infants/children. The EECs for chronic analysis of water are 0.3 µg/L (ground water) and 10 µg/L (surface water). EPA does not expect the chronic aggregate exposure to exceed 100% of the chronic RfD. Therefore, EPA has concluded with reasonable certainty that no harm will result from chronic (non-cancer) aggregate exposure to tebuconazole residues.

2. *Non-dietary exposure*. Tebuconazole is currently registered for use on the following residential non-food sites: the formulation of wood-based composite products, wood products for in-ground contact, plastics, exterior paints, glues and adhesives. EPA has determined (64 FR 1132) that exposure via incidental ingestion (by children) and inhalation are not a concern for these products which are used outdoors. No paints or other end-use products containing tebuconazole are available for interior use. Therefore, EPA has determined that no risk is expected for residential nonfood sites.

D. Cumulative Effects

Tebuconazole is a member of the triazole class of systemic fungicides which included other triazoles such as bitertanol, cyproconazole, diclobutrazole, difenoconazole, diniconazole, fenbuconazole, flusilazole, hexaconazole, myclobutanil, penconazole, propiconazole, tetraconazole, triadimefon, and triadimenol. At this time, the EPA has not made a determination that tebuconazole and other substances that may have a common mechanism of toxicity would have cumulative effects. Therefore, for these tolerance petitions, it is assumed that tebuconazole does not have a common mechanism of toxicity with other substances and only the potential risks of tebuconazole in its aggregate exposure are considered.

E. Safety Determination

1. *U.S. population*. Based on the exposure assessments described above under Unit C. Aggregate Exposure and on the completeness and reliability of the toxicity data, it can be concluded that aggregate exposure estimates from all label and pending uses of tebuconazole are 36.49% of the aPAD and 0.1% of the cPAD for dietary exposures. Since EPA found no concern from drinking water or non-dietary exposure (64 FR 1132), it can be concluded with reasonable certainty that the potential risks to the overall U.S. population would not exceed the Agency's level of concern.

2. *Infants and children*. In assessing the potential for additional sensitivity of infants and children to residues of tebuconazole, data from developmental toxicity studies in mice, rats, rabbits and a 2-generation reproduction study in the rat are considered. The developmental toxicity studies are designed to evaluate adverse effects on the developing organism resulting from maternal pesticide exposure during gestation. Reproduction studies provide information relating to effects from exposure to the pesticide on the reproductive capability of mating animals and data on systemic toxicity.

Using the conservative exposure assumptions described above under Unit C. Aggregate Exposure, it can be concluded that the aggregate dietary exposure estimates from the proposed uses of tebuconazole would not exceed 70.20% of the aPAD and 0.3% of the cPAD for the most sensitive population subgroup children (1-6 years). Since EPA found no concern from drinking water or non-dietary exposure (64 FR 1132), it can be concluded with reasonable certainty that the potential risks to infants and children would not exceed the Agency's level of concern.

F. International Tolerances

There are no established Codex or Canadian Maximum Residue Levels (MRLs) for tebuconazole. A Mexican MRL has been established on barley for tebuconazole.

[FR Doc. 01–6711 Filed 3–16–01; 8:45 a.m.]

BILLING CODE 6560–50–S

ENVIRONMENTAL PROTECTION AGENCY

[PF–997; FRL–6766–7]

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

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

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

DATES: Comments, identified by docket control number PF–000, must be received on or before April 18, 2001.

ADDRESSES: Comments may be submitted by mail, electronically, or in person. Please follow the detailed instructions for each method as provided in Unit I.C. of the **SUPPLEMENTARY INFORMATION**. To ensure proper receipt by EPA, it is imperative that you identify docket control number PF–000 in the subject line on the first page of your response.

FOR FURTHER INFORMATION CONTACT: By mail: Joseph Tavano, Registration Support Branch, Registration Division (7505C), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460; telephone number: (703) 305–6411; e-mail address: tavano.joseph@epa.gov.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

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

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

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

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

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

2. *In person*. The Agency has established an official record for this

action under docket control number PF–000. The official record consists of the documents specifically referenced in this action, any public comments received during an applicable comment period, and other information related to this action, including any information claimed as confidential business information (CBI). This official record includes the documents that are physically located in the docket, as well as the documents that are referenced in those documents. The public version of the official record does not include any information claimed as CBI. The public version of the official record, which includes printed, paper versions of any electronic comments submitted during an applicable comment period, is available for inspection in the Public Information and Records Integrity Branch (PIRIB), Rm. 119, Crystal Mall #2, 1921 Jefferson Davis Highway, Arlington, VA, from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The PIRIB telephone number is (703) 305–5805.

C. How and to Whom Do I Submit Comments?

You may submit comments through the mail, in person, or electronically. To ensure proper receipt by EPA, it is imperative that you identify docket control number PF–000 in the subject line on the first page of your response.

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

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

3. *Electronically.* You may submit your comments electronically by e-mail to: opp-docket@epa.gov, or you can submit a computer disk as described above. Do not submit any information electronically that you consider to be CBI. Avoid the use of special characters and any form of encryption. Electronic submissions will be accepted in Wordperfect 6.1/8.0 or ASCII file format. All comments in electronic form must be identified by docket control number PF–000. Electronic comments may also be filed online at many Federal Depository Libraries.

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

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

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

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

1. Explain your views as clearly as possible.

2. Describe any assumptions that you used.

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

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

5. Provide specific examples to illustrate your concerns.

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

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

II. What Action is the Agency Taking?

EPA has received a pesticide petition as follows proposing the establishment and/or amendment of regulations for residues of a certain pesticide chemical 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 this petition contains 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 support granting of the petition. Additional data may be needed before EPA rules on the petition.

List of Subjects

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

Dated: February 26, 2001.

James Jones,

Director, Registration Division, Office of Pesticide Programs.

Summary of Petitions

Petitioner summaries of the pesticide petitions are printed below as required by section 408(d)(3) of the Federal Food, Drug, and Cosmetic Act (FFDCA). The summaries of the petitions were prepared by the petitioner and represent the view of the petitioner. 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. Rohm and Haas Company

PP 0F6176

EPA has received a pesticide petition (0F6176) from Rohm and Haas Company, 100 Independence Mall West, Philadelphia, PA 19106–02399 proposing, pursuant to section 408(d) of the FFDCA, 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-(4-4-ethylbenzoyl) hydrazide in or on the raw agricultural commodity citrus crop group (Crop Group 10) at 0.8 parts per million (ppm) and in or on citrus oil at 15 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. *Nature of the residue—Plants.* The qualitative nature of the residue in plants is adequately understood based

upon acceptable apple, sugar beet, and rice metabolism studies. The Agency has concluded that the residue of regulatory concern is tebufenozide *per se*.

2. *Nature of the residue—Animal*. The results of the ruminant and poultry metabolism studies have been reviewed by the Agency and the determination was made that the tebufenozide residues of regulatory concern in animals are the parent tebufenozide and the four metabolites designated: RH-2703 [benzoic acid, 3,5-dimethyl-1-(1,1-dimethylethyl)-2-((4-carboxymethyl)benzoyl)hydrazide], RH-9886 [benzoic acid, 3-hydroxymethyl,5-methyl-1-(1,1-dimethylethyl)-2-(4-ethylbenzoyl)hydrazide], the stearic acid conjugate of RH-9886, and RH-0282 [benzoic acid, 3-hydroxymethyl-5-methyl-1-(1,1-dimethylethyl)-2-(4-(1-hydroxyethyl) benzoyl)hydrazide].

3. *Analytical method*— i. *Plant tissues*. Rohm and Haas method TR 34-96-184, with minor modifications, was used to determine tebufenozide residue levels in/on lemons, grapefruit and oranges. This method was independently validated. 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 (LOQ) of the method for all matrices is 0.02 ppm for tebufenozide and the limit of detection (LOD) is 0.006 ppm.

ii. *Animal tissues*. A submitted high performance liquid chromotography (HPLC/UV) Method, Rohm and Haas Method TR 34-96-109, has been determined to be adequate for collecting data on residues of tebufenozide in animal tissues. The validated LOQ for tebufenozide in animal tissue is 0.02 ppm. The LOQ for each of the metabolites studied are as follows: RH-2703 in liver, 0.02 ppm; RH-9886 and RH-0282 in meat, 0.02 ppm; RH-9526 in fat, 0.02 ppm. The LODs for the analytes are 0.006 ppm in tissues.

iii. *Multi-residue methods*. Rohm and Haas has previously submitted data involving multi-residue method testing.

a. *Magnitude of residues*. Field residue trials were conducted in the representative citrus fruit crops lemons, grapefruit and oranges and residues of tebufenozide were measured in whole fruit, peel and fresh pulp. The highest average field trial residue observed was in oranges at 047 ppm. Results of analyses showed that residues of tebufenozide will not exceed 0.8 ppm in whole fruit. Residues were found to be mainly associated in the peel and not in the fresh pulp.

b. *Processed food/feed*. Grapefruit and orange processing studies were conducted. Residues of tebufenozide did not concentrate in dry pulp or juice. Residues of tebufenozide concentrated in citrus oil. The average concentration factor for citrus oil was determined to be 26. The Highest Average Field Trial residue was in oranges at 0.47 ppm. Residues of tebufenozide in citrus oil should not exceed 15 ppm (rounded up from 0.47 ppm X 26).

B. Toxicological Profile

1. *Acute toxicity*. Acute toxicity studies with technical grade: Oral LD_{50} in the rat is > 5 grams for males and females - Toxicity Category IV; dermal LD_{50} in the rat is = 5,000 milligram/kilogram (mg/kg) for males and females - Toxicity Category III; inhalation LD_{50} in the rat is > 4.5 mg/l - Toxicity Category III; primary eye irritation study in the rabbit is a non-irritant; primary skin irritation in the rabbit > 5 mg - Toxicity Category IV. Tebufenozide is not a sensitizer.

In a 21-day dermal toxicity study, Crl: CD rats (6/sex/dose) received repeated dermal administration of either the technical 96.1% product RH-75,992 at 1,000 mg/kg/day Limit-Dose or the formulation 23.1% a.i. product RH-755,992 2F at 0, 62.5, 250, or 1,000 mg/kg/day, 6 hours/day, 5 days/week for 21 days. Under conditions of this study, RH-75,992 Technical or RH-75,992 2F demonstrated no systemic toxicity or dermal irritation at the highest dose tested 1,000 mg/kg/ during the 21-day study. Based on these results, the NOAEL for systemic toxicity and dermal irritation in both sexes is 1,000 mg/kg/day highest dose tested (HDT). A lowest-observable-effect level (LOAEL) for systemic toxicity and dermal irritation was not established.

2. *Genotoxicity*. Several mutagenicity tests which were all negative. These include an Ames assay with and without metabolic activation, an *in vivo* cytogenetic assay in rat bone marrow cells, and *in vitro* chromosome aberration assay in CHO cells, a CHO/HGPRT assay, a reverse mutation assay with *E. Coli*, and an unscheduled DNA synthesis assay (UDS) in rat hepatocytes.

3. *Reproductive and developmental toxicity*. In a prenatal developmental toxicity study in Sprague-Dawley rats 25/group Tebufenozide was administered on gestation days 6-15 by gavage in aqueous methyl cellulose at dose levels of 50, 250, or 1,000 mg/kg/day and a dose volume of 10 ml/kg. There was no evidence of maternal or developmental toxicity; the maternal and developmental toxicity NOAEL was 1,000 mg/kg/day.

In a prenatal developmental toxicity study conducted in New Zealand white rabbits 20/group Tebufenozide was administered in 5 ml/kg of aqueous methyl cellulose at gavage doses of 50, 250, or 1,000 mg/kg/day on gestation days 7-19. No evidence of maternal or developmental toxicity was observed; the maternal and developmental toxicity NOAEL was 1,000 mg/kg/day.

In a 1993 two-generation reproduction study in Sprague-Dawley rats tebufenozide was administered at dietary concentrations of 0, 10, 150, or 1,000 ppm (0, 0.8, 11.5, or 154.8 mg/kg/day for males and 0, 0.9, 12.8, or 171.1 mg/kg/day for females). The parental systemic NOAEL was 10 ppm (0.8/0.9 mg/kg/day for males and females, respectively) and the LOAEL was 150 ppm (11.5/12.8 mg/kg/day for males and females, respectively) based on decreased body weight, body weight gain, and food consumption in males, and increased incidence and/or severity of splenic pigmentation. In addition, there was an increased incidence and severity of extra-medullary hematopoiesis at 2,000 ppm. The reproductive NOAEL was 150 ppm. (11.5/12.8 mg/kg/day for males and females, respectively) and the LOAEL was 2,000 ppm (154.8/171.1 mg/kg/day for males and females, respectively) based on an increase in the number of pregnant females with increased gestation duration and dystocia. Effects in the offspring consisted of decreased number of pups per litter on postnatal days 0 and/or 4 at 2,000 ppm (154.8/171.1 mg/kg/day for males and females, respectively) with a NOAEL of 150 ppm (11.5/12.8 mg/kg/day for males and females, respectively).

In a 1995 two-generation reproduction study in rats tebufenozide was administered at dietary concentrations of 0, 25, 200, or 2,000 ppm (0, 1.6, 12.6, or 126.0 mg/kg/day for males and 0, 1.8, 14.6, or 143.2 mg/kg/day for females). For parental systemic toxicity, the NOAEL was 25 ppm (1.6/1.8 mg/kg/day in males and females, respectively), and the LOAEL was 200 ppm (12.6/14.6 mg/kg/day in males and females), based on histopathological findings (congestion and extra-medullary hematopoiesis) in the spleen. Additionally, at 2,000 ppm (126.0/143.2 mg/kg/day in M/F), treatment-related findings included reduced parental body weight gain and increased incidence of hemosiderin-laden cells in the spleen. Columnar changes in the vaginal squamous epithelium and reduced uterine and ovarian weights were also observed at

2,000 ppm, but the toxicological significance was unknown. For offspring, the systemic NOAEL was 200 ppm. (12.6/14.6 mg/kg/day in males and females), and the LOAEL was 2,000 ppm (126.0/143.2 mg/kg/day in M/F) based on decreased body weight on postnatal days 14 and 21.

4. *Subchronic toxicity*. A 1-year dog feeding study with a (LOAEL) of 250 ppm, 9 mg/kg/day for male and female dogs based on decreases in RBC, HCT, and HGB, increases in Heinz bodies, methemoglobin, MCV, MCH, reticulocytes, platelets, plasma total bilirubin, spleen weight, and spleen/body weight ratio, and liver/body weight ratio. Hematopoiesis and sinusoidal engorgement occurred in the spleen, and hyperplasia occurred in the marrow of the femur and sternum. The liver showed an increased pigment in the Kupffer cells. The no-observed effect level (NOAEL) for systemic toxicity in both sexes is 50 ppm (1.9 mg/kg/day).

5. *Chronic toxicity*. An 18-month mouse carcinogenicity study with no carcinogenicity observed at dosage levels up to and including 1,000 ppm.

A 2-year rat carcinogenicity with no carcinogenicity observed at dosage levels up to and including 2,000 ppm (97 mg/kg/day and 125 mg/kg/day for males and females, respectively).

6. *Animal metabolism*. The pharmacokinetics and metabolism of tebufenozide were studied in female Sprague-Dawley rats (3-6/sex/group) receiving a single oral dose of 3 or 250 mg/kg of RH-5992 ^{14}C labeled in one of three positions (A-ring, B-ring or N-butyl carbon). The extent of absorption was not established. The majority of the radio labeled material was eliminated or excreted in the feces within 48 hours within 48 hours; small amounts (1 to 7% of the administered dose) were excreted in the urine and only traces were excreted in expired air or remained in the tissues. There was no tendency for bioaccumulation. Absorption and excretion were rapid. A total of 11 metabolites, in addition to the parent compound, were identified in the feces; the parent compound accounted for 96 to 99% of the administered radioactivity in the high dose group and 35 to 43% in the low dose group. No parent compound was found in the urine; urinary metabolites were not characterized. The identity of several fecal metabolites was confirmed by mass spectral analysis and other fecal metabolites were tentatively identified by cochromatography with synthetic standards. A pathway of metabolism was proposed based on these data. Metabolism proceeded primarily by oxidation of the three benzyl carbons, two methyl groups on the B-ring and an ethyl group on the A-ring to alcohols, aldehydes or acids. The type of metabolite produced varies depending on the position oxidized and extent of oxidation. The butyl group on the quaternary nitrogen also can be cleaved (minor), but there was no fragmentation of the molecule between the benzyl rings. No qualitative differences in metabolism were observed between sexes, when high or low dose groups were compared or when different labeled versions of the molecule were compared.

The absorption and metabolism of tebufenozide were studied in a group of male and female bile-duct cannulated rats. Over a 72 hour period, biliary excretion accounted for 30%[M] to 34%[F] of the administered dose while urinary excretion accounted for about 5% of the administered dose and the carcass accounted for <0.5% of the administered dose for both males and females. Thus systemic absorption (percent of dose recovered in the bile, urine and carcass) was 35%[M] to 39%[F]. The majority of the radioactivity in the bile (20%[M] to 24%[F] of the administered dose) was excreted within the first 6 hours post-dosing indicating rapid absorption. Furthermore, urinary excretion of the metabolites was essentially complete within 24 hours post-dosing. A large amount [67%[F] to 70%[M]] of the administered dose was unabsorbed and excreted in the feces by 72 hours. Total recovery of radioactivity was 105% of the administered dose.

7. *Metabolite toxicology*. A total of 13 metabolites were identified in the bile; the parent compound was not identified, i.e. unabsorbed compound, nor were the primary oxidation products seen in the feces in the pharmacokinetics study. The proposed metabolic pathway proceeded primarily by oxidation of the benzylic carbons to alcohols, aldehydes or acids. Bile contained most of the other highly oxidized products found in the feces. The most significant individual bile metabolites accounted for 5% to 18% of the total radioactivity (F and/or M). Bile also contained the previously undetected (in the pharmacokinetics study) ''A'' Ring ketone and the ''B'' Ring diol. The other major components were characterized as high molecular weight conjugates. No individual bile metabolite accounted for 5% of the total administered dose. Total bile radioactivity accounted for about 17% of the total administered dose.

No major qualitative differences in biliary metabolites were observed between sexes. The metabolic profile in the bile was similar to the metabolic profile in the feces and urine.

8. *Short- and intermediate-term toxicity*. No dermal or systemic toxicity was seen in rats receiving 15 repeated dermal applications of the technical (97.2%) product at 1,000 mg/kg/day (Limit- Dose) as well as a formulated (23% a.i) product at 0, 62.5, 250, or 1,000 mg/kg/day over a 21-day period. In spite of the hematological effects seen in the dog study, similar effects were not seen in the rats receiving the compound via the dermal route indicating poor dermal absorption. Also, no developmental endpoints of concern were evident due to the lack of developmental toxicity in either rat or rabbit studies. This risk is considered to be negligible.

C. Aggregate Exposure

1. *Dietary exposure*—i. *Food— From food and feed uses*. Tolerances have been established (40 CFR 180.482) for the residues of tebufenozide, in or on a variety of raw agricultural commodities. The current petition requests establishment of tolerances in or on the crop group Citrus Fruit at 0.8 ppm and in citrus oil at 15 ppm. Risk assessments were conducted by Rohm and Haas to assess dietary exposures and risks from tebufenozide, benzoic acid, 3,5-dimethyl-1-(1,1-dimethylethyl)-2-(4-ethylbenzoyl) hydrazide as follows:

a. *Acute exposure and risk*. Acute dietary risk assessments are performed for a food-use pesticide if a toxicological study has indicated the possibility of an effect of concern occurring as a result of a one day or single exposure. Neither neurotoxicity nor systemic toxicity was observed in rats given a single oral administration of tebufenozide at 0, 500, 1,000 or 2,000 mg/kg. No maternal or developmental toxicity was observed following oral administration of tebufenozide at 1,000 mg/kg/day (Limit-Dose) during gestation to pregnant rabbits. This risk is considered to be negligible.

b. *Chronic exposure and risk*. The RfD used for the chronic dietary analysis is 0.018 mg/kg/day. In conducting the DEEM (Dietary Exposure Evaluation Model) analysis for chronic exposure to and risk from tebufenozide residues in food, Rohm and Haas used tolerance level residues for all crops and other commodities with established or pending tebufenozide tolerances; and percent crop-treated (PCT) information for some of these crops. The following tolerances were used: Citrus fruit at 0.8 ppm, citrus oil at 15 ppm, tree nut crop group at 0.1 ppm, pome fruit at 1.5 ppm, cotton at 1.5 ppm, leafy and cole crop groups ranging from 2.0 to 10.0 ppm,

turnip tops at 9.0 ppm, turnip roots at 0.25 ppm, canola seed at 1.75 ppm, canola oil at 3.75 ppm, mint at 10.0 ppm, fruiting vegetables at 1.0 ppm, sugarcane at 1.0 ppm, molasses at 0.6 ppm, cranberries at 1.0 ppm, berry crops at 3.0 ppm, imported kiwifruit at 1.0 ppm and imported wine grapes at 0.5 ppm, and the livestock commodities milk, meat and meat by-products ranging from 0.05 to 0.25 ppm. The % CT information utilized is found in Table 1 below:

TABLE 1.—MAXIMUM PERCENT CROP TREATED VALUES FOR VARIOUS CROPS UTILIZED IN CHRONIC DIETARY EXPOSURE ANALYSES

Crop	Maximum PCT (Percent)
Cranberries	100
Kiwifruit	100
Canola	100
Mint	100
Grapes	100
Citrus	100
Meat, Meat By-Products, Milk	100
Sugarcane	82
Turnips	75
Pecans	40
Walnuts	30
Berry Crops	25
Cotton	19
Cole Crop Vegetables	18
Almonds	16
Leafy Vegetables	14
Pome Fruit	10
Fruiting Vegetables	10

The Novigen DEEM system (version 7.075) was used for this chronic dietary exposure analysis. The analysis evaluates individual food consumption as reported by respondents in the USDA Continuing Surveys of Food Intake by Individuals conducted in 1989 through 1992. Summaries of the exposures and their representations as percentages of the cPAD for the general population and subgroups of interest are presented in Table 2 below. The subgroups listed below are (1) the U.S. Population (48 states); (2) those for infants and children; and (3) the other subgroups (adult) for which the percentage of the RfD occupied is greater than that occupied by the subgroup U.S. Population (48 states). cPAD% is defined as Exposure X 100% divided by the cPAD. The results are summarized below in Table 2:

TABLE 2.—CHRONIC EXPOSURE ANALYSIS BY THE DEEM SYSTEM FOR TEBUFENOZIDE

Population	Exposure (mg/kg/day)	cPAD (Percent)
U.S. Population	0.0038	21.1
All Infants (< 1 year)	0.0041	23.0
Nursing Infants (< 1 year)	0.0023	12.9
Non-Nursing Infants (< 1 year)	0.0049	27.3
Children (1-6 years old)	0.0092	51.0
Children (7-12 years old)	0.0057	31.8
Females (13+ years, nursing)	0.0043	23.9
U.S. Population Autumn	0.0038	21.4
U.S. Population Winter	0.0039	21.9
Hispanics	0.0042	23.1
Non-Hispanic Blacks	0.0043	23.6
Non-Hispanic Other than Black or White	0.0049	27.5
Northeast Region	0.0042	23.1
Western Region	0.0042	23.5
Pacific Region	0.0043	24.1

This chronic dietary (food only) risk assessment should be viewed as conservative. Further refinement using anticipated residue values and additional PCT information would result in a lower estimate of chronic dietary exposure from food.

ii. *Drinking water*— a. *Acute exposure and risk*. Because no acute dietary endpoint was determined, Rohm and Haas concludes that there is a reasonable certainty of no harm from acute exposure from drinking water.

b. *Chronic exposure and risk*. The Agency calculated the Tier I Estimated Environmental Concentrations (EECs) for tebufenozide using generic expected environmental concentration (GENEEC) (surface water) and screening concentration in ground water (SCI-GROW) (ground water) models for use in the human health risk assessment. For chronic exposure, the worst case EECs for surface water and ground water were 16.5 parts per billion (ppb) and 1.04 ppb, respectively. These values represent upper-bound estimates of the concentrations that might be found in surface and ground water. These modeling data were compared to the chronic drinking water levels of comparison (DWLOC) for tebufenozide in ground and surface water.

For purposes of chronic risk assessment, the estimated maximum concentration for tebufenozide in surface and ground waters (16.5 ppb) was compared to the back-calculated human health DWLOCs for the chronic (non-cancer) endpoint. These DWLOCs for various population categories are summarized below in Table 3:

TABLE 3.—DRINKING WATER LEVELS OF COMPARISON FOR CHRONIC EXPOSURE TO TEBUFENOZIDE[1]

Population Category[2]	Chronic RfD (mg/kg/day)	Food exposure (mg/kg/day)	exposure Max. water (mg/kg/day)[3]	DWLOC (µg/L)[4,5,6]	EEC[7] calc. max. (µg/L) (in percent)
U.S. Population (48 contiguous states)	0.018	0.0038	0.0142	497	16.5
Females (13+ years)	0.018	0.0043	0.0137	411	16.5
Children (1-6 years)	0.018	0.0092	0.0088	88	16.5

[1] Values are expressed to 2 significant figures.
[2] Within each of these categories, the subgroup with the highest food exposure was selected.
[3] Maximum water exposure (chronic) (mg/kg/day) = Chronic PAD (mg/kg/day).
[4] DWLOC (µg/L) = Max. water exposure (mg/kg/day) x body wt (kg) divided by 10^{-3} mg/µg) x water consumed daily (L/day).
[5] HED Default body weights are: General U.S. population, 70 kg; females (13+ years old), 60 kg; other adult populations, 70 kg; and, all infants/children, 10 kg.
[6] HED Default daily drinking rates are 2 L/day for adults and 1 L/day for children.
[7] EEC: Estimated Environmental Concentration. (Chronic 56-day value).

2. *Non-dietary exposure*. There is a potential for occupational exposure to tebufenozide during mixing, loading, and application activities. However, the Agency did not identify dermal or inhalation endpoints for tebufenozide and determined that risks from these routes of exposure are negligible.

D. Cumulative Effects

Cumulative exposure to substances with a common mechanism of toxicity. Section 408(b)(2)(D)(v) requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider ''available information'' concerning the cumulative effects of a particular pesticide's residues and ''other substances that have a common mechanism of toxicity''. EPA does not have, at this time, available data to determine whether tebufenozide has a common mechanism of toxicity with other substances or how to include this pesticide in a cumulative risk assessment. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, tebufenozide does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance petition, Rohm and Haas has not assumed that tebufenozide has a common mechanism of toxicity with other substances.

E. Safety Determination

1. *U.S. population— aggregate risks and determination of safety for U.S. population*—i. *Acute risk*. The Agency did not identify an acute dietary toxicological endpoint, therefore, the risk from this route of exposure is negligible.

ii. *Chronic risk*. Using the exposure assumptions described above, and taking into account the completeness and reliability of the toxicity data, Rohm and Haas has concluded that dietary (food only) exposure to tebufenozide will utilize 21% of the cPAD for the U.S. population, and 51% of the cPAD for the most highly exposed population subgroup (children 1-6 years old). EPA generally has no concern for exposures below 100% of the cPAD. Submitted environmental fate studies suggest that tebufenozide is moderately persistent to persistent and mobile; thus, tebufenozide could potentially leach to ground water and runoff to surface water under certain environmental conditions. The modeling data for tebufenozide indicate levels less than the Agency's DWLOCs. There are no chronic non- occupational/residential exposures expected for tebufenozide. Therefore, the Rohm and Haas concludes that there is a reasonable certainty that no harm will result to adults, infants and children from chronic aggregate exposure to tebufenozide residues.

iii. *Short- and intermediate-term risk*. There are potential non-occupational/ residential short-term post application exposures (incidental non-dietary ingestion) to toddlers from the use of tebufenozide on ornamentals. However, since the Agency did not identify acute dietary endpoint, the short-term post application exposure risk assessment is expected to be negligible. Intermediate-term incidental non-dietary exposures are not expected.

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

2. *Infants and children—aggregate risk and determination of safety for infants and children*— i. *Safety factor for infants and children*. In assessing the potential for additional sensitivity of infants and children to residues of tebufenozide, EPA considered data from developmental toxicity studies in the rat and rabbit and a two-generation reproduction study in the rat. The developmental toxicity studies are designed to evaluate adverse effects on the developing organism resulting from maternal pesticide exposure gestation. Reproduction studies provide information relating to effects from exposure to the pesticide on the reproductive capability of mating animals and data on systemic toxicity.

FFDCA section 408 provides that EPA shall apply an additional tenfold margin of safety for infants and children in the case of threshold effects to account for pre- and post-natal toxicity and the completeness of the database unless EPA determines that a different margin of safety will be safe for infants and children. Margins of safety are incorporated into EPA risk assessments either directly through use of a MOE analysis or through using uncertainty (safety) factors in calculating a dose level that poses no appreciable risk to humans. EPA believes that reliable data support using the standard uncertainty factor (usually 100 for combined inter- and intra-species variability) and not the additional tenfold MOE/uncertainty factor when EPA has a complete data base under existing guidelines and when the severity of the effect in infants or children or the potency or unusual toxic properties of a compound do not raise concerns regarding the adequacy of the standard MOE/safety factor.

ii. *Conclusion*. There is a complete toxicity data base for tebufenozide and exposure data are complete or are estimated based on data that reasonably accounts for potential exposures. For the reasons summarized above, Rohm and Haas concludes that an additional safety factor is not needed to protect the safety of infants and children.

iii. *Acute risk*. Since no acute toxicological endpoints were established, it is unlikely that acute aggregate risk exists.

iv. *Chronic risk*. Using the exposure assumptions described above, and taking into account the completeness and reliability of the toxicity data, the Agency has concluded that dietary (food only) exposure to tebufenozide will utilize 21% of the cPAD for the U.S. population, and 51% of the cPAD for the most highly exposed population subgroup (children 1-6 years old). EPA generally has no concern for exposures below 100% of the cPAD. Despite the potential for exposure to tebufenozide in drinking water and from non-dietary, non- occupational exposure, Rohm and Haas does not expect the aggregate exposure to exceed 100% of the RfD.

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

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

F. International Tolerances

Codex MRLs have been established for residues of tebufenozide in/on pome fruit (1.0 ppm), husked rice (0.1 ppm) and walnuts (0.05 ppm). Tebufenozide is registered in Canada, and a tolerance for residues in/on apples is established at 1.0 ppm. EPA has set the pome fruit tolerance at 1.5 ppm based on U.S. field residue trials.

2. Rohm and Haas Company

PP 0F6201

EPA has received a pesticide petition (0F6201) 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 (FFDCA), 21 U.S.C. 346a(d), to amend 40 CFR part 180 by establishing time-limited tolerances for indirect or inadvertent residues of methoxyfenozide [benzoic acid, 3-methoxy-2-methyl-, 2–(3,5-dimethylbenzoyl)-2–(1,1-dimethylethyl) hydrazide] and its metabolites RH–117,236 (free phenol of methoxyfenozide; 3,5-dimethylbenzoic

acid N-tert-butyl-N'-(3-hydroxy- 2-methylbenzoyl) hydrazide), RH–151,055 (the glucose conjugate of RH–117,236; 3,5-dimethylbenzoic acid N-tert- butyl-N–[3(-D-glucopyranosyloxy)-2-methylbenzoyl]-hydrazide) and RH–152,072 (the malonylglycosyl conjugate of RH–117,236) in or on the raw agricultural commodities root and tuber vegetables at 0.05 parts per million (ppm); leaves of root and tuber vegetables at 0.1 ppm; bulb vegetables at 0.1 ppm; leafy vegetables (except Brassica) at 0.2 ppm; Brassica vegetables at 0.2 ppm; legume vegetables at 0.05 ppm; foliage of legume vegetables at 8 ppm; forage, fodder, hay and straw of cereal grains at 7 ppm; grass forage, fodder and hay at 7 ppm; forage, fodder, straw and hay of non-grass animal feeds at 8 ppm; and herbs and spices at 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 qualitative nature of methoxyfenozide residues in plants is adequately understood based upon acceptable cotton, apple and grape metabolism studies. EPA has determined that the residue of concern for dietary exposure and tolerance setting purposes in primary crops and water is the parent compound, methoxyfenozide. The qualitative nature of methoxyfenozide residues in rotation crop plants is adequately understood based upon ^{14}C confined rotation crop studies. The residue of concern for dietary exposure and tolerance setting purposes in rotation crops is the parent compound, methoxyfenozide and its metabolites RH–117,236 (free phenol of methoxyfenozide; 3,5-dimethylbenzoic acid N-tert-butyl-N'-(3-hydroxy-2-methylbenzoyl) hydrazide), RH–151,055 (the glucose conjugate of RH–117,236; 3,5-dimethylbenzoic acid N-tert-butyl-N–[3(-D-glucopyranosyloxy)-2-methylbenzoyl]-hydrazide) and RH–152,072 (the malonylglycosyl conjugate of RH–117,236).

The qualitative nature of the residue in animals is adequately understood based on acceptable studies conducted on goats and laying hens. EPA has determined that the residue of concern in milk and ruminant tissues (other than liver and kidney) is the parent compound, methoxyfenozide. The residue of concern in ruminant liver and kidney is the parent compound, methoxyfenozide, and its glucuronide metabolite designated as RH–141,518 (also referred to as RH–1518).

2. *Analytical method*. An HPLC/UV Method TR 34–00–41 for the enforcement of tolerances in rotation crops has been developed. Confirmatory method validation, radiovalidation, and independent method validation data have been submitted for this method. The validated limit of quantitation (LOQ) of the analytical method was 0.02 ppm in all matrices for methoxyfenozide and RH–117,236 and 0.05 ppm for RH–151,055.

3. *Magnitude of residues*. Magnitude of the residue in rotation crops. Two geographically representative field trials were submitted to support the proposed time-limited tolerances on rotation crops. Turnips, onions, mustard greens, tomatoes, cucumbers, soybeans and wheat were planted back 7 days after the last application to growing lettuce crops of methoxyfenozide 80WP formulation according to the maximum proposed use patterns. The rotated crops were harvested at maturity. Residues of methoxyfenozide in turnip roots, turnip tops, onions, mustard greens, tomatoes and cucumbers ranged from no-detectable residues to 0.07 ppm.

The results of the field trials indicate that residues of methoxyfenozide will not exceed the proposed tolerances of 0.05 ppm in root and tuber vegetables, 0.1 ppm in the leaves of root and tuber vegetables, 0.1 ppm in bulb vegetables, 0.2 ppm in leafy and cole crop vegetables. No residues were found in fruiting vegetables or cucurbit vegetables. Residues of methoxyfenozide and its metabolites RH–117236, RH–151055 and RH–152072 in soybean seeds did not exceed 0.033 ppm and no residues were detected in wheat grain. Residues of methoxyfenozide and its metabolites concentrated in the dry matrices soybean hay and wheat straw at 7.1 ppm and 6.4 ppm, respectively. The results of the field trials indicate that residues of methoxyfenozide and its metabolites will not exceed the proposed tolerances of 7 ppm in forage, fodder and straw of cereal grains and grass forage, fodder and hay. Residues of methoxyfenozide and its metabolites will not exceed the proposed tolerances of 8 ppm in foliage of legume vegetables, forage, fodder, straw and hay of non-animal feeds, or in herbs and spices. Additional rotation crop trials are in progress to support these time-limited tolerances.

Residues in meat, milk, poultry, and eggs. The maximum theoretical dietary burden of methoxyfenozide for dairy or beef cattle associated with this petition is estimated to be less than 20 ppm. The established tolerances of 0.02 ppm in the milk and meat of cattle, goats, hogs, horses, and sheep, 0.1 ppm in the fat of cattle, goats, hogs, horses, and sheep, 0.1 ppm in liver and 0.02 ppm in meat byproduct (except liver) of cattle, goat, hogs, horses, and sheep were established based on a dairy cow feeding level of 45 ppm. These tolerances are adequate for the proposed rotation crop tolerances.

The maximum theoretical dietary burden of methoxyfenozide for poultry animals associated with this petition (from cotton meal and soybean seed) would contribute a maximum theoretical dietary burden for methoxyfenozide at 0.41 ppm. A poultry metabolism study was conducted at feeding levels of 58 ppm, 60 ppm, and 68 ppm which are equivalent to 145x, 150x, and 170x, respectively, the maximum theoretical dietary burden for poultry. Assuming a linear relationship between dose and residues, the expected residues in eggs and poultry tissues would be below the LOD for methods used to measure residues in poultry products. Rohm and Haas concludes that there is no reasonable expectation of finite residues in eggs and poultry tissues and that a poultry feeding study is not required at this time.

B. Toxicological Profile

1. *Acute toxicity*. Acute toxicity studies with technical grade: Oral LD_{50} in the rat is 5,000 milligrams/kilograms (mg/kg) for males and females- Toxicity Category IV; Oral LD_{50} in the mouse is 5,000 mg/kg for males and females-Toxicity Category IV; Dermal LD_{50} in the rat is > 2,000 mg/kg-Toxicity Category III; Inhalation LC_{50} in the rat is > 4.3 milligram/liter (mg/L)-Toxicity Category IV; Primary Eye Irritation in the rabbit-very mild irritant-Toxicity Category IV; Primary skin irritation in the rabbit-not a skin irritant-Toxicity Category IV. Methoxyfenozide is not a skin sensitizer.

In an acute neurotoxicity study in rats, statistically significant decreased hind limb grip strength was observed in male rats at 3 hours (approximate time of peak effect) following a single oral dose of 2,000 mg/kg (limit dose) of methoxyfenozide. Decreased hindlimb grip strength was also observed in the male rats at 7 and 14 days, but was not statistically significant. No other systemic or neurotoxic effects were observed in the male rats or in the female rats at any time in this study. Since this marginal effect occurred only in one sex, was statistically significant at only one time, was observed only at the high dose (limit dose) and no other

signs of toxicity were observed in the rats in this study, this possible effect is not considered to be biologically significant. In addition, neither decreased hindlimb grip strength nor any other signs of neurotoxicity were observed in any of the animals at any time in a 90–day subchronic neurotoxicity study in rats.

2. *Genotoxicity*. In a battery of four mutagenicity studies (with and without metabolic activation, as appropriate for the specific study), technical grade methoxyfenozide was negative for genotoxicity in all four studies. The four studies satisfy the new revised mutagenicity guideline requirements for a new chemical (published in 1991). An additional mutagenicity study, performed on RH–117,236 (Metabolite M-B), a metabolite of methoxyfenozide, was also negative for genotoxicity.

3. *Reproductive and developmental toxicity*. In a developmental toxicity study in rats, no signs of maternal toxicity in dams or of developmental toxicity in fetuses were observed at the limit dose of 1,000 mg/kg/day. The No Observed Adverse Effect Level (NOAEL) in this study for both maternal toxicity and developmental toxicity was 1,000 mg/kg/day. The Lowest Observed Adverse Effect Level (LOAEL) > 1,000 mg/kg/day. Similarly, in a developmental toxicity study in rabbits, no signs of maternal toxicity or of developmental toxicity were observed at the limit dose of 1,000 mg/kg/day. The NOAEL in this study for both maternal toxicity and developmental toxicity was 1,000 mg/kg/day. The LOAEL was > 1,000 mg/kg/day.

In neither the developmental toxicity study in rats nor in the developmental toxicity study in rabbits was there any evidence for increased susceptibility of fetuses to in utero exposure to methoxyfenozide. In these studies, methoxyfenozide was determined not to be a developmental toxicant.

In a 2–generation (1 litter/generation) reproduction study in rats, treatment-related parental toxicity was observed only at 20,000 ppm, the highest dose tested (HDT). At this dose, increased liver weights were observed in males and females of both generations and midzonal to periportal hepatocellular hypertrophy was observed in the livers of all males and females of both generations. The LOAEL for parental toxicity was 20,000 ppm (1,552/1,821 mg/kg/day for males/females,respectively) and the NOAEL was 2,000 ppm (153/181 mg/kg/day for males/females, respectively). There were no treatment-related effects on reproductive parameters for adult (parent) animals. The NOAEL for reproductive toxicity was 20,000 ppm. Since no treatment-related effects were observed in the pups, the NOAEL for neonatal toxicity was also, 20,000 ppm. The NOAEL for parental toxicity in this reproduction study is higher than the NOAEL for the 2–year combined chronic feeding/carcinogenicity study in rats because many of the toxic effects observed in the 2–year study at the LOAEL (hematological changes, liver toxicity, histopathological changes in the thyroid gland and increased adrenal weights) were not examined in the reproduction study.

4. *Subchronic toxicity*. In a 2–week range-finding dietary study in rats, treatment-related effects were observed at > 5,000 ppm in the liver (increased liver weights and hepatocellular hypertrophy in males and females), in the thyroid gland (hypertrophy/hyperplasia of follicular cells in males and females), and in the adrenal gland (increased adrenal weights and/or hypertrophy of the zona fasciculata in females). Hypertrophy/hyperplasia of thyroid follicular cells was also observed in males and females at 1,000 ppm, the lowest observed adverse effect level (LOAEL) in this study. The no observed adverse effect level (NOAEL) was 250 ppm. Treatment-related hematological changes were not observed in the rats in this study.

In a 3–month feeding study in rats, the predominant treatment-related effects were increased liver weights in males and females and periportal hepatocellular hypertrophy in all males and females at 20,000 ppm highest dose tested (HDT) and at 5,000 ppm. In addition, at 20,000 ppm, a slightly decreased (7–8%) RBC count and slightly decreased (7–8%) hemoglobin concentration, compared to control rats, were observed in the females. The LOAEL in this study was 5,000 ppm (353/379 mg/kg/day in males/females, respectively). The NOAEL was 1,000 ppm (69/72 mg/kg/day in males/females, respectively). Although observed in the 2–week dietary study and in the 2–year chronic feeding/carcinogenicity study in rats, treatment-related effects in the thyroid and adrenal glands were not observed in the rats in this 3–month study. There is no available biological explanation for this difference in findings in the studies.

In a 2–week range-finding study in dogs, treatment-related hematological changes were observed in both males and females at 3,500 ppm, 7,000 ppm, 15,000 ppm, and 30,000 ppm (HDT). These changes included decreased RBC counts, decreased hemoglobin concentrations, decreased hematocrits, decreased MCHC, increased MCV, increased MCH, increased Heinz bodies, methemoglobinemia, changes in RBC morphology such as Howell-Jolly bodies and polychromasia, increased reticulocyte counts, increased nucleated RBC and increased platelet counts. At the same dose levels (> 3,500 ppm), increased spleen weights and/or enlarged spleens were also observed. At 7,000 ppm, plasma total bilirubin was increased. The LOAEL in this study was 3,500 ppm (90–184 mg/kg/day in males and females). The NOAEL was 300 ppm (11–16 mg/kg/day in males and females).

In a 3–month feeding study in dogs, no treatment-related effects other than a suggestion of decreased body weight gains in males and females were observed in either males or females at the HDT viz. 5,000 ppm (198/209 mg/kg/day in males/females, respectively). Although hematological effects were noted in dogs in the 2–week range-finding study > 3,500 ppm (90–184 mg/kg/day) and in the 1–year chronic feeding study at > 3,000 ppm (106/111 mg/kg/day), hematological changes were not observed in this 3–month study at 5,000 ppm (198/209 mg/kg/day). There is no available biological explanation for this difference in findings in the studies.

As part of the 3–month study in dogs, some male and female dogs were given 15 ppm (0.6 mg/kg/day) of methoxyfenozide in the diet for 15 weeks followed by an increase in the dietary dose to 15,000 ppm (422/460 mg/kg/day in males/females, respectively) for an additional 6 weeks. After about 2 weeks and 6 weeks at 15,000 ppm, hematological examinations were conducted. No hematological changes in these dogs were observed. Apparently, pretreatment of the dogs at 15 ppm for 15 weeks prevented the occurrence of hematological changes which would have been expected to occur based on results in the 2–week and 1–year feeding studies. One possible explanation is that the liver microsomal enzyme system may have been stimulated so much during pretreatment at 15 ppm that the metabolic (detoxification) rate of methoxyfenozide was increased to the point where blood levels of methoxyfenozide may have remained below critical effect levels at 15,000 ppm. Another possible explanation is that compensatory mechanisms for replacing damaged RBC in pretreated dogs may have been so efficient that hematological changes were not observed in these dogs even at 15,000 ppm. Other explanations for this finding are also possible.

5. *Chronic toxicity*. In a 2–year combined chronic feeding/

carcinogenicity study in rats, the following treatment-related effects were observed at 20,000 ppm (highest dose tested): decreased survival in males, decreased body weight and food efficiency in females during the last year of the study, hematological changes (decreased RBC counts, hemoglobin concentrations, and/or hematocrits; methemoglobinemia; and increased platelet counts) in males and females, increased liver weights and periportal hepatocellular hypertrophy in males and females, thyroid follicular cell hypertrophy in males, altered thyroid colloid in males and females, and increased adrenal weights in males and females. At 8,000 ppm, the following treatment-related effects were observed: hematological changes (decreased RBC counts, hemoglobin concentrations, and/or hematocrits in males and females), liver toxicity (increased liver weights in males and periportal hepatocellular hypertrophy in males and females), histopathological changes in the thyroid (increased follicular cell hypertrophy in males and altered colloid in males) and possible adrenal toxicity (increased adrenal weights in males and females). The LOAEL in this study was 8,000 ppm (411/491 mg/kg/day in males/females, respectively), based on the effects described above. The NOAEL was 200 ppm (10.2/11.9 mg/kg/day in males/females, respectively). This NOAEL was used to establish the reference dose (RfD) for methoxyfenozide. Utilizing an uncertainty factor of 100 to account for both interspecies extrapolation (10x) and intraspecies variability (10x), the chronic RfD for methoxyfenozide was calculated to be 0.10 mg/kg/day. No evidence of carcinogenicity was observed in this study. Dosing was considered adequate because of the decreased survival in males and the decreased body weights and food efficiency in females at 20,000 ppm. In addition, the HDT for both males and females, 20,000 ppm (1,045/1,248 mg/kg/day in males/females, respectively), is higher than the limit dose of 1,000 mg/kg/day.

In a 1–year chronic feeding study in dogs, the predominant toxic effects were anemia and signs of an associated compensatory response. At 30,000 ppm, the HDT, the following treatment-related effects were observed in both males and females: decreased RBC counts, decreased hemoglobin concentrations, decreased hematocrits, methemoglobinemia, nucleated RBC, increased platelets, increased serum total bilirubin, bilirubinurea, increased hemosiderin in macrophages in liver and spleen, and increased hyperplasia in bone marrow of rib and sternum. Increased liver weights in males and females and increased thyroid weights in males were also observed at 30,000 ppm. Signs of anemia were also noted at 3,000 ppm and included decreased RBC counts, decreased hemoglobin concentrations, decreased hematocrits, methemoglobinemia, increased platelets, and increased serum total bilirubin and bilirubinurea. The LOAEL in this study was 3,000 ppm (106/111 mg/kg/day in males/females, respectively). The NOAEL was 300 ppm (9.8/12.6 mg/kg/day in males/females, respectively).

6. *Animal metabolism*. In a metabolism study in rats, 14_C-methoxyfenozide was rapidly absorbed, distributed, metabolized and almost completely excreted within 48 hours. The major route of excretion was feces (86–97%) with lesser amounts in the urine (5–13%). An enterohepatic circulation was observed. The test material was metabolized principally by O-demethylation of the A-ring methoxy group and oxidative hydroxylation of the B-ring methyl groups followed by conjugation with glucuronic acid. No significant sex-related or dose-dependent differences in metabolic disposition were noted. Seven metabolites and the parent accounted for 74–90% of the administered dose in all groups. The glucuronide conjugates are considered to be less toxic than the parent compound because glucuronide conjugation is well known to be a commonly occurring ''detoxification'' mechanism in mammalian species since it results in the formation of more polar, more water-soluble metabolites which are readily and easily excreted from the body (in this case, in the bile and urine). Further, based on similarities of chemical structure, the non-conjugated metabolites would be expected to be no more toxic than the parent compound. In a dermal absorption study in rats using an 80% wettable powder formulation as the test material, the cumulative dermal absorption of test material after a 10– or 24–hour dermal exposure was determined to be 2%. In a 28–day dermal toxicity study in rats, no treatment-related systemic or skin effects were observed at the limit dose of 1,000 mg/kg/day (HDT). Regarding effects on endocrine organs, methoxyfenozide affected the thyroid gland and adrenal gland in the 2–week and 2–year feeding studies in rats. In the thyroid gland, hypertrophy/hyperplasia of follicular cells and altered colloid were observed in males and females at or near the LOAEL in both of these studies. In the adrenal gland, increased adrenal weights and hypertrophy of the zona fasciculata were also observed in males and females at or near the LOAEL. In addition, in the 1–year chronic feeding study in dogs, increased thyroid weight in males was observed, but only at the very high dose of 30,000 ppm. Since the definition and regulatory significance of the term ''endocrine disruptor chemical'' has not yet been established by the Agency, it is not clear whether methoxyfenozide, on the basis of these effects on the thyroid gland and adrenal gland, should be considered to be an ''endocrine disruptor chemical.'' Other than the morphological changes described above, there were no signs of thyroid or adrenal dysfunction in these or in any other studies on methoxyfenozide.

7. *Endocrine disruption*. Regarding effects on endocrine organs, methoxyfenozide affected the thyroid gland and adrenal gland in the 2–week and 2–year feeding studies in rats. In the thyroid gland, hypertrophy/hyperplasia of follicular cells and altered colloid were observed in males and females at or near the LOAEL in both of these studies. In the adrenal gland, increased adrenal weights and hypertrophy of the zona fasciculata were also observed in males and females at or near the LOAEL. In addition, in the 1–year chronic feeding study in dogs, increased thyroid weight in males was observed, but only at the very high dose of 30,000 ppm. Since the definition and regulatory significance of the term ''endocrine disruptor chemical'' has not yet been established by the Agency, it is not clear whether methoxyfenozide, on the basis of these effects on the thyroid gland and adrenal gland, should be considered to be an ''endocrine disruptor chemical.'' Other than the morphological changes described above, there were no signs of thyroid or adrenal dysfunction in these or in any other studies on methoxyfenozide.

C. Aggregate Exposure

1. *Dietary exposure*—i. *Food.— From food and feed uses*. Tolerances have been established (40 CFR 180.544) for residues of methoxyfenozide on cotton, undelinted seed; cotton gin byproducts; pome fruit; apple pomace, wet; milk; meat of cattle, goats, hogs, horses and sheep and fat of cattle, goats, hogs, horses and sheep at 2.0, 35.0, 1.5, 7.0, 0.02, 0.02, 0.1 ppm and tolerances for the combined residues of methoxyfenozide and its glucuronide metabolite in liver of cattle, goats, hogs, horses and sheep and meat byproducts (except liver) of cattle, goats, hogs, horses and sheep at 0.1 and 0.02 ppm

respectively. Other petitions pending request tolerances for grapes at 1.0 ppm, raisins at 1.5 ppm, fruiting vegetables at 2.0 ppm, Leafy Vegetables (4A) at 25 ppm, Leaf Petioles (4B) at 10.0 ppm, Head and Stem Brassica (5A) at 6.5 ppm and Leafy Brassica Greens (5B) at 20.0 ppm. The current petition requests establishment of tolerances due to indirect or inadvertent residues of methoxyfenozide [benzoic acid, 3-methoxy-2-methyl-, 2–(3,5-dimethylbenzoyl)-2–(1,1-dimethylethyl) hydrazide] in or on root and tuber vegetables at 0.05 parts per million (ppm); leaves of root and tuber vegetables at 0.1 ppm; bulb vegetables at 0.1 ppm; leafy vegetables (except Brassica) at 0.2 ppm; Brassica vegetables at 0.2 ppm; and for indirect or inadvertent combined residues of methoxyfenozide and its metabolites RH–117,236 (free phenol of methoxyfenozide; 3,5-dimethylbenzoic acid N-tert-butyl-N'-(3-hydroxy-2-methylbenzoyl) hydrazide), RH–151,055 (the glucose conjugate of RH–117,236; 3,5-dimethylbenzoic acid N-tert-butyl-N-[3(-D-glucopyranosyloxy)-2-methylbenzoyl]-hydrazide) and RH–152,072 (the malonylglycosyl conjugate of RH–117,236) in or on legume vegetables at 0.05 ppm; foliage of legume vegetables at 8 ppm; forage, fodder, hay and straw of cereal grains at 7 ppm; grass forage, fodder and hay at 7 ppm; forage, fodder, straw and hay of non-grass animal feeds at 8 ppm; and herbs and spices at 8 ppm.

Risk assessments were conducted by Rohm and Haas to assess dietary exposures and risks from methoxyfenozide as follows:

a. *Acute exposure and risk.* Acute dietary risk assessments are performed for a food-use pesticide if a toxicological study has indicated the possibility of an effect of concern occurring as a result of a 1–day or single exposure. No appropriate toxicological endpoint attributable to a single exposure was identified in the available toxicology studies on methoxyfenozide including the acute neurotoxicity study in rats, the developmental toxicity study in rats and the developmental toxicity study in rabbits. This risk is considered to be negligible.

b. *Chronic exposure and risk.* Rohm and Haas used the Dietary Exposure Evaluation Model (DEEM) software for conducting a chronic dietary (food) risk analysis. DEEM is a dietary exposure analysis system that is used to estimate exposure to a pesticide chemical in foods comprising the diets of the U.S. population, including population subgroups. DEEM contains food consumption data as reported by respondents in the USDA Continuing Surveys of Food Intake by Individuals conducted in 1989–1992. Rohm and Haas assumed 100% of crops would be treated and contain methoxyfenozide residues at the tolerance level. The following tolerance levels were used in the analysis:

Commodity	Tolerance Level (parts per million) (ppm)
Cotton, undelinted seed	2.0
Pome fruits	1.5 ppm
Grapes	1.0 ppm
Raisins	1.5 ppm
Leafy Vegetables (4A)	25 ppm
Leaf Petioles (4B)	10.0 ppm
Head and Stem Brassica (5A)	6.5 ppm
Leafy Brassica Greens (5B)	20.0 ppm
Fruiting vegetables	2.0 ppm
Root and tuber vegetables	0.05 ppm
Leaves of root and tuber vegetables	0.1 ppm
Bulb vegetables	0.1 ppm
Leafy vegetables (except Brassica)	0.2 ppm
Brassica vegetables	0.2ppm
Legume vegetables	0.05 ppm
Herbs and spices	8 ppm
Milk	0.02 ppm
Meat*	0.02 ppm
Meat byproducts* (except liver)	0.02 ppm
Fat*	0.1 ppm
Liver	0.1 ppm

* of cattle, goats, hogs, horses and sheep.

Processing factors were also applied to grape juice (1.2x), grape juice concentrate (3.6x), apple juice/cider (1.3x), apple juice concentrate (3.9x), dried apples (8x), dried beef (1.92x), dried pears (6.25x), tomato juice (1.5x), tomato puree (3.3x), tomato paste (5.4x), tomato catsup (2.5x), dried tomatoes (14.3x), dehydrated onions (9x), white dry potatoes (6.5x), and dried veal (1.92x). The processing factors are default values from DEEM.

As shown in the following table, the resulting dietary food exposures occupy up to 28.3% of the Chronic PAD for the most highly exposed population subgroup, children 1–6 years old. These results should be viewed as conservative (health protective) risk estimates. Refinements such as use of percent crop-treated information and/or anticipated residue values would yield even lower estimates of chronic dietary exposure.

SUMMARY: CHRONIC DIETARY EXPOSURE ANALYSIS BY DEEM (TIER 1)

Population Subgroup[1]	Exposure (mg/kg/day)	Percent of Chronic PAD[2]
U.S. Population – 48 States	0.0149	14.9
All infants (<1 year)	0.0144	14.4
Nursing Infants<1 year old	0.0084	8.4
Non-Nursing Infants < 1 year old	0.0169	6.9
Children 1–6 years old	0.0283	28.3
Children 7–12 years old	0.0193	19.3
Females 13 + (nursing)	0.0172	17.2
U.S. population (autumn season)	0.0150	15.0
U.S. population (winter season)	0.0151	15.1
U.S. population (spring season)	0.0152	15.2
Northeast region	0.0161	16.1
Western region	0.0161	16.1
Non-Hispanic whites	0.0150	15.0
Non-Hispanic/non-white/non-black	0.0171	17.1
Pacific region	0.0162	16.2

[1]The subgroups listed are: (1) The U.S. population (total); (2) Those for infants and children; (3) The other subgroup(s), if any, for which the percentage of the Chronic PAD occupied is greater than that occupied by the subgroup U.S.population (total); and, (4) The most highly exposed of the females subgroups (in this case, females, (13+ years, nursing).

[2]Percent chronic PAD = (Exposure divided by Chronic PAD) x 100%.

ii. *Drinking water— From drinking water.* The are no water-related exposure data from monitoring to complete a quantitative drinking water exposure analysis and risk assessment for methoxyfenozide. GENEEC and/or PRZM/EXAMS (both produce estimates of pesticide concentration in a farm pond) are used to generate EECs for surface water and SCI-GROW (an empirical model based upon actual monitoring data collected for a number of pesticides that serve as benchmarks) predicts EECs in ground water. These models take into account the use patterns and the environmental profile of a pesticide, but do not include consideration of the impact that processing raw water for distribution as drinking water would likely have on the removal of pesticides from the source water. The primary use of these models at this stage is to provide a coarse screen for assessing whether a pesticide is likely to be present in drinking water at concentrations which would exceed human health levels of concern.

A drinking water level of comparison (DWLOC) is the concentration of a pesticide in drinking water that would be acceptable as a theoretical upper limit in light of total aggregate exposure to that pesticide from food, water, and residential uses. HED uses DWLOCs internally in the risk assessment process as a surrogate measure of potential exposure associated with pesticide exposure through drinking water. In the absence of monitoring data for a pesticide, the DWLOC is used as a point of comparison against the conservative EECs provided by computer modeling (SCI-GROW, GENEEC, PRZM/EXAMS).

a. *Acute exposure and risk*. Because no acute dietary endpoint was determined, Rohm and Haas concludes that there is a reasonable certainty of no harm from acute exposure from drinking water.

b. *Chronic exposure and risk*. Tier II screening-level assessments can be conducted using the simulation models SCI-GROW and PRZM/EXAMS to generate EECs for ground and surface water, respectively. The modeling was conducted based on the environmental profile and the maximum seasonal application rate proposed for methoxyfenozide (1.0 lb ai/acre/season). PRZM/EXAMS was used to generate the surface water EECs, because it can factor the persistent nature of the chemical into the estimates.

The EECs for assessing chronic aggregate dietary risk used by HED are 6 parts per billion (ppb) (in ground water, based on SCI-GROW) and 98.5 ppb (in surface water, based on the PRZM/EXAMS, long-term mean). The back-calculated DWLOCs for assessing chronic aggregate dietary risk range from 720 ppb for the most highly exposed population subgroup (children 1–6 years old) to 2,979 ppb for the U.S. population (48 contiguous States—all seasons).

The SCI-GROW and PRZM/EXAMS chronic EECs are less than the Agency's level of comparison (the DWLOC value for each population subgroup) for methoxyfenozide residues in drinking water as a contribution to chronic aggregate exposure. Rohm and Haas thus concludes with reasonable certainty that residues of methoxyfenozide in drinking water will not contribute significantly to the aggregate chronic human health risk and that the chronic aggregate exposure from methoxyfenozide residues in food and drinking water will not exceed the Agency's level of concern (100% of the cPAD) for chronic dietary aggregate exposure by any population subgroup. EPA generally has no concern for exposures below 100% of the cPAD, because it is a level at or below which daily aggregate dietary exposure over a lifetime will not pose appreciable risks to the health and safety of any population subgroup. This risk assessment is considered high confidence, conservative, and very protective of human health.

DRINKING WATER LEVELS OF COMPARISON FOR CHRONIC EXPOSURE TO METHOXYFENOZIDE

Population Subgroup	Chronic PAD (mg/kg/d)	Food Exposure (m/kg/d)	Max. Water Exposure (mg/kg/d)[1]	SCI-GROW (µg/L)	GENEEC 56–Day Average (µg/L)	DWLOC (µ/L)%
U.S. Population –48 States	0.10	0.0149	0.0851	6	98.5	2,979
Females 13+ (nursing)	0.10	0.0171	0.0829	6	98.5	2,487
Non-Nursing>1 year old	0.10	0.0169	0.083	6	98.5	830
Children 1–6 years old	0.10	0.0283	0.0720	6	98.5	720
Children 7–12 years old	0.10	0.0193	0.0807	6	98.5	807

[1]Maximum Water Exposure (mg/kg/d) = Chronic PAD (mg/kg/day) - Chronic Food Exposure DWLOC (µ/L) = [Maximum water Exposure (mg/kg/d) x body weight (kg)] divided by [1/1000 mg/µ x water consumed daily (L/day)].

2. *Non-dietary exposure*. From non-dietary exposure. Methoxyfenozide is not currently registered for use on any residential non-food sites. Therefore, there is no non-dietary acute, chronic, short- or intermediate-term exposure.

D. Cumulative Effects

Cumulative exposure to substances with a common mechanism of toxicity. Section 408(b)(2)(D)(v) requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider ''available information'' concerning the cumulative effects of a particular pesticide's residues and ''other substances that have a common mechanism of toxicity.''

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

E. Safety Determination

1. *U.S. population* — i. *Acute risk.* Since no acute toxicological endpoints were established, Rohm and Haas considers acute aggregate risk to be negligible.

ii. *Chronic risk*. Using the DEEM exposure assumptions described in this unit, Rohm and Haas has concluded that aggregate exposure to methoxyfenozide from food will utilize 14.9% of the cPAD for the U.S. population. The major identifiable subgroup with the highest aggregate exposure is children 1–6 years old at 28.3% of the cPAD and is discussed below. EPA generally has no concern for exposures below 100% of the cPAD because the cPAD represents the level at or below which daily aggregate dietary exposure over a lifetime will not pose appreciable risks to human health. Despite the potential for exposure to methoxyfenozide in drinking water, the aggregate exposure is not expected to exceed 100% of the cPAD. Rohm and Haas concludes that there is a reasonable certainty that no harm will result from aggregate exposure to methoxyfenozide residues.

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

Since there are currently no registered indoor or outdoor residential non-dietary uses of methoxyfenozide and no short or intermediate term toxic endpoints, Rohm and Haas considers short or intermediate term aggregate risks to be negligible.

iv. *Aggregate cancer risk for U.S. population.* Methoxyfenozide is classified as a ''not likely'' human carcinogen. Therefore this risk does is negligible.

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

2. *Safety factor for infants and children*— i. *In general.* In assessing the potential for additional sensitivity of infants and children to residues of methoxyfenozide, EPA considered data from developmental toxicity studies in the rat and rabbit and a 2–generation reproduction study in the rat. The developmental toxicity studies are designed to evaluate adverse effects on the developing organism resulting from maternal pesticide exposure during gestation. Reproduction studies provide information relating to effects from exposure to the pesticide on the reproductive capability of mating animals and data on systemic toxicity.

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

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

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

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

v. *Chronic risk.* Using the exposure assumptions described in this unit, Rohm and Haas has concluded that aggregate exposure to methoxyfenozide from food will utilize 28.3% of the cPAD for infants and children. EPA generally has no concern for exposures below 100% of the cPAD because the cPAD represents the level at or below which daily aggregate dietary exposure over a lifetime will not pose appreciable risks to human health. Despite the potential for exposure to methoxyfenozide in drinking water, Rohm and Haas does not expect the aggregate exposure to exceed 100% of the cPAD.

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

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

F. International Tolerances

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

3. Rohm and Haas Company

PP OF6213

EPA has received a pesticide petition (0F6213) 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 (FFDCA), 21 U.S.C. 346a(d), to amend 40 CFR part 180 by establishing tolerances for residues of methoxyfenozide [benzoic acid, 3-methoxy-2-methyl-, 2-(3,5-dimethylbenzoyl)-2-(1,1- dimethylethyl) hydrazide] in or on the raw agricultural commodities field corn grain at 0.05 parts per million (ppm), sweet corn (K +CWHR) at 0.05 ppm, field corn forage at 15 ppm, field corn stover (fodder) at 105 ppm, corn oil at 0.2 ppm, aspirated grain factions at 1.0 ppm, corn silage at 5.0 ppm, sweet corn forage at 30 ppm, and sweet corn stover (fodder) at 60 ppm. In addition, this petition requests an increase in the established tolerance for residues of methoxyfenozide to 0.1 ppm in milk and an increase in the established tolerances for residues of methoxyfenozide and its glucuronide metabolite to 0.5 ppm in fat, to 0.4 ppm in liver and to 0.1 ppm in meat by products (except liver) of cattle, goats, horses, hogs and sheep. 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 qualitative nature of methoxyfenozide residues in plants and animals is adequately understood and was previously published in the **Federal Register** of July 5, 2000 (65 FR 41355)(FRL–6496–5). The qualitative nature of methoxyfenozide residues in rotation crop plants is adequately understood based upon ^{14}C confined rotation crop studies. The residue of concern for dietary exposure and tolerance setting purposes in rotation crops is the parent compound, methoxyfenozide and its metabolites RH-–117,236 (free phenol of methoxyfenozide; 3,5-dimethylbenzoic acid N-tert-butyl-N'-(3-hydroxy-2-methylbenzoyl) hydrazide), RH–151,055 (the glucose conjugate of RH-117,236; 3,5-dimethylbenzoic acid N-tert-butyl-N-[3(-D-glucopyranosyloxy)-2-methylbenzoyl]-hydrazide) and RH–152,072 (the malonylglycosyl conjugate of RH–117,236).

2. *Analytical method.* An high performance liquid chromatography using ultra violet Method TR 34-00-38 for the enforcement of tolerances in field and sweet corn matrices has been developed. Confirmatory method validation, radiovalidation, and independent method validation data have been submitted for this method. The validated limit of quantitation (LOQ) of the analytical method was 0.02 ppm in all matrices for methoxyfenozide.

3. *Magnitude of residues*— i. *Magnitude of the residue.* Geographically representative field trials with methoxyfenozide 80WP and 2F formulations were conducted to support the proposed tolerances on field and sweet corn. The results of the field trials indicate that residues of methoxyfenozide will not exceed the proposed tolerances of 0.05 ppm in field grain and sweet corn (K+CWHR), 15 ppm in field corn forage, 105 ppm in

field corn stover (fodder), 1.0 ppm in aspirated grain factions, 5.0 ppm in corn silage, 30 ppm in sweet corn forage and 60 ppm in sweet corn stover (fodder). A processing study was conducted and showed that residues concentrated in oil and a tolerance of 0.2 ppm is proposed.

ii. *Residues in meat, milk, poultry, and eggs*. The maximum theoretical dietary burden of methoxyfenozide for dairy or beef cattle associated with this petition and previous petition is estimated to be less than 75 ppm. Based on a feeding study with methoxyfenozide at 150 ppm, tolerances should be increased to 0.1 ppm in milk, to 0.5 ppm in fat, to 0.4 ppm in liver and to 0.1 ppm in meat by-products (except liver). The maximum theoretical dietary burden of methoxyfenozide for poultry animals associated with this petition (from cotton meal, corn meal and grain) was calculated to be 0.03 ppm.

A poultry feeding study was conducted at levels of 2 ppm, 6 ppm, and 20 ppm which are equivalent to 67x, 200x, and 1,500x, respectively, the maximum theoretical dietary burden for poultry. No detectable residues of methoxyfenozide were found in any of the muscle, fat or liver samples from any dose level. In eggs, no quantifiable residues (i.e., greater than the limit of quantitation of 0.01 ppm) of either methoxyfenozide or its glucuronide metabolite were found in any of the samples. Average residues of RH–1518 in liver from hens dosed at 6 ppm were 0.016 ppm while those in the liver of hens dosed at 20 ppm were 0.031 ppm. After a 7–day depuration period, no detectable residues of RH–1518 were found in the liver of hens dosed at 20 ppm. Assuming a linear relationship between dose and residues, the expected residues in eggs and poultry tissues would be below the LOD of 0.01 ppm for methods used to measure residues in poultry products. Rohm and Haas concludes that there is no reasonable expectation of finding finite residues in eggs and poultry tissues.

B. Toxicological Profile

1. *Acute toxicity*. Acute toxicity studies with technical grade: Oral LD_{50} in the rat is > 5,000 milligrams/kilograms (mg/kg) for males and females- Toxicity Category IV; Oral LD_{50} in the mouse is > 5,000 mg/kg for males and females-Toxicity Category IV; Dermal LD_{50} in the rat is > 2,000 mg/kg-Toxicity Category III; Inhalation LD_{50} in the rat is > 4.3 milligram/liter (mg/L)-Toxicity Category IV; Primary Eye Irritation in the rabbit -very mild irritant-Toxicity Category IV; Primary skin irritation in the rabbit-not a skin irritant-Toxicity Category IV. Methoxyfenozide is not a skin sensitizer.

In an acute neurotoxicity study in rats, statistically significant decreased hind limb grip strength was observed in male rats at 3 hours (approximate time of peak effect) following a single oral dose of 2,000 mg/kg (limit dose) of methoxyfenozide. Decreased hindlimb grip strength was also observed in the male rats at 7 and 14 days, but was not statistically significant. No other systemic or neurotoxic effects were observed in the male rats or in the female rats at any time in this study. Since this marginal effect occurred only in one sex, was statistically significant at only one time, was observed only at the high dose (limit dose) and no other signs of toxicity were observed in the rats in this study, this possible effect is not considered to be biologically significant. In addition, neither decreased hindlimb grip strength nor any other signs of neurotoxicity were observed in any of the animals at any time in a 90–day subchronic neurotoxicity study in rats.

2. *Genotoxicity*. In a battery of four mutagenicity studies (with and without metabolic activation, as appropriate for the specific study), technical grade methoxyfenozide was negative for genotoxicity in all four studies. The four studies satisfy the new revised mutagenicity guideline requirements for a new chemical (published in 1991). An additional mutagenicity study, performed on RH–117,236 (Metabolite M-B), a metabolite of methoxyfenozide, was also negative for genotoxicity.

3. *Reproductive and developmental toxicity*. In a developmental toxicity study in rats, no signs of maternal toxicity in dams or of developmental toxicity in fetuses were observed at the limit dose of 1,000 mg/kg/day. The No Observed Adverse Effect Level (NOAEL) in this study for both maternal toxicity and developmental toxicity was 1,000 mg/kg/day. The Lowest Observed Adverse Effect Level (LOAEL) 1,000 mg/kg/day. Similarly, in a developmental toxicity study in rabbits, no signs of maternal toxicity or of developmental toxicity were observed at the limit dose of 1,000 mg/kg/day. The NOAEL in this study for both maternal toxicity and developmental toxicity was 1,000 mg/kg/day. The LOAEL was > 1,000 mg/kg/day.

In neither the developmental toxicity study in rats nor in the developmental toxicity study in rabbits was there any evidence for increased susceptibility of fetuses to *in utero* exposure to methoxyfenozide. In these studies, methoxyfenozide was determined not to be a developmental toxicant.

In a 2–generation (1 litter/generation) reproduction study in rats, treatment-related parental toxicity was observed only at 20,000 ppm, the HDT. At this dose, increased liver weights were observed in males and females of both generations and midzonal to periportal hepatocellular hypertrophy was observed in the livers of all males and females of both generations. The LOAEL for parental toxicity was 20,000 ppm (1,552/1,821 mg/kg/day for males/females, respectively) and the NOAEL was 2,000 ppm (153/181 mg/kg/day for males/females, respectively). There were no treatment-related effects on reproductive parameters for adult (parent) animals. The NOAEL for reproductive toxicity was 20,000 ppm. Since no treatment-related effects were observed in the pups, the NOAEL for neonatal toxicity was also, 20,000 ppm. The NOAEL for parental toxicity in this reproduction study is higher than the NOAEL for the 2–year combined chronic feeding/carcinogenicity study in rats because many of the toxic effects observed in the 2–year study at the LOAEL (hematological changes, liver toxicity, histopathological changes in the thyroid gland and increased adrenal weights) were not examined in the reproduction study.

4. *Subchronic toxicity*. In a developmental toxicity study in rats, no signs of maternal toxicity in dams or of developmental toxicity in fetuses were observed at the limit dose of 1,000 mg/kg/day. The NOAEL in this study for both maternal toxicity and developmental toxicity was 1,000 mg/kg/day. The LOAEL > 1,000 mg/kg/day. Similarly, in a developmental toxicity study in rabbits, no signs of maternal toxicity or of developmental toxicity were observed at the limit dose of 1,000 mg/kg/day. The NOAEL in this study for both maternal toxicity and developmental toxicity was 1,000 mg/kg/day. The LOAEL was > 1,000 mg/kg/day.

In neither the developmental toxicity study in rats nor in the developmental toxicity study in rabbits was there any evidence for increased susceptibility of fetuses to *in utero* exposure to methoxyfenozide. In these studies, methoxyfenozide was determined not to be a developmental toxicant.

In a 2–generation (1 litter/generation) reproduction study in rats, treatment-related parental toxicity was observed only at 20,000 ppm, the HDT. At this dose, increased liver weights were observed in males and females of both generations and midzonal to periportal hepatocellular hypertrophy was observed in the livers of all males and females of both generations. The LOAEL

for parental toxicity was 20,000 ppm (1,552/1,821 mg/kg/day for males/females, respectively) and the NOAEL was 2,000 ppm (153/181 mg/kg/day for males/females, respectively). There were no treatment-related effects on reproductive parameters for adult (parent) animals. The NOAEL for reproductive toxicity was 20,000 ppm. Since no treatment-related effects were observed in the pups, the NOAEL for neonatal toxicity was also, 20,000 ppm. The NOAEL for parental toxicity in this reproduction study is higher than the NOAEL for the 2–year combined chronic feeding/carcinogenicity study in rats because many of the toxic effects observed in the 2–year study at the LOAEL (hematological changes, liver toxicity, histopathological changes in the thyroid gland and increased adrenal weights) were not examined in the reproduction study.

5. *Chronic toxicity*. In a 2–year combined chronic feeding/carcinogenicity study in rats, the following treatment-related effects were observed at 20,000 ppm (highest dose tested): decreased survival in males, decreased body weight and food efficiency in females during the last year of the study, hematological changes (decreased RBC counts, hemoglobin concentrations, and/or hematocrits; methemoglobinemia; and increased platelet counts) in males and females, increased liver weights and periportal hepatocellular hypertrophy in males and females, thyroid follicular cell hypertrophy in males, altered thyroid colloid in males and females, and increased adrenal weights in males and females. At 8,000 ppm, the following treatment-related effects were observed: hematological changes (decreased RBC counts, hemoglobin concentrations, and/or hematocrits in males and females), liver toxicity (increased liver weights in males and periportal hepatocellular hypertrophy in males and females), histopathological changes in the thyroid (increased follicular cell hypertrophy in males and altered colloid in males) and possible adrenal toxicity (increased adrenal weights in males and females). The LOAEL in this study was 8,000 ppm (411/491 mg/kg/day in males/females, respectively), based on the effects described above. The NOAEL was 200 ppm (10.2/11.9 mg/kg/day in males/females, respectively). This NOAEL was used to establish the reference dose (RfD) for methoxyfenozide. Utilizing an uncertainty factor of 100 to account for both interspecies extrapolation (10x) and intraspecies variability (10x), the chronic RfD for methoxyfenozide was calculated to be 0.10 mg/kg/day. No evidence of carcinogenicity was observed in this study. Dosing was considered adequate because of the decreased survival in males and the decreased body weights and food efficiency in females at 20,000 ppm. In addition, the HDT for both males and females, 20,000 ppm (1,045/1,248 mg/kg/day in males/females, respectively), is higher than the limit dose of 1,000 mg/kg/day.

In a 1–year chronic feeding study in dogs, the predominant toxic effects were anemia and signs of an associated compensatory response. At 30,000 ppm, the HDT, the following treatment-related effects were observed in both males and females: decreased RBC counts, decreased hemoglobin concentrations, decreased hematocrits, methemoglobinemia, nucleated RBC, increased platelets, increased serum total bilirubin, bilirubinurea, increased hemosiderin in macrophages in liver and spleen, and increased hyperplasia in bone marrow of rib and sternum. Increased liver weights in males and females and increased thyroid weights in males were also observed at 30,000 ppm. Signs of anemia were also noted at 3,000 ppm and included decreased RBC counts, decreased hemoglobin concentrations, decreased hematocrits, methemoglobinemia, increased platelets, and increased serum total bilirubin and bilirubinurea. The LOAEL in this study was 3,000 ppm (106/111 mg/kg/day in males/females, respectively). The NOAEL was 300 ppm (9.8/12.6 mg/kg/day in males/females, respectively).

6. *Animal metabolism*. In a metabolism study in rats, 14C-methoxyfenozide was rapidly absorbed, distributed, metabolized and almost completely excreted within 48 hours. The major route of excretion was feces (86–97%) with lesser amounts in the urine (5–13%). An enterohepatic circulation was observed. The test material was metabolized principally by O-demethylation of the A-ring methoxy group and oxidative hydroxylation of the B-ring methyl groups followed by conjugation with glucuronic acid. No significant sex-related or dose-dependent differences in metabolic disposition were noted. Seven metabolites and the parent accounted for 74–90% of the administered dose in all groups. The glucuronide conjugates are considered to be less toxic than the parent compound because glucuronide conjugation is well known to be a commonly occurring ''detoxification'' mechanism in mammalian species since it results in the formation of more polar, more water-soluble metabolites which are readily and easily excreted from the body (in this case, in the bile and urine). Further, based on similarities of chemical structure, the non-conjugated metabolites would be expected to be no more toxic than the parent compound. In a dermal absorption study in rats using an 80% wettable powder formulation as the test material, the cumulative dermal absorption of test material after a 10- or 24–hour dermal exposure was determined to be 2%. In a 28–day dermal toxicity study in rats, no treatment-related systemic or skin effects were observed at the limit dose of 1,000 mg/kg/day (HDT). Regarding effects on endocrine organs, methoxyfenozide affected the thyroid gland and adrenal gland in the 2–week and 2–year feeding studies in rats. In the thyroid gland, hypertrophy/hyperplasia of follicular cells and altered colloid were observed in males and females at or near the LOAEL in both of these studies. In the adrenal gland, increased adrenal weights and hypertrophy of the zona fasciculata were also observed in males and females at or near the LOAEL. In addition, in the 1–year chronic feeding study in dogs, increased thyroid weight in males was observed, but only at the very high dose of 30,000 ppm. Since the definition and regulatory significance of the term ''endocrine disruptor chemical'' has not yet been established by the Agency, it is not clear whether methoxyfenozide, on the basis of these effects on the thyroid gland and adrenal gland, should be considered to be an ''endocrine disruptor chemical.'' Other than the morphological changes described above, there were no signs of thyroid or adrenal dysfunction in these or in any other studies on methoxyfenozide.

7. *Endocrine disruption*. Regarding effects on endocrine organs, methoxyfenozide affected the thyroid gland and adrenal gland in the 2–week and 2–year feeding studies in rats. In the thyroid gland, hypertrophy/hyperplasia of follicular cells and altered colloid were observed in males and females at or near the LOAEL in both of these studies. In the adrenal gland, increased adrenal weights and hypertrophy of the zona fasciculata were also observed in males and females at or near the LOAEL. In addition, in the 1–year chronic feeding study in dogs, increased thyroid weight in males was observed, but only at the very high dose of 30,000 ppm. Since the definition and regulatory significance of the term ''endocrine disruptor chemical'' has not yet been established by the Agency, it is not clear whether methoxyfenozide, on the basis of these effects on the thyroid

gland and adrenal gland, should be considered to be an ''endocrine disruptor chemical.'' Other than the morphological changes described above, there were no signs of thyroid or adrenal dysfunction in these or in any other studies on methoxyfenozide.

C. Aggregate Exposure

1. *Dietary exposure*— i. *Food.*— *From food and feed uses.* Tolerances have been established (40 CFR 180.544) for residues of methoxyfenozide on cotton, undelinted seed; cotton gin byproducts; pome fruit; apple pomace, wet; milk; meat and fat of cattle, goats, hogs, horses and sheep and for the combined residues of methoxyfenozide and its glucuronide metabolite in liver and meat byproducts (except liver) of cattle, goats, hogs, horses and sheep. The established tolerances are listed in the table below. Other petitions pending request tolerances for grapes, raisins, fruiting vegetables, Leafy Vegetables (4A), Leaf Petioles (4B), Head and Stem Brassica (5A) and Leafy Brassica Greens (5B), and tolerances due to indirect or inadvertent residues of methoxyfenozide [benzoic acid, 3-methoxy-2-methyl-, 2-(3,5-dimethylbenzoyl)-2-(1,1-dimethylethyl) hydrazide] in or on root and tuber vegetables; leaves of root and tuber vegetables; bulb vegetables; leafy vegetables (except Brassica); Brassica vegetables; and for indirect or inadvertent combined residues of methoxyfenozide and its metabolites RH-117,236 (free phenol of methoxyfenozide; 3,5-dimethylbenzoic acid N-tert-butyl-N'-(3-hydroxy-2-methylbenzoyl) hydrazide), RH–151,055 (the glucose conjugate of RH–117,236; 3,5-dimethylbenzoic acid N-tert-butyl-N-[3(-D-glucopyranosyloxy)-2-methylbenzoyl]-hydrazide) and RH–152,072 (the malonylglycosyl conjugate of RH–117,236) in or on legume vegetables; foliage of legume vegetables; forage, fodder, hay and straw of cereal grains; grass forage, fodder and hay; forage, fodder, straw and hay of non-grass animal feeds; and herbs and spices. The proposed tolerances are listed in the table below. The current petition requests establishment of tolerances in field corn grain at 0.05 ppm, sweet corn (K+CWHR) at 0.05 ppm, field corn forage at 15 ppm, field corn stover (fodder) at 105 ppm, corn oil at 0.2 ppm, aspirated grain factions at 1.0 ppm, corn silage at 5.0 ppm, sweet corn forage at 30 ppm, and sweet corn stover (fodder) at 60 ppm. In addition, this petition requests an increase in the established tolerance for residues of methoxyfenozide to 0.1 ppm in milk and an increase in the established tolerances for residues of methoxyfenozide and its glucuronide metabolite to 0.5 ppm in fat, to 0.4 ppm in liver and to 0.1 ppm in meat by products (except liver) of cattle, goats, horses, hogs and sheep.

Risk assessments were conducted by Rohm and Haas to assess dietary exposures and risks from methoxyfenozide as follows:

a. *Acute exposure and risk.* Acute dietary risk assessments are performed for a food-use pesticide if a toxicological study has indicated the possibility of an effect of concern occurring as a result of a 1–day or single exposure. No appropriate toxicological endpoint attributable to a single exposure was identified in the available toxicology studies on methoxyfenozide including the acute neurotoxicity study in rats, the developmental toxicity study in rats and the developmental toxicity study in rabbits. Since no acute toxicological endpoints were established, Rohm and Haas considers acute aggregate risk to be negligible.

b. *Chronic exposure and risk.* Rohm and Haas used the Dietary Exposure Evaluation Model (DEEM) software for conducting a chronic dietary (food) risk analysis. DEEM is a dietary exposure analysis system that is used to estimate exposure to a pesticide chemical in foods comprising the diets of the U.S. population, including population subgroups. DEEM contains food consumption data as reported by respondents in the USDA Continuing Surveys of Food Intake by Individuals conducted in 1994–1996. Rohm and Haas assumed 100 percent of crops would be treated and contain methoxyfenozide residues at the tolerance level. The following table shows the tolerance levels which were used in the analysis:

Commodity	Tolerance Level (parts per) million (ppm)
Cotton, undelinted seed	2.0
Pome fruit	1.5
Grapes	1.0
Raisins	1.5
Leafy Vegetables (4A)	25
Leaf Petioles (4B)	10.0
Head and Stem Brassica (5A)	6.5
Leafy Brassica Greens (5B)	20.0
Fruiting vegetables	2.0
Root and tuber vegetables	0.05
Leaves of root and tuber vegetables	0.1
Bulb vegetables	0.1
Legume vegetables	0.05
Herbs and spices	8
Corn, field, grain	0.05
Corn, field, forage	15
Corn, field, stover (fodder)	105
Corn, oil	0.2
Corn, aspirated grain fractions	1.0
Corn, silage	5.0
Corn, sweet (K+CWHR)	0.05
Corn, sweet, forage	30
Corn, sweet, stover (fodder)	60
Milk	0.1
Meat[1]	0.02
Meat byproducts[1] (except liver)	0.1
Fat[1]	0.5
Liver	0.4

[1]of cattle, goats, hogs, horses and sheep.

Processing factors were also applied to grape juice (1.2x), grape juice concentrate (3.6x), apple juice/cider (1.3x), apple juice concentrate (3.9x), dried apples (8x), dried pears (6.25x), tomato juice (1.5x), tomato puree (3.3x), tomato paste (5.4x), tomato catsup (2.5x), dried tomatoes (14.3x), dehydrated onions (9x), white dry potatoes (6.5x), sprouted soybean seeds (0.33x), corn grain sugar (high fructose corn syrup; 1.5x), dried beef (1.92x), and dried veal (1.92x). The processing factors are default values from DEEM.

As shown in the following table the resulting dietary food exposures occupy up to 34.5% of the Chronic PAD for the most highly exposed population subgroup, children 1–6 years old. These results should be viewed as conservative (health protective) risk estimates. Refinements such as use of percent crop-treated information and/or anticipated residue values would yield even lower estimates of chronic dietary exposure.

SUMMARY: CHRONIC DIETARY EXPOSURE ANALYSIS BY DEEM (TIER 1)

Population Subgroup	Exposure (mg/kg/day)	% of Chronic PAD*
U.S. Population — 48 States	0.0176	17.6
All infants (< 1 year)	0.226	22.6
Nursing Infants < 1 year old	0.00678	6.8
Non-Nursing Infants < 1 year old	0.0273	27.3
Children 1-6 years old	0.0345	34.5

SUMMARY: CHRONIC DIETARY EXPOSURE ANALYSIS BY DEEM (TIER 1)—Continued

Population Subgroup	Exposure (mg/kg/day)	% of Chronic PAD*
Children 7-12 years old	0.0200	20.0
Females 13+ (nursing)	0.0177	17.7
U.S. population (autumn season)	0.0181	18.1
U.S. population (winter season)	0.0178	17.8
U.S. population (spring season)	0.0178	17.8
Northeast region	0.0193	19.3
Western region	0.0195	19.5
Hispanics	0.0177	17.7
Non-Hispanic/non-white/non-black	0.0237	23.7

*Percent chronic PAD = (Exposure divided by Chronic PAD) x 100%

The subgroups listed are: (1) The U.S. population (total); (2) those for infants and children; (3) the other subgroup(s), if any, for which the percentage of the Chronic PAD occupied is greater than that occupied by the subgroup U.S. population (total); and, (4) the most highly exposed of the females subgroups (in this case, females, (13+ years, nursing).

ii. *Drinking water— From drinking water.* The are no water-related exposure data from monitoring to complete a quantitative drinking water exposure analysis and risk assessment for methoxyfenozide. GENEEC and/or PRZM/EXAMS (both produce estimates of pesticide concentration in a farm pond) are used to generate EECs for surface water and SCI-GROW (an empirical model based upon actual monitoring data collected for a number of pesticides that serve as benchmarks) predicts EECs in ground water. These models take into account the use patterns and the environmental profile of a pesticide, but do not include consideration of the impact that processing raw water for distribution as drinking water would likely have on the removal of pesticides from the source water. The primary use of these models at this stage is to provide a coarse screen for assessing whether a pesticide is likely to be present in drinking water at concentrations which would exceed human health levels of concern.

A drinking water level of comparison (DWLOC) is the concentration of a pesticide in drinking water that would be acceptable as a theoretical upper limit in light of total aggregate exposure to that pesticide from food, water, and residential uses. HED uses DWLOCs internally in the risk assessment process as a surrogate measure of potential exposure associated with pesticide exposure through drinking water. In the absence of monitoring data for a pesticide, the DWLOC is used as a point of comparison against the conservative EECs provided by computer modeling (SCI-GROW, GENEEC, PRZM/EXAMS).

a. *Acute exposure and risk.* Because no acute dietary endpoint was determined, Rohm and Haas concludes that there is a reasonable certainty of no harm from acute exposure from drinking water.

b. *Chronic exposure and risk.* Tier II screening-level assessments can be conducted using the simulation models SCI-GROW and PRZM/EXAMS to generate EECs for ground and surface water, respectively. The modeling was conducted based on the environmental profile and the maximum seasonal application rate proposed for methoxyfenozide (1.0 lb ai/acre/season). PRZM/EXAMS was used to generate the surface water EECs, because it can factor the persistent nature of the chemical into the estimates.

The EECs for assessing chronic aggregate dietary risk used by HED are 6 parts per billion (ppb) (in ground water, based on SCI-GROW) and 98.5 ppb (in surface water, based on the PRZM/EXAMS, long-term mean). The back-calculated DWLOCs for assessing chronic aggregate dietary risk range from 655 ppb for the most highly exposed population subgroup (children 1–6 years old) to 2,884 ppb for the U.S. population (48 contiguous States—all seasons).

The SCI-GROW and PRZM/EXAMS chronic EECs are less than the Agency's level of comparison (the DWLOC value for each population subgroup) for methoxyfenozide residues in drinking water as a contribution to chronic aggregate exposure. Rohm and Haas thus concludes with reasonable certainty that residues of methoxyfenozide in drinking water will not contribute significantly to the aggregate chronic human health risk and that the chronic aggregate exposure from methoxyfenozide residues in food and drinking water will not exceed the Agency's level of concern (100% of the cPAD) for chronic dietary aggregate exposure by any population subgroup. EPA generally has no concern for exposures below 100% of the cPAD, because it is a level at or below which daily aggregate dietary exposure over a lifetime will not pose appreciable risks to the health and safety of any population subgroup. This risk assessment is considered high confidence, conservative, and very protective of human health. The following table shows the drinking water level of comparison for chronic exposure to methoxyfenozine:

DRINKING WATER LEVELS OF COMPARISON FOR CHRONIC EXPOSURE TO METHOXYFENOZIDE

Population Subgroup	Chronic PAD (mg/kg/d)	Food Exposure (m/kg/d)	Max. Water Exposure (mg/kg/d)	SCI-GROW (µg/L)	GENEEC 56–Day Average (µg/L)	DWLOC (µg/L) %
U.S. Population - 48 States	0.10	0.0176	0.0824	6	98.5	2,884
Females 13+ (nursing)	0.10	.0177	0.0823	6	98.5	2,469
Non-Nursing Infants < 1 year old	0.10	0.0273	0.0727	6	98.5	727
Children 1-6 years old	0.10	0.0345	0.0655	6	98.5	655
Children 7-12 years old	0.10	0.0200	0.080	6	98.5	800

Maximum Water Exposure (mg/kg/d) = Chronic PAD (mg/kg/day) - Chronic Food Exposure DWLOC (µg/L) = [Maximum water Exposure (mg/kg/d) x body weight (kg)] divided by [1/1,000 mg/µg x water consumed daily (L/day)]. Body weights (kg) for adults is 70, for females 13+ is 60 kg and for all children is 10 kg. Drinking water consumption is 2 liters per day for adults and 1 liter per day for children.

2. *Non-dietary exposure.* Methoxyfenozide is not currently registered for use on any residential non-food sites. Therefore, there is no non-dietary acute, chronic, short- or intermediate-term exposure.

D. Cumulative Effects

Cumulative exposure to substances with a common mechanism of toxicity. Section 408(b)(2)(D)(v) requires that,

when considering whether to establish, modify, or revoke a tolerance, the Agency consider ''available information'' concerning the cumulative effects of a particular pesticide's residues and ''other substances that have a common mechanism of toxicity.''

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

E. Safety Determination

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

2. *Safety factor for infants and children*—i. *In general*. In assessing the potential for additional sensitivity of infant and children to residues of methoxyfenozide, EPA considered data from developmental toxicity studies in the rat and rabbit and a 2–generation reproduction study in the rat. The developmental toxicity studies are designed to evaluate adverse effects on the developing organism resulting from maternal pesticide exposure during gestation. Reproduction studies provide information relating to effects from exposure to the pesticide on the reproductive capability of mating animals and data on systemic toxicity.

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

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

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

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

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

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

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

F. International Tolerances

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

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ENVIRONMENTAL PROTECTION AGENCY

[PF–999; FRL–6766–8]

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

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

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

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

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

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