certainty that no harm will result to infants, children or adults from dietary food consumption exposure to clomazone residues from tuberous and corm vegetable (except potato) crop subgroup and cucurbit vegetable crop group plus all other clomazone treated human dietary food sources.

F. International Tolerances

There are Codex residue limits for residues of clomazone in or on oilseed rape, potatoes, tobacco, soybeans, rice, cottonseed, sugarcane and peas.

[FR Doc. 00–31058 Filed 12–5–00; 8:45 am]

BILLING CODE 6560–50–S

ENVIRONMENTAL PROTECTION AGENCY

[PF–983; FRL–6573–7]

Notice of Filing Pesticide Petitions to Establish and to Extend Tolerances 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–983, must be received on or before January 5, 2001.

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–983 in the subject line on the first page of your response.

FOR FURTHER INFORMATION CONTACT: For Pesticide Petition (PP 9F5079) contact: Cynthia Giles-Parker, Registration Division (7505C), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington DC 20460; Telephone number: (703) 305–7740; e-mail address: giles-parker.cynthia@epa.gov.

For Pesticide Petitions (PP 8F3654 8F3674) contact: Mary Waller, Registration Division (7505C), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington DC 20460; Telephone number: (703) 308–9354; e-mail address: waller.mary@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 codes	Examples of potentially affected entities
Industry	111 112 311 32532	Crop production Animal production Food manufacturing 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–983. 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 (CM #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–983 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, 1200 Pennsylvania Ave., NW., 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, CM#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–983. 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 pesticide petitions as follows proposing the establishment and/or amendment of regulations for residues of certain pesticide chemicals in or on various food commodities under section 408 of the Federal Food, Drug, and Comestic Act (FFDCA), 21 U.S.C. 346a. EPA has determined that these petitions contain data or information regarding the elements set forth in section 408(d)(2); however, EPA has not fully evaluated the sufficiency of the submitted data at this time or whether the data supports granting of the petition. Additional data may be needed before EPA rules on the petition.

List of Subjects

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

Dated: November 21, 2000.

James Jones,

Director, Registration Division, Office of Pesticide Programs.

Summaries of Petitions

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

1. ISK Biosciences Corporation (PP 9F5079)

Summary of Petition

EPA has received a pesticide petition (PP 9F5079) from ISK Biosciences Corporation, 5970 Heisley Road, Suite 200, Mentor, Ohio, 44060, 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 fluazinam in or on the raw agricultural commodities potato and peanut at 0.02 parts per million (ppm) and wine grapes 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 residue of concern is best defined as the parent, fluazinam. The metabolism of fluazinam in plants (potatoes, peanuts, and wine grapes) is adequately understood for the purposes of these tolerances. The metabolism of fluazinam involves initial reduction of the nitro groups, hydrolysis of the trifluoromethyl group as well as replacement of chlorine by glutathione with subsequent reactions along the glutathione pathway. Parent fluazinam is rapidly degraded and is either not found or barely detectable in peanuts and potatoes. Fluazinam parent was the major identifiable residue in a grape metabolism study. Identifiable residues in plant metabolism studies either closely resemble fluazinam in structure or are the result of re-incorporation of the fluazinam carbon pool into natural products.

Ruminant and poultry metabolism studies demonstrated that the transmittal of residues from the feed of goats and hens through to meat, milk, and eggs was low. Total 14C residues were below 1 ppm in all tissues, milk and eggs. Identifiable residues were less than 2% of the administered dose in all matrices, except for chicken fat and liver.

2. *Analytical method.* An analytical method using gas chromatography with electron capture detection (GC-ECD) for the determination of fluazinam residues on potatoes, peanuts, grapes and the processing fractions thereof has been developed and validated. The method involves solvent extraction followed by liquid-liquid partitioning and concentration prior to a final purification using column chromatography. The method has been successfully validated by an independent laboratory using peanut nutmeat as the matrix. The limit of quantitation of the method is 0.02 ppm in peanuts and 0.01 ppm in potatoes and grapes.

3. *Magnitude of residues*—i. *Potatoes.* Data from 11 field trials in potatoes showed that mean fluazinam residues from duplicate samples were <0.01 ppm in the RAC commodity at all locations. The result of a processing study using a 3.5X application rate showed no concentration into the processing fractions dry peels, french fries and chips. A calculated processing factor of 2.4 for the animal feed commodity wet peels was determined based on residue levels just slightly above the limit of quantitation.

ii. *Peanuts.* A total of 15 field trials were conducted over three growing seasons at nine sites representative of peanut production. Residues of fluazinam in nutmeat from all location were below 0.01 ppm. Residues in peanut hay, a grazing restriction commodity, ranged from 0.16 to 10.2 ppm in the six locations where it was harvested. In a processing study, residues concentrated 3x in crude oil and 5x in soapstock, but did not concentrate in refined oil or presscake.

iii. *Wine grapes.* A total of 20 field trials were conducted over three growing seasons in major wine grape growing regions worldwide. Residues of fluazinam in grapes ranged from 0.03 to 2.27 ppm. Vinification of grapes from two locations showed a reduction of fluazinam in wine to non-detectable levels.

iv. *Secondary residues.* Since levels of fluazinam in potatoes and peanut nutmeat were below detectable levels

(the fluazinam label includes a peanut hay grazing restriction, and only wine grapes which are imported are included in this tolerance petition), no residues of concern are expected on animal feed items. Furthermore, since animal metabolism studies do not show potential for significant residue transfer, detectable secondary residues in animal tissues, milk or eggs are not expected. Therefore, tolerances are not needed for these commodities.

B. Toxicological Profile

1. *Acute toxicity.* A battery of acute toxicity studies was conducted which placed technical fluazinam in Toxicity Category III for oral LD_{50}, dermal LD_{50}, dermal irritation, Category II for inhalation LC_{50} and Category I for eye irritation. Technical fluazinam showed potential for dermal sensitization.

In an acute neurotoxicity study, the no observed affect effect level (NOAEL) for neurotoxicity was 2,000 milligram/kilogram (mg/kg) highest dose tested (HDT) and the NOAEL for systemic effects was 50 mg/kg.

2. *Genotoxicty.* A battery of tests has been conducted to assess the genotoxic potential of technical fluazinam. Assays conducted included two gene mutation tests in bacteria, a chromosomal aberration test in mammalian cells, a mouse micronucleus test and a DNA repair test in bacteria. Technical fluazinam did not elicit a genotoxic response in any of the studies conducted.

3. *Reproductive and developmental toxicity.* In a 2–generation reproductive toxicity study, the NOAEL for reproductive effects was 100 ppm (10.1 mg/kg/day). The NOAEL for parental toxicity was 20 ppm (2.1 mg/kg/day).

In a rat developmental study, there were no developmental effects observed at non-maternally toxic doses. The developmental NOAEL was 50 mg/kg/day and the lowest observed adverse effect level (LOAEL) was 250 mg/kg/day, based upon statistically significant decreased mean fetal body weight and other evidence suggestive of delayed fetal development related to maternal toxicity. The maternal NOAEL was shown to be 50 mg/kg/day.

In a rabbit developmental study, there were no developmental effects observed at non-maternally toxic doses. The developmental NOAEL was 7 mg/kg/day and the LOAEL was 12 mg/kg/day, based on increased incidence of total litter loss and possible slightly increased incidences of fetal findings at this dose. It was concluded that the maternal NOAEL was 4 mg/kg/day.

4. *Subchronic toxicity.* The NOAEL for the 13 week feeding study in rats was 50 ppm (4.1 mg/kg/day). The LOAEL was 500 ppm (41 mg/kg/day), based on periacinar hepatocellular hypertrophy and sinusoidal chronic inflammation in males, increased liver weights in males and increased lung weights in females.

In a 13 week dog study, the NOAEL was 10 mg/kg/day. The LOAEL was 100 mg/kg/day, based on ocular change observed ophthalmoscopically and liver effects consisting of increased relative liver to body weight, bile duct hyperplasia with or without cholangiofibrosis and increased plasma phosphatase levels.

In a 21 day dermal study, the NOAEL for systemic effects was 10 mg/kg/day. The LOAEL was 100 mg/kg/day, based on hepatocelluar hypertrophy and increases in AST and cholesterol levels.

In a subchronic neurotoxicity study, no effects considered to be indicative of neurotoxicity were observed at the highest dose tested, 3,000 ppm (233 mg/kg/day). The NOAEL for systemic toxicity (body weight differences) was 1,000 ppm (74 mg/kg/day).

5. *Chronic toxicity.* Fluazinam was not carcinogenic in rats. A NOAEL of 10 ppm (0.43 mg/kg/day) of fluazinam was established based on the following effects at 1,000 and/or 100 ppm: lower food consumption and efficiency of food utilization, slight anemia, elevated cholesterol, increased liver weights, an increased number of macroscopic liver and testes lesions and an increased incidence of microscopically observed lung, liver, pancreas, lymph node and testes lesions.

An additional study was conducted to further define the NOAEL for long-term effects in the rat. In the second study, a NOAEL of 50 ppm (2.2 mg/kg/day) was established based on liver and testes effects.

Two long-term feeding studies were conducted in mice. In the first, the NOAEL for all effects was 10 ppm (1.14 mg/kg/day) and the LOAEL was 100 ppm (11.2 mg/kg/day) based on the treatment-related effects observed in the liver.

A second oncogenicity study in mice was conducted at 1,000, 3,000 and 7,000 ppm to ensure that an maximum tolerance dose (MTD) was studied. Findings included increased female mortality, reduced body weight gains, increased brain weights and/or liver weights. An impurity in the test material used in this study resulted in vacuolation of the white matter of the brain and cervical spinal cord in treated animals. A statistically significant higher incidence of hepatocellular adenomas was observed in the 3,000 ppm dose males. Hepatocellular adenomas are common tumors in male mice. There was no dose relationship in the induction of the adenoma and no increase in hepatocellular carcinomas. It was concluded that fluazinam is not carcinogenic in the mouse.

In a chronic dog study, the NOAEL was determined to be 1 mg/kg/day. The LOAEL was 10 mg/kg/day based on generalized, nonspecific toxicity. No ocular effects were observed ophthalmoscopally at any dose in this study.

6. *Animal metabolism.* After an oral dose of fluazinam the median peak time for blood concentration of radiolabel activity for both sexes was 6 hours. The major route of excretion was the feces with urine contributing as a minor route. Less than 1% of the administered dose was found in the terminated animals. The highest concentration was found in the liver. There were no major differences related to sex or dose level in the findings. It was concluded that fluazinam is metabolized by both reduction and glutathione and glucuronide conjugation and further metabolism.

7. *Metabolite toxicology.* The same metabolic processes occur in plants and animals but metabolism in plants is more extensive than in animals. All of the major identified metabolites in both plants and animals retain the phenylpyridinylamine structure. Many of the metabolites resulting from fluazinam are similar in plants and animals and, therefore, have already been evaluated toxicologically.

Because of the rapid and complete elimination (in animals) and re-incorporation (in plants) of fluazinam, the toxicity of metabolites is expected to be similar to but lower than the toxicity of the parent compound. The residue of concern is parent fluazinam only.

8. *Endocrine disruption.* The toxicological profile of fluazinam shows no evidence of physiological effects characteristic of the disruption of the hormone estrogen in mammalian chronic studies or in mammalian or avian reproduction studies. It is therefore considered that there is an adequate level of safety over the reference dose for possible endocrine effects and that an additional safety factor for possible endocrine effects is not warranted.

C. Aggregate Exposure

1. *Dietary exposure.* An RfD of 0.01 mg/kg/day is proposed for humans, based on the NOAEL from the one year dog study (1 mg/kg/day) and dividing by an uncertainty factor of 100.

i. *Food—a. Acute risk.* Tier 1 acute dietary exposure analyses were

conducted for fluazinam in/on peanuts, potatoes and imported wine grapes to determine the exposure contribution of these commodities to the diet and to ascertain the acute risk potential. The estimates were based on proposed tolerance level residues for all three crops, peanut and potato processing studies, market share assumptions of 100% crop treated, and consumption data from the 1994 through 1996 USDA continuing survey of food intake.

Even using all of the worst case exposure scenarios listed above, the Tier 1 acute assessment for the U.S. population resulted in a margin of safety (MOS) of 270,507 at the 95th percentile. This corresponded to an estimated exposure of 0.000185 mg/kg/day. The highest acute exposure estimate (95th percentile) was observed in the seniors (55 years and over) subpopulation: 0.001285 mg/kg/day. This correlates to an MOE of 38,908.

b. Chronic risk. Tier 1 dietary exposure analyses were conducted for fluazinam in/on peanuts, potatoes and imported wine grapes to determine the exposure contribution of these commodities to the diet and to ascertain the chronic risk potential. The estimates were based on proposed tolerance level residues for all three crops, peanut and potato processing studies, market share assumptions of 100% crop treated, and consumption data from the 1994 through 1996 USDA continuing survey of food intake.

Even using all of the worst case exposure scenarios listed above, the Tier 1 chronic dietary exposure estimates resulted in an estimated exposure for the U.S. population of 0.000104 mg/kg/day. This exposure corresponds to 1.0% of the reference dose (RfD) of 0.01mg/kg/day. The highest exposure estimate was calculated for the Females 20+ years (non-pregnant/non-nursing) population subgroup. This exposure was determined to be 0.000156 mg/kg/day (1.6% of the RfD).

It can be concluded that acute or long-term dietary exposure to fluazinam through residues on treated peanuts, potatoes and imported wine grapes should not be of cause for concern.

ii. *Drinking water.* Since fluazinam is intended for application outdoors to field grown peanut and potato crops, the potential exists for parent and or metabolites to reach ground or surface water that may be used for drinking water. The calculated drinking water levels of concern (DWLOC) for chronic exposure for adult males, adult females and toddlers were estimated to be 355 parts per billion (ppb), 296 ppb, and 149 ppb, respectively. The calculated DWLOCs for acute exposure for all adults, adult females and toddlers were estimated to be 17,943 ppb, 14,993 ppb, and 7,497 ppb, respectively. The chronic and acute DWLOC values are well above the modeled chronic and acute DWECs of 0.17 ppb (GENEEC 56–day/3) and 15.1 ppb (GENEEC instantaneous value), respectively. Therefore, there is comfortable certainty that no harm will result from combined dietary (food and water) exposure due to the use of fluazinam on peanuts, potatoes and imported wine grapes.

2. *Non-dietary exposure.* No petition for registration of fluazinam is being made for either indoor or outdoor residential use. Non-occupational exposure of fluazinam to the general population is therefore not expected and is not considered in aggregate exposure estimates.

D. Cumulative Effects

Fluazinam is a phenylpyridinylamine fungicide. Since there are no other members of this class of fungicides, it is considered unlikely that fluazinam would have a common mechanism of toxicity with any other pesticide in use at this time.

E. Safety Determination

1. *U.S. population.* Based on a NOAEL of 1 mg/kg bwt/day from a one year feeding study in dogs, and using an uncertainty factor of 100, a reference dose of 0.01 mg/kg bwt/day is proposed for assessment of long-term risk. The estimate of dietary intake was based on proposed tolerance level residues for all three crops, peanut and potato processing studies, market share assumptions of 100% crop treated and consumption data. Even using those conservative intake estimates, the proposed tolerances will utilize only 1% of the RfD for the U.S. population. The estimated exposure of fluazinam from drinking water, 0.17 ppb is at least three orders of magnitude below the calculated drinking water level of concern, 355 ppb.

2. *Infants and children.* Data from developmental toxicity studies in the rat and rabbit and a 2–generation reproduction study were considered. These studies which were described earlier, demonstrated no increased sensitivity of rats or rabbits to *in utero* exposure to fluazinam. In addition, the multigeneration reproductive toxicity study did not identify any increased sensitivity of rats to *in utero* or postnatal exposure. For all three studies, parental NOAELs were lower than or equivalent to the developmental or offspring NOAELs. It is concluded that the standard margin of safety will protect the safety of infants and children and that an additional safety factor is not warranted.

The dietary exposure of fluazinam to infants and children is estimated to be much lower than adults because 80% to 90% of the exposure is expected from sherry and wine. The proposed tolerances will utilize <0.5% of the RfD for infants and children. The estimated exposure of fluazinam from drinking water, 0.17 ppb is three orders of magnitude below the calculated drinking water level of concern, 149 ppb.

F. International Tolerances

There are presently no Codex maximum residue levels established for residues of fluazinam on any crop.

2. Novartis Crop Protection, Inc.,

Summary of Petitions:

EPA has received two pesticide petitions (PP 8F3654, PP 8F3674) from Novartis Crop Protection, Inc., P.O. Box 18300, Greensboro, NC 27419 proposing,pursuant to section 408(d) of the FFDCA, 21 U.S.C. 346a(d), to amend 40 CFR part 180 by extending the expiration date for tolerances for residues of propiconazole in or on the raw agricultural commodities corn, field, stover (12.0 parts per million (ppm)); corn, field, forage (12.0 ppm); corn, field, grain (0.1 ppm); corn, sweet (0.1 ppm); pineapple (0.1 ppm); pineapple, fodder (0.1 ppm) (PP 8F3674); peanut (0.2 ppm); peanut, hay (20 ppm); and peanut, hulls (1.0 ppm) (PP 8F3654). 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.* Novartis believes the studies supporting propiconazole adequately characterize metabolism in plants and animals. The metabolism profile supports the use of an analytical enforcement method that accounts for combined residues of propiconazole and its metabolites which contain the 2,4-dichlorobenzoic acid (DCBA) moiety.

2. *Analytical method.* Novartis has submitted a practical analytical method involving extraction, filtration, conversion, partition, derivitization, and solid phase cleanup with analysis by confirmatory gas chromatography using electron capture detection (ECD). The total residue method is used for

determination of propiconazole and its metabolites. The limit of quantitation (LOQ) for the method is 0.05 ppm.

3. *Magnitude of residues*. Field residue trials have been conducted at various rates, timing intervals, and applications methods to represent the use patterns which would most likely result in the highest residues. For all samples, the total residue method was used for determination of the combined residues of parent and its metabolites which contain the DCBA moiety.

B. Toxicological Profile

1. *Acute toxicity*. Propiconazole exhibits low toxicity. Data indicated the following: a rat acute oral LD_{50} of 1,517 milligrams/kilograms (mg/kg); a rabbit acute dermal LD_{50} > 6,000 mg/kg; a rat inhalation LC_{50} >5.8 g/liter air; minimal skin and slight eye irritation; and nonsensitization.

2. *Genotoxicty*. Propiconazole exhibits no mutagenic potential based on the following data: *In vitro gene* mutation test (Ames assay, rat hepatocyte DNA repair test, (human fibroblast DNA repair test), *In vitro* chromosome test, (human lymphocyte cytogenetic test), *In vivo* mutagenicity test, (Chinese hamster bone marrow cell nucleus anomaly test, Chinese hamster bone marrow cell micronucleus test, mouse dominant lethal test), and other mutagenicity test (BALB/3T3 cell transformation assay).

3. *Reproductive and developmental toxicity*. In an oral teratology study in the rabbit, a maternal no observed adverse effect level (NOAEL) of 30 mg/kg was based on reduced food intake but without any fetotoxicity even at the top dose of 180 mg/kg. In an oral teratology study in the rabbit, a maternal NOAEL of 100 mg/kg was based on reductions in body weight gain and food consumption and a fetal NOAEL of 250 mg/kg was based on increased skeletal variations at 400 mg/kg. In an oral teratology study in the rat, a maternal and fetal NOAEL of 100 mg/kg was based on decreased survival, body weight gain, and food consumption in the dams and delayed ossification in the fetuses at 300 mg/kg. In a second teratology study in the rat, a maternal and fetal NOAEL of 30 mg/kg was based on reductions in body weight gain and food consumption in the dams and delayed development in the fetuses at 90 and 360/300 mg/kg. A supplemental teratology study in the rat involving eight times as many animals per group as usually required showed no teratogenic potential for the compound. A 2-generation reproduction study in the rat showed excessive toxicity at 5,000 ppm without any teratogenic effects. A 2-generation reproduction study in the rat showed no effects on reproductive or fetal parameters at any dose level. Postnatal growth and survival were affected at the top dose of 2,500 ppm, and parental toxicity was also evident. The NOAEL for development toxicity is 500 ppm.

4. *Subchronic toxicity*. In a 21 day dermal study in the rabbit, a NOAEL of 200 mg/kg was based on clinical signs of systemic toxicity. In a 28 day oral toxicity study in the rat, a NOAEL of 50 mg/kg was based on increased liver weight. In a subchronic feeding study in the mouse, a NOAEL of 20 ppm (3 mg/kg) was based on liver pathologic changes. In a 13 week feeding study in the male mouse, a NOAEL of 20 ppm (3 mg/kg) was based on liver pathologic changes. In a 90 day feeding study in rats, the NOAEL was 240 ppm (24 mg/kg) based on a reduction in body weight gain. In a 90 day feeding study in dogs,the NOAEL was 250 ppm (6.25 mg/kg) based on reduced food intake and stomach histologic changes.

5. *Chronic toxicity*. In a 12 month feeding study in the dog, a NOAEL of 50 ppm (1.25 mg/kg) was based on stomach histologic changes. In a 24 month oncogenicity feeding study in the mouse, the NOAEL was 100 ppm (15 mg/kg). The MTD was exceeded at 2,500 ppm in males based on decreased survival and body weight. Increased incidence of liver tumor was seen in these males but no evidence of carcinogenicity was seen at the next lower dose of 500 ppm in either sex. In a 24 month chronic feeding/oncogenicity study in the rat, a NOAEL of 100 ppm (5 mg/kg) was based on body weight and blood chemistry. The MTD was 2,500 ppm based on reduction in body weight gain and no evidence of oncogenicity was seen. Based on the available chronic toxicity data, Novartis believes the Reference dose (RfD) for propiconazole is 0.0125 mg/kg/day. This RfD is based on a 1 year feeding study in dogs with a NOAEL of 1.25 mg/kg/day (50 ppm) and an uncertainly factor of 100. No additional modifying factor for the nature of effects was judged to be necessary as stomach mucous hyperemia was the most sensitive indicator of toxicity in that study.

Using the Guidelines for Carcinogenic Risk Assessment published on September 24, 1986 (51 FR 33992), the USEPA has classified propiconazole in group C for carcinogenicity (evidence of possible carcinogenicity for humans). The compound was tested in 24 month studies with both rats and mice. The only evidence of carcinogenicity was an increase in liver tumor incidence in male mice at a dose level that exceeded the maximum tolerated dose (MTD). Dosage levels in the rat study were appropriate for identifying a cancer risk. The Cancer Peer Review Committee recommended the RfD approach for quantitation of human risk. Therefore, the RfD is deemed protective of all chronic human health effects, including cancer.

C. Aggregate Exposure

1. *Dietary exposure*. The RfD for propiconazole is 0.0125 mg/kg/day and is based on a 1 year feeding study in dogs with a NOAEL of 1.25 mg/kg/day (50 ppm) and an uncertainly factor of 100.

i. *Food—Acute risk*. The risk from acute dietary exposure to propiconazole is considered to be very low. The lowest NOAEL in a short term exposure scenario, identified as 30 mg/kg in the rat teratology study, is 24-fold higher than the chronic NOAEL. Based on worst-case assumptions, the chronic exposure assessment did not result in any margin of exposure (MOE) less than 150 for even the most impacted population subgroup. Novartis believes that the MOE for acute exposure would be more than 100 for any population groups; MOE of 100 or more are considered satisfactory.

ii. *Chronic risk*. For the purposes of assessing the potential dietary exposure under the existing, pending, and proposed tolerances for the residue of propiconazole and its metabolites determined as 2,4-dichlorobenzoic acid, Novartis has estimated aggregate exposure based upon the Theoretical Maximum Residue Concentration (TMRC). The TMRC is a ''worst case'' estimate of dietary exposure since it assumes 100% of all crops for which tolerances are established are treated and that pesticide residues are at the tolerance levels, resulting in an overestimation of human exposure.

Currently established tolerances range from 0.05 ppm in milk to 60 ppm in grass seed screenings and include: apricots (1.0 ppm); bananas (0.2 ppm); barley grain (0.1 ppm); barley straw (1.5 ppm); cattle kidney and liver (2.0 ppm); cattle meat, fat, and meat by products except kidney and liver (0.1 ppm); celery (5.0 ppm); corn forage and fodder (12.0 ppm); corn grain and sweet (0.1); eggs (0.1 ppm); goat kidney and liver (2.0 ppm); goat meat, fat, and meat by products except kidney and liver (0.1 ppm); grass forage (0.5 ppm); grass hay/straw (40.0 ppm); grass seed screenings (60.0 ppm); hogs kidney and liver (2.0 ppm); hog meat, fat, and meat by products except kidney and liver (0.1 ppm); horses kidney and liver (2.0 ppm); horse meat, fat, and meat by

products except kidney and liver (0.1 ppm); milk (0.05 ppm); mint tops (0.3 ppm - regional tolerance west of Cascade Mountains); mushrooms (0.1 ppm); nectarines (1.0 ppm); oat forage (10.0 ppm); oat grain (0.1 ppm); oat hay (30.0 ppm); oat straw (1.0 ppm); peaches (1.0 ppm); peanut hay (20.0 ppm); peanut hulls (1.0 ppm); peanuts (0.2 ppm);, pecans (0.1 ppm); pineapple (0.1 ppm); pineapple fodder (0.1 ppm); plums (1.0 ppm); poultry liver and kidney (0.2 ppm); poultry meat, fat, and meat by products except kidney and liver (0.1 ppm); prunes, fresh (1.0 ppm); rice grain (0.1 ppm); rice straw (3.0 ppm); wild rice (0.5 ppm regional tolerance Minnesota); rye grain (0.1 ppm); rye straw (1.5 ppm); sheep kidney and liver (2.0 ppm); sheep meat, fat, and meat by products except kidney and liver (0.1 ppm); stone fruit crop group 12 (1.0 ppm); wheat grain (0.1 ppm); and wheat straw (1.5 ppm). In addition, time-limited regional tolerances for sorghum grain and stover at 0.1 ppm and 1.5 ppm, respectively were established to support a section 18 Crisis exemption in Texas (expiration date December 31, 2000) and Nebraska, Kansas, and Oklahoma (expiration date September 30, 2000).

Additional uses of propiconazole have been requested in several pending petitions. Proposed tolerances include: PP 5F4424 for use of propiconazole on dry bean and soybean - dry bean forage (8.0 ppm); dry bean hay (8.0 ppm); dry bean vines (0.5 ppm); dry bean (0.5 ppm), soybeans (0.5 ppm); soybean fodder (8.0 ppm); soybean forage (8.0 ppm); soybean hay (25.0 ppm); and soybean straw (0.1 ppm); PP 5F4591 for use of propiconazole on berries, carrots and onions - berry crop grouping (1.0 ppm); dry bulb onion (0.3 ppm); green onion (8.0); PP 5F3740 - tree nut crop grouping (0.1 ppm); PP 5F4498 - inadvertent/rotational crop tolerances for alfalfa forage (0.1 ppm), alfalfa hay (0.1 ppm), grain sorghum fodder (0.3 ppm), grain sorghum forage (0.3 ppm) and grain sorghum grain (0.2 ppm).

ii. *Drinking water*. Other potential sources of exposure of the general population to residues of propiconazole are residues in drinking water and exposure from non-occupational sources. Review of environmental fate data by the Environmental Fate and Effects Division of USEPA indicates that propiconazole is persistent and moderately mobile to relatively immobile in most soil and aqueous environments. No Maximum Concentration Level (MCL) currently exists for residues of propiconazole in drinking water and no drinking water health advisory levels have been established for propiconazole.

The degradation of propiconazole is microbially mediated with an aerobic soil metabolism half-life of 70 days. While propiconazole is hydrolytically and photochemically stable ($T_{\frac{1}{2}}$ >100 days), it binds very rapidly and tightly to soil particles following application. Adsorption/desorption and aged leaching data indicate that propiconazole and its degradates will primarily remain in the top 0–6 inches of the soil. It has been determined that under field conditions propiconazole will degrade with a half-life of approximately 100 days.

2. *Non-dietary exposure*. Propiconazole is registered for residential use as a preservative treatment for wood and for lawn and ornamental uses. At this time, no reliable data exist which would allow quantitative incorporation of risk from these uses into a human health risk assessment. The exposure to propiconazole from contacting treated wood products is anticipated to be very low since the surface of wood is usually coated with paint or sealant when used in or around the house. The non-occupational exposure from lawn and ornamental applications is also considered to be minor. It is estimated that less than 0.01% of all households nationally use propiconazole in a residential setting.

D. Cumulative Effects

Consideration of a common mechanism of toxicity is not appropriate at this time since there is no reliable information to indicate that toxic effects produced by propiconazole would be cumulative with those of any other types of chemicals. While other triazoles are available on the commercial or consumer market, sufficient structural differences exist among these compounds to preclude any categorical grouping for cumulative toxicity. Consequently, Novartis is considering only the potential risks of propiconazole in its aggregate exposure assessment.

E. Safety Determination

1. *U.S. population—Reference dose.* Using the conservative exposure assumptions described above (100% stone fruit acres treated and tolerance level residues) and based on the completeness and reliability of the toxicity data base for propiconazole, Novartis has calculated aggregate exposure levels for this chemical. The calculation shows that only 16% of the RfD will be utilized for the U.S. population based on chronic toxicity endpoints. EPA generally has no concern for exposures below 100% of the RfD because the RfD represents the level at or below which daily aggregate dietary exposure over a lifetime will not pose appreciable risks to human health. Novartis concludes that there is a reasonable certainty that no harm will result from aggregate exposure to propiconazole residues.

2. *Infants and children*. Developmental toxicity (e.g., reduced pup weight and ossification) was observed in the rat teratology studies and 2–generation rat reproduction studies at maternally toxic doses. Some of these findings are judged to be nonspecific, secondary effects of maternal toxicity. The lowest NOAEL for developmental toxicity was established in the rat teratology study at 30 mg/kg, a level 24–fold higher than the NOAEL of 1.25 mg/kg on which the RfD is based.

3. *Reference dose.* Using the same conservative exposure assumptions as employed for the determination in the general population, Novartis has calculated that the percent of the RfD that will be utilized by aggregate exposure to residues of propiconazole is 26% for nursing infants less than 1 year old, 65% for non-nursing infants less than 1 year old, 35% for children 1–6 years old, and 23% for children 7–12 years old. Therefore, based on the completeness and reliability of the toxicity data base and the conservative exposure assessment, Novartis concludes that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to propiconazole residues.

F. International Tolerances

International CODEX values are established for almond, animal products, bananas, barley, coffee, eggs, grapes, mango, meat, milk, oat, peanut-whole, peanut grains, pecans, rape, rye, stone fruit, sugar cane, sugar beets, sugar beet tops, and wheat. The U.S. residue definition includes both propiconazole and metabolites determined as 2,4-dichlorobenzoic acid (DCBA), while the CODEX definition is for propiconazole, per se, i.e. parent only. This difference results in unique tolerance expressions with the U.S. definition resulting in the higher tolerance levels.

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