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.''

EPA does not have, at this time, available data to determine whether methoxyfenozide has a common mechanism of toxicity with other substances or how to include this pesticide in a cumulative risk assessment. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, methoxyfenozide does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, it is assumed that methoxyfenozide does not have a common mechanism of toxicity with other substances.

E. Safety Determination

1. *U.S. population.* Using the DEEM exposure assumptions described in this unit, Rohm and Haas has concluded that aggregate exposure to methoxyfenozide from food will utilize 17.6% of the cPAD for the U.S. population. The major identifiable subgroup with the highest aggregate exposure is children 1–6 years old at 34.5% of the cPAD and is discussed below. EPA generally has no concern for exposures below 100% of the cPAD because the cPAD represents the level at or below which daily aggregate dietary exposure over a lifetime will not pose appreciable risks to human health. Despite the potential for exposure to methoxyfenozide in drinking water, the aggregate exposure is not expected to exceed 100% of the cPAD. Rohm and Haas concludes that there is a reasonable certainty that no harm will result from aggregate exposure to methoxyfenozide residues.

2. *Safety factor for infants and children*—i. *In general.* In assessing the potential for additional sensitivity of infant and children to residues of methoxyfenozide, EPA considered data from developmental toxicity studies in the rat and rabbit and a 2–generation reproduction study in the rat. 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.

FFDCA section 408 provides that EPA shall apply an additional tenfold margin of safety for infants and children in the case of threshold effects to account for prenatal and postnatal 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 (MOE) analysis or through using uncertainty (safety) factors in calculating a dose level that poses no appreciable risk to humans. EPA believes that reliable data support using the standard uncertainty factor (usually 100 for combined interspecies and intraspecies variability) and not the additional tenfold MOE/UF when EPA has a complete data base under existing guidelines and when the severity of the effect in infants or children or the potency or unusual toxic properties of a compound do not raise concerns regarding the adequacy of the standard MOE/safety factor.

ii. *Prenatal and postnatal sensitivity.* The toxicology data base for methoxyfenozide included acceptable developmental toxicity studies in both rats and rabbits as well as a 2–generation reproductive toxicity study in rats. The data provided no indication of increased sensitivity of rats or rabbits to in utero and/or postnatal exposure to methoxyfenozide.

iii. *Conclusion.* There is a complete toxicity data base for methoxyfenozide and exposure data are complete or are estimated based on data that reasonably accounts for potential exposures. Based on the completeness of the data base and the lack of prenatal and postnatal toxicity, EPA determined that an additional safety factor was not needed for the protection of infants and children.

iv. *Acute risk.* Since no acute toxicological endpoints were established, acute aggregate risk is considered to be negligible.

v. *Chronic risk.* Using the exposure assumptions described in this unit, Rohm and Haas has concluded that aggregate exposure to methoxyfenozide from food will utilize 34.5% of the cPAD for infants and children. EPA generally has no concern for exposures below 100% of the cPAD because the cPAD represents the level at or below which daily aggregate dietary exposure over a lifetime will not pose appreciable risks to human health. Despite the potential for exposure to methoxyfenozide in drinking water, Rohm and Haas does not expect the aggregate exposure to exceed 100% of the cPAD.

vi. *Short- or intermediate-term risk.* Short and intermediate term risks are judged to be negligible due to the lack of significant toxicological effects observed.

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

F. International Tolerances

There are no established or proposed Codex, Canadian or Mexican limits for residues of methoxyfenozide in/on plant or animal commodities. Therefore, no compatibility issues exist with regard to the proposed U.S. tolerances discussed in this petition review.

[FR Doc. 01–6721 Filed 3–16–01; 8:45 am]

BILLING CODE 6560–50–S

ENVIRONMENTAL PROTECTION AGENCY

[PF–999; FRL–6766–8]

Notice of Filing Pesticide Petitions to Establish a Tolerance for Certain Pesticide Chemicals in or on Food

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: This notice announces the initial filing of pesticide petitions proposing the establishment of regulations for residues of certain pesticide chemicals in or on various food commodities.

DATES: Comments, identified by docket control number PF–999, must be received on or before April 18, 2001.

ADDRESSES: Comments may be submitted by mail, electronically, or in person. Please follow the detailed instructions for each method as provided in Unit I.C. of the **SUPPLEMENTARY INFORMATION**. To ensure proper receipt by EPA, it is imperative that you identify docket control number PF–999 in the subject line on the first page of your response.

FOR FURTHER INFORMATION CONTACT: The product manager listed in the table below:

Product Manager	Office location/telephone number/e-mail address	Petition(s) number
Shaja Brothers	Registration Division (7505C), Office of Pesticide Programs, Environmental Protection Agency, Ariel Rios Bldg., 1200 Pennsylvania Ave., NW.,Washington, DC 20460; telephone number: (703) 308–3194; and e-mail address: brothers.shaja@epamail.epa.gov..	PP 0E6183, 0E6083, 0E6175
Joseph Tavano	Registration Division (7505C), Office of Pesticide Programs, Environmental Protection Agency, Ariel Rios Bldg., 1200 Pennsylvania Ave., NW.,Washington, DC 20460; telephone number: (703) 305–6411; and e-mail address: tavano.joe@epamail.epa.gov..	PP 0F6220

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

You may be affected by this action if you are an agricultural producer, food manufacturer or pesticide manufacturer. Potentially affected categories and entities may include, but are not limited to:

Categories	NAICS	Examples of potentially affected entities
Industry	111 112 311 32532	Crop production Animal production Food manufacturing Pesticide manufacturing

This listing is not intended to be exhaustive, but rather provides a guide for readers regarding entities likely to be affected by this action. Other types of entities not listed in the table could also be affected. The North American Industrial Classification System (NAICS) codes have been provided to assist you and others in determining whether or not this action might apply to certain entities. If you have questions regarding the applicability of this action to a particular entity, consult the person listed under **FOR FURTHER INFORMATION CONTACT**.

B. How Can I Get Additional Information, Including Copies of this Document and Other Related Documents?

1. *Electronically*. You may obtain electronic copies of this document, and certain other related documents that might be available electronically, from the EPA Internet Home Page at *http://www.epa.gov/*. To access this document, on the Home Page select ''Laws and Regulations'' and then look up the entry for this document under the ''**Federal Register**—Environmental Documents.'' You can also go directly to the **Federal Register** listings at *http://www.epa.gov/fedrgstr/*.

2. *In person*. The Agency has established an official record for this action under docket control number PF–999. The official record consists of the documents specifically referenced in this action, any public comments received during an applicable comment period, and other information related to this action, including any information claimed as confidential business information (CBI). This official record includes the documents that are physically located in the docket, as well as the documents that are referenced in those documents. The public version of the official record does not include any information claimed as CBI. The public version of the official record, which includes printed, paper versions of any electronic comments submitted during an applicable comment period, is available for inspection in the Public Information and Records Integrity Branch (PIRIB), Rm. 119, Crystal Mall #2, 1921 Jefferson Davis Highway, Arlington, VA, from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The PIRIB telephone number is (703) 305–5805.

C. How and to Whom Do I Submit Comments?

You may submit comments through the mail, in person, or electronically. To ensure proper receipt by EPA, it is imperative that you identify docket control number PF–999 in the subject line on the first page of your response.

1. *By mail*. Submit your comments to: Public Information and Records Integrity Branch (PIRIB), Information Resources and Services Division (7502C), Office of Pesticide Programs (OPP), Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460.

2. *In person or by courier*. Deliver your comments to: Public Information and Records Integrity Branch (PIRIB), Information Resources and Services Division (7502C), Office of Pesticide Programs (OPP), Environmental Protection Agency, Rm. 119, Crystal Mall #2, 1921 Jefferson Davis Highway, Arlington, VA. The PIRIB is open from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The PIRIB telephone number is (703) 305–5805.

3. *Electronically*. You may submit your comments electronically by e-mail to: opp-docket@epa.gov, or you can submit a computer disk as described above. Do not submit any information electronically that you consider to be CBI. Avoid the use of special characters and any form of encryption. Electronic submissions will be accepted in Wordperfect 6.1/8.0 or ASCII file format. All comments in electronic form must be identified by docket control number PF–999. Electronic comments may also be filed online at many Federal Depository Libraries.

D. How Should I Handle CBI That I Want to Submit to the Agency?

Do not submit any information electronically that you consider to be CBI. You may claim information that you submit to EPA in response to this document as CBI by marking any part or all of that information as CBI. Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR part 2. In addition to one complete version of the comment that includes any information claimed as CBI, a copy of the comment that does not contain the information claimed as CBI must be submitted for inclusion in the public version of the official record. Information not marked confidential will be included in the public version of the official record without prior notice. If you have any questions about CBI or the procedures for claiming CBI, please consult the person identified under **FOR FURTHER INFORMATION CONTACT**.

E. What Should I Consider as I Prepare My Comments for EPA?

You may find the following suggestions helpful for preparing your comments:

1. Explain your views as clearly as possible

2. Describe any assumptions that you used.

3. Provide copies of any technical information and/or data you used that support your views.

4. If you estimate potential burden or costs, explain how you arrived at the estimate that you provide.

5. Provide specific examples to illustrate your concerns.

6. Make sure to submit your comments by the deadline in this notice.

7. To ensure proper receipt by EPA, be sure to identify the docket control number assigned to this action in the subject line on the first page of your response. You may also provide the name, date, and **Federal Register** citation.

II. What Action is the Agency Taking?

EPA has received pesticide petitions as follows proposing the establishment and/or amendment of regulations for residues of certain pesticide chemicals in or on various food commodities under section 408 of the Federal Food, Drug, and Comestic Act (FFDCA), 21 U.S.C. 346a. EPA has determined that these petitions contain data or information regarding the elements set forth in section 408(d)(2); however, EPA has not fully evaluated the sufficiency of the submitted data at this time or whether the data supports granting of the petition. Additional data may be needed before EPA rules on the petition.

List of Subjects

Environmental protection, Agricultural commodities, Feed additives, Food additives, Pesticides and pests, Reporting and recordkeeping requirements.

Dated: February 23, 2001.

Peter Caulkins,

Acting Director, Registration Division, Office of Pesticide Programs.

Summaries of Petitions

Petitioner summaries of the pesticide petitions are printed below as required bysection 408(d)(3) of the FFDCA. The summaries of the petitions were prepared by the petitioners and represent the views of the petitioners. EPA is publishing the petition summaries verbatim without editing them in any way. The petition summary announces the availability of a description of the analytical methods available to EPA for the detection and measurement of the pesticide chemical residues or an explanation of why no such method is needed.

1. Valent U.S.A. Corporation

0F6220

EPA has received a pesticide petition (OF6220) from Valent U.S.A. Corporation, 1333 North California Street, Suite 600, Walnut Creek, CA 945968025 proposing, pursuant to section 408(d) of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 346a(d), to amend 40 CFR part 180 by establishing a tolerance for residues of pyriproxyfen, 2-[1-methyl-2-(4-phenoxyphenoxy)ethoxy]pyridine in or on the raw agricultural commodity stone fruit at 1.0 parts per million (ppm). EPA has determined that the petition contains data or information regarding the elements set forth in section 408(d)(2) of the FFDCA; however, EPA has not fully evaluated the sufficiency of the submitted data at this time or whether the data supports granting of the petition. Additional data may be needed before EPA rules on the petition.

A. Residue Chemistry

1. *Plant metabolism*. Metabolism of ^{14}C-pyriproxyfen labelled in the phenoxyphenyl ring and in the pyridyl ring has been studied in cotton, apples, tomatoes, lactating goats, and laying hens (and rats). The major metabolic pathways in plants is aryl hydroxylation and cleavage of the ether linkage, followed by further metabolism into more polar products by further oxidation and/or conjugation reactions. However, the bulk of the radiochemical residue on RAC samples remained as parent. Comparing metabolites detected and quantified from cotton, apple, tomato, goat and hen (and rat) shows that there are no significant aglycones in plants which are not also present in the excreta or tissues of animals. The residue of concern is best defined as the parent, pyriproxyfen. Ruminant and poultry metabolism studies demonstrated that transfer of administered ^{14}C-residues to tissues was low. Total ^{14}C-residues in goat milk, muscle and tissues accounted for less than 2% of the administered dose, and were less than 1 ppm in all cases. In poultry, total ^{14}C-residues in eggs, muscle and tissues accounted for about 2.7% of the administered dose, and were less than 1 ppm in all cases except for gizzard.

2. *Analytical method*. Practical analytical methods for detecting and measuring residue levels of pyriproxyfen (and relevant metabolites) have been developed and validated in/on all appropriate agricultural commodities, respective processing fractions, milk, animal tissues, and environmental samples. The extraction methodology has been validated using aged radiochemical residue samples from metabolism studies. The methods have been validated in cottonseed, apples, soil, and oranges at independent laboratories. EPA has successfully validated the analytical method for analysis of cottonseed raw agricultural commodity. The limit of detection of pyriproxyfen in the methods is 0.01 ppm which will allow monitoring of food with residues at the levels proposed for the tolerances.

3. *Magnitude of residues—stone fruit*. Seven field trials in cherries were conducted in 1998 through 1999. Similarly, 10 field trials were conducted for peaches, and 7 field trials were conducted for plums. The proposed use pattern for the three stone fruit crops is identical. The analytical data show that the average measured residue in/on cherry samples was 0.33 ppm (n = 14, σ_{n-1} = 0.20 ppm) pyriproxyfen. Similarly, the analytical data show that the average measured residue in/on peach samples was 0.16 ppm (n = 20, σ_{n-1} = 0.06 ppm), and in/on plum samples was 0.06 ppm (n = 14, σ_{n-1} = 0.06 ppm), of pyriproxyfen. A processing study in prunes demonstrated that pyriproxyfen concentrated in prunes (2.9–fold). The highest average residue (HAR) from field trials was 0.20 ppm. All these data support proposed tolerances for pyriproxyfen in/on stone fruit crop group at 1.0 ppm and no processed commodity tolerance is necessary.

i. *Secondary residues*. Using proposed tolerances to calculate the maximum feed exposure to fed animals, and using the very low potential for residue transfer documented in the milk cow feeding residue study, finite, detectable secondary residues in animal tissues, milk, and eggs are not expected. Therefore, tolerances are not proposed for these commodities.

ii. *Rotational crops*. The results of a confined rotational crops accumulation study indicate that no rotational crop planting restrictions or rotational crop tolerances are required.

B. Toxicological Profile

1. *Acute toxicity*. The acute toxicity of technical grade pyriproxyfen is low by all routes. The compound is classified as Category III for acute dermal and inhalation toxicity, and Category IV for acute oral toxicity, and skin/eye irritation. Pyriproxyfen is not a skin sensitizing agent.

2. *Genotoxicty*. Pyriproxyfen does not present a genetic hazard. Pyriproxyfen was negative in the following tests for mutagenicity: Ames assay with and

without S9, *in vitro* unscheduled DNA synthesis in HeLa S3 cells, *in vitro* gene mutation in V79 Chinese hamster cells, and *in vitro* chromosomal aberration with and without S9 in Chinese hamster ovary cells.

3. *Reproductive and developmental toxicity*. Pyriproxyfen is not a developmental or reproductive toxicant. Developmental toxicity studies have been performed in rats and rabbits, and multigenerational effects on reproduction were tested in rats. These studies have been reviewed and found to be acceptable to the Agency.

In the developmental toxicity study conducted with rats, technical pyriproxyfen was administered by gavage at levels of 0, 100, 300, and 1,000 milligrams/kilogram of body weight/day (mg/kg bw/day) during gestation days 7–17. Maternal toxicity (mortality, decreased body weight gain and food consumption, and clinical signs of toxicity) was observed at doses of 300 mg/kg bw/day and greater. The maternal NOAEL was 100 mg/kg bw/day. A transient increase in skeletal variations was observed in rat fetuses from females exposed to 300 mg/kg bw/day and greater. These effects were not present in animals examined at the end of the postnatal period, therefore, the NOAEL for prenatal developmental toxicity was 100 mg/kg bw/day. An increased incidence of visceral and skeletal variations was observed postnatally at 1,000 mg/kg bw/day. The NOAEL for postnatal developmental toxicity was 300 mg/kg bw/day.

In the developmental toxicity study conducted with rabbits, technical pyriproxyfen was administered by gavage at levels of 0, 100, 300, and 1,000 mg/kg bw/day during gestation days 6–18. Maternal toxicity (clinical signs of toxicity including one death, decreased body weight gain and food consumption, and abortions or premature deliveries) was observed at oral doses of 300 mg/kg bw/day or higher. The maternal NOAEL was 100 mg/kg bw/day. No developmental effects were observed in the rabbit fetuses. The NOAEL for developmental toxicity in rabbits was 1,000 mg/kg bw/day.

In the rat reproduction study, pyriproxyfen was administered in the diet at levels of 0, 200, 1,000, and 5,000 ppm through 2 generations of rats. Adult systemic toxicity (reduced body weights, liver and kidney histopathology, and increased liver weight) was produced at the 5,000 ppm dose (453 mg/kg bw/day in males, 498 mg/kg bw/day in females) during the pre-mating period. The systemic NOAEL was 1,000 ppm (87 mg/kg bw/day in males, 96 mg/kg bw/day in females). No effects on reproduction were produced at 5,000 ppm, the highest dose tested.

4. *Subchronic toxicity*. Subchronic oral toxicity studies conducted with pyriproxyfen technical in the rat, mouse and dog indicate a low level of toxicity. Effects observed at high dose levels consisted primarily of decreased body weight gain; increased liver weights; histopathological changes in the liver and kidney; decreased red blood cell counts, hemoglobin and hematocrit; altered blood chemistry parameters; and, at 5,000 and 10,000 ppm in mice, a decrease in survival rates. The NOAELs from these studies were 400 ppm (23.5 mg/kg bw/day for males, 27.7 mg/kg bw/day for females) in rats, 1,000 ppm (149.4 mg/kg bw/day for males, 196.5 mg/kg bw/day for females) in mice, and 100 mg/kg bw/day in dogs.

In a 4–week inhalation study of pyriproxyfen technical in rats, decreased body weight and increased water consumption were observed at 1,000 mg/m^3. The NOAEL in this study was 482 mg/m^3.

A 21–day dermal toxicity study in rats with pyriproxyfen technical did not produce any signs of dermal or systemic toxicity at 1,000 mg/kg bw/day, the highest dose tested (HDT). In a 21–day dermal study conducted with KNACK®. Insect Growth Regulator the test material produced a NOAEL of 1,000 mg/kg bw/day (HDT) for systemic effects, and a NOAEL for skin irritation of 100 mg/kg bw/day.

5. *Chronic toxicity*. Pyriproxyfen technical has been tested in chronic studies with dogs, rats and mice. EPA has established a reference dose (RfD) for pyriproxyfen of 0.35 mg/kg bw/day, based on the NOAEL in female rats from the 2–year chronic/oncogenicity study. Effects cited by EPA in the Reference Dose Tracking Report include negative trend in mean red blood cell volume, increased hepatocyte cytoplasm and cytoplasm: nucleus ratios, and decreased sinusoidal spaces.

Pyriproxyfen is not a carcinogen. Studies with pyriproxyfen have shown that repeated high dose exposures produced changes in the liver, kidney and red blood cells, but did not produce cancer in test animals. No oncogenic response was observed in a rat 2–year chronic feeding/oncogenicity study or in a 78 week study on mice. The oncogenicity classification of pyriproxyfen is ''E'' (no evidence of carcinogenicity for humans).

Pyriproxyfen technical was administered to dogs in capsules at doses of 0, 30, 100, 300 and 1,000 mg/kg bw/day for 1–year. Dogs exposed to dose levels of 300 mg/kg bw/day or higher showed overt clinical signs of toxicity, elevated levels of blood enzymes and liver damage. The NOAEL in this study was 100 mg/kg bw/day.

Pyriproxyfen technical was administered to mice at doses of 0, 120, 600 and 3,000 ppm in diet for 78 weeks. The NOAEL for systemic effects in this study was 600 ppm (84 mg/kg bw/day in males, 109.5 mg/kg bw/day in females), and a LOAEL of 3,000 ppm (420 mg/kg bw/day in males, 547 mg/kg bw/day in females) was established based on an increase in kidney lesions.

In a 2–year study in rats, pyriproxyfen technical was administered in the diet at levels of 0, 120, 600, and 3,000 ppm. The NOAEL for systemic effects in this study was 600 ppm (27.31 mg/kg bw/day in males, 35.1 mg/kg bw/day in females). A LOAEL of 3,000 ppm (138 mg/kg bw/day in males, 182.7 mg/kg bw/day in females) was established based on a depression in body weight gain in females.

6. *Animal metabolism*. The absorption, tissue distribution, metabolism and excretion of ^{14}C-labeled pyriproxyfen were studied in rats after single oral doses of 2 or 1,000 mg/kg bw (phenoxyphenyl and pyridyl label), and after a single oral dose of 2 mg/kg bw (phenoxyphenyl label only) following 14 daily oral doses at 2 mg/kg bw of unlabelled material. For all dose groups, most (88–96%) of the administered radiolabel was excreted in the urine and feces within 2 days after radiolabeled test material dosing, and 92–98% of the administered dose was excreted within 7 days. Seven days after dosing, tissue residues were generally low, accounting for no more than 0.3% of the dosed ^{14}C. Radiocarbon concentrations in fat were higher than in other tissues analyzed. Recovery in tissues over time indicates that the potential for bioaccumulation is minimal. There were no significant sex or dose-related differences in excretion or metabolism.

7. *Metabolite toxicology*. Metabolism studies of pyriproxyfen in rats, goats and hens, as well as the fish bioaccumulation study demonstrate that the parent is very rapidly metabolized and eliminated. In the rat, most (88–96%) of the administered radiolabel was excreted in the urine and feces within 2 days of dosing, and 92–98% of the administered dose was excreted within 7 days. Tissue residues were low 7 days after dosing, accounting for no more than 0.3% of the dosed ^{14}C. Because parent and metabolites are not retained in the body, the potential for acute toxicity from *in situ,* formed metabolites is low. The potential for chronic toxicity is adequately tested by chronic exposure

to the parent at the MTD and consequent chronic exposure to the internally formed metabolites.

Seven metabolites of pyriproxyfen, 4'-OH-pyriproxyfen, 5''-OH-pyriproxyfen, desphenyl-pyriproxyfen, POPA, PYPAC, 2-OH-pyridine and 2,5-diOH-pyridine, have been tested for mutagenicity (Ames) and acute oral toxicity to mice. All seven metabolites were tested in the Ames assay with and without S9 at doses up to 5,000 micro-grams per plate or up to the growth inhibitory dose. The metabolites did not induce any significant increases in revertant colonies in any of the test strains. Positive control chemicals showed marked increases in revertant colonies. The acute toxicity to mice of 4'-OH-pyriproxyfen, 5''-OH-pyriproxyfen, desphenyl-pyriproxyfen, POPA, and PYPAC did not appear to markedly differ from pyriproxyfen, with all metabolites having acute oral LD_{50} values greater than 2,000 mg/kg bw. The two pyridines, 2-OH-pyridine and 2,5-diOH-pyridine, gave acute oral LD_{50} values of 124 (male) and 166 (female) mg/kg bw, and 1,105 (male) and 1,000 (female) mg/kg bw, respectively.

8. *Endocrine disruption*. Pyriproxyfen is specifically designed to be an insect growth regulator and is known to produce juvenoid effects on arthropod development. However, this mechanism-of-action in target insects and other arthropods has no relevance to any mammalian endocrine system. While specific tests, uniquely designed to evaluate the potential effects of pyriproxyfen on mammalian endocrine systems have not been conducted, the toxicology of pyriproxyfen has been extensively evaluated in acute, sub-chronic, chronic, developmental, and reproductive toxicology studies including detailed histopathology of numerous tissues. The results of these studies show no evidence of any endocrine-mediated effects and no pathology of the endocrine organs. Consequently, it is concluded that pyriproxyfen does not possess estrogenic or endocrine disrupting properties applicable to mammals.

C. Aggregate Exposure

1. *Dietary exposure*. An evaluation of chronic dietary exposure to include drinking water has been performed for the U.S. population and various sub-populations including infants and children. Because no acute dietary endpoint was determined, the Agency concludes that there is a reasonable certainty of no harm from acute exposure from drinking water.

i. *Food*. a. Chronic dietary exposure to pyriproxyfen residues was calculated for the U.S. population and 26 population subgroups assuming tolerance level residues and 100% of the crop treated. The results from several representative subgroups are listed in the table below. Chronic dietary exposure was at or below 0.705% of the reference dose, with stone fruit commodities contributing the most to chronic exposure. Generally speaking, the Agency has no cause for concern if total residue contribution for published and proposed tolerances is less than 100% of the RfD.

TIER I CALCULATED CHRONIC DIETARY EXPOSURES TO THE TOTAL U.S. POPULATION AND SELECTED SUB-POPULATIONS TO PYRIPROXYFEN RESIDUES IN FOOD

Population Subgroup	Exposure (mg/kg bw/day)	Percent of RfD
Total U.S. Population (all seasons)	0.000535	0.153
Females (13+/Nursing)	0.000597	0.171
Females (20+ years, not preg. or nursing)	0.000415	0.119
Children (1–6 Years)	0.001381	0.395
All Infants (<1 Year Old)	0.002156	0.616
Non-Nursing Infants (<1 Year Old)	0.002467	0.705
Nursing Infants (<1 Year Old)	0.001096	0.313

b. 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 the result of a one day or single exposure. No acute dietary endpoint and dose was identified in the toxicology database for pyriproxyfen, therefore the Agency has concluded that there is a reasonable certainty of no harm from acute dietary exposure.

ii. *Drinking water*. Since pyriproxyfen is applied outdoors to growing agricultural crops, the potential exists for pyriproxyfen or its metabolites to reach ground or surface water that may be used for drinking water. Because of the physical properties of pyriproxyfen, it is unlikely that pyriproxyfen or its metabolites can leach to potable groundwater. To quantify potential exposure from drinking water, surface water concentrations for pyriproxyfen were estimated using GENEEC 1.3. The average 56–day concentration predicted in the simulated pond water was 0.16 ppb. Using standard assumptions about body weight and water consumption, the chronic exposure to pyriproxyfen from this drinking water would be 4.57 x 10^{-6} and 1.6 x 10^{-5} mg/kg bw/day for adults and children, respectively; 0.0046 percent of the RfD (0.35 mg/Kg/day) for children. Based on this worse case analysis, the contribution of water to the dietary risk is negligible.

2. *Non-dietary exposure*. Pyriproxyfen is the active ingredient in numerous registered products for household use — primarily for indoor, non-food applications by consumers. The consumer uses of pyriproxyfen typically do not involve chronic exposure. Instead, consumers are exposed intermittently to a particular product (e.g., pet care pump spray) containing pyriproxyfen. Since pyriproxyfen has a relatively short elimination half-life, cumulative toxicological effects resulting from bioaccumulation are not plausible following short-term, intermittent exposures. Further, pyriproxyfen is short-lived in the environment and this indoor domestic use of pyriproxyfen provides only relatively short-term reservoirs. Thus, consumer use of these products results in acute- and short-term intermittent exposures.

No acute dermal, or inhalation dose or endpoint was identified in the toxicity data for pyriproxyfen. Similarly, doses and endpoints were not identified for short- and intermediate-term dermal or inhalation exposure to pyriproxyfen. The Agency has concluded that there are reasonable certainties of no harm from acute-, short-term, and intermediate-term dermal and inhalation occupational and residential exposures due to the lack of significant toxicological effects observed. Thus, no detailed exposure and risk analyses for non-dietary exposures to pyriproxyfen are necessary.

D. Cumulative Effects

Section 408(b)(2)(D)(v) requires that the Agency must consider ''available information'' concerning the cumulative effects of a particular pesticide's residues and ''other substances that have a common mechanism of toxicity.'' Available information in this context 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.

There are no other pesticidal compounds that are structurally related to pyriproxyfen and have similar effects on animals. In consideration of potential cumulative effects of pyriproxyfen and other substances that may have a common mechanism of toxicity, there are currently no available data or other reliable information indicating that any toxic effects produced by pyriproxyfen would be cumulative with those of other chemical compounds. Thus, only the potential risks of pyriproxyfen have been considered in this assessment of aggregate exposure and effects.

Valent will submit information for EPA to consider concerning potential cumulative effects of pyriproxyfen consistent with the schedule established by EPA at 62 FR 42020 (Aug. 4, 1997) (FRL–5734–6) and other subsequent EPA publications pursuant to the Food Quality Protection Act.

E. Safety Determination

1. *U.S. population*—i. *chronic dietary exposure and risk —adult sub-populations*. Using the Tier I dietary exposure assessment procedures described above for pyriproxyfen, calculated chronic dietary exposure resulting from residue exposure from existing and proposed uses of pyriproxyfen is minimal. The estimated chronic dietary exposure from food for the overall U.S. population and many non-child/infant subgroups is from 0.000338 to 0.000652 mg/kg bw/day, 0.097 to 0.186% of the RfD. Addition of the small but worse case potential chronic exposure from drinking water (calculated above) increases exposure by only 4.57 x 10^{-6} mg/kg bw/day and does not change the maximum occupancy of the RfD significatly. Generally, the Agency has no cause for concern if total residue contribution is less than 100% of the RfD. It can be concluded that there is a reasonable certainty that no harm will result to the overall U.S. Population and many non-child/infant subgroups from aggregate, chronic exposure to pyriproxyfen residues.

ii. *Acute dietary exposure and risk—adult sub-populations*. An acute dietary dose and endpoint was not identified. Thus, the risk from acute aggregate exposure is considered to be negligible.

iii. *Non-dietary exposure and aggregate risk—adult sub-populations*. Acute-, short-term, and intermediate-term dermal and inhalation risk assessments for residential exposure are not required due to the lack of significant toxicological effects observed.

2. *Infants and children* —i. *safety factor for infants and children*. In assessing the potential for additional sensitivity of infants and children to residues of pyriproxyfen, FFDCA section 408 provides that EPA shall apply an additional margin of safety, up to 10–fold, for added protection for infants and children in the case of threshold effects unless EPA determines that a different margin of safety will be safe for infants and children.

The toxicological database for evaluating pre- and post-natal toxicity for pyriproxyfen is complete with respect to current data requirements. There are no special pre- or post-natal toxicity concerns for infants and children, based on the results of the rat and rabbit developmental toxicity studies or the 2-generation reproductive toxicity study in rats. Valent concludes that reliable data support use of the standard 100–fold uncertainty factor and that an additional uncertainty factor is not needed for pyriproxyfen to be further protective of infants and children.

ii. *Chronic dietary exposure and risk— infants and children*. Using the conservative Tier I exposure assumptions described above, the percentage of the RfD that will be utilized by chronic dietary (food only) exposure to residues of pyriproxyfen ranges from 0.000714 mg/kg bw/day for children (7–12 years old), up to 0.002467 mg/kg bw/day for non-nursing infants (<1 year old), 0.204 to 0.705% of the RfD, respectively. Adding the worse case potential incremental exposure to infants and children from pyriproxyfen in drinking water (1.6 x 10^{-5} mg/kg bw/day) does not materially increase the aggregate, chronic dietary exposure and only increases the occupancy of the RfD by 0.0046% to 0.710% for non-nursing infants (<1 year old). EPA generally has no concern for exposures below 100% of the RfD because the RfD represents the level at or below which daily aggregate dietary exposure over a lifetime will not pose appreciable risks to human health. It can be concluded that there is a reasonable certainty that no harm will result to infants and children from aggregate, chronic exposure to pyriproxyfen residues.

iii. *Acute dietary exposure and risk — infants and children*. An acute dietary dose and endpoint was not identified. Thus, the risk from acute aggregate exposure is considered to be negligible.

iv. *Non-dietary exposure and aggregate risk — infants and children*. Acute-, short-term, and intermediate-term dermal and inhalation risk assessments for residential exposure are not required due to the lack of significant toxicological effects observed.

F. International Tolerances

There are no presently existing Codex MRLs for pyriproxyfen.

2. Interregional Research Project Number 4 (IR-4)

0E6083 and 0E6175

EPA has received pesticide petitions (0E6083 and 0E6175) from the Interregional Research Project Number 4 (IR-4), Technology Centre of New Jersey, 681 U.S. Highway #1 South, North Brunswick, New Jersey 08902–3390 proposing, pursuant to section 408(d) of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 346a(d), to amend 40 CFR part 180 by establishing tolerances for the combined residues of the herbicide, pendimethalin, *N*-(1-ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzenamine, and its 3,5-dinitrobenzyl alcohol metabolite (CL 202347) in or on the following raw agricultural commodities: tree nuts (crop group 14) and pistachio at 0.1 parts per million (ppm), almond hull at 0.4 ppm, and fruiting vegetable (crop group 8) at 0.1 ppm. EPA has determined that the petitions contain data or information regarding the elements set forth in section 408(d)(2) of the FFDCA; however, EPA has not fully evaluated the sufficiency of the submitted data at this time or whether the data support granting of the petitions. Additional data may be needed before EPA rules on the petitions. This notice includes a summary of the petitions prepared by American Cyanamid Company, One Campus Drive, Parsippany, NJ 07054.

A. Residue Chemistry

1. *Plant metabolism*. The qualitative nature of the residues of pendimethalin in plants is understood based on adequate studies conducted with ^{14}C pendimethalin on various crops. Pendimethalin and its 3,5-dinitrobenzyl alcohol metabolite (CL202347) are the residues of concern.

2. *Analytical method*. Section 408 (b)(3) of the amended FFDCA requires EPA to determine that there is a practical method for detecting and measuring levels of the pesticide chemical residue in or on food and that the tolerance be set at a level at or above the limit of detection of the designated method. Gas Chromatography (GC) analytical methods, M691 and M692, are proposed as the enforcement method in tree nuts and pistachio as well as fruiting vegetables, for the residues of pendimethalin and the alcohol metabolite (CL 202347), respectively. Both methods have a limit of quantitation (LOQ) of 0.05 ppm for pendimethalin and the alcohol metabolite.

B. Toxicological Profile

1. *Acute toxicity*. The acute oral lethal dose (LD_{50}) values for pendimethalin technical ranged from 1,050 to 1,250 milligrams/kilogram(mg/kg) body weight (bw) in the rat. The acute dermal LD_{50} was greater than 5,000 mg/kg in rabbits. The 4–hour rat inhalation lethal concentration (LC_{50}) was >320 mg/cubic meter (m^3) air (aerosol). Pendimethalin was not irritating to rabbit skin or eyes. Pendimethalin did not cause skin sensitization in guinea pigs.

2. *Genotoxicity*. Extensive mutagenicity studies conducted to investigate point and gene mutations, DNA damage and chromosomal aberration, both using *in vitro* and *in vivo* test systems show pendimethalin to be non-genotoxic.

3. *Reproductive and developmental toxicity*. A 2–generation rat reproduction study gave a no observed adverse effect level (NOAEL) of 2,500 ppm (172 and 216 mg/kg bw/day in males and females, respectively) for reproductive toxicity and a lowest observed adverse effect level (LOAEL) of 5,000 ppm (346 and 436 mg/kg bw/day in males and females, respectively). Rat and rabbit developmental toxicity studies were negative at doses up to 500 mg/kg/bw and 60 mg/kg bw/day, respectively.

4. *Subchronic toxicity*. Ninty-day feeding studies were conducted in rats and dogs. The NOAELs for these tests were 500 ppm (50 mg/kg bw/day) and 62.5 mg/kg bw/day for the rat and dog studies, respectively.

5. *Chronic toxicity*. The reference dose (RfD) of 0.1 mg/kg/day was established based on a combination of three studies in male rats:

i. A 56–day oral thyroid function study,

ii. A 92–day thyroid function study; and

iii. A 14–day intrathyroidal metabolism study.

The NOAEL was established at 10 mg/kg/day. The LOAEL of 31 mg/kg/day was based on thyroid hormonal changes and histologic thyroid changes. An Uncertainty Factor (UF) of 100 was applied to account for both interspecies and intraspecies variability.

6. *Carcinogenicity*. Pendimethalin has been classified as a Group C, ''possible human carcinogen'', chemical by EPA, based on a statistically significant increased trend and pairwise comparison between the high dose group and controls for thyroid follicular cell adenomas in male and female rats. EPA recommends using the RfD approach for quantification of human risk. Therefore, the RfD is deemed protective of all chronic human health effects, including cancer.

7. *Animal metabolism*. Although not relevant to this petition, adequate goat and poultry metabolism studies are available for pendimethalin. The Agency has determined that there is no reasonable expectation of finite pendimethalin residues of concern in animal commodities as a result of use on multiple crops and no tolerances for pendimethalin residues of concern in livestock commodities are needed.

8. *Endocrine disruption*. It is known that pendimethalin affects the pituitary thyroid axis. However, as the RfD (0.10 mg/kg/day) is based on the reversible, non-adverse hormonal and histologic thyroid changes observed in the subchronic studies, these effects are already taken into consideration in the characterization of potential risks to humans.

C. Aggregate Exposure

1. *Dietary exposure*—i. *Food*. Tolerances have been established (40 CFR 180.361) for the combined residues of pendimethalin and its 3,5-dinitrobenzyl alcohol metabolite (CL 202347), in or on a variety of raw agricultural commodities at levels ranging from 0.05 ppm in rice grain to 0.1 ppm in corn, peanuts, soybeans and other commodities. Based on conservative assumptions of tolerance level residues and 100% crop treatment with pendimethalin, the EPA's Dietary Risk Elimination System (DRES) estimates chronic dietary exposure to pendimethalin from all currently registered uses to be only 0.00042 mg/kg/day (< 1% RfD) for the overall U.S. population. The estimated most highly exposed DRES subgroup for pendimethalin is non-nursing infants at a level of 0.00140 mg/kg/day (<2% RfD). Thus, American Cyanamid Company believes that the additional dietary burdens (0.000002 mg/kg/day, 0.002% RfD for the general U.S. population), that will result from the proposed tolerances of pendimethalin in tree nuts and pistachio will be insignificant. Also, American Cyanamid Company believes that the additional dietary burdens (0.000217 mg/kg/day, 0.2% RfD for the general U.S. population and (0.000085 mg/kg/day, 0.1% RfD for non-nursing infants), that will result from the proposed tolerances of pendimethalin in fruiting vegetables will be insignificant.

ii. *Drinking water*. Pendimethalin has low water solubility and a strong absorption to soil, which makes it essentially immobile in all soil types. Thus, there is no concern for the potential for pendimethalin to runoff to surface water or leach to ground water. No Maximum Concentration Level and no Health Advisory Level has been established for residues of pendimethalin in drinking water. The Agency has conducted a pendimethalin drinking water exposure analysis for a 10 kg child and determined that a chronic exposure from a worse-case dietary intake of 0.0018 mg/kg/day would utilize < 2% of the RfD. Thus, American Cyanamid Company believes that contributions to the dietary burden from residues of pendimethalin in water would be inconsequential.

2. *Non-dietary exposure*. Pendimethalin is currently registered for use on the following residential and non-food sites: Ornamental lawns, grasses, ground covers, turf, and ornamental plantings. The Agency has stated that it does not consider that these types of outdoor residential uses constitute a chronic residential exposure scenario. Although there may be short- and intermediate-term non-occupational exposure scenarios, American Cyanamid Company has concluded that the margins of exposure for residential applicators exposure (MOE 833) and residential post-application exposures to children (MOE 111) are more than adequate.

D. Cumulative Effects

The Agency has not yet published guidelines to determine whether pendimethalin has a common mechanism of toxicity with other substances or how to include this pesticide in a cumulative risk assessment. Unlike other pesticides for

which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, pendimethalin does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, it is assumed that pendimethalin does not have a common mechanism of toxicity with other substances.

E. Safety Determination

1. *U.S. population*. Using the conservative exposure assumptions described above and based on the completeness and reliability of the toxicity data, American Cyanamid Company concludes that the total aggregate exposure to pendimethalin from food will utilize less than 1% of the RfD for the overall U.S. population. EPA generally has no concern for exposures below 100% of the RfD because the RfD represents the level at or below which daily aggregate dietary exposure over a lifetime will not pose appreciable risks to human health. Despite the potential for exposure to pendimethalin in drinking water and from non-dietary, non-occupational exposures, American Cyanamid Company does not expect the aggregate exposure to exceed 100% of the RfD. The additional dietary burden for the general U.S. population that will result from the proposed tolerances of pendimethalin in tree nuts and pistachio will be only 0.000002 mg/kg/day, 0.002% RfD. Also, the additional dietary burden for the general U.S. population that will result from the proposed tolerances of pendimethalin in fruiting vegetables will be only 0.000217 mg/kg/day, 0.2% RfD. Thus, American Cyanamid Company concludes that there is a reasonable certainty that no harm will result from aggregate exposure to pendimethalin residues as a result of the establishment of the proposed tolerances in tree nuts and pistachio and the establishment of the proposed tolerances in fruiting vegetables.

2. *Infants and children*. The major identifiable subgroup with the highest aggregate exposure is non-nursing infants less than 1 year old. In assessing the potential for additional sensitivity of infants and children to residues of pendimethalin, the data from developmental toxicity studies in the rat and rabbit and a 2–generation reproduction study in the rat have been considered. The developmental toxicity studies are designed to evaluate adverse effects on the developing organism resulting from pesticide exposure during prenatal development to one or both parents. Reproduction studies provide information relating to effects from exposure to the pesticide on the reproductive capability of mating animals and data on systemic toxicity. The pre- and post-natal toxicology database for pendimethalin is complete with respect to current toxicological data requirements. The database does not indicate a potential for increased sensitivity from pre- and post-natal exposure. No developmental toxicity was observed in either the rat or rabbit developmental toxicity studies, nor was there any evidence in the 2-generation toxicity study that there was developmental or reproductive toxicity at dose levels below those in which parental toxicity was observed. For rabbits, the developmental toxicity NOAEL was > 60 mg/kg/day, at the highest dose tested (HDT). The maternal NOAEL was > 60 mg/kg/day, based upon mortality observed at 125 mg/kg/day in a pilot study. For rats, there were no maternal or developmental effects at any dose level and the NOAELs were > 500 mg/kg/day, the HDT. In the 2-generation reproductive toxicity study in rats, the reproductive NOAEL was 172 mg/kg/day. The reproductive LOAEL of 346 mg/kg/day was based on decreased pup weight, which occurred in the presence of parental (systemic) toxicity at 346 mg/kg/day.

FFDCA section 408 provides that EPA may apply an additional 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 database. Based on current toxicological data requirements, the toxicology database for pendimethalin is complete.

Furthermore, for pendimethalin, the reproductive NOAEL of 172 mg/kg/day is 17–fold higher than the NOAEL of 10 mg/kg/day used for the RfD. Additionally, the reproductive LOAEL occurred in the presence of parental (systemic) toxicity and there was no evidence of developmental toxicity in either the rat or the rabbit studies. Therefore, American Cyanamid Company believes that these proposed tolerances do not represent any unacceptable pre- or post-natal risk to infants and children.

Using the conservative exposure assumptions described above, EPA has previously concluded that aggregate exposure to pendimethalin from food will utilize less than 2% of the RfD for infants and children. The additional dietary burden for non-nursing infants, (<1 year old) that will result from the proposed tolerances of pendimethalin in tree nuts and pistachio will be zero. The additional dietary burden for non-nursing infants, (<1 year old) that will result from the proposed tolerances of pendimethalin in fruiting vegetables will be only 0.000085 mg/kg/day, 0.1% of the RfD. EPA generally has no concern for exposures below 100% of the RfD because the RfD represents the level at or below which daily aggregate dietary exposure over a lifetime will not pose appreciable risks to human health. Despite the potential for exposure to pendimethalin in drinking water and from non-dietary, non-occupational exposure, American Cyanamid Company does not expect the aggregate exposure to exceed 100% of the RfD. Thus, American Cyanamid Company concludes that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to pendimethalin residues.

F. International Tolerances

There are no CODEX, Canadian or Mexican International Maximum Residue Levels (MRLs) established for residues of pendimethalin in tree nuts and pistachio, almond hull or in fruiting vegetables at this time.

3. Interregional Research Project Number 4 (IR)

0E6183

EPA has received a pesticide petition (0E6183) from the Interregional Research Project Number 4 (IR 4), Rutgers University, New Brunswick, NJ, 08903–0231 proposing, pursuant to section 408(d) of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 346a(d), to amend 40 CFR part 180 by establishing a tolerance for residues of the herbicide carfentrazone-ethyl (ethyl-α-2-dichloro-5-[4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl]-4-fluorobenzene-propanoate)and the metabolite carfentrazone-ethyl chloropropionic acid (α, 2-dichloro-5-[-4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl]-4-fluorobenzenepropanoic acid) in or on the raw agricultural commodity within the crop subgroup caneberry at 0.1 parts per million (ppm). EPA has determined that the petition contains data or information regarding the elements set forth in section 408(d)(2) of the FFDCA; however, EPA has not fully evaluated the sufficiency of the submitted data at this time or whether the data support granting of the petition. Additional data may be needed before EPA rules on the petition. This notice includes a summary of the petition prepared by FMC Corporation, Agricultural Products Group, Philadelphia, PA 19103.

A. Residue Chemistry

1. *Plant metabolism*. The metabolism of carfentrazone-ethyl in plants is adequately understood. The residues of concern are the combined residues of carfentrazone-ethyl and carfentrazone-ethyl-chloropropionic acid.

2. *Analytical method*. There is a practical analytical method for detecting and measuring levels of carfentrazone and its metabolites in or on food with a limit of quantitation that allows monitoring of food with residues at or above the levels set in the tolerances. The analytical method for carfentrazone-ethyl involves separate analyses for parent and its metabolites. The parent is analyzed by gas chromatography/electron capture detection (GC/ECD). The metabolites are derivatized with boron trifluoride and acetic anhydride for analysis by gas chromatography/mass spectrometry detection (GC/MSD) using selective ion monitoring.

3. *Magnitude of residues*. Carfentrazone-ethyl 40 DF was applied to 4 caneberry trials in the appropriate EPA regions. The caneberries were harvested at the appropriate growth stages and subsequent analyses determined that the residues of carfentrazone-ethyl and its metabolites would not exceed the proposed tolerances of 0.1 ppm.

B. Toxicological Profile

1. *Acute toxicity*. Carfentrazone-ethyl demonstrates low oral, dermal and inhalation toxicity. The acute oral lethal dose (LD_{50}) value in the rat was greater than 5,000 mg/kg, acute dermal LD_{50} value in the rat was greater than 4,000 mg/kg, and the acute inhalation lethal concentration(LC_{50}) value in the rat was greater than 5.09 mg/L/4h. Carfentrazone-ethyl is non-irritating to rabbit skin and minimally irritating to rabbit eyes. It did not cause skin sensitization in guinea pigs. An acute neurotoxicity study in the rat had a systemic No Observed Adverse Effect Level (NOAEL) of 500 mg/kg based on clinical signs and decreased motor activity levels; the NOAEL for neurotoxicity was greater than 2,000 mg/kg highest dose tested (HDT) based on the lack of neurotoxic clinical signs or effects on neuropathology.

2. *Genotoxicity*. Carfentrazone-ethyl did not cause mutations in the Ames assay with or without metabolic activation. There was a positive response in the chromosome aberration assay without activation but a negative response with activation. The mouse micronucleus assay (an *in vivo* test which also measures chromosome damage), the CHO/HGPRT forward mutation assay and the unscheduled DNA synthesis assay were negative. The overwhelming weight of the evidence supports the conclusion that carfentrazone-ethyl is not genotoxic.

3. *Reproductive and developmental toxicity*. Carfentrazone-ethyl is not considered to be a reproductive or a developmental toxin. In the 2-generation reproduction study, the NOAEL for reproductive toxicity was greater than 4,000 ppm (greater than 323 to greater than 409 mg/kg/day). In the developmental toxicity studies, the rat and rabbit maternal NOAELs were 100 mg/kg/day and 150 mg/kg/day, respectively. The developmental NOAEL for the rabbit was greater than 300 mg/kg/day (HDT), and for the rat the NOAEL was 600 mg/kg/day based on increased litter incidences of thickened and wavy ribs at 1,250 mg/kg/day. These two findings (thickened and wavy ribs) are not considered adverse effects of treatment but related delays in rib development which are generally believed to be reversible.

4. *Subchronic toxicity*. Ninty-day feeding studies were conducted in mice, rats and dogs with carfentrazone-ethyl. The NOAEL for the mouse study was 4,000 ppm (571 mg/kg/day), for the rat study was 1,000 ppm (57.9 mg/kg/day for males; 72.4 mg/kg/day for females) and for dogs was 150 mg/kg/day. A 90–day subchronic neurotoxicity study in the rat had a systemic NOAEL of 1,000 ppm (59.0 mg/kg/day for males; 70.7 mg/kg/day for females) based on decreases in body weights, body weight gains and food consumption at 10,000 ppm; the neurotoxicity NOAEL was greater than 20,000 ppm (1,178.3 mg/kg/day for males; 1,433.5 mg/kg/day for females) (HDT).

5. *Chronic toxicity*. Carfentrazone-ethyl is not carcinogenic to rats or mice. A 2–year combined chronic toxicity/carcinogenicity study in the rat was negative for carcinogenicity and had a chronic toxicity NOAEL of 200 ppm (9 mg/kg/day) for males and 50 ppm (3 mg/kg/day) for females based on red fluorescent granules consistent with porphyrin deposits in the liver at the 500 and 200 ppm levels, respectively. An 18 month carcinogenicity study in the mouse had a carcinogenic NOAEL that was greater than 7,000 ppm (>1,090 mg/kg/day for males; >1,296 mg/kg/day for females) based on no evidence of carcinogenicity at the HDT. A 1–year oral toxicity study in the dog had a NOAEL of 50 mg/kg/day based on isolated increases in urine porphyrins in the 150 mg/kg/day group (this finding was not considered adverse).

Using the Guidelines for Carcinogen Risk Assessment, carfentrazone-ethyl should be classified as Group ''E'' for carcinogenicity — no evidence of carcinogenicity — based on the results of carcinogenicity studies in two species. There was no evidence of carcinogenicity in an 18–month feeding study in mice and a 2–year feeding study in rats at the dosage levels tested. The doses tested are adequate for identifying a cancer risk. Thus, a cancer risk assessment is not necessary.

6. *Animal metabolism*. The metabolism of carfentrazone-ethyl in animals is adequately understood. Carfentrazone-ethyl was extensively metabolized and readily eliminated following oral administration to rats, goats, and poultry via excreta. All three animals exhibited a similar metabolic pathway.

7. *Endocrine disruption*. An evaluation of the potential effects on the endocrine systems of mammals has not been determined; however, no evidence of such effects was reported in the chronic or reproductive toxicology studies described above. There was no observed pathology of the endocrine organs in these studies. There is no evidence at this time that carfentrazone-ethyl causes endocrine effect.

C. Aggregate Exposure

1. *Dietary exposure—Acute*. Based on the available toxicity data, the EPA has established an acute Reference Dose (aRfD) for carfentrazone-ethyl of 5 mg/kg/day. The aRfD for carfentrazone-ethyl is based on acute neurotoxicity study in rats with a threshold NOAEL of 500 mg/kg/day and an uncertainty factor of 100.

Chronic. Based on the available toxicity data, the EPA has established a chronic Reference Dose (cRfD) for carfentrazone-ethyl of 0.03 mg/kg/day. The cRfD for carfentrazone-ethyl is based on a 2–year chronic toxicity/carcinogenicity study in rats with a threshold NOAEL of 3 mg/kg/day and an uncertainty factor of 100. For purposes of assessing the potential chronic dietary exposure, a Tier 1 dietary risk assessment was conducted based on the Theoretical Maximum Residue Contribution (TMRC) from the established and proposed tolerances for carfentrazone-ethyl, as follows: 0.1 ppm in or on wheat grain; 0.3 ppm in or on wheat hay; 0.2 ppm in or on wheat straw; 1.0 ppm in or on cereal grain forage (except corn and sorghum); 0.1 ppm in or on sorghum and corn (sweet and field) forage, 0.15 ppm in or on stover and 0.1 ppm in or on sweet corn, K+ CWHR (kernels plus cob with husk removed), in or on the soybean seed at 0.1 ppm, in or on cotton at 3.5 ppm, in

or on cotton gin byproducts, in or on cottonseed (undelinted) and 0.2 ppm in/on caneberry at 0.1 ppm. (The TMRC is a ''worse case'' estimate of dietary exposure since it is assumed that 100% of all crops for which tolerances are established are treated and that pesticide residues are present at the tolerance levels). In conducting this exposure assessment, the following very conservative assumptions were made-100% of soybeans, cotton and cereal grains will contain carfentrazone-ethyl residues and those residues would be at the level of the tolerance which result in an overestimate of human exposure.

i. *Food*. Dietary exposure from the proposed uses would account for 0.1% or less of the aRfD in subpopulations (including infants and children). Dietary exposure from the proposed uses would account for 3.2% or less of the cRfD in subpopulations (including infants and children).

ii. *Drinking water*. Studies have indicated that carfentrazone-ethyl will not move into groundwater, therefore water has not been included in the dietary risk assessment.

2. *Non-dietary exposure*. The potential for non-occupational exposure to the general population has not been fully assessed.

D. Cumulative Effects

EPA is also required to consider the potential for cumulative effects of carfentrazone-ethyl and other substances that have a common mechanism of toxicity. FMC does not have information to indicate that toxic effects produced by carfentrazone-ethyl would be cumulative with those of any other chemical compounds; thus only the potential risks of carfentrazone-ethyl are considered in this exposure assessment.

E. Safety Determination

1. *U.S. population*. Using the conservative exposure assumptions described and based on the completeness and reliability of the toxicity data, the aggregate exposure to carfentrazone-ethyl will utilize 0.06% of the aRfD and 1.4% of the cRfD for the U.S. population. EPA generally has no concern for exposures below 100% of the RfD. Therefore, based on the completeness and reliability of the toxicity data and the conservative exposure assessment, there is a reasonable certainty that no harm will result from aggregate exposure to residues of carfentrazone-ethyl, including all anticipated dietary exposure and all other non-occupational exposures.

2. *Infants and children*. In assessing the potential for additional sensitivity of infants and children to residues of carfentrazone-ethyl, EPA considers data from developmental toxicity studies in the rat and rabbit and the 2–generation reproduction study in the rat. The developmental toxicity studies are designed to evaluate adverse effects on the developing organism resulting from pesticide exposure during prenatal development. Reproduction studies provide information relating to effects on the reproductive capacity of males and females exposed to the pesticide. Developmental toxicity was not observed in developmental toxicity studies using rats and rabbits. Subsequently, there was no reproductive toxicity observed in the 2–generation reproduction study in rats as well.

FFDCA section 408 provides that EPA may apply an additional safety factor for infants and children in the case of threshold effects to account for pre- and post-natal toxicity and the completeness of the database. Based on the current toxicological data requirements, FMC concludes that the database relative to pre- and post-natal effects for children is complete and an additional uncertainty factor is not warranted. Therefore at this time, the RfD of 0.03 mg/kg/day is appropriate for assessing aggregate risk to infants and children.

Using the conservative exposure assumptions described above, the percent of the RfD that will be utilized by aggregate exposure to residues of carfentrazone-ethyl for non-nursing infants (<1 year old) would be 0.08% of the aRfD and 3.0% of the cRfD; for children 1–6 years of age would be 0.08% of the aRfD and 3.2% of the cRfD, (the most highly exposed group). Based on the completeness and reliability of the toxicity data and the conservative exposure assessment, there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the residues of carfentrazone-ethyl including all anticipated dietary exposure.

F. International Tolerances

There are no Codex Alimentarius Commission (Codex) Maximum Residue Levels (MRLs) for carfentrazone-ethyl on any crops at this time.

[FR Doc. 01–6731 Filed 3–16–01; 8:45 am]

BILLING CODE 6560–50–S

ENVIRONMENTAL PROTECTION AGENCY

[OPP–181080; FRL–6772–3]

Bifenazate; Receipt of Application for Emergency Exemption, Solicitation of Public Comment

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: EPA has received a specific exemption request from the Texas Department of Agriculture to use the pesticide bifenazate (CAS No. 149877–41–8) to treat up to 200 acres of greenhouse tomatoes to control spider mites. The Applicant proposes a first food use of this pesticide. EPA is soliciting public comment before making the decision whether or not to grant the exemption.

DATES: Comments, identified by docket control number OPP–181080, must be received on or before April 3, 2001.

ADDRESSES: Comments may be submitted by mail, electronically, or in person. Please follow the detailed instructions for each method as provided in Unit I. of the **SUPPLEMENTARY INFORMATION**. To ensure proper receipt by EPA, it is imperative that you identify docket control number OPP–181080 in the subject line on the first page of your response.

FOR FURTHER INFORMATION CONTACT: Stephen Schaible, Registration Division (7505C), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460; telephone number: 703 308–9362; fax number: 703 308–5433; e-mail address: schaible.stephen@epa.gov.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

You may be potentially affected by this action if you petition EPA for emergency exemption under section 18 of FIFRA. Potentially affected categories and entities may include, but are not limited to:

Categories	NAICS Codes	Examples of potentially affected entities
State government	9241	State agencies that petition EPA for section 18 pesticide exemption

This listing is not intended to be exhaustive, but rather provides a guide for readers regarding entities likely to be