C. Safety Determination

Based on the very low level of substance toxicity, relatively short period of environmental fate and its usage pattern, Mival exhibits very minimal risk exposure both in dietary and non-occupational exposures to children.

D. International Tolerances

There are no Codex maximum residue levels established for residues of Mival.

[FR Doc. 97–31549 Filed 12–2–97; 8:45 am]

BILLING CODE 6560–50–F

ENVIRONMENTAL PROTECTION AGENCY

[PF–780; FRL–5756–1]

Notice of Filing of Pesticide Petitions

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

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

DATES: Comments, identified by the docket control number PF–780, must be received on or before January 2, 1998.

ADDRESSES: By mail submit written comments to: Public Information and Records Integrity Branch, Information Resources and Services Division (7502C), Office of Pesticides Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. In person bring comments to: Rm. 1132, CM #2, 1921 Jefferson Davis Highway, Arlington, VA.

Comments and data may also be submitted electronically to: opp-docket@epamail.epa.gov. Follow the instructions under ''SUPPLEMENTARY INFORMATION.'' No confidential business information should be submitted through e-mail.

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

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

Product Manager	Office location/telephone number	Address
Joanne Miller (PM 23) ...	Rm. 237, CM #2, 703–305–6224, e-mail:miller.joanne@epamail.epa.gov.	1921 Jefferson Davis Hwy, Arlington, VA
James Tompkins (PM 25).	Rm. 239, CM #2, 703–305–5697, e-mail: tompkins.james@epamail.epa.gov.	1921 Jefferson Davis Hwy, Arlington, VA.

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

The official record for this notice of filing, as well as the public version, has been established for this notice of filing under docket control number [PF–780] (including comments and data submitted electronically as described below). A public version of this record, including printed, paper versions of electronic comments, which does not include any information claimed as CBI, is available for inspection from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The official record is located at the address in ''ADDRESSES'' at the beginning of this document.

Electronic comments can be sent directly to EPA at:

opp-docket@epamail.epa.gov

Electronic comments must be submitted as an ASCII file avoiding the use of special characters and any form of encryption. Comment and data will also be accepted on disks in Wordperfect 5.1 file format or ASCII file format. All comments and data in electronic form must be identified by the docket number (insert docket number) and appropriate petition number. Electronic comments on notice may be filed online at many Federal Depository Libraries.

List of Subjects

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

Dated: November 21, 1997

Peter Caulkins,

Acting Director, Registration Division, Office of Pesticide Programs.

Summaries of Petitions

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

1. Valent U.S.A. Corporation

PP 7F4873

EPA has received a pesticide petition (PP 7F4873) from Valent U.S.A. Corporation, 1333 N. California Blvd., Walnut Creek, CA 94596. proposing pursuant to section 408(d) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. 346a(d), to amend 40 CFR part 180 by establishing a tolerance for residues of clethodim in or on the raw agricultural commodities tuberous and corm vegetables (crop subgroup 1-C) at 1.0 parts per million (ppm), potato flakes/granules at 2.0 ppm, sunflower seed at 5.0 ppm, sunflower meal at 10.0 ppm, canola seed at 0.5 ppm, and canola meal at 1.5 ppm. The crop subgroup 1-C tolerance should replace the 0.5 ppm tolerance that already exists for clethodim in/or potato tubers which was based on data from Canada. The

proposed analytical method for these commodities is EPA-RM-26D-3, a high-performance liquid chromatography (HPLC) method. 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*. Clethodim is used for postemergent control of grasses in a wide variety of crops including cotton, soybeans, sugar beets, onions, tomatoes, etc. Plant metabolism studies have been performed in carrots, soybeans, and cotton. Studies were performed with clethodim radiolabeled in the ring structure and in the side chain to follow both parts of the molecule.

The major metabolic pathway in plants is initial sulfoxidation to form clethodim sulfoxide followed by further sulfoxidation to form clethodim sulfone; elimination of the chloroallyloxy side chain to give the imine sulfoxide and sulfone; and hydroxylation to form the 5-OH sulfoxide and 5-OH sulfone. Clethodim sulfoxide and clethodim sulfone conjugates were also detected as major or minor metabolites, depending on plant species and subfractions. Once cleaved from clethodim, the chloroallyloxy moiety udergoes extensive metabolism to eliminate the chlorine atom and incorporate the three-carbon moieties into natural plant components.

Based on these metabolism studies, the residues of concern in crops are clethodim and its metabolites containing the cyclohexene moiety, and their sulfoxides and sulfones.

2. *Analytical method*. Adequate analytical methodology is available for detecting and measuring levels of clethodim and its metabolites in crops. For most commodities, the primary enforcement method is EPA-RM-26D-3, an HPLC method capable of distinguishing clethodim from the structurally related herbicide sethoxydim. However, for milk natural interferences prevent adequate quantitation of clethodim moieties and the common-moiety method (RM-26B-2) is the primary enforcement method with EPA-RM-26D-3 as the secondary method if needed to determine whether residues are clethodim or sethoxydim. Both of these methods have successfully undergone petition method validations at EPA.

3. *Magnitude of residues*. Clethodim is the active ingredient in SELECT 2 EC Herbicide (EPA Reg. No. 59639-3) and SELECT Herbicide (also known as PRISM and ENVOY Herbicides, EPA Reg. No. 59639-78). Tolerances have been established for residues in cotton, soybean, sugar beet, onion (dry bulb), and animal commodities, and tolerances are expected soon for alfalfa, peanut, dry bean, and tomato commodities. A summary of available field residue data for the pending tolerances on tuberous and corm vegetables (crop subgroup 1-C), sunflower, and canola commodities is presented below.

In 17 field trials, potatoes were treated with two post-emergent applications of 0.25 lb. a.i./A each, approximately 14–days apart, and harvested approximately 30 days after the last application. Trials were performed in EPA Regions 1, 2, 3, 5, 9, 10, and 11. Residues for potato tuber samples ranged from < 0.1 ppm to 0.80 ppm total clethodim. The highest average field trial (HAFT) residue was 0.775 ppm. The average residue value for all trials, excluding samples less than the limit of detection, was 0.42 ppm. Two processing studies were also performed for potatoes. Residues were found to concentrate in flakes, but not wet peel or chips. The average concentration factor for flakes was 2.4. Since potato is the only representative crop for crop subgroup 1-C per 40 CFR 180.41, these data support time-limited tolerances of 1.0 ppm in tuberous and corm vegetables (crop subgroup 1-C) and 2.0 ppm in flakes/granules.

In 8 field trials, sunflowers were treated with two post-emergent applications of 0.25 lb. a.i./A each. Sunflower seeds were harvested 56 to 72 days after the last application. Trials were performed in EPA Regions 5, 7, and 8. Residues for sunflower seed samples ranged from 0.46 ppm to 4.4 ppm total clethodim. The highest average field trial (HAFT) residue was 4.2 ppm. The average residue level was 1.6 ppm. A processing study was also performed for sunflowers. Residues were found to concentrate in meal, but not in refined oil. The concentration factor for meal was 2.1. These data support tolerances of 5.0 ppm in sunflower seed and 10.0 ppm in sunflower meal.

In 18 field trials, canola or rape was treated with one post-emergent application of 0.11 to 0.32 lb. a.i./A and harvested approximately 70 to 98 days after the application. Most of the trials were performed in Canada in growing regions adjacent to the U.S. areas where canola is grown. These data were used to support a maximum residue level in Canada and are being cited in order to harmonize maximum residue levels between the U.S. and Canada and remove the existing trade barrier. Residues in canola seed samples ranged from < 0.05 ppm to 0.54 ppm. The highest average field trial (HAFT) residue was 0.505 ppm. The average residue value for all trials, including samples less than the limit of detection at one-half the limit, was 0.162 ppm. A processing study was also performed for canola and residues were found to concentrate in meal, but not in crude oil. Since the highest residues were the result of application rates higher than those proposed for the U.S., these data support tolerances of 0.5 ppm in canola seed and 1.5 ppm in canola oil.

B. Toxicological Profile

1. *Acute toxicity*. Clethodim Technical is slightly toxic to animals following acute oral (Toxicity Category III), dermal (Toxicity Category IV), or inhalation exposure (Toxicity Category IV under current guideline interpretation). Clethodim is a moderate eye irritant (Category III), a severe skin irritant (Category II), and does not cause skin sensitization in the modified Buehler test in guinea pigs. In addition, an acute oral no-observed effect level (NOEL) has been determined in rats to be 300 milligrams/kilograms (mg/kg). Since this NOEL is significantly higher than the lowest chronic NOEL of 1 mg/kg/day, chronic exposures are expected to be of the most concern and this summary will focus on repeated exposures.

2. *Genotoxicty*. Clethodim Technical did not induce gene mutation in microbial in vitro assays. A weak response in an in vitro assay for chromosome aberrations was not confirmed when clethodim was tested in an in vivo cytogenetics assay up to the maximally tolerated dose level, nor was the response observed in vitro using technical material of a higher purity. No evidence of unscheduled DNA synthesis was seen following in vivo exposure up to a dose level near the LD_{50} (1.5 g/kg). This evidence indicates that clethodim does not present a genetic hazard to intact animal systems.

3. *Reproductive and developmental toxicity*. No reproductive toxicity was observed with Clethodim Technical at feeding levels up to 2,500 ppm. Developmental toxicity was observed in two rodent species, but only at maternally toxic dose levels. In rats, the developmental NOEL was 300 mg/kg/day while the maternal toxicity NOEL was only 150 mg/kg/day. In rabbits, the developmental NOEL was >300 mg/kg/day and the maternal NOEL was only 25 mg/kg/day. Valent therefore does not

consider clethodim to be a reproductive or developmental hazard. These studies also indicate that clethodim does not adversely affect endocrine function.

4. *Subchronic toxicity*. High doses of Clethodim Technical cause decreased body weights, increased liver size (increased weight and cell hypertrophy), and anemia (decreased erythrocyte counts, hemoglobin, or hematocrit) in rats and dogs. No observable effect levels have been determined to be 100 mg/kg/day for a 4-week dermal study in rats, 200 to 1,000 ppm for 4- or 5-week feeding studies in rats or mice, 500 ppm in a 13-week feeding study in rats, and 25 mg/kg/day in a 90-day oral study in dogs.

5. *Chronic toxicity and oncogenicity*. In chronic studies conducted in rats, mice, and dogs, compound-related effects noted at high doses included decreased body weight, increased liver size (liver weight and hypertrophy), and anemia (decreased hemoglobin, hematocrit, and erythrocyte count). Bone marrow hyperplasia was observed in dogs at the highest dose tested. No treatment-related increases in incidence of neoplasms were observed in any study. Chronic NOELs were 200 ppm for an 18-month feeding study in mice and 500 ppm for a 24-month study in rats. The lowest NOEL is from the 1-year oral dog study and is 1 mg/kg/day clethodim technical. Based on this study and a 100-fold safety factor, the reference dose (RfD) for clethodim was determined to be 0.01 mg/kg/day. Valent believes that clethodim is not carcinogenic. These studies also indicate that clethodim does not adversely affect endocrine function.

6. *Animal metabolism*. The *in vivo* metabolism of clethodim in rats was tested at a high dose (468 mg/kg), low dose (4.4 mg/kg), and a low dose (4.8 mg/kg) following 14-days of treatment with Clethodim Technical. A single oral dose of [14C]-clethodim was given to each rat and expired carbon dioxide and excreta were collected over the next 2- and 7-days, respectively, to determine radiolabel recovery. Several organs and tissues, and the remaining carcass, were collected after sacrifice to determine radiolabel recovery. In all treatment groups, nearly all of the radiolabel was eliminated in the urine (87-93%), feces (9-17%), and carbon dioxide (0.5-1%) and less than 1% of the dose was recovered in the organs and tissues after 7- days.

Elimination was rapid as most of the recovered dose was eliminated within 48 hours. The low dose groups eliminated clethodim slightly faster than the high dose group, and repeated exposure to clethodim prior to radiolabel dosing did not affect the rate of elimination or distribution of recovered radiolabel. There were no apparent sex differences with respect to elimination or distribution of metabolites.

The primary excretory metabolites were identified as clethodim sulfoxide (48-63%), clethodim *S*-methyl sulfoxide (6-12%), clethodim imine sulfoxide (7-10%), and clethodim 5-hydroxy sulfoxide (3-5%). Minor metabolites included clethodim oxazole sulfoxide (2-3%), clethodim trione sulfoxide (1%), clethodim (1%), clethodim 5-hydroxy sulfone (0.3-1%), clethodim sulfone (0.1-1%), aromatic sulfone (0.2-0.7%), and *S*-methyl sulfone (0-0.4%).

7. *Dermal penetration*. The dermal penetration of SELECT 2 EC Herbicide, the end-use product, was tested on unabraded, shaved skin of rats. Single doses of approximately 0.05, 0.5, and 5.0 mg of radiolabeled (14C-clethodim) SELECT 2 EC Herbicide, were applied topically to 10 cm^2 sites on the dorsal trunk. After 2, 10, or 24 hours, urine, feces, volatiles, scrubbings of the skin, skin at treatment site, blood, several tissues, and the carcass were collected and counted for radioactivity. Clethodim was found to be slowly absorbed through the skin in a time-dependent manner. The percent of dose absorbed increased with length of exposure and decreased with increasing dose. 10-hour absorption rates ranged from 7.5% to 30.0%. Most of the absorbed material was found in the urine and carcass, and most of the unabsorbed material was found in the skin scrubbings indicating that material was still on the skin surface.

8. *Metabolite toxicology*. 2 metabolites of clethodim, clethodim imine sulfone (RE-47719) and clethodim 5-hydroxy sulfone (RE-51228), have been tested in toxicity screening studies to evaluate the potential impact of these metabolites on the toxicity of clethodim. In general, these metabolites were found to be less toxic than Clethodim Technical for acute and oral toxicity studies; reproduction and teratology screening studies; and several mutagenicity studies.

C. Aggregate Exposure

1. *Dietary exposure*—i. *Food*. Clethodim is approved for use in the production of commercial agricultural crops including cotton, soybeans, sugar beets, and onions (dry bulb). Approval is expected soon for several additional crops. Dietary exposures are expected to represent the major route of exposure to the public. Since chronic exposures are of more concern than acute exposures for clethodim, this summary will focus primarily on chronic issues. Chronic dietary assessments for clethodim have been conducted by the registrant for all currently approved crops, all pending crops, and the crops proposed in this petition (tuberous and corm vegetables, sunflower, and canola).

In Valent's assessment, anticipated residues were used for all crop and animal commodities. Anticipated residue levels were the mean levels found in crop field trial data after treatment with the maximum recommended rate and harvested at minimum allowable intervals. These values are, therefore, slightly conservative. An assessment was performed assuming 100% of crop treated (still conservative) as well as assuming a more realistic percent of crop treated based on market survey data for existing uses or market projections for proposed uses. Adjusting for percent of crop treated is justified because most of treated commodities are combined in central locations and broadly distributed to the public; none of the clethodim tolerances or uses are limited to specific regions in the U.S.; and the primary concern is with chronic dietary exposure which minimizes the variance of single serving residues. The results of these assessments are summarized below in the Safety Determination section and indicate that chronic dietary exposures for existing and proposed uses of clethodim are well below the reference dose in either case.

ii. *Drinking water*. Since clethodim is applied outdoors to growing agricultural crops, the potential exists for clethodim or its metabolites to leach into groundwater. Drinking water, therefore, represents a potential route of exposure for clethodim and should be considered in an aggregate exposure assessment.

Based on available studies used in EPA's assessment of environmental risk for clethodim (memo from E. Brinson Conerly dated June 26, 1990), clethodim itself was classified as mobile in soil, but very non-persistent, representing a minimal groundwater concern. Metabolites of clethodim were also classified as mobile, but are slightly more persistent (half-lives up to 30– days versus up to 3-days for parent). Regarding clethodim metabolites, the Agency concluded that the ''potential for groundwater contamination may be somewhat higher than for clethodim but would still be expected to be relatively low in most cases due to their moderately low persistence''.

There is no established Maximum Concentration Level for residues of clethodim in drinking water under the Safe Drinking Water Act.

Based on this information, Valent believes that clethodim appears to represent an insignificant risk for exposure through drinking water.

2. *Non-dietary exposure*. Clethodim is currently approved for the commercial production of agricultural crops including soybeans, cotton, sugar beets, onions, and ornamental plants as well as for use on non-crop areas. The new uses proposed in this notice of filing are all agricultural crops. While there is a potential for clethodim to be used in non-crop areas (e.g. around parks and rights-of-way) where the public does spend some time, the likelihood of significant exposure is very small. First, this grass herbicide cannot be sprayed on lawns where the public does spend significant amounts of time, but instead must be used where there is no crop or around ornamental plants that are tolerant to the chemical. The public does not spend significant amounts of time in these areas. And second, clethodim is not persistent in the environment so the potential for public exposure is short term. Therefore, Valent believes that the potential for non-occupational exposure to the general public, other than through the diet or drinking water, is insignificant.

D. Cumulative Effects

There is one other pesticide compound registered in the United States, sethoxydim, which is structurally related to clethodim and has similar effects on animals. Sethoxydim is approved for use on a variety of agricultural crops, in non-crop areas, and around the home. This chemical should be considered in an aggregate exposure assessment along with clethodim. Dietary exposure is expected to represent the major route of exposure for sethoxydim as well as for clethodim.

The reference dose for sethoxydim is 0.09 mg/kg/day based on the 1–year dog feeding study NOEL and a 100-fold safety factor. This in on the same order of magnitude as clethodim, 0.01 mg/kg/day, which is also based on a 1–year dog study and a 100-fold safety factor.

A discussion of the cumulative effects from clethodim and sethoxydim exposures is presented below in the Safety Determination section.

E. Safety Determination

1. *U.S. population*. Using the dietary exposure assessment procedures described above for clethodim, chronic dietary exposures resulting from existing and proposed uses of clethodim were compared to the reference dose (RfD) of clethodim. In Valent's conservative assessment (using anticipated residues and assuming 100% treated for all crops), exposure for the U.S. population would occupy 13.6% of the RfD and non-nursing infants (< 1–year) are most highly exposed with total exposure occupying 32.3% of the RfD. Exposure to children 1 to 6 years old would occupy 27.1% of the RfD. In Valent's realistic analysis (using anticipated residues and estimated percent of crop treated for all crops), exposure for the U.S. population would occupy only 0.6% of the RfD and non-nursing infants are still the highest and would be at only 1.6% of the RfD.

For sethoxydim, recent EPA dietary assessments have been performed in conjunction with the extension of several time-limited tolerances. In a Final Rule published in the **Federal Register** of April 11, 1997 (62 FR 17735) (FRL-5598-7), EPA estimated that exposure to all existing tolerances for sethoxydim would occupy 36% of the sethoxydim RfD for the U.S. population and 72% of the RfD for the most exposed subpopulation of children aged 1– to 6-years. The assumptions used were conservative and the final rule stated that ''actual risks using more realistic assumptions would likely result in significantly lower risk estimates.''

Since clethodim and sethoxydim have similar toxicological effects in mammals, the contributions to the individual reference doses may need to be considered in an aggregate exposure assessment. The EPA generally has no concern for exposures below 100% of the RfD because the RfD represents the level at or below which daily aggregate exposure over a lifetime will not pose appreciable risks to human health. Directly summing the results of the conservative sethoxydim and the conservative clethodim contributions to RfD would be approaching 100%. However, reliable information is not available to indicate that directly summing the percent of RfD for these two chemicals is the most appropriate thing to do. Since using realistic assumptions for clethodim, including adjustment for percent of crop treated, result in large decreases in dietary risk (about 20-fold) Valent expects that the sethoxydim risk estimates would also be reduced significantly. Therefore, Valent believes that the cumulative chronic dietary risk of sethoxydim and clethodim is likely to be well below the 100% level for all population subgroups.

Regarding drinking water exposures, sethoxydim is similar to clethodim representing a minimal risk for leaching into groundwater due to its rapid degradation in the environment. There is no established Maximum Concentration Level for residues of sethoxydim in drinking water under the Safe Drinking Water Act.

Regarding non-occupational exposures, sethoxydim is registered for use in non-crop areas and around the home and may have some potential for exposure to the general public. However, as discussed for clethodim, sethoxydim cannot be applied to grass where public contact is expected and sethoxydim is not persistent in the environment. Valent therefore expects that non-occupational exposures to the public be minimal for sethoxydim.

In summary, dietary exposure for clethodim and sethoxydim are each expected to occupy less than 10% of their RfD's when anticipated residue levels and percent of crop treated values are considered. Exposures through the drinking water or other non-occupational routes are expected by Valent to be minimal. Collectively, Valent believes that the aggregate risks associated with the uses of these two chemicals is small and demonstrates a reasonable certainty of no harm to the public.

2. *Infants and children*. As discussed above, dietary exposure for clethodim and sethoxydim is greatest for children ages 1–6-years or non-nursing infants less than 1–year old. However, using a realistic approach to estimating exposures, exposures are expected to be below 10% of the RfD for each chemical even for infants and children. The databases for clethodim and sethoxydim are complete relative to current pre- and post-natal toxicity testing requirements including developmental toxicity studies in two species and multi-generation reproduction studies in rats. Reproduction and developmental effects have been found in toxicology studies for clethodim and sethoxydim, but the effects were seen at levels that were also maternally toxic. This indicates that developing animals are not more sensitive than adults. FQPA requires an additional safety factor of up to 10 for chemicals which represent special risks to infants or children. Clethodim and sethoxydim do not meet the criterion for application of an additional safety factor for infants and children. Valent believes that this demonstrates a reasonable certainty of no harm to children and infants from the proposed uses of clethodim.

F. International Tolerances

Although some have been proposed, there are no Mexican or Codex tolerances or maximum residue limits established for clethodim on potatoes, sunflower, or canola commodities. In

Canada, there are maximum residue limits established for potato tubers at 0.5 ppm and canola oil at 0.1 ppm. The use rates proposed for the use on tuberous and corm vegetables (crop subgroup 1-C) may exceed the 0.5 ppm level in tubers so a higher level is necessary. In Canada, canola oil is the only canola commodity considered for a residue limit since this is the commodity consumed by humans. In the U.S., a tolerance is not being proposed for the processed commodity canola oil since concentration did not occur in the processing study. Consequently, residue in oil up to 0.5 ppm would be allowed in the U.S. However, the residue data indicate that residues in oil are not expected to exceed 0.1 ppm and Valent does not believe this would represent a barrier against exporting U.S.-treated canola oil into Canada.

2. Zeneca Ag Products

PP 6F4609

EPA has received a pesticide petition (PP 6F4609) from Zeneca Ag Products, 1800 Concord Pike, P.O. Box 15458, Wilmington, DE 19850. proposing pursuant to section 408(d) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 346a(d), to amend 40 CFR part 180 by establishing a tolerance for residues of diquat dibromide in or on the raw agricultural commodity dried shelled pea and bean (except soybean) subgroup (seed) at 0.80 ppm. The proposed analytical method is a spectrophotometric method measuring absorption following derivitisation of the diquat with alkaline sodium dithionite. EPA has determined that the petition contains data or information regarding the elements set forth in section 408(d)(2) of the FFDCA; however, EPA has not fully evaluated the sufficiency of the submitted data at this time or whether the data supports granting of the petition. Additional data may be needed before EPA rules on the petition.

A. Residue Chemistry

1. *Plant metabolism*. The metabolism of diquat in plants is adequately understood. The residue of concern in plants is diquat per se. No further plant metabolism data are necessary for this proposed use.

2. *Analytical method*. The method of analysis is a spectrophotometic method measuring absorption following derivitisation of the diquat with alkaline sodium dithinoite.

3. *Magnitude of residues*. Dry Pea - Six residue field trials were conducted during 1994 in California, Idaho, Oregon, Texas, and Washington. The seed samples were analyzed for the active ingredient diquat. Diquat residues in dry pea seed ranged from 0.05 to 0.56 ppm.

Lentil - Five residue field trials were conducted during 1994 in Idaho, North Dakota, and Washington. The seed samples were analyzed for the active ingredient diquat. Diquat residues in lentil seed ranged from < 0.05 to 0.54 ppm.

Dry Bean - Eight residue field trials were conducted during 1994 in California, Colorado, Idaho, Michigan, Minnesota, North Dakota, Nebraska, and New York. The bean seed were analyzed for the active ingredient diquat. Diquat residues were less than the limit of quantitation (<0.05 ppm) in all the bean seed samples.

B. Toxicological Profile

1. *Acute toxicity*. In studies using laboratory animals, diquat dibromide has been shown generally to be of moderate toxicity. It can cause slight to severe eye irritation and has been placed in Toxicity Category II for acute dermal eye irritation effects. It is slightly acutely toxic by the oral and inhalation routes and has been placed in Toxicity Category III for these effects. Diquat dibromide causes slight dermal irritation and has been placed in Toxicity Category IV for this effect. It is not a skin sensitizer.

2. *Genotoxicty*. Diquat dibromide was negative for mutagenicity in the following test: 1 gene mutation (Ames), 2 structural chromosome aberration (mouse micronucleus and dominant lethal in mice) and 1 other genotoxic effects (unscheduled DNA synthesis in rat hepatocytes *in vitro*). Diquat was positive in 1 gene mutation test (mouse lymphoma cell assay) and in 1 chromosome aberration test (human blood lymphocytes, depending on the concentration of diquat dibromide and the presence or absence of the metabolic activation system). EPA has concluded that Diquat does not appear to present a mutagenicity concern in (in vivo) studies and for heritable risk considerations based on available information.

3. *Reproductive and developmental toxicity*. In a rat multigeneration study, diquat was fed at dose levels equivalent to 0, 16, 80 or 400/240 ppm of diquat cation. There was evidence of toxicity in both adults and offspring at 400/240 ppm diquat. A low incidence of toxicity was seen at 80 ppm in the adult rats only. Based on the findings, the NOEL and LOEL for systemic toxicity are 16 ppm (0.8 mg/kg/day) and 80 ppm (4 mg/kg/day), respectively, expressed as diquat cation. The NOEL and LOEL for reproductive toxicity are 80 ppm (4 mg/kg/day) and 400/240 ppm (20/12 mg/kg/day) respectively, expressed as diquat cation.

In a developmental toxicity study in rabbits, diquat dibromide was administered by gavage at dose levels of 0, 1, 3, or 10 mg/kg/day. There was no evidence to suggest that diquat was teratogenic to the rabbit at any dose level tested. Based on the findings, the NOEL and LOEL for maternal toxicity are 1 mg/kg/day and 3 mg/kg/day, respectively, expressed as diquat cation. The developmental toxicity NOEL and LOEL are, respectively, 3 mg/kg/day and 10 mg/kg/day, expressed as diquat cation.

In a developmental toxicity study in the rat, diquat dibromide was administered by oral gauge dose levels of 0, 4, 12 or 40 mg/kg/day. Diquat was not a rat teratogen at any of the dose levels tested. Maternal toxicity and foetotoxicity were in evidence at 40 mg/kg/day with mild and transient maternal toxicity persisting to the lowest dose level tested (4 mg/kg/day). The developmental toxicity NOEL and LOEL are, respectively, 12 mg/kg/day and 40 mg/kg/day expressed as diquat cation.

4. *Subchronic toxicity*. A supplemental subchronic dermal toxicity study using rabbits exposed to technical diquat dibromide at doses of 0, 20, 40, 80, or 160 mg/kg/day with a toxicological NOEL and LOEL for systemic toxicity, for both sexes, of 20 mg/kg/day and 40 mg/kg/day, respectively.

A repeated dermal toxicity study using rats exposed to technical diquat dibromide at doses of 0, 5, 20, 40 or 80 mg/kg of body weight/day with a toxicological NOEL and LOEL for systemic toxicity, for both sexes, of 5 mg/kg/day and 20 mg/kg/day, respectively.

An inhalation study using rats resulted in increase in lung weight, lung/body weight and lung/brain weight, lung lesions, and mottling and reddening of the lungs in females; however, all effects except the latter were reversible. A second inhalation study using rats showed no effects on any of the parameters examined at a dose of 0.1 µg/l. Based on both studies the NOEL and LOEL on inhalation exposure are 0.1µg/L and 0.49 µg/L, respectively.

5. *Chronic toxicity*.— i. *2–Year rat study*. - A chronic feeding carcinogenicity study was conducted on rats which were fed diets containing 0, 5, 15, 75 or 375 ppm of diquat cation. The systemic NOEL for both sexes was 15 ppm (0.58 mg/kg/day for males and

0.72 mg/kg/day for females, expressed as diquat cation); and the systemic LOEL was 75 ppm (2.91 mg/kg/day for males and 3.64 mg/kg/day for females, expressed as diquat cation).

ii. *1–Year dog study*. - A chronic dog study was conducted on beagles which were fed diets containing 0, 0.5, 2.5, or 12.5 mg/kg/day, expressed as diquat cation. The systemic NOEL for both sexes was 0.5 mg/kg/day and systemic LOEL was 2.5 mg/kg/day.

iii. *2–Year mice study*. - A chronic feeding/carcinogenicity study was conducted on mice which were fed diets containing 0,30,100 or 300 ppm, expressed as diquat cation. The systemic NOEL for both sexes was 30 ppm. The systemic LOEL was 100 ppm. Zeneca believes that diquat was not carcinogenic in this study.

The carcinogenic potential of diquat dibromide was evaluated by the Health Effects Division Reference Dose (RfD)/ Peer Review Committee on March 31, 1994. The Committee classified diquat dibromide into Group E (evidence of noncarcinogenicity for humans, based on a lack of evidence of carcinogenicity in acceptable studies with two animal species, rat and mouse.

6. *Animal metabolism*. The reregistration requirements for animal metabolism are fulfilled. The qualitative nature of the residue in animals is adequately understood based on acceptable poultry, ruminant, and fish metabolism studies. There are no animal feed items associated with this proposed use. The diquat metabolism and magnitude of residue in animals is not germane to this petition.

7. *Metabolite toxicology*. The qualitative nature of the residue in plants is adequately understood based on an acceptable potato metabolism study and rat bioavailabilty study. The terminal residue of concern in plants is diquat per se. The qualitative nature of the residue in animals is adequately understood.

C. Aggregate Exposure

Diquat is a non-selective, contact herbicide with both food and non-food uses. As such, aggregate non-occupational exposure would include exposures resulting from consumption of potential residues in food and water, as well as from residue exposure resulting from non-crop use around trees, shrubs, lawns, walks, driveways, etc. Thus, the possible human exposure from food, drinking water and residential uses has been assessed below.

1. *Dietary exposure*— i. *Food*. Acute dietary - The EPA did not identify an acute toxicity endpoint of concern for diquat in the Reregistration Eligibility Decision (RED) document, and determined that an acute dietary risk assessment is not required for this chemical.

ii. *Chronic dietary*. For purposes of assessing the potential chronic dietary exposure, Zeneca has estimated the aggregate exposure based on Theoretical Maximum Residue Contribution (TMRC) for all existing tolerances and the proposed tolerances of diquat on dry beans and dry peas at 0.8 ppm. The TMRC is obtained by multiplying the tolerance level residues (existing and proposed) by the consumption data which estimates the amount of those food products eaten by various population subgroups. Exposure of humans to residues could also result if such residues are transferred to meat, milk, poultry or eggs. The following assumptions were used in conducting this exposure assessment: 100% of the crops were treated, the RAC residues would be at the level of the tolerance, and certain processed food residues would be at anticipated (average) levels based on processing studies. In addition, residues of diquat in tap water at the Maximum Contaminant Level (MCL) of 0.02 ppm was included in the dietary assessment. These conservative assumptions result in a ''worst-case'' risk assessment and a significant overestimate of actual human exposure. An assessment was also performed using Anticipated Residues Contributions (ARC) derived from field trial data for sorghum, soybeans, potatoes, dry beans and peas. The ARC assessment also included percent crop treated data as cited in the July 1995 Diquat RED, as well as market projections for dry beans and peas. The resulting TMRC for the US population is 0.002946 mg/kg body weight/day (58.9% of the RfD). For this same group, the Anticipated Residue Contribution (ARC) is 0.000711 mg/kg body weight/ day (14.2% RfD). For children ages 1 to 6 and non-nursing infants the TMRC was 0.004571 mg/kg body-weight/day (91.4% RfD) and 0.003620 mg/kg body-weight/day (72.4% RfD), respectively. For these same groups the ARC was 0.001513 mg/kg body-weight/day (30.3% RfD) for children ages 1 to 6, and 0.002795 mg/kg body-weight/day (55.9% RfD) for non-nursing infants. None of the subgroups assessed exceeded 100% of the RfD.

iii. *Drinking water*. In examining aggregate exposure, FQPA directs EPA to consider available information concerning exposures from the pesticide residue in food and all other non-occupational exposures. The primary non-food sources of exposure the Agency looks at, include drinking water (whether from groundwater or surface water), is exposure through pesticide use in gardens, lawns, etc (residential uses).

The lifetime health advisory and maximum contaminant level (MCL) set by EPA for diquat are the same and given as 0.02 parts per million (ppm) as required under the Drinking Water Regulations under the Safe Drinking Water Act. Drinking water which meets the EPA standard is associated with little to no risk and should be considered safe. Inclusion of MCL level residues of diquat in water in the dietary assessment demonstrated a safe exposure level to all subgroups in the US population. The Agency no longer establishes tolerances for residues in potable water; the tolerance for diquat dibromide has been replaced with a designated maximum contaminant level goal (MCLG) of 0.02 ppm for residues of diquat in potable water.

The primary route of environmental dissipation of diquat is strong adsorption to soil particles. Diquat does not hydrolyse or photodegrade and is resistant to microbial degradation under aerobic and anaerobic conditions. There were no major degradates isolated from any of the environmental fate studies. When used as an aquatic herbicide, diquat is removed from the water column by adsorption to soil sediments, aquatic vegetation, and organic matter. Adsorbed diquat is persistent and immobile, and is not expected to be a ground-water contaminant. The environmental fate data base for diquat is complete for reregistration of diquat dibromide.

2. *Non-dietary exposure*. As a non-selective, contact herbicide, homeowner use of diquat will consist primarily of spot spraying of weeds around trees, shrubs, walks, driveways, flower beds, fence lines, etc. The potential for exposure following application as a spot treatment in residential gardens, driveway edges, patios, etc. is low due to the limited frequency and duration of exposure. The exposures which would result from the use of diquat are determined to be of an intermittent nature. Any exposures to diquat would result from dermal exposure. These exposures are not expected to pose any acute toxicity concerns. Based on the US EPA National Home and Garden Pesticide Use Survey (RTI/5100/17-01F, March 1992), the average homeowner is expected to use non-selective herbicides only about four times a year. Thus, these exposure have not been factored into a chronic exposure assessment. Also, diquat has extremely low skin permeation, is not volatile, presenting

no inhalation risk, and has rapid and strong binding characteristics to leaf surfaces and soil. The Agency concludes that non-occupational and non-dietary exposure to diquat will not be significant and has not been aggregated with dietary exposures in estimating chronic risk.

D. Cumulative Effects

The only other compound in the bipyridilium chemical family is paraquat dichloride. Since diquat dibromide and paraquat dichloride have different toxicological endpoints and therefore do not have a common mode of action, there is no need for an assessment of cumulative effects.

E. Safety Determination

1. *U.S. population*. The proposed uses utilize 58.9% of the RfD for the general U.S. population, based on the assumptions of 100% crop treated, MCL level residues in tap water and all residues at tolerance levels; 72.4% of the RfD for non-nursing infants under 1-year old, 19.6% of the RfD for nursing infants under 1-year old; 91.4% of the RfD for children 1-6 years old; and 71.5% of the RfD for children 7-12 years old. An additional risk assessment for residential uses is unnecessary because there is no evidence for toxicological concern via the dermal or inhalation routes of exposure. Given diquat's strong binding characteristics, exposure via drinking water is highly unlikely. Zeneca concludes that there is reasonable certainty that no harm will occur from aggregate exposure to diquat.

2. *Infants and children*. FFCDA section 408 provides that EPA shall apply an additional ten fold margin of exposure 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 exposure will be safe for infants and children. EPA believes that reliable data support using the standard margin of exposure (usually 100 x for combined inter- and intra-species variability) and not the additional tenfold margin of exposure when EPA has a complete data base under existing guidelines and when the severity of the potential effect in infants and children or the potency or unusual toxic properties of a compound do not raise concerns regarding the adequacy of the standard margin of exposure.

Risk to infants and children was determined by the use of a rat multigeneration reproduction study and developmental toxicity studies in rabbits and rats. The reproduction study provides information on potential effects from exposure on the reproductive capability of mating parents and on systemic toxicity. The developmental studies provide information on the potential for adverse effects from exposure on the developing organism during prenatal development.

The toxicological data base for evaluating pre- and post-natal toxicity for diquat is considered to be complete. In the rat reproduction study, systemic toxicity to the mating parents was observed at 4 and 20/12 mg diquat cation/kg body weight/day, and reproductive effects in the form of decreased pups per litter and decreased body weight gain were seen at 20/12 mg/kg/day. Given that the effects seen in the pups and litters were at doses that clearly affected the parents at this dose level and below, diquat is considered not to affect reproductive performance without significantly compromising the health of the parental animals.

Developmental effects in the rat and rabbit studies, including decreased body weights, kidney and liver effects, and delayed ossification, were only observed at the highest doses tested and are considered to be related to the significant maternal toxicity exhibited at these dose levels. There was no evidence in these studies that diquat caused teratogenic effects.

Furthermore, the RfD is currently based on effects seen at 0.5 mg/kg/day in the dog. Effects seen at maternally toxic doses in the rat developmental study were 80 times higher, and in the rabbit study were 20 times higher than the level on which the RfD is based. Thus, Zeneca does not believe the effects seen in these studies are of such a concern to require an additional safety factor. Accordingly, Zeneca concludes that the RfD has an adequate margin of protection for infants and children and there is reasonable certainty that no harm will occur to infants and children from aggregate exposure to diquat.

F. International Tolerances

Codex lists diquat cation in dry beans and peas at 0.2 ppm. Diquat is listed in Canada in beans and peas at 0.1 ppm. There are no Mexican maximum residue limits for diquat on dry beans or peas.

3. E.I. DuPont de Nemours and Co., Inc.

PP 7F4849

EPA has received a pesticide petition (PP 7F4849) from E.I. DuPont de Nemours and Co., Inc. (DuPont), Barley Mill Plaza, P.O. Box 80083, Wilmington, DE 19880-0038. proposing pursuant to section 408(d) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. 346a(d), to amend 40 CFR part 180 by establishing a tolerance for residues of for azafenidin, 2-[2,4-dichloro-5-(2-propynyloxy) phenyl]-5,6,7,8-tetrahydro-1,2,4-triazolo [4,3-*a*] pyridin-3(*2H*)-1 in or on the raw agricultural commodities of the crop grouping of citrus, grapes, sugarcane and sugarcane molasses. The proposed analytical method involves homogenization, filtration, partition and cleanup with analysis by gas chromatography using mass selective detection. 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 the residues of azafenidin in citrus, grapes and sugarcane is adequately understood for the purposes of registration. Metabolic pathways in grapefruit, grapes and sugarcane are similar, consisting of rapid O-dealkylation and production of hydroxyl derivatives, with subsequent formation of glucuronide and sulfate.

2. *Analytical method*. The proposed analytical method involves homogenization, filtration, partition and cleanup with analysis by gas chromatography using mass selective detection.

3. *Magnitude of residues*. DuPont proposes establishing tolerances for residues azafenidin, 2-[2,4-dichloro-5-(2-propynyloxy)phenyl]-5,6,7,8-tetrahydro-1,2,4-triazolo[4,3-*a*]pyridin-3(*2H*)-1 (Milestone*) in or on the agricultural commodities of the crop grouping of citrus at 0.1 ppm, grapes at 0.02 ppm, sugarcane at 0.02 ppm and sugarcane molasses at 0.1 ppm .

B. Toxicological Profile

1. *Acute toxicity*. Technical azafenidin has been placed in acute toxicology category III based on overall results from several studies. Results from the following studies indicate toxicology category III: acute dermal toxicity (LD_{50} > 2,000kg; rabbits) and eye irritation (effects reversible within 72 hours; rabbits). Acute oral toxicity (LD_{50} > 5,000 mg/kg; rats), acute inhalation toxicity (LC_{50} > 5.4 mg/L, rats) and skin irritation (slight effects resolved within 48 hours; rabbits) results were assigned toxicology category IV. Technical azafenidin is not a dermal sensitizer.

An acute neurotoxicity study was conducted in rats administered

azafenidin via gavage at 0, 100, 300 or 900 mg/kg. Azafenidin was not neurotoxic at any dose. The systemic NOEL was 100 mg/kg for males and females based on reduced food consumption and body weights at 300 mg/kg and above.

2. *Genotoxicty*. Technical azafenidin was negative for genotoxicity in a battery of *in vitro* and *in vivo* tests. These tests included the following: mutagenicity in bacterial (Ames test) and mammalian (CHO/HGPRT assay) cells; *in vitro* cytogenetics (chromosomal aberration in human lymphocytes); *in vivo* cytogenetics (bone marrow micronucleus assay in mice); and unscheduled DNA synthesis in rat primary hepatocytes.

3. *Reproductive and developmental toxicity*. A 2-generation reproduction study was conducted in rats with dietary technical azafenidin concentrations of 0, 5, 30, 180 or 1,080 ppm. The NOEL was 30 ppm (1.7 to 2.8 mg/kg/day for P_1 and F_1 males and females and their offspring). This was based on the following effects at 180 ppm (10.1 to 17.8 mg/kg/day for P_1 and F_1 males and females and/or their offspring): slight reductions in mean body weights for F_1 males and females; reductions in mean gestation body weight gain and implantation efficiency; slightly increased gestation lengths; decreased offspring survival, body weights and other indices of offspring health; and increased incidence of diarrhea among F_1 parental males.

A developmental study was conducted in rats administered technical azafenidin by gavage at 0, 3, 8, 16 or 24 mg/kg/day. Azafenidin was not teratogenic. The NOEL was 16 mg/kg/day based on the following observations at 24 mg/kg/day: reduced maternal body weight, increased resorptions, reductions in litter size and fetal weights and increased sternebral variations. The maternal effects consisted of transient body weight reductions; however, the nature of these effects suggested that fetal resorptions contributed to these weight reductions.

A developmental study was conducted in rabbits administered technical azafenidin by gavage at 0, 12, 36, 100 or 300 mg/kg/day. Azafenidin was not teratogenic. The NOELs for maternal and offspring toxicity were 12 and 100 mg/kg/day, respectively. The maternal NOEL was based on reduced body weight at 36 and 100 mg/kg/day and mortality at higher doses. Excessive maternal toxicity at 300 mg/kg/day precluded a Crop field trial residue data from citrus, grape and sugarcane studies show that the proposed tolerances on these commodities will not be exceeded when Milestone* is used as directed. Assessment of developmental effects at this level. However, the developmental NOEL was considered to be 100 mg/kg/day since there were no indications of fetal toxicity up to and including this dose level.

4. *Subchronic toxicity*. A 90–day study in mice was conducted at dietary concentrations of 0, 50, 300, 900 or 1,500 ppm. The NOEL was 300 ppm (47.2 and 65.8 mg/kg/day for male and female mice, respectively). This was based on reduced body weight gain in males and microcytic and hypochromic anemia in males and females at 900 ppm (or 144 and 192 mg/kg/day for males and females, respectively).

Technical azafenidin was administered in the diets of rats at 0, 50, 300, 900 or 1,500 ppm for 90 days. The NOEL was 300 ppm (24.2 and 28.2 mg/kg/day for male and female rats, respectively). This was based on methemoglobinemia and microcytic and hypochromic anemia in males and females at 900 ppm (or 71.9 and 83.8 mg/kg/day for male and female rats, respectively).

Dogs were administered technical azafenidin in their diets at 0, 10, 60, 120 or 240 ppm for 90–days. The NOEL was 10 ppm (0.34 and 0.33 mg/kg/day for males and females, respectively). This was based on enlarged hepatocytes and increased serum alkaline phosphatase and alanine aminotransferase activities at 60 ppm (2.02 and 2.13 mg/kg/day for male and female dogs, respectively).

A 90–day subchronic neurotoxicity study was conducted in rats at 0, 50, 750 or 1,500 ppm. There were no neurological effects observed in this study. The NOEL for systemic toxicity was 50 ppm (3.0 mg/kg/day) and 750 ppm (54.5 mg/kg/day) for male and female rats, respectively. These were based on reduced food consumption and body weights and increased incidences of clinical signs of toxicity at the higher doses.

A 28–day dermal study was conducted in rats at 0, 80, 400 or 1,000 mg/kg/day. There was no dermal irritation or systemic toxicity among males or females at the highest dose tested. The NOEL was > 1,000 mg/kg/day.

5. *Chronic toxicity*. An 18–month mouse study was conducted with dietary concentrations of 0, 10, 30, 300 or 900 ppm technical azafenidin. This product was not oncogenic in mice. The systemic NOEL was 300 ppm (39.8 and 54.1 mg/kg/day for males and females, respectively). This was based on hepatotoxicity among males and reduced body weights and food efficiency among females at 900 ppm (or 122 and 163 mg/kg/day for males and females, respectively).

A 2–year chronic toxicity/oncogenicity study was conducted in rats fed diets that contained 0, 5, 15, 30, 300 or 900 ppm technical azafenidin. This product was not oncogenic in rats. The systemic NOEL was 300 ppm (12.1 and 16.4 mg/kg/day males and females, respectively). The NOEL was defined by microcytic, hypochromic and hemolytic anemia and mortality at 900 (or 35.2 and 50.2 mg/kg/day for male and female rats, respectively).

Technical azafenidin was administered for 1–year to dogs at dietary concentrations of 0, 5, 10, 120 and 360 ppm. The NOEL was 10 ppm (0.30 mg/kg/day for males and females). This was based on observations of altered hepatocyte morphology, hydropic degeneration and elevated alanine aminotransferase and alkaline phosphatase at 30 ppm (0.86 and 0.87 mg/kg/day for male and female dogs, respectively) and above.

6. *Animal metabolism*. The metabolism of azafenidin in animals (rat and goat) is adequately understood and is similar among the species evaluated. Azafenidin was readily absorbed following oral administration, extensively metabolized and rapidly eliminated in the urine and feces. The terminal elimination half-life in plasma was 40 hours in rats. Less than 1% of the administered dose was present in rat tissues at 120 hours. There were no volatile metabolites of azafenidin. The major metabolic pathways in the rat and goat consisted of rapid O-dealkylation and production of hydroxyl derivatives, subsequent formation of glucuronide and sulfate conjugates and elimination of these conjugates in feces and urine. There was no evidence of accumulation of azafenidin or its metabolites in the tissues of either species or in the goat's milk.

7. *Metabolite toxicology*. There is no evidence that the metabolites of azafenidin identified in animal or plant metabolism studies are of any toxicological significance. The existing metabolism studies indicate that the metabolites formed are unlikely to accumulate in humans or in animals that may be exposed to these residues in the diet. The fact that no quantifiable residues were found in edible portions of treated crops further indicates that exposures to and accumulation of metabolites are unlikely.

C. Aggregate Exposure

1. *Food*—i. *Acute dietary exposure*. Since there were no acute affects appropriate for assessment of the general population, the NOEL of 16 mg/

kg/day from the rat developmental toxicity study was used to assess acute dietary risk for females 13–years of age and older. Exposures were estimated using the DEEM computer software (version 5.03b, Novigen Sciences, Inc, 1997). The proposed azafenidin tolerances for the raw agricultural commodities and processed fractions that were used in the calculations included: grapes, 0.02 ppm; citrus, 0.1 ppm; and sugarcane - 0.02 ppm for cane sugar and 0.1 ppm for molasses. The following exposures indicate margins of exposure > 11,000 at the 95th percentile and provides a reasonable certainty that no harm to the individual or the developing child will occur under these conservative exposure assumptions (i.e., all labeled crops are treated, residues are present at the proposed tolerances and there is no reduction of residues prior to consumption of these food commodities).

Subpopulations	Exposure - 95th Percentile (mg/kg/day)	MOE[a]
13+/Pregnant; Not Nursing.	0.000868	86,800
13+/Nursing	0.001384	11,561
13 - 19/ Not Pregnant; Not Nursing.	0.001119	14,561
20+/Not Pregnant; Not Nursing.	0.000832	0.19,231
13 - 50 Years ..	0.000938	17,056

[a] MOE - Margin of Exposure = NOEL from rat developmental study (16 mg/kg/day) divided by the 95th percentile exposure.

ii.*Chronic dietary exposure.* A Reference Dose (RfD) of 0.003 mg/kg/day has been proposed based on the NOEL from the most sensitive chronic study (NOEL of 0.3 mg/kg/day from the 1–year dog study) and applying a 100-fold uncertainty factor. General and subpopulation exposures were estimated using the DEEM computer software (version 5.03b, Novigen Sciences, Inc, 1997). The following proposed azafenidin tolerances for the raw agricultural commodities and processed fractions were used in the calculations: grapes, 0.02 ppm; citrus, 0.1 ppm; and sugarcane - 0.02 ppm for cane sugar and 0.1 ppm for molasses. Exposure assessments assumed 100% of the crops were treated with azafenidin, that residues were present at the tolerance level and that no residues were removed prior to consumption of treated crops. These assessments indicated adequate margins of exposure for all subpopulations and that only 21% or less of the RfD was utilized by any group. For example, the TMRCs were 0.000237 mg/kg/day (7.9% RfD) for the general population and 0.000619 mg/kg/day (20.6% RfD) for the subpopulation with the highest potential exposure, children ages 1 through 6 years.

2. *Drinking water.* Other potential dietary sources of exposure of the general population to pesticides are residues in drinking water. There is no Maximum Contaminant Level established for residues of azafendidin. The petitioner is reporting to the Environmental Fate and Groundwater Branch of EPA (EFGWB) the interim results of a prospective groundwater monitoring study conducted at a highly vulnerable site. Based on the preliminary results of this study the petitioner does not anticipate residues of azafenidin in drinking water and exposure from this route is unlikely. However, given that less than 21% of the RfD is attained by the TMRC for the population subgroup with the highest theoretical dietary exposure (children 1-6 years of age), there is ample allowance for safe exposure to azafenidin via drinking water should it ever be detected.

3. *Non-dietary exposure.* Azafenidin is proposed for use in weed control in selective non-food crop situations including certain temperate woody crops, and in non-crop situations including industrial sites and unimproved turf areas. Azafenidin is not be used in on residential temperate woody plantings, or on lawns, walkways, driveways, tennis courts, golf courses, athletic fields, commercial sod operations, or other high maintenance fine turf grass areas, or similar areas. Any non-occupational exposure to azafenidin is likely to be negligible.

C. Cumulative Effects

The herbicidal activity of azafenidin is due to its inhibition of an enzyme involved with synthesis of the porphyrin precursors of chlorophyll, protoporphyrinogen oxidase. Mammals utilize this enzyme in the synthesis of heme. Although there are other herbicides that also inhibit this enzyme, there is no reliable information that would indicate or suggest that azafenidin has any toxic effects on mammals that would be cumulative with those of any other chemicals. In addition there is no valid methodology for combining the risks of adverse effects of overexposures to these compounds.

D. Safety Determination

1. *U.S. population.* Based on the completeness and reliability of this azafenidin toxicology database and using the conservative aggregate exposure assumptions presented earlier, it has been concluded that azafenidin products may be used with a reasonable certainty of no harm relative to exposures from food and drinking water. A chronic RfD of 0.003 mg/kg/day has been proposed from the NOEL of the most sensitive chronic dietary study and the use of a 100-fold uncertainty factor. The TMRC determined for proposed tolerances in citrus, grapes and sugar cane utilized only 7.9% of the RfD (an exposure of 0.000237 mg/kg/day). Although there was no data to accurately assess potential exposures through drinking water, the small fraction of the RfD utilized for food by the general and subpopulations indicate that is unlikely that aggregate exposures will exceed acceptable limits. In addition, the use patterns and physical chemical properties of azafenidin suggest that the potential for significant concentrations in drinking water are remote. It has been concluded that the aggregate exposure for the proposed tolerances on citrus, grapes and sugar cane provide a reasonable certainty of no harm to the general population. Because of effects observed in the rat developmental toxicology study, an acute safety determination based on margins of exposure was calculated from the NOEL of 16 mg/kg/day. The subpopulation potentially at risk was considered to be females 13–years of age and older. However, based on the MOEs presented previously of >11,000 at the 95th exposure percentile, it was concluded that these potential dietary exposures represented a reasonable certainty of no harm for this group. An MOE of 100 or greater is generally considered protective.

2. *Infants and children.* In assessing the potential for additional sensitivity of infants and children to residues of azafenidin, data from the previously discussed developmental and multigeneration reproductive toxicity studies were considered. Developmental studies are designed to evaluate adverse effects on the developing organism resulting from pesticide exposure during pre-natal development. Reproduction studies provide information relating to reproductive and other effects on adults and offspring from pre-natal and post-natal exposures to the pesticide. The rat reproduction and developmental studies indicated developmental effects in this species at exposures that produced minimal maternal effects. A clear dose-response and developmental NOEL has been defined for these effects. FFDCA section

408 provides that EPA may apply an additional uncertainty factor for infants and children in the case of threshold effects to account for pre- and post-natal toxicity and the completeness of the database. The additional uncertainty factor may increase the MOE from the usual 100- up to 1,000-fold. Based on current toxicological data requirements, the database for azafenidin relative to pre- and post-natal effects for children is complete. In addition, the NOEL of 0.3 mg/kg/day in the 1–year dog study and upon which the RfD is based is much lower than the NOELs defined in the reproduction and developmental toxicology studies. Conservative assumptions utilized to estimate aggregate dietary exposures of infants and children to azafenidin (0.000619 mg/kg/day) demonstrated that only 20.6% of the RfD was utilized for the proposed tolerances. Based on these exposure estimates and the fact that MOEs in excess of 1,000-fold exist relative to the NOELs in the rat reproduction study (NOEL = 1.7 mg/kg/day and MOE = 2,746) and the rat developmental toxicity study (NOEL = 16 mg/kg/day and MOE = 25,848), the extra 10-fold uncertainty factor is not warranted for these groups. Therefore, it may be concluded that there is reasonable certainty that no harm will result to infants and children from aggregate exposures to azafenidin].

E. International Tolerances

There are no established Canadian, Mexican or Codex MRLs for azafenidin. Compatibility is not a problem.

[FR Doc. 97–31542 Filed 12–2–97; 8:45 am]

BILLING CODE 6560–50–F

FEDERAL COMMUNICATIONS COMMISSION

[Report No. 2240]

Petitions for Reconsideration and Clarification of Action in Rulemaking Proceedings

November 28, 1997.

Petitions for reconsideration and clarification have been filed in the Commission's rulemaking proceedings listed in this Public Notice and published pursuant to 47 CFR Section 1.429(e). The full text of these documents are available for viewing and copying in Room 239, 1919 M Street, N.W., Washington, D.C. or may be purchased from the Commission's copy contractor, ITS, Inc. (202) 857–3800. Oppositions to these petitions must be filed December 18, 1997. See Section 1.4(b)(1) of the Commission's rule (47 CFR 1.4(b)(1)). Replies to an opposition must be filed within 10 days after the time for filing oppositions has expired.

Subject: Investigation of Special Access Tariffs of Local Exchange Carriers (CC Docket No. 85–166, Phase I).

Number of Petitions Filed: 1.

Subject: Amendments of Parts 73 and 74 of the Commission's Rules To Permit Certain Minor Changes in Broadcast Facilities Without a Construction Permit (MM Docket No. 96–58).

Number of Petitions Filed: 4.

Subject: Anthony T. Easton (WT Docket No. 97–199).

Number of Petitions Filed: 1.

Federal Communications Commission.

Magalie Roman Salas,

Secretary.

[FR Doc. 97–31592 Filed 12–2–97; 8:45 am]

BILLING CODE 6712–01–M

FEDERAL MARITIME COMMISSION

Notice of Agreement(s) Filed

The Commission hereby gives notice of the filing of the following agreement(s) under the Shipping Act of 1984.

Interested parties can review or obtain copies of agreements at the Washington, DC offices of the Commission, 800 North Capitol Street, NW., Room 962. Interested parties may submit comments on an agreement to the Secretary, Federal Maritime Commission, Washington, DC 20573, within 10 days of the date this notice appears in the **Federal Register**.

Agreement No.: 202–010689–068.

Title: Transpacific Westbound Rate Agreement (''TWRA'').

Parties:

American President Lines, Ltd.
Hapag-Lloyd Container Linie GmbH
Kawasaki Kisen Kaisha, Ltd.
A.P. Moller-Maersk Line
Mitsui O.S.K. Lines, Ltd.
Neptune Orient Lines, Ltd.
Nippon Yusen Kaisha Line
Orient Overseas Container Line, Inc.
P&O Nedlloyd Limited
P&O Nedlloyd Lijnen, B.V.
Sea-Land Service, Inc.

Synopsis: The proposed modification authorizes the parties to consider and act upon proposals and recommendations of the Equipment Interchange Discussion Agreement (FMC Agreement No. 202–011284) with respect to activities within the scope of the TWRA agreement.

Dated: November 26, 1997.

By Order of the Federal Maritime Commission.

Joseph C. Polking,

Secretary.

[FR Doc. 97–31670 Filed 12–2–97; 8:45 am]

BILLING CODE 6730–01–M

FEDERAL MARITIME COMMISSION

Request for Additional Information

Agreement No.: 203–011075–041

Title: Central America Discussion Agreement

Parties:

Concorde Shipping, Inc.
Global Reefer Carriers Ltd.
Dole Fresh Fruit
King Ocean Central America, S.A.
Crowley American Transport, Inc.
Seaboard Marine, Ltd.
A.P. Moller-Maersk Line
Sea-Land Service, Inc.
NPR, Inc.

Synopsis: Notice is hereby given that the Federal Maritime Commission, pursuant to section 6(d) of the Shipping Act of 1984 (46 U.S.C. app. 1701–1720), has requested additional information from the parties to the Agreement as required by the Act. This action extends the review period as provided in section 6(c) of the Act

Dated: November 28, 1997.

By Order of the Federal Maritime Commission.

Joseph C. Polking,

Secretary.

[FR Doc. 97–31671 Filed 12–2–97; 8:45 am]

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FEDERAL RESERVE SYSTEM

Change in Bank Control Notices; Acquisitions of Shares of Banks or Bank Holding Companies

The notificants listed below have applied under the Change in Bank Control Act (12 U.S.C. 1817(j)) and § 225.41 of the Board's Regulation Y (12 CFR 225.41) to acquire a bank or bank holding company. The factors that are considered in acting on the notices are set forth in paragraph 7 of the Act (12 U.S.C. 1817(j)(7)).

The notices are available for immediate inspection at the Federal Reserve Bank indicated. The notices also will be available for inspection at the offices of the Board of Governors. Interested persons may express their views in writing to the Reserve Bank indicated for that notice or to the offices of the Board of Governors. Comments must be received not later than December 16, 1997.