Dated: July 22, 1997.

William D. Dickerson,

Director, NEPA Compliance Division, Office of Federal Activities.

[FR Doc. 97–19658 Filed 7–24–97; 8:45 am]

BILLING CODE 6560–50–M

ENVIRONMENTAL PROTECTION AGENCY

[ER–FRL–5482–6]

Environmental Impact Statements and Regulations; Availability of EPA Comments

Availability of EPA comments prepared June 30, 1997 through July 04, 1997 pursuant to the Environmental Review Process (ERP), under Section 309 of the Clean Air Act and Section 102(2)(c) of the National Environmental Policy Act as amended. Requests for copies of EPA comments can be directed to the Office of Federal Activities at (202) 564–7167.

An explanation of the ratings assigned to draft environmental impact statements (EISs) was published in FR dated April 04, 1997 (62 FR 16154).

Draft EISs

ERP No. D–BLM–K67043–AZ Rating E02, Cyprus Miami Mining Leach Facility Expansion Project, Construction and Operation, Plan of Operations Approval and COE Section 404 Permit, Gila County, AZ.

Summary: EPA expressed environmental objections since the proposed alternative does not appear to be the least environmentally damaging practicable alternative in accordance with guidelines pursuant to Clean Water Act, Section 404. EPA believed additional financial assurance is needed for the contingency of collecting and managing mine leachate. A Clean Air Act conformity analysis is needed as the proposed facility would generate an increase of over 100 tons per year of pollutants.

Final EISs

ERP No. F–AFS–L39041–OR Metolius Wild and Scenic River Management Plan, Implementation, Deschutes National Forest, Sisters Range District, Jefferson County, OR.

Summary: Review of the Final EIS was not deemed necessary. No formal comment letter was sent to the preparing agency.

ERP No. F–COE–E90015–00, Pearl River in the Vicinity of Walkiah Bluff, Wetland Restoration, Implementation, Picayune, Pearl River County, MS and St. Tammany Parish, LA.

Summary: EPA expressed environmental concerns over the ability of the project to maintain the proposed redirected flow regime on a long-term basis, and suggested that the Corps develop a monitoring program to review the project's status over a five-year period.

ERP No. F–SFW–L99005–WA, Plum Creek Timber Sale, Issuance of a Permit to Allow Incidental Take and Habitat Conservation Plan (HCP) for Threatened and Endangered Species, Implementation, Eastern and Western Cascade Provinces in the Cascade Mountains, King and Kittitas Counties, WA.

Summary: Review of the Final EIS was not deemed necessary. No formal comment letter was sent to the preparing agency.

Dated: July 22, 1997.

William D. Dickerson,

Director, NEPA Compliance Division, Office of Federal Activities.

[FR Doc. 97–19659 Filed 7–24–97; 8:45 am]

BILLING CODE 6560–50–M

ENVIRONMENTAL PROTECTION AGENCY

[PF–744; FRL–5726–4]

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–744, must be received on or before August 25, 1997.

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

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

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

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

Product Manager	Office location/telephone number	Address
Mary Waller (PM 21)	Rm. 265, CM #2, 703–308–9354, e-mail:waller.mary@epamail.epa.gov.	1921 Jefferson Davis Hwy, Arlington, VA
Cynthia Giles-Parker (PM 22).	Rm. 247, CM #2, 703–305–7740, e-mail:giles-parker.cynthia@epamail.epa.gov.	Do.

SUPPLEMENTARY INFORMATION: EPA has received pesticide petitions as follows proposing the establishment and/or amendment of regulations for residues of certain pesticide chemicals in or on various raw 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 grantinig of the petition. Additional data may be needed before EPA rules on the petition.

The official record for this notice, as well as the public version, has been established for this notice of filing under docket control number PF–744

(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''.

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 control number (insert docket number) and appropriate petition number. Electronic comments on this notice may be filed online at many Federal Depository Libraries.

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

List of Subjects

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

Dated: July 11, 1997.

James Jones,

Director, Registration Division, Office of Pesticide Programs.

Summaries of Petitions

Below summaries of the pesticide petitions are printed. The summaries of the petitions were prepared by the petitioners. The petition summary announces the availability of a description of the analytical methods available to EPA for the detection and measurement of the pesticide chemical residues or an explanation of why no such method is needed.

1. Bayer

PP 3E2938

EPA has received a pesticide petition (PP) 3E2938 from Bayer Corporation, 8400 Hawthorn Rd., P.O. Box 4913, Kansas City, MO 64120-0013 proposing to amend 40 CFR 180.410 by establishing tolerances for residues of the fungicide triadimefon, 1-(4-Chlorophenoxy)-3,3-dimethyl-1-(1*H*-1,2,4-triazol-1-yl)-2-butanone, and its metabolites containing chlorophenoxy and triazole moieties expressed as the fungicide in or on the raw agricultural commodities coffee beans at 0.1 ppm. The nature of the residue in plants and livestock is adequately understood. The analytical method for determining residues uses gas-liquid chromatography coupled with a thermionic detector.

A. Residue Chemistry

1. *Plant and livestock metabolism.* The nature of the residue in plants and animals is adequately understood. The residue of concern is triadimefon and its triazole and chlorophenoxy metabolites. Since there are no livestock feedstuffs derived from coffee, the nature of the residue in poultry and ruminants is not of concern here.

2. *Analytical method.* Adequate analytical methods are available for analysis of triadimefon and its triazole and chlorophenoxy metabolites in or on coffee. These methods are available in PAM II as Method I.

3. *Magnitude of residue.* Fifteen separate residue trials have been conducted and submitted to the EPA with triadimefon on coffee. These trials were conducted in Brazil (4 trials), Mexico (4 trials), Costa Rica (2 trials), El Salvador (2 trials), Guatemala (1 trial) and Columbia (2 trials). The EPA has determined that these data show that residues of triadimefon and its metabolites containing chlorophenoxy and triazole moieties (expressed as the fungicide) in the raw agricultural commodity coffee beans will not exceed the proposed tolerance of 0.1 ppm. Although no data on roasted beans or instant coffee were submitted, the EPA has concluded that food additive tolerances are not required. There are no livestock feed stuffs from coffee and therefore, secondary residues in meat, milk, poultry and eggs are not expected. Since this is an import tolerance petition and since coffee is not normally rotated, the nature of residue in rotational crops is not of concern.

B. Toxicological Profile

1. *Acute toxicity. Rat acute oral study with an* LD_{50} of 568 + 61 mg/kg (male) and 363 + 41 mg/kg (female). Rabbit acute dermal study with a LD_{50} of >2000 mg/kg. Rat acute inhalation study with a LC_{50} of > 3.570 mg/l. Primary eye irritation study in the rabbit which showed practically no irritation. Primary dermal irritation study which showed practically no irritation. Primary dermal sensitization study which indicated that triadimefon is a skin sensitizer.

2. *Genotoxicity.* Triadimefon has been found to be negative in the Ames reverse mutation test and in the Structural Chromosome Aberration Test

3. *Reproductive and developmental toxicity.* A rat developmental toxicity study showed a maternal systemic NOEL of 30 mg/kg/day and the LOEL 90 mg/kg/day. The NOEL for developmental toxicity was 30 mg/kg/day and the LOEL was 90 mg/kg/day. In the developmental toxicity study in rabbits, the maternal systemic NOEL was 50 mg/kg/day and the LOEL 120 mg/kg/day. The NOEL for developmental toxicity was 20 mg/kg/day and the LOEL was 50 mg/kg/day. Effects seen at the developmental LEL in the rabbit study were irregular spinous process and ossification of various bones. A 3-generation rat reproduction study showed decreases in maternal body weight gain, fertility, and in litter size, pups survival during the lactation phase, and pups weights. The maternal NOEL was 300 ppm and the reproductive NOEL was 50 ppm. A 2-generation rat reproductive study showed reductions in litter size, pups viability, birth and lactational weights. The reproductive NOEL was 50 ppm.

4. *Subchronic toxicity.* A 3-month feeding study in the rat with a NOEL of 2,000 ppm based on decreased body weight gain and food consumption attributed to palatability. A rat 30-day feeding study with a NOEL of 10 mg/kg. A thirteen-week dog-feeding study with a NOEL of 2,400 ppm based on decreased body weight gain and food consumption due to palatability. There was also a decreased hematocrit, RBC count, hemoglobin volume and microsomal induction. A 28-day rabbit dermal study with a NOEL >250 mg/kg. A rat 21-day inhalation study with a NOEL = 78.7 mg/$m^{3/6}$ hrs. per day/ 15 exposures.

5. *Chronic toxicity.* A 2-year rat chronic feeding study defined a NOEL for systemic effect as 300 ppm (males = 16.4 mg/kg/day; females = 22.5 mg/kg/day). The systemic LOEL was 1,800 ppm (males = 114.0 mg/kg/day; females = 199.0 mg/kg/day) based on neoplastic and systemic effects. A dog feeding study showed only minimal toxic effects (decrease in body weight, increase in liver weight and in hepatic *N*-demethylase activity, and an increase in serum alkaline phosphatase activity. The NOEL was established at 100 ppm. A mouse oncogenicity study showed hepatocellular adenomas in both sexes of NMRI mice. The NOEL was established for males at 50 ppm. No NOEL was reached for females. A mouse oncogenicity study using CF1–W74 mice was negative for oncogenicity.

6. *Animal metabolism.* In a general rat metabolism study triadimefon was initially converted to triadimefon. This conversion was more rapid in males.

The major metabolites were the acid and alcohol of triadimefon. In males radioactivity was found mainly in feces, whereas, in females, radioactivity was equally distributed between urine and feces. No radioactivity was recovered in the expired air. Peak tissue levels were found in 2 to 4 hours and were highest in fat, liver and kidney.

7. *Endocrine effects.* No special studies investigating potential estrogenic or endocrine effects of triadimefon have been conducted. However, the standard battery of required studies has been completed. These studies include an evaluation of the potential effects on reproduction and development, and an evaluation of the pathology of the endocrine organs following repeated or long-term exposure. These studies are generally considered to be sufficient to detect any endocrine effects, but no such effects were noted in any of the studies with either triadimefon or its metabolites.

8. *Carcinogenicity.* Using its Guidelines for Carcinogen Risk Assessment published in the **Federal Register** of September 24, 1986 (51 FR 33992), EPA has classified triadimefon as Group ''C'' for carcinogenicity (possible human carcinogen) based on the results of carcinogenicity studies in 2 species. The classification as Group C was based on borderline statistically significant increases in thyroid adenomas in male rats, and increases in liver adenomas in both sexes of mice. Because the tumors were benign, and there were no apparent genotoxicity concerns, the Cancer Peer Review Committee recommended the RfD approach for quantitation of human risk.

C. Aggregate Exposure

1. *Dietary (food) exposure*—a. *Chronic*. For purposes of assessing the potential dietary exposure from food under the proposed tolerances, Bayer has estimated exposure based on the Theoretical Maximum Residue Contribution (TMRC) derived from the previously established tolerances for triadimefon as well as the proposed tolerance for triadimefon on coffee beans at 0.1 ppm. The TMRC is obtained by using a model which multiplies the tolerance level residue for each commodity by consumption data which estimate the amount of each commodity and products derived from the commodities that are eaten by the U.S. population and various population subgroups. In conducting this exposure assessment, very conservative assumptions--100% of all commodities will contain triadimefon residues, and those residues would be at the level of the tolerance--which result in a large overestimate of human exposure. Thus, in making a safety determination for these tolerances, Bayer took into account this very conservative exposure assessment.

b. *Acute.* EPA has not estimated non-occupational exposures other than dietary for triadimefon. Acceptable, reliable data are not currently available with which to assess acute risk. Triadimefon is registered for outdoor residential use (lawn use). While dietary and residential scenarios could possibly occur in a single day, triadimefon would rarely be present on both the food eaten and the lawn on that single day. Even assuming this were the case, it is yet more unlikely that residues would be present at tolerance level on all food eaten that day for which triadimefon tolerances exist, as is assumed in the acute dietary risk analysis, and on the lawn that same day. Because the acute dietary exposure estimate assumes tolerance level residues and 100% crop treated for all crops evaluated, it is a large over-estimate of exposure and is considered to be protective of any acute exposure scenario.

2. *Drinking water exposure.* Based on the available studies used in EPA's assessment of environmental risk, triadimefon and its metabolites are mobile and persistent and have the potential to leach into groundwater. There is no established Maximum Concentration Level for residues of triadimefon in drinking water. No drinking water health advisory levels have been issued for triadimefon or its metabolite triadimenol. The ''Pesticides in Groundwater Database'' (EPA 734–12–92–001, September 1992) indicated that triadimefon was monitored for in 14 wells in California from 1984 to 1989. There were no detectable residues (limit of detection was not stated). Although the Agency does not have available data to perform a quantitative drinking water risk assessment for triadimefon at this time, Bayer is currently conducting 2 prospective groundwater monitoring studies. Previous experience with more persistent and mobile pesticides for which there have been available data to perform quantitative risk assessments have demonstrated that drinking water exposure is typically a small percentage of the total exposure when compared to the total dietary exposure. This observation holds even for pesticides detected in wells and drinking water at levels nearing or exceeding established MCLs. Based on this experience and the Agency's best scientific judgement, EPA concludes that it is not likely that the potential exposure from residues of triadimefon in drinking water added to the current dietary exposure will result in an exposure which exceeds the RfD.

3. *Non-occupational exposure.* Triadimefon is currently registered for use on turf and ornamentals. Bayer has conducted and submitted to the EPA an exposure study designed to measure the upper bound acute exposure potential of adults and children from contact with triadimefon treated turf. The population considered to have the greatest potential exposure from contact with pesticide treated turf soon after pesticides are applied are young children. The estimated safe residue levels for triadimefon on treated turf for 10-year-old children ranged from 1.3 – 6.4 µg/cm^2 and for 5-year-old children from 1.1 – 5.6 µg/cm^2. This compares with the average triadimefon transferable residue level of 1.0 µg/cm^2 present immediately after the sprays have dried. These data indicate that children can safely contact triadimefon-treated turf as soon after application as the spray has dried.

D. Cumulative Effects

At this time, the Agency has not made a determination that triadimefon and other substances that may have a common mode of toxicity would have cumulative effects. For purposes of this tolerance, only the potential risks of triadimefon in its aggregate exposure are being considered.

E. Safety Determination

1. *U.S. population*.—a. *Chronic risk*. Based on the available chronic toxicity data, EPA has established the RfD for triadimefon at 0.04 milligrams(mg)/kilogram(kg)/day. This RfD is based on a 2-year dog feeding study with a NOEL of 11.4 mg/kg/day and an uncertainty factor of 300. An uncertainty factor of 300 was applied to account for inter-species extrapolation (10), intra-species variability (10), and the lack of an adequate reproduction study (3). Decreased food intake, depression in weight gain, and significantly ($p < 0.05$) increased alkaline phosphatase activity in both sexes were the effects observed at the lowest effect level (LEL). Using the conservative exposure assumptions described above, Bayer has determined that aggregate dietary exposure to triadimefon from the previously established and the proposed tolerance on coffee will utilize 12.32% of the RfD for the U.S. population (48 states). There is generally no concern for exposures below 100 percent 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. Acceptable, reliable data are not available to quantitatively assess risk from drinking water or from

residential uses. However, there is a reasonable certainty that no harm will result from aggregate exposure to triadimefon residues.

b. *Acute risk.* The EPA has recommended that the developmental NOEL from the rabbit developmental toxicity study (20 mg/kg/day) be used for acute dietary risk calculations. Based on the NFCS 1989–92 data base, the population of concern for this risk assessment is children 1–6 years old. The calculated Margin Of Exposure (MOE) value is 531. This MOE does not exceed the Agency's level of concern for acute dietary exposure.

2. *Infants and children.* In assessing the potential for additional sensitivity of infants and children to residues of triadimefon, the data from developmental studies in both rat and rabbit and a 2-generation reproduction study in the rat should be considered. The developmental toxicity studies evaluate any potential adverse effects on the developing animal resulting from pesticide exposure of the mother during prenatal development. The reproduction study evaluates any effects from exposure to the pesticide on the reproductive capability of mating animals through 2-generations, as well as any observed systemic toxicity. A rat and rabbit developmental toxicity studies and a 2-generation and 3-generation rat reproduction studies have been conducted with triadimefon as described above under Toxicology Profile. Maternal and developmental toxicity NOELs of 30 mg/kg/day were determined in the rat developmental toxicity studies. In the rabbit developmental toxicity study, the maternal NOEL was 50 mg/kg bwt/day and the developmental NOEL was 20 mg/kg bwt/day. Although EPA has accepted the rat and rabbit developmental toxicity studies, they have determined that the rat reproduction studies are not acceptable and question whether another study would adequately answer the question about the potential reproductive toxicity of triadimefon. The EPA believes that the additional information my be collected from the 90-day neurotoxicity study which was submitted to the EPA on October 30, 1996.

a. *Chronic risk.* FFDCA Section 408 provides that EPA may apply an additional safety factor for infants and children in the case of threshold effects to account for pre- and post-natal effects and the completeness of the toxicity database. Therefore, EPA has incorporated an additional 3-fold uncertainty factor into the calculation of the RfD because of the absence of an acceptable reproduction study. The Agency notes that there is approximately a 2-fold difference between the developmental NOEL of 20 mg/kg/day from the rabbit developmental toxicity study and the NOEL of 11.4 mg/kg/day from the 2-year dog feeding study which was the basis of the RfD. It is further noted that in the rabbit developmental toxicity study, the developmental NOEL of 20 mg/kg/day is lower than the maternal systemic NOEL of 50 mg/kg/day, suggesting the possibility of increased sensitivity for the pre-natal child. The TMRC value for the most highly exposed infant and children subgroup (non-nursing infants <1 year old) occupies 35.1% of the RfD. However, this calculation also assumes 100% crop treated and uses tolerance level residues for all commodities. Refinement of the dietary risk assessment by using percent of crop treated and anticipated residue data would likely greatly reduce the dietary exposure estimate and result in an anticipated residue contribution (ARC) which would occupy a percent of the RfD that is substantially lower than the currently calculated TMRC value. Should an additional uncertainty factor be deemed appropriate, when considered in conjunction with a refined exposure estimate, it is unlikely that the dietary risk will exceed 100 percent of the RfD. Therefore, taking into account the completeness and reliability of the toxicity data and the conservative exposure assessment, there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to triadimefon residues.

b. *Acute risk.* The EPA has recommended that the developmental NOEL from the rabbit developmental toxicity study (20 mg/kg/day) be used for acute dietary risk calculations. Based on the NFCS 1989–92 data base, the population of concern for this risk assessment is children 1-6 years old. The calculated Margin Of Exposure (MOE) value is 531. This MOE does not exceed the Agency's level of concern for acute dietary exposure.

F. International Issues

A Codex Maximum Residue Level (MRL) of 0.1 ppm has been established for residues of triadimefon and triadimenol.

G. Mode of Action

Triadimefon is a sterol demethylation inhibitor (DMI) fungicide. It is systemic and shows activity against rust infecting coffee. Triadimefon provides protective activity by preventing completion of the infection process by direct inhibition of sterol synthesis. It is rapidly absorbed by plants and translocated systemically in the young growing tissues. (PM 22)

2. E.I. duPont de Nemours & Co. (DuPont)

PP 7F4805

EPA has received a pesticide petition (PP) 7F4805 from E.I. duPont de Nemours & Co. (DuPont), P.O. Box 80038, Wilmington, DE 19880–0038 proposing, pursuant to section 408(d) of the Federal Food, Drug and Cosmetic Act (FFDCA), 21 U.S.C. Section 346a, to amend 40 CFR 180.474 by establishing tolerances for residues of the fungicide cymoxanil: 2-cyano-*N*-[(ethylamino)carbonyl]-2-(methoxyimino)acetamide in or on the raw agricultural commodity potatoes at 0.1 ppm. The proposed analytical method for determining residues is high performance liquid chromatography.

A. Residue Chemistry

1. *Plant metabolism.* The metabolism of cymoxanil in plants is adequately understood for the purposes of this tolerance. Cymoxanil degrades rapidly and extensively in potatoes to natural products. The primary metabolite is glycine (a natural amino acid), which is reincorporated into other naturally occurring products.

2. *Animal metabolism.* The metabolism of cymoxanil in animals is adequately understood. Cymoxanil degrades rapidly and extensively in ruminants to natural products, including fatty acids, glycerol, glycine and other amino acids, lactose, and acid hydrolyzable formyl and acetyl groups.

3. *Analytical method.* The proposed practical analytical method utilizes high performance liquid chromatography for detecting and measuring levels of cymoxanil in or on potatoes with a general limit of quantitation of 0.05 ppm. This method allows monitoring of food with residues at or above the levels proposed in this tolerance. This method has been validated by an independent laboratory.

4. *Magnitude of the residue in plants.* Field residue trials were conducted with cymoxanil on potatoes at 19 test sites in the U.S. at rates equal to or higher than (up to 5×) the proposed maximum use rate with pre-harvest intervals as short as 0 days. No detectable cymoxanil residue (detection limit = 0.02 ppm) was found in any sample at any of the tested sites or rates.

5. *Magnitude of the residue in processed commodities.* Because there were no detectable residues present in potato samples treated at highly exaggerated rates, no detectable residues are expected in processed potatoes at

rates which would appear on the product label.

6. *Magnitude of the residue in animals.* Based on a ruminant metabolism study, no secondary tolerances in animal commodities are necessary.

B. Toxicological Profile of Cymoxanil

1. *Acute toxicity.* Technical cymoxanil has low acute toxicity. The acute oral LD_{50} is 960 mg/kg in rats. The acute dermal LD_{50} is >2000 mg/kg in rabbits. The 4-hour rat inhalation LC_{50} is >5.06 mg/L. Minimal transient irritation of the skin and eyes was observed in rabbits. Cymoxanil did not cause skin sensitization in guinea pigs. Cymoxanil should be classified as Toxicity Category III for oral and dermal toxicity and Toxicity Category IV for inhalation toxicity and skin and eye irritation potential.

2. *Genotoxicity.* A battery of *in vitro* and *in vivo* tests were conducted to determine the genotoxic potential of cymoxanil. Cymoxanil was negative for mutagenicity in *in vitro* bacterial (*Salmonella typhimurium* or *Escherichia coli* tester strains) and mammalian cell assays (Chinese hamster ovary (CHO) cells) and is therefore considered not mutagenic. Cymoxanil was positive for induction of chromosome aberrations in *in vitro* assays (CHO cells and human lymphocytes), but negative in 2 species of *in vivo* assays (rat clastogenicity and mouse micronucleus). The weight-of-evidence indicates that cymoxanil is not clastogenic. Cymoxanil was negative for induction of unscheduled DNA synthesis (UDS) in 1 *in vitro* assay but positive in another; however, it was negative for induction of UDS in both hepatocytes and spermatocytes when evaluated in *in vivo* assays.

Therefore, Dupont believes that the weight-of-evidence indicates that cymoxanil does not produce DNA damage. In summary, cymoxanil is not considered genotoxic, nor does it have the potential to induce heritable effects.

3. *Reproductive and developmental toxicity.* A 2-generation reproduction study in rats fed diets containing 0, 100, 500, or 1,500 ppm resulted in no-observed-adverse-effects-level (NOAELs) of 100 ppm for both parental rats (equivalent to 6.50 and 7.85 mg/kg/day for P1 males and females, respectively) and offspring (equivalent to 7.39 and 8.85 mg/kg/day for F1 males and females, respectively). The NOAELs were based on alterations in body weight parameters, food consumption and food efficiency in the parents at 500 ppm, and decreases in pup weights and viability in the offspring at 500 ppm. Based on these results, cymoxanil is not a reproductive toxin.

A developmental toxicity study was conducted with cymoxanil in rats at 0, 10, 25, 75, or 150 mg/kg/day on days 7-16 of gestation. The no-observable-effect levels (NOELs) for maternal and developmental effects were considered to be 10 mg/kg/day for both maternal toxicity (based on reduced weight gain and food consumption at 25 ppm and above) and developmental toxicity (based on effects that included fetal variations in ossification at 25 ppm and above).

A developmental toxicity study was conducted in rabbits at dose levels of 0, 4, 8 and 16 mg/kg/day. Cymoxanil was not considered maternally or fetally toxic at any dose level. A second rabbit study at 0, 8, 16 and 32 mg/kg/day demonstrated toxicity to the doe at 16 mg/kg/day. Changes in axial skeleton of the fetus were observed at all dose levels, but without direct relation to dosage. A third rabbit study was conducted at 0, 1, 4, 8, and 32 mg/kg/day. Maternal toxicity was observed at 8 mg/kg/day. Although skeletal variations were seen in some fetal groups, they were not considered related to cymoxanil since they were not statistically increased or dose related. A reevaluation of the combined results of all three rabbit studies using current statistical methods demonstrated NOAELs of 8 mg/kg/day for the doe and 4 mg/kg/day for the fetus.

In the absence of significant differences between maternal and fetal effect levels (revealed in both the rat and combined rabbit studies), cymoxanil is not considered a developmental toxin.

4. *Subchronic toxicity.* A 90-day feeding study was conducted in rats at dietary levels of 0, 100, 750, 1,500 or 3,000 ppm. Body weight effects, increased food consumption, decreased food efficiency, increased mean relative organ weights, and testicular (elongate spermatid degeneration) and epididymal histopathologic effects were observed at 1,500 and 3,000 ppm. The NOEL was 750 ppm (47.6 mg/kg/day males; 59.9 mg/kg/day females).

The potential neurotoxicity of cymoxanil was evaluated in rats as part of the 90-day feeding study at dietary levels of 0, 100, 750, 1,500 or 3,000 ppm. The NOEL for neurotoxicity was the highest dietary level tested, 3,000 ppm for male (224 mg/kg/day) and female (333 mg/kg/day) rats. Cymoxanil is judged not to be a neurotoxicant.

A 90-day feeding study was conducted in mice at dietary levels of 0, 50, 500 and 1,750, 3,500 or 7,000 ppm. The highest dietary level was terminated by the third week of the study due to severe toxicity. The NOEL was established at 50 ppm for female mice (11.3 mg/kg/day) based on body weight effects at 500 ppm; no NOEL was established for male mice due to body weight effects and increased liver weights at all dietary levels. Liver weight increases were observed in female mice at 1,750 and 3,500 ppm. No histopathologic alterations were found in male or female mice at levels up to 3,500 ppm.

A 90-day feeding study was conducted in dogs at dietary levels of 0, 100, 200 or 250/500 ppm (250 ppm for weeks 1 and 2; 500 ppm for the remainder of the study). No NOEL was established for female dogs due to lower body weight gain, food consumption and food efficiency at all dietary levels. The NOEL in males was 100 ppm (3 mg/kg/day) based on decreased body weight gain.

A 28-day repeated dose dermal study was conducted with rats at dosages of 50, 500 or 1,000 mg/kg with daily 6-hour exposures. No toxicologically significant effects were observed in any treatment group. The NOEL is considered to be 1,000 mg/kg/day.

5. *Chronic toxicity/oncogenicity.* A 12-month chronic feeding study was conducted in male dogs at dietary levels of 0, 50, 100 and 200 ppm and in female dogs at 0, 25, 50 and 100 ppm. The NOAELs for chronic toxicity were 100 ppm in male dogs (3.0 mg/kg/day) and 50 ppm in female dogs (1.6 mg/kg/day), based on body weight and food consumption effects in both sexes and decreased red cell parameters in males. No gross or histopathological effects were observed.

An 18-month oncogenicity study was conducted in mice at dietary levels of 0, 30, 300, 1,500 or 3,000 ppm. The NOEL was 30 ppm (4.19 and 5.83 mg/kg/day for males and females, respectively) based on histopathological effects in testis and liver for males and the mucosal lining of the gastrointestinal tract for females at 300 ppm. Cymoxanil is not considered oncogenic.

A 2-year combined chronic toxicity/oncogenicity study was conducted in rats at dietary levels of 0, 50, 100, 700 or 2,000 ppm. The NOEL for chronic effects was 100 ppm (4.08 and 5.36 mg/kg/day for male and female rats, respectively), based on decreased mean body weights, mean body weight gains, food consumption, and food efficiency; and gross and/or histopathological alterations of the retina, lymph nodes, lung, intestine, testes, and sciatic nerve at 700 ppm. Cymoxanil is not considered oncogenic.

6. *Animal metabolism*. An oral dose of radiolabelled cymoxanil was extensively metabolized and rapidly eliminated in the rat. More than 85% of the dosed radioactivity is eliminated in the excreta, mostly in the urine, within 48 hours. After 96 hours, less than 1% of the administered dose remained in the tissues. The major excretory products were polar metabolites such as 2-cyano-2-methoxyimino acetic acid, glycine and other amino acid conjugates. These metabolites are rapidly metabolized to other natural products. A minor metabolite, 1-ethyl-5,6-di-2,4(1*H*,3*H*)pyridinedione, was also identified and is postulated as an intermediate metabolite.

7. *Metabolite toxicology.* Cymoxanil breaks down rapidly in plants and animals into naturally occurring compounds. Because of this, no significant risk is expected from exposure to potatoes or other crops treated with cymoxanil.

8. *Endocrine effects.* No evidence of endocrine effects were observed upon comprehensive evaluation of data from the standard battery of EPA required toxicology studies. These animal studies were conducted at exposure levels that far exceed those likely to be experienced by a human. Thus, adverse endocrine effects are not expected to occur in humans (general population or sub-groups, including nursing infants and children).

This battery of tests included, but is not limited to, the following studies: reproductive, developmental, subchronic, chronic/oncogenicity and metabolism. Most of these studies included gross and histopathologic assessment of the endocrine organs (e.g., thyroid, mammary glands, and testes).

C. Aggregate Exposure

Cymoxanil is a fungicide used on crops including potatoes, tomatoes, and grapes. Cymoxanil is not registered for non-crop use in any country. Although cymoxanil is not registered in the U.S., DuPont's request for import tolerances on grapes and tomatoes is pending review at EPA.

No aggregate exposure considerations are required for cymoxanil because no residues are anticipated to occur in drinking water or from other non-occupational exposures. Human exposure to residues in food is the primary exposure consideration when calculating risk. Total chronic dietary exposure to the most sensitive sub-population (children 1–6 yrs.) is determined to be less than 3% of the Reference Dose (RfD). Details are given below:

1. *Dietary (Food) Exposure.* A complete and reliable database is available for the assessment of threshold effects of cymoxanil. Comparison of no effect levels (NOEL) for subchronic and chronic studies found that the dog was the most sensitive species with a NOEL of 1.6 mg/kg/day in the 1year study. The endpoint effects noted in this study were reduced body weight gain, food consumption, and food efficiency in females.

Applying a 100-fold safety factor, 0.016 mg/kg/day was selected as the reference dose (RfD) in the dietary risk evaluation system (DRES) analysis. No additional safety factor was used for infants or children since they are not more sensitive to cymoxanil toxicity as discussed in section E.2 of this document.

The ''worst-case'' DRES analysis included total potential dietary intake of cymoxanil residues from potatoes, grapes, and tomatoes. It was also assumed that 100% of these crops were treated with cymoxanil and that all commodities contained residues at the proposed tolerance levels (0.1 ppm). Analyses of actual field samples have detected no residues of cymoxanil above the limit of detection (0.02 ppm). Potato cells and processed potato waste may be fed to livestock. However, the lack of detectable cymoxanil residues in any feed item and the lack of transfer of cymoxanil to meat or milk in a ruminant metabolism study indicate there is no reasonable expectation of cymoxanil residue in meat and milk. Potatoes do not serve as a source of poultry feed, thus no residues are expected in poultry or eggs.

Using this conservative exposure scenario, the DRES estimates a theoretical maximum daily intake of 0.000216 mg/kg/day or 1.35% of the RfD for the general U.S. population. Since cymoxanil is unlikely to occur in drinking water, water was not included in this assessment (see Section D.2 of this document). The most sensitive sub-population is children (1–6 yrs.) with a predicted intake of 2.63% of the RfD. Using the conservative exposure assumptions described above, it is estimated that the cymoxanil exposure for infants and children ranges from 0.29% of the RfD for nursing infants to 2.63% for children 1–6 years old.

An acute dietary risk exposure analysis for cymoxanil was not performed. Since potatoes are the only commodity for which registration of cymoxanil is being sought, significant dietary impact to any U.S. population is not anticipated. Cymoxanil is not registered on grapes in Chile or tomatoes in Mexico, the major countries that import these commodities to the U.S. Therefore, exposure to cymoxanil from grapes and tomatoes imported into the United States would not be expected to contribute significantly to the U.S. diet. In addition, exposure to cymoxanil through drinking water is unlikely since cymoxanil degrades rapidly in soil and water as discussed in section D.2 of this document.

2. *Dietary (Drinking Water) Exposure.* It is unlikely that there will be exposure to significant residues of cymoxanil through drinking water supplies. Cymoxanil degrades rapidly in the environment. Studies to satisfy the environmental fate data requirements are included with this submission. Evaluation of these studies indicates the potential for cymoxanil residues to be detected in drinking water supplies at significant levels is minimal. Degradation from photolysis and both anaerobic and aerobic metabolism in soils occur rapidly. Degradation products also decline rapidly. The half-life of cymoxanil in soil under field conditions was 1 to 9 days. Although cymoxanil and its degradates are weakly adsorbed to the soil, they degrade so rapidly that movement into groundwater is unlikely. Should movement into surface or ground water occur, degradation will be very rapid. In water the photolytic half-life of cymoxanil is less than 2-days at neutral and acidic conditions, and its hydrolytic half-life at pH 9 is less than 1 hour.

3. *Non-dietary exposure.* Since cymoxanil is to be used on food crops only there will be no non-dietary non-occupational exposure.

D. Cumulative Effects

Given cymoxanil's unique chemistry, low acute toxicity, the absence of genotoxic, oncogenic, developmental, or reproductive effects, and low exposure potential (see section C), the expression of cumulative human health effects with cymoxanil and other natural or synthetic pesticides is not anticipated. The potential for cumulative effects of cymoxanil and other substances, that have a common mechanism of toxicity, has been considered and is not applicable. Cymoxanil is a unique cyanoacetamide and is chemically unrelated to any other commercial plant disease control agents. Its biochemical mode of action in fungi appears to be unique; it is theorized to act through inhibition of multiple cellular processes, but a definitive mechanism is not completely elucidated. Similarly, the mechanism of action underlying observed toxicological effects in mammals is not fully characterized and there is no reliable information to

suggest that cymoxanil has a mechanism of toxicity in common with any other compound.

E. Safety Determination

1. *U.S. population*. Dupont believes that the chronic dietary risk assessment demonstrates that an adequate margin of safety exists for all U.S. sub-populations under DRES consideration.

A ''worst case'' DRES analysis was performed using proposed tolerance levels for potatoes, tomatoes, and grapes and assuming 100% of all crops are treated. Using these conservative assumptions, the percentage of the RfD utilized by the general U.S. population is 1.35%. The most sensitive sub-population, children 1–6 yrs., utilized 2.63% of the RfD. These levels are well below those which would cause an appreciable risk of harm from aggregate exposure to cymoxanil residues.

2. *Infants and children*. Based on the current toxicological requirements, a complete and reliable database exists to assess the potential for additional sensitivity of infants and children to the residues of cymoxanil. Data from developmental and reproductive toxicity studies (see section B.3) show that developing and young animals are no more susceptible to prenatal and postnatal effects of cymoxanil than the adult animals. In addition, the NOAEL from the dog study proposed as the basis for the RfD is already more than 3-fold lower than the lowest NOAEL observed in immature animals in the developmental or reproductive studies. Therefore, Dupont concludes that the safety factor used for protection of adults is fully appropriate for the protection of infants and children; no additional safety factor is necessary.

Thus toxicity of cymoxanil to developing and young animals is no greater than to adults as demonstrated in the developmental and reproductive toxicity studies.

Nonetheless, children 1–6 yrs. are identified as the most sensitive sub-population in the chronic dietary risk analysis based on potential for exposure (i.e., food consumption patterns). This sub-population consumes more potatoes, grapes, and tomatoes than the general U.S. population and other sub-populations. The chronic DRES found children 1–6 yrs. utilized 2.63% of the RfD. The general U.S. population utilized 1.35% of the RfD and the exposure for infants and children ranged from 0.29% of the RfD for nursing infants to 2.63% for children 1–6 yrs.

F. International Tolerances

Cymoxanil, a fungicide used to control potato late blight, is currently registered for use on potatoes in 35 countries, including the major European countries. The following Codex Alimentarius Commission (Codex) Maximum Residue Levels (MRL's) for cymoxanil on potatoes have been established: Belgium, Germany, Indonesia, Mexico, Netherlands, Portugal, Spain, Switzerland - 0.05 ppm, Austria, Brazil, Japan, Italy - 0.10 ppm, Hungary - 0.50 ppm, and Luxembourg - 2.0 ppm.

The U.S. Tolerance for potatoes being proposed is 0.10 ppm which is twice the limit of quantitation of 0.05 ppm in the residue enforcement method. Tolerances are not required for processed potatoes because no residues were detected (detection limit = 0.02 ppm) in the magnitude of residue study at highly exaggerated rates.

MRL's are also established internationally for cymoxanil on grapes, tomatoes, hops, tobacco and various other vegetables. MRL's on grapes range from 0.05–1.0 ppm and on tomatoes from 0.05–2.0 ppm. MRL's for all other crops range from 0.05–2.0 ppm. (PM 21)

3. Novartis Crop Protection, Inc.

PP 5E4526

EPA has received a pesticide petition (PP 5E4526) from Novartis Crop Protection, Inc. 410 Swing Road, Greensboro, NC 27401, proposing to amend 40 CFR Part 180 by establishing a tolerance for residues of the fungicide, difenoconazole, in or on the raw agricultural commodity bananas at 0.2 ppm.

Analytical method AG-575B (MRID 42806504) is proposed as the regulatory enforcement method. It is a revised version of AG-575A, which was used to determine residues of difenoconazole in or on bananas. The procedures in AG-575A remain unaltered in the revised method, AG-575B, which incorporates specificity data and methodology for megabore column gas chromatography. Procedural recoveries on banana substrates (peel and pulp), fortified prior to extraction at levels ranging from 0.02 ppm to 0.2 ppm, averaged 90.7+12% (n=42). Recoveries ranged from 60 to 115%. Storage stability has been demonstrated under frozen conditions for periods of up to 364 days.

A. Chemical Uses

Difenoconazole is the active ingredient in Sico 25EC, Sico 250EC, Score 25EC, and Score 250EC, fungicides that offer broad-spectrum control of several diseases in bananas and plantains. In the current petition, Sico and Score are being developed as foliar treatments for bananas. Difenoconazole is highly active at rates of 75 to 100 g a.i./ha.

B. Difenoconazole Safety

Novartis has submitted over 20 toxicity studies in support of tolerances for difenoconazole. Difenoconazole has a low order of acute toxicity, minimal irritation potential, and no sensitization potential. There was no evidence of genotoxicity, and it is not fetotoxic, embryolethal, or teratogenic. It is not a reproductive toxin. The main target organ of toxicity was the liver in the species tested. There was an increase in liver tumors only in mice, and only, according to the Carcinogenicity Peer Review Committee, at doses considered excessively high for carcinogenicity testing. The EPA has concluded that for the purpose of risk characterization, the Margin of Exposure (MOE) approach (threshold model) should be used for quantification of human risk. Margins of exposure are extremely high for the US population and all population subgroups for both chronic effects and acute toxicity.

The following mammalian toxicity studies were conducted and submitted in support of tolerances for difenoconazole. No-observable-effect levels are consistent with those published in the **Federal Register** of August 24, 1994 (FR 59 43491).

A rat acute oral study with an LD_{50} of 1,453 mg/kg.

A rabbit acute dermal study with an LD_{50} of >2010 mg/kg.

A rat acute inhalation study with an LC_{50} of >3.285 mg/L.

A primary eye irritation study in the rabbit which showed slight irritation.

A primary dermal irritation study in the rabbit which showed slight irritation.

A dermal sensitization study in the guinea pig which showed no irritation.

A 13-week rat feeding study identified liver as a target organ and had a no-observable-effect level (NOEL) of 20 ppm.

A 13-week mouse feeding study identified liver as a target organ and had a NOEL of 20 ppm.

A 26-week dog feeding study identified liver and eye as target organs and had a NOEL of 100 ppm.

A 21-day dermal study in rabbits had a NOEL of 10 mg/mg/day based on decreased body weight gain at 100 and 1,000 mg/kg/day.

A 24-month feeding study in rats had a NOEL of 20 ppm based on liver toxicity at 500 and 2,500 ppm. There

was no evidence of an oncogenic response.

An 18-month mouse feeding study had an overall NOEL of 30 ppm based on decreased body weight gain and liver toxicity at 300 ppm. There was an increase in liver tumors only at dose levels that exceeded the maximum tolerated dose (MTD). The oncogenic NOEL was 300 ppm.

A 12-month feeding study in dogs had a NOEL of 100 ppm based on decreased food consumption and increased alkaline phosphatase levels at 500 ppm.

An oral teratology study in rats had a maternal NOEL of 16 mg/kg/day based on excess salivation and decreased body weight gain and food consumption. The developmental NOEL of 85 mg/kg/day was based on effects seen secondary to maternal toxicity including slightly reduced fetal body weight and minor changes in skeletal ossification.

An oral teratology study in rabbits had maternal NOEL of 25 mg/kg/day based on decreased body weight gain, death, and abortion. The developmental NOEL of 25 mg/kg/day was based on effects seen secondary to maternal toxicity including slight increase in post-implantation loss and resorptions, and decreased fetal weight.

A 2-generation reproduction study in rats had a parental and reproductive NOEL of 25 ppm based on significantly reduced female body weight gain, and reductions in male pup weights at 21 days.

There was no evidence of the induction of point mutations in an Ames test.

There was no evidence of mutagenic effects in a mouse lymphoma test.

There was no evidence of mutagenic effects in a nucleus anomaly test with Chinese hamsters.

There was no evidence of induction of DNA damage in a rat hepatocyte DNA repair test.

There was no evidence of induction of DNA damage in a human fibroblast DNA repair test.

C. Threshold Effects

1. *Chronic effects.* Based on the data from chronic studies in rats, mice, and dogs, the Reference Dose (RfD) for difenoconazole is 0.01 mg/kg/day **Federal Register** of August 24, 1994 (FR 59 43492). The RfD for difenoconazole is based on the chronic study in rats with a threshold No-Observable-Effect Level of 1 mg/kg/day and an uncertainty factor of 100.

2. *Acute toxicity.* The EPA has concluded that the dietary acute margin of exposure (MOE) for developmental toxicity was 25,000 for high exposure in the females 13+ subgroup. The agency is generally not concerned unless the MOE is below 100 for substances whose acute NOEL is based on animals studies.

Novartis concurs, and has also considered that since the percentage of the RfD utilized in the chronic exposure analysis for all population subgroups is less than 10, it is highly unlikely that any acute dietary exposure scenario would utilize a significant percentage of the RfD.

Since margins of exposure of 100 or more are considered satisfactory, there is no concern for acute dietary exposure for the US population, for various population subgroups, or for either gender.

3. *Non-threshold effects (Carcinogenicity).* The Health Effects Division Carcinogenicity Peer Review Committee (CPRC) evaluated the weight-of-the-evidence on difenoconazole with reference to its carcinogenic potential. The CPRC concluded that difenoconazole should be classified a Group C carcinogen, and for the purpose of risk characterization the Margin of Exposure (MOE) approach should be used for quantification of human risk.

In the 18-month study with CD-1 mice, there was a statistically significant increase in hepatocellular adenomas, carcinomas, and combined adenomas/ carcinomas in both sexes, but only at dose levels which were considered excessively high for carcinogenicity testing. This is considered very weak evidence of carcinogenic potential. Additionally, there was no evidence of carcinogenicity in either sex of CD rat after 24 months, and there was no evidence of genotoxicity. Therefore, a threshold model should be used for estimating risk. The CPRC determined that a NOEL of 4.7 mg/kg/day, based on endpoints related to hepatic tumor development, should be used for calculating MOE's. The margin of exposure, calculated using worst case assumptions, was 9,958 for the US population.

D. Aggregate Exposure

When the potential dietary exposure to difenoconazole is calculated, the theoretical maximum residue concentration (TMRC) of 0.00041 mg/ kg/day utilizes 4% of the RfD for the overall US population. For the most exposed population subgroups, children and non-nursing infants, the TMRC is 0.000946 mg/kg/day, utilizing 9% of the RfD (**Federal Register**, August 24, 1994 FR 59 43492).

Novartis has conducted another exposure analysis using additional crops and similar conservative assumptions. In this analysis, oats, barley, and bananas (pending import tolerance) were included in addition to wheat. Tolerances or proposed tolerances were 0.1 ppm each for wheat, oats, and barley, and 0.2 ppm for bananas. Tolerances were 0.01 ppm for milk and 0.05 ppm for all other commodities: beef, goat, horse, rabbit, sheep, pork, turkey, eggs, chicken, and other poultry. Very conservative assumptions were used to estimate residues (i.e. 100% of all wheat, oats, barley and imported bananas used for human consumption or forage was treated and all RACs contained tolerance level residues). These estimates result in a extreme overestimate of human dietary exposure. Calculated TMRC values from these assumptions utilize 4.7% of the RfD for the US population and 12.51% of the RfD for non-nursing infants.

Although the import tolerance for bananas would not lead to the exposure of the general population to residues of pesticides in drinking water, this source of exposure was considered in the risk assessment. Difenoconazole is currently used in the U.S. as a seed treatment and residues are, therefore, incorporated into the soil at very low rates (0.0125 to 0.025 lb a.i./100 lb of seed). The likelihood of contamination of surface water from run-off is essentially negligible. In addition, parent and aged leaching, soil adsorption/ desorption, and radiolabeled pipe studies indicated that difenoconazole has a low potential to leach in the soil and would not be expected to reach aquatic environments. For these reasons and because of the low use rate, exposures to residues in ground water are not anticipated.

Non-occupational exposure for difenoconazole has not been estimated since the current registration in the U.S. is limited to seed treatment. Therefore, the potential for non-occupational exposure to the general population is insignificant.

Novartis has considered the potential for cumulative effects of difenoconazole and other substances of common mechanism of toxicity. Novartis has concluded that consideration of a common mechanism of toxicity in aggregate exposure assessment is not appropriate at this time. Novartis has no information to indicate that the toxic effects (generalized liver toxicity) seen at high doses of difenoconazole would be cumulative with those of any other compound. Thus, Novartis is considering only the potential risk of difenoconazole from dietary exposure in its aggregate and cumulative exposure assessment.

E. Safety Determination

1.*U.S. population*. Reference Dose (RfD); using the very conservative exposure assumptions described above, and based on the completeness of the toxicity data base for difenoconazole, Novartis calculates that aggregate exposure to difenoconazole utilizes <5% of the RfD for the US population based on chronic toxicity endpoints (NOEL = 1 mg/kg/day). When using the carcinogenic NOEL of 4.7 mg/kg/day and the margin of exposure approach recommended by the CPRC, approximately 1% of the RfD is utilized.

If more realistic assumptions were used to estimate anticipated residues and appropriate market share, this percentage would be considerably lower, and would be significantly lower than 100%, even for the highest exposed population subgroup. EPA generally has no concern for exposures below 100% of the RfD. Therefore, Novartis concludes that there is reasonable certainty that no harm will result from daily aggregate exposure to residues of difenoconazole over a lifetime.

2. *Infants and children.* Developmental toxicity and 2-generation toxicity studies were evaluated to determine if there is a special concern for the safety of infants and children from exposure to residues of difenoconazole. There was no evidence of embryotoxicity or teratogenicity, and no effects on reproductive parameters, including number of live births, birth weights, and post-natal development, at dose levels which did not cause significant maternal toxicity. In addition, there were no effects in young post-weaning animals that were not seen in adult animals in the 2-generation reproduction study. Therefore, Novartis concludes that it is inappropriate to assume that infants and children are more sensitive than the general population to effects from exposure to residues of difenoconazole.

F. Estrogenic Effects

Developmental toxicity studies in rats and rabbits and a 2-generation reproduction study in rats gave no specific indication that difenoconazole may have effects on the endocrine system with regard to development or reproduction. Furthermore, histologic investigations were conducted on endocrine organs (thyroid, adrenal, and pituitary, as well as endocrine sex organs) from long-term studies in dogs, rats and mice. There was no indication that the endocrine system was targeted by difenoconazole, even when animals were treated with maximally tolerated doses over the majority of their lifetime.

Difenoconazole has not been found in raw agricultural commodities at the limit of quantification. Based on the available toxicity information and the lack of detected residues, it is concluded that difenoconazole has no potential to interfere with the endocrine system, and there is no risk of endocrine disruption in humans.

G. Chemical Residues

The nature of the residue is adequately understood in plants and animals. The metabolism of difenoconazole has been studied in wheat, tomatoes, potatoes, and grapes. The metabolic pathway was the same in these 4 separate and distinct crops. There are no Codex maximum residue levels established for residues of difenoconazole in bananas. Novartis has submitted a practical analytical method for detecting and measuring levels of difenoconazole in or on food with the limit of quantitation that allows monitoring of food with residues at or above the levels set in the proposed tolerances. EPA will provide information on this method to FDA. The method is available to anyone who is interested in pesticide residue enforcement from the Field Operations Division, Office of Pesticide Programs. Confirmatory methods have also been supplied.

Eleven field residue studies were conducted in the major banana-producing regions of Central America (Belize, Costa Rica, Guatemala), South America (Ecuador), and Mexico. Up to 8 applications were made at the label maximum of 100 g a.i./ha. Some applications were made at a 200 g a.i./ha (2×) rate for comparison purposes. Samples of bagged (standard commercial practice in many countries) and unbagged bananas were obtained 0, 1, and 2 days after the last application. Ten studies were conducted using ground equipment and one study was applied by air. Six replicate bunches were collected in several studies to determine sample variation. Selected samples were split; one-half was frozen immediately and the other half was stored under refrigerated or room temperature conditions to mimic typical transport to market. Samples were separated into peel and pulp for analysis using analytical method AG-575A.

Difenoconazole was found in only 4 of 76 pulp samples at the 1× rate and 5 of 36 samples at the exaggerated (2×) rate. The maximum residues found in pulp were 0.03 ppm and 0.05 ppm for the 1× and 2× treatments, respectively. On a whole fruit basis, the maximum residues found for the 1× and 2× treatments were 0.16 ppm and 0.24 ppm, respectively. Residues in bagged fruit were generally lower than unbagged fruit. Residues were independent of the preharvest intervals (PHIs) used in these studies. The data support a 0.2 ppm tolerance in bananas with no PHI.

There were no differences in residues between samples of green fruit frozen immediately and fruit allowed to ripen at temperatures normally encountered in transit to the US, indicating some residue stability even at temperatures above freezing.

Freezer storage stability has also been demonstrated. Banana whole fruit samples were macerated, fortified at 0.2 ppm with difenoconazole, and stored for one year in the freezer. Samples analyzed at 0-, 28-, 84-, 168-, and 364-day intervals exhibited no degradation of the difenoconazole, demonstrating stability under these storage conditions.

Information on the transfer of residues to animals is not required or relevant to this petition. Since there are no animal feedstuffs produced from this use on bananas, transfer of residues to livestock will not occur.

There are no Codex tolerances established for difenoconazole in bananas.

H. Environmental Fate

Although the import tolerance for bananas would not lead to the exposure of the general population to residues of pesticides in the environment, these sources of exposure were considered in the risk assessment. Difenoconazole is hydrolytically stable in solution at 25 degrees Celcius at pH 5, 7, and 9. The aerobic soil metabolism half-life ranges from 75 to over 1,000 days in various soils and environmental conditions. Difenoconazole is considered to be immobile in soil. (PM 22)

4. Novartis Crop Protection Inc.

PP 6F4723

EPA has received a pesticide petition (PP) 6F4723 from Novartis Crop Protection, Inc. (Novartis), P.O. Box 18300, Greensboro, NC 27419 proposing, pursuant to section 408(d) of the Federal Food, Drug and Cosmetic Act (FFDCA), 21 U.S.C. Section 346a, to amend 40 CFR 180.474 by establishing revised tolerances for residues of the fungicide CGA329351 ([(R)-2-[(2,6-dimethylphenyl)-methoxyacetylamino]-propionic acid methyl ester). CGA329351 is the more active enantiomer contained in the racemic fungicide metalaxyl. Novartis believes

that because of its systemic and intrinsic activity, effective disease control can be obtained with mefenoxam at one-half the rate required for metalaxyl. This petition reflects the reduced dietary exposure associated with using CGA329351.

A. Residue Chemistry

1. *CGA329351 uses.* CGA329351 is highly efficacious against Pythium spp., Phytophthora spp., and fungi which cause downy mildews of turf, ornamental, and agricultural crops. Application methods include seed treatment, in-furrow, soil drenches, and/or foliar.

2. *Metabolism*. Novartis believes the studies supporting this CGA329351 petition well characterize metabolism in plants and animals. The metabolism profile supports the use of an analytical enforcement method that accounts for combined residues of CGA329351 and its metabolites which contain the 2,6-dimethylaniline (DMA) moiety.

3. *Analytical methodology.* Novartis has submitted a practical analytical method involving extraction, filtration, acid reflux, steam distillation, and solid phase cleanup with analysis by confirmatory gas chromatography using Nitrogen/Phosphorous (N/P) detection. A total residue method is used for determination of the combined residues of CGA329351 and its metabolites which contain the 2,6-dimethylaniline (DMA) moiety. The limit of quantitation (LOQ) for the method is 0.05 ppm.

4. *Magnitude of residue.* This petition is supported by field residue trials conducted at various rates, timing intervals, and applications methods to represent the use patterns which would most likely result in the highest residues. In comparative side-by-side residue tests where CGA329351 was applied at one-half the labeled use rate of metalaxyl, resultant CGA329351 residues averaged one-half of those produced from the use of metalaxyl. For all samples, the total residue method was used for determination of the combined residues of parent and its metabolites which contain the DMA moiety.

B. Toxicological Profile of CGA329351

Rat acute oral study with a LD_{50} value of 490 mg/kg.

Rat acute dermal study with a LD_{50} > 2000 mg/kg.

Rat inhalation study with a LC_{50} > 2.29 mg/liter air.

Primary eye irritation study in rabbit showing CGA329351 as severely irritating.

Primary dermal irritation study in rabbit showing CGA329351 as slightly irritating.

Skin sensitization studies in guinea pigs (Maximization and Buehler Test) showing CGA329351 is not a sensitizer.

A 28-days cumulative toxicity study in rats with a No Observed Effect Level (NOEL) of 50 mg/kg based on liver changes.

A 90-day subchronic dietary toxicity study in rats with a NOEL of 250 ppm based on liver changes.

A 90-day subchronic dietary toxicity study in dogs with a NOEL of 250 ppm basedon changes in blood biochemistry and hematology indicative of functional liver changes.

A 21-day dermal toxicity study in rats with a NOEL equal to or higher than the limit dose of 1,000 mg/kg. No local or systemic signs of toxicity were found.

A 6-month dietary toxicity study in dogs with a NOEL of 250 ppm based on changes in blood biochemistry indicative of hepatocellular damage.

A 24-month combined chronic toxicity / carcinogenicity study conducted in rats with a NOEL of 250 ppm based on liver changes. No evidence of oncogenicity was seen.

A 24-month oncogenicity study conducted in mice with a NOEL of 250 ppm based on liver changes. No evidence of oncogenicity was seen.

Teratology study in rats with a maternal NOEL of 10 mg/kg based on reduced body weight gain. The fetuses remained entirely unaffected at the highest dose tested, 250 mg/kg.

Teratology study in rabbits with a maternal NOEL of 150 mg/kg based on body weight loss. The developmental NOEL was greater than or equal to the highest dose tested, 300 mg/kg.

3-generation reproduction study in rats with a NOEL of 1,250 ppm, which was the highest dose tested. The treatment had no effect on reproduction or fertility.

In vitro gene mutation test: Ames test - negative.

In vitro chromosomal aberration test: Chinese hamster ovary (CHO)- negative.

In vitro gene mutation tests: Ames tests (3 independent studies) - negative; gene mutation in mouse lymphoma cells - negative; reverse mutation in *Saccharomyces cerevisiae* - negative.

In vitro chromosomal aberration tests: Chinese hamster bone marrow cytogenetic test - negative.

DNA repair study in rat hepatoctes - negative.

Dominant lethal study in mouse - negative.

C. Threshold Effects

1. *Chronic effects.* Based upon chronic toxicity data, Novartis believes the Reference Dose (RfD) for CGA329351 is 0.08 mg/kg/day. This RfD is based on a 6-months feeding study conducted in dogs using an uncertainty factor of 100. The No-Observed Effect Level was 8 mg/kg/day.

2. *Acute toxicity.* The risk from acute dietary exposure to CGA329351 is considered to be very low. The NOEL in a 28-day study was 50 mg/kg, which is 6-fold higher than the chronic NOEL. Since chronic exposure assessment did not result in any unacceptable exposure for even the most impacted population subgroup, it is anticipated that also the acute exposure will be in an acceptable range.

3. *Non-threshold effects.* From toxicity studies supporting the registration of CGA329351, the active ingredient is classified as a Group ''E'' compound (evidence of noncarcinogenicty for humans). There was no evidence of carcinogenicity in a 24-month feeding trial in mice nor in a 24-month feeding study in rats at the dosage levels tested. The doses tested were adequate for identifying a cancer risk.

D. Aggregate Exposure

1. *Dietary Exposure.* For the purposes of assessing the potential dietary exposure under the proposed tolerances, Novartis has estimated aggregate exposure based upon the Theoretical Maximum Residue Concentration (TMRC). The TMRC is a ''worst case'' estimate of dietary exposure since it assumes 100 percent of all crops for which tolerances are established are treated. Residue studies indicate a significant reduction in plant residue levels for CGA329351 relative to those for metalaxyl. With use rates that are one-half that of metalaxyl, CGA329351 plant residue levels are also 50% lower. Novartis has requested the following tolerances for CGA329351:

commodity	parts per million (ppm)
Alfalfa, forage	3.0 ppm
Alfalfa, hay	10.0 ppm
Almonds	0.3 ppm
Almond, hulls	5.0 ppm
Apples	0.1 ppm
Asparagus	3.5 ppm
Berries Group 1.0 ppm.	
Brassica (Cole) Leafy Vegetable Crop Grouping (Except Broccoli, Cabbage, Cauliflower, Brussels Sprouts, Mustard Greens).	0.05 ppm
Broccoli	1.0 ppm
Brussels Sprouts	1.0 ppm

commodity	parts per million (ppm)
Cabbage	0.5 ppm
Cattle (fat, liver, and kidney)	0.2 ppm
Cattle, meat and meat by products (except kidney and liver).	0.05 ppm
Cauliflower	0.5 ppm
Cereal Grains (Except Barley, Oats, and Wheat).	0.05 ppm
Citrus Fruits Group	0.5 ppm
Clover, forage	0.5 ppm
Clover, hay	1.3 ppm
Cottonseed, undelinted seed	0.05 ppm
Cranberries	2.0 ppm
Cucurbit Vegetables Group	0.5 ppm
Eggs	0.05 ppm
Fruiting Vegetables	0.5 ppm
Ginseng	1.5 ppm
Goats (fat, liver, and kidney)	0.2 ppm
Goat, meat and meat by products (except kidney and liver).	0.05 ppm
Grapes	1.0 ppm
Grass, Forage	5.0 ppm
Grass, Hay	12.5 ppm
Hogs (fat, liver, and kidney)	0.2 ppm
Hogs, meat and meat by products (except kidney and liver).	0.05 ppm
Hops cones, dried	10.0 ppm
Horses (fat, liver, and kidney)	0.2 ppm
Horses, meat and meat by products (except kidney and liver).	0.05 ppm
Leafy Vegetables Group (Except Brassica, Except Spinach).	2.5 ppm
Leaves of Root and Tuber Vegetables (human food or animal feed) Group.	7.5 ppm
Legume Vegetable Group, Foliage of.	4.0 ppm
Legume Vegetables (succulent or dried) Group, except Soybeans.	0.1 ppm
Milk	0.01 ppm
Mustard Greens	2.5 ppm
Bulb Vegetables Group	5.0 ppm
Peanut, hay	10.0 ppm
Peanut, nutmeat	0.1 ppm
Pineapples	0.05 ppm
Poultry (fat, liver, and kidney)	0.2 ppm
Poultry, meat and meat by products (except kidney and liver).	0.05 ppm
Root and Tuber Vegetables, Except Ginseng.	0.3 ppm
Sheep (fat, liver, and kidney)	0.2 ppm
Sheep, meat and meat by products (except kidney and liver).	0.05 ppm
Soybeans	0.5 ppm
Spinach	5.0 ppm
Stone Fruit Group	0.5 ppm
Strawberries	5.0 ppm
Sunflower, seed	0.05 ppm
Walnuts	0.3 ppm
Papaya (Regional tolerance for Hawaii).	0.05 ppm
Citrus Oil	3.5 ppm
Potatoes, granules / flakes	1.0 ppm
Potatoes, chips	1.0 ppm
Prunes	2.0 ppm
Raisins	3.0 ppm
Tomatoes, puree	1.5 ppm
Apples, pomace	0.2 ppm
Citrus, dried pulp	3.5 ppm
Peanut, meal	0.5 ppm
Pineapple, process residue	0.3 ppm
Potato, waste from processing	5.0 ppm
Soybeans, hulls	1.0 ppm
Soybeans, meal	1.0 ppm
Sugar beets, molasses	2.5 ppm
Sunflower seeds, meal	0.1 ppm
Wheat, milling byproducts	1.0 ppm

The following indirect or inadvertent tolerances also have been requested:

commodity	parts per million (ppm)
Barley, forage	2.0 ppm
Barley, grain	0.2 ppm
Barley, hay	6.0 ppm
Barley, straw	2.0 ppm
Forage, Fodder, and Straw of Cereal Grains Group (except wheat, barley, and oats) Fodder, Forage and Straw.	1.0 ppm
Forage, Fodder, and Straw of Cereal Grains Group (except wheat, barley, and oats) Fodder, Forage and Hay.	3.0 ppm
Oat, forage	2.0 ppm
Oat, hay	6.0 ppm
Oat, grain	0.2 ppm
Oat, straw	2.0 ppm
Wheat, forage	2.0 ppm
Wheat, hay	6.0 ppm
Wheat, grain	0.2 ppm
Wheat, straw	2.0 ppm
Barley, milling fractions	1.0 ppm
Oat, milling fractions	1.0 ppm
Wheat, milling fractions	1.0 ppm

In conducting this exposure assessment, Novartis has made very conservative assumptions -- 100% of all requested commodities will contain CGA329351 at tolerance levels which result in an overestimate of human exposure.

2. *Drinking water exposure.* Novartis anticipates the potential exposure from residues of CGA329351 in drinking water to be relatively low. Although the potential for groundwater contamination cannot be completely excluded where soils are highly permeable and the water table is shallow, the reduced use rate associated with CGA329351 reduces potential groundwater contamination relative to that for metalaxyl. Based on historical groundwater monitoring data for metalaxyl from 5 states, levels typically do not exceed 3 ppb. This contamination level would lead to a potential uptake of 0.09 x 10-3 mg/kg/day CGA329351 (for an adult person consuming 2 liters of water per day), which is equivalent to 0.1% of the RfD. On the basis of this worst case estimate for CGA329351, Novartis concludes that the contribution of any potential groundwater contamination will be negligible.

3. *Non-dietary exposure.* In addition to uses on agricultural crops, CGA329351 is registered for use against soil-borne disease in turf and ornamentals. The product, however, is not used residentially by homeowners and potential exposure to the general public is extremely low. Novartis believes the non-occupational exposure to the general public from turf andornamentals uses of CGA329351 to be negligible.

Novartis believes that 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 CGA329351 would be cumulative with those of any other chemicals. Consequently, Novartis is considering only the potential exposure to CGA329351 in its aggregate risk assessment.

E. Safety Determination

1. *U.S. population.* Under the conservative exposure assumptions of 100 percent of all crops for which tolerances are established are treated, and CGA329351 residue levels are at tolerance level (i.e., TMRC), less than 9% of the RfD will be utilized by the U.S. general population. EPA generally has no concern for exposures below 100 percent of the RfD. Therefore, based on the completeness and reliability of the toxicity data supporting this petition, Novartis believes that there is a reasonable certainty that no harm will result from aggregate exposure to residues of CGA329351, including anticipated dietary exposure and all other types of non-occupational exposures.

2. *Infants and children.* There is no indication that CGA329351 interferes with the pre-or neonatal development, even when experimental animals were exposed to very high doses leading to maternal toxicity. Infants and children are not expected to show any particular sensitivity to CGA329351. Calculated on the basis of the TMRC, utilization of RfD from dietary exposure of children is estimated as: 6% for nursing infants less than 1 year old, 16% for non-nursing infants less than 1 year old, 18% for 1 to 6 year old and 13% for children 7–12 years old.

Novartis believes that under the worst case assumptions which overestimate exposure to infants and children, there is a reasonable certainty that no harm

will result to infants and children form aggregate exposure to CGA329351.

F. Estrogenic Effects

CGA329351 does not belong to a class of chemicals known or suspected of having adverse effects on the endocrine system. Furthermore, supporting developmental toxicity studies in rats and rabbits and a reproduction study in rats gave no indication of any effects on endocrine function related to development and reproduction. Subchronic and chronic treatment did not induce any morphological changes in endocrine organs and tissues.

G. International Tolerances

There are no Codex Alimentarius Commission (CODEX) maximum residue levels (MRL's) established for residues of CGA329351 in or on raw agricultural commodities. (PM 21)

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ENVIRONMENTAL PROTECTION AGENCY

[FRL–5860–9]

Proposed Administrative Settlement Under the Comprehensive Environmental Response, Compensation and Liability Act; Dorney Road Landfill Superfund Site; De Minimis Settlement

AGENCY: Environmental Protection Agency (EPA).

ACTION: Request for public comment.

SUMMARY: The United States Environmental Protection Agency is proposing to enter into a *de minimis* settlement pursuant to sections 104 and 122(g)(4) of the Comprehensive Environmental Response, Compensation, and Liability Act of 1980, as amended, (CERCLA), 42 U.S.C. 9604 and 9622(g)(4). This proposed settlement is intended to resolve the liabilities under CERCLA of Dorothy and Russell Kulp for response costs incurred by the United States Environmental Protection Agency at the Dorney Road Landfill Superfund Site, Lehigh and Berks Counties, Pennsylvania.

DATES: Comments must be provided on or before August 25, 1997.

ADDRESSES: Comments should be addressed to the Docket Clerk, United States Environmental Protection Agency, Region III, 841 Chestnut Building, Philadelphia, Pennsylvania, 19107, and should refer to: In Re: Dorney Road Landfill Superfund Site, Lehigh and Berks Counties, Pennsylvania, U.S. EPA Docket No. III–97–85–DC.

FOR FURTHER INFORMATION CONTACT: Pamela Lazos (215) 566–2658, United States Environmental Protection Agency, Office of Regional Counsel, (3RC22), 841 Chestnut Building, Philadelphia, Pennsylvania, 19107.

Notice of de minimis settlement: In accordance with section 122(i)(1) of CERCLA, 42 U.S.C. 9622(i)(1), notice is hereby given of a proposed administrative settlement concerning the Dorney Road Landfill Superfund Site in Lehigh and Berks Counties, Pennsylvania. The administrative settlement was signed by the United States Environmental Protection Agency, Region III's Regional Administrator on May 14, 1997, and is subject to review by the public pursuant to this document. The agreement is also subject to the approval of the Attorney General, United States Department of Justice or her designee.

The settling parties have agreed to provide the United States Environmental Protection Agency, or its designee, access to their property so that response actions may be conducted on that property, and not to interfere with those response actions. This administrative settlement is subject to the contingency that the Environmental Protection Agency may elect not to complete the settlement based on matters brought to its attention during the public comment period established by this document.

EPA is entering into this agreement under the authority of sections 122(g)(4), 104 and 107 of CERCLA, 42 U.S.C. 9622(g)(4), 9604 and 9607. Section 122(g)(4) of CERCLA, 42 U.S.C. 9622(g)(4), authorizes early settlements with *de minimis* parties to allow them to resolve their liabilities under, inter alia, section 107 of CERCLA, 42 U.S.C. 9607, to reimburse the United States for response costs incurred in cleaning up Superfund sites without incurring substantial transaction costs.

The Environmental Protection Agency will receive written comments upon this proposed administrative settlement until August 25, 1997. A copy of the proposed Administrative Order on Consent can be obtained from the Environmental Protection Agency, Region III, Office of Regional Counsel, (3RC20), 841 Chestnut Building, Philadelphia, Pennsylvania, 19107 by contacting Pamela Lazos at (215) 566-2658.

Stanley L. Laskowski,

Acting Regional Administrator, EPA, Region III.

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ENVIRONMENTAL PROTECTION AGENCY

[FRL–5860–8]

Proposed Administrative Settlement Under the Comprehensive Environmental Response, Compensation and Liability Act; Dorney Road Landfill Superfund Site

AGENCY: Environmental Protection Agency (EPA).

ACTION: Request for public comment.

SUMMARY: The United States Environmental Protection Agency is proposing to enter into an administrative settlement pursuant to sections 122 and 104 of the Comprehensive Environmental Response, Compensation, and Liability Act of 1980, as amended (CERCLA), 42 U.S.C. 9622 and 9604. This proposed settlement is intended to resolve the liability under CERCLA of Robert and Melinda Tercha for response costs incurred by the United States Environmental Protection Agency at the Dorney Road Landfill Superfund Site, located in both Lehigh and Berks Counties, Pennsylvania.

DATES: Comments must be provided on or before August 25, 1997.

ADDRESSES: Comments should be addressed to the Docket Clerk, United States Environmental Protection Agency, Region III, 841 Chestnut Building, Philadelphia, Pennsylvania, 19107, and should refer to: In Re: Dorney Road Landfill Superfund Site, Lehigh and Berks Counties, Pennsylvania, U.S. EPA Docket No. III–97–84–DC.

FOR FURTHER INFORMATION CONTACT: Pamela Lazos, (215) 566–2658, United States Environmental Protection Agency, Office of Regional Counsel, (3RC22), 841 Chestnut Building, Philadelphia, Pennsylvania, 19107.

Notice of administrative settlement: In accordance with section 122(i)(1) of CERCLA, 42 U.S.C. 9622(i)(1), notice is hereby given of a proposed administrative settlement concerning the Dorney Road Landfill Superfund Site in Lehigh and Berks Counties, Pennsylvania. The administrative settlement was signed by the United States Environmental Protection