TABLE B.—LIST OF REQUIREMENTS

Active Ingredient	Registrant Affected	Requirement Name	Guideline Reference Number	Original Due Date
Bacillus popillae and *Bacillus lentimorbus*	Fairfax Biological Laboratories	90–Day Response	**	12/20/92
		Acute Pulmonary Toxicity/Pathogenicity	152-30	10/20/93
		Acute Intravenous Toxicity/Pathogenicity	152-32	10/20/93
		Avian Oral Toxicity/Pathogenicity	154-16	10/20/93
		Non-Target Insects	154-23	10/20/93

IV. Attachment III Suspension Report--Explanatory Appendix

This Explanatory Appendix provides a discussion of the basis for the Notice of Intent to Suspend issued herewith.

On September 30, 1992, EPA issued the Phase 5 Reregistration Eligibility Document Data Call-In Notice imposed pursuant to section 4(g)(2)(B) of FIFRA which required registrants of products containing *Bacillus popillae* and *Bacillus lentimorbus* used as the active ingredients to develop and submit certain data. These data/information were determined to be necessary to satisfy reregistration data requirements of section 4(g). Failure to comply with the requirements of a Phase 5 Reregistration Eligibility Document Data Call-In Notice is a basis for suspension under section 3(c)(2)(B) of FIFRA.

The *Bacillus popillae* and *Bacillus lentimorbus* Phase 5 Reregistration Eligibility Document Data Call-In Notice dated September 30, 1992 required each affected registrant to submit data/information to the Agency to address each of the data requirements. Those data/information were required to be received by the Agency within 8 months of the registrant's receipt of the Notice. Fairfax Biological Laboratories was sent the original 1992 Data Call-In. According to a U.S. Postal Service return receipt, you received the original Data Call-In Notice on October 10, 1992. You subsequently failed to respond within 90 days of receipt as required, and failed to submit the required data within 8 months as required. Repeated attempts to contact the company via telephone were unsuccessful. Fairfax was sent a letter on March 25, 1996, with a May 1, 1996 deadline for response to the Data Call-In and its requirements. You received the letter on April 2, 1996, as evidenced by the U.S. Postal Service return receipt. The Agency received no response.

Because you have failed to submit appropriate or adequate data/information within the time provided for the data/information requirements listed in Attachment II and have yet to provide the required response to date, the Agency is issuing this Notice of Intent to Suspend.

V. Conclusions

EPA has issued Notices of Intent to Suspend on the dates indicated. Any further information regarding these Notices may be obtained from the contact person noted above.

List of Subjects

Environmental protection.

Dated: February 18, 1998.

Elaine G. Stanley,

Director, Office of Compliance.

[FR Doc. 98–5855 Filed 3–5–98; 8:45 am]

BILLING CODE 6560–50–F

ENVIRONMENTAL PROTECTION AGENCY

[PF–798; FRL–5777–5]

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 agricultural commodities.

DATES: Comments, identified by the docket control number PF–798, must be received on or before April 6, 1998.

ADDRESSES: By mail submit written comments to: Public Information and Records Integrity Branch, Information Resources and Services Divison (7502C), Office of Pesticides Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. In person bring comments to: Rm. 119, CM #2, 1921 Jefferson Davis Highway, Arlington, VA.

Comments and data may also be submitted electronically to: opp-docket@epamail.epa.gov. 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. 119 at the address given above, from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays.

FOR FURTHER INFORMATION CONTACT: By mail: Joseph Tavano, Product Manager (PM) 10, Registration Division, (7505C), Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. Office location, telephone number, and e-mail address: Rm. 214, CM#2, 1921 Jefferson Davis Hwy., Arlington, VA. 22202, (703) 305–6411; e-mail: tavano.joe@epamail.epa.gov.

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 raw agricultural 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 grantinig of the petition. Additional data may be needed before EPA rules on the petition.

The official record for this notice, as well as the public version, has been established for this notice of filing under docket control number PF–798 (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 5.1/6.1 file format or ASCII file format. All comments and data in electronic form must be identified by the docket control number PF–798 and appropriate petition number. Electronic comments on this notice may be filed online at many Federal Depository Libraries.

Authority: 21 U.S.C. 346a.

List of Subjects

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

Dated: March 2, 1998.

Peter Caulkins,

Acting Director, Registration Division, Office of Pesticide Programs.

Summaries of Petitions

Below summaries of the pesticide petitions are printed. The summaries of the petitions were prepared by the petitioners. 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. Rohm and Haas Company

PP 3G4274

EPA has received a pesticide petition (PP 3G4274)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 triazamate [Acetic acid, [{1-{(dimethylamino) carbonyl}-3-(1,1-dimethylethyl)-1*H*-1,2,4-triazol-5-y1} thio]-,ethyl ester] and its metabolite Acetic acid,[{1-{(dimethylamino) carbonyl}-3-(1,1-dimethylethyl)-1*H*-1,2,4-triazol-5-y1}thio]-(code number RH–0422 in or on the raw agricultural commodity fresh apples 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 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 triazamate in plants (apples) is adequately understood for the purposes of this tolerance. The metabolism of triazamate involves oxidative demethylation of the carbamoyl group. Parent compound is rapidly metabolized and is either not found or found at trace levels in apples. The majority of the total dosage is present as other non-cholinesterase inhibiting metabolites whose structures do not contain the dimethylcarbamoyl moiety. Because the proposed experimental use program is for fresh apples, livestock metabolism studies are not required. Tolerances for residues of triazamate should be expressed as the total residue from triazamate and its only cholinesterase-inhibiting metabolite RH–0422.

2. *Analytical method*. The metabolism of triazamate in plants (apples) is adequately understood for the purposes of this tolerance. The metabolism of triazamate involves oxidative demethylation of the carbamoyl group. Parent compound is rapidly metabolized and is either not found or found at trace levels in apples. The majority of the total dosage is present as other non-cholinesterase inhibiting metabolites whose structures do not contain the dimethylcarbamoyl moiety. Because the proposed experimental use program is for fresh apples, livestock metabolism studies are not required. Tolerances for residues of triazamate should be expressed as the total residue from triazamate and its only cholinesterase-inhibiting metabolite RH–0422.

3. *Magnitude of residues*. A total of 14 field residue trials in apples was conducted with a 25WP formulation in geographically representative regions of the U.S. Three applications were made at either 0.25 or 0.38 lb. a.i./acre. Fruit were harvested at 40 days after the last application. Only trace residues of triazamate were detected and residues of RH–0422 did not exceed 0.06 ppm.

B. Toxicological Profile

1. *Acute toxicity*. Triazamate is a moderately toxic cholinesterase inhibitor belonging to the carbamate class. Triazamate Technical was moderately toxic to rats following a single oral dose (LD_{50} = 50-200 milligram/kilograms (mg/kg)), and after a 4-hr inhalation exposure (LC_{50} value of >0.47 mg/L); and was minimally to slightly toxic to rats following a single dermal dose (LD_{50} >5,000 mg/kg). In a guideline acute neurotoxicity study with triazamate in the rat, the NOEL for clinical signs was 5 mg/kg based on the observation of cholinergic signs in 1 of 10 male rats at 25 mg/kg. Triazamate was practically non-irritating to the skin, moderately irritating to eyes in rabbits and did not produce delayed contact hypersensitivity in the guinea pig.

2. *Genotoxicity*. Triazamate is not mutagenic or genotoxic. Triazamate Technical was negative (non-mutagenic) in an Ames assay with and without hepatic enzyme activation. Triazamate 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, triazamate did not induce unscheduled DNA synthesis (UDS) or repair when tested up to the maximum soluble concentration in culture medium. Triazamate did not produce chromosome aberrations in an *in vitro* assay using Chinese hamster ovary cells (CHO) or an *in vivo* mouse micronucleus assay.

3. *Reproductive and developmental toxicity*. In a developmental toxicity study in rats with Triazamate Technical, the no-observed-effect-level (NOEL) for developmental toxicity was 64 mg/kg (highest dose tested) (HDT). The NOEL for maternal toxicity was 16 mg/kg based on clinical signs of cholinergic toxicity at 64 mg/kg.

In a developmental toxicity study in rabbits with Triazamate Technical, the NOEL for developmental toxicity was 10 mg/kg (HDT). The NOEL for maternal toxicity was 0.5 mg/kg based on clinical signs and decreased body weight at 10 mg/kg.

In a 2-generation reproduction study in rats with Triazamate Technical, the NOEL for reproductive effects was 1,500 ppm (101 and 132 milligram/kilograms/day (mg/kg/day) for males and females, respectively; HDT). The NOEL for parental toxicity was 10 ppm (0.7 and 0.9 mg/kg/day for males and females, respectively) based on decreased plasma and RBC cholinesterase activities at 250 ppm (17 and 21 mg/kg/day for males and females, respectively).

The acceptable developmental studies (prenatal developmental toxicity studies in rats and rabbits and 2-generation reproduction study in rats) provided no

indication of increased sensitivity of rats or rabbits to *in utero* and or post-natal exposure to triazamate. Triazamate Technical is not a developmental or reproductive toxicant.

4. *Subchronic toxicity.* In subacute and subchronic dietary toxicity studies, Triazamate Technical produced no evidence of adverse effects other than those associated with cholinesterase inhibition:

i. In a 90-day dietary toxicity study with Triazamate Technical in the rat, the NOEL for blood cholinesterase inhibition was 50 ppm (3.2 and 3.9 mg/kg/day for males and females, respectively), based on decreases in plasma and RBC cholinesterase activities at 500 ppm (32 and 39 mg/kg/day for males and females, respectively). The NOEL for brain cholinesterase inhibition and/or clinical signs was 500 ppm (32 and 39 mg/kg/day for males and females respectively) based on decreased brain cholinesterase activity and decreased body weight gain and feed consumption at 1,500 ppm (93 and 117 mg/kg/day for males and females, respectively).

ii. In a guideline subchronic neurotoxicity study (90-day dietary feeding) with Triazamate Technical in the rat, the NOEL for blood cholinesterase inhibition was 10 ppm (0.6 and 0.7 mg/kg/day for males and females, respectively), based on reductions in plasma and RBC cholinesterase activities at 250 ppm (14.3 and 17.1 mg/kg/day for males and females, respectively). The NOEL for brain cholinesterase inhibition and/or clinical signs was 250 ppm (14.3 and 17.1 mg/kg/day for males and females respectively) based on decreases in brain cholinesterase activity and cholinergic signs at 1,500 ppm (87 and 104 mg/kg/day for males and females, respectively).

iii. In a 90-day dietary toxicity study with Triazamate Technical in the mouse, the NOEL for blood cholinesterase inhibition was 2 ppm (0.4 and 0.5 mg/kg/day for males and females, respectively) based on decreases in plasma cholinesterase activity at 25 ppm (4 and 6 mg/kg/day for males and females, respectively). The NOEL for brain cholinesterase and/or clinical signs was 250 ppm (46 and 67 mg/kg/day for males and females, respectively) based on decreases brain cholinesterase and decreases body weight and feed consumption at 1,000 ppm (164 and 222 mg/kg/day for males and females, respectively).

iv. In a 90-day dietary toxicity study with Triazamate Technical in the dog, the NOEL for blood cholinesterase inhibition was 1 ppm for males only (0.03 mg/kg/day) based on decreases in plasma cholinesterase at 10 ppm (0.3 mg/kg/day). The dose of 1 ppm was a lowest-observed-effect-level (LOEL) for females based on the presence of decreased plasma cholinesterase activity (24%). The NOEL for clinical signs was 10 ppm (0.3 mg/kg/day for males and females) based a few clinical signs at 100 ppm (3.1 mg/kg/day for males and females).

v. In a 21-day dermal toxicity study with Triazamate Technical, the NOEL blood and brain cholinesterase inhibition was 10 mg/kg based on decreases plasma, RBC and brain cholinesterase activities at 100 mg/kg.

5. *Chronic toxicity*— i. *Rat, mouse, and dog studies.* In chronic dietary toxicity studies, Triazamate Technical produced no evidence of adverse effects other than those associated with cholinesterase inhibition and was not oncogenic in the rat and mouse.

In a combined chronic dietary toxicity/oncogenicity study (24 months) in rats with Triazamate Technical, no evidence of oncogenicity was observed at doses up to 1,250 ppm (62.5 mg/kg/day for males and females; HDT). The NOEL for blood cholinesterase inhibition was 10 ppm (0.5 and 0.6 mg/kg/day for males and females, respectively) based on decreases in plasma and RBC cholinesterase activity at 250 ppm (11.5 and 14.5 mg/kg/day in males and females, respectively). The NOEL for brain cholinesterase inhibition and/or clinical signs was 250 ppm (11.5 and 14.5 mg/kg/day in males and females, respectively) based on clinical signs and decreases in brain cholinesterase inhibition at 1,250 ppm (62.5 mg/kg/day for males and females).

In a combined chronic dietary toxicity study (18 months) in mice with Triazamate Technical, no evidence of oncogenicity was observed at doses up to 1,000-1,500 ppm (130-195 mg/kg/day for males and females; HDT). The NOEL for blood cholinesterase inhibition was 1 ppm (0.1 and 0.2 mg/kg/day for males and females, respectively) based on decreased plasma cholinesterase activity at 50 ppm (6.7 and 8.4 mg/kg/day for males and females, respectively). The NOEL for brain cholinesterase inhibition and/or clinical signs was 50 ppm (6.7 and 8.4 mg/kg/day for males and females, respectively) based on decreased brain cholinesterase activity and other evidence of systemic toxicity at 1,000-1,500 ppm (130-195 mg/kg/day for males and females).

In a chronic dietary toxicity study (12 months) in dogs with Triazamate Technical, the NOEL for blood cholinesterase inhibition was 0.9 ppm (0.023 and 0.025 mg/kg/day for males and females, respectively) based on decreased plasma cholinesterase activity at 15.0 ppm (0.42 mg/kg/day for both males and females). The NOEL for brain cholinesterase inhibition was 15.0 ppm (0.42 mg/kg/day for both males and females) based on decreased brain cholinesterase activity at 150 ppm (4.4 and 4.7 mg/kg/day for males and females, respectively).

ii. *Human studies.* A randomized double blind ascending dose study was conducted in human male volunteers to determine the safety and tolerability of Triazamate Technical and to establish a NOEL for adverse clinical toxicity. Single doses of Triazamate Technical, when administered orally by capsule to healthy male subjects, were tolerated up to and including a dose of 1.0 mg/kg. The 3.0 mg/kg dose of triazamate was not clinically tolerated well. Clinically, the NOEL was 0.3 mg/kg of triazamate based on minimal clinical signs at 1.0 mg/kg that were considered possibly related to treatment. Transient decreases in plasma and RBC cholinesterase occurred at doses lower than the dose that elicited adverse clinical signs.

Using its Guidelines for Carcinogen Risk Assessment published September 24, 1986 (51 FR 33992), Rohm and Haas Company considers triazamate to be classified as a Group ''E,'' not a likely human carcinogen.

A Reference dose (RfD) of 0.01 mg/kg/day is proposed for humans, based on the clinical NOEL in the human study (0.3 mg/kg) and dividing by a safety factor of 30. The dose of 0.3 mg/kg was the highest dose in humans that did not produce toxicologically significant adverse effects (i.e., signs of cholinergic toxicity) and is 10 times lower than a dose that produced unequivocal signs of cholinergic toxicity in man. In addition, the clinical NOEL in humans is comparable to the no-observable-adverse-effect level (NOAEL) of 0.42 mg/kg/day following chronic dosing in the dog, the most sensitive laboratory animal species. A safety factor of 10 is applied to the clinical NOEL in humans to account for potential variability within humans with respect to sensitivity towards triazamate. An additional, safety factor of 3 is included, since at 0.03 mg/kg (i.e., $1/10^{th}$ the dose that was a clinical NOEL) there was a transient but measurable depression in plasma cholinesterase in humans. Although a change in the plasma pseudo-cholinesterase (i.e., butyl-cholinesterase) is not toxicologically significant since this enzyme is not molecularly similar to acetyl-cholinesterase, the additional uncertainty factor of 3 establishes a RfD at a level where one would predict no

measurable response of any kind, irrespective of the toxicological significance of the finding.

6. *Animal metabolism*. The adsorption, distribution, excretion and metabolism of triazamate in rats, dogs and goats was investigated. Triazamate is rapidly absorbed when given orally (capsule or gavage) but slower following dietary intake. Peak blood levels following dietary administration were 10-fold lower than after gavage administration of an equivalent mg/kg/dose. Elimination is predominately by urinary excretion and triazamate does not accumulate in tissues. The metabolism of triazamate proceeds via ester hydrolysis and then a rapid stepwise cleavage of the carbamoyl group. The free acid, (RH–0422) is the only toxicologically significant metabolite, given that it contains the carbamoyl group. Other metabolites of triazamate, which are seen in other animal and plant metabolism studies, do not contain the carbamoyl group and do not produce cholinesterase inhibition.

7. *Metabolite toxicology*. Common metabolic pathways for triazamate have been identified in both plants (apple) and animals (rat, goat, hen). The metabolic pathway common to both plants and animals involves oxidative demethylation of the carbamoyl group. 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 triazamate shows no evidence of physiological effects characteristic of the disruption of mammalian hormones. In developmental and reproductive studies there was no evidence of developmental or reproductive toxicity. In addition, the molecular structure of triazamate does not suggest that this compound would disrupt the mammalian hormone system. Overall, the weight of evidence provides no indication that triazamate has endocrine activity in vertebrates.

C. Aggregate Exposure

1. *Dietary exposure*. A RfD of 0.01 mg/kg/day is proposed for humans, based on the clinical NOEL in the human study (0.3 mg/kg) and dividing by a safety factor of 30.

2. *Food*— i. *Acute risk*. An acute dietary risk assessment (Dietary Exposure Evaluation Model, Novigen Sciences Inc., 1997) was conducted for triazamate using two approaches: (a) a Tier 1 approach using a tolerance level residue of 0.1 ppm and (b) Monte Carlo simulations using an entire distribution of field trial residues for pome fruit and adjusted for percent crop treated (Tier 3). Using the Tier 1 approach margins of exposure (MOEs) at the 95th and 99th percentiles of exposure for the overall U.S. population were 572 and 199, respectively. Using the Tier 3 procedure in which residues were adjusted for percent crop treated, the MOEs for the 95th and 99th percentiles were 8,769 and 1,511, respectively. Acute exposure was also estimated for non-nursing infants, the most sensitive sub-population. For this population, MOEs at the 95th and 99th percentiles of exposure were 113 and 83, respectively. Using the Tier 3 method, MOEs were 909 and 396, respectively. Acute dietary risk is considered acceptable if the MOE is greater than 30, an appropriate safety factor when based on a human clinical study. Even under the conservative assumptions presented here, the more realistic estimates of dietary exposure (Tier 3 analyses) clearly demonstrate adequate MOEs up to the 99th percentile of exposure for all population subgroups.

ii. *Chronic risk*. Chronic dietary risk assessments (Dietary Exposure Evaluation Model, Novigen Sciences Inc., 1997) were conducted for triazamate using two approaches: (a) using a tolerance level residue of 0.1 ppm assuming 100% of crop is treated and (b) using a tolerance level residue of 0.1 ppm adjusted for projected percent crop treated. The Theoretical Maximum Residue Contribution (TMRC) from the proposed pome fruit tolerance represents 0.91% of the 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 6.3% of the RfD. The chronic dietary risks from this use do not exceed EPA's level of concern.

3. *Drinking water*. Both triazamate and its cholinesterase-inhibiting metabolite RH-0422 are degraded rapidly in soil. This rapid degradation has been observed in both laboratory and field studies and makes it highly unlikely that measurable residues of either compound would be found in ground or surface water when triazamate is applied according to the proposed EUP label directions.

4. *Non-dietary exposure*. Triazamate 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 triazamate with other substances that have a common mechanism of toxicity was considered. It is recognized the triazamate, although structurally a pseudo-carbamate, exhibits toxicity similar to the carbamate class of insecticides, and that these compounds produce a reversible inhibition of the enzyme cholinesterase. However, Rohm and Haas Company concludes that consideration of a common mechanism of toxicity is not appropriate at this time since EPA does not have the methodology to resolve this complex scientific issue concerning common mechanisms of toxicity. Based on these points, Rohm and Haas Company has considered only the potential risks of triazamate and RH–0422 in its cumulative exposure assessment.

E. Safety Determination

1. *U.S. population*. The acute and chronic dietary exposure to triazamate and its metabolite from the proposed use on pome fruit were evaluated. Exposure to triazamate and its toxicologically significant metabolite on pome fruit does not pose an unreasonable health risk to consumers including the sensitive subgroup non-nursing infants. In Tier 1 and Tier 3 acute analyses for the 95th percentile exposures, MOEs were greater than 100 for the general U.S. population. Using the TMRC and assuming 100% of crop treated, the most conservative chronic approach, chronic dietary exposures represents 0.6% of the RfD for the 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.

Using the two conservative exposure assessments described above and taking into account the completeness and reliability of the toxicity data, Rohm and Haas Company concludes that there is a reasonable certainty that no harm will result from aggregate exposure to residues of triazamate and its toxicologically significant metabolite to the U.S. population.

2. *Infants and children*. In assessing the potential for additional sensitivity of infants and children to residues of triazamate, 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 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.

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 effects and the completeness of the toxicity database. Based on current toxicological data requirements, the toxicology database for triazamate relative to pre- and post- natal effects is complete. For triazamate, developmental toxicity was not observed in developmental studies using rats and rabbits. The NOEL for developmental effects in rats was 64 mg/kg/day and rabbits was 10 mg/kg/day. In the 2-generation reproductive toxicity study in the rat, the reproductive/ developmental toxicity NOEL was 101-132 mg/kg/day. These NOELs are 10-fold or higher than those observed for systemic toxicity, i.e., cholinesterase inhibition.

In Tier 1 and Tier 3 acute dietary analyses for the 95th percentile exposures, MOEs were greater than 100 for non-nursing infants. Using the TMRC and assuming 100% of crop treated, the most conservative chronic approach, chronic dietary exposures represents 6.3% of the RfD for non-nursing infants under 1 year old. Therefore Rohm and Haas Company concludes that there is a reasonable certainty that no harm will result from aggregate exposure to residues of triazamate and its toxicologically significant metabolite to infants and children.

F. International Tolerances

There are no approved CODEX maximum residue levels (MRLs) established for residues of triazamate. MRLs have been established for apples at 0.1 ppm in the Czech Republic, at 0.02 ppm in Hungary, and at 0.2 ppm in Korea.

2. Rohm and Haas Company

PP 6E4679

EPA has received a pesticide petition (PP 6E4679) from Rohm and Haas Company, 100 Independence Mall West, Philadelphia, PA 19106. 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 wine grapes at 0.5 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 and hens proceeds along the same metabolic pathway as observed in plants. No accumulation of residues in tissues, milk or eggs occurred. Because wine grape processed fractions are not fed to livestock, there is no reasonable expectation that measurable residues of tebufenozide will occur in meat, milk, eggs, or poultry.

2. *Analytical method*. A high performance liquid chromatographic (HPLC) analytical method using ultraviolet (UV) detection has been validated for grapes and wine. For these matrices, 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 limit of quantitation of the method is 0.01 ppm for grapes and 0.005 ppm for wine.

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 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-hour 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. *Genotoxicity*. 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*. NOELs for developmental and maternal toxicity to tebufenozide were established at 1,000 mg/kg/day (HDT) in both the rat and rabbit. No signs of developmental toxicity were exhibited.

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.

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*. 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 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 = 1,330 mg/kg/day for males, 1,650 mg/kg/day for females).

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.

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.

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 weeks, 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-week 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.

In a 28-day dermal toxicity study in the rat, the NOEL was 1,000 mg/kg/day, the highest dose tested. 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*. 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.

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.

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*— i. *Acute risk*. 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 values are used and the assumption that all of these crops which are consumed in the U.S. will contain residues at the tolerance level. The TMRC using existing and future potential tolerances for tebufenozide on food crops is obtained by multiplying the tolerance level residues (existing and proposed) 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 grown in the U.S. are treated with tebufenozide. The TMRC from current and future tolerances 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 20.1% of the 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 52.0% of the RfD. Using anticipate residue levels for these crops utilizes 3.38% of the RfD for the U.S. population and 12.0% for non-nursing infants. The chronic dietary risks from these uses do not exceed EPA's level of concern.

2. *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). In addition to this action, a request to establish a tolerance in or on wine grapes, other petitions are pending for the following tolerances: pome fruit, livestock commodities, pecans, cotton, the crop subgroups leafy greens, leaf petioles, head and stem *Brassica* and leafy *Brassica* greens, and kiwifruit (import tolerance).

3. *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.

4. *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 future tolerances will utilize 20.1% of the RfD for the U.S. population and 52.0% for non-nursing infants under 1-year old. Using anticipate residue levels for these crops utilizes 3.38% of the RfD for the U.S. population and 12.0% for non-nursing infants. 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 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. 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 grapes and proposed an MRL (Step 3) of 0.5 mg/kg.

3. Valent U.S.A. Corporation

PP 6F4737

EPA has received a pesticide petition (PP 6F4737) 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 of pyriproxyfen, 2-[1-methyl-2-(4-phenoxyphenoxy) ethoxy) ethoxy] pyridine in or on the raw agricultural commodity cottonseed at 0.05 ppm and cotton gin byproducts at 2.0 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—Nature of the residues in food, feed and secondary residues.* The residue of concern is best defined as the parent, pyriproxyfen.

The nature of the residues in cotton, apples, and animals is adequately understood. Metabolism of ^{14}C-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 residue 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 ^{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— Pyriproxyfen and metabolites.* Practical analytical methods for detecting and measuring levels of pyriproxyfen (and relevant metabolites) have been developed and validated in cotton raw agricultural commodities, respective processing fractions, animal tissues, and environmental samples. The methods have been independently validated in cottonseed, apples, soil, and oranges and the extraction methodology has been validated using aged radiochemical residue samples from metabolism studies. EPA has successfully validated the analytical method for analysis of cottonseed raw agricultural commodity (personal communication). 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 proposed for the tolerances.

3. *Magnitude of residues*— i. *Cotton.* Data from fifteen field trials in cotton conducted in 1994 and 1995, showed that mean pyriproxyfen residues from duplicate samples were <0.01 - 0.04 ppm in cottonseed, and 0.35 - 2.3 ppm in gin trash, following two or three treatments totaling 80 grams active ingredient per acre at 14 day intervals with a 28 day pre-harvest interval. The seasonal use rate tested in the residue trials was approximately 2.6 times the maximum seasonal use rate presently proposed for cotton in the pending KNACK® Insect Growth Regulator label. No concentration of residues was observed from processing cottonseed treated with an 12.8 x application rate into hulls, meal, crude oil or refined oil.

ii. *Secondary residues.* Since low residues were detected in cotton derived animal feed items and since 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.

iii. *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. *Genotoxicity.* 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 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 body weight/day (bw/day) and greater. The maternal NOEL 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 NOEL 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 NOEL 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 NOEL was 100 mg/kg bw/day. No developmental effects were observed in the rabbit fetuses. The NOEL 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 two 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 NOEL 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 HDT.

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 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 four week inhalation study of pyriproxyfen technical in rats, decreased body weight and increased water consumption were observed at 1,000 mg/m^3. The NOEL 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. In a 21-day dermal study conducted with KNACK® Insect Growth Regulator the test material produced a NOEL of 1,000 mg/kg bw/day (HDT) for systemic effects, and a NOEL 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 RfD for pyriproxyfen of 0.35 mg/kg bw/day, based on the NOEL in female rats from the two 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 two-year chronic feeding/oncogenicity study or in a seventy-eight 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 one 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 NOEL 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 NOEL 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 LOEL 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 two-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 bw/day in males, 35.1 mg/kg bw/day in females). A LOEL 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 mammalian metabolism of pyriproxyfen is understood. 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 the 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. Seven days after dosing, tissue residues were low, 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 mammalian endocrine systems. 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 Sumilarv does not possess estrogenic or endocrine disrupting properties applicable to mammals.

C. Aggregate Exposure

1. *Dietary exposure*. EPA has established a RfD for pyriproxyfen of 0.35 mg/kg bw/day, based on the rat 2 year chronic/oncogenicity study and a safety factor of 100. The chronic dietary risk can be evaluated using this endpoint. 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 bw/day as the short term study with the lowest exposure endpoint. This figure will be used for all acute and short term risk analyses.

2. *Food*. Chronic and acute dietary exposure analyses have been performed for pyriproxyfen using (proposed) tolerance level and anticipated residues and 100% of the crop treated. Included in the analyses are cottonseed, cotton gin trash and secondary residues in meat, milk, and eggs. These exposure/risk analyses have been submitted to the Agency along with a detailed description of the methodology and assumptions used.

i. *Chronic*. Long term dietary exposure was calculated for the U.S. population and 26 population subgroups. The results from several

representative subgroups are listed below. The highest exposed sub-population, Children (1 - 6 Years) with tolerance level exposure, showed an occupancy of the RfD of 0.03%. In all other cases, chronic dietary exposure was below 0.03 % of the RfD.

POTENTIAL CHRONIC DIETARY EXPOSURE TO PYRIPROXYFEN RESIDUES

Population Subgroup	Exposure (mg/kg bw/day)	
	Tolerances	Anticipated
U.S.population - 48 States - All seasons	0.000026	0.000016
U.S. population - Autumn season	0.000027	0.000017
Midwest Region	0.000030	0.000018
All infants	0.000049	0.000030
Non-nursing infants (<1 year old)	0.000065	0.000040
Children (1 - 6 years)	0.000095	0.000058
Females (13+/pregnant/not nursing)	0.000025	0.000015

ii. *Acute*. A tier 2 acute dietary exposure analysis assuming 100% of crop treated was performed for the U.S. population and six subgroups -- All Infants, Non-Nursing Infants (<1 Year), Children 1-6, Children 7-12, Females 13-50, and males 20+. The calculated exposures are all very low, ranging from 0.000002 to 0.000018 mg/kg bw/day, for the higher exposed proportions, 95 th and 99.9 th percentiles, of the subgroups. It should be noted that the population sizes are small at the lower probability exposures (e.g. 99 th and 99.9 th percentiles) oftentimes leading to unrealistically high calculated exposures. In all cases, MOEs to pyriproxyfen residues exceed one-million.

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

i. *Ground water*. Pyriproxyfen is extremely insoluble in water (0.367 mg/L at 25°C), with high octanol/water partitioning coefficient (Log P o/w = 5.37 at 25°C), 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.

ii. *Surface water*. In connection with the potential for dietary exposure from surface potable water, a simulation of expected environmental concentration (EEC) values in aquatic systems has been performed using the Pesticide Root Zone Model (PRZM-2.3) and the Exposure Analysis Modeling System, version 2.95 (EXAMSII). The simulation was designed to approximate as closely as possible the conditions associated with two aerial applications totaling 0.084 lb. a.i. per acre to cotton with a 28-day interval. This use pattern exceeds the presently proposed use pattern by approximately 1.2 x. The results of the modeling estimate that the maximum upper tenth percentile concentrations modeled in water adjacent to treated fields are instantaneous, 0.23 ppb; 96-hour, 0.14 ppb; and 21 day, 0.08 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 (static, stagnant farm ponds) adjacent to treated cotton fields. Standard, conservative exposure assumptions of body weight and water consumption (adult 70 kg, 2 kg water per day; child 10 kg, 1 kg water) will be used.

iii *Chronic*. The 21 day concentration, 0.08 ppb (0.00008 mg/kg), is used to represent chronic exposure. The highest possible exposure would be 2.3×10^{-6} and 8×10^{-6} mg/kg bw/day for an adult and child, respectively. This very small, but probably exaggerated, exposure would occupy 0.00065 (adult) and 0.0023 (child) percent of the chronic RfD of 0.35 mg/kg bw/day.

iv. *Acute*. The modeled instantaneous concentration of 0.23 ppb (0.00023 mg/kg), can be used to represent potential acute exposure to pyriproxyfen in surface source drinking water. A corresponding calculation shows that the maximum acute exposure would be 6.6×10^{-6} and 2.3×10^{-5} mg/kg bw/day for the adult and child, respectively. When compared to the short term endpoint of 23.5 mg/kg bw/day, MOEs for both adults and children exceed one million.

4. *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.

This non-dietary exposure assessment for pyriproxyfen conservatively focuses on upper-bound estimates of potential applicator (adult) and post-application (adult and child - less than one 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 estimates exposures for selected consumer uses that are 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 applicator exposures (dermal and inhalation), and post-application adult (inhalation) and child (inhalation, dermal, incidental oral ingestion associated with hand-to-mouth behavior) exposures associated with consumer use of an aerosol carpet spray product.

The risk analyses use a combination of representative models. Information from the pesticide handlers exposure data base (PHED) was used to estimate exposures to applicators (adult). Surrogate data from a study of exposure to indoor broadcast applications were used to calculate a series of absorbed dose estimates 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}
		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. Application exposures on non-application days would be zero.

Further, the Agency has not identified acute or short term toxicity endpoints of concern for oral inhalation or dermal exposure. Endpoints that could be considered for short term and intermediate exposures include developmental toxicity NOEL values of 100 mg/kg bw/day (rat and rabbit), rat 21-day dermal systemic NOEL values of 1,000 mg/kg bw/day (technical grade and end-use product), a four week rat inhalation toxicity NOEL of 482 mg/m^3, and, the endpoint chosen by Valent to be used in these analyses, the 90-day rat oral toxicity NOEL of 23.5 mg/kg bw/day. There are no dermal absorption data for pyriproxyfen.

The largest 1 day exposure is calculated for the applicator of the pet spray (0.085 mg/kg bw/day). This value 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 (1.5×10^{-3} mg/kg bw/day). Furthermore, the return frequency is much different. Label instructions allow treatment of the pet every 14-days during the flea season, while the carpet can be treated only each 120 days. The 1 day exposure is compared to the smallest short term endpoint choosen by Valent, the 90-day rat oral toxicity NOEL of 23.5 mg/kg bw/day, and a MOE can be calculated. This compares an acute, one day, dermal exposure to a sub-chronic 90-day dietary endpoint.

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

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

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

$MOE_{\text{Pet Spray Applicator}} = 3{,}900$

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 subsequent exposure must be less than exposure on the day of application.

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

There is usually no cause for concern if MOEs exceed 100. All other MOEs 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.

5. *Summary of acute and chronic 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.

i. *Acute and short term non-occupational exposures.* Potential acute and short term non-occupational exposures to pyriproxyfen are associated with food, water, and household uses -- applicator 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 MOE. Valent has identified the 90-day rat oral toxicity with a NOEL of 23.5 mg/kg bw/day as the short term study with the lowest exposure endpoint. In general, if exposure estimates are conservative and the resulting MOE values are greater than 100, the Agency has no cause for concern.

It is possible to sum calculated acute exposures from various sources as shown in the table below. However, summation is exceedingly conservative because the approach assumes that two or more low probability events occurr symultaneously. For example, it is highly unlikely that an individual consuming the 99.9th percentile dietary exposure (one-in-a-thousand), also treats a large dog for fleas, and consumes all drinking water from a pond surrounded by treated cotton fields in a single day. Even so, the short term non-occupational exposures shown below that sum exposures from food, drinking water and household uses of pyriproxyfen gives MOE values all much larger than 100. These calculated acute and short term exposures are very conservative, and are small enough to be of little significance.

AGGREGATE ACUTE EXPOSURE TO PYRIPROXYFEN FOR TWO REPRESENTATIVE U.S. POPULATIONS
(SUMMATION OF LOW PROBABILITY MAXIMUM VALUES)

Exposure Medium	Exposure (mg/kg bw/day)	
	U.S. Population (all seasons)	Non-Nursing Infant (less than 1 year)
Non-dietary	0.085	0.0015
Food	0.000012	0.000012
Drinking water	0.0000066	0.000023
Sum of acute exposures	0.0850186	0.001535
Margin of exposure	276	15,300

ii. *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 of 0.35 mg/kg bw/day. If the occupancy of the RfD is less than 100%, the Agency usually has little cause for concern. From the table, it can be seen that the total potential chronic exposure to pyriproxyfen is truly insignificant, and should not be cause for concern.

AGGREGATE CHRONIC EXPOSURE TO PYRIPROXYFEN FOR TWO REPRESENTATIVE U.S. POPULATIONS

Exposure Medium	Exposure (mg/kg bw/day)		
	U.S. Population (all seasons)	Non-Nursing Infant (less than 1 year)	Children (1 - 6 Years)
Food	0.000026	0.000065	0.000095
Drinking water	0.0000023	0.000008	0.000008
Sum of chronic exposures	0.0000283	0.000073	0.000103
Occupancy of RfD (percent)	0.0081	0.021	0.029

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 appear to be structurally, closely related to pyriproxyfen and may 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 EPA publications pursuant to the Food Quality Protection Act.

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 bw/day using the NOEL from the chronic rat feeding study and a 100-fold uncertainty factor.

i. *Chronic*. The aggregate chronic exposure to pyriproxyfen will utilize much less than 0.1% of the RfD for the U.S. population. Because estimated exposures are far below 100% of the RfD, Valent concludes that there is a reasonable certainty that no harm will result from chronic aggregate exposure to pyriproxyfen residues.

ii. *Acute*. Assessment of aggregate acute exposure to food and non-food uses of pyriproxyfen to the U.S. population and numerous subpopulations has demonstrated that exposures are small. MOE values using very conservative assumptions and a conservative toxicity endpoint are all greater than 100 and it can be concluded that there is reasonable certainty of no harm from acute exposures to pyriproxyfen.

2. *Infants and children*— i. *Chronic*. 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 0.021% for Non-Nursing Infants, and 0.029% for Children (1 - 6 Years), the most highly exposed child population subgroup. Because estimated exposures to infants and children are far below 100% of the RfD, Valent concludes that there is a reasonable certainty that no harm will result from chronic aggregate exposure to pyriproxyfen residues.

ii. *Acute*. Assessment of aggregate acute exposure to food and non-food uses of pyriproxyfen to infants and children has demonstrated that exposures allow calculation of acceptable MOE values. Using very conservative assumptions and a

conservative toxicity endpoint are all MOE values are greater than 100. Therefore, it can be concluded that there is reasonable certainty of no harm to infants and children from potential acute exposures to pyriproxyfen.

3. *Additional safety factor to provide additional protection to infants and children*. Pyriproxyfen is supported by a complete, reviewed and reliable toxicology database. 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 unique pathology or other effects to fetal or developing young experimentsl animals. In all these studies there is no indication that young or developing animals are any more sensitive to toxicity from pyriproxyfen or its metabolites than adult animals. The developmental toxicity studies and reproduction study all demonstrated that any toxicity attributable to pyriproxyfen was observed in adults at lower levels than in fetuses or in developing young animals. There is no indication that a higher safety factor, other than 100, is needed for additional protection for infants and children.

F. International Tolerances

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

[FR Doc. 98–5985 Filed 3–5–98; 8:45 am]

BILLING CODE 6560–50–F

ENVIRONMENTAL PROTECTION AGENCY

[FRL–5972–6]

Rhode Island Marine Sanitation Device Standard; Receipt of Petition

Notice is hereby given that a petition has been received from the State of Rhode Island requesting a determination from the Regional Administrator, U.S. Environmental Protection Agency, pursuant to section 312(f)(3) of Pub. L. 92–500 as amended by Pub. L. 95–217 and Pub. L. 100–4, that adequate facilities for the safe and sanitary removal and treatment of sewage from all vessels are reasonably available for all waters within the 3 mile territorial limit of Rhode Island's coastline and all coastal shore ponds which would include Point Judith and Potter Ponds, Quonochontaug Pond, Ninigret and Green Hill Ponds, Winnapaug Pond, the Pawcatuck River and also within the 3 mile territorial waters surrounding Block Island. The areas covered under this petition include Latitude 71°22′55″ Longitude 41°53′36″ at the Providence River, Latitude 71°13′09″, 71°12′18″ Longitude 41°42′11″, 41°41′09″ in Mount Hope Bay, Latitude 71°07′04″, Longitude 41°26′25″ at the Massachusetts state border, and Latitude 71°55′48″ Longitude 41°16′40″ at the Connecticut border.

The State of Rhode Island has certified that there are forty-three disposal facilities available to service vessels operating in the marine waters of Rhode Island. A list of the facilities, phone numbers, locations, and hours of operation is appended at the end of this petition. Six additional facilities are pending or under construction. Of the forty-three facilities, thirty-eight are fixed shore based facilities, one is a mobile cart, and four are pump-out boats. Fourteen of the thirty-eight fixed, shore based facilities discharge to holding tanks. The other twenty-four discharge directly to municipal sewerage systems. The four pump-out boats also discharge to the sewer. In addition there are shoreside restrooms at all of the marinas as mandated by § 300.4 of the Rhode Island Coastal Resources Management Program Rules and Regulations.

Rhode Island mandates that all fixed facilities connect to available sewers, and holding tanks will ONLY be approved in locations where direct connection to an existing sewer system is not possible. The facilities which use holding tanks for boater wastes are required to use licensed septage haulers who must abide by § 6.00 of the Rules and Regulations set forth by the Division of Waste Management, Department of Environmental Management. The state conducts periodic inspections for the purpose of record keeping and facility evaluation to assure pump-out facilities are operational and functioning.

The pump-out facilities are capable of evacuating and discharging at head differentials of 25 feet. The capacity of the holding tanks is 5,000 gallons as recommended under Rhode Island's Clean Vessel Act grant guidelines. The tanks are fitted with alarms that activate to ensure waste removal before the capacity is reached.

There are 31,608 boats registered with the Rhode Island Department of Environmental Management Boating Office, 27,697 of which are recreational and 3,911 of which are commercial. Rhode Island estimates there are 11,203 registered boats larger than 20 feet and approximately 5,033 transient boats larger than 20 feet. Rhode Island calculates that approximately 16,236 boats use pump-outs in their marine waters.

In 1985 the Environmental Protection Agency designated Narragansett Bay as an ''estuary of national significance''. The Narragansett Bay Comprehensive Conservation and Management Plan recommends that the Bay become a No Discharge Area to achieve greater water quality protection. The area supports 25 State parks, 160 marinas, and approximately 1.3 million visits are made to bayside beaches each year. Nearly 300,000 residents and nonresidents participate in recreational and commercial fishing.

Comments and reviews regarding this request for action may be filed on or before May 5, 1998. Communications or requests for information should be addressed to Ann Rodney, U.S. Environmental Protection Agency—New England Region, Office of Environmental Protection, Water Quality Unit (CWQ), JFK Federal Building, Boston, MA 02203. *Telephone:* 617–565–4885.

Dated: February 23, 1998.

John P. DeVillars,

Regional Administrator.

PUMP-OUT FACILITIES AVAILABLE IN RHODE ISLAND WATERS

Marina name	Number	Water body	Hours of operation
City of Providence	454–4447	Seekonk River	F–Su 10 am–9:30 pm/M–Th 10 am–8 pm.
Bootlegger Marina	273–2444	Seekonk River	F–Su 10 am–9:30 pm/M–Th 10 am–8 pm.
Edgewood Yacht Club	466–1000/ext: 3245	Providence River	24 Hours.
Port Edgewood Marina	941–2000	Providence River	24 Hours.
Pawtuxet Cove Marina	941–2000	Providence River	24 Hours.
Rhode Island Yacht Club	941–0220	Providence River	24 Hours.