Appendix A, ''proposed data requirements,'' by contacting Mr. Dan Peacock at (703) 305–5407]. Within two months of receipt of a complete EUP application, EPA will review all information contained in the EUP application and will provide the Registrant with lists of:

(a) the terms and conditions EPA intends to impose upon issuance of the EUP;

(b) revised data requirements for registration of a CPT Perch Solution product (if changed by the EUP review); and

(c) the results of all reviews of data and rationales for extrapolating data from Starlicide to satisfy CPT requirements.

6. After receipt by the Registrant of the above EUP review, EPA agrees to meet with the Registrant and/or its representatives at least once, if requested, to discuss any issue involving the EUP and registration of CPT.

7. EPA agrees to review any complete application submitted by the Registrant for registration of a perch solution product containing the active ingredient CPT within 4 months of receipt. If EPA's total review time for complete EUP and registration applications for perch solution products containing CPT exceeds 6 months in the aggregate, the existing stocks provisions of the cancellation order as set forth in paragraph 1(b), and the date for the recall of all canceled product as set forth in paragraph 4, shall each be extended by a period equal to the additional time utilized by EPA for the review of the applications. The effective date of cancellation under paragraph 1(a) shall not be extended unless EPA determines, in its discretion, to extend the date.

8. The parties acknowledge that the labeling restrictions set forth in paragraph 2 apply only to the Rid-A-Bird Perch 1100 Solution and are not necessarily applicable to the registration of a CPT perch product by the Registrant. The acceptability of labeling and proposed uses for a CPT perch product will be evaluated on their own merits by EPA pursuant to section 3 of FIFRA.

9. The Registrant agrees that failure to comply with any of the conditions of registration set forth in this Agreement shall be grounds for cancellation of the Rid-A-Bird Perch 1100 Solution under section 6(e) of FIFRA.

10. The Registrant agrees that it will not challenge or assist any person in challenging this Agreement in any forum.

11. This Agreement constitutes the complete agreement reached by EPA and the Registrant.

12. This Agreement shall take effect if the Registrant and EPA sign the Agreement. The effective date shall be the date that the last party signs the Agreement.

Dated this 3rd and 5th day of November, 1997.

Steven Johnson, Acting Director, Office of Pesticide Programs, U.S. Environmental Protection Agency, /s/ 11/5/97.

Keith Wilson, President, Rid-A-Bird, Inc., /s/ 11/3/97.

List of Subjects

Environmental protection, Agricultural commodities, Pesticides and pests.

Dated: March 18, 1998

Linda A. Travers,

Director, Information Resources and Services Division, Office of Pesticide Programs.

[FR Doc. 98–8067 Filed 3–26–98; 8:45 am]

BILLING CODE 6560–50–F

ENVIRONMENTAL PROTECTION AGENCY

[PF–799; FRL–5579–6]

Notice of Filing of Pesticide Petitions

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 the docket control number PF–799, must be received on or before April 27, 1998.

ADDRESSES: By mail submit written comments to: Public Information and Records Integrity Branch, Information Resources and Services Division (7506C), Office of Pesticides Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. In person bring comments to: Rm. 1132, CM #2, 1921 Jefferson Davis Highway, Arlington, VA.

Comments and data may also be submitted electronically by following the instructions under ''SUPPLEMENTARY INFORMATION.'' No confidential business information should be submitted through e-mail.

Information submitted as a comment concerning this document may be claimed confidential by marking any part or all of that information as ''Confidential Business Information'' (CBI). CBI should not be submitted through e-mail. Information marked as CBI will not be disclosed except in accordance with procedures set forth in 40 CFR part 2. A copy of the comment that does not contain CBI must be submitted for inclusion in the public record. Information not marked confidential may be disclosed publicly by EPA without prior notice. All written comments will be available for public inspection in Rm. 1132 at the address given above, from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays.

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

Product Manager	Office location/telephone number	Address
Ann Sibold	Rm. 212, CM #2, 703–305–6502, e-mail:sibold.ann@epamail.epa.gov.	1921 Jefferson Davis Hwy, Arlington, VA
Joseph M. Tavano	Rm. 214, CM #2, 703–305–6411, e-mail: tavano.joseph@epamail.epa.gov.	Do.

SUPPLEMENTARY INFORMATION: 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.

The official record for this notice of filing, as well as the public version, has been established for this notice of filing under docket control number [PF–799] (including comments and data submitted electronically as described below). A public version of this record, including printed, paper versions of electronic comments, which does not include any information claimed as CBI, is available for inspection from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The official record is located at the address in ''ADDRESSES'' at the beginning of this document.

Electronic comments can be sent directly to EPA at:

opp-docket@epamail.epa.gov

Electronic comments must be submitted as an ASCII file avoiding the use of special characters and any form of encryption. Comment and data will also be accepted on disks in

Wordperfect 5.1 file format or ASCII file format. All comments and data in electronic form must be identified by the docket number (insert docket number) and appropriate petition number. Electronic comments on notice may be filed online at many Federal Depository Libraries.

List of Subjects

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

Dated: March 19, 1998

Peter Caulkins,

Acting Director, Registration Division, Office of Pesticide Programs.

Summaries of Petitions

Petitioner summaries of the pesticide petitions are printed below as required by section 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. American Cyanamid Company

PP 6F4623

EPA has received a pesticide petition (PP 6F4623) from American Cyanamid Company, P.O. Box 400, Princeton, NJ 08543-0400, proposing pursuant to section 408(d) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. 346a(d), to amend 40 CFR part 180 by establishing a tolerance of 0.5 ppm for residues of 4-bromo-2-(4-chlorophenyl)-1-(ethoxymethyl)-5-(trifluoromethyl)-1-pyrrole-3-carbonitrile, (chlorfenapyr) in or on the raw agricultural commodity citrus. As citrus processed commodities fed to food animals may be transferred to milk and edible tissues, tolerances are also proposed for the following ruminant food items: milk at 0.01 parts per million (ppm); milk fat at 0.15 ppm; meat at 0.01 ppm; and meat by-products (including fat) at 0.10 ppm.

The proposed analytical method is capillary gas chromatography using an electron capture detector. 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*. The nature of the residues of chlorfenapyr in plants is adequately understood and the residue of concern in citrus consists of the parent molecule. Expressed on a whole basis, the parent compound accounted for 56-75% of the total radioactive residue (TRR), 98% of which was associated with the external rinse and peel.

2. *Analytical method*. The GC analytical method, M2284, which is proposed as the enforcement method for the residues of chlorfenapyr in citrus, has a limit of detection (LOD) of 0.01 ppm (0.025 ppm for juice) and a limit of quantitation (LOQ) of 0.05 ppm.

3. *Magnitude of residues*. Extensive citrus field trials have been conducted over multiple growing seasons in all major citrus growing regions of the US. The results of these studies indicate that at the highest proposed use rate of 1.05 lbs ai/A, the maximum expected chlorfenapyr residues are 0.4 ppm in oranges, 0.38 ppm in lemons and 0.27 ppm in grapefruit in/on citrus samples harvested 7 days following the last application. These field trial data are adequate to support the proposed tolerance of 0.5 ppm in/on citrus harvested 7-days following the last application. The results of processing studies indicate that chlorfenapyr residues do not concentrate in molasses and juice. The actual concentration factors in dried pulp (2.4x) and citrus oil (70x) are well below the maximum theoretical concentration factors for these commodities. Although citrus oil is not considered to be a ready-to-eat item and is not expected to contribute to the dietary exposure, a tolerance at 35 ppm (0.5 ppm x 70) is proposed for enforcement purposes.

B. Toxicological Profile

1. *Acute toxicity*. Based on the EPA's toxicity category criteria, the acute toxicity category for chlorfenapyr technical is Category II or moderately toxic (signal word WARNING) and the acute toxicity category for the 2SC formulation is Category III or slightly toxic (signal word CAUTION). Males appear to be more sensitive to the effects of chlorfenapyr than females. The acute toxicity profile indicates that absorption by the oral route appears to be greater than by the dermal route. The following are the results from the acute toxicity tests conducted on the technical material:

i. Rat Oral LD_{50}: 441/1152 milligram/kilograms (mg/kg) bwt.(M/F) -- Tox. Category II

ii. Rabbit Dermal LD_{50}: >2,000 mg/kg bwt.(M/F) -- Tox. Category III

iii. Acute Inhal. LC_{50}: 0.83/>2.7 mg/L (M/F) -- Tox. Category III

iv. Eye Irritation: Moderately Irritating -- Tox. Category III

v. Dermal Irritation: Non-Irritating -- Tox. Category IV

vi. Dermal Sensitization: Non-Sensitizer -- Non Sensitizer

vii. Acute Neurotoxicity: NOEL 45 mg/kg bwt. -- Not An Acute Neurotoxicant

2. *Genotoxicty*. Chlorfenapyr technical (94.5% a.i.) was examined in a battery of*in vitro* and *in vivo* tests to assess its genotoxicity and its potential for carcinogenicity. These tests are summarized below.

Microbial/Microsome Mutagenicity Assay: Non-mutagenic

Mammalian Cell CHO/HGPRT Mutagenicity Assay: Non-mutagenic

In Vivo Micronucleus Assay: Non-genotoxic

In Vitro—Chromosome Aberration Assay in CHO: Non-clastogenic

In Vitro—Chromosome Aberration Assay in CHLC: Non-clastogenic

Unscheduled DNA Synthesis (UDS) Assay: Non-genotoxic.

3. *Reproductive and developmental toxicity*. Chlorfenapyr is neither a reproductive or developmental toxicant and is not a teratogenic agent in the Sprague-Dawley rat or the New Zealand white rabbit. This is demonstrated by the results of the following studies:

Rat Oral Teratology -- No-Observed-Effect-Level (NOEL) for maternal toxicity 25 mg/kg bwt./day and NOEL for fetal/develop. toxicity 225 milligram/kilograms body weight/day (mg/kg bwt./day)

Rabbit Oral Teratology -- NOEL for maternal toxicity 5 mg/kg bwt./day and NOEL for fetal/develop. toxicity 30 mg/kg bwt./day

Rat 2-Generation Reproduction -- NOEL for parental toxicity /growth and offspring development 60 ppm (5 mg/kg bwt./day)
NOEL for reproductive performance 600 ppm (44 mg/kg bwt./day).

4. *Subchronic toxicity*. The following are the results of the subchronic toxicity tests that have been conducted with chlorfenapyr:

28-Day Rabbit Dermal -- NOEL 100 mg/kg bwt./day

28-Day Rat Feeding -- NOEL >600 ppm (< 71.6 mg/kg bwt./day)

28-Day Mouse Feeding -- NOEL >160 ppm (<32 mg/kg bwt./day)

13-Week Rat Dietary -- NOAEL 150 ppm (11.7 mg/kg bwt./day)

13-Week Mouse Dietary -- NOEL 40 ppm (8.2 mg/kg bwt./day)

13-Week Dog Dietary -- NOAEL 120 ppm (4.2 mg/kg bwt./day)

5. *Chronic toxicity*. Chlorfenapyr is not oncogenic in either Sprague Dawley rats or CD-1 mice and is not likely to be carcinogenic in humans. The following are the results of the chronic toxicity tests that have been conducted with chlorfenapyr:

1-Year Neurotoxicity in Rats -- NOEL 60 ppm (2.6/3.4 mg/kg bwt./day M/F)

1-Year Dog Dietary -- NOEL 120 ppm (4.0/4.5 mg/kg bwt./day M/F)

24-Month Rat Dietary -- NOEL for Chronic Effects 60 ppm (2.9/3.6 mg/kg bwt./day M/F) and NOEL for Oncogenic Effects 600 ppm (31/37 mg/kg bwt./day M/F)

18-Month Mouse Dietary -- NOEL for Chronic Effects 20 ppm (2.8/3.7 mg/kg bwt./day M/F) and NOEL for Oncogenic Effects 240 ppm (34.5/44.5 mg/kg bwt./day M/F)

6. *Animal metabolism*. A metabolism study was conducted in Sprague Dawley rats at approximately 20 and 200 mg/kg bwt. using radiolabeled chlorfenapyr. Approximately 65% of the administered dose was eliminated during the first 24 hours (62% in feces and 3% in urine) and by 48 hours following dosing, approximately 85% of the dose had been excreted (80% in feces and 5% in urine). The absorbed chlorfenapyr-related residues were distributed throughout the body and detected in tissues and organs of all treatment groups. The principal route of elimination was via feces, mainly as unchanged parent plus minor N-dealkylated, debrominated and hydroxylated oxidation products.

The metabolic pathway of chlorfenapyr in the laying hen and the lactating goat was also similar to that in laboratory rats.

7. *Metabolite toxicology*. The parent molecule is the only moiety of toxicological significance which needs regulation in plant and animal commodities.

8. *Endocrine effects*. Collective organ weights and histopathological findings from the 2-generation rat reproduction study, as well as from the subchronic and chronic toxicity studies in two or more animal species, demonstrate no apparent estrogenic effects or effects on the endocrine system. There is no information available which suggests that chlorfenapyr would be associated with endocrine effects.

C. Aggregate Exposure

1. *Dietary exposure*— i. *Food*. For purposes of assessing the potential dietary exposure, a Theoretical Maximum Residue Contribution (TMRC) has been calculated from the tolerance of chlorfenapyr in/on citrus at 0.5 ppm. This exposure assessment is based on very conservative assumptions, namely 100% of all citrus is treated with chlorfenapyr and that the residues of chlorfenapyr in citrus are at the tolerance level. Although there are no other established US permanent tolerances for chlorfenapyr, a petition for a permanent tolerance at 0.5 ppm in cottonseed is pending at the Agency. Therefore, the dietary exposures to residues of chlorfenapyr in or on food will be limited to residues in cottonseed, citrus and food and feed items derived from them. As dried citrus pulp is a dairy and beef cattle feed item, a cold feeding study with dairy cattle was conducted. Since this study demonstrated that measurable residues of chlorfenapyr may occur in milk, meat and meat by products, appropriate residue tolerances for these items are proposed. The contribution of the citrus tolerances alone to the daily consumption uses only 0.23% of the reference dose (RfD) for the overall US population. The combined contributions of the citrus and the pending cottonseed tolerances to the daily consumption uses less than 1% (actual 0.85%) of the reference dose for the overall US population and less than 3% (actual 2.23%) and less than 1% (actual 0.89%) of the reference doses for children aged 1-6 and for non-nursing infants, respectively.

ii. *Drinking water*. There is no available information about chlorfenapyr exposures via levels in drinking water. There is no concern for exposure to residues of chlorfenapyr in drinking water because of its extremely low water solubility (120 ppb at 25°). Chlorfenapyr is also immobile in soil and does not leach because it is strongly adsorbed to all common soil types. In addition, the label explicitly prohibits applications near aquatic areas

There is a reasonable certainty that no harm will result from dietary exposure to chlorfenapyr, because dietary exposure to residues on food will use only a small fraction of the (RfD) (including exposure of sensitive subpopulations), and exposure through drinking water is expected to be insignificant.

2. *Non-dietary exposure*. There is no available information quantifying non-dietary exposure to chlorfenapyr. However, based on the physico-chemical characteristics of the compound, the proposed use pattern and available information concerning its environmental fate, non-dietary exposure is expected to be negligible. The vapor pressure of chlorfenapyr is less than 1×10^{-7} mm of Hg; therefore, the potential for non-occupational exposure by inhalation is insignificant. Moreover, the current proposed registration is for outdoor, terrestrial uses which severely limit the potential for non-occupational exposure.

D. Cumulative Effects

The pyrrole insecticides represent a new class of chemistry with a unique mechanism of action. The parent molecule, AC 303,630 is a pro-insecticide which is converted to the active form, CL 303,268, via rapid metabolism by mixed function oxidases (MFOs). The active form uncouples oxidative phosphorylation in the insect mitochondria by disrupting the proton gradient across the mitochondrial membrane. The production of ATP is inhibited resulting in the cessation of all cellular functions. Because of this unique mechanism of action, it is highly unlikely that toxic effects produced by chlorfenapyr would be cumulative with those of any other pesticide chemical.

In mammals, there is a lower titer of MFOs, and chlorfenapyr is metabolized by different pathways (including dehalogenation, oxidation and ring hydroxylation) to other polar metabolites without any significant accumulation of the potent uncoupler, CL—303,268. In the rat, approximately 85 % of the administered dose is excreted in the feces within 48-hours, thereby reducing the levels of AC 303,630 and CL 303,268 that are capable of reaching the mitochondria. This differential metabolism of AC 303,630 to CL 303,268 in insects versus to other polar metabolites in mammals is responsible for the selective insect toxicity of the pyrroles.

E. Safety Determination

1. *U.S. population*. The RfD of 0.03 mg/kg bwt./day for the residues of chlorfenapyr in citrus is calculated by applying a 100-fold safety factor to the overall NOEL of 3 mg/kg bwt./day. This NOEL is of based on the results of the chronic feeding studies in the rat and mouse and the 2-generation reproduction study in the rat (see Item 2). The TMRC for the proposed tolerances in citrus alone, (0.0000692 mg/kg bwt./day), will utilize only 0.23% of the RfD for the general U.S. population and the combined TMRC for the proposed chlorfenapyr tolerances in cottonseed, citrus, milk and meat (0.0002558 mg/kg bwt./day) will utilize approximately 0.85% of the RfD for the general U.S. population.

2. *Infants and children*. The TMRC in milk consumed by a non-nursing infant

(>1-year of age) is 0.0002435 mg/kg bwt./day. The combined tolerances will use less than 1% (actual 0.89%) of the RfD for non-nursing infants. The TMRC in milk consumed by a child (1-6 years of age) is 0.0003886 mg/kg bwt./day. The combined TMRC for the proposed chlorfenapyr tolerances in cottonseed, citrus meat and milk consumed by a child 1-6 years of age is 0.0006708 mg/kg bwt./day, which is less than 3% (actual 2.23%) of the RfD. Therefore, the results of the toxicology and metabolism studies support both the safety of chlorfenapyr to humans based on the intended use as an insecticide-miticide on citrus and cottonseed and the granting of the requested tolerances in cottonseed, citrus, milk, milk fat solids, meat and meat by-products.

Based on the conservative assumptions used in proposing the above tolerances and the absence of other non-dietary routes of exposure to chlorfenapyr, and since the calculated exposures are well below 100% of the reference dose, there is a reasonable certainty that no harm will result from aggregate exposure to residues of chlorfenapyr, including all anticipated dietary exposure and all other non-occupational exposures. The use of a 100-fold safety factor ensures an acceptable margin of safety for both the overall U. S. population as well as infants and children. As the toxicology database (reproduction/developmental and teratology studies) is complete, valid and reliable, no additional safety factor is needed.

The 100-fold margin of safety is adequate to assure a reasonable certainty of no harm to infants and children from the proposed use. As stated earlier, the NOEL is based on the effects observed in the rat and mouse chronic oncogenicity studies, (reduced body weight gains, increased globulin and cholesterol values and increased liver weights in the rat and reduced body weight gains and vacuolation of white matter of the mouse brain), the one-year neurotoxicity study in the rat, (reduced body weight gains and vacuolar myelinopathy of the brain and spinal cord that is completely reversible following termination of treatment and is not associated with any damage to neuronal cell bodies or axons; vacuolation of the white matter is a consequence of edema (water) formation between the myelin layers which result from the unrestricted movement of ions across the cell membranes) and the 2-generation rat reproduction study, (reduced body weight gains for parental animals and reduced pup body weights for the F1 and F2 litters; however no behavioral changes were observed in either F1 or F2 offsprings in the 2-generation reproduction study). Moreover, as the NOELs for fetal/developmental toxicity are significantly higher than those for maternal toxicity, the results indicate that chlorfenapyr is neither a developmental toxicant nor a teratogenic agent in either the Sprague-Dawley rat or New Zealand White rabbit. Thus, there is no reliable information to indicate that there would be a variability in the sensitivities of infants and children and adults to the effects of exposure to chlorfenapyr.

F. International Tolerances

Section 408 (b)(4) of the amended FFDCA requires EPA to determine whether a maximum residue level has been established for the pesticide chemical by the Codex Alimentarius Commission.

There is neither a Codex proposal, nor Canadian or Mexican tolerances/limits for residues of chlorfenapyr in/on citrus. Therefore, a compatibility issue is not relevant to the proposed tolerance.

2. Rohm and Haas Company

PP 6G4681

EPA has received a pesticide petition (PP 6G4681) from Rohm and Haas Company, 100 Independence Mall West, Philadelphia, PA 19106-2399. proposing pursuant to section 408(d) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. 346a(d), to amend 40 CFR part 180 by establishing a tolerance for residues of tebufenozide, benzoic acid, 3,5-dimethyl-,1-(1,1-dimethylethyl)-2-(4-ethylbenzoyl)hydrazide in or on the raw agricultural commodity pears at 1.5 (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*. The metabolism of tebufenozide in plants (grapes, apples, rice and sugar beets) is adequately understood for the purposes of these tolerances. The metabolism of tebufenozide in all crops was similar and involves oxidation of the alkyl substituents of the aromatic rings primarily at the benzylic positions. The extent of metabolism and degree of oxidation are a function of time from application to harvest. In all crops, parent compound comprised the majority of the total dosage. None of the metabolites were in excess of 10% of the total dosage. The metabolism of tebufenozide in goats proceeds along the same metabolic pathway as observed in plants. No accumulation of residues in tissues or milk occurred. Because apple pomace is not fed to poultry, there is no reasonable expectation that measurable residues of tebufenozide will occur in eggs, poultry meat or poultry meat by-products.

2. *Analytical method*. A high performance liquid chromatographic (HPLC) analytical method using ultraviolet (UV) or mass selective detection have been validated for apples. The method involves extraction by blending with solvents, purification of the extracts by liquid-liquid partitions and final purification of the residues using solid phase extraction column chromatography. The limits of quantitation is 0.02 ppm for apples.

B. Toxicological Profile

1. *Acute toxicity*. Tebufenozide has low acute toxicity. Tebufenozide Technical was practically non-toxic by ingestion of a single oral dose in rats and mice (LD_{50} > 5,000 milligram/kilograms (mg/kg) and was practically non-toxic by dermal application (LD_{50} > 5,000 mg/kg). Tebufenozide Technical was not significantly toxic to rats after a 4-hr inhalation exposure with an LC_{50} value of 4.5 mg/L (highest attainable concentration), is not considered to be a primary eye irritant or a skin irritant and is not a dermal sensitizer. An acute neurotoxicity study in rats did not produce any neurotoxic or neuropathologic effects.

2. *Genotoxicty*. Tebufenozide technical was negative (non-mutagenic) in an Ames assay with and without hepatic enzyme activation and in a reverse mutation assay with *E. coli*. Tebufenozide technical was negative in a hypoxanthine guanine phophoribosyl transferase (HGPRT) gene mutation assay using Chinese hamster ovary (CHO) cells in culture when tested with and without hepatic enzyme activation. In isolated rat hepatocytes, tebufenozide technical did not induce unscheduled DNA synthesis (UDS) or repair when tested up to the maximum soluble concentration in culture medium. Tebufenozide did not produce chromosome effects *in vivo* using rat bone marrow cells or *in vitro* using Chinese hamster ovary cells (CHO). On the basis of the results from this battery of tests, it is concluded that tebufenozide is not mutagenic or genotoxic.

3. *Reproductive and developmental toxicity*—i. NOELs for developmental and maternal toxicity to tebufenozide

were established at 1,000 milligram/kilograms/day (mg/kg/day) highest dose tested (HDT) in both the rat and rabbit. No signs of developmental toxicity were exhibited.

ii. In a 2-generation reproduction study in the rat, the reproductive/developmental toxicity (NOEL) of 12.1 mg/kg/day was 14-fold higher than the parental (systemic) toxicity NOEL 10 ppm 0.85 mg/kg/day. Equivocal reproductive effects were observed only at the 2,000 ppm dose.

iii. In a second rat reproduction study, the equivocal reproductive effects were not observed at 2,000 ppm (the NOEL equal to 149-195 mg/kg/day) and the NOEL for systemic toxicity was determined to be 25 ppm (1.9-2.3 mg/kg/day).

4. *Subchronic toxicity*— i. The NOEL in a 90-day rat feeding study was 200 ppm (13 mg/kg/day for males, 16 mg/kg/day for females). The lowest-observed-effect-level (LOEL) was 2,000 ppm (133 mg/kg/day for males, 155 mg/kg/day for females). Decreased body weights in males and females was observed at the LOEL of 2,000 ppm. As part of this study, the potential for tebufenozide to produce subchronic neurotoxicity was investigated. Tebufenozide did not produce neurotoxic or neuropathologic effects when administered in the diets of rats for 3-months at concentrations up to and including the limit dose of 20,000 ppm (NOEL = 1330 mg/kg/day for males, 1,650 mg/kg/day for females).

ii. In a 90-day feeding study with mice, the NOEL was 20 ppm (3.4 and 4.0 mg/kg/day for males and females, respectively). The LOEL was 200 ppm (35.3 and 44.7 mg/kg/day for males and females, respectively). Decreases in body weight gain were noted in male mice at the LOEL of 200 ppm.

iii. A 90-day dog feeding study gave a NOEL of 50 ppm (2.1 mg/kg/day for males and females). The LOEL was 500 ppm (20.1 and 21.4 mg/kg/day for males and females, respectively). At the LOEL, females exhibited a decrease in rate of weight gain and males presented an increased reticulocyte

iv. A 10-week study was conducted in the dog to examine the reversibility of the effects on hematological parameters that were observed in other dietary studies with the dog. Tebufenozide was administered for 6-weeks in the diet to 4 male dogs at concentrations of either 0 or 1,500 ppm. After the 6-week, the dogs receiving treated feed were switched to the control diet for 4-weeks. Hematological parameters were measured in both groups prior to treatment, at the end of the 6-weeks treatment, after 2-weeks of recovery on the control diet and after 4-weeks of recovery on the control diet. All hematological parameters in the treated/recovery group were returned to control levels indicating that the effects of tebufenozide on the hemopoietic system are reversible in the dog.

v. In a 28-day dermal toxicity study in the rat, the NOEL was 1,000 mg/kg/day, (HDT). Tebufenozide did not produce toxicity in the rat when administered dermally for 4-weeks at doses up to and including the limit dose of 1,000 mg/kg/day.

5. *Chronic toxicity*—i. A 1-year feeding study in dogs resulted in decreased red blood cells, hematocrit, and hemoglobin and increased Heinz bodies, reticulocytes, and platelets at the (LOEL) of 8.7 mg/kg/day. The NOEL in this study was 1.8 mg/kg/day.

ii. An 18-month mouse carcinogenicity study showed no signs of carcinogenicity at dosage levels up to and including 1,000 ppm, the highest dose tested.

iii. In a combined rat chronic/oncogenicity study, the NOEL for chronic toxicity was 100 ppm (4.8 and 6.1 mg/kg/day for males and females, respectively) and the LOEL was 1,000 ppm (48 and 61 mg/kg/day for males and females, respectively). No carcinogenicity was observed at the dosage levels up to 2,000 ppm (97 mg/kg/day and 125 mg/kg/day for males and females, respectively).

6. *Animal metabolism*. The adsorption, distribution, excretion and metabolism of tebufenozide in rats was investigated. Tebufenozide is partially absorbed, is rapidly excreted and does not accumulate in tissues. Although tebufenozide is mainly excreted unchanged, a number of polar metabolites were identified. These metabolites are products of oxidation of the benzylic ethyl or methyl side chains of the molecule. These metabolites were detected in plant and other animal (rat, goat, hen) metabolism studies.

7. *Metabolite toxicology*. Common metabolic pathways for tebufenozide have been identified in both plants (grape, apple, rice and sugar beet) and animals (rat, goat, hen). The metabolic pathway common to both plants and animals involves oxidation of the alkyl substituents (ethyl and methyl groups) of the aromatic rings primarily at the benzylic positions. Extensive degradation and elimination of polar metabolites occurs in animals such that residue are unlikely to accumulate in humans or animals exposed to these residues through the diet.

8. *Endocrine disruption*. The toxicology profile of tebufenozide shows no evidence of physiological effects characteristic of the disruption of the hormone estrogen. Based on structure-activity information, tebufenozide is unlikely to exhibit estrogenic activity. Tebufenozide was not active in a direct *in vitro* estrogen binding assay. No indicators of estrogenic or other endocrine effects were observed in mammalian chronic studies or in mammalian and avian reproduction studies. Ecdysone has no known effects in vertebrates. Overall, the weight of evidence provides no indication that tebufenozide has endocrine activity in vertebrates.

C. Aggregate Exposure

1. *Dietary exposure*. Use of an agricultural pesticide may result, directly or indirectly in pesticide residues in food. These residues are determined by chemical analysis. Data from field studies are evaluated to determine the appropriate level of residue that would not be exceeded if the pesticide were used according to the label use directions.

2. *Plant and animal metabolism*. The metabolism of tebufenozide in plants (grapes, apples, rice and sugar beets) is adequately understood for the purposes of these tolerances. The metabolism of tebufenozide in all crops was similar and involves oxidation of the alkyl substituents of the aromatic rings primarily at the benzylic positions. The extent of metabolism and degree of oxidation are a function of time from application to harvest. In all crops, parent compound comprised the majority of the total dosage. None of the metabolites were in excess of 10% of the total dosage. The metabolism of tebufenozide in goats proceeds along the same metabolic pathway as observed in plants. No accumulation of residues in tissues or milk occurred. Because apple pomace is not fed to poultry, there is no reasonable expectation that measurable residues of tebufenozide will occur in eggs, poultry meat or poultry meat by-products.

3. *Analytical methods*. A high performance liquid chromatographic (HPLC) analytical method using ultraviolet (UV) or mass selective detection have been validated for apples. The method involves extraction by blending with solvents, purification of the extracts by liquid-liquid partitions and final purification of the residues using solid phase extraction column chromatography. The limits of quantitation is 0.02 ppm for apples.

4. *Food*. Tolerances for residues of tebufenozide are currently expressed as benzoic acid, 3,5-dimethyl-1-(1,1-dimethylethyl)-2(4-ethylbenzoyl) hydrazide. Tolerances currently exist for residues on apples at 1.0 ppm (import

tolerance) and on walnuts at 0.1 ppm (see 40 CFR 180.482).

5. *Acute risk*—i. No appropriate acute dietary endpoint was identified by the Agency. This risk assessment is not required.

ii. *Chronic risk*. For chronic dietary risk assessment, the tolerance and temporary tolerance values are used and the assumption that all walnuts, imported apples and pears which are consumed in the U.S. will contain residues at the tolerance level. The theoretical maximum residue contribution (TMRC) using existing tolerances and temporary tolerances for tebufenozide on food crops is obtained by multiplying the tolerance level residues by the consumption data which estimates the amount of those food products consumed by various population subgroups and assuming that 100% of the food crops are treated with tebufenozide. The Theoretical Maximum Residue Contribution (TMRC) from current tolerances and temporary tolerances (MRID 44319101) is calculated using the Dietary Exposure Evaluation Model (Version 5.03b, licensed by Novigen Sciences Inc.) which uses USDA food consumption data from the 1989-1992 survey.

With the current and proposed uses of tebufenozide, the TMRC estimate represents 4.31% of the Reference dose (RfD) for the U.S. population as a whole. The subgroup with the greatest chronic exposure is non-nursing infants (less than 1-year old), for which the TMRC estimate represents 20.3% of the RfD. The chronic dietary risks from these uses do not exceed EPA's level of concern.

6. *Drinking water*. An additional potential source of dietary exposure to residues of pesticides are residues in drinking water. Review of environmental fate data by the Environmental Fate and Effects Division concludes that tebufenozide is moderately persistent to persistent and mobile, and could potentially leach to groundwater and runoff to surface water under certain environmental conditions. However, in terrestrial field dissipation studies, residues of tebufenozide and its soil metabolites showed no downward mobility and remained associated with the upper layers of soil. Foliar interception (up to 60% of the total dosage applied) by target crops reduces the ground level residues of tebufenozide. There is no established Maximum Concentration Level (MCL) for residues of tebufenozide in drinking water. No drinking water health advisory levels have been established for tebufenozide.

There are no available data to perform a quantitative drinking water risk assessment for tebufenozide at this time. However, in order to mitigate the potential for tebufenozide to leach into groundwater or runoff to surface water, precautionary language has been incorporated into the product label. Also, to the best of our knowledge, previous experience with more persistent and mobile pesticides for which there have been available data to perform quantitative risk assessments have demonstrated that drinking water exposure is typically a small percentage of the total exposure when compared to the total dietary exposure. This observation holds even for pesticides detected in wells and drinking water at levels nearing or exceeding established MCLs. Considering the precautionary language on the label and based on our knowledge of previous experience with persistent chemicals, significant exposure from residues of tebufenozide in drinking water is not anticipated.

7. *Non-dietary exposure*. Tebufenozide is not registered for either indoor or outdoor residential use. Non-occupational exposure to the general population is therefore not expected and not considered in aggregate exposure estimates.

D. Cumulative Effects

The potential for cumulative effects of tebufenozide with other substances that have a common mechanism of toxicity was considered. Tebufenozide belongs to the class of insecticide chemicals known as diacylhydrazines. The only other diacylhydrazine currently registered for non-food crop uses is halofenozide. Tebufenozide and halofenozide both produce a mild, reversible anemia following subchronic/chronic exposure at high doses; however, halofenozide also exhibits other patterns of toxicity (liver toxicity following subchronic exposure and developmental/systemic toxicity following acute exposure) which tebufenozide does not. Given the different spectrum of toxicity produced by tebufenozide, there is no reliable data at the molecular/mechanistic level which would indicate that toxic effects produced by tebufenozide would be cumulative with those of halofenozide (or any other chemical compound).

In addition to the observed differences in mammalian toxicity, tebufenozide also exhibits unique toxicity against target insect pests. Tebufenozide is an agonist of 20-hydroxyecdysone, the insect molting hormone, and interferes with the normal molting process in target lepidopteran species by interacting with ecdysone receptors from those species. Unlike other ecdysone agonists such as halofenozide, tebufenozide does not produces symptoms which may be indicative of systemic toxicity in beetle larvae (*Coleopteran* species). Tebufenozide has a different spectrum of activity than other ecdysone agonists. In contrast to the other agonists such as halofenozide which act mainly on coleopteran insects, tebufenozide is highly specific for lepidopteran insects.

Based on the overall pattern of toxicity produced by tebufenozide in mammalian and insect systems, the compound's toxicity appears to be distinct from that of other chemicals, including organochlorines, organophosphates, carbamates, pyrethroids, benzoylureas, and other diacylhydrazines. Thus, there is no evidence to date to suggest that cumulative effects of tebufenozide and other chemicals should be considered.

E. Safety Determination

1. *U.S. population*. Using the conservative exposure assumptions described above and taking into account the completeness and reliability of the toxicity data, the dietary exposure to tebufenozide from the current and proposed tolerances will utilize 4.31% of the RfD for the U.S. population and 20.3% for non-nursing infants under 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. Rohm and Haas concludes that there is a reasonable certainty that no harm will result from aggregate exposure to tebufenozide residues to the U.S. population and non-nursing infants.

2. *Infants and children*. In assessing the potential for additional sensitivity of infants and children to residues of tebufenozide, data from developmental toxicity studies in the rat and rabbit and 2-generation reproduction studies in the rat are considered. The developmental toxicity studies are designed to evaluate adverse effects on the developing organism resulting from pesticide exposure during prenatal development to 1 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. Developmental toxicity was not observed in developmental studies using rats and rabbits. The NOEL for developmental effects in both rats and rabbits was 1,000 mg/kg/day, which is the limit dose for testing in developmental studies.

In the 2-generation reproductive toxicity study in the rat, the reproductive/ developmental toxicity NOEL of 12.1 mg/kg/day was 14-fold higher than the parental (systemic) toxicity NOEL (0.85 mg/kg/day). The reproductive (pup) LOEL of 171.1 mg/kg/day was based on a slight increase in both generations in the number of pregnant females that either did not deliver or had difficulty and had to be sacrificed. In addition, the length of gestation increased and implantation sites decreased significantly in F1 dams. These effects were not replicated at the same dose in a second 2-generation rat reproduction study. In this second study, reproductive effects were not observed at 2,000 ppm (the NOEL equal to 149-195 mg/kg/day) and the NOEL for systemic toxicity was determined to be 25 ppm (1.9-2.3 mg/kg/day).

Because these reproductive effects occurred in the presence of parental (systemic) toxicity and were not replicated at the same doses in a second study, these data do not indicate an increased pre-natal or post-natal sensitivity to children and infants (that infants and children might be more sensitive than adults) to tebufenozide exposure. FFDCA section 408 provides that EPA shall 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 data base unless EPA concludes that a different margin of safety is appropriate. Based on current toxicological data discussed above, an additional uncertainty factor is not warranted and the RfD at 0.018 mg/kg/day is appropriate for assessing aggregate risk to infants and children. Rohm and Haas concludes that there is a reasonable certainty that no harm will occur to infants and children from aggregate exposure to residues of tebufenozide.

F. International Tolerances

There are no approved CODEX maximum residue levels (MRLs) established for residues of tebufenozide. At the 1996 Joint Meeting for Pesticide Residues, the FAO expert panel considered residue data for pome fruit and proposed an MRL (Step 3) of 1.0 mg/kg.

3. Valent U.S.A. Corporation

PP 7F4882

EPA has received a pesticide petition (PP 7F4882) from Valent U.S.A. Corporation, 1333 N. California Blvd., Walnut Creek, CA 94596. proposing pursuant to section 408(d) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. 346a(d), to amend 40 CFR part 180 by establishing a tolerance for residues pyriproxyfen, 2-[1-methyl-2-(4-phenoxyphenoxy)ethoxy]pyridine in or on the raw agricultural commodity Pome Fruits(Crop Group 11, including apples and pears) at 0.2 (ppm), Walnuts at 0.02 ppm, and Apple Pomace,wet at 0.8 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*. The nature of the residues in cotton, apples, and animals is adequately understood. Metabolism of 14C-pyriproxyfen labelled in the phenoxyphenyl ring and in the pyridyl ring was studied in cotton, apples, lactating goats, and laying hens (and rats). The nature of the residue is defined by the metabolism studies primarily as pyriproxyfen. The major metabolic pathways in plants is hydroxylation and cleavage of the ether linkage, followed by further metabolism into more polar products by oxidation or conjugation reactions, however, the bulk of the radiochemical residues was parent. Comparing metabolites from cotton, apple, goat and hen (and rat) shows that there are no significant metabolites in plants which are not also present in the excreta or tissues of animals.

Ruminant and poultry metabolism studies demonstrated that transfer of administered 14C residues to tissues was low. Total 14C 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 14C 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 levels of pyriproxyfen (and relevant metabolites) have been developed and validated for the raw agricultural commodities, their respective processing fractions, and animal tissues. The methods have been independently validated in cottonseed and apples (and oranges) and the extraction methodology has been validated using aged radiochemical residue samples from metabolism studies. EPA has(personal communication) 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 or above the levels set for the proposed tolerance.

3. *Magnitude of residues*—i. *Apples*. A total of fifteen trials were conducted in 1994, 1995, and 1996 to determine the magnitude of the residue in apples and apple processing commodities from regions representing approximately 97% of the commercial U.S. apple acreage. The mean residue of pyriproxyfen found in these samples was 0.091 ppm with a standard deviation (δ, n-1 degrees of freedom) of 0.035 ppm and a maximum residue of 0.18 ppm. Apples from two sites were processed into juice and wet pomace. The results from the processing samples show that pyriproxyfen was substantially retained with the wet pomace fraction, resulting in a 5 x concentration in this fraction. The average processing concentration factor for pyriproxyfen from fruit into apple pomace, wet, was 4.89 x. No residues of pyriproxyfen above the 0.01 LOD was detected in the juice fractions.

ii. *Pears*. A total of eight trials were conducted in 1994, 1995, and 1996 to determine the magnitude of the residue of pyriproxyfen in pears from regions representing approximately 95% of the commercial U.S. pear acreage. The mean residue of pyriproxyfen found in these samples was 0.039 ppm with a standard deviation (δ, n-1 degrees of freedom) of 0.016 ppm and a maximum residue of 0.07 ppm.

iii. *Walnuts*. A total of 4 trials were conducted in 1996 to determine the magnitude of the residue of pyriproxyfen in walnut nutmeats all in region x where 98% of the commercial walnut acreage is located. No residues of pyriproxyfen above the 0.01 ppm limit of detection were found in any walnut nutmeat collected for this study.

4. *Secondary residues*. Since low residues were detected in animal feed items (cotton gin byproducts, apple pomace, wet) and animal metabolism studies do not show potential for significant residue transfer, detectable secondary residues in animal tissues, milk, and eggs are not expected. Therefore, tolerances are not needed for these commodities.

B. Toxicological Profile

1. *Acute toxicity*. The acute toxicity of technical grade pyriproxyfen is low by all routes, 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 toxicant. In the rat teratology study, maternal toxicity was observed at doses of 300 mg/kg/day and greater, the NOEL for prenatal developmental toxicity was 100 mg/kg/day. A rabbit teratology study resulted in a maternal NOEL of 100 mg/kg/day, with no developmental effects observed in the rabbit fetuses.

In the study conducted with rats, technical pyriproxyfen was administered by gavage at levels of 0, 100, 300, and 1,000 mg/kg/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/day and greater. The maternal NOEL was 100 mg/kg/day. A transient increase in skeletal variations was observed in rat fetuses exposed to 300 mg/kg/day and greater. These effects were not present in animals examined at the end of the postnatal period, therefore, the NOEL for prenatal developmental toxicity was 100 mg/kg/day. An increased incidence of visceral and skeletal variations was observed postnatally at 1,000 mg/kg/day. The NOEL for postnatal developmental toxicity was 300 mg/kg/day. In the study conducted with rabbits, technical pyriproxyfen was administered by gavage at levels of 0, 100, 300, and 1,000 mg/kg/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/day or higher. The maternal NOEL was 100 mg/kg/day. No developmental effects were observed in the rabbit fetuses. The NOEL for developmental toxicity in rabbits was 1,000 mg/kg/day.

Pyriproxyfen is not a reproductive toxicant. 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/day in males, 498 mg/kg/day in females during the pre-mating period). The systemic NOEL was 1,000 ppm (87 mg/kg/day in males, 96 mg/kg/day in females). No effects on reproduction were produced even 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 NOELs from these studies were 400 ppm (23.5 mg/kg/day for males, 27.7 mg/kg/day for females) in rats, 1,000 ppm (149.4 mg/kg/day for males, 196.5 mg/kg/day for females) in mice, and 100 mg/kg/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/m3 . The NOEL in this study was 482 mg/m3.

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/day, the highest dose tested. In a 21-day dermal study conducted with KNACK Insect Growth Regulator the test material produced a NOEL of 1,000 mg/kg/day (highest dose tested) for systemic effects, and a NOEL for skin irritation of 100 mg/kg/day.

5. *Chronic toxicity*. Pyriproxyfen technical has been tested in chronic studies with dogs, rats and mice.

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

Pyriproxyfen technical was administered to mice at doses of 0, 120, 600 and 3,000 ppm in diet for 78-weeks. The NOEL for systemic effects in this study was 600 ppm (84 mg/kg/day in males, 109.5 mg/kg/day in females), and a LOEL of 3,000 ppm (420 mg/kg/day in males, 547 mg/kg/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 NOEL for systemic effects in this study was 600 ppm (27.31 mg/kg/day in males, 35.1 mg/kg/day in females). A LOEL of 3,000 ppm (138 mg/kg/day in males, 182.7 mg/kg/day in females) was established based on a depression in body weight gain in females.

EPA has established a RfD for pyriproxyfen of 0.35 mg/kg/day, based on the rat 2-year chronic/oncogenicity study. Effects cited by EPA in the RfD 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 show 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/oncogenicitystudy or in a 78-week study on mice.

Pyriproxyfen's oncogenicity classification is ''E'' (no evidence of carcinogenicity for humans).

6. *Animal metabolism*. The mammalian metabolism of pyriproxyfen is understood. The absorption, tissue distribution, metabolism and excretion of 14C-labeled pyriproxyfen were studied in rats after single oral doses of 2 or 1,000 mg/kg (phenoxyphenyl and pyridyl label), and after a single oral dose of 2 mg/kg (phenoxyphenyl label only) following 14 daily oral doses at 2 mg/kg of unlabelled material.

Both the phenoxyphenyl-label and pyridyl-label studies exhibited very similar results. 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. 7-days after dosing, tissue residues were generally low, accounting for no more than 0.3% of the dosed 14^C. 14^C concentrations in fat were the highest in tissues analyzed. Recovery in tissues over time indicates that the potential for bioaccumulation is minimal. There are no significant sex or dose-related differences in excretion or metabolism.

7. *Endocrine disruption*. Pyriproxyfen is specifically designed to be an insect growth regulator and is known to produce juvenile hormone-mediated effects in arthropods. However, this mechanism-of-action in target insects has no relevance to the 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. 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 Sumilarv does not possess estrogenic or endocrine disrupting properties applicable to mammals.

C. Aggregate Exposure

1. *Dietary exposure.* A chronic dietary exposure and risk assessment based on anticipated residues from samples from field residue studies was performed in cotton, apple, pear, and walnut and assumed that 100% of the crops were treated. The exposure analysis also reflected the contribution of meat and milk residues, without regard to detectability, based on commodities used for feed containing residues at anticipated residue levels.

Using mean anticipated residue values and 100% of the crop treated, exposure to the U.S. population - 48 States - all seasons is calculated to be only 0.000049 mg/kg body-wt/day. The most exposed sub-population, non-nursing infants (<1-year), is calculated to be 0.000273 mg/kg bwt./day. These calculated exposures represent, respectively, 0.014, and 0.078 percent occupancy of the RfD of 0.35 mg/kg body-wt/day. Chronic dietary risk from exposure to pyriproxyfen residues on the proposed crops may be characterized as negligible.

2. *Drinking water.* Since pyriproxyfen is to be applied outdoors to growing agricultural crops, the potential exists for the parent or its metabolites to reach ground or surface water that may be used for drinking water.

3. *Ground water.* Pyriproxyfen is extremely insoluble in water (0.367 mg/L at 25°, with high octanol/water partitioning constant (Log P O/W = 5.37 at 25°, and relatively short soil half-life (aerobic soil metabolism T ½ = 6 to 9 days). Given the low use rates, the immobility of the parent and the instability of the soil metabolites in soil, it is very unlikely that pyriproxyfen or its metabolites could leach to and contaminate potable groundwater.

4. *Surface water.* In connection with the potential for dietary exposure from surface potable water, a simulation of expected exposure concentration (EEC) values in aquatic systems has been performed using the Pesticide Root Zone Model (PRZM-3) and the Exposure Analysis Modeling System, version 2.97 (EXAMSII). The simulation was designed to approximate as closely as possible the conditions associated with the high rate proposed use on tree crops. The results of the modelingdemonstrate that the maximum upper tenth percentile concentrations modeled in water adjacent to treated fields are instantaneous, 0.36 ppb; 96-hour, 0.23 ppb; and 21-day, 0.14 ppb.

To obtain a very conservative estimate of a possible dietary exposure from drinking water, it could be assumed that all water consumed contains pyriproxyfen at the maximum upper tenth percentile concentrations modeled in aquatic systems adjacent to treated orchards. The 21-day concentration, 0.14 ppb (0.00014 mg/kg), is used because drinking water is considered to be a chronic exposure, and there are no identified acute or short term endpoints of concern. Using standard assumptions of body weight and water consumption (adult 70 kg, 2 kg water per day; child 10 kg, 1 kg water), the highest possible exposure would be 4.0 x 10-6 and 1.4 x 10-5 mg/kg bwt./day for the adult and child, respectively. This very small, but probably exaggerated, exposure would occupy 0.00114 (adult) and 0.004 (child) percent of the chronic reference dose of 0.35 mg/kg body-wt/day.

5. *Non-dietary exposure.* Pyriproxyfen has numerous registered products for household use primarily of 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 the pharmacokinetics of pyriproxyfen indicate a relatively short elimination half-life, cumulative toxicological effects resulting from bioaccumulation are not plausible following these short-term, intermittent exposures. Further, pyriproxyfen is very short-lived in the environment and this indoor domestic use of pyriproxyfen may provide only relatively short-term reservoirs.

The most relevant exposure for non-dietary exposure assessment is short-term to intermediate average daily exposure estimates. The non-dietary exposure assessment for pyriproxyfen conservatively focuses on upper-bound estimates of potential applicator (adult) and post-application (adult and child - less than 1-year old) exposures on the day of application. Subsequent days present no applicator exposure, and a decreasing contribution to short-term total exposure.

The assessment presented herein estimates exposures for selected consumer uses that are considered representative, plausible, and reasonable worst case exposure scenarios. The scenarios selected include:

(i) Potential exposures associated with adult application (dermal and inhalation exposures) and post-application (adult and child inhalation exposures) of pyriproxyfen-containing pet care products; and

(ii) Potential adult application exposures (dermal and inhalation), and adult (inhalation) and child exposures (inhalation, dermal, incidental oral ingestion associated with hand-to-mouth behavior) post-application exposures associated with consumer use of a carpet spray product.

Using a combination of representative information from the PHED data base for applicators (adult), and surrogate data from a study of exposure to indoor broadcast applications (post-application adult and child) a series of adsorbed dose estimates were calculated for adult applicators, and post-application exposures to adults and children by dermal, inhalation, and (hand-to-mouth) oral routes. The methodology, assumptions, and estimates are presented in detail in the full FQPA exposure analysis, the table below presents the results.

SUMMARY OF ESTIMATED HUMAN APPLICATION AND POST-APPLICATION EXPOSURES ASSOCIATED WITH USE OF PET SPRAY AND CARPET SPRAY PRODUCTS CONTAINING PYRIPROXYFEN AS THE ACTIVE INGREDIENT

Product	Population	Timing of Exposure	Daily Dose (mg/kg bw/day)			
			Inhalation[1]	Dermal[2]	Oral[1]	Total
Pet Spray	Adults	Application	4.3×10^{-6}	0.085	[3]NA	0.085
		Post-Application ...	1.8×10^{-5}	NA	NA	1.8×10^{-5}
		TOTAL	2.2×10^{-5}	0.085	NA	0.085
	Children	Post-Application ...	3.7×10^{-5}	NA	NA	3.7×10^{-5}
Carpet Spray	Adults	Application	1.3×10^{-6}	5.1×10^{-4}	NA	5.1×10^{-4}
		Post-Application ...	5.4×10^{-6}	NA	NA	5.4×10^{-6}

SUMMARY OF ESTIMATED HUMAN APPLICATION AND POST-APPLICATION EXPOSURES ASSOCIATED WITH USE OF PET SPRAY AND CARPET SPRAY PRODUCTS CONTAINING PYRIPROXYFEN AS THE ACTIVE INGREDIENT—Continued

Product	Population	Timing of Exposure	Daily Dose (mg/kg bw/day)			
			Inhalation[1]	Dermal[2]	Oral[1]	Total
		TOTAL	6.7×10^{-6}	5.1×10^{-4}	NA	5.2×10^{-4}
	Crawling Infant	Post-Application ...	1.5×10^{-5}	1.3×10^{-3}	2.1×10^{-4}	1.5×10^{-3}

[1] 100 % adsorption.
[2] Conservatively assumes a dermal absorption factor of 50%.
[3] Exposure pathway not applicable.

It is important to emphasize that the exposures summarized in the table are based on conservative assumptions and surrogate data. Further, the exposures are calculated for the day of application. Subsequent daily exposures would be less as pyriproxyfen is adsorbed into substrate, or dissipates and becomes unavailable by other mechanisms. Exposures to applicators on non-application days would be zero.

Further, the Agency has not identified acute or short term toxicity endpoints of concern. Endpoints that could be considered for short term and intermediate exposures include a developmental toxicity no observed effect level (NOEL) of 100 mg/kg/day (rat and rabbit), a rat 21-day dermal systemic NOEL of 1,000 mg/kg/day (technical grade and end-use products), a 4-week rat inhalation toxicity NOEL of 482 mg/m3, and a 90-day rat oral toxicity NOEL of 23.5 mg/kg/day. There are no dermal absorption data for pyriproxyfen. The 1-day exposure calculated for the applicator of the pet spray (0.085 mg/kg/day) is 57-times larger than the next highest calculated exposure which is the total exposure to a crawling infant on the day of application of the carpet spray (1.5 x 10-3 mg/kg/day). Furthermore, the return frequency is much different. Label instructions allow treatment of the dog every 14-days during the flea season, while the carpet can be treated only each 120-days. The 1-day exposure can be compared to the smallest short term endpoint, that from the 90-day rat oral toxicity NOEL of 23.5 mg/kg/day, and a Margin of Exposure (MOE) can be calculated. This compares an acute exposure to a sub-chronic endpoint.

MOE = Toxicity Endpoint (mg/kg/day) ÷ Daily Short Term Exposure (mg/kg/day)

$MOE_{Pet\ Spray\ Applicator,\ One\ day} = 276$

Probably more realistic, a short term daily exposure to the adult applicator can be calculated and compared to the same endpoint.

Daily Exposure (mg/kg/day) = Applicator Exposure (mg/kg/day) ÷ Frequency (days)

$MOE_{Pet\ Spray\ Applicator} = 3900$

Based on the available toxicity data and the conservative exposure assumptions, and because infants and children are not applicators in the household, the smallest acute and short term MOE value for children is based on post-application exposures. The day of application exposure to a crawling infant is the sum of inhalation, dermal adsorption, and oral (hand to mouth) exposures. Subsequent daily exposures are not quantified, but because of dissipation of the active ingredient in the home environment but must be smaller than on the day of application.

$MOE_{Carpet\ Spray,\ Crawling\ Infant} = 15{,}700$

There is usually no cause for concern if margins of exposure exceed 100. All other margins of exposure that can be calculated from the non-occupational, non-dietary exposures summarized in the table above are considerably larger than that for the pet spray applicator and (post carpet spray application) crawling infant.

Summary of Aggregate Non-Occupational Exposures. Aggregate exposure is defined as the sum all non-occupational exposures to the general U.S. population and relevant sub-populations to the single active ingredient, pyriproxyfen. These exposures can be classified as acute, short term, and chronic.

Acute and Short Term Non-Occupational Potential acute and short term non-occupational exposures to pyriproxyfen are associated with household uses -- applicator, bystander, and post-application exposures. For preliminary risk analysis, these exposures, oftentimes calculated using conservative assumptions and surrogate data, are compared to appropriate acute and short term toxicity endpoints to yield margins of exposure (MOE). In general, if exposure estimates are conservative and the resulting MOE values are greater than 100, the Agency is not concerned. In contrast, if conservative MOE values are less than 100, then more refined exposure estimates and/or exposure mitigation are required.

The Agency has not identified acute or short term toxicity endpoints of concern for pyriproxyfen. Valent has identified the 90-day rat oral toxicity with a NOEL of 23.5 mg/kg/day as the short term study with the lowest exposure endpoint. Comparing this endpoint with the short term non-occupational exposures calculated for the household uses of pyriproxyfen gives MOE values all much larger than 100. These acute and short term exposures are small enough to be of little significance.

C. Chronic Exposures

Potential chronic exposures to pyriproxyfen are considered to be derived from dietary exposures to primary and secondary residues in food, and to potential residues in drinking water. To calculate the total potential chronic exposure from food and drinking water, the calculated exposures from both media can be summed. To assess risk these totals can then be compared to the chronic RfD.

Summation of the Calculated Potential Chronic Exposure to Pyriproxyfen in Food and Drinking Water and Percent Occupancy of the RfD for Two U.S. Populations

Medium(mg/kg body-wt/day)	General Population(adult)	Non-NursingInfant (1)
Food	0.000049	0.000273
Drinking Water	0.000004	0.000014

Summation of the Calculated Potential Chronic Exposure to Pyriproxyfen in Food and Drinking Water and Percent Occupancy of the RfD for Two U.S. Populations—Continued

Medium(mg/kg body-wt/day)	General Population(adult)	Non-NursingInfant (1)
Total	0.000053	0.000287
%RfD(0.35 mg/kg body-wt/day)	0.015	0.082

If the occupancy of the RfD is less than 100%, the Agency usually has little cause for concern. From the table above, it can be seen that the total potential chronic exposure to pyriproxyfen is truly insignificant, and should not be cause for concern.

D. Cumulative Effects

Valent has considered the potential for cumulative exposure to substances with a common mechanism of toxicity to pyriproxyfen. However, a cumulative exposure assessment is not appropriate at this time because there is no available information to indicate that the effects of pyriproxyfen would be cumulative with those of any other chemical compound. Therefore, Valent is considering only the potential risk of pyriproxyfen in its aggregate exposure assessment.

E. Safety Determination

1. *U.S. population*. Based on a complete and reliable toxicity database, EPA has established an RfD value of 0.35 mg/kg bwt./day using the NOEL from the chronic rat feeding study and a 100-fold uncertainty factor. The aggregate chronic exposure to pyriproxyfen will utilize less than 0.1% of the RfD for the U.S. population. Because estimated exposures are far below 100 percent of the RfD, Valent concludes that there is a reasonable certainty that no harm will result from aggregate exposure to pyriproxyfen residues.

2. *Infants and children*. Using the same conservative exposure assumptions as for the general population, the percent of the RfD utilized by aggregate chronic exposure to residues of pyriproxyfen is 0.082% for non-nursing infants, the most highly exposed population subgroup. Valent concludes that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to residues of pyriproxyfen.

F. International Tolerances

There are presently no Codex maximum residue levels established for residues of pyriproxyfen on any crop.

[FR Doc. 98–8065 Filed 3–26–98; 8:45 am]
BILLING CODE 6560–50–F

ENVIRONMENTAL PROTECTION AGENCY

[OPP–181058; FRL–5780–4]

Triazamate; 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 Washington Department of Agriculture (hereafter referred to as the ''Applicant'') to use the pesticide triazamate (CAS 112143-82-5) to treat up to 5,000 acres of true fir Christmas trees to control root aphids.

The Applicant proposes the use of a new (unregistered) chemical. Therefore, in accordance with 40 CFR 166.24, EPA is soliciting public comment before making the decision whether or not to grant the exemption.

DATES: Comments must be received on or before April 13, 1998.

ADDRESSES: Three copies of written comments, bearing the identification notation ''OPP-18058 ,'' should be submitted by mail to: Public Information and Records Integrity Branch, Information Resources and Division (7502), Office of Pesticide Programs, Environmental Protection Agency, 401 M St. SW, Washington, DC 20460. In person, bring comments to: Rm. 119, Crystal Mall #2 1921 Jefferson Davis Highway, Arlington, VA.

Comments and data may also be submitted electronically to: opp-docket@epamail.epa.gov. Follow the instruction under ''SUPPLEMENTARY INFORMATION.'' No Confidential Business Information (CBI) should be submitted through e-mail.

Information submitted in any comment concerning this notice may be claimed confidential 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. A copy of the comment that does not contain CBI must be submitted for inclusion in the public record. Information not marked confidential may be included in the public record by EPA without prior notice. The public docket is available for public inspection in 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.

FOR FURTHER INFORMATION CONTACT: By mail: Stephen Schaible, Registration Division (7505C), Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW, Washington, DC 20460. Office location and telephone number: Floor 2, Crystal Mall #2, 1921 Jefferson Davis Highway, Arlington, VA, (703-308-9362); e-mail: schaible.stephen@epamail.epa.gov.

SUPPLEMENTARY INFORMATION:. Pursuant to section 18 of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) (7 U.S.C. 136p), the Administrator may, at her discretion, exempt a state agency from any registration provision of FIFRA if she determines that emergency conditions exist which require such exemption. The Applicant has requested the Administrator to issue a specific exemption for the use of triazamate on true fir Christmas trees to control root aphids. Information in accordance with 40 CFR part 166 was submitted as part of this request.

According to the Applicant, the root aphid is not new to the Northwest, but has only recently been identified as posing a serious economic threat to true fir Christmas tree plantations. Root aphids feed on the roots of true fir trees, causing stunting and color loss in the foliage, and increasing susceptibility to disease. Losses extend from the first year through the life of the plantation. Attempts to chemically control the aphids during the winged stage during migration to and from fir trees have not been successful. Foliar and soil drench applications of several insecticides have also been tested, with none being adequately successful.

Under the proposed exemption, a maximum of two applications, at least 30 days apart and when aphids are present, at a rate of 0.5 lb/acre of formulated product (0.25 lb/acre active ingredient) would be applied by ground or air. A maximum of 5,000 acres in Kitsap, Lewis, Mason and Thurston counties would be treated. Do not apply