TABLE 3.— PRIORITY GROUP 1 PESTICIDES SUBJECT TO REREGISTRATION REVIEW AND TOLERANCE REASSESSMENT UNDER FQPA (WAVES 1–11)—Continued

| Chemical | Chemical Class or Toxicology Concern |
|---|---|
| Myclobutanil | azole |
| Tebuconazole | azole |
| Triflumazole | azole |
| Triadimenol | azole |
| Difenoconazole | azole |
| **WAVE 11** | |
| Diphenamid | |
| Dipropyl isocinchomeronate | |
| DNOC | |
| TCMB | |
| Tetradifon | |
| 2,4-D | aryloxyalkanoic acid |
| Cycloate | |
| Chloramben | |
| Chloroxuron | |
| Diethatyl ethyl | |
| Hexythiazox | |
| Benfluralin | 2,6-dinitroaniline |
| Ethalfluralin | 2,6-dinitroaniline |
| Oryzalin | 2,6-dinitroaniline |
| Pendimethalin | 2,6-dinitroaniline |
| Trifluralin | 2,6-dinitroaniline |
| Butralin | 2,6-dinitroaniline |
| Dinocap | dinitrophenol derivative |

[1] These Organophosphates (OPs) are not in the reregistration queue--REDs were completed for them prior to FQPA, or they are not subject to reregistration (initially registered prior to November 1, 1984). However, for most, tolerances still must be re-assessed under FQPA. The other OPs are scheduled for REDs in Waves 1 through 5.

*H. Projected Year of Completion of Reregistrations*

EPA is committed to completing the pesticide reregistration program by the year 2002.

## III. Electronic Submissions and Public Response

This notice is not subject to a formal public comment period. Nevertheless, EPA welcomes input from interested parties and the general public. Public responses to this notice should be submitted to the address in the ADDRESS section above, with an additional copy sent to Wanda Daughtry, Special Review and Reregistration Division, at the address and telephone number listed above in the section titled, ''FOR FURTHER INFORMATION CONTACT.''

The official record for this notice, as well as the public version, has been established under docket number OPP–34128 (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 ''ADDRESS'' at the beginning of this document.

Electronic comments can be sent directly to EPA at: opp-docket@.epa.gov. Electronic responses must be submitted in ASCII file format, avoiding the use of special characters and any form of encryption. Comments will also be accepted on disks in WordPerfect 5.1/6.1 file format or ASCII file format. All comments in electronic form must be identified by the docket control number OPP–34128. Electronic responses to this schedule may be filed on line at many Federal Depository libraries.

## List of Subjects

Environmental protection.

Dated: September 30, 1998.

**Lynn R. Goldman,**

*Assistant Administrator, Office of Prevention, Pesticides, and Toxic Substances.*

[FR Doc. 98–26909 Filed 10–6–98; 8:45 am]

BILLING CODE 6560–50–F

## ENVIRONMENTAL PROTECTION AGENCY

**[PF–831; FRL–6026–3]**

## Notice of Filing of Pesticide Tolerance 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–831, must be received on or before November 6, 1998.

**ADDRESSES:** By mail submit written comments to: Public Information and Records Integrity Branch, Information Resources and Services Divison (7502C), Office of Pesticides Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. In person bring comments to: Rm. 119, Crystal Mall (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 (CBI) 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 CBI. CBI should not be submitted through e-mail. Information marked as CBI will not be disclosed except in accordance with procedures set forth in 40 CFR part 2. A copy of the comment that does not contain CBI must be submitted for inclusion in the public record. Information not marked confidential may be disclosed publicly by EPA without prior notice. All written comments will be available for public inspection in Rm. 119 at the address given above, from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays.

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

| Product Manager | Office location/telephone number | Address |
|---|---|---|
| Leonard Cole | Rm. 209, CM #2, 703–305–5412; e-mail: cole.leonard@epamail.epa.gov. | 1921 Jefferson Davis Hwy, Arlington, VA |
| Mark Dow | Rm. 214, CM #2, 703–305–5533; e-mail: Dow.mark@epamail.epa.gov. | Do. |
| James Tompkins | Rm. 239, CM #2, 703 305–5697; e-mail: tompkins.james@epamail.epa.gov. | Do. |

**SUPPLEMENTARY INFORMATION:** EPA has received pesticide petitions as follows proposing the establishment 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 document control number PF–831 (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 5.1/6.1 file format or ASCII file format. All comments and data in electronic form must be identified by the document control number (PF–831) 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: September 29, 1998.

**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. FMC Corporation

*PP 8F5014*

EPA has received a pesticide petition (PP 8F5014) from FMC Corporation, 1735 Market Street, Philadelphia, PA 19103 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 Bifenthrin: (2-methyl [1,1′-biphenyl]-3-yl)methyl 3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2 dimethylcyclopropanecarboxylate in or on the raw agricultural commodity corn, grain (sweet) at 0.05 and corn, forage at 3.0 parts per million (ppm). EPA has determined that the petition contains data or information regarding the elements set forth in section 408(d)(2) of the FFDCA; however, EPA has not fully evaluated the sufficiency of the submitted data at this time or whether the data supports granting of the petition. Additional data may be needed before EPA rules on the petition.

*A. Residue Chemistry*

1. *Plant metabolism*. The metabolism of bifenthrin in plants is adequately understood. Studies have been conducted to delineate the metabolism of radiolabelled bifenthrin in various crops all showing similar results. The residue of concern is the parent compound only.

2. *Analytical method*. There is a practical method for detecting and measuring levels of bifenthrin in or on food with a limit of detection that allows monitoring of food with residues at or above the levels set in these tolerances (Gas Chromatography with Electron Capture Detection (GC/ECD) analytical method P–2132M, PP 0E3921, MRID 41658601).

3. *Magnitude of residues*. Field residue trials meeting EPA study requirements have been conducted at the maximum label rate for the crop sweet corn. Results from these trials demonstrate that the proposed bifenthrin tolerances on corn, sweet (k+cwhr) at 0.05 ppm and on corn, forage at 3.0 ppm will not be exceeded when the product is applied following the proposed use directions.

*B. Toxicological Profile*

1. *Acute toxicity*. For the purposes of assessing acute dietary risk, FMC has used the maternal No-Observed-Adverse-Effects-Level (NOAEL) of 1.0 milligram/kilogram/day (mg/kg/day) from the oral developmental toxicity study in rats. The maternal Lowest Effect Level (LEL) of this study of 2.0 mg/kg/day was based on tremors from day 7–17 of dosing. This acute dietary endpoint is used to determine acute dietary risks to all population subgroups.

2. *Genotoxicty*. The following genotoxicity tests were all negative:

gene mutation in *Salmonella* (Ames); chromosomal aberrations in Chinese hamster ovary and rat bone marrow cells; Hypoxanthine guanine phophoribosyl transferase (HGPRT) locus mutation in mouse lymphoma cells; and unscheduled DNA synthesis in rat hepatocytes.

3. *Reproductive and developmental toxicity*. i. In the rat reproduction study, parental toxicity occurred as decreased body weight at 5.0 mg/kg/day with a NOAEL of 3.0 mg/kg/day. There were no developmental (pup) or reproductive effects up to 5.0 mg/kg/day (highest dose tested).

ii. Post-natal sensitivity. Based on the absence of pup toxicity up to dose levels which produced toxicity in the parental animals, there is no evidence of special post-natal sensitivity to infants and children in the rat reproduction study.

4. *Subchronic toxicity*. Short- and intermediate-term toxicity. The maternal NOAEL of 1.0 mg/kg/day from the oral developmental toxicity study in rats is also used for short- and intermediate-term Margins of Exposure (MOE) calculations (as well as acute, discussed in (1) above). The maternal LEL of this study of 2.0 mg/kg/day was based on tremors from day 7–17 of dosing.

5. *Chronic toxicity*. i. The Referenced Dose (RfD) has been established at 0.015 mg/kg/day. This RfD is based on a 1–year oral feeding study in dogs with a NOAEL of 1.5 mg/kg/day, based on intermittent tremors observed at the Lowest Observed Effects Level (LOEL) of 3.0 mg/kg/day; an uncertainty factor of 100 is used.

ii. Bifenthrin is classified as a Group C chemical (possible human carcinogen) based upon urinary bladder tumors in mice; assignment of a Q* has not been recommended.

6. *Animal metabolism*. The metabolism of bifenthrin in animals is adequately understood. Metabolism studies in rats with single doses demonstrated that about 90% of the parent compound and its hydroxylated metabolites are excreted.

7. *Metabolite toxicology*. The Agency has previously determined that the metabolites of bifenthrin are not of toxicological concern and need not be included in the tolerance expression.

8. *Endocrine disruption*. No special studies investigating potential estrogenic or other endocrine effects of bifenthrin have been conducted. However, no evidence of such effects were reported in the standard battery of required toxicology studies which have been completed and found acceptable. Based on these studies, there is no evidence to suggest that bifenthrin has an adverse effect on the endocrine system.

*C. Aggregate Exposure*

1. *Dietary exposure. — Food*. Tolerances have been established for the residues of bifenthrin, in or on a variety of raw agricultural commodities. Tolerances, in support of registrations, currently exist for residues of bifenthrin on hops; strawberries; corn (field, seed, and pop) grain, forage, and fodder; cottonseed; and from the associated meat, milk and meat by-products from livestock commodities of cattle, goats, hogs, horses, sheep, and poultry. Additionally, time-limited tolerances associated with emergency exemptions were established for broccoli, cauliflower, raspberries, cucurbits and canola. A pending tolerance for artichokes also exists. For the purposes of assessing the potential dietary exposure for these existing and pending tolerances as well as the existing time-limited tolerances under FIFRA section 18 emergency exemptions, FMC has utilized available information on anticipated residues, monitoring data and percent crop treated as follows:

i. *Acute exposure and risk*. Acute dietary exposure risk assessments are performed for a food-use pesticide if a toxicological study has indicated the possibility of an effect of concern occurring as a result of a 1 day or single exposure. For the purposes of assessing acute dietary risk for bifenthrin, the maternal NOAEL of 1.0 mg/kg/day from the oral developmental toxicity study in rats was used. The maternal LEL of this study of 2.0 mg/kg/day was based on tremors from day 7–17 of dosing. This acute dietary endpoint was used to determine acute dietary risks to all population subgroups. Available information on anticipated residues, monitoring data and percent crop treated was incorporated into a Tier 3 analysis, using Monte Carlo modeling for commodities that may be consumed in a single serving. These assessments show that the MOE are significantly greater than the EPA standard of 100 for all subpopulations. The 95th percentile of exposure for the overall U. S. population was estimated to be 0.001105 mg/kg/day (MOE of 905); 99th percentile 0.002064 mg/kg/day (MOE of 484); and 99.9th percentile 0.003955 mg/kg/day (MOE of 253). The 95th percentile of exposure for all infants < 1 year old was estimated to be 0.002234 mg/kg/day (MOE of 448); 99th percentile 0.004459 mg/kg/day (MOE of 224); and 99.9th percentile 0.006945 mg/kg/day (MOE of 144). The 95th percentile of exposure for nursing infants < 1 year old was estimated to be 0.00061 mg/kg/day (MOE of 1,639); 99th percentile 0.001376 mg/kg/day (MOE of 727); and 99.9th percentile 0.002009 mg/kg/day (MOE of 498). The 95th percentile of exposure for non-nursing infants < one year old was estimated to be 0.002804 mg/kg/day (MOE of 357); 99th percentile 0.004831 mg/kg/day (MOE of 207); and 99.9th percentile 0.007236 mg/kg/day (MOE of 138). The 95th percentile of exposure for children 1 to 6 years old (the most highly exposed population subgroup) was estimated to be 0.002377 mg/kg/day (MOE of 421); 99th percentile 0.003483 mg/kg/day (MOE of 287); and 99.9th percentile 0.00628 mg/kg/day (MOE of 159). Therefore, FMC concludes that the acute dietary risk of bifenthrin, as estimated by the dietary risk assessment, does not appear to be of concern.

ii. *Chronic exposure and risk*. The acceptable RfD is based on a NOAEL of 1.5 mg/kg/day from the chronic dog study and an uncertainty factor of 100 is 0.015 mg/kg/day. The endpoint effect of concern were tremors in both sexes of dogs at the LEL of 3.0 mg/kg/day. A chronic dietary exposure/risk assessment has been performed for bifenthrin using the above RfD. Available information on anticipated residues, monitoring data and percent crop treated was incorporated into the analysis to estimate the anticipated residue contribution (ARC). The ARC is generally considered a more realistic estimate than an estimate based on tolerance level residues. The ARC are estimated to be 0.000384 mg/kg body weight (bwt)/day and utilize 2.6% of the RfD for the overall U. S. population. The ARC for non-nursing infants (<1 year) and children 1–6 years old (subgroups most highly exposed) are estimated to be 0.000837 mg/kg bwt/day and 0.001265 mg/kg bwt/day and utilizes 5.6% and 8.4% of the RfD, respectively. Generally speaking, the EPA has no cause for concern if the total dietary exposure from residues for uses for which there are published and proposed tolerances is less than 100% of the RfD. Therefore, FMC concludes that the chronic dietary risk of bifenthrin, as estimated by the dietary risk assessment, does not appear to be of concern.

2. *Drinking water*. Laboratory and field data have demonstrated that bifenthrin is immobile in soil and will not leach into groundwater. Other data show that bifenthrin is virtually insoluble in water and extremely lipophilic. As a result, FMC concludes that residues reaching surface waters from field runoff will quickly adsorb to sediment particles and be partitioned

from the water column. Further, a screening evaluation of leaching potential of a typical pyrethroid was conducted using EPA's Pesticide Root Zone Model (PRZM3). Based on this screening assessment, the potential concentrations of a pyrethroid in groundwater at depths of 1 and 2 meters are essentially zero (<<0.001 parts per billion (ppb)). Surface water concentrations for pyrethroids were estimated using PRZM3 and Exposure Analysis Modeling System (EXAMS) using standard EPA cotton runoff and Mississippi pond scenarios. The maximum concentration predicted in the simulated pond was 0.052 ppb. Concentrations in actual drinking water would be much lower than the levels predicted in the hypothetical, small, stagnant farm pond model since drinking water derived from surface water would normally be treated before consumption. Based on these analyses, the contribution of water to the dietary risk estimate is negligible. Therefore, FMC concludes that together these data indicate that residues are not expected to occur in drinking water.

3. *Non-dietary exposure*. Analyses were conducted which included an evaluation of potential non-dietary (residential) applicator, post-application and chronic dietary aggregate exposures associated with bifenthrin products used for residential flea infestation control and agricultural/commercial applications. The aggregate analysis conservatively assumes that a person is concurrently exposed to the same active ingredient via the use of consumer or professional flea infestation control products and to chronic level residues in the diet.

In the case of potential non-dietary health risks, conservative point estimates of non-dietary exposures, expressed as total systemic absorbed dose (summed across inhalation and incidental ingestion routes) for each relevant product use category (i.e., lawn care) and receptor subpopulation (i.e., adults, children 1 - 6 years and infants < 1 year) are compared to the systemic absorbed dose NOAEL for bifenthrin to provide estimates of the MOEs. Based on the toxicity endpoints selected by EPA for bifenthrin, inhalation and incidental oral ingestion absorbed doses were combined and compared to the relevant systemic NOAEL for estimating MOEs.

In the case of potential aggregate health risks, the above mentioned conservative point estimates of inhalation and incidental ingestion non-dietary exposure (expressed as systemic absorbed dose) are combined with estimates (arithmetic mean values) of chronic average dietary (oral) absorbed doses. These aggregate absorbed dose estimates are also provided for adults, children 1 - 6 years and infants < 1 year. The combined or aggregated absorbed dose estimates (summed across non-dietary and chronic dietary) are then compared with the systemic absorbed dose NOAEL to provide estimates of aggregate MOEs.

The non-dietary and aggregate (non-dietary + chronic dietary) MOEs for bifenthrin indicate a substantial degree of safety. The total non-dietary (inhalation + incidental ingestion) MOEs for post-application exposure for the lawn care product evaluated was estimated to be >51,000 for adults, 1,900 for children 1–6 years old and 1,800 for infants < 1 year. The aggregate MOE (inhalation + incidental oral + chronic dietary, summed across all product use categories) was estimated to be 2,479 for adults, 559 for children 1–6 years old and 712 for infants (<1 year). It can be concluded that the potential non-dietary and aggregate (non-dietary + chronic dietary) exposures for bifenthrin are associated with substantial margins of safety.

*D. Cumulative Effects*

In consideration of potential cumulative effects of bifenthrin and other substances that may have a common mechanism of toxicity, to our knowledge there are currently no available data or other reliable information indicating that any toxic effects produced by bifenthrin would be cumulative with those of other chemical compounds; thus only the potential risks of bifenthrin have been considered in this assessment of its aggregate exposure. FMC intends to submit information for the EPA to consider concerning potential cumulative effects of bifenthrin consistent with the schedule established by EPA published in the **Federal Register** of August 4, 1997 (62 FR 42020) (FRL 5734–6) and other EPA publications pursuant to the Food Quality Protection Act (FQPA).

*E. Safety Determination*

1. *U.S. population*. Based on a complete and reliable toxicology database, the acceptable RfD is 0.015 mg/kg/day, based on a NOAEL of 1.5 mg/kg/day from the chronic dog study and an uncertainty factor of 100. Available information on anticipated residues, monitoring data and percent crop treated was incorporated into an analysis to estimate the Anticipated Residue Contribution (ARC) for 26 population subgroups. The ARC is generally considered a more realistic estimate than an estimate based on tolerance level residues. The ARC are estimated to be 0.000384 mg/kg bwt/day and utilize 2.6% of the RfD for the overall U. S. population. The ARC for non-nursing infants (<1 year) and children 1–6 years old (subgroups most highly exposed) are estimated to be 0.000837 mg/kg bwt/day and 0.001265 mg/kg bwt/day and utilizes 5.6% and 8.4% of the RfD, respectively. Generally speaking, the EPA has no cause for concern if the total dietary exposure from residues for uses for which there are published and proposed tolerances is less than 100% of the RfD. Therefore, FMC concludes that the chronic dietary risk of bifenthrin, as estimated by the aggregate risk assessment, does not appear to be of concern.

For the overall U.S. population, the calculated MOE at the 95th percentile was estimated to be 905; 484 at the 99th percentile; and 253 at the 99.9th percentile. For all infants < one year old, the calculated MOE at the 95th percentile was estimated to be 448; 224 at the 99th percentile; and 144 at the 99.9th percentile. For nursing infants < 1 year old, the calculated MOE at the 95th percentile was estimated to be 1,639; 727 at the 99th percentile; and 498 at the 99.9th percentile. For non-nursing infants < 1 year old, the calculated MOE at the 95th percentile was estimated to be 357; 207 at the 99th percentile; and 138 at the 99.9th percentile. For the most highly exposed population subgroup, children 1 - 6 years old, the calculated MOE at the 95th percentile was estimated to be 421; 287 at the 99th percentile; and 159 at the 99.9th percentile. Therefore, FMC concludes that there is reasonable certainty that no harm will result from acute exposure to bifenthrin.

2. *Infants and children*. —i. *General*. In assessing the potential for additional sensitivity of infants and children to residues of bifenthrin, FMC considered data from developmental toxicity studies in the rat and rabbit, and a 2–generation reproductive study in the rat. The developmental toxicity studies are designed to evaluate adverse effects on the developing organism resulting from pesticide exposure during prenatal development to one or both parents. Reproduction studies provide information relating to effects from exposure to the pesticide on the reproductive capability of mating animals and data on systemic toxicity. FFDCA section 408 provides that EPA may apply an additional margin of safety for infants and children in the case of threshold effects to account for pre- and post-natal toxicity and the completeness of the database.

ii. *Developmental toxicity studies.* In the rabbit developmental study, there were no developmental effects observed in the fetuses exposed to bifenthrin. The maternal NOAEL was 2.67 mg/kg/day based on head and forelimb twitching at the LOEL of 4 mg/kg/day. In the rat developmental study, the maternal NOAEL was 1 mg/kg/day, based on tremors at the LOEL of 2 mg/kg/day. The developmental (pup) NOAEL was also 1 mg/kg/day, based upon increased incidence of hydroureter at the LOEL 2 mg/kg/day. There were 5/23 (22%) litters affected (5/141 fetuses since each litter only had one affected fetus) in the 2 mg/kg/day group, compared with zero in the control, 1, and 0.5 mg/kg/day groups. According to recent historical data (1992–1994) for this strain of rat, incidence of distended ureter averaged 11% with a maximum incidence of 90%.

iii. *Reproductive toxicity study.* In the rat reproduction study, parental toxicity occurred as decreased body weight at 5.0 mg/kg/day with a NOAEL of 3.0 mg/kg/day. There were no developmental (pup) or reproductive effects up to 5.0 mg/kg/day (highest dose tested).

iv. *Pre- and post-natal sensitivity. —a. Pre-natal.* Since there was not a dose-related finding of hydroureter in the rat developmental study and in the presence of similar incidences in the recent historical control data, the marginal finding of hydroureter in rat fetuses at 2 mg/kg/day (in the presence of maternal toxicity) is not considered a significant developmental finding. Nor does it provide sufficient evidence of a special dietary risk (either acute or chronic) for infants and children which would require an additional safety factor.

*b. Post-natal.* Based on the absence of pup toxicity up to dose levels which produced toxicity in the parental animals, there is no evidence of special post-natal sensitivity to infants and children in the rat reproduction study.

v. *Conclusion.* Based on the above, FMC concludes that reliable data support use of the standard 100-fold uncertainty factor, and that an additional uncertainty factor is not needed to protect the safety of infants and children. As stated above, aggregate exposure assessments utilized significantly less than 1% of the RfD for either the entire U. S. population or any of the 26 population subgroups including infants and children. Therefore, it may be concluded that there is reasonable certainty that no harm will result to infants and children from aggregate exposure to bifenthrin residues.

*F. International Tolerances*

There are no Codex, Canadian, or Mexican residue limits for residues of bifenthrin in or on corn, sweet. (Mark Dow)

**2. Norvartis Crop Protection**

*PP 8F4984*

EPA has received a pesticide petition (PP 8F4984) from Norvartis Crop Protection, P.O. Box 18300 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 Prymetrozine in or on the raw agricultural commodity cotton at 0.4 parts per million (ppm), and on cotton gin by-products at 3.0 ppm. EPA has determined that the petition contains data or information regarding the elements set forth in section 408(d)(2) of the FFDCA; however, EPA has not fully evaluated the sufficiency of the submitted data at this time or whether the data supports granting of the petition. Additional data may be needed before EPA rules on the petition.

*A. Residue Chemistry*

1. *Plant metabolism.* The metabolism of CGA-215944 in plants is understood for the purposes of the proposed tolerance. Studies in rice, tomatoes, cotton and potatoes gave similar results. Identified metabolic pathways have demonstrated that pymetrozine is the residue of concern for tolerance setting purposes.

2. *Analytical method*—i. *Crops.* Novartis has submitted two analytical methods for the determination of pymetrozine and its major crop metabolite, in crop substrates. For both methods, the limit of detection (LOD) is 1.0 nanogram (ng) and the limit of quantitation (LOQ) of 0.02 ppm. Samples are extracted using acetonitrile: 0.05M sodium borate and an aliquot is taken for each method. The aliquots were cleaned up with solid-phase and/or liquid-liquid partitions and analyzed by high preformance liquid chromatography (HPLC) with column-switching and Ultra violet (UV) detection. Both methods have undergone independent laboratory validation. The pymetrozine Analytical Method is proposed as the tolerance enforcement method.

ii. *Livestock.* Novartis has submitted an analytical methods for the determination of pymetrozine in eggs, milk and poultry, dairy and goat tissues. The LOD for the analytical method is 1.0 ng and the LOQ is 0.01 ppm. Samples are extracted using acetonitrile:water, cleaned up with solid-phase and liquid-liquid partitions, and analyzed for pymetrozine by HPLC with column switching and UV detection.

Novartis has also submitted an analytical method for the determination of the major livestock metabolite of pymetrozine in dairy and goat tissues and milk. This method also accounts for a phosphate conjugate, which is a significant metabolite found only in milk. The LOD for the metabolite method is 1.5 ng and the is LOQ of 0.01 ppm. Samples are extracted using methanol:water. Milk samples are heated to hydrolyze the phosphate conjugate, and all samples are cleaned up with solid-phase partitions and analyzed by HPLC with UV detection. The parent Analytical Method has successfully undergone independent laboratory validation.

3. *Magnitude of residues* —i. *Cotton.* The maximum residues of pymetrozine detected in samples of undelinted cottonseed from cotton supporting the maximum proposed application rate of 3 x 0.086 lbs. active ingredient/Acre (ai/A) = 0.258 lbs. ai/A (residue program performed at 1 x 0.099 lbs. ai/A + 2 x 0.132 lbs. ai/A = 0.363 lbs. ai/A) harvested with a 21–day pre-harvest interval (PHI) were 0.32 ppm. The maximum residues of the major metabolite GS–23199 detected in samples of undelinted cottonseed resulting from cotton treated as described above and harvested with a 21–day PHI were 0.04 ppm.

The maximum residues of pymetrozine detected in samples of cotton gin trash from cotton supporting the maximum proposed application rate of 3 x 0.086 lbs. ai/A = 0.258 lbs. ai/A (residue program performed at 1 x 0.099 lbs. ai/A + 2 x 0.132 lbs. ai/A = 0.363 lbs. ai/A) harvested with a 21–day PHI were 2.4 ppm. The maximum residues of GS–23199 detected in samples of cotton gin trash resulting from cotton treated as described above and harvested with a 21–day PHI were 0.31 ppm.

The maximum residues of pymetrozine detected in samples of cottonseed hulls from cotton supporting the maximum proposed application rate of 3 x 0.086 lbs. ai/A = 0.258 lbs. ai/A (residue program performed at 1 x 0.099 lbs. ai/A + 2 x 0.132 lbs. ai/A = 0.363 lbs. ai/A) harvested with a 21–day PHI were 0.08 ppm. No residues of GS–23199 were detected in samples of cottonseed hulls.

No detectable residues of either pymetrozine or GS–23199 were found in samples of cottonseed meal or refined oil from cotton supporting the maximum proposed application rate of

3 x 0.086 lbs. ai/A = 0.258 lbs. ai/A (residue program performed at 1 x 0.099 lbs. ai/A + 2 x 0.132 lbs. ai/A = 0.363 lbs. ai/A) harvested with a 21–day PHI.

ii. *Livestock*. A 3–level dairy feeding study was conducted using pymetrozine as the test substance. Holstein dairy cows were dosed daily with pymetrozine at levels equivalent to 0 (Control), 1.0 ppm, 3.0 ppm and 10 ppm. These rates represent 1.6, 5 and 16 times the maximum contribution to the diet that could be expected from cotton. This study was designed to provide data concerning the level of residues of pymetrozine, and CGA–313124, in milk and tissues which could occur as a result of feeding crops treated with pymetrozine to dairy cows. The results are used to estimate the transfer of residues from the diet to the tissues and milk of livestock.

No detectable residues of pymetrozine or CGA–313124 were observed in samples of liver, kidney, perirenal fat, omental fat, round muscle, or tenderloin muscle from cows dosed with 10 ppm (16×) pymetrozine. No detectable residues of pymetrozine were observed in samples of milk from cows dosed with 10 ppm (16×), 3 ppm (5×), or 1 ppm 1.6×) pymetrozine at any sampling interval. Detectable residues of CGA–313124 occurred only in milk samples from 80× dosed cows at a maximum level of 0.05 ppm.These results indicate that there is no need to establish a meat and milk tolerance.

*B. Toxicological Profile*

1. *Acute toxicity*. Pymetrozine has low acute toxicity. The oral $LD_{50}$ in rats is >5,820 milligram/kilograms (mg/kg) for males and females, combined. The rat dermal $LD_{50}$ is > 2,000 mg/kg and the rat inhalation $LC_{50}$ is > 1.8 mg/liter (L) air. Pymetrozine is not a skin sensitizer in guinea pigs and does not produce dermal irritation in rabbits. It produces minimal eye irritation in rabbits. End-use water-dispersible granule formulations of pymetrozine have similar low acute toxicity profiles.

2. *Genotoxicty*. Pymetrozine has low acute toxicity. The oral $LD_{50}$ in rats is > 5,820 mg/kg for males and females, combined. The rat dermal $LD_{50}$ is > 2,000 mg/kg and the rat inhalation $LC_{50}$ is > 1.8 mg/L air. Pymetrozine is not a skin sensitizer in guinea pigs and does not produce dermal irritation in rabbits. It produces minimal eye irritation in rabbits. End-use water-dispersible granule formulations of pymetrozine have similar low acute toxicity profiles.

3. *Reproductive and developmental toxicity*. In a teratology study in rats, pymetrozine caused decreased body weights (bwts) and food consumption in females given 100 and 300 mg/kg/day during gestation. This maternal toxicity was accompanied by fetal skeletal anomalies and variations consistent with delayed ossification. The no-observed-adverse-effect-level (NOAEL) for maternal and fetal effects in rats was 30 mg/kg/day. A teratology in rabbits showed that pymetrozine caused maternal death and reduced body weight gain and food consumption at 125 mg/kg/day highest dose tested (HDT). Maternal toxicity was accompanied by embryo- and feto-toxicity (abortion in one female and total resorptions in two females). Body weight and food consumption decreases, early resorptions and postimplantation losses were also observed in maternal rabbits given 75 mg/kg/day. There was an increased incidence of fetal skeletal anomalies and variations at these maternally toxic doses. The NOAEL for maternal and fetal effects in rabbits was 10 mg/kg/day. Pymetrozine is not teratogenic in rats or rabbits. In a 2-generation reproduction study in rats, parental body weight and food consumption were decreased, liver and spleen weights were reduced and histopathological changes in liver, spleen and pituitary were observed at 2,000 ppm HDT. Liver hypertrophy was observed in parental males at 200 ppm (approximately 10–40 mg/kg/day). Reproductive parameters were not affected by treatment with pymetrozine. The NOAEL for reproductive toxicity is 2,000 ppm (approximately 110–440 mg/kg/day). Offspring bwts were slightly reduced at 2,000 and 200 ppm and eye opening was slightly delayed in pups at 2,000 ppm. Effects on offspring were secondary to parental toxicity. The NOAEL for toxicity to adults and pups is 20 ppm (approximately 1–4 mg/kg/day).

4. *Subchronic toxicity*. Pymetrozine was evaluated in 13–week subchronic toxicity studies in rats, dogs and mice. Liver, kidneys, thymus and spleen were identified as target organs. The NOAEL was 500 ppm (33 mg/kg/day) in rats and 100 ppm (3 mg/kg/day) in dogs. In mice, increased liver weights and microscopical changes in the liver were observed at all doses tested. The NOAEL in mice was <1,000 ppm (198 mg/kg/day). No dermal irritation or systemic toxicity occurred in a 28–day repeated dose dermal toxicity study with pymetrozine in rats given 1,000 mg/kg/day. Minimum direct dermal absorption (1.1%) of pymetrozine was detected in rats over a 21 hour period of dermal exposure. Maximum radioactivity left on or in the skin at the application site and considered for potential absorption was 11.9%.

5. *Chronic toxicity*. Based on chronic toxicity studies in the dog and rat, a reference dose (RfD) of 0.0057 mg/kg/day is proposed for pymetrozine. This RfD is based on a NOAEL of 0.57 mg/kg/day established in the chronic dog study and an uncertainty factor of 100 to account for interspecies extrapolation and interspecies variability. Minor changes in blood chemistry parameters, including higher plasma cholesterol and phospholipid levels, were observed in the dog at the lowest-observed-effect level (LOEL) of 5.3 mg/kg/day. The NOAEL established in the rat chronic toxicity study was 3.7 mg/kg/day, based on reduced bwt gain and food consumption, hematology and blood chemistry changes, liver pathology and biliary cysts.z.

6. *Animal metabolism*. The metabolism of pymetrozine (CGA–215944) in the rat is well understood. Metabolism involves oxidation of the 5-methylene group of the triazine ring yielding 4,5-dihydro-5-hydroxy-6-methyl-4–[(3-pyridinylmethylene)amino]-1,2,4-triazin-3(2*H*)-one (CGA–359009). Oxidation of the methyl substituent of the triazine ring led to 4,5-dihydro-6-(hydroxymethyl)-4-[(3-pyridinylmethylene)amino]-1,2,4-triazin-3(2*H*)-one (CGA–313124) which was further oxidized to the corresponding carboxylic acid, 4,5-dihydro-6-carboxy-4-[(3-pyridinylmethylene)amino]-1,2,4-triazin-3(2*H*)-one. Hydrolysis of the enamino bridge yielded 4-amino-6-methyl-1,2,4-triazin-3,5(2*H*,4*H*)-dione (CGA–294849). This was further degraded to 6-methyl-1,2,4-triazin-3,5(2*H*,4*H*)-dione (metabolite). Hydrolysis of the enamino bridge of CGA–215944 produced CGA–215525 which undergoes either acylation (CGA–259168) or deamination yielding 4,5-dihydro-6-methyl-1,2,4-triazin-3(2*H*)-one (CGA–249257). Hydrolysis of the enamino bridge also formed 3-pyridinecarboxaldehyde (CGA–300407), nicotinic acid (CGA–180777), nicotinamide (CGA–180778), 3-pyridinemethanol (CGA–128632) and 1,6-dihydro-1-methyl-6-oxo-3-pyridinecarboxamide. Identified metabolic pathways in animals and plants are similar.

7. *Metabolite toxicology*. The residue of concern for tolerance setting purposes is the parent compound. Metabolites of pymetrozine are considered to be of equal or lesser toxicity than the parent.

8. *Endocrine disruption*. Pymetrozine does not belong to a class of chemicals known or suspected of having adverse

effects on the endocrine system. There is no evidence that pymetrozine has any effect on endocrine function in developmental and reproduction studies. Furthermore, histological investigation of endocrine organs in chronic dog, rat and mouse studies did not indicate that the endocrine system is targeted by pymetrozine.

*C. Aggregate Exposure*

1. *Dietary exposure— Food/Water.* Dietary exposure to pymetrozine was estimated based on tolerance level residues on fruiting vegetables, tuberous and corm vegetables, cucurbits, cotton, hops (import/domestic), associated dairy products and drinking water. Maximum expected exposure to the U.S. population (48 States, all seasons) was calculated to be 6.66% of the RfD described as 0.0057 mg/kg/bwt/day. Maximum expected exposure to the most sensitive population subgroup, non-nursing infants was calculated to be 14.4% of the RfD. The above values were determined by using tolerance level values for each appropriate crop with an assumption of 100% market share (most conservative scenario). In addition, the drinking water component was evaluated using the Generic expected environmental concentration (GENEEC) surface water model (worst case scenario) and the resulting calculated value was then incorporated into the crop and animal aspect of the diet and is included in the above values. There is a reasonable certainty that no harm will result from exposure to dietary residues (including drinking water) of pymetrozine. There are no proposed residential uses of pymetrozine, therefore the potential for non-occupational exposure to the general population is not significant.

2. *Non-dietary exposure.* There are no other uses currently registered for pymetrozine. The proposed uses involve application of pymetrozine to crops grown in an agricultural environment. There are no proposed uses which would be expected to result in residential exposure of pymetrozine. Therefore, there is no potential for non-occupational exposure to the general population.

*D. Cumulative Effects*

The potential for cumulative effects of pymetrozine and other substances that have a common mechanism of toxicity has also been considered. Pymetrozine belongs to a new chemical class known as pyridine azomethines. It exhibits a unique mode of action which can be characterized as nervous system inhibition of feeding behavior. It does not have a general toxic or paralyzing effect on insects, but selectively interferes with normal feeding activities by affecting nervous system regulation of fluid intake. There is no reliable information to indicate that toxic effects produced by pymetrozine would be cumulative with those of any other chemical including another pesticide. Therefore, Novartis believes it is appropriate to consider only the potential risks of pymetrozine in an aggregate risk assessment.

*E. Safety Determination*

1. *U.S. population.* Using the conservative exposure assumptions and the proposed RfD described above, the aggregate exposure to pymetrozine will utilize 6.66% of the RfD for the U.S. population. EPA generally has no concern for exposures below 100% of the RfD because the RfD represents the level at or below which daily aggregate exposure over a lifetime will not pose appreciable risks to human health. Therefore, Novartis concludes that there is a reasonable certainty that no harm will result from aggregate exposure to pymetrozine residues.

2. *Infants and children.* In assessing the potential for additional sensitivity of infants and children to residues of pymetrozine, data from developmental toxicity studies in the rat and rabbit and a 2-generation reproduction study in the rat have been considered.

In a teratology study in rats, developmental toxicity anomalies and variations associated was observed only at maternally toxic doses. Similarly, in a rabbit teratology study, was observed only at maternally toxic doses. The NOAELs in the rat and rabbit teratology studies were 30 and 10 mg/kg/day, respectively. In the 2-generation reproduction study, there were no effects on reproductive parameters. Offspring bwts were slightly reduced and eye opening was slightly delayed at dose levels producing parental toxicity. The NOAEL for parental and offspring toxicity was 20 ppm (approximately 1–4 mg/kg/day).

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 toxicity and the completeness of the database. Based on the current toxicological requirements, the database relative to pre- and post-natal effects for children is complete. Further, for pymetrozine, the NOAEL of 0.57 from the chronic feeding study in dogs, which was used to calculate the RfD (0.0057 mg/kg/day), is already lower than the developmental NOAELs (30 and 10 mg/kg/day) from the teratogenicity studies in rats and rabbits by a factor of more than 10 fold. In the pymetrozine rat reproduction study, the mild nature of the effects observed (decreased bwt) at the systemic LOEL (10-40 mg/kg/day) and the fact that the effects were observed at a dose that is more than 10 times greater than the NOAEL in the chronic dog study (0.57 mg/kg/day) suggest that there is no additional sensitivity for infants and children. Therefore, it is concluded that an additional uncertainty factor is not warranted to protect the health of infants and children and that an RfD of 0.0057 mg/kg/day based on the chronic dog study is appropriate for assessing aggregate risk to infants and children from pymetrozine.

Using the exposure assumptions (residues at proposed tolerance levels on all crops and a 100% market share), the percent of the RfD that will be utilized by aggregate exposure to residues of pymetrozine is 3.83% for nursing infants less than 1 year old, 14.4% for non-nursing infants and 10.17% for children 1–6 years old. Therefore, based on the completeness and reliability of the toxicity database, Novartis concludes that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to pymetrozine residues.

*F. International Tolerances*

There are no Codex maximum levels established for residues of pymetrozine. (Leonard Cole)

**3. Zeneca Ag. Products**

*PP 5F1625/5H5088*

EPA has received pesticide petitions PP 5F1625 and 5H5088 from Zeneca Ag Products, 1800 Concord Pike, P.O. Box 15458, Wilmington, Delaware 19850–5458, proposing pursuant to section 408(d) of the Federal Food, Drug, and Cosmetic Act, (FFDCA) 21 U.S.C. 346a(d), to amend 40 CFR part 180 by establishing a tolerance for residues of the herbicide paraquat (1,1-dimethyl-4,4′-bypyridinium) derived from the corn harvest-aid application of the dichloride salt (calculated as the cation) in or on the raw agricultural commodities corn, pop, grain at 0.05 part per million (ppm); corn, field, grain at 0.05 ppm; corn, field, forage at 3.0 ppm; corn, pop, forage at 3.0 ppm; corn, field, stover at 10.0 ppm; corn, pop, stover at 10 ppm; and corn, flour at 0.1 ppm.

An adequate analytical method (spectrophotometric method) has been accepted and published in the Pesticide Analytical Manual (PAM Vol. II) for the enforcement of tolerances in plant

commodities. 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 residue in plants is adequately understood based on studies depicting the metabolism of paraquat in carrots and lettuce following pre-emergence treatments and in potatoes and soybeans following desiccant treatment. The residue of concern in plants is the parent, paraquat; the current tolerance expression for plant commodities, as defined in 40 CFR 180.205(a) and (b).

2. *Analytical method.* An adequate analytical method (spectrometric method) has been accepted and published in the The Pesticide Analytical Manual (PAM Vol. II) for the enforcement of tolerances in plant commodities.

3. *Magnitude of residues.* Paraquat residues on corn forage ranged from <0.025 to 3 ppm and on corn fodder ranged from 0.025 to 6 ppm following preemergence and post-directed applications as described for MRID 41151523 and 41151506. Residue data submitted in tolerance petition PP 5F1625 (MRID 00114426) for corn harvest-aid use of paraquat indicate that corn grain residues would not exceed the established tolerance of 0.05 ppm when applied broadcast postemergence at 0.5 lbs ai/A with a 7–day pre-harvest interval. Residue data submitted in tolerance petition PP 5F1625 (MRID 00114426) for corn harvest-aid use of paraquat indicate that corn fodder (stover) residues range from 1.3 to 10.0 ppm when applied broadcast postemergence at 0.5 lbs ai/A with a 7–day pre-harvest interval. These data support a corn forage tolerance of 3 ppm and a corn stover tolerance of 10 ppm.

*B. Toxicological Profile*

1. *Acute Toxicity.* Acute toxicity studies conducted with the 45.6% paraquat dichloride technical concentrate give the following results: oral $LD_{50}$ in the rat of 344 mg/kg (males) and 283 mg/kg (females) (Category II); dermal $LD_{50}$ in the rat of ≤ 2,000 mg/kg for males and females (Category III); the primary eye irritation study showed corneal involvement with clearing within 17 days (Category II); and dermal irritation of slight erythema and edema at 72 hours (Category IV). Paraquat is not a dermal sensitizer. Acute inhalation studies conducted to EPA guideline with aerosolized sprays result in $LD_{50}$ of 0.6 to 1.4 µg paraquat cation/Liter (L) (Category I). However, since paraquat dichloride has no measurable vapor pressure; and hydraulic spray droplets are too large to be respirable, inhalation exposure is not a concern in practice.

2. *Genotoxicity.* Paraquat dichloride was not mutagenic in the Ames test using *Salmonella typhinurium* strains TA1535, TA1538, TA98, and TA100; the chromosomal aberrations in the bone marrow test system; or in the dominant lethal mutagenicity study with CD-1 mice. Additionally, paraquat dichloride was negative for unscheduled DNA synthesis in rat hepatocytes in *in vitro* and *in vivo*. Paraquat was weakly positive in the mouse lymphoma cell assay only in the presence of metabolic activation. Paraquat dichloride was weakly positive in mammalian cells (lymphocytes) and positive in the sister chromatid exchange (SCE) assay in Chinese hamster lung fibroblasts. Paraquat is non-mutagenic.

3. *Reproductive and developmental toxicity.* A 3–generation reproduction study in rats fed diets containing 0, 25, 75, and 150 ppm which correspond to 0, 1.25, 3.75 or 7.5 mg of paraquat cation/kg/day, respectively. Paraquat, at all levels tested, had no effect on body weight gain, food consumption and utilization, fertility and length of gestation of the $F_0$ $F_1$ and $F_2$ parents. The NOAEL and LOEL for systemic toxicity are 25 ppm (1.25 mg/kg/day) and 75 ppm (3.75 mg/kg/day), respectively, expressed as paraquat cation. The NOAEL for reproductive toxicity is ≥150 ppm (7.5 mg/kg/day; HDT) expressed as paraquat cation, as there were no reproductive effects observed.

Two developmental toxicity studies were conducted in rats given gavage doses of 0, 1, 5, and 10 mg/kg/day and 0, 1, 3, and 8 mg/kg/day, respectively, expressed as paraquat cation. In the first study, the NOAEL for maternal toxicity was 1 mg/kg/day based on clinincal signs of toxicity and decreased body weight gain at 5 mg/kg/day (the LOEL). The NOAEL for developmental toxicity was set at 5 mg/kg/day based on delayed ossification of the forelimb and hindlimb digits. In the second, study, the maternal and developmental NOAEL is 8 mg/kg/day (HDT) as there were no effects observed at any dose level even though the animals were examined more carefully in the manus and pes assessment. Based on both studies the overall NOAEL for maternal and developmental toxicity is at least 3 mg/kg/day.

Two developmental toxicity studies were conducted in mice given gavage doses of 0, 1, 5, and 10 mg/kg/day and 0, 7.5, 15, or 25 mg/kg/day paraquat ion, respectively. Both the maternal and developmental NOAEL's are at 15 mg/kg/day in the second study. The maternal LOEL of 25 mg paraquat cation/kg/day is based on death, decreases in body weight and body weight gain, and other clinical signs. The developmental LOEL is 25 mg/kg/day. In the first study there was a statistically significant effect on ''partial ossification'' of the 4th sternebra at 10 mg/kg/day (HDT). However, it is not believed the ossification pattern of the 4th sternebra was affected by paraquat as evidenced by the lack of increase in ''4th sternebra - not ossified.''

Additionally there were no statistically significant skeletal abnormalities seen in the second study. The developmental/maternal NOAEL should be based on the second study and is 15 mg/kg/day. Paraquat dichloride is not a developmental toxin.

4. *Subchronic toxicity.* A 90 day feeding study in dogs fed doses of 0, 7, 20, 60 or 120 ppm with a NOAEL of 20 ppm based on long effects such as alveolitis and alveolar collapse seen at the LOEL of 60 ppm.

A 21 day dermal toxicity study in rabbits exposed dermally to doses of 0, 1.5, 3.4, 7.8 or 17.9 mg/kg/day with a NOAEL of 1.15 mg/kg/day and a LOEL of 2.6 mg/kg/day based on dermal irritation.

A 21 day inhalation toxicity study in rats were exposed to respirable aerosols of paraquat at doses of 0, 0.01, 0.1, 0.5 and 1.0 µg/L with a NOAEL of 0.01 µg/L and a LOEL of 0.10 µg/L based on histopathological changes to the epithelium of the larynx and nasal discharge.

5. *Chronic toxicity.* In a 12-month feeding study in dogs fed dose levels of 0, 15, 30, or 50 ppm, expressed as paraquat cation. These levels corresponded to 0, 0.45, 0.93 or 1.51 mg of paraquat cation/kg/day, respectively, in male dogs or 0, 0.48, 1.00 or 1.58 mg of paraquat cation/kg/day, respectively for female dogs. There was a dose-related increase in the severity and extent of chronic pneumonitis in the mid-dose and high-dose male and female dogs. This effect was also noted in the low-dose male group, but was minimal when compared with the male controls. The systemic NOAEL is 15 ppm (0.45 mg/kg/day for males and 0.48 mg/kg/day for females, expressed as paraquat cation). The systemic LOEL is 30 ppm (0.93 mg/kg/day for males and

1.00 mg/kg/day for females, expressed as paraquat cation).

In a 2-year chronic feeding/carcinogenicity study, rats were fed doses of paraquat dichloride at 0, 25, 75, or 150 ppm which corresponded to 0, 1.25, 3.75, or 7.5 mg of paraquat cation/kg/day. Paraquat enhanced the development of ocular lesions in all of the treated groups. The predominant lesions detected opthalmoscopically were lenticular opacities and cataracts. At test week 103, dose-related statistically significant (P<0.001) increases in the incidence of ocular lesions were observed only in the mid-dose and high-dose male and female groups. Based on these findings, the NOAEL (approximate) and the LOEL for systemic toxicity, for both sexes, are 25 ppm (1.25 mg/kg/day) and 75 ppm (3.75 mg/kg/day), respectively.

In another 2-year chronic feeding/carcinogenicity study, rats were dosed at 0, 6, 30, 100 or 300 ppm, expressed as paraquat dichloride (nominal concentrations), equivalent to 0, 0.25, 1.26, 4.15, or 12.25 mg/kg/day, respectively (males) and 0, 0.30, 1.5, 5.12 or 15.29 mg/kg/day respectively (females), expressed as paraquat dichloride. The incidence of ocular changes were low and not caused by paraquat in this study. The systemic NOAEL is 100 ppm of paraquat dichloride (4.15 and 5.12 mg/kg/day, for males and females, respectively); or 3.0 mg/kg/day (males) and 3.7 mg/kg/day (females), expressed as paraquat cation. The systemic LOEL is 300 ppm of paraquat dichloride (12.25 and 15.29 mg/kg/day, for males and females, respectively); or 9.0 mg/kg/day (males) and 11.2 mg/kg/day (females), expressed as paraquat cation.

A chronic feeding/carcinogenicity study in rats fed dose levels of 0, 25, 75 or 150 ppm, expressed as paraquat cation (nominal concentrations). These doses corresponded to 0, 1.25, 3.75, or 7.5 mg paraquat cation/kg/day, respectively. There was uncertain evidence of carcinogenicity (squamous cell carcinomas in the head region; ears, nasal cavity, oral cavity and skin) in males at 7.5 mg/kg/day (HDT) with a systemic NOAEL of 1.25 mg/kg/day. Upon submission of additional data to EPA, the incidence of pulmonary adenomas and carcinomas was well within historical ranges and it was determined that paraquat was not carcinogenic in the lungs and the head region of the rat.

In another chronic feeding/carcinogenicity study, rats were fed dose levels of 0, 6, 30, 100 or 300 ppm, expressed as paraquat dichloride. There were no carcinogenic findings in this study at the highest dose tested. In a two year chronic feeding/oncogenicity study, SPF Swiss derived mice were fed paraquat dichloride at dose levels of 0, 12.5, 37.5, or 100/125 ppm, expressed as paraquat cation. These rates correspond to 0, 1.87, 5.62, and 15 mg/kg/day as cation. Because no toxic signs appeared after 35 weeks of dosing, the 100 ppm level was increased to 125 ppm at week 36. There were no carcinogenic effects observed in this study.

The systemic NOAEL for both sexes is 12.5 ppm (1.87 mg/kg/day) and the systemic LOEL is 37.5 ppm (5.6 mg/kg/day), each expressed as paraquat cation based on renal tubular degeneration in males and weight loss and decreased food intake in females.

Paraquat is classified Category E for carcinogenicity (no evidence of carcinogenicity in animal studies).

6. *Animal metabolism*. The qualitative nature of the residue in animals is adequately understood based on the combined studies conducted with ruminants (goats and cows), swine, and poultry. The residue of concern in eggs, milk, and poultry and livestock tissues is the parent, paraquat.

7. *Metabolite toxicology.* The nature of residues in plants and animals is adequately understood. The residue of concern in eggs, milk, poultry, livestock, and in crops is the parent paraquat. There are no metabolites.

8. *Endocrine disruption.* EPA is required to develop a screening program to determine whether certain substances (including all pesticides and inerts) ''may have an effect produced by a naturally occurring estrogen, or such other endocrine effect .'' The Agency is currently working with interested stakeholders, including other government agencies, public interest groups, industry and research scientist in developing a screening and testing program and a priority setting scheme to implement this program. Congress has allowed 3 years from passage of FQPA (August 3, 1999) to implement this program. At that time, EPA may require further testing of this active ingredient and end use products for endocrine disrupter effects.

*C. Aggregate Exposure*

In examining aggregate exposure, FQPA directs EPA to take into account available information concerning exposures from the pesticide residue in food and all other exposures for which there is reliable information. These other sources of exposure including drinking water, and non-occupational exposures, e.g., to pesticides used in and around the home. For estimating acute and chronic risks the Agency considers aggregate exposures from the diet and from drinking water. Exposures from uses in and around the home that may be short term, intermediate or other duration may also be aggregated as appropriate for specific chemicals.

1. *Dietary exposure.* The Residue Chemistry data base for paraquat is substantially complete, and the nature of the residues in plants and animals is adequately understood. The residue of concern is the parent, paraquat; the current tolerance expression for plants and animal commodities, as defined in 40 CFR 180.205(a) and (b), is adequate. The Reference Dose (RfD) for chronic dietary assessments is 0.0045 mg/kg/day, based on a NOAEL of 0.45 mg/kg/day from a 1 year dog study and the addition of a standard uncertainty factor of 100.

2. *Food.* —i. *Chronic dietary assessment.* A chronic dietary exposure analysis was performed using current and reassessed tolerance level residues, contributions from the proposed use as a corn harvest aid, and 100% crop treated information to estimate the Theoretical Maximum Residue Contribution (TMRC) for the general population and 22 subgroups. The resulting TMRC for the general U.S. population from all established uses is 0.001669 mg/kg/day (37% of the RfD). For children ages 1–6, the most highly exposed subgroup, the resulting TMRC is 0.003679 mg/kg/day (82% of the RfD). A refined chronic dietary assessment using percent crop treated data provided a more accurate estimate of exposure, called the Anticipated Residue Contribution (ARC). The resulting ARC for the general population is 0.00037 mg/kg/day (8.0% of the RfD), and 0.001 mg/kg/day (22% of the RfD) for children ages one to six.

ii. *Acute dietary assessment.* EPA has determined that current data on paraquat shows no acutedietary endpoint of concern. Therefore, an acute dietary risk assessment is not required for paraquat.

3. *Drinking water.* Paraquat is not expected to be a contaminant of groundwater. Paraquat dichloride binds strongly to soil clay particles and it did not leach from the surface in terrestrial field dissipation studies. There were, however, detections of paraquat in drinking water wells from 2 states cited in the Pesticides in Ground Water Database (1991). These detections are not considered to be representative of normal paraquat use. Therefore, paraquat is not expected to be a groundwater contaminant or concern based on normal use patterns.

Due to its persistent nature, paraquat could potentially be found in surface

water systems associated with soil particles carried by erosion, however, paraquat is immobile in most soils, and at very high application rates (50–1,000X), there was no desorption of paraquat from soils. Therefore, based on paraquat's normal use patterns and unique environmental fate characteristics, exposures to paraquat in drinking water are not expected to be obtained from surface water sources.

4. *Non-dietary exposure.* Paraquat dichloride has no residential or other non-occupational uses that might result in non-occupational, non-dietary exposure for the general population. Paraquat products are Restricted Use, for use by Certified Applicators only, which means the general public cannot buy or use paraquat products.

*D. Cumulative Effects*

In assessing the potential risk from cumulative effects of paraquat and other chemical substances, the Agency has considered structural similarities that exist between paraquat and other bipyridylium compounds such as diquat dibromide. Examination of the toxicology databases of paraquat and diquat dibromide, indicates that the two compounds have clearly different target organs. Based on available data, the Agency does not believe that the toxic effects produced by paraquat would be cumulative with those of diquat dibromide.

*E. Safety Determination*

1. *U.S. population.* Based on the information provided in this notice, EPA has determined that for the aggregate exposure assessment the only exposure route of concern for paraquat is chronic dietary. The toxicology database for paraquat is considered by EPA to be complete and reliable. Using the conservative assumptions presented earlier, EPA has established an RfD of 0.0045 mg/kg/day. This was based on the NOAEL for the 1-year dog study of 0.45 mg/kg/day and employed a 100-fold uncertainty factor. Results of this aggregate exposure assessment, which includes EPA's reassessment of tolerances for existing crops and the addition of corn harvest aid, utilize a maximum of 22% of the RfD. Generally, exposures below 100% of the RfD are of no concern because it represents the level at or below which daily aggregate dietary exposure over a lifetime will not pose appreciable risk to human health. Thus, there is reasonable certainty that no harm will result from aggregate exposures to paraquat residues.

2. *Infants and children.* EPA has determined that the established tolerances for paraquat, with amendments and changes as specified in this notice, meet the safety standards under the FQPA amendments to section 408(b)(2)(*C*) for infants and children. The safety determination for infants and children considers the factors noted above for the general population, but also takes into account the possibility of increased dietary exposure due to specific consumption patterns of infants and children, as well as the possibility of increased susceptibility to the toxic effects of paraquat residues in this population subgroup.

In determining whether or not infants and children are particularly susceptible to toxic effects from paraquat residues, EPA considered the completeness of the database for developmental and reproductive effects, the nature and severity of the effects observed, and other information.

Based on the current data requirements, paraquat has a complete database for developmental and reproductive toxicity. In the developmental studies effects were seen (delayed ossification in the forelimb and hindlimb digits) in the fetuses only at the same or higher dose levels than effects in the mother. In the reproduction study, no effects on reproductive performance were seen. Also because the NOAELs from the developmental and reproduction studies were equal to or greater than the NOAEL used for establishing the reference dose, EPA concludes that it is unlikely that there is additional risk concern for immature or developing organisms. Finally, the Agency has no epidemiological information suggesting special sensitivity of infants and children to paraquat. Therefore, the Agency finds that the uncertainty factor (100X) routinely used in RfD calculations is adequately protective of infants and children, and an additional uncertainty factor is not warranted for paraquat.

Zeneca estimates that paraquat residues in the diet of non-nursing infants (less than 1 year) account for 18% of the RfD and 22% of the RfD for children aged 1–6 years. Further, residues in drinking water are not expected. Therefore, the Zeneca has determined that there is reasonable certainty that dietary exposure to paraquat will not cause harm to infants and children.

*F. International Tolerances*

Codex maximum residue levels (MRL) are established for residues of paraquat for corn grain at 0.1 ppm. The proposed tolerances for corn grain at 0.05 ppm differ from the Codex MRL's based on field residue data generated in the United States for this use (Pesticide Petitions 5F1625 and 5H5088 for corn grain. Differences in use patterns and pre-harvest intervals may account for the differences between the Codex MRLs and the tolerance values generated from the pesticide residue trials in the United States. (Jim Tompkins)

[FR Doc. 98–26783 Filed 10–6–98; 8:45 am]

BILLING CODE 6560–50–F

## ENVIRONMENTAL PROTECTION AGENCY

**[FRL–6173–6]**

## State and Tribal Water Quality Standards; Notice of EPA Approvals

**AGENCY:** Environmental Protection Agency (EPA).

**ACTION:** Notice.

**SUMMARY:** This document contains a listing of State and Tribal submissions of new or revised water quality standards that EPA approved during the period September 1, 1995 through March 31, 1998. This document is published in accordance with a requirement contained in the Water Quality Standards Regulation (40 CFR 131.21). Additionally, this notice contains a listing of Indian Tribes that obtained EPA approval to administer a water quality standards program during the same period. It also contains a list of EPA actions to promulgate or remove Federal water quality standards during the same period.

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