bases this conclusion on a cursory review of the cited studies. These studies were not extensively reviewed for this Section 18 request.**

Analytical Enforcement Methodology

2. Adequate enforcement methodology is available (MRID#439841-14) to enforce the tolerance expression. The method involves extraction, methylation, separation by gas chromoatography (GC), and detection by Mass Spectroscopy (MS).

Magnitude of the Residues

3. As a result of this Section 18 use, residues of mefenpyr-diethyl (HOE-107892) and its regulated metabolites (HOE-113225, 109453, and 094270) are not expected to exceed the following levels: 0.05 ppm in grain, 0.5 ppm in hay, and 1.0 ppm in straw. In addition, residues of HOE-107892 and its regulated metabolites are not expected to exceed the following levels in processed by-products of barley grain: 0.1 ppm in pearled barley, 0.4 ppm in bran, and 0.1 ppm in flour. The tolerance levels on processed barley by-products are based on the tolerance level for barley grain and theoretical concentration factors (OPPTS Test Guidelines, Series 860.1520). Time-limited tolerances should be established at the above levels.

4. HED does not expect detectable residues in livestock commodities as a result of this Section 18 use.

Rotational Crop Restrictions

5. For this Section 18 only, a 60 day plant back interval will be required for all crops other than wheat and barley. **RD is advised that the label needs to be revised to provide for this requirement.** This decision is based on results of laboratory environmental fate studies and the long PHI which is stipulated. Within one month of application of HOE-107892, ^{14}C activity from both mefenpyr diethyl and a major metabolite, HOE-113225, decreased to less than 6% of the original activity. A second major metabolite, HOE-094270, had a longer residence time in soil. It reached maximum activity of about 72% after 30-60 days of incubation, and has a much longer estimated DT50 (time required for compound to decay to 50% of the initial quantity) of 100-200 days. In this Section 18 a 60 day PHI is stipulated. In effect, HOE-107892 automatically has 60 days to decay before re-planting can be done. For the purposes of this Section 18 only, HED is willing to allow rotation to any crops 60 days after application. For Section 3 registration, actual rotational crop data will need to be reviewed to determine an appropriate plant back interval for crops other than wheat and barley.

International Residue Limits

6. There are no CODEX, Canadian, or Mexican Maximum Residue Limits (MRLs) for HOE-107892 on barley. Thus, harmonization is not an issue for this Section 18 request.

SUPPLEMENTAL INFORMATION

DIETARY EXPOSURE

Table 8. Residue Consideration Summary Table

PARAMETER	PROPOSED USE	RESIDUE DATA
CHEMICAL	PUMA (Mefenpyr- diethyl)	HOE-107892, 113225, 109453, and 094270
FORMULATION	Solution Concentrate	Unspecified
CROP	Barley	Barley (12 trials)
TYPE APPLICATION	Ground or Aerial	Unspecified
# APPLICATIONS	1	1
TIMING	Apply from 2 leaf to 6 leaf stage.	Application made 57-60 days prior to harvest
RATE/APPLICATION	0.08 lbs ai/A 0.02 lbs safener/A	0.08 lbs ai/A 0.02 lbs safener/A
RATE/YEAR or SEASON	0.08 lbs ai/A/year 0.02 lbs. safener/A/year	0.08 lbs ai/A/year 0.02 lbs safener/A/year
MAXIMUM RESIDUE	N/A	hay <0.3 ppm 54-day PHI grain <0.04 ppm 60-day PHI straw <0.58 ppm 60-day PHI
RESTRICTIONS	60 day PHI	
RESIDUE DATA SOURCE	N/A	PP#7F4850
PERFORMING LAB	N/A	Unspecified

ADDITIONAL INFORMATION

Animal Feedstuffs Considerations. The theoretical maximum dietary burden to livestock is 0.5 ppm (dairy cattle). The theoretical maximum dietary burden to poultry is 0.04 ppm. The information used to calculate these theoretical dietary burdens included the percentage dry matter (% DM) in each feed item; the percentage of each feed item in the animal diets (Table 1, OPPTS Test Guidelines, Series 860); and maximum residues in the feed items based on proposed tolerances

for barley grain, hay, and straw. For poultry, a dry matter value of 100% is used in calculating dietary burden.

Theoretical Maximum Dietary Burden for Dairy Cattle:

Crop	Feedstuff	% DM	Tolerance Level (ppm)	% in Diet	Dietary Burden (ppm)
Barley	grain	88	0.05	30	0.017
	hay	88	0.5	60	0.34
	straw	89	1.0	10	0.11
Theoretical Maximum Dietary Burden (Dairy Cattle)					0.47

Theoretical Maximum Dietary Burden for Poultry:

Crop	Feedstuff	% DM	Tolerance Level (ppm)	% in Diet	Dietary Burden (ppm)
Barley	grain	100	0.05	40	0.038
	hay	100	0.5	0	0
	straw	100	1.0	0	0
Theoretical Maximum Dietary Burden (Poultry)					0.038

No meat, milk, poultry, and egg tolerances are established or proposed. The theoretical maximum residue levels in meat, milk, poultry, and eggs are all below the limit of quantitation of 0.01 ppm. A cursory review was done of ruminant and poultry metabolism studies (MRID #s 443029-06 and 443029-07). A lactating goat was dosed with HOE-107892 so that the mean level in the diet was 11.2 ppm. This dose level is equivalent to a 22 fold increase over the maximum theoretical dietary burden for dairy cattle. The total radioactive residue levels in tissues were highest in the kidney and liver (0.17 mg equivalents/kg and 0.061 mg equivalents/kg, respectively). Extrapolating to a dose of 0.5 ppm, the total radioactive residue levels would be less than the limit of quantitation. The poultry dose was equivalent to 13 ppm in the diet. This dose level is equivalent to a 300 fold increase over the maximum theoretical dietary burden for poultry. The total radioactive residue levels in egg yolks (which were higher than those in egg whites) and in subcutaneous and abdominal fat (the highest levels in poultry tissues) were 0.018 mg equivalents/kg and 0.015 mg equivalent/kg, respectively. Extrapolating to a dose of 0.04 ppm, the residue levels would be considerably lower than the limit of quantitation.

Progress Toward Registration. The initial filing of the petition (PP#7F4850) proposing the establishment of a tolerance for residues of HOE-107892 on wheat and barley was published in the Federal Register on September 26, 1997. The petition will be reviewed by HED in fiscal year 1999.

Reregistration Status. HOE-107892 is not a reregistration list chemical.

Attachments: DEEM Runs: Chronic: Cutchin, 6/18/98
Acute: Cutchin, 6/18/98

cc with Attachments: P. Hurley, D. Dotson, S. Weiss, DRES (B. Steinwand), RAB2 reading file

RDI: RAB2 7/2/98

Filename: c:\novigen\resdata\hoe-c.R95
Chemical Name: HOE-107892
RfD(Chronic): .510000 mg/kg/DAY NOEL(Chronic): .000000 mg/kg/day
RfD(Acute): .000000 mg/kg/DAY NOEL(Acute): 100.000000 mg/kg/day
Q* = .0000 Date created/last modified: /8 Program ver. 6.13
Comment: Safener - Fenoxyprop-ethyl, no CAS, no PCode/3x females 13+

FoodCrop Code	Grp	Food Name	RESIDUE (ppm)	RDF #	Adj.Factors #1	#2	Comment
265	O	BARLEY	000.050000		01.000	01.000	98ND00
Full comment: 98ND0007							
276	O	WHEAT-ROUGH	000.010000		01.000	01.000	Sec18
277	O	WHEAT-GERM	000.010000		01.000	01.000	Sec18
278	O	WHEAT-BRAN	000.010000		01.000	01.000	Sec18
279	O	WHEAT-FLOUR	000.010000		01.000	01.000	

U.S. Environmental Protection Agency Ver. 6.13
DEEM96 ACUTE96 analysis for HOE-107892 (1994-95 data)
Residue file name: HOE-C.R95 Adjustment factor #2 NOT used.
Analysis Date 06-18-1998 Residue file dated: 06-18-1998/08:26:56/8
NOEL (ACUTE96) = 100.000000 mg/kg body-wt/day
COMMENT 1: Safener - Fenoxyprop-ethyl, no CAS, no PCode/3x females 13+
COMMENT 2: 98ND0007/Hurley-RAB2

Residue file listing

Food Code	EPA Code	Crop Group	Food Name	Residue (ppm)	Adj. Fctrs #1	#2
265	24001AA	O	BARLEY	0.050000	1.00	1.00
276	24007AA	O	WHEAT-ROUGH	0.010000	1.00	1.00
277	24007GA	O	WHEAT-GERM	0.010000	1.00	1.00
278	24007HA	O	WHEAT-BRAN	0.010000	1.00	1.00
279	24007WA	O	WHEAT-FLOUR	0.010000	1.00	1.00

U.S. Environmental Protection Agency Ver. 6.13
DEEM96 ACUTE96 analysis for HOE-107892 (1994-95 data)
Residue file name: HOE-C.R95 Adjustment factor #2 NOT used.
Analysis Date 06-18-1998 Residue file dated: 06-18-1998/08:26:56/8
NOEL (ACUTE96) = 100.000000 mg/kg body-wt/day
Bin intervals calibrated using computed means.
COMMENT 1: Safener - Fenoxyprop-ethyl, no CAS, no PCode/3x females 13+
COMMENT 2: 98ND0007/Hurley-RAB2

U.S. pop - all seasons

Daily Exposure Analysis 1/
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.000023	0.000023
Standard Deviation	0.000035	0.000035
Standard Error	0.000000	0.000000
Margin of Exposure 2/	>1,000,000	>1,000,000

Percent of Person-Days that are User-Days = 96.86%

Estimated percentile of user-days exceeding calculated exposure in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

Percentile	Exposure	MOE	Percentile	Exposure	MOE
90.00	0.000004	>1,000,000	10.00	0.000048	>1,000,000
80.00	0.000007	>1,000,000	5.00	0.000072	>1,000,000
70.00	0.000009	>1,000,000	2.50	0.000104	963,458
60.00	0.000011	>1,000,000	1.00	0.000167	600,451
50.00	0.000014	>1,000,000	0.50	0.000212	470,957
40.00	0.000018	>1,000,000	0.25	0.000300	333,054
30.00	0.000022	>1,000,000	0.10	0.000428	233,666
20.00	0.000031	>1,000,000			

Estimated percentile of per-capita days exceeding calculated exposure in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

Percentile	Exposure	MOE	Percentile	Exposure	MOE
90.00	0.000003	>1,000,000	10.00	0.000048	>1,000,000
80.00	0.000006	>1,000,000	5.00	0.000071	>1,000,000
70.00	0.000009	>1,000,000	2.50	0.000103	973,128
60.00	0.000011	>1,000,000	1.00	0.000165	605,375
50.00	0.000014	>1,000,000	0.50	0.000211	474,270
40.00	0.000017	>1,000,000	0.25	0.000297	336,242
30.00	0.000022	>1,000,000	0.10	0.000425	235,181
20.00	0.000030	>1,000,000			

1/ Analysis based on all 2-day participant records in CSFII 1994-95 survey.
2/ Margin of Exposure = NOEL/ Dietary Exposure.

U.S. Environmental Protection Agency — Ver. 6.13
DEEM96 ACUTE96 analysis for HOE-107892 — (1994-95 data)
Residue file name: HOE-C.R95 — Adjustment factor #2 NOT used.
Analysis Date 06-18-1998 — Residue file dated: 06-18-1998/08:26:56/8
NOEL (ACUTE96) = 100.000000 mg/kg body-wt/day

Nursing infants (<1 year)

Daily Exposure Analysis (mg/kg body-weight/day)

	per Capita	per User
Mean	0.000004	0.000028
Standard Deviation	0.000022	0.000053
Standard Error	0.000002	0.000010
Margin of Exposure	>1,000,000	>1,000,000

Percent of Person-Days that are User-Days = 14.49%

Estimated percentile of user-days exceeding calculated exposure in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

Percentile	Exposure	MOE	Percentile	Exposure	MOE
90.00	0.000001	>1,000,000	10.00	0.000051	>1,000,000
80.00	0.000001	>1,000,000	5.00	0.000131	765,017
70.00	0.000002	>1,000,000	2.50	0.000177	566,530
60.00	0.000003	>1,000,000	1.00	0.000204	490,217
50.00	0.000005	>1,000,000	0.50	0.000213	469,152
40.00	0.000011	>1,000,000	0.25	0.000218	459,284
30.00	0.000020	>1,000,000	0.10	0.000220	453,560
20.00	0.000034	>1,000,000			

Estimated percentile of per-capita days exceeding calculated exposure in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

Percentile	Exposure	MOE	Percentile	Exposure	MOE
90.00	0.000000	>1,000,000	10.00	0.000002	>1,000,000
80.00	0.000000	>1,000,000	5.00	0.000016	>1,000,000
70.00	0.000000	>1,000,000	2.50	0.000039	>1,000,000
60.00	0.000000	>1,000,000	1.00	0.000101	994,461
50.00	0.000000	>1,000,000	0.50	0.000159	628,589
40.00	0.000000	>1,000,000	0.25	0.000191	524,389
30.00	0.000000	>1,000,000	0.10	0.000210	476,951
20.00	0.000000	>1,000,000			

U.S. Environmental Protection Agency Ver. 6.13
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Residue file name: HOE-C.R95 Adjustment factor #2 NOT used.
Analysis Date 06-18-1998 Residue file dated: 06-18-1998/08:26:56/8
NOEL (ACUTE96) = 100.000000 mg/kg body-wt/day

Females (13+/preg/not nsg)

Daily Exposure Analysis (mg/kg body-weight/day)	per Capita	per User
Mean	0.000015	0.000015
Standard Deviation	0.000011	0.000010
Standard Error	0.000001	0.000001
Margin of Exposure	>1,000,000	>1,000,000

Percent of Person-Days that are User-Days = 96.94%

Estimated percentile of user-days exceeding calculated exposure in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

Percentile	Exposure	MOE	Percentile	Exposure	MOE
90.00	0.000005	>1,000,000	10.00	0.000028	>1,000,000
80.00	0.000008	>1,000,000	5.00	0.000033	>1,000,000
70.00	0.000010	>1,000,000	2.50	0.000037	>1,000,000
60.00	0.000011	>1,000,000	1.00	0.000039	>1,000,000
50.00	0.000013	>1,000,000	0.50	0.000055	>1,000,000
40.00	0.000014	>1,000,000	0.25	0.000067	>1,000,000
30.00	0.000018	>1,000,000	0.10	0.000074	>1,000,000
20.00	0.000022	>1,000,000			

Estimated percentile of per-capita days exceeding calculated exposure in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

Percentile	Exposure	MOE	Percentile	Exposure	MOE
90.00	0.000004	>1,000,000	10.00	0.000028	>1,000,000
80.00	0.000008	>1,000,000	5.00	0.000033	>1,000,000
70.00	0.000009	>1,000,000	2.50	0.000037	>1,000,000
60.00	0.000011	>1,000,000	1.00	0.000039	>1,000,000
50.00	0.000012	>1,000,000	0.50	0.000055	>1,000,000
40.00	0.000014	>1,000,000	0.25	0.000067	>1,000,000
30.00	0.000017	>1,000,000	0.10	0.000074	>1,000,000
20.00	0.000022	>1,000,000			

U.S. Environmental Protection Agency Ver. 6.13
DEEM96 ACUTE96 analysis for HOE-107892 (1994-95 data)
Residue file name: HOE-C.R95 Adjustment factor #2 NOT used.
Analysis Date 06-18-1998 Residue file dated: 06-18-1998/08:26:56/8
NOEL (ACUTE96) = 100.000000 mg/kg body-wt/day

Females (13+/nursing)

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000017	0.000017
Standard Deviation	0.000013	0.000013
Standard Error	0.000002	0.000002
Margin of Exposure	>1,000,000	>1,000,000

Percent of Person-Days that are User-Days =100.00%

Estimated percentile of user-days exceeding calculated exposure in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

Percentile	Exposure	MOE	Percentile	Exposure	MOE
90.00	0.000005	>1,000,000	10.00	0.000036	>1,000,000
80.00	0.000007	>1,000,000	5.00	0.000043	>1,000,000
70.00	0.000010	>1,000,000	2.50	0.000050	>1,000,000
60.00	0.000012	>1,000,000	1.00	0.000057	>1,000,000
50.00	0.000013	>1,000,000	0.50	0.000059	>1,000,000
40.00	0.000015	>1,000,000	0.25	0.000060	>1,000,000
30.00	0.000019	>1,000,000	0.10	0.000061	>1,000,000
20.00	0.000024	>1,000,000			

Estimated percentile of per-capita days exceeding calculated exposure in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

Percentile	Exposure	MOE	Percentile	Exposure	MOE
90.00	0.000005	>1,000,000	10.00	0.000036	>1,000,000
80.00	0.000007	>1,000,000	5.00	0.000043	>1,000,000
70.00	0.000010	>1,000,000	2.50	0.000050	>1,000,000
60.00	0.000012	>1,000,000	1.00	0.000057	>1,000,000
50.00	0.000013	>1,000,000	0.50	0.000059	>1,000,000
40.00	0.000015	>1,000,000	0.25	0.000060	>1,000,000
30.00	0.000019	>1,000,000	0.10	0.000061	>1,000,000
20.00	0.000024	>1,000,000			

U.S. Environmental Protection Agency Ver. 6.13
DEEM96 ACUTE96 analysis for HOE-107892 (1994-95 data)
Residue file name: HOE-C.R95 Adjustment factor #2 NOT used.
Analysis Date 06-18-1998 Residue file dated: 06-18-1998/08:26:56/8
NOEL (ACUTE96) = 100.000000 mg/kg body-wt/day

Children (1-6 years)

Daily Exposure Analysis (mg/kg body-weight/day)	per Capita	per User
Mean	0.000038	0.000039
Standard Deviation	0.000026	0.000026
Standard Error	0.000000	0.000000
Margin of Exposure	>1,000,000	>1,000,000

Percent of Person-Days that are User-Days = 98.60%

Estimated percentile of user-days exceeding calculated exposure in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

Percentile	Exposure	MOE	Percentile	Exposure	MOE
90.00	0.000011	>1,000,000	10.00	0.000072	>1,000,000
80.00	0.000018	>1,000,000	5.00	0.000087	>1,000,000
70.00	0.000024	>1,000,000	2.50	0.000102	981,182
60.00	0.000029	>1,000,000	1.00	0.000128	781,285
50.00	0.000034	>1,000,000	0.50	0.000144	693,384
40.00	0.000040	>1,000,000	0.25	0.000154	650,317
30.00	0.000047	>1,000,000	0.10	0.000184	544,209
20.00	0.000057	>1,000,000			

Estimated percentile of per-capita days exceeding calculated exposure in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

Percentile	Exposure	MOE	Percentile	Exposure	MOE
90.00	0.000010	>1,000,000	10.00	0.000072	>1,000,000
80.00	0.000018	>1,000,000	5.00	0.000087	>1,000,000
70.00	0.000023	>1,000,000	2.50	0.000102	983,201
60.00	0.000028	>1,000,000	1.00	0.000128	782,800
50.00	0.000034	>1,000,000	0.50	0.000144	694,497
40.00	0.000040	>1,000,000	0.25	0.000154	650,893
30.00	0.000047	>1,000,000	0.10	0.000183	545,054
20.00	0.000056	>1,000,000			

U.S. Environmental Protection Agency Ver. 6.13
DEEM96 ACUTE96 analysis for HOE-107892 (1994-95 data)
Residue file name: HOE-C.R95 Adjustment factor #2 NOT used.
Analysis Date 06-18-1998 Residue file dated: 06-18-1998/08:26:56/8
NOEL (ACUTE96) = 100.000000 mg/kg body-wt/day

Males (13-19 years)

Daily Exposure Analysis (mg/kg body-weight/day)	per Capita	per User
Mean	0.000021	0.000022
Standard Deviation	0.000028	0.000028
Standard Error	0.000001	0.000001
Margin of Exposure	>1,000,000	>1,000,000

Percent of Person-Days that are User-Days = 97.66%

Estimated percentile of user-days exceeding calculated exposure in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

Percentile	Exposure	MOE	Percentile	Exposure	MOE
90.00	0.000006	>1,000,000	10.00	0.000039	>1,000,000
80.00	0.000009	>1,000,000	5.00	0.000050	>1,000,000
70.00	0.000011	>1,000,000	2.50	0.000065	>1,000,000
60.00	0.000014	>1,000,000	1.00	0.000135	743,185
50.00	0.000017	>1,000,000	0.50	0.000259	385,939
40.00	0.000019	>1,000,000	0.25	0.000315	317,602
30.00	0.000023	>1,000,000	0.10	0.000358	279,534
20.00	0.000029	>1,000,000			

Estimated percentile of per-capita days exceeding calculated exposure in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

Percentile	Exposure	MOE	Percentile	Exposure	MOE
90.00	0.000004	>1,000,000	10.00	0.000039	>1,000,000
80.00	0.000008	>1,000,000	5.00	0.000050	>1,000,000
70.00	0.000011	>1,000,000	2.50	0.000065	>1,000,000
60.00	0.000014	>1,000,000	1.00	0.000133	749,342
50.00	0.000016	>1,000,000	0.50	0.000256	390,442
40.00	0.000019	>1,000,000	0.25	0.000314	318,957
30.00	0.000023	>1,000,000	0.10	0.000357	280,071
20.00	0.000028	>1,000,000			

U.S. Environmental Protection Agency Ver. 6.13
DEEM96 ACUTE96 analysis for HOE-107892 (1994-95 data)
Residue file name: HOE-C.R95 Adjustment factor #2 NOT used.
Analysis Date 06-18-1998 Residue file dated: 06-18-1998/08:26:56/8
NOEL (ACUTE96) = 100.000000 mg/kg body-wt/day

Males (20+ years)

Daily Exposure Analysis (mg/kg body-weight/day)	per Capita	per User
Mean	0.000027	0.000028
Standard Deviation	0.000048	0.000048
Standard Error	0.000001	0.000001
Margin of Exposure	>1,000,000	>1,000,000

Percent of Person-Days that are User-Days = 97.90%

Estimated percentile of user-days exceeding calculated exposure in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

Percentile	Exposure	MOE	Percentile	Exposure	MOE
90.00	0.000005	>1,000,000	10.00	0.000064	>1,000,000
80.00	0.000007	>1,000,000	5.00	0.000101	987,771
70.00	0.000009	>1,000,000	2.50	0.000154	648,482
60.00	0.000011	>1,000,000	1.00	0.000222	449,585
50.00	0.000014	>1,000,000	0.50	0.000323	309,533
40.00	0.000017	>1,000,000	0.25	0.000430	232,772
30.00	0.000023	>1,000,000	0.10	0.000567	176,296
20.00	0.000033	>1,000,000			

Estimated percentile of per-capita days exceeding calculated exposure in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

Percentile	Exposure	MOE	Percentile	Exposure	MOE
90.00	0.000004	>1,000,000	10.00	0.000064	>1,000,000
80.00	0.000006	>1,000,000	5.00	0.000100	995,549
70.00	0.000009	>1,000,000	2.50	0.000153	653,305
60.00	0.000011	>1,000,000	1.00	0.000221	451,569
50.00	0.000014	>1,000,000	0.50	0.000321	311,620
40.00	0.000017	>1,000,000	0.25	0.000427	234,019
30.00	0.000022	>1,000,000	0.10	0.000565	176,911
20.00	0.000032	>1,000,000			

U.S. Environmental Protection Agency Ver. 6.13
DEEM96 ACUTE96 analysis for HOE-107892 (1994-95 data)
Residue file name: HOE-C.R95 Adjustment factor #2 NOT used.
Analysis Date 06-18-1998 Residue file dated: 06-18-1998/08:26:56/8
NOEL (ACUTE96) = 100.000000 mg/kg body-wt/day

Females (13-50 years)

Daily Exposure Analysis (mg/kg body-weight/day)	per Capita	per User
Mean	0.000016	0.000017
Standard Deviation	0.000025	0.000025
Standard Error	0.000000	0.000000
Margin of Exposure	>1,000,000	>1,000,000

Percent of Person-Days that are User-Days = 96.79%

Estimated percentile of user-days exceeding calculated exposure in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

Percentile	Exposure	MOE	Percentile	Exposure	MOE
90.00	0.000004	>1,000,000	10.00	0.000030	>1,000,000
80.00	0.000006	>1,000,000	5.00	0.000042	>1,000,000
70.00	0.000008	>1,000,000	2.50	0.000065	>1,000,000
60.00	0.000010	>1,000,000	1.00	0.000120	835,785
50.00	0.000011	>1,000,000	0.50	0.000178	562,271
40.00	0.000014	>1,000,000	0.25	0.000204	489,653
30.00	0.000017	>1,000,000	0.10	0.000283	352,935
20.00	0.000021	>1,000,000			

Estimated percentile of per-capita days exceeding calculated exposure in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

Percentile	Exposure	MOE	Percentile	Exposure	MOE
90.00	0.000003	>1,000,000	10.00	0.000030	>1,000,000
80.00	0.000005	>1,000,000	5.00	0.000042	>1,000,000
70.00	0.000007	>1,000,000	2.50	0.000064	>1,000,000
60.00	0.000009	>1,000,000	1.00	0.000118	844,343
50.00	0.000011	>1,000,000	0.50	0.000176	568,444
40.00	0.000013	>1,000,000	0.25	0.000203	491,761
30.00	0.000016	>1,000,000	0.10	0.000282	355,129
20.00	0.000021	>1,000,000			

U.S. Environmental Protection Agency Ver. 6.13
DEEM96 ACUTE96 analysis for HOE-107892 (1994-95 data)
Residue file name: HOE-C.R95 Adjustment factor #2 NOT used.
Analysis Date 06-18-1998 Residue file dated: 06-18-1998/08:26:56/8
NOEL (ACUTE96) = 100.000000 mg/kg body-wt/day
Bin intervals calibrated using computed means.
COMMENT 1: Safener - Fenoxyprop-ethyl, no CAS, no PCode/3x females 13+
COMMENT 2: 98ND0007/Hurley-RAB2

Summary calculations:

	95th Percentile Exposure	95th Percentile MOE	99th Percentile Exposure	99th Percentile MOE	99.9 Percentile Exposure	99.9 Percentile MOE
U.S. pop - all seasons:	0.000071	1000000	0.000165	605375	0.000425	235181
Nursing infants (<1 year):	0.000016	1000000	0.000101	994461	0.000210	476951
Females (13+/preg/not nsg):	0.000033	1000000	0.000039	1000000	0.000074	1000000
Females (13+/nursing):	0.000043	1000000	0.000057	1000000	0.000061	1000000
Children (1-6 years):	0.000087	1000000	0.000128	782800	0.000183	545054
Males (13-19 years):	0.000050	1000000	0.000133	749342	0.000357	280071
Males (20+ years):	0.000100	995549	0.000221	451569	0.000565	176911
Females (13-50 years):	0.000042	1000000	0.000118	844343	0.000282	355129

U.S. Environmental Protection Agency Ver. 6.11
DEEM96 CHRONIC analysis for HOE-107892 (1994/95 data)
Residue file name: HOE-C Adjustment factor #2 NOT used.
Analysis Date 06-18-1998 Residue file dated: 06-18-1998/08:26:56/8
Reference dose (RfD, CHRONIC) = 0.510000 mg/kg body-wt/day
COMMENT 1: Safener - Fenoxyprop-ethyl, no CAS, no PCode/3x females 13+
COMMENT 2: 98ND0007/Hurley-RAB@

Residue file listing

Food Code	EPA Code	Crop Group	Food Name	Residue (ppm)	Adj. Fctrs #1	#2
265	24001AA	O	BARLEY	0.050000	1.00	1.00
276	24007AA	O	WHEAT-ROUGH	0.010000	1.00	1.00
277	24007GA	O	WHEAT-GERM	0.010000	1.00	1.00
278	24007HA	O	WHEAT-BRAN	0.010000	1.00	1.00
279	24007WA	O	WHEAT-FLOUR	0.010000	1.00	1.00

U.S. Environmental Protection Agency Ver. 6.11
DEEM96 CHRONIC analysis for HOE-107892 (1994/95 data)
Residue file name: HOE-C Adjustment factor #2 NOT used.
Analysis Date 06-18-1998 Residue file dated: 06-18-1998/08:26:56/8
Reference dose (RfD, CHRONIC) = 0.510000 mg/kg body-wt/day
COMMENT 1: Safener - Fenoxyprop-ethyl, no CAS, no PCode/3x females 13+
COMMENT 2: 98ND0007/Hurley-RAB@

Total exposure by population subgroup

Population Subgroup	Total Exposure mg/kg body wt/day	Total Exposure Percent of Rfd
U.S. Pop - 48 states - all seasons	0.000023	0.0%
U.S. Population - spring season	0.000025	0.0%
U.S. Population - summer season	0.000022	0.0%
U.S. Population - autumn season	0.000022	0.0%
U.S. Population - winter season	0.000021	0.0%
Northeast region	0.000022	0.0%
Midwest region	0.000025	0.0%
Southern region	0.000021	0.0%
Western region	0.000023	0.0%
Hispanics	0.000021	0.0%
Non-hispanic whites	0.000024	0.0%
Non-hispanic blacks	0.000020	0.0%
Non-hispanic other than black or white	0.000018	0.0%
All infants (<1 year)	0.000007	0.0%
Nursing infants (<1 year)	0.000004	0.0%
Non-nursing infants (<1 year)	0.000008	0.0%
Children (1-6 years)	0.000038	0.0%
Children (7-12 years)	0.000027	0.0%
Females (13-19 yrs/not preg. or nursing)	0.000015	0.0%
Females (20+ years/not preg. or nursing)	0.000016	0.0%
Females (13-50 years)	0.000016	0.0%
Females (13+/pregnant/not nursing)	0.000015	0.0%
Females (13+/nursing)	0.000017	0.0%
Males (13-19 years)	0.000021	0.0%
Males (20+ years)	0.000027	0.0%
Seniors (55+)	0.000015	0.0%

13544

R104559

Chemical:	**Diethyl-1-(2,4-dichlorophenyl)-5-methyl-**
PC Code:	**811800**
HED File Code	**14000 Risk Reviews**
Memo Date:	**07/02/98**
File ID:	**DPD244654**
Accession Number:	**412-05-0088**

HED Records Reference Center
01/10/2005