tumorigenic in animals even at maximally tolerated doses and has a different spectrum of toxicological effects.

E. Safety Determination

1. *US population*. The Rohm and Haas Company estimates the risk to the U.S. adult population from use of fenbuconazole on wheat as utilizing approximately 0.36% of the RfD. Using the EPA low dose extrapolation model and the risk factor based on the mouse data (0.36×10^{-6} (mg/kg/day)-1) the excess cancer risk from dietary sources for fenbuconazole use on wheat and the associated animal commodities is estimated at 0.3×10^{-6}. The upper bound estimate on excess cancer risk for all uses including wheat is 0.7×10^{-6}.

This assumes that all of the wheat consumed in the U.S. will contain residues of fenbuconazole (in actuality a small fraction of the total crop is likely to be treated). The combined risk for wheat plus registered uses will not exceed either the dietary risk standard established by the Food Quality Protection Act (FQPA) for the US population, (one $\times 10^{-6}$), or the RfD.

The sole acute risk would be for women of childbearing age. The EPA/OREB calculated that the worst-case Margin of Exposure (MOE) for fenbuconazole measured against the developmental LOEL would be greater than 30,000. This is clearly adequate. The MOE would be even higher for consumer dietary exposure from any source. Thus, there is adequate safety for this group and there is a reasonable certainty that no harm will result from fenbuconazole use on wheat.

2. *Infants and children*. The reproductive and developmental toxicity data base for fenbuconazole is complete. There is no selective increase in toxicity to developing animals. Thus, there is no evidence that prenatal and postnatal exposure would present unusual or disproportionate hazard to infants or children. Therefore, there is no need to impose an additional uncertainty factor to protect infants and children.

The EPA calculated the dietary risk to infants and children for existing tolerances. The estimated dietary exposure (TMRC) for this subpopulation is 0.00522 mg/kg/day which represents only 17% of the RfD; no other subgroup used in excess of 17% of the RfD. The EPA estimated lifetime oncogenic risk in the range of one in a million at 0.9×10^{-6}, using ($Q1^* = 1.06 \times 10^{-2}$ (mg/kg/day)-1). (60 FR 27420; May 24,1995).

For the wheat use the most sensitive subgroup is children 1 to 6 years old and the estimated risk to this subgroup is less than 18% of the RfD. Utilizing the risk factor ($Q1^* = 0.36 \times 10^{-2}$ (mg/kg/day)-1), the estimated excess cancer risk for the U.S. population is less than 1×10^{-6}. Therefore the wheat use is safe within the meaning of the FQPA and there is a reasonable certainty that no harm will result to infants or children from the approval of fenbuconazole use on wheat.

F. International Tolerances

There are no Codex Maximum Residue Levels (MRLs) for fenbuconazole, but the fenbuconazole database will be evaluated by the WHO and the FAO Expert Panels at the Joint Meeting on Pesticide Residues (JMPR) in September 1997. An Allowable Daily Intake (ADI (RfD)) of 0.03 mg/kg/day is proposed and a total of 36 Codex MRLs are proposed in the data submission.

G. Environmental Fate Summary

Fenbuconazole has little to no mobility in soil (Koc = 4425). It is stable to hydrolysis and aqueous photolysis in buffered solutions, but does degrade photolytically in natural waters and soil (half–life 87 and 79 days, respectively). Laboratory soil metabolism half–lives or DT_{50} values for fenbuconazole range from 29 to 532 days under terrestrial conditions and from 442 to 906 in soil exposed to aquatic conditions. Field-trial soil dissipation studies had half–lives ranging from 157 to 407 days and indicated no significant downward movement of residues. These field trials show fenbuconazole degrades more rapidly outdoors than in laboratory metabolism studies. When material was applied in a single application, fenbuconazole degraded to about 50% of the applied material in less than 60 days. In wheat the DT_{50} in green heads was measured as 18 days and in green wheat stalks the DT_{50} was 84.4 days. These results only reflect foliar dissipation in wheat at the particular growth stage(s) during the study and not at all stages of wheat. The results of residue decline analyses in a number of environmental media support the EPA conclusion that there is no environmental hazard associated with the proposed agricultural use of this chemical.

[FR Doc. 97–24693 Filed 9–16–97; 8:45 am]

BILLING CODE 6560–50–F

ENVIRONMENTAL PROTECTION AGENCY

[PF–754; FRL–5735–8]

Notice of Filing of Pesticide Petitions

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

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

DATES: Comments, identified by the docket control number PF–754, must be received on or before October 17, 1997.

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

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

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

FOR FURTHER INFORMATION CONTACT: By mail: Sidney Jackson, Product Manager (PM) 43, Minor Use, Inerts, Emergency Response Branch, Registration Division (7505C), Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. Office location and telephone number: Rm. 274, CM#2, 1921 Jefferson Davis Highway, Arlington, VA., (703) 305–7610. e-mail: jackson.sidney@epamail.epa.gov.

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

The official record for this notice, as well as the public version, has been established for this notice of filing under docket control number PF–754 (including comments and data submitted electronically as described below). A public version of this record, including printed, paper versions of electronic comments, which does not include any information claimed as CBI, is available for inspection from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The official record is located at the address in ''ADDRESSES''.

Electronic comments can be sent directly to EPA at:

opp-docket@epamail.epa.gov

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

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

List of Subjects

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

Dated: September 5, 1997.

James Jones,

Acting 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. DowElanco Products Co.

PP 5E4573

EPA has received a pesticide petition (PP 5E4573) from the Interregional Research Project number 4 (IR-4), 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 Fenarimol, alpha-(2 chlorophenyl)-alpha-(4-chlorophenyl)-5-pyrimidine methanol, in or on the raw agricultural commodity filbert (hazelnuts) at 0.02 parts per million (ppm).

A. Residue Chemistry

1. *Plant metabolism*. The nature of the residue in fenarimol-treated filberts has not been directly determined. Radioactive metabolism studies with apples and cherries indicate that fenarimol is the only significant component of the residue in apples and cherries. The residue of concern is fenarimol.

2. *Analytical method*. Analytical methodology used for filberts is a slight modification of the basic PAM II method for fenarimol (Method R039). Residues are extracted with methanol. Aqueous sodium chloride (5%) is added and the extract is partitioned with dichloromethane. Residues are cleaned up on a Florisil column and detected by GC/ECD. Recoveries ranged from 84–97% in samples fortified with fenarimol at 0.02–0.2 ppm. The limit of detection via this method is >0.02 ppm.

3. *Magnitude of residues*. IR-4 data from 4 residue trials show residues of fenarimol were <0.02 ppm in composite samples of filberts treated at 0.09 pounds active ingredient per acre (lb ai/A) and composite samples treated at 0.18 lb ai/A or two times the proposed maximum application rate. These data indicate that fenarimol residues would not be expected to accumulate to significant levels in filberts. Based on these results and for purposes of this petition, it is appropriate to base the magnitude of total terminal residues and proposed tolerance only on residues of the parent compound, fenarimol.

B. Toxicological Profile

1. *Acute toxicity*. The acute oral lethal dose $(LD)_{50}$ in the rat is 2,500 milligrams (mg)/kilogram (kg) and the acute dermal LD_{50} in the rabbit is >2,000 mg/kg. The inhalation lethal concentration $(LC)_{50}$ in the rat is >2.04 mg/liter(l) of air, which is the highest obtainable respirable aerosol concentration. Fenarimol produced no indications of dermal irritation in rabbits or sensitization in the guinea pig. End use formulations of fenarimol have similar low acute toxicity profiles.

2. *Genotoxicity*. Fenarimol tested negative in several assay systems for gene mutation, structural chromosome aberration and other genotoxic effects. In a micronucleus test in the mouse, fenarimol did produce a significant increase in the percent of polychromatic erythrocytes with micronucleus at 24 hours but not at 48 or 72 hours. Moreover, a second test run at a higher dosage, which produced significant toxicity including death, was unequivocally negative.

3. *Reproductive and developmental toxicity*. A developmental toxicity study in rabbits was negative for teratogenic effects at all doses tested (0, 5, 10, and 35 mg/kg). A developmental toxicity study in rats demonstrated hydronephrosis at 35 mg/kg (doses tested were 0, 5, 10, and 35 mg/kg). A second developmental toxicity study in rats (with a postpartum evaluation) again demonstrated hydronephrosis at 35 mg/kg. Maternal toxicity (decreased body weight) was also observed at the 35 mg/kg/day dose level. The no observed effect level (NOEL) for hydronephrosis and maternal toxicity is 13 mg/kg.

A 3-generation reproduction study in rats dosed at 0, 12.5, 25 or 50 ppm (equivalent to 0, 0.625, 1.25 or 2.5 mg/kg/day) demonstrated decreased fertility in males at 25 ppm and delayed parturition and dystocia in females at 25 and 50 ppm. The NOEL for reproductive effects was 12.5 ppm (0.625 mg/kg/day). The infertility effect in males is considered to be a species-specific effect mediated by the inhibition of aromatase an enzyme which catalyzes the conversion of testosterone to estradiol. Estradiol plays an essential role in the developmental and maintenance of sexual behavior in rats.

Multigeneration reproduction studies in guinea pigs and mice were negative for reproductive effects at the highest dose levels tested 35 mg/kg/day and 20 mg/kg/day, respectively. A NOEL of 35 mg/kg/day for reproductive effects relevant to humans was established based on the NOEL from the multi-generation reproduction study in guinea pigs.

4. *Chronic toxicity*. A 2-year chronic toxicity/carcinogenicity study in rats fed diets containing 0, 50, 130, or 350 ppm (equivalent to 2.5, 6.5, or 17.5 mg/kg/day) with a systemic NOEL of 130 ppm

(equivalent to 6.5 mg/kg/day). An increase in fatty liver changes was observed in rats fed diets containing 350 ppm. There were no carcinogenic effects observed under the conditions of the study.

A second 2-year carcinogenicity study was conducted in rats fed diets containing 0, 12.5, 25, or 50 ppm (equivalent to 0, 0.63, 1.25, or 2.5 mg/kg/day). There was no apparent effect on survival which was reduced in all treatment groups due to chronic respiratory disease. An increase incidence of fatty changes in the liver was observed at the top dose level of 50 ppm, and the NOEL was established as 25 ppm (1.2 mg/kg/day) in this study. A third 2-year study carcinogenicity was conducted at the same dose levels as above. The incidence of liver lesions was similar in the treated and control groups, thus the NOEL for liver effects in this study was greater than 50 ppm (2.5 mg/kg/day).

A 2-year dietary feeding study in mice fed diets containing concentrations of 0, 50, 170, or 600 ppm equivalent to 0, 7, 24.3, or 85.7 mg/kg/day). A 600 ppm dose level was shown to increase liver weight. There was no increase in cancer and no toxicologically significant treatment related effects were observed at any dose level. The NOEL was determined to be 600 parts per million(ppm) (85.7 mg/kg/day).

A 1-year chronic toxicity study in dogs fed diets containing 0, 1.25, 12.5, or 125 mg/kg/day, the NOEL was 12.5 mg/kg/day based upon an increase in serum alkaline phosphatase, increased liver weights, an increase in p-nitroanisole o-demethylase activity, and mild hepatic bile stasis at the high dose level (125 mg/kg/day).

Based on the chronic toxicity data, the Reference Dose (RfD) for fenarimol is established at 0.065 mg/kg/day. The RfD for fenarimol is based on a 2-year chronic feeding study in rats with a NOEL of 6.5 mg/kg/day and an uncertainty factor of 100.

There is no evidence to suggest that fernarimol effects any endocrine system or that fernarimol would elicit neurotoxic response.

5. *Animal metabolism*. Metabolism studies conducted in rats show fenarimol is rapidly metabolized and excreted. Major metabolic pathways were oxidation of the carbinol-carbon atom, the phenyl rings and the pyrimidine ring.

6. *Carcinogenicity*. Fenarimol is classified as Group ''E'' for carcinogenicity (no evidence of carcinogenicity) based on the results of the carcinogenicity studies. There was no evidence of carcinogenicity in 2-year feeding studies in mice and rats at the dosage levels tested. The doses tested were adequate for identifying a cancer risk. Thus, a cancer assessment would not be appropriate.

C. Aggregate Exposure

1. *Dietary (food) exposure*. For the purposes of assessing the potential dietary exposure from use of fenarimol on filberts, an estimate of aggregate exposure is determined by basing the TMRC from previously established tolerances and the proposed tolerance on filberts for fenarimol at 0.02 parts per million(ppm) and assuming that 100% of the filbert crop has a residue of fenarimol at the tolerance level.

Exposure to humans to residues could also result if such residues are transferred to meat, milk, poultry or eggs. Since there is no livestock feed commodities associated with filberts, there is no reasonable expectation that measurable secondary residues of fenarimol will occur in meat, milk, poultry or eggs under the terms of the proposed use. Other established U.S. tolerances for fenarimol on food or feed crops in the United States are established under 40 CFR part 180.421, 40 CFR part 185.3200 and 40 CFR part 186.3200. The use of a tolerance level and 100% of crop treated clearly results in an overestimate of human exposure and a safety determination for use of fenarimol on filberts that is based on a conservative exposure assessment.

2. *Drinking water*. Based upon the available environmental studies conducted with fenarimol wherein it's properties show little potential for mobility in soil and extremely rapid photolysis in water, DowElanco concludes, there is no anticipated exposure to residues of fenarimol in drinking water.

3. *Non-dietary exposure*. The proposed use on filberts involves application of fenarimol to a crop grown in an agricultural environment. Thus, the potential for non-occupational, non-dietary exposure to the general population is not expected to be significant.

D. Cumulative Effects

DowElanco concludes that there is no evidence that there is a common mechanism of toxicity with any other chemical compound or that potential toxic effects of fenarimol would be cumulative with those of any other pesticide chemical. Thus DowElanco believes it is appropriate to consider only the potential risks of fenarimol in its exposure assessment.

E. Safety Determination

1. *U.S. population*. DowElanco has concluded that aggregate exposure to fenarimol will utilize less than 2% of the RfD for the U.S. general 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 dietary exposure over a lifetime will not pose appreciable risks to human health. DowElanco concludes that there is a reasonable certainty that no harm will result from aggregate exposure to fenarimol residues in or on filberts. The complete toxicology profile for fenarimol shows no evidence of physiological effects characteristic of the disruption of the hormone estrogen. Based upon this observation, DowElanco concludes that fenarimol does not meet the criteria for an estrogenic compound.

2. *Infants and children*. In assessing the potential for additional sensitivity of infants and children to residues of fenarimol, data from developmental toxicity studies in rats and rabbits and a multigeneration reproduction study in the rat are considered. 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 and potential systemic toxicity of mating animals and on various parameters associated with the well-being of offspring.

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 data base. Based on the current toxicological data requirements, the data base for fenarimol relative to pre- and post-natal effects for children is complete. Further, for fenarimol, the NOEL in the chronic feeding study which was used to calculate the RfD (6.5 mg/kg/day used by EPA or 1.2 mg/kg/day used by The World Health Organization) is already lower than the NOELs from the developmental studies in rats and rabbits.

Concerning the multi-generation reproduction study, the effects on reproduction are considered to be specific effect caused by aromatase inhibition. The aromatase enzyme promotes normal sexual behavior in rats and mice, but not in guinea pigs, or primates (including humans). A NOEL of 35 mg/kg/day for reproductive effects

relevant to humans was established based on the NOEL from the multi-generation reproduction study in guinea pigs. In addition, a NOEL of 13 mg/kg/day for developmental effects was established based upon the NOEL from the teratology study in rats. Therefore, DowElanco concludes that an additional uncertainty factor is not needed and that the RfD at 0.065 mg/kg/day is appropriate for assessing risk to infants and children.

Using the exposure assumptions previously described, the percent RfD utilized by the aggregate exposure to residues of fenarimol from previously established tolerance and the proposed tolerance on filberts is less than 2% for children 1 to 6 years of age, the population subgroup most highly exposed to dietary residues of fenarimol. Thus, based on the completeness and reliability of the toxicity data and the conservative exposure assessment, DowElanco concludes that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to fenarimol on filberts.

F. International Tolerances

A temporary tolerance of 0.02 ppm for fenarimol on pecans; and a 0.1 ppm Mexican limit for fenarimol on walnuts exist. Since there are not Codex, Mexican or Canadian limits for fenarimol on filberts, international compatibility is not considered to be at issue.

2. ISK Biosciences Corporation

PP 2E4042, 2E4018 and 6E4672

EPA has received pesticide petitions (PP 2E4042, 2E4018 and 6E4672) from the Interregional Research Project Number 4 (IR-4), 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 tolerances for residues of Chlorothalonil (tetrachloroisophthalonitrile) and its metabolite 4-hydroxy-2,5,6-trichloro-isophthalonitrile in or on the raw agricultural commodities at levels of 0.1 parts per million(ppm) for asparagus, 1.0 ppm for mangoes, and 0.2 ppm for pistachios.

A. Residue Chemistry

1. *Plant metabolism*. The nature of the residue of chlorothalonil in asparagus, mangoes and pistachios is adequately understood. The parent compound and its metabolite (4-hydroxy-2,5,6-trichloro-isophthalonitrile) are the regulated residues. Chlorothalonil is not systemic in plants.

2. *Analytical method*. An adequate analytical method (gas chromatography) is available for enforcement purposes. The method is listed in the Pesticide Analytical Manual, Vol. II (PAM II).

3. *Magnitude of residues*. Residue data from studies conducted with asparagus, mangoes and pistachios support the proposed tolerances for combined residues of chlorothalonil and its metabolite, 4-hydroxy-2,5,6-trichloro-isophthalonitrile in/on these raw agricultural commodities.

B. Toxicological Profile

1. *Acute toxicity*. Acute toxicity studies on technical grade chlorothalonil show: an oral lethal dose $(LD)_{50}$ >10,000 milligrams(mg)/kilogram(kg) (Toxicity Category IV) in rats; a dermal LD_{50} >10,000 mg/kg (Toxicity Category IV) in rabbits; a four-hour inhalation lethal concentration $(LC)_{50}$ of 0.092 mg/L in female rats and 0.094 mg/L in male rats (Toxicity Category II); and a primary eye irritation study showing chlorothalonil as corrosive causing irreversible eye effects (Toxicity Category I) in the rabbit at 21 days. Chlorothalonil was shown not to be a dermal irritant (Toxicity Category IV) in a primary dermal irritation study in rabbits and not a skin sensitizer in a dermal sensitization study in guinea pigs.

2. *Genotoxicity*. Mutagenicity studies with chlorothalonil include gene mutation assays in bacterial and mammalian cells; in vitro and in vivo chromosomal aberration assays; DNA repair assays in bacterial systems; and cell transformation assays. All were negative with the following two exceptions:

Chlorothalonil was positive in an *in vitro* chromosomal aberration assay in chinese hamster ovary (CHO) cells without metabolic activation but was negative with metabolic activation. *In vivo* chromosomal aberration studies in rats and mice were negative and one study in the Chinese hamster was equivocal. These results suggest that chlorothalonil is not mutagenic and does not have clastogenic potential in intact mammalian systems.

In bacterial DNA repair tests, chlorothalonil was negative in *Bacillus subtilis*, but was positive in *Salmonella typhimurium*. In an *in vivo* DNA binding study in rats with ^{14}C-chlorothalonil, there was no covalent binding of the radiolabel to the DNA of the kidney, the target organ for chlorothalonil toxicity in rodents.

3. *Reproductive and developmental toxicity*. A developmental toxicity study with rats fed doses of 0, 25, 100, and 400 mg/kg body weight/day from days 6 through 15 of gestation resulted in a no observed effect level (NOEL) for maternal toxicity of 100 mg/kg/day based on increased mortality, reduced body weight, and a slight increase in early resorptions at the highest dose. There were no developmental effects observed at any dose in this study.

A developmental toxicity study in rabbits fed doses of 0, 5, 10, or 20 mg/kg/day on days 7 through 19 of gestation resulted in a maternal NOEL of 10 mg/kg/day. Effects observed in the dams in the high-dose group were decreased body weight gain and reduced food consumption. There were no developmental effects observed in this study.

A two-generation reproduction study in rats fed diets containing 0, 500, 1,500 and 3,000 ppm resulted in a reproductive NOEL of 1500 ppm (equivalent to 115 mg/kg/day) based on lower neonatal body weights by day 21. There were no effects seen on any other reproductive parameter at any dose level in this study.

4. *Subchronic toxicity*. A subchronic toxicity study was conducted in rats at doses of 0, 1.5, 3.0, 10 and 40 mg/kg/day for 13 weeks. Treatment related hyperplasia and hyperkeratosis of the forestomach was observed at the two highest dose levels. Initial histopathological evaluation did not demonstrate any nephrotoxicity, however, a subsequent evaluation observed a treatment-related increase in hyperplasia of the proximal tubule epithelium at 40 mg/kg/day. Based on these findings, the NOEL was 3.0 mg/kg/day and the lowest observed effect level (LOEL) in rats was 10.0 mg/kg/day.

A 90-day oral toxicity study was conducted in dogs with dose levels of technical chlorothalonil of 15, 150 and 750 mg/kg/day. The two highest dosages resulted in lower body weight gain in male dogs. The NOEL was 15 mg/kg/day, and the LOEL was 150 mg/kg/day based on decreased body weight gain in males.

Two 21-day dermal toxicity studies were conducted with technical chlorothalonil. In the initial study, rabbits were dosed at 50, 2.5 and 0.1 mg/kg/day. The NOEL and LOEL for systemic effects and dermal effects were both greater than 50 mg/kg/day. The NOEL for dermal irritation was 0.1 mg/kg/day. A subsequent 21-day dermal study was conducted in male rats, to specifically evaluate the potential for nephrotoxicity in this laboratory species following dermal dosing. In this study the doses were 60, 100, 250 and 600 mg/kg/day. The NOEL for nephrotoxicity was greater than 600 mg/kg/day.

Estrogenic effects. ISK Biosciences concludes that based upon all of the chronic toxicity, developmental toxicity, mutagenicity and reproductive studies conducted with chlorothalonil and its metabolites, results did not indicate any potential to cause estrogenic effects, or endocrine disruption.

5. *Chronic toxicity*. A 12-month chronic oral toxicity study in Beagle dogs was conducted with technical chlorothalonil at dose levels of 15, 150 and 500 mg/kg/day. The no observed adverse effect level (NOAEL) was 150 mg/kg/day based on lower blood albumin levels at the highest dose. There was no nephrotoxicity observed at any dose in this study.

A chronic feeding/carcinogenicity study with Fischer 344 rats fed diets containing 0, 800, 1,600 or 3,500 ppm (equivalent to 0, 40, 80 or 175 mg/kg body weight (body weight (bwt))/day) for 116 weeks in males or 129 weeks in females, resulted in a statistically higher incidence of combined renal adenomas and carcinomas. At the high dose, which was above the maximum tolerated dose (MTD), there was also a statistically significant higher incidence of tumors of the forestomach in female rats.

In a second chronic feeding/carcinogenicity study with Fischer 344 rats, designed to define the NOEL for tumors and the preneoplastic hyperplasia, animals were fed diets containing 0, 2, 4, 15 or 175 mg/kg/day. The NOEL in this study, based on renal tubular hyperplasia, was a nominal dose of 2 mg/kg body weight (bwt)/day. Because of the potential for chlorothalonil to bind to diet, the 2 mg/kg bwt/day dose, expressed as unbound chlorothalonil is 1.8 mg/kg body weight(bwt)/day. The NOEL for hyperplasia and hyperkeratosis of the forestomach was 4 mg/kg body weight(bwt)/day or a dose of 3.8 mg/kg bwt/day based on unbound chlorothalonil.

A 2-year carcinogenicity study in CD-1 mice at dietary levels of 0, 750 and 1,500 or 3,000 ppm (equivalent to 0, 107, 214 or 428 mg/kg/day), resulted in a statistically higher incidence of squamous cell carcinomas of the forestomach in both sexes, and a statistically higher incidence of combined renal adenomas/carcinomas in only the male mice receiving the low dose. There were no renal tumors in any female mouse in this study.

A 2-year carcinogenicity study in male CD-1 mice for the purpose of establishing the no effect level for renal and forestomach effects, was conducted at dietary levels of 0, 10/15, 40, 175, or 750 ppm (equivalent to 0, 1.4/2.1, 5.7, 25 or 107 mg/kg/day). The NOEL level for renal effects was 40 ppm and the NOEL for forestomach effects was 15 ppm.

The Agency classifies and regulates chlorothalonil as a B2 (probable human carcinogen). This classification was based on statistically significant increases in the incidence of renal adenomas and carcinomas in male and female Fisher 344 rats, a statistically significant increase in combined renal adenoma/carcinoma of the forestomach in male and female Osborne-Mendel rats, and statistically significant increases in carcinoma of the forestomach in male and female CD-1 mice, as well as positive dose-related trend for combined renal adenoma/carcinoma in male mice.

A carcinogenic potency factor, Q1*, of 0.00766 $(mg/kg/day)^{-1}$ is used by the Agency when conducting mathematical modeling to estimate carcinogenic risk to humans. The carcinogenic potency factor was calculated based upon female rat renal (adenoma and/or carcinoma) tumor rates.

The Agency is currently evaluating recently submitted mechanistic data in connection with the registrants' assertions regarding the carcinogenicity of chlorothalonil. No conclusions are available at this time.

Reference Dose (RfD): A RfD of 0.02 mg/kg/day was determined based on the NOEL of 2 mg/kg/day established in a 2-year dietary study in rats and using an uncertainty factor of 100.

The no effect level (NOEL) for chlorothalonil is based on the nephrotoxicity observed in the chronic rat study. The Agency considers the NOEL to be 2.0 mg/kg/bwt, which is the nominal dose.

No effect levels for maternal toxicity from developmental studies are 10 mg/kg body weight (bwt) in rabbits and 100 mg/kg body weight (bwt) in the rat. The no effect level for pup growth in the reproduction study was 1,500 mg/kg body weight(bwt) which would be most conservatively estimated as equating to approximately 75 mg/kg/bwt.

6. *Animal metabolism*. Approximately 33% of chlorothalonil at dose levels at or below 50 mg/kg was orally absorbed. Of this amount, 80 to 90% was eliminated in the feces and 15–20% of the dose was excreted into the bile. No significant levels of chlorothalonil were found in any tissues. The compound was metabolized primarily via glutathione conjugation (mono, di and triglutathione conjugates; possibly tetra). These conjugates were excreted directly into bile; some were shown to have been transported to the kidneys where they were cleaved to thio metabolites, the excretion of which was rate-limited, and therefore, could lead to nephrotoxicity.

7. *Metabolite toxicology*. The primary metabolite of chlorothalonil is 4-Hydroxy-2,5,6-Trichloroisophthalonitrile (4-OH or SDS-3701). The toxicity data base for SDA-3701 is adequate. Two data gaps currently exist for a 1-year chronic toxicity study in dogs and a developmental toxicity study in rats. SDS-3701 has been show to be a minor residue in soil and rotated crops. The existing toxicity data base can be summarized as follows:

a. *Acute toxicity*. The acute oral LD_{50} for male rats was 422 mg/kg and for female rats was 242 mg/kg, with the combined sexes value being 332 mg/kg.

b. *Subchronic toxicity*. Sprague-Dawley rats dosed with SDS-3701 at 0, 0.5, 2.5, 5 or 10 mg/kg/day in a 4-month feeding study resulted in a NOEL at 5 mg/kg/day and the LOEL at 10 mg/kg/day based on depressed body weight and an increase in liver weight. Sprague-Dawley rats of both sexes dosed for 61-69 days at doses of 0, 10, 20, 40, 75, 125, 250, 500 or 750 mg/kg/day. The NOEL was 20 mg/kg/day and the LOEL was 40 mg/kg/day based on decreased body weights, anemia and renal cortical atrophy. In a 3-month feeding study in beagle dogs with SDS-3701 fed at 0, 1.25, 2.5 or 5.0 mg/kg/day, the NOEL was 2.5 mg/kg/day and the LOEL was 5.0 mg/kg/day based on renal tubular degeneration and vacuolation in males.

c. *Chronic toxicity and carcinogenicity*. In a 2-year study SDS-3701 was fed to Sprague-Dawley rats at 0, 0.5, 3.0, 15 (reduced to 10 at week 30) or 30 (reduced to 20 at week 30) mg/kg/day. The NOEL was 3.0 mg/kg/day. The LOEL was 10 mg/kg/day based on reduced body weight, microcyticanemia, hemosiderin and decreased serum potassium. In a 2-year study with CD-mice and SDS-3701 were fed at 0, 54, 107 or 214 mg/kg/day, the NOEL was not established; the LOEL was <54 mg/kg/day based on increased liver-to-body weight ratios in males. In both the above studies, there was no evidence of carcinogenicity in either sex.

d. *Developmental toxicity*. SDS-3701 was fed to pregnant Dutch Belted rabbits at dose levels of 1, 2.5, or 5 mg/kg/day on gestation days six through fifteen. For maternal toxicity the NOEL was 1 mg/kg/day and the LOEL was 2.5 mg/kg/day based on a dose dependent increase in maternal death and abortion. The developmental toxicity NOEL was 5 mg/kg/day. No LOEL was established.

e. *Reproductive toxicity*. In a 1-generation reproduction study, SDS-3701 was fed to Sprague-Dawley CD rats at 0, 0.5, 1.0, 1.5, 3.0 or 6.0 mg/kg/day. For paternal systemic toxicity, the NOEL was 1.5 mg/kg/day. In a 3-generation reproduction study with the same rat species fed SDS-3701 at 0, 0.5, 3.0, or 6.25 mg/kg/day the parental systemic NOEL was 0.5 mg/kg/day. In both the 1 and 3-generation studies the LOEL was the same, 3.0 mg/kg/day based on reduced weaning body weight and the reproductive toxicity NOEL was similar at 6.0 and 6.25 mg/kg/day.

f. *Mutagenicity*. SDS–3701 did not cause DNA damage in *S. Typhimurium* or induce a mutagenic response when tested in this species or in tests with cultured Chinese hamster V 79 cells or BALB/3T3 mouse fibroblasts. No evidence of mutagenesis was found in host mediated assay using *S. typhimurium* tester strains and mice exposed daily for 5 days to 6.5 mg/kg/day of the compound.

C. Aggregate Exposure

1. *Dietary exposure*. Available information on anticipated residues was incorporated into the analysis to estimate the Anticipated Residue Contribution (ARC) from each existing use. Potential dietary exposure determinations were based on estimates of anticipated residues of chlorothalonil in food and drinking water.

a. *Food*. Chlorothalonil would be applied to asparagus ferns which regrow after harvest of the spears to protect the ferns from diseases. There is no harvest until the following crop season and little chance of chemical residues of chlorothalonil or its major metabolite on the spears. ISK Biosciences determined that anticipated actual residues of chlorothalonil on asparagus spears would be 0.0000000891 mg/kg body weight(bwt)/day to the U.S. population and 0.0000000719 mg/kg body weight(bwt)/day to children ages 1–6.

Chlorothalonil would be applied to mango trees during the growing season for control of diseases. ISK Biosciences determined that anticipated actual residues of chlorothalonil on mangoes would be 0.0000000633 mg/kg body weight(bwt)/day to the U.S. population and 0.000000129 mg/kg body weight(bwt)/day to children ages 7–12.

Chlorothalonil would be applied to pistachio trees during the growing season for control of diseases. The nuts used for human consumption are not directly exposed to the sprays. Thus, there is little chance of significant levels of residues of chlorothalonil or its major metabolite on pistachio nutmeats. ISK Biosciences determined that anticipated actual residues of chlorothalonil on pistachios would be 0.0000000167 mg/kg body weight(bwt)/day to the U.S. population and 0.0000000304 mg/kg body weight(bwt)/day to children ages 1–6.

There is no reasonable expectation that secondary residues will occur in milk, eggs, or meat, fat, or meat byproducts of livestock or poultry as a result of this action; there are no livestock feed items associated with asparagus, mangoes or pistachios.

ISK Biosciences believes that exposure, based on the current registered uses for chlorothalonil, is 0.0000642 mg/kg body weight(bwt)/day for the general U.S. population and 0.000105 mg/kg body weight(bwt)/day for infants and children 1–6 years of age. For all published and pending tolerances, the respective exposures are 0.0000651 mg/kg body weight(bwt)/day and 0.000106 mg/kg body weight(bwt)/day.

b. *Drinking water*. Results of monitoring studies in the National Survey of Pesticides in Drinking Water Wells conducted by EPA showed that no chlorothalonil residues were detected in any of the 1,300 community water systems and domestic wells (using methodology for chlorothalonil having a limit of detection (LOD) of 0.06 micro grams(µg/l) and limit of quantitation of 0.12 µg/l). The absence of chlorothalonil detections in the National Survey suggests that chlorothalonil is not a contaminant in drinking water wells and that the population is not exposed to chlorothalonil in these water sources. These findings are consistent with the physical and chemical properties of chlorothalonil, including low water solubility (0.9 ppm) and high affinity for organic matter including soil. It has also been demonstrated that chlorothalonil does not leach into groundwater from applications made to growing crops.

Aerobic aquatic metabolism studies with chlorothalonil establish a half-life in natural aquatic habitats of less than 10 hours, depending on environmental conditions. The short half-life of chlorothalonil in natural water/sediment systems and practiced water treatment techniques prior to consumption, suggest that chlorothalonil is not likely to be present in drinking water obtained from natural surface water systems.

An exposure estimate, based on surface water concentration recently cited by EPA, would conclude that the average concentration in surface water would be less than 0.002 parts per billion (ppb). Assuming that everyone in the US consumed untreated surface water, the exposure to chlorothalonil of the general population would be less than 0.00000058 mg/kg body weight(bwt)/day. This would be a worst case scenario, which would greatly overestimate exposure.

2. *Non-dietary exposure*. Potential non-dietary exposures to chlorothalonil may result from the following uses of chlorothalonil. In each case, the exposure would be from the dermal route and only for an intermittent duration. The two 21-day dermal studies that have been conducted in the rabbit and rat indicate that there is no nephrotoxicity associated with the dermal exposure to chlorothalonil at dose levels up to 600 mg/kg/day. Therefore, ISK Biosciences concludes the exposures from the uses of chlorothalonil listed below, would not be expected to add to the carcinogenic risk associated with chlorothalonil.

a. *Residential owner uses*. ISK Biosciences contends that application of chlorothalonil to home lawns and gardens represents minor uses and would be expected to present very little potential for homeowner exposure.

b. *Paint*. Chlorothalonil is used in paints and stains for control of mildew and molds on exterior surfaces of buildings and occasionally for interior paints. The company estimates that only about 2% of the chlorothalonil used in paint is used in interior paint and only 0.2% or less of interior paints in the United States contains chlorothalonil. In paints chlorothalonil is tightly bound within the paint matrices; thus, effective control of mildew may last for several years and the potential for exposure is very limited.

c. *Grouts*. Chlorothalonil is used in cement tile grouts, also for control of mildew and molds. Chlorothalonil is bound within the grout matrices and presents little exposure opportunity. This is a minor use of chlorothalonil and non-occupational dermal exposure of humans to chlorothalonil from this source is extremely low.

d. *Wood treatment*. Chlorothalonil is used for control of sapstain as a surface treatment on rough-cut, newly-sawn lumber to protect it from molds and mildews while drying. Chlorothalonil does not occur in structural wood used for residential or occupational scenarios.

D. Cumulative Effects

ISK Biosciences has considered the potential for cumulative effects of chlorothalonil and other substances that have a common mechanism of toxicity. Chlorothalonil is a halogenated benzonitrile fungicide which readily undergoes displacement of chlorine in

the 2, 4 and 6 positions by glutathione and other thiol containing amino acids and proteins. In the rat, the glutathione conjugates are sufficiently absorbed from the gut and subsequently metabolized to form di- and tri-thiol metabolites which may produce a nephrotoxic effect. In dogs where this absorption and subsequent metabolism to di- and tri-thiol metabolites does not occur, nephrotoxicity does not occur. ISK Biosciences does not have any information to indicate that toxic effects observed in rats occur through a mechanism which is common to any other agricultural chemical. Thus, it appears inappropriate to group chlorothalonil with any other pesticide at this time.

E. Safety Determination

1. *U.S. population*.Exposure to anticipated actual residues of chlorothalonil on asparagus, as discussed above, would represent only 0.0005% of the RfD (0.018 mg/kg/day) in the diets of the U.S. population with a corresponding carcinogenic risk of 6.8 X 10^{-10}.

Exposure to anticipated actual residues of chlorothalonil on mangoes, as discussed above, would represent only <0.0004% of the RfD (0.018 mg/kg/day) in the diets of the U.S. population with a corresponding oncogenic risk of 4.8 X 10^{-10}. For infants and children ages 1–6, residues on mangoes would represent <0.0008% of the RfD. Exposure to anticipated actual residues of chlorothalonil on pistachios, as discussed above, would represent only <0.0001% of the RfD (0.018 mg/kg/day) in the diets of the U.S. population with a corresponding oncogenic risk of 6.8 X $10-^{-10}$. For infants and children ages 1–6, residues on pistachios would represent <0.0002% of the RfD.

All published and pending tolerances for chlorothalonil utilize less than 1% of the RfD for all segments of the U.S. population with corresponding oncogenic risks of 5.0 X 10^{-7} for the general U.S. population.

Because the worst case assumptions for human exposure from drinking water indicate that exposure would be only 1% of the dietary exposure, the risk assessment is not significantly altered by considering the exposure from drinking water.

2. *Infants and children*. There is a complete database for chlorothalonil which includes pre- and post-natal developmental toxicity data as well as mechanistic data related to the rodent specific nephrotoxicity observed in subchronic and chronic studies. The toxicological effects of chlorothalonil in rodents are well understood. Chlorothalonil has a low level of toxicity in dogs.

In a two-generation reproduction study in rats, all reproductive parameters investigated showed no treatment-related effects except pup weight gain. Specifically, the weights of pups exposed to chlorothalonil were comparable to controls at parturition through day four of lactation. It was only after day four of lactation, when the pups begin to consume the test diet, that body weight gain lags behind controls. This only occurred at the highest dose tested; 3,000 ppm. The dose of chlorothalonil the pups would receive would be far in excess of the estimated adult dose of 150 mg/kg body weight(bwt)/day (3,000 ppm ÷ 20). The doses for the pups could have easily exceeded 500 mg/kg body weight (bwt)/day. Dose levels of 375 mg/kg body weight (bwt) and above have been shown to significantly affect body weight in the rat. Therefore, the reduction of body weight gain observed in the reproduction study is considered to be comparable to the effects that have been observed in older rats. The NOEL for this effect was 1,500 ppm.

In developmental toxicity studies conducted in the rat and the rabbit, chlorothalonil did not cause any developmental effects even at dose levels that produced significant maternal toxicity. In the rabbit a dose level of 20 mg/kg body weight (bwt) caused maternal toxicity, but there were no developmental effects and in the rat, a dose level of 400 mg/kg body weight (bwt) caused maternal toxicity without developmental toxicity.

The extensive data base that is available for chlorothalonil is devoid of any indication that chlorothalonil would represent any unusual or disproportionate hazard to infants or children. Therefore, ISK Biosciences believes that there is no need to impose an additional 10X safety factor for infants or children and argues that the standard uncertainty factor of 100X should be used for all segments of the human population when calculating risks associated with chlorothalonil.

F. International Tolerances

A maximum residue level has not been set for chlorothalonil on pistachios by the Codex Alimentarius Commission.

3. Zeneca Ag Products

PP 6E4653

EPA has received a pesticide petition (PP 6E4653) from the Interregional Research Project No. 4 (IR-4), New Jersey Agricultural Experiment Station, P.O. Box 231, Rutgers University, New Brunswick, NJ 08903, 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 the herbicide sodium salt of fomesafen (also referred to in this document as fomesafen, 5-[2-chloro-4-(trifluoromethyl)phenoxy]-*N*-(methylsulfonyl)-2-nitrobenzamide, in or on the raw agricultural commodity snap beans at 0.05 parts per million (ppm).

A. Residue Chemistry

1. *Plant metabolism*. Fomesafen metabolism has been extensively studied in soybeans. Once in the plant, fomesafen shows very rapid metabolism with either cleavage or conjugation of the intermediate degradation products to a complex mixture of low level degradation products. There is no significant translocation. For purposes of regulation, the parent compound fomesafen is the residue of concern on harvested bean crops.

2. *Analytical method*. The method of analysis uses High Pressure Liquid Chromatography. It is method GAM-RM-001/86, which was developed for analytical work on soybeans and adapted for use on snap beans. The limit of detection of the analytical method is 0.025 ppm.

3. *Magnitude of residues*. Residue data are available for fomesafen applied post-emergence on snap beans at the maximum label rate of 0.375 pounds active ingredient/acre (lb ai/A). The residue field trials were conducted by the IR-4 project in the States of Florida, North Carolina, New York, Oregon, and Wisconsin, representing approximately 50% of the national snap bean acreage. Each treated plot received a single post-emergence, prebloom application at either 0.25 or 0.375 lb ai/A. Four snap bean samples per treatment were collected from each trial. Samples were harvested 22 to 31 days after treatment, a normal range for snap beans. There are no detectable residues in snap beans when fomesafen is applied up to 0.375 lb ai/A prior to pod development, pre-bloom application.

Based on the results of the poultry and ruminant metabolism studies, fomesafen is rapidly metabolized and excreted. There are no expected residues of fomesafen in meat, milk, or eggs. Snap beans are not a significant livestock feed commodity.

B. Toxicological Profile

1. *Acute toxicity*. The acute toxicity profile of technical fomesafen is low by oral, dermal and inhalation routes. Similarly the formulated fomesafen

product (REFLEX) is of low oral, dermal and inhalation toxicity but is classed as Category I toxicity based on the highest hazard, severe eye irritancy. Fomesafen is not a skin sensitizer and only a slight irritant to the skin.

Results of the acute toxicity testing with REFLEX show acute oral in the rat lethal dose $(LD)_{50}$ > 2,000 milligram (mg)/kilogram (kg), acute dermal in the rabbit LD_{50} > 2,000 mg/kg, acute inhalation in the rat LD_{50} > 5.48 mg/liter (L), eye irritation in the rabbit showed severe irritancy, and skin irritation in the rabbit showed a slight irritancy. REFLEX is not a skin sensitizer.

2. *Genotoxicity*. Fomesafen tested negative in assay systems for gene mutation, structural chromosome aberration and other genotoxic effects. However fomesafen did produce a weak clastogenic response in the rat bone marrow when the analysis of the data was undertaken with gap-type aberrations both included and excluded.

In the registrant's view, gap-type aberrations (small discontinuities in the staining of the chromosomes, as distinct from breaks), do not indicate significant chromosomal damage and should be excluded from the evaluation of such assays. Their conclusion therefore is that these data should be considered to indicate no clastogenic effect of fomesafen with no biologically significant genotoxic effects.

3. *Reproductive and developmental toxicity*. In a 2-generation reproduction study in rats fed diets containing 0, 50, 250 or 1,000 ppm fomesafen (equivalent to 2.5, 12.5 or 50 mg/kg/day) no reproductive effects were observed. The no observed effects level (NOEL) for systemic toxicity (reduction in body weight gain and liver necrosis) is established at 250 ppm for this study.

In a developmental toxicity study in rats given oral doses of fomesafen at 0, 50, 100, or 200 mg/kg/day on gestation days 6 to 15 there was no developmental toxicity and the NOEL was established at 50 mg/kg/day, following evaluation of a second study at lower doses.

A developmental toxicity study in rabbits given oral doses of 0, 2.5, 10, or 40 mg/kg/day on gestation days 6 to 18 with no developmental toxicity.

4. *Subchronic toxicity*. Subchronic oral toxicity studies in the rat (90-day) and dog (26 weeks) show that the liver is the primary target of toxicity in both sexes. Rats were dosed at 1, 5, 100, and 1,000 ppm in the diet. The lowest observed effect level (LOEL) in this study was 100 ppm (5 mg/kg/day) and the NOEL was 5 ppm (0.25 mg/kg/day). The dogs were dosed at 0.1, 1 and 25 mg/kg/day. The LOEL in this study was 25 mg/kg/day and the NOEL was 1 mg/kg/day.

A 21-day dermal toxicity study in the rabbit at doses of 10, 100, and 1,000 mg/kg/day showed moderate to severe skin irritation at the application site but no systemic effects at doses up to 1,000 mg/kg/day. The LOEL for skin irritation was 100 mg/kg/day and the NOEL was 10 mg/kg/day.

5. *Chronic toxicity*. Beagle dogs were administered fomesafen in gelatin capsules at dose levels of 0, 0.1, 1.0 or 25 mg/kg body weight (bwt)/day for 26 weeks with a NOEL of 1.0 mg/kg/day. There were no deaths, no clinical signs of toxicity and no treatment related effects on bodyweight or food consumption. Evidence of toxicity was observed at 25 mg/kg/day. Hypolipidemia was present in dogs of both sexes. At autopsy liver weight was increased at 25 mg/kg/day; microscopic examination revealed eosinophilic damage and peroxisome proliferation in both sexes.

A 2-year feeding/carcinogenicity study with rats fed diets containing 0, 5, 100, or 1,000 ppm of fomesafen gave a NOEL for systemic effects of 5 ppm (0.25 mg/kg/day). At the lowest-effect level (LEL) 100 ppm (5 mg/kg/day) there were minor changes associated with liver toxicity. There were no carcinogenic effects observed under the conditions of the study.

A carcinogenicity study was conducted in CD-1 mice fed diets containing 0, 1, 10, 100 or 1,000 ppm fomesafen (equivalent to 0.15, 1.5, 15 or 150 mg/kg/day) for up to 89 weeks. Increased mortality was seen at 1,000 ppm in both males and females and liver weights were increased at 100 and 1,000 ppm. A dose-related increase in the incidence of benign and malignant hepatocellular tumors was observed. Both tumor types were statistically significant in males and females at 1,000 ppm. At the 100 ppm feeding level (male and female), the increased incidence was confined to benign tumors. The increase in benign liver tumors at 1 ppm in males only was not considered related to fomesafen, due to the lack of any increase at 10 ppm.

The Agency has classified fomesafen as a Group C carcinogen (possible human carcinogen) with a potency factor (Q1*) of 0.0019 mg/kg/day.

6. *Animal metabolism*. Fomesafen is well absorbed and completely metabolized in the rat. Excretion is rapid with 90% of the compound excreted within 7 days of ingestion. There is no accumulation of fomesafen.

7. *Metabolite toxicology*. Toxicity testing results for the fomesafen parent compound is indicative of any metabolites, either in the plant or animal.

C. Aggregate Exposure

1. *Dietary exposure*. For purposes of assessing the potential dietary exposure, ZENECA estimated aggregate exposure based on the tolerance for fomesafen on soybeans and snap beans at 0.05 ppm. Dietary exposure to residues of fomesafen in or on food will be limited to residues on soybean and snap beans. Based on the animal metabolism data, and because there are no residues on the crops at time of harvest, the company has concluded that there is reasonable expectation that no measurable residues of fomesafen will occur in meat, milk, poultry, or eggs from this use. There are no other established U.S. tolerances for fomesafen.

2. *Food*. On the bases of the Group C carcinogen classification of fomesafen the upper-bound carcinogenic risk from dietary exposure to fomesafen was calculated using a potency factor (Q*) of 0.19 $(mg/kg/day)^{-1}$ and dietary exposure as estimated by the Anticipated Residue Contribution (ARC) for existing tolerances and the proposed tolerance for snap beans. The upper-bound carcinogenic risk from established tolerances and the proposed tolerance for snap beans is calculated at 1.56×10^{-6} for the U.S. Population. The upper-bound carcinogenic risk from the proposed use on snap beans is calculated at 1.4×10^{-6}. Therefore, the potential cancer risk from residues of fomesafen resulting from the combined established tolerance on soybeans and the proposed tolerance for snap beans is negligible.

3. *Drinking water*. Other potential sources of exposure of the general population to residues of pesticides are residues in drinking water and exposure from non-occupational sources. Field dissipation data and a prospective groundwater study indicate that fomesafen is persistent and has the potential to leach to groundwater. There is no established Maximum Concentration Level (MCL) for residues in drinking water. No drinking water health advisory has been established.

Risk of contaminating surface water. Zeneca contends that fomesafen is unlikely to enter surface water bodies to any significant degree except by direct accidental over-spray. Should this arise, fomesafen will be readily degraded by a number of contributory processes. Fomesafen is not persistent in water in sunlit aquatic conditions. All these processes will ensure that any fomesafen entering surface water bodies will be short-lived and will not result in

any significant contamination of potential drinking water sources.

Therefore, Zeneca concludes that potential exposures from residues of fomesafen in drinking water added to the current dietary exposure will not present significant risk to the U.S. population.

4. *Non-dietary exposure*. Since fomesafen is not registered for residential or turf uses, exposures from other than dietary or occupational sources are extremely unlikely. At this time there are no reliable data to assess the potential risk from non-dietary sources.

D. Cumulative Effects

Fomesafen is a diphenyl ether class of chemicals. At this time, EPA has not made a determination that fomesafen and other compounds have a common mechanism of toxicity resulting in cumulative effects. Therefore, aggregate exposure is evaluated on the uses of fomesafen only.

E. Safety Determination

1. *U.S. population*. The Reference Dose (RfD) for fomesafen has not been established by the Agency's. For purposes of this action, the RfD is calculated at 0.0025 mg/kg of body weight/day. The RfD is based on a NOEL of 0.25 mg/kg/day from the rat feeding/carcinogenicity study and an uncertainty factor of 100. The ARC for the overall U.S. population from established tolerances and the proposed tolerance for snap beans utilizes 1.4% of the RfD. EPA generally has no concern for exposures below 100% of the RfD.

The upper-bound carcinogenic risk from established tolerance on soybeans and the proposed tolerance for snap beans is calculated at 1.56×10^{-6} for the U.S. population, based on the available market share data. The upper-bound carcinogenic risk from the proposed use on snap beans is calculated at 1.4×10^{-6}. Therefore, Zeneca believes that the potential cancer risk from residues of fomesafen resulting from the combined established tolerance on soybeans and the proposed tolerance for snap beans is negligible.

2. *Infants and children*. Zeneca noted that the potential for additional sensitivity for infants and children to residues of fomesafen have been considered based on the three-generation reproductive study in rats and the developmental toxicity studies in rat and rabbit. Zeneca concluded that fomesafen showed no evidence of reproductive toxicity and caused no developmental toxicity in the rabbit or in the rat.

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 data requirements, the database relative to pre- and post-natal effects for children is complete for fomesafen. Zeneca AG Products concludes that there is reasonable certainty that no harm will result to infants and children from aggregate exposure to fomesafen.

F. International Tolerances

There are no Codex Maximum Residue Levels established for fomesafen residues.

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ENVIRONMENTAL PROTECTION AGENCY

[PF–763; FRL–5742–9]

Notice of Filing of Pesticide Petitions

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

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

DATES: Comments, identified by the docket control number PF–763, must be received on or before October 17, 1997.

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

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

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

FOR FURTHER INFORMATION CONTACT: By mail: Beth Edwards, Registration Division (7505C), Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. Office location and telephone number: Rm. 206, CM #2, 1921 Jefferson Davis Highway, Arlington, VA 22202, (703) 305–5400; e-mail: edwards.beth@epamail.epa.gov.

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

The official record for this notice of filing, as well as the public version, has been established for this notice of filing under docket control number [PF–763] (including comments and data submitted electronically as described below). A public version of this record, including printed, paper versions of electronic comments, which does not include any information claimed as CBI, is available for inspection from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The official record is located at the address in ''ADDRESSES'' at the beginning of this document.

Electronic comments can be sent directly to EPA at:
opp-docket@epamail.epa.gov

Electronic comments must be submitted as an ASCII file avoiding the use of special characters and any form of encryption. Comment and data will also be accepted on disks in Wordperfect 5.1 file format or ASCII file format. All comments and data in electronic form must be identified by the docket number [pf–763] and appropriate petition number. Electronic comments on this notice may be filed