comments received electronically into printed, paper form as they are received and will place the paper copies in the official rulemaking record which will also include all comments submitted directly in writing. The official record is the paper record maintained at the address in ''ADDRESSES'' at the beginning of this document.

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

List of Subjects

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

Dated: January 16, 1997.

Flora Chow,

Acting Director, Biopesticides and Pollution Prevention Division, Office of Pesticide Programs.

[FR Doc. 97–1753 Filed 1–23–97; 8:45 am]

BILLING CODE 6560–50–F

[PF-689; FRL-5582-7]

Rhone-Poulenc Ag Company; Pesticide Tolerance Petition Filing

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice of filing.

SUMMARY: This notice announces the filing of a pesticide petition proposing the extension of the temporary tolerances for the combined residues of the fungicide iprodione [3-(3,5-dichlorophenyl)-*N*-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide], its isomer [3-(1-methylethyl)-*N*-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide], and its metabolite [3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide] (CAS Number 36734-19-7, PC Code 109801) in or on the raw agricultural commodities tangerines and tangelos at 3.0 ppm. The notice includes a summary of the petition prepared by the petitioner, Rhone-Poulenc Ag Company.

DATES: Comments, identified by the docket control number [PF-689], must be received on or before, February 24, 1997.

ADDRESSES: By mail, submit written comments to: Public Response and Program Resources Branch, Field Operations Division (7506C), Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. In person, bring comments to: Crystal Mall #2, Room 1132, 1921 Jefferson Davis Highway, Arlington, VA.

Comments and data may also be submitted electronically by sending electronic mail (e-mail) to: 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. Comments and data will also be accepted on disks in WordPerfect in 5.1 file format or ASCII file format. All comments and data in electronic form must be identified by the docket control number [PF-689]. Electronic comments on this notice may be filed online at many Federal Depository Libraries. Additional information on electronic submissions can be found below in this document.

Information submitted as comments concerning this document may be claimed confidential by marking any part or all of that information as ''Confidential Business Information'' (CBI). The 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 Room 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: Connie Welch, Product Manager (PM 21), Registration Division (7505C), Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. Office location, telephone number, and e-mail address: Crystal Mall #2, Room 227, 1921 Jefferson Davis Highway, Arlington, VA, 703-305-6226, e-mail: welch.connie@epamail.epa.gov.

SUPPLEMENTARY INFORMATION: EPA has received a pesticide petition (PP 3G4210) from Rhone-Poulenc Ag Company (Rhone-Poulenc), P.O. Box 12014, T.W. Alexander Drive, Research Triangle Park, NC 27709 proposing pursuant to section 408(d) of the Federal Food, Drug and Cosmetic Act (FFDC), 21 U.S.C. 346(d), to extend the temporary tolerances for the fungicide iprodione [3-(3,5-dichlorophenyl)-*N*-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide], its isomer [3-(1-methylethyl)-*N*-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide], and its metabolite [3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide] in or on the raw agricultural commodities tangerines and tangelos at 3.0 ppm. The current temporary tolerances expire on April 15, 1997. EPA has determined that the petition contains data or information regarding the elements set forth in section 408(d)(2) of the FFDC; 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. As required by section 408(d) of the FFDC, as recently amended by the Food Quality Protection Act (FQPA), Pub. L. 104-170), Rhone-Poulenc included in the petition a summary of the petition and authorization for the summary to be published in the Federal Register in a notice of receipt of the petition. The summary represents the views of Rhone-Poulenc. EPA is in the process of evaluating the petition. As required by section 408(d)(3) of the FFDC, EPA is including the summary as a part of this notice of filing. EPA may have made minor edits to the summary for the purpose of clarity.

I. Petition Summary

There is an extensive data base supporting the registration of iprodione. All the studies required under the reregistration process mandated by FIFRA 88 have been submitted. Most of these studies have been reviewed by the Agency and accepted.

The temporary tolerances for iprodione on tangelos and tangerines at 3.0 ppm are considered adequate to cover residues resulting from the limited use of iprodione in the proposed experimental use program. The tolerance level is based on field trial data with an overall mean residue of 1.19 ppm for tangelos and tangerines. The nature of the residue in plants is adequately defined. Plant metabolism studies have been reviewed in connection with previous petitions for tolerances. The residues of concern are iprodione, its isomer RP 30228, and its metabolite RP 32490. The Phase IV Review concluded that additional plant metabolism studies are not needed.

The nature of the residue in animals is adequately understood considering the limited use of iprodione on tangerines and tangelos as proposed in the experimental use permit (EUP). The residues of concern in animals are iprodione, its isomer RP 30228, its metabolites RP 32490 and RP 36114. The established tolerances for iprodione and its metabolites in meat, milk, poultry, and eggs are adequate to cover secondary residues in animal commodities resulting from the experimental use on tangerines and tangelos. Citrus feedstuff theoretically accounts only for a maximum of 20% of beef and dairy cattle diet. Citrus

feedstuff is not fed to poultry and swine. Since the EUP covers only a maximum of 4,000 acres which represents less than 0.4% of total U.S. bearing citrus fruit production for 1996, the actual iprodione contribution to the diet of livestock is not significant.

An adequate analytical method, gas liquid chromatography using an electron-capture detector, is available in the Pesticide Analytical Manual, Vol. II, for enforcement purposes. In the Phase IV Review, EPA requested that a substitute for benzene be used in the method of analysis used in new crop field trials. In response to this request, Rhone-Poulenc developed a common moiety GC method with a 0.05 ppm limit of quantitation (LOQ). An Independent Laboratory Validation for this method was submitted.

Iprodione is an important product for growers of several minor crops. These include garlic, ginseng, chinese mustard, broccoli, caneberries (blackberries, loganberries, and raspberries), and bushberries (blueberries, currant, elderberries, gooseberries, and huckleberries).

There are no Codex tolerances for iprodione on citrus commodities.

The following mammalian toxicity studies have been conducted to support the extension of the temporary tolerances for iprodione on tangerines and tangelos.

A. Toxicological Profile

1. *Acute toxicity*. A complete battery of acute toxicity studies for iprodione were completed. Iprodione has low acute toxicity. The acute oral toxicity study in the rat resulted in LD_{50}s of 3,629 mg/kg and 4,468 mg/kg for females and the combined sexes, respectively. The acute dermal LD_{50} in both rats and rabbits is >2,000 mg/kg. The acute inhalation LC_{50} for a 4–hour exposure to rats is >5.16 mg/L. No skin or eye irritation or dermal sensitization are produced by iprodione. Based on the results of these studies, iprodione was placed in toxicity category III.

Conclusion. Based on the acute toxicity data cited above, Rhone-Poulenc believes that iprodione does not pose any acute dietary risks.

2. *Mutagenicity*. Mutagenicity studies completed include *Salmonella typhimurium* and *Escherichia coli* reverse mutation (all negative), induction tests with *Escherichia coli* (all negative), DNA repair test in *Escherichia coli* (negative), DNA damage in *Bacillus subtilis* (positive), Rec assay in *Bacillus subtilis* (negative), mutagenicity in *Saccharomyces cerevisiae* D7 (negative), forward mutation in CHO/HGPRT assay (negative), chromosome aberrations in CHO cells (negative), sister chromatid exchange in CHO cells (negative), *in vivo* micronucleus test (negative), *in vivo* host mediated assay with *Salmonella typhimurium* G46 (negative) and dominant lethal test in male mice (negative).

Conclusion. Based on the data cited above, Rhone-Poulenc believes that the weight of evidence indicates that iprodione does not pose a mutagenic hazard to humans.

3. *Rat metabolism*. ^{14}C-Iprodione was absorbed readily from the gastrointestinal tract, metabolized, and excreted by rats of both sexes following single low [50 mg/kg] and high [900 mg/kg] oral doses and 14 repeated low [50 mg/kg] doses. Peak blood levels were observed at 4 and 2 hours, respectively, in low-dose males and females and at 6 hours in high-dose rats of both sexes. The elimination of ^{14}C from the blood was slower in males than females. There were both dose and sex-related differences noted in absorption: males absorbed a greater percentage of the low and repeated doses than females. Although levels of ^{14}C were found in most tissues monitored, the levels were ≤0.5% of the total amount administered. It is to be noted that the testes of the low-dose [50 mg/kg] males showed no detectable amount of ^{14}C; the high dose in the rat chronic toxicity/carcinogenicity study where testicular tumors were observed was 69 mg/kg. The primary route of elimination of ^{14}C following single and repeat low-dose exposure was the urine, and the feces was the primary route following high-dose exposure. Dealkylation and cleavage of the hydantoin ring were the two primary steps in the metabolism of iprodione. Hydroxylation of the phenyl ring and oxidation of the alkyl chain also occurred. The primary metabolites recovered from the urine [both sexes] included a dealkylated derivative of iprodione and two polar but unidentified compounds. Males produced larger amounts of a hydantoin ring-opened metabolite than females, and the urine of the females contained a higher proportion of unchanged parent compound than that of the males. Several urinary metabolites were not identified. The feces contained much larger amounts of unchanged parent compound than the urine, which the authors suggested was unabsorbed iprodione and metabolites or hydrolyzed conjugates of absorbed material.

In another single oral administration study in rats using 50 mg/kg, no sex differences were apparent in the excretion profile, and both urinary elimination [37%M/28%F] and fecal excretion [56%M/50%F] are major routes of excretion. The metabolism of iprodione was extensive and characterized by the large number of metabolites formed. In the urine, RP 36115, RP 32490, RP 36112, RP 36119, and RP 30228 were either confirmed or indicated. The feces contained a large proportion of parent compound; the major fecal metabolites were RP 36115, RP 36114, RP 32490, and RP 30228. A general metabolic pathway for iprodione in the rat indicates that biotransformation results in hydroxylation of the aromatic ring, degradation of the isopropylcarbamoyl chain and rearrangement followed by cleavage of the hydantoin moiety. Additionally, structural isomers of iprodione resulting from molecular rearrangement, as well as intermediates in the pathway were detected.

4. *Chronic effect*. The chronic toxicity of iprodione has been extensively studied in three species, i.e. dog, rat, and mouse:

a. *Dog*—i. In the first study, conducted at dose levels of 100, 600, and 3,600 ppm a clear no observed effect level (NOEL) was established at 100 ppm (4.2 mg/kg/day). The lowest effect level (LEL) was set at 600 ppm based on equivocal effects such as decreased prostate weight and an increased incidence of Heinz bodies in erythrocytes in males.

ii. A second study (MRID 00144391, 41327001, 42211101), conducted at dose levels of 200, 300, 400, and 600 ppm, was performed as a bridging study for EPA in order to establish a higher NOEL. In this study no clear indications of any toxicological effects were noted. From the results of the two complementary studies, a conservative NOEL of 400 ppm (17.5 mg/kg/day in males and 18.4 mg/kg/day in females) and a LEL of 600 ppm (24.6 mg/kg/day in males and 26.4 mg/kg/day in females) based on depressed blood cell parameters were established.

b. *Rat*—i. In an initial study, Charles River outbred CD albino rats were fed diets containing 125, 250, or 1,000 ppm (6.25, 12.5, and 50 mg/kg/day) of iprodione technical for 24 months. In this study, the NOEL of iprodione in rats was observed to be greater than 1,000 ppm (i.e. >50 mg/kg/day).

ii. In a repeat study, Sprague Dawley rats were administered 150, 300, or 1,600 ppm iprodione technical in the diet for 24 months. The NOEL for chronic toxicity was set at 150 ppm (mean intake of males and females was 7.25 mg/kg/day) and the LEL was 300 ppm (12.4 mg/kg/day for males and 16.5 mg/kg/day for females).

c. *Mouse*—i. In an initial study, Carworth CF-1 outbred albino mice were fed diets containing 200, 500, 1,250 ppm (28.6, 71.4, and 178.6 mg/kg/day) of iprodione technical for 18 months. In this study, the NOEL of iprodione in mice was greater than 1,250 ppm (i.e. >178.6 mg/kg/day).

ii. In a repeat study, iprodione technical was administered at dietary concentrations of 160, 800, or 4,000 ppm to CD-1 mice for 99 weeks. The NOEL for chronic toxicity was set at 160 ppm (23 mg/kg/day for males and 27 mg/kg/day for the females) and the LEL at 800 ppm (115 mg/kg/day for males and 138 mg/kg/day for females).

Conclusion. The chronic reference dose (RfD) for iprodione is 0.0725 mg/kg/day. This RfD is based on the NOEL of 7.25 mg/kg/day determined from the rat combined chronic toxicity and carcinogenicity study. An uncertainty factor of 100 has been included in the RfD value to account for inter and intra-species variations.

5. *Carcinogenicity*—a. *Rat*—i. In the initial 2-year combined toxicity/carcinogenicity study, Charles River outbred CD albino rats were fed diets containing 125, 250, or 1,000 ppm of iprodione technical. In this study, no increase in neoplastic lesions were observed at any of the treatment levels. The NOEL for oncogenicity in rats was observed to be greater than 1,000 ppm (>50 mg/kg/day).

ii. In the repeat study conducted with Sprague Dawley rats administered 150, 300, or 1,600 ppm iprodione technical in the diet, no increase in tumor incidence was noted at interim sacrifice. Microscopic examination of animals found dead, sacrificed in extremis, or killed at termination after 104 weeks revealed an increased incidence of benign interstitial cell tumors in rats treated with 1,600 ppm (29/60 animals) compared with controls (3/60). No increased incidence of any other tumor type was recorded. No treatment-related neoplastic lesions were observed in the 150 or 300 ppm treatment groups. The NOEL for oncogenicity in males in this study was 300 ppm (12.4 mg/kg/day) and the LEL 1,600 ppm (69 mg/kg/day). There was no indications of oncogenicity in females at any dose level.

b. *Mouse*—i. In the initial study, Carworth CF-1 outbred albino mice were fed diets containing 200, 500, 1,250 ppm of iprodione technical for 18 months. In this study, no increase in neoplastic lesions were observed at any of the treatment levels. The NOEL for oncogenicity in mice was observed to be greater than 1,250 ppm (>178.6 mg/kg/day).

ii. In the repeat mouse oncogenicity study, iprodione technical was administered at dietary concentrations of 0, 160, 800, or 4,000 ppm to CD-1 mice for 99 weeks. Microscopic examination of animals found dead, sacrificed in extremis, or killed at termination after 99 weeks revealed an increased incidence of benign and malignant liver cell tumors in both sexes. A slight increase in the incidence of luteomas in the ovaries of females was also noted at 4,000 ppm. No increased incidence of any other tumor type was recorded. No treatment-related neoplastic lesions were observed in the 160 or 800 ppm treatment groups. The NOEL for oncogenicity in this study was 800 ppm (115 mg/kg/day in males and 138 mg/kg/day in females) and the LEL was 4,000 ppm (604 mg/kg/day in males and 793 mg/kg/day in females).

Discussion. A number of mechanistic studies have been conducted in order to elucidate the mechanism of testicular toxicity and carcinogenicity in the rat and hepatic toxicity and carcinogenicity in the mouse.

c. *Testicular toxicity and carcinogenicity in the rat*. The results of recently completed mechanistic studies have further elucidated the mechanism of iprodione testicular toxicity. The available evidence suggests that the primary mode of action of iprodione in the testes is via a disruption of testosterone biosynthesis in the interstitial cells. The resulting reduction in testosterone secretion may lead to a compensatory hyperplasia in order to maintain normal hormonal homeostasis. Tumors may then develop in sensitive species, such as the rat, due to the persistent hyperplasia. The evidence supporting such a mechanism of action can be summarized as follows:

- Iprodione and certain metabolites (RP 36112 and RP 36115) have been shown to inhibit testosterone secretion from cultures of porcine Leydig cells. Recently, it has been demonstrated that iprodione inhibits testosterone synthesis and release from rat testicular sections *in vitro*.
- The site of action whereby iprodione and its metabolites (RP 36112 and RP 36115) appear to modulate Leydig cell steroidogenesis has recently been identified using porcine Leydig cell cultures. Iprodione appears to act through a rapid, reversible, interaction with cholesterol and/or steroid hormones at the level of some transport proteins and/or steroidogenic enzymes.
- Hormonal perturbation has been observed in a rat *in vivo* study with iprodione. These were however limited to increases in LH and FSH levels following 15 days of iprodione treatment and slight differences in the secretion pattern of LH and testosterone following 30-days of treatment. In the same study, decreases in absolute and relative weights of total accessory sex organs and seminal vesicles (but not the prostate or epididymides) were noted at final sacrifice. By contrast, treatment with flutamide induced marked and persistent increases in plasma levels of testosterone, estradiol, LH and FSH and these were associated with marked decreases in the epididymides and accessory sex organs weights (ventral prostate and seminal vesicles).
- Data from subchronic and chronic toxicity studies show that several major target organs (adrenals, testicular and ovarian interstitial cells) are tissues which secrete steroid hormones.
- No clear evidence of competitive binding to the androgen receptor was found for iprodione or its major metabolites (RP 32490, RP 36114, RP 36118, and RP 36119). Several minor metabolites did exhibit a binding activity close to the reference compound flutamide. However, it is generally accepted that the anti-androgenic activity of flutamide is due to its major metabolite hydroxyflutamide, which binds to the androgen receptor with a greater affinity than flutamide (Simard *et al*, 1986).

It is well established that a threshold can be expected for hormonally mediated oncogenic mechanisms. In the rat chronic/oncogenicity study, Leydig cell tumors were only observed at highly toxic dose levels which were at or above the MTD (mean body weight gains were reduced from 13.7% to 16.4% between weeks 0 to 12, 12 to 22, and 0 to 104 of the study in high dose males) and clear thresholds exist for both non-neoplastic lesions and tumors. In addition, the cellular effects of iprodione have been demonstrated to be reversible since the inhibition of testosterone biosynthesis in porcine Leydig cells was removed following removal of the iprodione from the cell culture. It can also be noted that the rat appears to be one of the most sensitive species to benign interstitial cell tumors. They are, however, a very uncommon tumor type in humans. It is evident that the rat is much more sensitive to chemical insult of the Leydig cells than is man and, consequently, that humans are at less risk for Leydig cell testicular tumors than rats. This implies that the threshold dose for humans would be greater than for rats (See C. C. Capen, *Leydig Cell Tumors: Pathology, Physiology, and Mechanistic Considerations in Rats*, The Toxicology Forum, 1994 Annual Summer Meeting, p. 110).

d. *Hepatotoxicity and carcinogenicity in male and female mice*. In the mouse oncogenicity study, the development of hepatocellular tumors in mice appeared secondary to hepatic toxicity at a dose level at which body weight gain was severely reduced indicating that the MTD was probably exceeded (over the duration of the study, weight gain was reduced 14% and 11% in high dose males and females respectively. During weeks 18 to 45, weight gain was reduced 44% and 47%, respectively. This severity of the weight gain decrement is compounded by the fact that the livers in these animals weighed more than double their respective controls, i.e., the weight gain decrement is even more serious than the body weights alone would indicate). The animals at the highest dose level, and to a lesser extent, the mid-dose group, exhibited signs of liver toxicity, including increased liver weights, hepatocytic hypertrophy, enlarged eosinophilic hepatocytes, pigmented macrophages, centrilobular necrosis, amyloid deposits, and statistically significant increases in levels of the liver enzymes GPT and GOT. Clear NOELs exist for these effects. In a recently completed 14-day toxicity study in male mice, dose levels similar to those at which tumors were observed in the mouse carcinogenicity study induced a number of hepatic changes including the induction of Cytochrome P450 isoenzymes and cellular proliferation.

The HED Carcinogenicity Peer Review Committee (CPRC) met in 1994 and determined that iprodione should be classified a group B2 carcinogen. The CPRC recommended that a low dose quantitative risk assessment for iprodione be estimated from the benign rat interstitial cell tumors of the testes, and also from the mouse male and female liver tumors separately. It is the opinion of Rhone-Poulenc that the B2 classification as well as the use of low dose quantitative risk assessment for iprodione is inappropriate.

The male interstitial cell tumors seen only at the high dose in the lifetime rat study with iprodione were due to a mode of action with a clear threshold. This conclusion is based on the following rationale: (i) The tumors were benign and only observed at a dose level at or above the MTD, (ii) the mechanistic toxicological research designed to elucidate the biochemical mode of action, and (iii) the consensus of scientific experts that benign Leydig cell tumors in the rat are not useful predictors of human disease. Thus, because the mechanism of action shows a clear threshold, and because the potential toxicological hazard has no direct relevance for human health, Rhone-Poulenc believes that the dose response assessment for the benign interstitial cell effects in the rat testes should rely on threshold, non-linear, margin of exposure procedures and not on linear low dose extrapolations.

The mouse liver tumors also arose from a toxicological mechanism having a clear threshold. A study conducted to elucidate the mode of action of the mouse liver tumorigenesis has been described above. The relationship between hormonally active compounds and the etiology of mouse liver cancer is well established. Rhone-Poulenc therefore contends that a complete evaluation of the carcinogenicity issue indicates that iprodione is a threshold carcinogen acting through a non-genotoxic mechanism of toxicity. The application of a low dose quantitative risk assessment for iprodione is inappropriate. Rhone-Poulenc therefore recommends the use of an uncertainty factor approach and a RfD of 0.0725 mg/kg/day.

6. *Teratology rat*—a. The embryo/fetal toxicity and teratogenicity of iprodione were evaluated in Sprague-Dawley rats at oral (gavage) dose levels of 40, 90, or 200 mg/kg/day. Iprodione showed no embryotoxicity or teratogenicity at any of the dose levels examined. Although no maternal effects were detected at any treatment level in the definitive study, dose selection was justified from the pilot study in which maternal toxicity was noted at 120 and 240 mg/kg/day. In addition, an increase in the average number of late resorptions per litter was observed at 240 mg/kg/day. A clear and conservative developmental and maternal NOEL was observed at 90 mg/kg/day.

b. *Rabbit*. The embryo/fetal toxicity and teratogenicity of iprodione were evaluated in rabbits at oral (gavage) dose levels of 20, 60, or 200 mg/kg/day. No treatment-related embryotoxicity or teratogenicity was noted at doses of 20 or 60 mg/kg/day. Even though iprodione at 200 mg/kg/day was too maternally toxic for a complete teratologic evaluation, no malformations were observed in the fetuses examined from this group. The developmental NOEL was 60 mg/kg/day and the maternal NOEL was 20 mg/kg/day based decreases in maternal body weight gain.

Conclusion. Based on the studies cited above, iprodione is not a developmental toxicant.

7. *Reproductive effects*. In a multi-generation study, iprodione was administered to male and female Sprague-Dawley rats via dietary admixture at dose levels of 300, 1,000, or 2,000/3,000 ppm (for males 18.5, 61.4, and 154.8 mg/kg/day and for females 22.49, 76.2, and 201.2 mg/kg/day, respectively). It was necessary to reduce the high dose from 3,000 to 2,000 ppm following the first mating period of the F1 parents owing to excessive toxicity. No effects on reproductive performance were observed at any of the treatment levels. Parental toxicity, as evidenced by reduced body weight, body weight gain and food consumption was observed at dietary levels of 1,000 ppm and higher. Effects on pup viability and pup weight were noted at 2,000/3,000 ppm. The NOELs for parental and offspring toxicity were 300 ppm and 1,000 ppm, respectively.

Conclusion. Based on the study cited above, Rhone-Poulenc believes that iprodione is not a reproductive toxicant.

8. *Neurotoxicity*. Iprodione does not have a chemical function associated with neurotoxicity. No neurotoxic symptoms have been recorded in any toxicity study conducted with iprodione. Iprodione is therefore not considered to be a neurotoxin.

B. Aggregate Exposure

In addition to dietary exposure, the FQPA lists three potential sources of exposure to the general population that must be addressed. These are pesticides in drinking water, exposure from non-occupational sources, and the potential cumulative effect of pesticides with similar toxicological modes of action.

1. *Drinking water*. Iprodione, applied according to labeled use and good agricultural management practices, is predicted and demonstrated to present no significant, if any, concentrations in drinking water sources. Iprodione's physical-chemical properties and actual measured environmental concentrations in field dissipation/monitoring studies provides support for this conclusion. There is no established Maximum Concentration Level or Health Advisory Level for iprodione under the Safe Drinking Water Act.

2. *Non-occupational exposure discussion*. Iprodione is included in a number of formulations used for professional treatment of golf-courses and turf. Posting and notification procedures ensure that there is no exposure to the general public either during or following treatment.

A single granular formulation containing low quantities of iprodione (1.02%) is available to the homeowner for use on residential ornamentals and lawns. Treatment rates (1.25 oz a.i./2,500 - 5,000 sq. ft.) and the number of treatments allowed per year (2-3 max.) are low. Rhone-Poulenc believes that

this minor use will not impact significantly on the aggregate exposure to iprodione since it represents less than 4% of total iprodione use. Two formulations are registered for home and garden use but they have not been commercialized. They therefore do not need to be included in the aggregate exposure risk estimate for iprodione.

Conclusion. Rhone-Poulenc does not expect that the ornamental and turf uses add significantly to the aggregate exposure for iprodione; thus, dietary exposure is the main consideration for risk assessment purposes.

3. *Common mechanism of action discussion*. Risk assessment based on exposure to multiple chemicals is not appropriate for the following reasons:

- Similar toxicological end-points may be induced by a number of different mechanisms of action that are unlikely to be additive.
- Toxicological end-points for RfD setting may be different even between chemicals acting via a common mechanism.
- Margins between NOELs and LELs may be large and variable from chemical to chemical.
- Multiple chemical dietary exposures are low and infrequent.
- For a majority of chemicals insufficient or incomplete data is available to identify a common mechanism of action.

However, the Agency has previously noted both structural and toxicological similarities between iprodione, procymidone, and vinclozolin. There are clear differences in both the type and magnitude of effects observed after exposure to iprodione in contrast to vinclozolin and procymidone. In multi-generation studies, iprodione had no adverse effects on reproductive performance, fertility, fecundity, or sex ratio, even at dose levels that induced dramatic parental toxicity. However in similar types of studies, procymidone induced adverse effects on fertility and abnormalities of male sex organs and vinclozolin induced infertility, genital and reproductive tract malformations and pseudohermaphroditism in male rats.

Vinclozolin and procymidone are known to exert their endocrine effects via a blockage of the androgen receptor in a similar way to the potent anti-androgen flutamide (Hosokawa *et al*, 1993a and 1993b, Kelce *et al*, 1994). By contrast, iprodione has poor binding affinity to the androgen receptor and the primary lesion appears to be a blockage of testosterone biosynthesis and secretion in a similar manner to ketoconazole; a therapeutic agent that also has no effects on fertility or fecundity (Heckman *et al*, 1992). Subsequently, iprodione only appears to induce transient changes in plasma hormone levels until compensatory mechanisms take effect. Consequently, iprodione does not possess the potent anti-androgenic activity of flutamide (or its structural analogs).

Conclusion. Therefore, Rhone-Poulenc believes that consideration of a common mechanism of toxicity is not appropriate at this time since there are no reliable data to indicate that the toxic effects caused by iprodione would be cumulative with those of any other compound. Based on this point, Rhone-Poulenc has considered only the potential risks of iprodione in its exposure assessment.

C. Safety Determination

1. *DRES–U.S. population–infants–children (1-6 yrs old).* According to EPA's Dietary Risk Evaluation System (DRES) chronic analysis, the % RfD falls within a safe margin even when considering tolerance levels and 100% crop treated. For the overall U.S. population, dietary exposure to iprodione uses 0.353% of the RfD when using Anticipated Residue Contribution (ARC) or 54.22 % of the RfD when using tolerance levels. Exposure to iprodione resulting from the use of the product on tangelos and tangerines is negligible considering the low residues and limited acreage covered in the EUP (maximum of 4,000 acres). Dietary contribution from tangerines and tangelos accounts for less than 1% of total exposure and the cancer risk for these uses is estimated to be less than 5×10^{-8}.

A DRES detailed acute exposure analysis was performed by EPA using conservative values. The resulting high end Margin of Exposure value of 100 for the DRES subgroup of concern (females 13 + years) is above the acceptable level and demonstrates no acute dietary concern.

For the reasons stated earlier (see Unit A.5.) Rhone-Poulenc considers the use of a low dose quantitative risk assessment for iprodione to be inappropriate. As previously indicated Rhone-Poulenc recommends the use of a safety factor approach and a RfD of 0.0725 mg/kg/day. The use the Q* (Q star) value of 0.0439 $(mg/kg/day)^{-1}$ previously calculated by EPA represents a very conservative estimate of the lifetime cancer risk from potential residues of iprodione.

Nevertheless, an assessment of the lifetime cancer risk from iprodione residues in food using a Q* value of 0.0439 $(mg/kg/day)^{-1}$ has been conducted. This assessment indicates the total cancer risk to be in the *de minimus* range of 10^{-6}, even with a very conservative Q* value. Based on results of the analyses, iprodione residues in currently registered foods would not be expected to result in significant levels of chronic toxicity to any segment of the U.S. population. The upper bound cancer risk attributed to the use of iprodione on tangerines and tangelos is calculated to be negligible. Therefore, the added use will not measurably increase the cancer risk estimate for any population subgroup.

2. *Infants and children–adequate margin of safety*. In assessing the potential for additional sensitivity of infants and children to residues of iprodione the available teratology and reproductive toxicity studies and the potential for endocrine modulation by iprodione were considered.

Developmental studies in two species indicate that iprodione has no teratogenic potential, even at maternally toxic dose levels. Maternal and developmental NOELs and lowest observed effect levels (LOELs) were generally comparable indicating no increased susceptibility of developing organisms. Multi-generation rodent reproduction studies indicated that iprodione has no adverse effects on reproductive performance, fertility, fecundity, or sex ratio. Effects on pup weight and viability were only noted in the presence of severe parental toxicity.

The mechanism of endocrine modulation associated with iprodione (inhibition of testosterone biosynthesis) appears to be distinct from that of anti-androgens acting at the level of the androgen receptor and may help to explain the lack of adverse effects on reproductive function observed with iprodione.

Therefore, based upon the completeness and reliability of the toxicity data and the conservative exposure assessment, Rhone-Poulenc believes that there is a reasonable certainty that no harm will result to infants and children from exposure to residues of iprodione and no additional uncertainty factor is warranted.

3. *Endocrine discussion and conclusion*. As indicated in unit A. 5., the primary lesion at the level of the target organs (testes, ovaries, and adrenals) is likely to be related to an inhibition of steroid/androgen biosynthesis. The resulting endocrine toxic effect due to iprodione is fairly moderate compared to that produced by potent endocrine disruptors such as flutamide (and other structural analogs) and is insufficiently potent to produce effects on reproduction or development.

The increased incidence in tumors in both rats and mice was only observed when animals were treated at or above the MTD. For all three tumor sites (testes, liver, ovary) tumors only develop on pre-existing non-neoplastic lesions (cell hypertrophy/vacuolation, hyperplasia) and a clear threshold level exist for both non-neoplastic lesions and tumors. Those thresholds are far in excess of those levels of iprodione that the general public would be exposed to.

Conclusion. Rhone-Poulenc believes that iprodione would not be expected to induce any adverse effects related to endocrine disruption in members of the general population via the consumption of food crops containing residues of this compound.

II. Public Record

EPA invites interested persons to submit comments on this notice of filing. Comments must bear a notation indicating the docket control number, [PF-689].

A record has been established for this notice of filing under docket control number [PF-689] (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 public record is located in Room 1132 of the Public Response and Program Resources Branch, Field Operations Division (7506C), Office of Pesticide Programs, Environmental Protection Agency, Crystal Mall #2, 1921 Jefferson Davis Highway, Arlington, VA.

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

Electronic comments must be submitted as ASCII file avoiding the use of special characters and any form of encryption.

The official record for this notice of filing, as well as the public version, as described above will be kept in paper form. Accordingly, EPA will transfer all comments received electronically into printed, paper form as they are received and will place the paper copies in the official rulemaking record which will also include all comments submitted directly in writing. The official rulemaking record is the paper record maintained at the address in ''ADDRESSES'' at the beginning of this document.

List of Subjects

Environmental protection, Administrative practice and procedure, Agricultural commodities, Pesticides and pests, Reporting and recordkeeping requirements.

Dated: January 15, 1997.

Stephen L. Johnson,

Director, Registration Division, Office of Pesticide Programs.

[FR Doc. 97–1752 Filed 1–23–97; 8:45 am]
BILLING CODE 6560–50–F

[PF-691; FRL-5583-6]

Rhone-Poulenc Ag Company; Pesticide Tolerance Petition Filing

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice of filing.

SUMMARY: This notice announces the filing of a pesticide petition proposing the extension of the time-limited tolerance for the combined residues of the fungicide iprodione [3-(3,5-dichlorophenyl)-*N*-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide], its isomer [3-(1-methylethyl)-*N*-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide], and its metabolite [3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide] (CAS Number 36734-19-7, PC Code 109801) in or on the raw agricultural commodity (RAC) cottonseed at 0.10 parts per million (ppm). The notice includes a summary of the petition prepared by the petitioner, Rhone-Poulenc Ag Company.

DATES: Comments, identified by the docket number [PF-691], must be received on or before February 24, 1997.

ADDRESSES: By mail, submit written comments to: Public Response and Program Resources Branch, Field Operations Division (7506C), Office of Pesticide 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 sending electronic mail (e-mail) to: 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. Comments 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-691]. Electronic comments on this notice of filing may be filed online at many Federal Depository Libraries. Additional information on electronic submissions can be found in Unit II. of this document.

Information submitted as comments 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: Connie Welch, Product Manager (PM 21), Registration Division (7505W), Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. Office location, telephone number, and e-mail address: Crystal Mall #2, Room 227, 1921 Jefferson Davis Highway, Arlington, VA, 703-305-6226, e-mail: welch.connie@epamail.epa.gov.

SUPPLEMENTARY INFORMATION: EPA has received a pesticide petition (PP 2F4111) from Rhone-Poulenc Ag Company (Rhone-Poulenc), P.O. Box 12014, T.W. Alexander Drive, Research Triangle Park, NC 27709 proposing pursuant to section 408(d) of the Federal Food, Drug and Cosmetic Act (FFDCA), 21 U.S.C. 346(d), to amend 40 CFR part 180 by extending the time-limited tolerance for the fungicide iprodione [3-(3,5-dichlorophenyl)-*N*-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide], its isomer [3-(1-methylethyl)-*N*-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide], and its metabolite [3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide] in or on the RAC cottonseed at 0.10 ppm. The current time-limited tolerance was established under pesticide petition (PP) 2F4111 and expires on March 15, 1997. 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.