in the control, 1, and 0.5 mg/kg/day groups. According to recent historical data 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 bwt 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 HDT.

iv. *Prenatal and postnatal sensitivity*—a. *Prenatal*. 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. *Postnatal*. Based on the absence of pup toxicity up to dose levels which produced toxicity in the parental animals, there is no evidence of special postnatal sensitivity to infants and children in the rat reproduction study.

c. *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 less than 10% of the cPAD 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 grape, peppers (bell and non-bell), lettuce, and caneberry.

[FR Doc. 99–33035 Filed 12–21–99; 8:45 am]

BILLING CODE 6560–50–F

ENVIRONMENTAL PROTECTION AGENCY

[PF–906; FRL–6398–6]

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

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

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

DATES: Comments, identified by docket control number PF–906, must be received on or before January 21, 2000.

ADDRESSES: Comments may be submitted by mail, electronically, or in person. Please follow the detailed instructions for each method as provided in Unit I.C. of the ''SUPPLEMENTARY INFORMATION.'' To ensure proper receipt by EPA, it is imperative that you identify docket control number PF–906 in the subject line on the first page of your response.

FOR FURTHER INFORMATION CONTACT: By mail: James Tompkins, Registration Support Branch, Registration Division (7505C), Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460; telephone number: (703) 305–5697; e-mail address: tompkins.jim@epa.gov.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

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

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

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

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

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

2. *In person.* The Agency has established an official record for this action under docket control number PF–906. The official record consists of the documents specifically referenced in this action, any public comments received during an applicable comment period, and other information related to this action, including any information claimed as confidential business information (CBI). This official record includes the documents that are physically located in the docket, as well as the documents that are referenced in those documents. The public version of the official record does not include any information claimed as CBI. The public version of the official record, which includes printed, paper versions of any electronic comments submitted during an applicable comment period, is available for inspection in the Public Information and Records Integrity Branch (PIRIB), Rm. 119, Crystal Mall #2, 1921 Jefferson Davis Highway, Arlington, VA, from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The PIRIB telephone number is (703) 305–5805.

C. How and to Whom Do I Submit Comments?

You may submit comments through the mail, in person, or electronically. To ensure proper receipt by EPA, it is imperative that you identify docket control number PF–906 in the subject line on the first page of your response.

1. *By mail.* Submit your comments to: Public Information and Records Integrity Branch (PIRIB), Information Resources and Services Division (7502C), Office of Pesticide Programs (OPP), Environmental Protection Agency, 401 M St., SW., Washington, DC 20460.

2. *In person or by courier.* Deliver your comments to: Public Information and Records Integrity Branch (PIRIB), Information Resources and Services Division (7502C), Office of Pesticide

Programs (OPP), Environmental Protection Agency, Rm. 119, Crystal Mall #2, 1921 Jefferson Davis Highway, Arlington, VA. The PIRIB is open from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The PIRIB telephone number is (703) 305–5805.

3. *Electronically.* You may submit your comments electronically by e-mail to: ''*opp-docket@epa.gov*,'' or you can submit a computer disk as described above. Do not submit any information electronically that you consider to be CBI. Avoid the use of special characters and any form of encryption. Electronic submissions will be accepted in Wordperfect 6.1/8.0 or ASCII file format. All comments in electronic form must be identified by docket control number PF–904. Electronic comments may also be filed online at many Federal Depository Libraries.

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

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

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

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

1. Explain your views as clearly as possible.

2. Describe any assumptions that you used.

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

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

5. Provide specific examples to illustrate your concerns.

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

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

II. What Action is the Agency Taking?

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

List of Subjects

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

Dated: December 10, 1999.

James Jones,

Director, Registration Division, Office of Pesticide Programs.

Summary of Petition

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

Nippon Soda Co. LtD with, BASF Corporation as Agent

PP 8F4945

EPA has received a pesticide petition (8F4945) from BASF Corporation , acting as Agent for Nippon Soda Company, LtD, Agricultural Products, PO Box 13528, Research Triangle Park, NC 27709-3528 proposing, pursuant to section 408(d) of the Federal Food, Drug, and Costmetic Act (FFDCA), 21 U.S.C. 346a(d), to amend 40 CFR part 180 by establishing a tolerance for residues of tepraloxydim [(EZ)-(RS)-2-1-[(2E)-3-chloroallyloxyimino]propyl-3-hydroxy-5-perhydropyran-4-ylcylohex-2-en-1-one] and its metabolites containing the 3-tetrahydroyrany-1-pentane-1,5-dione (GP) and/or 5-(4-tetrahydropyranyl)-3-hydroxy-cyclohex-2-en-1-one (5-OH-DP) moiety (calculated as the herbicide)] in or on the raw agricultural commodity (RAC) in cotton seed at 0.2 parts per million (ppm), cotton meal at 0.2 ppm, cotton hulls at 0.2 ppm, cotton gin trash at 3.0 ppm, soybean seed at 5.0 ppm, soybean meal at 5.0 ppm, soybean hulls, poultry meat at 0.5 ppm, poultry liver at 1.0 ppm, poultry fat at 0.5 ppm, and eggs at 0.2 ppm. EPA has determined that the petition contains data or information regarding the elements set forth in section 408(d)(2) of the FFDCA; however, EPA has not fully evaluated the sufficiency of the submitted data at this time or whether the data supports granting of the petition. Additional data may be needed before EPA rules on the petition.

A. Residue Chemistry

1. *Plant metabolism.* The qualitative nature of the residues in plants is adequately understood for the purposes of registration. Analytical methods for detecting levels of tepraloxydim and its metabolites 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 was submitted to EPA.

2. *Analytical method.* The proposed analytical method involves extraction, concentration, precipitation, centrifugation/filtration, oxidation, partition, and clean-up. Samples are then analyzed by GC-MS (selected ion monitoring). The limit of quantitation (LOQ) is 0.4 ppm in soybean matrices and 0.1 ppm in cotton matrices.

3. *Magnitude of residues.* Soybean samples from 22 locations in 16 states were analyzed for residues of tepraloxydim. The highest average total of tepraloxydim residues detected in soybean seed samples collected 45 days after application was 4.93 ppm. The average total of tepraloxydim residues in other soybean seed samples collected 45 days after application for the remaining sites ranged from 0.65 to 4.81 ppm. Forage and hay were not analyzed and these commodities will be restricted from feeding to livestock. The tepraloxydim residues for 2 residue decline sites did not exhibit any clear trends from the range of -10 days to +10 days around the 45–day harvest target.

In addition, soybeans were processed after treatment at the proposed label rate into hulls, meal, and refined oil. There was little or no concentration of tepraloxydim residues found in soybean meal or refined oil. Residues in the meal were roughly equal to those found in the seeds. Residues in the refined oil were less than 10% of the residues observed in the seeds. Residues concentrated slightly in the hull fractions. The average concentration factor in hulls was 1.45. Cotton samples from 13 locations in 8 States were analyzed for residues of tepraloxydim. The highest average total of tepraloxydim residues detected in cotton seed samples collected 40 days after application was 0.19 ppm. The average total of tepraloxydim residues in cotton seed for the remaining sites ranged from < 0.10 to 0.18 ppm. In gin trash, the highest average total of tepraloxydim residues detected was 2.10 ppm. The remaining sites contained tepraloxydim residues that ranged from < 0.10 to 1.34 ppm. The tepraloxydim residues for the residue decline site in North Carolina exhibited no clear trends from the -11 day harvest to the +10 day of the 41–day target. All 5-OH-DP residues were < 0.05 ppm level of quanification. Only the 36 and 51 days after last application (DALA) seed samples for tepraloxydim were at or above 0.05 ppm (0.054 and 0.05 ppm, respectively). The gin trash samples contained tepraloxydim residues ranging from < 0.05 ppm to 0.178 ppm at 36 and 46 DALA, respectively.

Available data support the proposed tolerances of poultry meat and fat at 0.5 ppm, poultry liver at 1.0 ppm, and eggs at 0.2 ppm.

B. Toxicological Profile

1. *Acute toxicity*. Based on available acute toxicity data tepraloxydim does not pose any acute toxicity risks. Acute toxicity studies place technical tepraloxydim in toxicity category III and for acute oral, dermal, and inhalation and toxicity category IV for eye and dermal irritation. The technical material is not a positive skin sensitizer. Additionally, tepraloxydim was not found to have a neurotoxic potential after acute exposure.

2. *Genotoxicity*. The following tests were conducted: An Ames Test (1 study; point mutation): negative; *in vitro* CHO cells/hypoxanthine-guanine phosphoribosyl transferase (CHO/HPRT) (1 study; point mutation): negative; *in vitro* cytogenetics - CHO Cells (1 study; chromosome aberrations): negative; *in vitro* unscheduled DNA synthesis (UDS) test using rat hepatocytes (1 study; DNA damage and repair): negative; mouse micronucleus - *in vivo* (1 study; chromosome aberrations): negative based on the studies mentioned above, tepraloxydim does not pose a mutagenic hazard to humans.

3. *Reproductive and developmental toxicity*. A 2-generation reproduction study was conducted with rats being fed dosages of 0, 11, 53, and 268 milligrams/kilograms/day (mg/kg/day) with a reproductive no observed adverse effect level (NOAEL) of 268 mg/kg/day, pup developmental NOAEL of 53 mg/kg/day, and maternal NOAEL of 11 mg/kg/day based on the following: (1) At the parental 268 mg/kg/day dose level, decreased food consumption, reduced body weights (bwts) and/or gains, increase in albumin and cholesterol, decrease in triglycerides and increase in white blood cell count were observed; (2) at the parental (F1 females) 53 mg/kg/day dose group only, increase in white blood cell count was observed; and (3) the only pup toxicity was observed at the 268 mg/kg/day dose group which consisted of reduced bwts and/or gains and delayed eye opening.

A developmental study in rats via oral gavage resulted in dosages of 0, 40, 120, and 360 mg/kg/day highest dose tested (HDT) with a developmental toxicity NOAEL of 40 mg/kg/day and a maternal toxicity of 120 mg/kg/day based on the following: (1) At the 360 mg/kg/day dose group, distinct maternal toxicity consisting of reduced food consumption, impairment in bwt gains, and reduced uterus weights; (2) at the 360 mg/kg/day dose group, increased resorptions and post implantation loss, lower mean percentage of live fetuses, and lower mean placental weights were observed; and (3) at the 360 and 120 mg/kg/day dose groups, slightly decreased mean fetal weights were observed with a progression of severity to the upper dose group, and, at the 360 mg/kg/day dose group, slightly increased malformation rates were observed.

A second developmental study was performed to clarify phenomenons (skeletal retardations and variations) which were observed in the preceding test also at the lowest dose level of 40 mg/kg/day, but which were still within historical control data and, therefore, assessed as not being substance-related. The dose levels in this study were 0, 10, 20, and 40 mg/kg/day HDT with a developmental toxicity NOAEL of 40 mg/kg/day and a maternal NOAEL of 40 mg/kg/day. There were no substance-related effects for all parameters measured in this study.

A developmental toxicity study in rabbits via oral gavage resulted in dosages of 0, 20, 60, and 180 mg/kg/day HDT with a developmental toxicity NOAEL of 180 mg/kg/day and a maternal toxicity NOAEL of 60 mg/kg/day based on the following: (1) At the HDT, reduced food consumption and impaired bwt gain were the only effects observed during the treatment period; and (2) no other signs of maternal toxicity were detected in this dose group or at the lower dose groups tested. No developmental or teratogenic effects were observed in this study.

4. *Subchronic toxicity*. A subchronic neurotoxicity study in rats fed dosages of 0, 28, 103, and 428 mg/kg/day (males) and 0, 33, 124, and 513 mg/kg/day (females) with a neurotoxicity NOAEL of 428 mg/kg/day (males) and 513 mg/kg/day (females) and a systemic NOAEL of ~28 mg/kg/day based on the following effects: (1) At the HDT, decreased food consumption and significantly reduced bwts and/or bwt changes were observed in both male and females rats; and (2) in the mid-dose level, reduced bwts and/or bwt changes were observed in female rats only. No signs of neurotoxicity and gross and microscopic pathology were observed at any dose level tested.

In an *in vivo* dermal absorption study, male Wistar rats were dosed with [^{14}C] - tepraloxydim. Dose levels of 0.005, 0.05, and 0.5 mg/cm^2 diluted in Solvesso 200 were administered to rats on a shaved area on the back. Groups of 4 rats per dose group were sacrificed at 8, 24, or 72 hours following application of the dose. Results indicated that after the 8–hour exposure, the total percent absorbed at all dose levels was 3-5%. Additionally, with increasing dose, the percentage of radioactivity absorbed tended to decrease indicating that saturation of skin with increasing dose occurred under the conditions tested. This effect was most striking at the high dose level (HDL).

5. *Chronic toxicity*. Based on review of the available data, BASF believes the reference dose (RfD) for tepraloxydim will be based on the 2–year feeding study in rats with a threshold NOAEL of 6 mg/kg/day in male and female rats. Using an uncertainty factor of 100, the RfD is calculated to be 0.06 mg/kg/day. The following are summaries of the pertinent toxicity data supporting tepraloxydim tolerances

Two 1 year feeding study in dogs fed dosages of 0, 3.0, 12.0, 58.0 (first study) and 257.0 mg/kg/day (second study) with a NOAEL of 12 mg/kg/day based on the following effects: (1) At the 257 mg/kg/day dose level a slight anemia was detected; (2) clinical chemistry revealed disturbances in lipid, protein, and carbohydrate metabolism in both sexes of the 257 mg/kg/day dose level and, to a minor extent, in males of the

58 mg/kg/day dose level; (3) the upper two dose levels caused reduced function of the epididymides, and degeneration and atrophy of the germinal epithelium in the testes were observed; (4) increased absolute and/or relative weights for the liver, kidney, and thyroid, and decreased absolute and or relative weights (males only) of the testes and epididymides were observed in the 257 mg/kg/day dose group; (5) increased absolute and/or relative weight for the liver and thyroid, and decreased absolute and/or relative epididymides (males only) weights were observed in the 58 mg/kg/day dose group (these increases were not statistically significant); and (6) microscopic findings in the urinary bladder, liver, gall bladder, spleen, bone marrow, thyroid, testes (males), epididymides (male), and prostate (male) were seen in the 257 mg/kg/day dose group and, in the 58 mg/kg/day dose group, urinary bladder, epididymides (male), and prostate (male) microscopic findings were seen at a lesser degree than the 258 mg/kg/day dose group.

A chronic feeding study and carcinogenicity study resulted in rats being fed dosages of 0, 6.0, 33, and 154 (males) and 273 (females) mg/kg/day with a NOAEL of 6.0 mg/kg/day for males and females based on the following effects: (1) Decreased bwt, bwt change, and food consumption in both male and female rats at dose levels > 154 mg/kg/day; (2) clinical chemical changes were observed in the mid- and high-dose groups; and (3) in the 273 mg/kg/day dose group of the carcinogenicity study, there was a trend towards a slightly elevated incidence for hepatocellular adenomas and carcinomas. However, the incidence for adenomas is within the range of historical control, the incidence for carcinomas was slightly above the range of historical controls, and, in the 154 mg/kg/day male dose group of the chronic study, a trend towards a slightly elevated increase of carcinomas was observed which was not considered to be statistically significant. The higher sensitivity of females may possibly be due to the higher dose that was fed to that sex, which clearly fulfilled the criteria for a Maximum Tolerated Dose (MTD).

A carcinogenicity study in mice fed dosages of 0, 37, 332, and 1,035 mg/kg/day (males) and 0, 52, 490, and 1,456 mg/kg/day (females) with a NOAEL of 37 mg/kg/day (males) and 52 mg/kg/day (females) based on the following effects: (1) Significantly decreased bwts/bwt changes were observed in both male and female mice at the mid-dose and high-dose levels with a progression of severity to the top dose which clearly fulfilled the criteria for a MTD for both dose levels; (2) in the 1,456 mg/kg/day female dose group, a slight increase in lymphocytes and decrease in polymorphonuclear neutrophils was seen; (3) relative liver weights were increased in both sexes of the high-dose group and in males of the 332 mg/kg/day dose group; (4) in females of the high-dose and mid-dose levels, hyalinization (sclerosis) of the endometrial stroma, muscularis, and/or perivascular areas were observed in the uterus; and (5) a very slightly increased incidence of neoplasms (adenomas and carcinomas) occurred at dose levels which fulfilled the criteria for a maximum tolerated dose in the liver of female mice. No substance-related neoplasms were observed in the top dose males or in both sexes at dose levels below the MTD.

i. *Mechanistic studies*—a. *Initiation potential study*. In order to determine if tepraloxydim will initiate the carcinogenic process, tepraloxydim was tested for its foci initiating potential after single oral administration of 2,000 mg/kg/day in 0.5% aqueous carboxymethyl-cellulose (CMC) solution to partially hepatectomized female Wistar rats according to a protocol of Prof. Schulte-Hermann, University of Vienna, Austria. N-Nitrosomorpholine (NNM) is known to induce liver foci and was used as a positive control for initiation at a dose of 25 mg/kg/day. Phenobarbitone (PB) was used as a promoter. Three different groups (test substance, negative and positive controls) were each divided into two sub-groups, one being maintained for 8 weeks on basal diet, while the other sub-group was treated with 500 ppm PB in the diet for the same period. Each sub-group consisted of 15 male and 15 female animals. The rats were subjected to an adaptation period of at least 17 days. After this adaptation period, partial hepatectomy was performed. Fourteen hours after partial hepatectomy, the test and control substances were administered once by gavage to 2 groups each (initiation period) and the animals were held on basal diet ad libitum for a 14–day recovery period. Thereafter, the groups received either 500 ppm PB or basal diet for another 8 weeks (promotion period). The state of health of the animals was checked at least once a day. Body weight was determined in weekly intervals and food consumption was measured in weekly intervals during the promotion period. At the end of the study the animals were subjected to gross-pathological assessment, giving special attention to the liver. Histopathologic evaluation of the liver was performed on Hematoxylin and Eosin stained slides as well as on slides stained for Glutathione-S-Transferase P (GST-P). GST-P positive foci were evaluated quantitatively (foci/cm^2 of liver tissue). The initiating potential of a chemical is expressed in the increased number of foci relative to control.

The mean numbers of GST-P positive foci per cm^2, which were detected in the different study groups, are given in the following table.

TABLE 1: MEAN NUMBER OF GST-P POSITIVE FOCI PER CM^2

Study group	Initiation	Promotion	Mean number of foci per cm^2
0	vehicle[1]	-	0.3
1	vehicle[1]	500 ppm PB[2]	0.45
2	25 mg/kg/day NNM[3]	-	7.78
3	25 mg/kg/day NNM[3]	500 ppm PB[2]	11.86
4	2,000 mg/kg/day tepraloxydim	-	0.08
5	2,000 mg/kg/day tepraloxydim	500 ppm PB[2]	0.17

[1]vehicle = 0.5% aqueous carboxymethyl cellulose
[2]PB = Phenobarbitone
[3]NNM = N-Nitrosomorpholine

The mean number of GST-P positive foci per cm^2 liver tissue was very low in groups 4 and 5 which were treated with the test substance, and there were no significant differences to the corresponding control groups 0 and 1.

As expected, the number of GST-P positive foci per cm^2 was significantly increased in groups 2 and 3, when compared with the corresponding control groups (group 0 or 1) demonstrating the known initiating capacity of NNM.

Therefore, tepraloxydim does not have an initiating potential.

A possible non-genotoxic mechanism, which could account for the increased incidence of liver tumors, is the induction of increased cell proliferation (S-phase response).

b. *S-Phase response*. In order to determine if tepraloxydim causes cell proliferation, tepraloxydim was administered to groups of 5 male and 5 female Wistar rats at dietary levels of 0, 100, 600, 3,000 (males only), and 4,000 (females only) ppm for different time periods: 1 week, 6 weeks, and 13 weeks. An additional group with a recovery period of 2 weeks was used after 1 week administration, and a 5–week recovery group was additionally used after 13–week administration. The influence of treatment on DNA-synthesis/cell proliferation (S-phase response) in the liver was determined using bromodeoxyuridine (BrdU), which is incorporated into the DNA if DNA-synthesis and cell proliferation is induced. One week prior to necropsy, osmotic minipumps containing BrdU were implanted subcutaneously. Food consumption and bwt were determined weekly. The state of health was checked each day. All animals were assessed by gross pathology. BrdU incorporated into the DNA of liver cells was detected by immunohistochemistry and evaluated microscopically.

Cell proliferation can be induced diffusely in all hepatocytes or it can be localized in a specific region of the lobule. Therefore, in each of the two liver lobes, five lobules were evaluated. In order to assess whether a localized liver cell proliferation occurs in the liver lobule, the lobule was subdivided into three zones (Rappaport) containing the portal tract (zone 1), the central vein (zone 3), and the zone in-between (zone 2). In total, more than 1,000 cells per zone and more than 3,000 hepatocytes per animal were recorded and the BrdU labeling index determined.

The results from the S-phase response study in the rat liver demonstrate that tepraloxydim can induce a selective increase in cell proliferation predominantly in zone 3 after 1, 6, and 13 weeks in females at 4,000 ppm and, to a minor degree, at 600 ppm. In the males, there was an increase in cell proliferation after 1 week treatment at 3,000 ppm and, to a minor degree, at 600 ppm. The enhanced cell proliferation after 1 week of administration was reversible after 1 weeks of recovery in both sexes and appeared to be reversible in females after 5 weeks of recovery following 13 weeks of administration. The more pronounced S-phase response in female rats also explains why liver neoplasia was predominantly found in the females. These studies indicate that the mode of action by which an enhancement of liver neoplasia was induced is a chronic increase in liver cell proliferation. It is emphasized that this mechanism results in an increased incidence of liver tumors only at dose levels at the MTD. It is therefore concluded that tepraloxydim does not have an oncogenic potential of biological relevance.

6. *Animal metabolism*. The qualitative nature of the residues in animals is adequately understood for the purposes of registration. Analytical methods for detecting levels of tepraloxydim and its metabolites 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 was submitted to EPA.

7. *Metabolite toxicology*. Available metabolism data indicate that the metabolites containing the GP and 5-OH-DP moiety should be included in the tolerance for expression for tepraloxydim.

8. *Endocrine disruption*. No specific tests have been performed with tepraloxydim to determine whether the chemical may have an effect in humans that is similar to an effect produced by naturally-occurring estrogen or other endocrine effects.

C. Aggregate Exposure

1. *Dietary exposure*. For purposes of assessing the potential dietary exposure, BASF has estimated aggregate exposure based on the Theoretical Maximum Residue Contribution (TMRC) from the proposed tolerances for tepraloxydim in or on the RAC cotton seed, meal, and hulls at 0.2 ppm; cotton gin trash at 3.0 ppm; soybean seed, meal, and hulls at 5.0 ppm; poultry meat and fat and 0.5 ppm; poultry liver at 1.0 ppm; and eggs at 0.2 ppm. The TMRC is a ''worst-case'' estimate of dietary exposure since it is assumed that 100% of all crops for which tolerances are established are treated and that pesticide residues are at the tolerance levels. There are no established U.S. tolerances for tepraloxydim, and there are no currently registered uses for tepraloxydim on food or feed crops in the United States.

i. *Food*. Dietary exposure to residues of tepraloxydim in or on food from these proposed tolerances would account for less than 4.0% of the RfD (0.06 mg/kg/day) for the overall U. S. population. BASF estimates indicate that dietary exposure will not exceed the RfD for any population subgroup for which EPA has data. The most highly exposed group in the subpopulation groups would be non-nursing infants < 1 year old, which uses ~15.0% of the RfD. This exposure assessment relies on very conservative assumptions--100% of crops will contain tepraloxydim residues and those residues would be at the level of the tolerance--which results in an overestimate of human exposure.

Tepraloxydim was evaluated for its potential mutagenicity and genotoxicity *in vitro* using bacterial and mammalian cells as well as in a cytogenetics assay. The results of these studies demonstrated the absence of a mutagenic or genotoxic effect.

In vivo, the compound was assessed for the induction of micronuclei in mice. The result of this study showed that tepraloxydim has no chromosome-damaging potential.

It is therefore, concluded that tepraloxydim has no mutagenic or genotoxic properties either *in vitro* or *in vivo*.

The results of a 24–month chronic toxicity study and a carcinogenicity study in rats show that the HDL (154 mg/kg/day in males and 273 mg/kg/day in females) clearly fulfilled the criteria for a MTD based on distinctly reduced bwts or bwt changes and histopathological alterations in the liver. The test substance induced changes in clinico-chemical parameters, which are considered to be associated with liver toxicity. Histopathologically, the liver was found to be affected, therefore, this organ was identified as a target. In the carcinogenicity study, in female animals of the top dose, a slight trend towards an increased incidence of hepatocellular adenomas and carcinomas was observed which was virtually within the historical control range. In top dose males of the chronic toxicity study, a trend towards a slightly elevated increase of carcinomas was detected. As this increase was not evident in the carcinogenicity study, which involves a far greater number of animals, it is likely that this finding was incidental.

Additional mechanistical investigations have demonstrated that tepraloxydim does not possess an initiating potential for a liver carcinogenic process. Combined with the proven absence of a gene or chromosome damaging effect, it can be concluded that the increased incidence of rat liver neoplasia was not related to a genotoxic mode of action.

The results from an S-phase response study in the rat liver demonstrate that tepraloxydim can induce a selective increase in cell proliferation predominantly in zone 3 after 1, 6, and 13 weeks in females at 4,000 ppm and, to a minor degree, at 600 ppm. In the males, there was an increase in cell proliferation after 1 week treatment at 3,000 ppm and, to a degree, at 600 ppm. The enhanced cell proliferation after 1 week of administration was reversible after 2 weeks of recovery in both sexes and appeared to be reversible in females after 5 weeks of recovery following 13 weeks of administration. The more pronounced S-phase response in female rats also explains why liver neoplasia was predominantly found in the females. These studies indicate that the mode of action, by which an enhancement of liver neoplasia was induced, is a chronic increase in liver cell proliferation. It is emphasized that this mechanism results in an increased incidence of liver tumors only at dose levels at the MTD. It is therefore, concluded that tepraloxydim does not have an oncogenic potential of biological relevance. The result of the carcinogenicity study in mice demonstrates that the HDL of 1,035 mg/kg/day (males) and 1,456 mg/kg/day (females) by far exceeded the criteria of a MTD as evidenced by drastically reduced bwts or bwt changes. A trend towards an increased incidence of liver neoplasia occurred only in females exclusively at that dose level and therefore cannot be extrapolated to dose levels below the MTD. Relative liver weights were distinctly increased at the HDL associated with foci of cellular alteration and hypertrophy of hepatocytes.

In female animals of the HDLs, hyalinization of the uterus was found as well as reduced ovarian activity which may be a consequence of the reduced terminal bwts.

In conclusion, in long-term feeding studies in rats and mice, there was a slight trend towards increased incidences of liver neoplasia at the HDLs. These dose levels were at or exceeded the MTD. As the liver was shown to be the target organ, the increased cell proliferation, resulting in neoplasia is considered to have been due to the toxicity exerted on this organ.

The overall lowest NOAELs obtained in long-term feeding studies were:
Rats: 6 mg/kg/day
Mice:
Males: 37 mg/kg/day
Females: 52 mg/kg/day
Dogs: 12 mg/kg/day.
These chronic NOAELs demonstrate that the rat is the most sensitive species.

Tepraloxydim does not possess mutagenic or genotoxic properties. As discussed above, it can be concluded that the compound has no biologically relevant oncogenic potential.

Therefore, based on the results of the carcinogenicity study in mice, the results of genotoxicity testing, the results of the 24–month chronic feeding/oncogenicity study in rats, and auxiliary mechanistic data showing that tepraloxydim is not an initiator of the carcinogenic process, BASF believes that the threshold approach to regulating tepraloxydim is appropriate.

ii. *Drinking water.* Based on the available studies, BASF does not anticipate exposure to residues of tepraloxydim in drinking water. There is no established Maximum Concentration Level (MCL) for residues of tepraloxydim in drinking water under the Safe Drinking Water Act (SDWA).

2. *Non-dietary exposure.* Tepraloxydim is not currently registered for any nonagricultural use. The potential for non-occupational exposure to the general population is therefore, not significant.

D. Cumulative Effects

BASF has considered the potential for cumulative effects of tepraloxydim and other substances that have a common mechanism of toxicity. No evidence or information exists to suggest that toxic effects produced by tepraloxydim would be cumulative with those of any other chemical compound.

E. Safety Determination

1. *U.S. population.* Using the conservative exposure assumptions described above and based on the completeness and the reliability of the toxicity data, BASF has estimated that aggregate exposure to tepraloxydim will utilize less than 4.0% of the RfD for the U.S. population. BASF concludes that there is a reasonable certainty that no harm will result from the aggregate exposure to residues of tepraloxydim, including anticipated dietary exposure and non-occupational exposures.

2. *Infants and children*—i. *Developmental toxicity.* The teratogenicity studies in rats resulted in a developmental toxicity NOAEL of 40 mg/kg/day and a maternal toxicity NOAEL of 40 mg/kg/day. These NOAEL values are 7x higher than the NOAEL from the 2–year feeding study in rats used to establish the RfD.

The teratogenicity study in rabbits resulted in a developmental toxicity NOAEL of 180 mg/kg/day and a maternal toxicity NOAEL of 60 mg/kg/day. These NOAEL values are 10x higher than the NOAEL from the 2–year feeding study in rats used to establish the RfD.

ii. *Reproductive toxicity.* The 2–generation reproduction study with rats resulted in a reproductive NOAEL of 268 mg/kg/day ppm and a maternal NOAEL of 53 mg/kg/day. These NOAEL values are significantly higher than the NOAEL from the 2–year feeding study in rats used to establish the RfD.

iii. *Reference dose.* Since developmental and reproductive toxicity occurs at levels at or above the levels shown to exhibit parental toxicity and since these levels are significantly higher than those used to calculate the RfD, BASF believes the RfD of 0.06 mg/kg/day is an appropriate measure of safety for infants and children.

Using the conservative exposure assumptions described above, BASF has concluded that the portion of the RfD that will be utilized by aggregate exposure to residues of tepraloxydim resulting from the proposed tolerances will be less than 15% for all populations of infants and children. The most highly exposed group in the subpopulation groups would be non-nursing infant < 1 year old, which uses 15% of the RfD. Therefore, based on the completeness and reliability of the toxicity data and the conservative exposure assessment, BASF concludes that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the residues of tepraloxydim, including all anticipated dietary exposure and all other non-occupational exposures.

F. International Tolerances

A maximum residue level has not been established for tepraloxydim by the Codex Alimentarius Commission.

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ENVIRONMENTAL PROTECTION AGENCY

[PF–907; FRL–6398–7]

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

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: This notice announces amendment of pesticide petitions (PP 5F4469), and (PP 4F4336), proposing the establishment of regulations for residues of certain pesticide chemicals in or on various food commodities.