0 estimate, 1.86 parts per billion (ppb), was used in the acute exposure analysis and the corrected 56–day drinking water concentration of 0.4667 ppb was used in the chronic exposure analysis. The SCI-GROW estimated ground water concentration for the prosulfuron uses of 0.406585 ppb contributed little to the overall exposure. The acute drinking water levels of concern (DWLOC) for prosulfuron were based on the acute RfD, a margin of exposure (MOE), the 99.9th percentile of the acute dietary exposure for U.S. population subgroups and the body weight - daily water consumption of each respective subgroup. The calculated acute DWLOC values for the population subgroups ranged from 978–3447 ppb. The estimated ground water concentration (0.406585 ppb) and the peak day–0 surface water concentration (1.86 ppb) of prosulfuron did not exceed the acute DWLOC values. The chronic (non-cancer) DWLOC for prosulfuron were based on the chronic RfD, any estimated residential exposure, the chronic dietary exposure for select U.S. population subgroups and the body weight - daily water consumption of each respective subgroup. The calculated chronic DWLOC values for the population subgroups ranged from 197–694. The estimated ground water concentration (0.406585 ppb) and the corrected average 56–day surface water concentration (0.4667 ppb) of prosulfuron did not exceed the chronic DWLOC values. Therefore, there is reasonable certainty that the residues of prosulfuron in the drinking water would not result in unacceptable levels of acute or chronic aggregate human health risk, and that such exposure would not exceed the exposure allowable by the risk cup.

Nondietary exposure. Nondietary exposure to prosulfuron is considered negligible as the chemical is registered for agricultural use only. For workers handling this chemical, acceptable MOE (in the range of thousands) have been obtained for both acute and chronic scenarios.

D. Cumulative Effects

Consideration of a common mechanism of toxicity is not appropriate at this time since there is no information to indicate that toxic effects produced by prosulfuron would be cumulative with those of any other types of chemicals.

E. Safety Determination

1. *U.S. population*. The calculation shows that less than 1% of the RfD will be utilized for the U.S. population based on chronic toxicity endpoints. EPA generally has no concern for exposures below 100% of the RfD because the RfD represents the level at or below which daily aggregate dietary exposure over a lifetime will not pose appreciable risks to human health. It is concluded that there is a reasonable certainty that no harm will result from aggregate exposure to prosulfuron residue.

2. *Infants and children*. The calculated percent of the RfD that will be utilized by aggregate exposure to residues of prosulfuron is only 2.4% for children (1 to 6 years old), the most impacted subpopulation. There were no adverse reproductive or developmental effects indicated in the prosulfuron toxicity data base, which is considered to be essentially complete with no data gaps. It is concluded that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to prosulfuron residues.

F. International Tolerances

No codex MRLs have been established for residues of prosulfuron.

[FR Doc. 02–32988 Filed 12–30–02; 8:45 am]

BILLING CODE 6560–50–S

ENVIRONMENTAL PROTECTION AGENCY

[OPP–2002–0349; FRL–7285–6]

Flumioxazin; Notice of Filing a Pesticide Petition to Establish a Tolerance for a Certain Pesticide Chemical 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 a certain pesticide chemical in or on various food commodities.

DATES: Comments, identified by docket ID number OPP–2002–0349, must be received on or before January 30, 2003.

ADDRESSES: Comments may be submitted electronically, by mail, or through hand delivery/courier. Follow the detailed instructions as provided in Unit I. of the **SUPPLEMENTARY INFORMATION**.

FOR FURTHER INFORMATION CONTACT: Joanne I. Miller, Registration Division (7505C), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001; telephone number: (703) 305–6224; e-mail address: Miller.Joanne@epamail.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:

- Crop production (NAICS 111)
- Animal production (NAICS 112)
- Food manufacturing (NAICS 311)
- Pesticide manufacturing (NAICS 32532)

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 Copies of this Document and Other Related Information?

1. *Docket*. EPA has established an official public docket for this action under docket identification (ID) number OPP–2002–0349. The official public docket consists of the documents specifically referenced in this action, any public comments received, and other information related to this action. Although a part of the official docket, the public docket does not include Confidential Business Information (CBI) or other information whose disclosure is restricted by statute. The official public docket is the collection of materials that is available for public viewing at the Public Information and Records Integrity Branch (PIRIB), Rm. 119, Crystal Mall #2, 1921 Jefferson Davis Hwy., Arlington, VA. This docket facility is open from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The docket telephone number is (703) 305–5805.

2. *Electronic access*. You may access this **Federal Register** document electronically through the EPA Internet under the ''**Federal Register**'' listings at http://www.epa.gov/fedrgstr/.

An electronic version of the public docket is available through EPA's electronic public docket and comment system, EPA Dockets. You may use EPA Dockets at http://www.epa.gov/edocket/ to submit or view public comments,

access the index listing of the contents of the official public docket, and to access those documents in the public docket that are available electronically. Although not all docket materials may be available electronically, you may still access any of the publicly available docket materials through the docket facility identified in Unit I.B.1. Once in the system, select ''search,'' then key in the appropriate docket ID number.

Certain types of information will not be placed in the EPA Dockets. Information claimed as CBI and other information whose disclosure is restricted by statute, which is not included in the official public docket, will not be available for public viewing in EPA's electronic public docket. EPA's policy is that copyrighted material will not be placed in EPA's electronic public docket but will be available only in printed, paper form in the official public docket. To the extent feasible, publicly available docket materials will be made available in EPA's electronic public docket. When a document is selected from the index list in EPA Dockets, the system will identify whether the document is available for viewing in EPA's electronic public docket. Although not all docket materials may be available electronically, you may still access any of the publicly available docket materials through the docket facility identified in Unit I.B. EPA intends to work towards providing electronic access to all of the publicly available docket materials through EPA's electronic public docket.

For public commenters, it is important to note that EPA's policy is that public comments, whether submitted electronically or in paper, will be made available for public viewing in EPA's electronic public docket as EPA receives them and without change, unless the comment contains copyrighted material, CBI, or other information whose disclosure is restricted by statute. When EPA identifies a comment containing copyrighted material, EPA will provide a reference to that material in the version of the comment that is placed in EPA's electronic public docket. The entire printed comment, including the copyrighted material, will be available in the public docket.

Public comments submitted on computer disks that are mailed or delivered to the docket will be transferred to EPA's electronic public docket. Public comments that are mailed or delivered to the docket will be scanned and placed in EPA's electronic public docket. Where practical, physical objects will be photographed, and the photograph will be placed in EPA's electronic public docket along with a brief description written by the docket staff.

C. How and To Whom Do I Submit Comments?

You may submit comments electronically, by mail, or through hand delivery/courier. To ensure proper receipt by EPA, identify the appropriate docket ID number in the subject line on the first page of your comment. Please ensure that your comments are submitted within the specified comment period. Comments received after the close of the comment period will be marked ''late.'' EPA is not required to consider these late comments. If you wish to submit CBI or information that is otherwise protected by statute, please follow the instructions in Unit I.D. Do not use EPA Dockets or e-mail to submit CBI or information protected by statute.

1. *Electronically*. If you submit an electronic comment as prescribed in this unit, EPA recommends that you include your name, mailing address, and an e-mail address or other contact information in the body of your comment. Also include this contact information on the outside of any disk or CD ROM you submit, and in any cover letter accompanying the disk or CD ROM. This ensures that you can be identified as the submitter of the comment and allows EPA to contact you in case EPA cannot read your comment due to technical difficulties or needs further information on the substance of your comment. EPA's policy is that EPA will not edit your comment, and any identifying or contact information provided in the body of a comment will be included as part of the comment that is placed in the official public docket, and made available in EPA's electronic public docket. If EPA cannot read your comment due to technical difficulties and cannot contact you for clarification, EPA may not be able to consider your comment.

i. *EPA Dockets*. Your use of EPA's electronic public docket to submit comments to EPA electronically is EPA's preferred method for receiving comments. Go directly to EPA Dockets at http://www.epa.gov/edocket, and follow the online instructions for submitting comments. Once in the system, select ''search,'' and then key in docket ID number OPP–2002–0349. The system is an ''anonymous access'' system, which means EPA will not know your identity, e-mail address, or other contact information unless you provide it in the body of your comment.

ii. *E-mail*. Comments may be sent by e-mail to opp-docket@epa.gov, Attention: Docket ID Number OPP–2002–0349. In contrast to EPA's electronic public docket, EPA's e-mail system is not an ''anonymous access'' system. If you send an e-mail comment directly to the docket without going through EPA's electronic public docket, EPA's e-mail system automatically captures your e-mail address. E-mail addresses that are automatically captured by EPA's e-mail system are included as part of the comment that is placed in the official public docket, and made available in EPA's electronic public docket.

iii. *Disk or CD ROM*. You may submit comments on a disk or CD ROM that you mail to the mailing address identified in Unit I.C.2. These electronic submissions will be accepted in WordPerfect or ASCII file format. Avoid the use of special characters and any form of encryption.

2. *By mail*. Send your comments to: Public Information and Records Integrity Branch (PIRIB) (7502C), Office of Pesticide Programs (OPP), Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001, Attention: Docket ID Number OPP–2002–0349.

3. *By hand delivery or courier*. Deliver your comments to: Public Information and Records Integrity Branch (PIRIB), Office of Pesticide Programs (OPP), Environmental Protection Agency, Rm. 119, Crystal Mall #2, 1921 Jefferson Davis Hwy., Arlington, VA, Attention: Docket ID Number OPP–2002–0349. Such deliveries are only accepted during the docket's normal hours of operation as identified in Unit I.B.1.

D. How Should I Submit CBI To the Agency?

Do not submit information that you consider to be CBI electronically through EPA's electronic public docket or by e-mail. You may claim information that you submit to EPA as CBI by marking any part or all of that information as CBI (if you submit CBI on disk or CD ROM, mark the outside of the disk or CD ROM as CBI and then identify electronically within the disk or CD ROM the specific information that is 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 docket and EPA's electronic public docket. If you submit the copy that does not contain CBI on disk or CD ROM, mark the outside of the disk or CD ROM clearly that it does not contain CBI.

Information not marked as CBI will be included in the public docket and EPA's electronic public docket without prior notice. If you have any questions about CBI or the procedures for claiming CBI, please consult the person listed 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 ID 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 Cosmetic Act (FFDCA), 21 U.S.C. 346a. EPA has determined that this petition contains data or information regarding the elements set forth in FFDCA 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: December 20, 2002.

Debra Edwards,

Acting Director, Registration Division, Office of Pesticide Programs.

Summary of Petition

The petitioner summary of the pesticide petitions is printed below as required by FFDCA section 408(d)(3). The summary of the petitions was prepared by the petitioner and represents the view of the petitioner. 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.

Valent U.S.A. Corporation

1F6296 and 0F6171

EPA has received pesticide petitions (PP 1F6296, 0F6171) from Valent U.S.A. Corporation, 1333 North California Boulevard, Suite 600, Walnut Creek, California 94596-8025 proposing, pursuant to section 408(d) of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 346a(d), to amend 40 CFR part 180 by establishing a tolerance for residues of the herbicide chemical flumioxazin, 2-[7-fluoro-3,4-dihydro-3-oxo-4-(2-propynyl)-2H-1,4-benzoxazin-6-yl]-4,5,6,7-tetrahydro-1H-isoindole-1,3(2H)-dione, in or on the raw agricultural commodities cotton at 0.02 parts per million (ppm), cotton, gin byproducts at 0.60 ppm, grape at 0.02 ppm, almonds at 0.02 ppm, almond, hulls at 0.70 ppm and sugarcane at 0.20 ppm. EPA has determined that the petitions contain data or information regarding the elements set forth in section 408(d)(2) of the FFDCA; however, EPA has not fully evaluated the sufficiency of the submitted data at this time or whether the data supports granting of the petition. Additional data may be needed before EPA rules on the petition.

A. Residue Chemistry

1. *Plant metabolism*. Metabolism of ^{14}C-flumioxazin labeled in the phenyl- or tetrahydrophthalimido-rings has been studied in soybeans, peanuts, grapes and corn. Flumioxazin was rapidly and extensively metabolized to many metabolites in all plants. Even with exaggerated treatment, individual metabolites and parent were only found at very low concentrations. Comparisons of metabolites detected and quantified from plants and animals show that there are no significant aglycones in plants which are not also present in the excreta or tissues of animals. The residue of concern is best defined as the parent.

2. *Analytical method*. Practical analytical methods for detecting and measuring levels of flumioxazin have been developed and validated in/on all appropriate agricultural commodities and respective processing fractions. The extraction methodology has been validated using aged radiochemical residue samples from ^{14}C-metabolism studies. The enforcement method has been validated in soybean at an independent laboratory and by EPA. The limit of quantitation (LOQ) of flumioxazin in the method is 0.02 ppm which will allow monitoring of food with residues at the levels proposed for the tolerances.

3. *Magnitude of residues*—i.*Cotton.* Thirteen field trials in cotton were conducted in 1999 in EPA Regions II (1 trial), IV (4 trials), VI (1 trial), VIII (4 trials), and X (3 trials), representing approximately 97% of the U.S. cotton growing regions. Seasonal treatment ranged from 0.190 to 0.375 pounds active ingredient per acre [two applications of 0.095 lb. a.i./A each or two applications of 0.187 lb. a.i./A each], 1.5- to 3-times the proposed application rate for high organic soils. Application of VALOR was done lay-by and post direct to the soil and not over the top. Finite residues of flumioxazin were detected in 7 of 26 duplicate samples cottonseed and in 14 of the 16 duplicate samples of gin trash. The LOQ of the residue method was 0.01 ppm, and the limit of detection (LOD) was 0.005 ppm. No residues of 1-OH-HPA were detected (<0.005 ppm) in any cottonseed or gin trash sample, including samples from trial treated at the 2X rate. The data demonstrate that 1-OH-HPA is not a residue of concern in cottonseed or cotton gin trash.

No residues of flumioxazin or its degradate were found in the processed commodities treated ginned seed, hulls, solvent extracted meal and refined oil.

All these data support proposed tolerance for flumioxazin in/on cotton at 0.02 ppm, and in/on cotton, gin byproducts at 0.60 ppm. No separate tolerances are needed for cotton processed commodities.

ii. *Grapes*. Twelve field trials in grapes were conducted in 1999 in EPA Regions I (2 trials) Region X (9 trials) and Region XI (1 trial), representing approximately 96% of the U.S. grapes growing regions. Seasonal treatment ranged from 0.75 to 3.75 pounds active ingredient per acre [two applications of 0.375 lb. a.i./A each or two applications of 1.87 lb. a.i./A each] 1 to 5-times the proposed application rate. Application on grapes was post direct and not over the top. At the proposed maximum seasonal rate of 0.75 lb. a.i./A, no residues of flumioxazin were found in/on grapes from all 12 trials. Residues of flumioxazin were detected in only one of six samples treated at 2X application rate (seasonal total of 1.5 lb. a.i./A). The residue found, 0.005 ppm, was below the LOQ of 0.01 ppm.

Grapes treated at 5X (seasonal total of 3.75 lb. a.i./A) the proposed use rate were processed into grape juice and raisins. The RAC grapes contained 0.006 ppm flumioxazin. No residues (<0.005 ppm) of flumioxazin were found in grape juice. In raisins 0.007 ppm flumioxazin was detected. These residues were below the LOQ of 0.01 ppm. The data demonstrate no concentration of flumioxazin residues in juice and raisins.

All these data support a proposed tolerance for flumioxazin in/on grapes of 0.02 ppm. No separate tolerances are needed for grapes processed commodities.

iii. *Almond.* Five field trials in almonds were conducted in 1999 in EPA Regions X, representative of all U.S. almond growing regions. Seasonal treatment ranged from 0.75 to 1.5 pounds active ingredient per acre [two applications of 0.375 lb. a.i./A each or two applications of 0.75 lb. a.i./A each] 1 to 2-times the proposed application rate. Application on almonds was done post direct and not over the top. At the proposed maximum seasonal rate of 0.75 lb. a.i./A, no residues of flumioxazin were found in/on almond nutmeat greater than the LOQ (0.01 ppm). The highest average field Trial for residues of flumioxazin in/on almond hulls was 0.552 ppm. Residues of 1-OH-HPA were not detected in any sample of almond hulls (<0.05 ppm).The LOQ and LOD of the residue method for 1-OH-HPA in/on almond hulls were 0.1 ppm and 0.05 ppm, respectively.

All these data support a proposed tolerance for flumioxazin in/on almond of 0.02 ppm, and in/on almond hulls of 0.6 ppm.

iv. *Sugarcane*. Nine field trials in sugarcane were conducted in 1998 in EPA Regions III (4 trials), IV (3 trials), VI (1 trial), and XIII (1 trial), representative of all of the U.S. sugarcane growing regions. Treatments ranged from 0.37 to 1.12 pounds active ingredient per acre, 1- to 3-times the proposed application rate for high organic soils. Finite residues of flumioxazin were detected in 14 of 18 duplicate samples. Residues of flumioxazin averaged 0.039 ppm (standard deviation = 0.033 ppm) from the trials conducted at the proposed maximum application rate. Analysis for the major plant metabolite, 1-OH-HPA, was conducted on all cane samples including those from the two 3X processing trials. No residues of the degradate were found in any cane sample.

No residues of flumioxazin or its degradate were found in the processed commodity refined sugar. In molasses, produced from cane treated at three times the proposed label rate, flumioxazin was detected (0.055 ppm) at approximately half of the concentration in the starting sugarcane. The degradate, 1-OH-HPA, was also detected in molasses (0.036 ppm). Because these detections were in a processed sample from cane treated at 3X, and are still less than the proposed RAC tolerance, no separate processed product tolerances are necessary.

All these data support a proposed tolerance for flumioxazin in/on sugarcane at 0.20 ppm. No separate tolerances for parent or degradate are needed for processed commodities.

B. Toxicological Profile

1. *Acute toxicity*. The acute toxicity of technical grade flumioxazin is low by all routes. The battery of acute toxicity studies place flumioxazin in Toxicity Category III.

i. No abnormal clinical signs, body weight changes, or gross pathological findings were observed and no rats died following administration of an oral dose of 5 g/kg of flumioxazin technical. The LD_{50} was greater than 5 g/kg.

ii. No deaths, abnormal clinical signs, body weight changes, or gross pathological findings were observed in rats exposed to a 2.0 g/kg dermal dose of flumioxazin technical. The LD_{50} was greater than 2.0 g/kg.

iii. Rats were exposed to a dust aerosol of flumioxazin technical for 4 hours at measured concentrations of 1.55 or 3.93 mg/l, the maximum attainable concentration. Irregular respiration, bradypnea and a decrease in spontaneous activity were observed in many of the rats, but these effects disappeared within 2 hours after termination of the exposure. No deaths, body weight changes, gross pathological findings or histopathological changes in the respiratory organs were observed. The LC_{50} for flumioxazin technical was determined to be greater than 3.93 mg/l.

iv. Flumioxazin technical produced minimal eye irritation in rabbits which cleared within 48 hours.

v. Flumioxazin technical did not produce any signs of skin irritation in abraded or intact skin of rabbits.

vi. Flumioxazin technical was not a skin sensitizer when tested in guinea pigs using the Magnussen and Kligman maximization test methodology.

2. *Genotoxicty*. Flumioxazin does not present a genetic hazard. Flumioxazin was evaluated in the following tests for mutagenicity:

i. A reverse gene mutation assay in *Salmonella typhimurium* and *Escherichia coli* was negative with or without metabolic activation.

ii. An *in vitro* chromosome aberration assay using Chinese hamster ovary (CHO) cells was negative in the absence of metabolic activation. However, an increase in cells with aberrations was observed at doses of 1×10^{-4} M and higher in the presence of S9.

iii. An *in vivo* chromosomal aberration study in the rat was negative. No significant increase in the incidence of chromosomal aberrations in bone marrow cells was observed following treatments as high as 5,000 mg/kg.

iv. An *in vitro* unscheduled DNA synthesis (UDS) assay with rat hepatocytes was negative.

v. A mouse micronucleus assay was negative following intraperitoneal injection of 5,000 mg/kg.

3. *Reproductive and developmental toxicity*. Flumioxazin shows developmental toxicity in the absence of maternal toxicity in rats. Mechanistic studies demonstrate that the effect is specifically related to the inhibition of heme synthesis, that the effect shows considerable species specificity, and that the rat is a conservative surrogate species for the potential for developmental toxicity in man. No developmental toxicity was observed in rabbits. Developmental toxicity to the pups was seen in the rat reproduction study at doses that were not toxic to the parental animals.

i. *Rat--developmental toxicity.* A pilot dose range-finding study was conducted to determine appropriate doses for the definitive oral developmental toxicity study. Flumioxazin technical was administered by oral gavage at dosages of 0, 30, 100, 200 and 500 mg/kg/day to pregnant rats on days 6 through 15 of gestation. No animals died during the course of this study and maternal toxicity was limited to decreased weight gain associated with high embryolethality observed in all dose groups. Fetuses obtained from the 30 mg/kg/day dams had significantly reduced body weights and were found to have both skeletal and visceral abnormalities--primarily wavy ribs and ventricular septal defects (VSD). Because of the high degree of embryolethality at doses of 100 mg/kg/day and greater, the highest dose selected for the definitive study was 30 mg/kg/day.

In the definitive study, pregnant rats were administered oral doses of 0, 1, 3, 10 or 30 mg/kg/day of flumioxazin technical on days 6 through 15 of gestation. No maternal deaths were observed at any dosage and no treatment-related effects on clinical signs or food consumption were noted.

A decrease in maternal body weight gain was found at 30 mg/kg/day. The number of live fetuses and fetal body weights were decreased in the 30 mg/kg/day group and the incidence of embryo mortality tended to be higher but was not statistically significant. No effects on the number of implantations, sex ratios, or external abnormalities were found. The incidence of fetuses with cardiovascular abnormalities, primarily VSD, was increased in the 30 mg/kg/day group. Other developmental effects observed at 30 mg/kg/day included an increase in the incidence of wavy ribs and curvature of the scapula, and a decrease in the number of ossified sacrococcygeal vertebral bodies. Based on these findings, a maternal NOEL of 30 mg/kg/day and a developmental NOEL of 3 mg/kg/day are proposed.

In a range-finding dermal developmental toxicity study flumioxazin technical was administered dermally at levels of 100, 200, 400 and 800 mg/kg/day in corn oil. No adverse effects on the dams were observed at doses up to 800 mg/kg/day. Because of the high degree of embryolethality at doses of 400 mg/kg/day and greater, the highest dose selected for the definitive study was 300 mg/kg/day.

On days 6-15 of gestation, pregnant rats were exposed dermally to dose levels of 30, 100, or 300 mg/kg/day of flumioxazin technical in corn oil. No adverse effects were observed in the dams throughout the study. Increased fetal mortality was accompanied by decreases in the number of live fetuses and fetal body weights at doses of 300 mg/kg/day. No external abnormalities were observed at any dose level. An increase in cardiovascular abnormalities, primarily VSD, an increase in wavy ribs and a decrease in the number of ossified sacrococcygeal vertebral bodies was observed at 300 mg/kg/day. Based on these results, a maternal NOEL of 300 mg/kg/day and a developmental NOEL of 30 mg/kg/day are proposed.

To measure the dermal penetration of flumioxazin under the conditions of the dermal teratology study, 13-day pregnant rats were dermally exposed to [phenyl-^{14}C] flumioxazin. The systemic absorption ranged from 3.8% at 2 hours to 6.9% of the recovered ^{14}C at 48 hours.

ii. *Mechanistic studies*. A series of scientific studies were conducted to examine the mechanism and species differences in the production of developmental toxicity by flumioxazin. This research demonstrates clear species differences between rats, rabbits, mice, and (*in vitro*) humans and indicates a high degree of correlation between the interruption of heme synthesis and the production of developmental toxicity in rats. The data support that the rat is a conservative model for use in the risk assessment for humans. Specifically the studies demonstrate that:

- Flumioxazin interferes with normal heme biosynthesis resulting in sidroblastic anemia and porphyria in adult rats.
- ^{14}C-Flumioxazin administered to pregnant rats on day 12 of gestation crosses the placenta and reaches the rat fetus at maximum levels of radiocarbon (and flumioxazin), 4 hours later.
- No clear pattern of adsorption, distribution, metabolism, or excretion was evident which could account for the species-specific development toxicity in rats.
- The critical period of sensitivity to the developmental effects of flumioxazin in rats is day 12 of gestation. This correlates with the peak period of protoporphyrin IX (PPIX) accumulation in maternal rat liver and the rat fetus.
- A histological examination of rat fetus indicated signs of fetal anemia within 6 hours after dosing, but no histological changes in the fetal rat heart were observed until 36 or 48 hour after treatment. No effects were observed in rabbit fetus treated in the same manner as the rats.
- Other observations in the pathogenesis of the developmental effects of flumioxazin in rat fetuses included: enlarged heart, edema, anemia (decreased red blood cell count and hemoglobin), delayed closure of the interventricular foramen, reduced serum protein and incomplete/delayed ossification of the ribs.
- The observation of enlarged heart, edema and anemia preceding the occurrence of fetal mortality suggest these effects may be instrumental in the cause of fetal deaths.
- The occurrence of an enlarged heart preceding the failure of interventricular foramen closure could be related to the pathogenesis rather than a direct toxic effect of flumioxazin on cardiac tissue.
- A strong correlation exists between PPIX accumulation, an indicator of disrupted heme synthesis, and developmental toxicity. Evidence of this correlation exists on the basis of species differences between rats and rabbits; the critical period of sensitivity in the rat; and compound-specific differences with two chemicals structurally related to flumioxazin, one which produces developmental effects in rats and one which does not.

iii. *Rabbits*. In a pilot dose range-finding study in rabbits, flumioxazin technical was administered to rabbits on days 7 through 19 of gestation via oral intubation at dosages of 0, 300, 500, 1,000 and 1,500 mg/kg/day. Clinical observations were recorded and on day 29 of gestation, all does were sacrificed, caesarean sectioned, and examined for gross lesions, number of corpora lutea, and number and placement of implantation sites, early and late resorptions and live and dead fetuses. No deaths, abortions or premature deliveries occurred during this study. Dosages of flumioxazin technical as high as 1,500 mg/kg/day did not result in significant clinical or necropsy observations nor affect maternal body weight gains or feed consumption values. Similarly, there were no adverse effects of dosages of flumioxazin technical up to 1,500 mg/kg/day on embryo-fetal viability, sex ratios, body weights or external morphology.

Based on these results, pregnant rabbits were administered 0, 300, 1,000, or 3,000 mg/kg/day of flumioxazin technical on days 7 - 19 of gestation by oral gavage. The highest dose was well in excess of the 1,000 mg/kg/day limit dose for developmental toxicity studies. The 3,000 mg/kg/day dosage tended to reduce maternal body weight gains and relative and absolute feed consumption values. No gross lesions were produced at any dose level. The 3,000 mg/kg/day dosage group litters tended to have reduced fetal body weights but these differences were not statistically different. No fetal external, soft tissue, or skeletal malformations or variants were attributable to the test substance. Based on these data, the maternal NOEL was 1,000 mg/kg/day and the developmental NOEL was 3,000 mg/kg/day.

iv. *Reproduction*. Two pilot range-finding rat reproduction studies were conducted with flumioxazin technical at dosages from 100 to 5,000 ppm in the diet. In the definitive two-generation reproduction study in the rat dietary levels of 0, 50, 100, 200 and 300 ppm established a systemic NOEL of 200 ppm based on increased clinical signs (both sexes and generations); mortality, gross and histopathology findings in the liver (F_1 females); decreased body weight/weight gain (F_0 and F_1 females during gestation, F_1 males during premating) and decreased food consumption (F_0 and F_1 females during lactation). The reproductive NOEL of 100 ppm was mainly based on developmental toxicity at 200 ppm. Observed at 200 ppm were a decreased number of live-born pups and reduced pup body weights. At 300 ppm the following effects were observed: decreased pup body weight (both generations); decreased number of live pups/litter and viability index (both

generations); increased incidence of abnormalities of the reproductive organs (predominately atrophied or hypoplastic testes and/or epididymides in F_1 males); decreased gestation index (F_0 females); decreased mating and fertility indices (F_1 males) and increased clinical signs (F_1 pups).

4. *Subchronic toxicity.* Subchronic toxicity studies conducted with flumioxazin technical in the rat (oral and dermal), mouse and dog indicate a low level of toxicity. Effects observed at high dose levels consisted primarily of anemia and histological changes in the spleen, liver and bone marrow related to the anemia.

i. *Rats.* A 90-day subchronic toxicity study was conducted in rats, with dietary intake levels of 0, 30, 300, 1,000 and 3,000 ppm flumioxazin technical (98.4% purity). The no-observed-effect-level (NOEL) of 300 ppm was based on decreased body weights; anemia; increases in absolute and/or relative liver, kidney, brain heart and thyroid weights; and histological changes in the spleen, liver and bone marrow related to the anemia.

A second 90–day subchronic toxicity study was conducted with a sample of Flumioxazin Technical of typical purity (94.8%) at dietary concentrations of 0, 30, 300, 1,000 and 3,000 ppm. The NOEL was 30 ppm based on anemia and related hematological changes; increases in liver, heart, kidney and thyroid weights; and histological changes in the spleen, liver and bone marrow related to the anemia.

ii. *Mice.* Dose levels for the mouse oncogenicity study were selected on the basis of results from a 4–week study of flumioxazin in the diets of mice at levels of 0, 1,000, 3,000 and 10,000 ppm. In this range-finding study, increases in absolute and/or relative liver weights were noted for males at 10,000 ppm and at 3,000 and 10,000 ppm for females.

iii. *Dogs.* A 90–day study was conducted in dogs given gelatin capsules containing 0, 10, 100 or 1,000 mg/kg/day. The NOEL of 10 mg/kg/day for this study was based on a slight prolongation of activated partial thromboplastin time; increased total cholesterol and phospholipid and elevated alkaline phosphatase activity; increased absolute and relative liver weights; and histological changes in the liver.

iv. *Rats.* A 21–day dermal toxicity study was conducted in rats at dose levels of 0, 100, 200 or 1,000 mg/kg/day. The NOEL was determined to be 300 mg/kg/day based on significantly decreased hemoglobin and hematocrit values for females.

5. *Chronic toxicity.* Flumioxazin technical has been tested in chronic studies with dogs, rats and mice. Valent proposes a chronic oral endpoint of 1.8 mg/kg bw/day, based on the NOEL for male rats in the two-year chronic toxicity oncogenicity feeding study.

i. *Rats.* In a 2–year study in rats, flumioxazin technical administered in the diet at levels of 0, 50, 500, and 1,000 ppm produced anemia and chronic nephropathy in rats of the 500 and 1,000 ppm groups. The anemia lasted throughout the treatment period, however, it was not progressive nor aplastic in nature. No evidence of an oncogenic effect was observed in rats and the NOEL for this study was 50 ppm (1.8 mg/kg/day for males and 2.2 mg/kg/day for females).

ii. *Mice.* Flumioxazin technical was administered to mice at doses of 0, 300, 3,000, and 7,000 ppm in diet for 78 weeks. An increased incidence of hypertrophy of centrilobular hepatocytes was observed in males of the 3,000 and 7,000 ppm groups. Increases in the incidence of diffuse hypertrophy and single cell necrosis of hepatocytes were observed in females of the 3,000 and 7,000 ppm groups. There was no evidence of any treatment-related effect on the incidence of tumors. Flumioxazin technical was not carcinogenic to mice, and the NOEL for this study was 300 ppm (31.1 mg/kg/day for males and 36.6 mg/kg/day for females).

iii. *Dogs.* Flumioxazin technical was administered to dogs in capsules at daily doses of 0, 10, 100, and 1,000 mg/kg bw/day for 1 year. Treatment-related changes in blood biochemistry included increased total cholesterol and phospholipid values, elevated *alpha*-2-globulin ratio at 1,000 mg/kg/day and increased alkaline phosphatase activity in the 100 and 1,000 mg/kg/day groups. The absolute and/or relative liver weights were elevated in one animal in the 100 mg/kg/day group and four animals of the 1,000 mg/kg/day group. Minimal treatment-related histological changes were noted in the livers of animals at the 1,000 mg/kg/day group. Based on these data the NOEL was determined to be 10 mg/kg/day.

iv. *Carcinogenicity.* Flumioxazin is not a carcinogen. Adequately designed studies with both rats and mice have shown that repeated high dose exposures produced anemia, liver effects and nephropathy, but did not produce cancer in test animals. No oncogenic response was observed in a rat 2–year chronic feeding/oncogenicity study or in a 78 week study on mice. Valent anticipates that the oncogenicity classification of flumioxazin will be ''E'' (no evidence of carcinogenicity for humans).

6. *Animal metabolism.* The absorption, tissue distribution, metabolism and excretion of phenyl-^{14}C-labeled flumioxazin were studied in rats after single oral doses of 1 or 100 mg/kg, and after a single oral dose of 1 mg/kg following 14 daily oral doses at 1 mg/kg of unlabelled material. For all dose groups, most (97.9-102.3%) of the administered radiolabel was excreted in the urine and feces within 7 days after radiolabeled test material dosing. Radiocarbon tissue residue levels were generally low on the seventh day post-dosing. Radiocarbon residues were higher in blood cells than tissues. Tissue ^{14}C-residue levels, including those for fat, were lower than blood levels which suggests little potential for bioaccumulation. Urinary radiocarbon excretion was greater in females than males in all dose groups.

Flumioxazin was extensively metabolized by rats and 35 metabolites were detected and quantitated. The main metabolic reactions in rats were (1) hydroxylation of the tetrahydrophthalimide moiety; (2) incorporation of the sulfonic acid group into the tetrahydrophthalimide moiety; (3) cleavage of the imide linkage; (4) cleavage of the benzoxazinoneamide and;(5) acetylation of the aniline nitrogen group.

7. *Metabolite toxicology.* Metabolism studies of flumioxazin in rats, goats, hens, soybeans, and peanuts, as well as the fish bioaccumulation study demonstrate that the parent is very rapidly metabolized and, in animals, eliminated. The metabolites detected and quantified from plants and animals show that there are no significant aglycones in plants which are not also present in the excreta or tissues of animals. Because parent and metabolites are not retained in the body, the potential for acute toxicity from *in situ* formed metabolites is low. The potential for chronic toxicity is adequately tested by chronic exposure to the parent at the MTD and consequent chronic exposure to the internally formed metabolites.

8. *Endocrine disruption.* No special studies to investigate the potential for estrogenic or other endocrine effects of flumioxazin have been performed. However, as summarized above, a large and detailed toxicology database exists for the compound including studies in all required categories. These studies include acute, sub-chronic, chronic, developmental, and reproductive toxicology studies including detailed histology and histopathology of numerous tissues, including endocrine organs, following repeated or long term

exposures. These studies are considered capable of revealing endocrine effects. The results of all of these studies show no evidence of any endocrine-mediated effects and no pathology of the endocrine organs. Consequently, it is concluded that flumioxazin does not possess estrogenic or endocrine disrupting properties.

C. Aggregate Exposure

1. *Dietary exposure*. A full battery of toxicology testing including studies of acute, chronic, oncogenicity, developmental, mutagenicity, and reproductive effects is available for flumioxazin. In these risk assessments Valent has chosen as the chronic oral toxic endpoint the NOEL for males from the rat chronic/oncogenicity feeding study, 1.8 mg/kg/day; and as the acute oral toxic endpoint the NOEL (proposed by EPA) from the rat oral developmental toxicity study of 3.0 mg/kg/day. Because the acute oral endpoint is for fetal toxicity to rats, Valent has chosen to use the full, extra 10X uncertainty factor for appropriate sub-groups of the population as mandated by FQPA.

i. *Food*. a. Acute dietary exposures to flumioxazin residues were calculated for the U.S. population, Women 13 years and older, and five children subgroups. The calculated exposure values are very conservative because tolerance-level residues and 100% of the crop treated are assumed. For refined sugar from sugarcane and juice from grapes for which processing is required, concentration factors were considered. The calculated exposures and margins of exposure (MOE) for the higher exposed proportions of the subgroups are listed below. In all cases, margins of exposure relative to the acute endpoint from the rat oral developmental toxicity study exceed 1,000.

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

Population Subgroup	95th Percentile		99.9th Percentile	
	Exposure (mg/kg/day)	MOE	Exposure (mg/kg/day)	MOE
Total U.S. Population	0.000063	47,737	0.000287	10,442
Women 13 Years and Older	0.000040	74,350	0.000128	23,527
Children 7 to 12 Years	0.000076	39,620	0.000310	9,675
Children 1 to 6 Years	0.000153	19,583	0.000599	5,008
All Infants	0.000205	14,608	0.000800	3,750
Non-Nursing Infants (<1 yr old)	0.000217	13,807	0.000799	3,753
Nursing Infants (<1 yr old)	0.000106	28,357	0.000283	10,612

b. Chronic dietary exposures to flumioxazin residues were calculated for the U.S. population and 25 population subgroups. This modified Tier I analysis assumes tolerance-level residues, processing factors for grape and cane sugar, and 100 percent of the crops treated. The results from several representative subgroups are listed below. All calculated chronic dietary exposures were below 5% of the c-PAD. The c-PAD was defined as the NOEL from the rat oral two-year combined chronic toxicity oncogenicity study (1.8 mg/kg/day for males) divided by the 100X uncertainty factor for the adult exposures (0.018 mg/kg/day), or divided by 1,000 to include the extra 10X uncertainty factor for adult females of child-bearing age and infant and children population subgroups (0.0018 mg/kg/day). Generally speaking, the Agency has no cause for concern if total residue contribution for published and proposed tolerances is less than 100 percent of the c-PAD.

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

Population Subgroup	Exposure (mg/kg/day)	Percent of c-PAD
Total U.S. Population (total) (0.018)*	0.000020	0.11
Females 13+ (nursing) (0.0018)*	0.000016	0.89
Females 13+ (preg./not nursing) (0.0018)*	0.000015	0.83
Children 7-12 yrs (0.018)*	0.000030	0.17
Children 1-6 yrs (0.0018)*	0.000052	2.89
All Infants (<1 year) (0.0018)*	0.000067	3.72
Non-Nursing Infants (0.0018)*	0.000082	4.56
Nursing Infants (0.0018)*	0.000016	0.89

*c-PAD value used to calculate percent of occupancy.

ii. *Drinking water*. Since flumioxazin is applied outdoors to growing agricultural crops, the potential exists for the parent or its metabolites to reach ground or surface water that may be used for drinking water. Because of the physical properties of flumioxazin, it is unlikely that flumioxazin or its metabolites can leach to potable groundwater. To quantify potential exposure from drinking water, surface water concentrations for flumioxazin were estimated using GENEEC 1.2. Because K_{OC} could not be measured

directly in adsorption- desorption studies because of chemical stability, GEEC values representative of a range of K_{OC} values were modeled. The simulation that was selected for these exposure estimates used an average K_{OC} of 385, indicating high mobility. The peak GEEC concentration predicted in the simulated pond water was 9.8 ppb. Using standard assumptions about body weight and water consumption, the acute exposure from this drinking water would be 0.00028 and 0.00098 mg/kg/day for adults and children, respectively. The 56-day GEEC concentration predicted in the simulated pond water was 0.34 ppb. Chronic exposure from this drinking water would be 0.0000097 and 0.000034 mg/kg/day for adults and children, respectively; 1.9 percent of the c-PAD of 0.0018 mg/kg/day for children. Based on this worse case analysis, the contribution of drinking water to the dietary exposure is comparable to that from food, but the risk is still negligible.

2. *Non-dietary exposure*. Flumioxazin is proposed only for agricultural uses and no homeowner or turf uses. Thus, no non-dietary risk assessment is needed.

D. Cumulative Effects

Section 408(b)(2)(D)(v) requires that the Agency must consider ''available information'' concerning the cumulative effects of a particular pesticide's residues and ''other substances that have a common mechanism of toxicity.'' Available information in this context include not only toxicity, chemistry, and exposure data, but also scientific policies and methodologies for understanding common mechanisms of toxicity and conducting cumulative risk assessments. For most pesticides, although the Agency has some information in its files that may turn out to be helpful in eventually determining whether a pesticide shares a common mechanism of toxicity with any other substances, EPA does not at this time have the methodologies to resolve the complex scientific issues concerning common mechanism of toxicity in a meaningful way.

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

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

E. Safety Determination

1. *U.S. population*—i. *Acute risk*. The potential acute exposure from food to the U.S. population and various non-child/infant population subgroups provide MOE values exceeding 1,000. Addition of the worse case, but small ''background'' dietary exposure from water reduces the MOE value at the 99.9th percentile from 10,442 to 5,291. In a conservative policy, the Agency has no cause for concern if total acute exposure to adults calculated for the 95th percentile (for the Tier I calculated acute dietary exposure using tolerance level residues and 100% crops treated) yields a MOE of 100 or larger. For women of child bearing age where an MOE of 1,000 or larger is appropriate, the addition of water to the diet of women, 13 years and older, reduces the MOE (99.9th percentile) from 23,527 to 7,353. It can be concluded that there is a reasonable certainty that no harm will result to the overall U.S. Population and many non-child/infant subgroups from aggregate, acute exposure to flumioxazin residues.

ii. *Chronic risk*. Using the dietary exposure assessment procedures described above for flumioxazin, calculated chronic dietary exposure resulting from residue exposure from proposed uses of flumioxazin is minimal. The estimated chronic dietary exposure from food for the overall U.S. Population and many non-child/infant subgroups is 0.11 to 0.89% of the appropriate c-PAD. Addition of the small but worse case potential exposure from drinking water (calculated above) increases exposure by 0.0000097 mg/kg /day and the maximum occupancy of the c-PAD from 0.89 to 1.43% (women 13 +). Generally, the Agency has no cause for concern if total residue contribution is less than 100% of the appropriate c-PAD. It can be concluded that there is a reasonable certainty that no harm will result to the overall U.S. Population and many non-child/infant subgroups from aggregate, chronic exposure to flumioxazin residues.

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

i. *Children*. The toxicological database for evaluating pre- and post-natal toxicity for flumioxazin is complete with respect to current data requirements. Developmental toxicity was observed by both oral and dermal routes in rats. Therefore, reliable data support use of the standard 100-fold uncertainty factor and an additional uncertainty factor of 10X for flumioxazin to be further protective of infants and children.

ii. *Developmental toxicity studies*. Flumioxazin shows developmental toxicity in the absence of maternal toxicity in rats. Mechanistic studies demonstrate that the effect is specifically related to the inhibition of heme synthesis, that the effect shows considerable species specificity, and that the rat is a conservative surrogate species for the potential for developmental toxicity in man. No developmental toxicity was observed in rabbits. Developmental toxicity to the pups was seen in the rat reproduction study at doses that were not toxic to the parental animals.

a. *Rats*. In the definitive rat oral developmental toxicity study, pregnant rats were administered oral doses of 0, 1, 3, 10 or 30 mg/kg/day of flumioxazin technical on days 6 through 15 of gestation. No maternal deaths were observed at any dosage and no treatment-related effects on clinical signs or food consumption were noted. A decrease in maternal body weight gain was found at 30 mg/kg/day. The number of live fetuses and fetal body weights were decreased in the 30 mg/kg/day group and the incidence of embryo mortality tended to be higher but was not statistically significant. No effects on the number of implantations, sex ratios, or external abnormalities were found. The incidence of fetuses with cardiovascular abnormalities, primarily VSD, was increased in the 30 mg/kg/day group. Other developmental effects observed at 30 mg/kg/day included an increase in the incidence of wavy ribs and curvature of the scapula, and a decrease in the number of ossified sacrococcygeal vertebral bodies. Based on these findings, a maternal NOEL of 30 mg/kg/day and a developmental NOEL of 3 mg/kg/day are proposed.

On days 6-15 of gestation, pregnant rats were exposed dermally to dose levels of 30, 100, or 300 mg/kg/day of flumioxazin technical in corn oil. No

adverse effects were observed in the dams throughout the study. Increased fetal mortality was accompanied by decreases in the number of live fetuses and fetal body weights at doses of 300 mg/kg/day. No external abnormalities were observed at any dose level. An increase in cardiovascular abnormalities, primarily VSD, an increase in wavy ribs and a decrease in the number of ossified sacrococcygeal vertebral bodies was observed at 300 mg/kg/day. Based on these results, a maternal NOEL of 300 mg/kg/day and a developmental NOEL of 30 mg/kg/day are proposed.

To measure the dermal penetration of flumioxazin under the conditions of the dermal teratology study, 13-day pregnant rats were dermally exposed to [phenyl-^{14}C] flumioxazin. The systemic absorption ranged from 3.8% at 2 hours to 6.9% of the recovered ^{14}C at 48 hours.

b. *Mechanistic studies.* A series of scientific studies were conducted to examine the mechanism and species differences in the production of developmental toxicity by flumioxazin. This research demonstrates clear species differences between rats, rabbits, mice, and (in vitro) humans and indicates a high degree of correlation between the interruption of heme synthesis and the production of developmental toxicity in rats. The data support that the rat is a conservative model for use in the risk assessment for humans. Specifically the studies demonstrate that:

• Flumioxazin interferes with normal heme biosynthesis resulting in sidroblastic anemia and porphyria in adult rats.

•^{14}C-Flumioxazin administered to pregnant rats on day 12 of gestation crosses the placenta and reaches the rat fetus at maximum levels of radiocarbon (and flumioxazin), 4 hours later.

• No clear pattern of adsorption, distribution, metabolism, or excretion was evident which could account for the species-specific development toxicity in rats.

• The critical period of sensitivity to the developmental effects of flumioxazin in rats is day 12 of gestation. This correlates with the peak period of protoporphyrin IX (PPIX) accumulation in maternal rat liver and the rat fetus.

• A histological examination of rat fetus indicated signs of fetal anemia within 6 hours after dosing, but no histological changes in the fetal rat heart were observed until 36 or 48 hour after treatment. No effects were observed in rabbit fetus treated in the same manner as the rats.

• Other observations in the pathogenesis of the developmental effects of flumioxazin in rat fetuses included: enlarged heart, edema, anemia (decreased red blood cell count and hemoglobin), delayed closure of the interventricular foramen, reduced serum protein and incomplete/delayed ossification of the ribs.

• The observation of enlarged heart, edema and anemia preceding the occurrence of fetal mortality suggest these effects may be instrumental in the cause of fetal deaths.

• The occurrence of an enlarged heart preceding the failure of interventricular foramen closure could be related to the pathogenesis rather than a direct toxic effect of flumioxazin on cardiac tissue.

• A strong correlation exists between PPIX accumulation, an indicator of disrupted heme synthesis, and developmental toxicity. Evidence of this correlation exists on the basis of species differences between rats and rabbits; the critical period of sensitivity in the rat; and compound-specific differences with two chemicals structurally related to flumioxazin, one which produces developmental effects in rats and one which does not.

c. *Rabbits.* Pregnant rabbits were administered 0, 300, 1,000, or 3,000 mg/kg/day of flumioxazin technical on days 7 - 19 of gestation by oral gavage. The highest dose was well in excess of the 1,000 mg/kg/day limit dose for developmental toxicity studies. The 3,000 mg/kg/day dosage tended to reduce maternal body weight gains and relative and absolute feed consumption values. No gross lesions were produced at any dose level. The 3,000 mg/kg/day dosage group litters tended to have reduced fetal body weights but these differences were not statistically different. No fetal external, soft tissue, or skeletal malformations or variants were attributable to the test substance. Based on these data, the maternal NOEL was 1,000 mg/kg/day and the developmental NOEL was 3,000 mg/kg/day.

iii. *Reproductive toxicity study.* In the two-generation reproduction study in the rat dietary levels of 0, 50, 100, 200 and 300 ppm established a systemic NOEL of 200 ppm based on increased clinical signs (both sexes and generations); mortality, gross and histopathology findings in the liver (F_1 females); decreased body weight/weight gain (F_0 and F_1 females during gestation, F1 males during premating) and decreased food consumption (F_0 and F_1 females during lactation). The reproductive NOEL of 100 ppm was mainly based on developmental toxicity at 200 ppm. Observed at 200 ppm were a decreased number of live-born pups and reduced pup body weights. At 300 ppm the following effects were observed: decreased pup body weight (both generations); decreased number of live pups/litter and viability index (both generations); increased incidence of abnormalities of the reproductive organs (predominately atrophied or hypoplastic testes and/or epididymides in F_1 males); decreased gestation index (F_0 females); decreased mating and fertility indices (F_1 males) and increased clinical signs (F_1 pups).

iv. *Prenatal and postnatal sensitivity.* Flumioxazin interferes with normal heme biosynthesis resulting in sidroblastic anemia and porphyria in adult rats. Clear species differences between rats, rabbits, mice, and (*in vitro*) humans were demonstrated. There is a high degree of correlation between the interruption of heme synthesis, consequent PPIX accumulation, and the production of developmental toxicity in rats. The data support that the rat is a conservative model for use in the risk assessment for humans.

v. *Acute exposure and risk.* The potential acute exposure from food to the various child and infant population subgroups all provide MOE values exceeding 1,000. Addition of the worse case, but small ''background'' dietary exposure from water (0.00098 mg/kg/day) to the 99.9th percentile food exposure for infants reduces the MOE value from 3,753 to 1,686. In a conservative policy with the addition of the FQPA extra 10X uncertainty factor, the Agency has no cause for concern if total acute exposure to infants and children calculated for the 95th percentile for the Tier I acute dietary exposure yields a MOE of 1,000 or larger. It can be concluded that there is a reasonable certainty that no harm will result to infants and children from aggregate, acute exposure to flumioxazin residues.

vi. *Chronic exposure and risk.* Using the conservative exposure assumptions described above, the percentage of the c-PAD that will be utilized by dietary (food only) exposure to residues of flumioxazin ranges from 0.17% for children 7-12 years, to 4.6% for Non-Nursing Infants. Adding the worse case potential incremental exposure to infants and children from flumioxazin in drinking water (0.000034 mg/kg/day) increases the aggregate, chronic dietary exposure by 1.9%. The addition of the exposure attributable to drinking water increases the occupancy of the c-PAD for Non-Nursing Infants to 6.44%. EPA generally has no concern for exposures below 100% of the c-PAD because the c-PAD, in this case including the extra 10X FQPA uncertainty factor, represents the level at or below which daily

aggregate dietary exposure over a lifetime will not pose appreciable risks to human health. It can be concluded that there is a reasonable certainty that no harm will result to infants and children from aggregate, chronic exposure to flumioxazin residues.

vii. *Determination of safety—Summary*. Aggregate acute or chronic dietary exposure to various sub-populations of children and adults demonstrate acceptable risk. Chronic dietary exposures to flumioxazin occupy considerably less than 100% of the appropriate c-PAD, and all acute dietary MOE values exceed 1,000. Chronic and acute dietary risk to children from flumioxazin should not be of concern. Further, flumioxazin has only agricultural uses and no other uses, such as indoor pest control, homeowner or turf, that could lead to unique, enhanced exposures to vulnerable sub-groups of the population. It can be concluded that there is a reasonable certainty that no harm will result to the U.S. Population or to any sub-group of the U.S. population, including infants and children, from aggregate chronic or aggregate acute exposures to flumioxazin residues resulting from proposed uses.

F. International Tolerances

Flumioxazin has not been evaluated by the World Health Organization, Joint Meeting on Pesticide Residues (JMPR) and there are no Codex Maximum Residue Limits (MRL) for flumioxazin. MRL values have been established to allow the following uses of flumioxazin in the following countries.

Country	Crop	MRL (ppm)
Brazil	Soybean	0.05
Argentina	Soybean Sunflower	0.015 0.02
Paraguay	Soybean	0.015
South Africa	Soybean Groundnut	0.02 0.02

[FR Doc. 02–32990 Filed 12–30–02; 8:45 am]
BILLING CODE 6560–50–S

ENVIRONMENTAL PROTECTION AGENCY

[OPPT–2002–0077; FRL–7286–8]

Certain New Chemicals; Receipt and Status Information

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: Section 5 of the Toxic Substances Control Act (TSCA) requires any person who intends to manufacture (defined by statute to include import) a new chemical (i.e., a chemical not on the TSCA Inventory) to notify EPA and comply with the statutory provisions pertaining to the manufacture of new chemicals. Under sections 5(d)(2) and 5(d)(3) of TSCA, EPA is required to publish a notice of receipt of a premanufacture notice (PMN) or an application for a test marketing exemption (TME), and to publish periodic status reports on the chemicals under review and the receipt of notices of commencement to manufacture those chemicals. This status report, which covers the period from November 20, 2002 to December 10, 2002, consists of the PMNs pending or expired, and the notices of commencement to manufacture a new chemical that the Agency has received under TSCA section 5 during this time period.

DATES: Comments identified by the docket ID number OPPT– 2002–0077 and the specific PMN number or TME number, must be received on or before January 30, 2003.

ADDRESSES: Comments may be submitted electronically, by mail, or through hand delivery/courier. Follow the detailed instructions as provided in Unit I. of the **SUPPLEMENTARY INFORMATION.**

FOR FURTHER INFORMATION CONTACT: Barbara Cunningham, Acting Director, Environmental Assistance Division, Office of Pollution Prevention and Toxics (7408M), Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001; telephone number: (202) 554–1404; e-mail address: TSCA-Hotline@epa.gov.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

This action is directed to the public in general. As such, the Agency has not attempted to describe the specific entities that this action may apply to. Although others may be affected, this action applies directly to the submitter of the premanufacture notices addressed in the action. If you have any 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 Copies of This Document and Other Related Information?

1. *Docket.* EPA has established an official public docket for this action under docket identification (ID) number OPPT–2002–0077. The official public docket consists of the documents specifically referenced in this action, any public comments received, and other information related to this action. Although a part of the official docket, the public docket does not include Confidential Business Information (CBI) or other information whose disclosure is restricted by statute. The official public docket is the collection of materials that is available for public viewing at the EPA Docket Center, Rm. B102-Reading Room, EPA West, 1301 Constitution Ave., NW., Washington, DC. The EPA Docket Center is open from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays. The EPA Docket Center Reading Room telephone number is (202) 566–1744 and the telephone number for the OPPT Docket, which is located in EPA Docket Center, is (202) 566–0280.

2. *Electronic access.* You may access this **Federal Register** document electronically through the EPA Internet under the ''**Federal Register**'' listings at http://www.epa.gov/fedrgstr/.

An electronic version of the public docket is available through EPA's electronic public docket and comment system, EPA Dockets. You may use EPA Dockets at http://www.epa.gov/edocket/ to submit or view public comments, access the index listing of the contents of the official public docket, and to access those documents in the public docket that are available electronically. Although not all docket materials may be available electronically, you may still access any of the publicly available docket materials through the docket facility identified in Unit I.B.1. Once in the system, select ''search,'' then key in the appropriate docket ID number.

Certain types of information will not be placed in the EPA Dockets. Information claimed as CBI and other information whose disclosure is restricted by statute, which is not included in the official public docket, will not be available for public viewing in EPA's electronic public docket. EPA's policy is that copyrighted material will not be placed in EPA's electronic public docket but will be available only in printed, paper form in the official public docket. To the extent feasible, publicly available docket materials will be made available in EPA's electronic public docket. When a document is selected from the index list in EPA Dockets, the