ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[OPP–300801; FRL–6064–6]

RIN 2070–AB78

Azoxystrobin; Pesticide Tolerance

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This regulation establishes tolerances for combined residues of azoxystrobin (methyl(*E*)-2-(2-(6-(2-cyanophenoxy)pyrimidin-4-yloxy)phenyl)-3-methoxyacrylate and its Z isomer (methyl(*Z*)-2-(2-(6-(2-cyanophenoxy)pyrimidin-4-yloxy)phenyl)-3-methoxyacrylate) in or on almond hulls, aspirated grain fractions, bananas (postharvest), canola, cucurbits, peanut hay, pistachios, potatoes, rice, stone fruits, and wheat; and residues of azoxystrobin (only) on fat of cattle, goats, hogs, horses, and sheep; meat of cattle, goats, hogs, horses, and sheep; meat byproducts of cattle, goats, hogs, horses, and sheep; and milk. Zeneca Ag Products requested these tolerances under the Federal Food, Drug, and Cosmetic Act, as amended by the Food Quality Protection Act of 1996.

DATES: This regulation is effective March 17, 1999. Objections and requests for hearings must be received by EPA on or before May 17, 1999.

ADDRESSES: Written objections and hearing requests, identified by the docket control number, [OPP–300801], must be submitted to: Hearing Clerk (1900), Environmental Protection Agency, Rm. M3708, 401 M St., SW., Washington, DC 20460. Fees accompanying objections and hearing requests shall be labeled ''Tolerance Petition Fees'' and forwarded to: EPA Headquarters Accounting Operations Branch, OPP (Tolerance Fees), P.O. Box 360277M, Pittsburgh, PA 15251. A copy of any objections and hearing requests filed with the Hearing Clerk identified by the docket control number, [OPP–300801], must also be submitted to: Public Information and Records Integrity Branch, Information Resources and Services Division (7502C), Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. In person, bring a copy of objections and hearing requests to Rm. 119, Crystal Mall #2, 1921 Jefferson Davis Hwy., Arlington, VA.

A copy of objections and hearing requests filed with the Hearing Clerk may be submitted electronically by sending electronic mail (e-mail) to: opp-docket@epa.gov. Copies of objections and hearing requests must be submitted as an ASCII file avoiding the use of special characters and any form of encryption. Copies of objections and hearing requests will also be accepted on disks in WordPerfect 5.1/6.1 file format or ASCII file format. All copies of objections and hearing requests in electronic form must be identified by the docket control number [OPP–300801]. No Confidential Business Information (CBI) should be submitted through e-mail. Electronic copies of objections and hearing requests on this rule may be filed online at many Federal Depository Libraries.

FOR FURTHER INFORMATION CONTACT: By mail: Cynthia Giles-Parker, 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: Rm. 249, Crystal Mall #2, 1921 Jefferson Davis Hwy., Arlington, VA, 703–305–7740, giles-parker.cynthia@epa.gov.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of October 8, 1997 (62 FR 52544)(FRL–5746–9) and December 11, 1998 (63 FR 68458)(FRL–6043–3), EPA issued notices pursuant to section 408 of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 346a as amended by the Food Quality Protection Act of 1996 (FQPA) (Pub. L. 104–170) announcing the filing of two pesticide petitions (PP) 8F4995 and 7F4864, for tolerances by Zeneca Ag Products, 1800 Concord Pike, P.O. Box 15458, Wilmington, DE 19850–5458. This notice included a summary of the petition prepared by Zeneca Ag Products, the registrant. There were no comments received in response to the notices of filing.

The petitions requested that 40 CFR part 180 be amended by establishing tolerances for combined residues of the fungicide azoxystrobin (methyl(*E*)-2-(2-(6-(2-cyanophenoxy)pyrimidin-4-yloxy)phenyl)-3-methoxyacrylate) and its Z isomer (methyl(*Z*)-2-(2-(6-(2-cyanophenoxy)pyrimidin-4-yloxy)phenyl)-3-methoxyacrylate) in or on almond hulls at 4.0 parts per million (ppm), bananas (postharvest) at 2.0 ppm, canola at 1.0 ppm, cucurbits at 0.3 ppm, peanut hay at 1.5 ppm, pistachios at 0.01 ppm, potatoes at 0.03 ppm, rice grain at 4.0 ppm, rice straw at 11 ppm, rice hulls at 20 ppm, stone fruits at 1.5 ppm, tree nuts at 0.01 ppm; wheat grain at 0.04 ppm, wheat bran at 0.12 ppm, wheat hay at 13.0 ppm, wheat straw at 4.0 ppm; wheat aspirated grain fractions at 15.0 ppm, and for the residues of azoxystrobin (only) in eggs at 0.4 ppm; fat of cattle, goats, hogs, horses, poultry, and sheep at 0.01 ppm; kidney of cattle at 0.06 ppm; liver of cattle, goats, horses, and sheep at 0.3 ppm; liver of hogs at 0.2 ppm; liver of poultry at 0.4 ppm; meat of cattle, goats, hogs, horses, poultry, and sheep at 0.01 ppm; and milk at 0.006 ppm.

I. Background and Statutory Findings

Section 408(b)(2)(A)(i) of the FFDCA allows EPA to establish a tolerance (the legal upper limit for a pesticide chemical residue in or on a food) only if EPA determines that the tolerance is ''safe.'' Section 408(b)(2)(A)(ii) defines ''safe'' to mean that ''there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information.'' This includes exposure through drinking water and in residential settings, but does not include occupational exposure. Section 408(b)(2)(C) requires EPA to give special consideration to exposure of infants and children to the pesticide chemical residue in establishing a tolerance and to ''ensure that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the pesticide chemical residue....''

EPA performs a number of analyses to determine the risks from aggregate exposure to pesticide residues. For further discussion of the regulatory requirements of section 408 and a complete description of the risk assessment process, see the final rule on Bifenthrin Pesticide Tolerances (62 FR 62961, November 26, 1997) (FRL–5754–7).

II. Aggregate Risk Assessment and Determination of Safety

Consistent with section 408(b)(2)(D) of the FFDCA, EPA has reviewed the available scientific data and other relevant information in support of this action. EPA has sufficient data to assess the hazards of azoxystrobin and to make a determination on aggregate exposure, consistent with section 408(b)(2), for establishment of permanent tolerances for combined residues of azoxystrobin (methyl(*E*)-2-(2-(6-(2-cyanophenoxy)pyrimidin-4-yloxy)phenyl)-3-methoxyacrylate) and its Z isomer (methyl(*E*)-2-(2-(6-(2-cyanophenoxy)pyrimidin-4-yloxy)phenyl)-3-methoxyacrylate) in or on almond hulls at 4.0 ppm, aspirated grain fractions at 10 ppm, bananas (pre-harvest and postharvest) at 2.0 ppm (of which not more than 0.1 ppm is

contained in the pulp), canola at 1.0 ppm, cucurbits at 0.3 ppm, peanut hay at 2.0 ppm, pistachios at 0.01 ppm, potatoes at 0.03 ppm, rice grain at 5.0 ppm, rice straw at 12 ppm, rice hulls at 20 ppm, stone fruits at 1.5 ppm, tree nuts at 0.010 ppm, wheat grain at 0.10 ppm, wheat bran at 0.20 ppm, wheat hay at 15 ppm, wheat straw at 4.0 ppm, and for the residues of azoxystrobin (only) in fat of cattle, goats, hogs, horses, and sheep at 0.010 ppm; meat of cattle, goats, hogs, horses, and sheep at 0.01 ppm; meat byproducts of cattle, goats, hogs, horses, and sheep at 0.010 ppm; and milk at 0.006 ppm. A permanent domestic tolerance of 0.5 ppm already exists for bananas and will be amended by this rule. Temporary tolerances already exist for fat of cattle, goats, hogs, horses, and sheep at 0.01 ppm; kidney of cattle, goats, hogs, and sheep at 0.06 ppm; liver of cattle, goats, horses, and sheep at 0.3 ppm; liver of hogs at 0.2 ppm; meat of cattle, goats, hogs, horses, and sheep at 0.01 ppm; cucurbits at 1.0 ppm; milk at 0.006 ppm; potatoes at 0.03 ppm; rice grain at 4 ppm; rice hulls at 20 ppm; and rice straw at 10 ppm. A tolerance of 0.8 ppm already exists for peaches; this will be superseded by the stone fruits tolerance of 1.5 ppm that is being established in this rule. Several of the tolerances that are being established by this rule are different from (often higher than) those proposed by Zeneca Ag Products. EPA review of the data submitted by the company lead to an Agency decision to modify the proposed tolerances. During these reviews it was also determined that azoxystrobin uses that have been registered so far do not lead to a need to establish tolerances for poultry commodities (including eggs). EPA's assessment of the exposures and risks associated with establishment of the above tolerances follows.

A. Toxicological Profile

EPA has evaluated the available toxicity data and considered its validity, completeness, and reliability as well as the relationship of the results of the studies to human risk. EPA has also considered available information concerning the variability of the sensitivities of major identifiable subgroups of consumers, including infants and children. The nature of the toxic effects caused by azoxystrobin is discussed in this unit.

1. *Acute toxicity.* The acute oral toxicity study in rats of technical azoxystrobin resulted in an LD_{50} of > 5,000 milligrams/kilogram (mg/kg) (limit test) for both males and females. The acute dermal toxicity study in rats of technical azoxystrobin resulted in an LD_{50} of > 2,000 mg/kg (limit dose). The acute inhalation study of technical azoxystrobin in rats resulted in an LC_{50} of 0.962 mg/liter (mg/L) in males and 0.698 mg/L in females. In an acute oral neurotoxicity study in rats dosed once by gavage with 0, 200, 600, or 2,000 mg/kg azoxystrobin, the systemic toxicity no observable adverse effect level (NOAEL) was < 200 mg/kg and the systemic toxicity lowest observed adverse effect level (LOAEL) was 200 mg/kg, based on the occurrence of transient diarrhea in both sexes. There was no indication of neurotoxicity at the doses tested.

2. *Mutagenicity.* Azoxystrobin was negative for mutagenicity in the salmonella/mammalian activation gene mutation assay, the mouse micronucleus test, and the unscheduled DNA synthesis in rat hepatocytes/mammalian cells (*in vivo*/*in vitro* procedure study). In the forward mutation study using L5178 mouse lymphoma cells in culture, azoxystrobin tested positive for forward gene mutation at the TK locus. In the *in vitro* human lymphocytes cytogenetics assay of azoxystrobin, there was evidence of a concentration related induction of chromosomal aberrations over background in the presence of moderate to severe cytotoxicity.

3. *Rat metabolism*. In this study, azoxystrobin--unlabeled or with a pyrimidinyl, phenylacrylate, or cyanophenyl label--was administered to rats by gavage as a single dose or as 14–day repeated doses. Less than 0.5% of the administered dose was detected in the tissues and carcass up to 7 days post-dosing and most of it was in excretion-related organs. There was no evidence of potential for bioaccumulation. The primary route of excretion was via the feces, though 9- to 18% was detected in the urine of the various dose groups. Absorbed azoxystrobin appeared to be extensively metabolized. A metabolic pathway was proposed showing hydrolysis and subsequent glucuronide conjugation as the major biotransformation process. This study was classified as supplementary but upgradeable; the company has submitted data intended to upgrade the study to acceptable and these data have been scheduled for review.

4. *Sub-chronic toxicity*. i. In a 90–day rat feeding study the NOAEL was 20.4 mg/kg/day for males and females. The LOAEL was 211.0 mg/kg/day based on decreased weight gain in both sexes, clinical observations of distended abdomens and reduced body size, and clinical pathology findings attributable to reduced nutritional status.

ii. In a subchronic toxicity study in which azoxystrobin was administered to dogs by capsule for 92 or 93 days, the NOAEL for both males and females was 50 mg/kg/day. The LOAEL was 250 mg/kg/day, based on treatment-related clinical observations and clinical chemistry alterations at this dose.

iii. In a 21–day repeated-dose dermal rat study using azoxystrobin, the NOAEL for both males and females was greater than or equal to 1,000 mg/kg/day (the highest dosing regimen); a LOAEL was therefore not determined.

5. *Chronic feeding toxicity and carcinogenicity*. i. In a 2–year feeding study in rats fed diets containing 0, 60, 300, and 750/1,500 ppm (males/females), the systemic toxicity NOAEL was 18.2 mg/kg/day for males and 22.3 mg/kg/day for females. The systemic toxicity LOAEL for males was 34 mg/kg/day, based on reduced body weights, food consumption, and food efficiency; and bile duct lesions. The systemic toxicity LOAEL for females was 117.1 mg/kg/day, based on reduced body weights. There was no evidence of carcinogenic activity in this study.

ii. In a 1–year feeding study in dogs to which azoxystrobin was fed by capsule at doses of 0, 3, 25, or 200 mg/kg/day, the NOAEL for both males and females was 25 mg/kg/day and the LOAEL was 200 mg/kg/day for both sexes, based on clinical observations, clinical chemistry changes, and liver weight increases that were observed in both sexes.

iii. In a 2–year carcinogenicity feeding study in mice using dosing concentrations of 0, 50, 300, or 2,000 ppm, the systemic toxicity NOAEL was 37.5 mg/kg/day for both males and females. The systemic toxicity LOAEL was 272.4 mg/kg/day for both sexes, based on reduced body weights in both sexes at this dose. There was no evidence of carcinogenicity at the dose levels tested.

According to the new proposed guidelines for Carcinogen Risk Assessment (April, 1996), the appropriate descriptor for human carcinogenic potential of azoxystrobin is ''Not Likely.'' The appropriate subdescriptor is ''has been evaluated in at least two well conducted studies in two appropriate species without demonstrating carcinogenic effects.''

6. *Developmental and reproductive toxicity*. i. In a prenatal development study in rats gavaged with azoxystrobin at dose levels of 0, 25, 100, or 300 mg/kg/day during days 7 through 16 of gestation, lethality at the highest dose caused the discontinuation of dosing at that level. The developmental NOAEL was greater than or equal to 100 mg/kg/

day and the developmental LOAEL was > 100 mg/kg/day because no significant adverse developmental effects were observed. In this same study, the maternal NOAEL was not established; the maternal LOAEL was 25 mg/kg/day, based on increased salivation.

ii. In a prenatal developmental study in rabbits gavaged with 0, 50, 150, or 500 mg/kg/day during days 8 through 20 of gestation, the developmental NOAEL was 500 mg/kg/day and the developmental LOAEL was > 500 mg/kg/day because no treatment-related adverse effects on development were seen. The maternal NOAEL was 150 mg/kg/day and the maternal LOAEL was 500 mg/kg/day, based on decreased body weight gain.

iii. In a two-generation reproduction study, rats were fed 0, 60, 300, or 1,500 ppm of azoxystrobin. The reproductive NOAEL was 32.2 mg/kg/day. The reproductive LOAEL was 165.4 mg/kg/day; reproductive toxicity was demonstrated as treatment-related reductions in adjusted pup body weights as observed in the F1a and F2a pups dosed at 1,500 ppm (165.4 mg/kg/day).

B. Toxicological Endpoints

1. *Acute toxicity*. The Agency evaluated the existing toxicology database for azoxystrobin and did not identify any acute dietary endpoint because there were no effects of concern attributable to a single dose (exposure) in oral toxicology studies including developmental toxicity studies in the rat and rabbit and acute neurotoxicity study in the rat. Therefore, this risk assessment is not required.

2. *Short- and intermediate-term toxicity*. The Agency evaluated the existing toxicology database for short-term and intermediate-term dermal and inhalation exposure and determined that this risk assessment is not required because no dermal or systemic effects were seen in the repeated dose dermal study at the limit dose. The only registered residential use for azoxystrobin is residential turf.

3. *Chronic toxicity*. EPA has established the Reference Dose (RfD) for azoxystrobin at 0.18 mg/kg/day. This RfD is based on a NOAEL of 18.2 mg/kg/day from the rat chronic toxicity/carcinogenicity feeding study. Effects observed at the LOAEL's (34 mg/kg/day for males, 117.1 mg/kg/day for females) included reduced body weights, food consumption and efficiency. Males also had bile duct lesions. An uncertainty factor of 100 was used to allow for interspecies sensitivity and intraspecies variability. There was no evidence of increased susceptibility of infants or children to azoxystrobin. Therefore, no additional uncertainty factor to protect infants and children is needed at this time.

4. *Carcinogenicity*. The Agency determined that azoxystrobin should be classified as ''Not Likely'' to be a human carcinogen according to the proposed revised Cancer Guidelines. This classification is based on the lack of evidence of carcinogenicity in long-term rat and mouse feeding studies.

C. Exposures and Risks

1. *From food and feed uses.* Permanent tolerances have been established (40 CFR 180. 507(a)) for the combined residues of azoxystrobin (methyl(*E*)-2(2-(6-(2-cyanophenoxy)pyrimidin-4-yloxy)phenyl)-3-methoxyacrylate) and its Z isomer (methyl (*Z*)-2-(2-(6-(2-cyanophenoxy)pyrimidin-4-yloxy)phenyl)-3-methoxyacrylate)), in or on the following raw agricultural commodities: pecans at 0.01 ppm, peanuts at 0.01 ppm, peanut oil at 0.03 ppm, grapes at 1.0 ppm, bananas at 0.5 ppm, peaches at 0.80 ppm, tomatoes at 0.2 ppm, and tomato paste at 0.6 ppm. In addition, time-limited tolerances have been established for crops, processed foods and animal commodities (40 CFR 180.507(b)) at levels ranging from 0.006 ppm in milk to 20 ppm in rice hulls and including cucurbits at 1.0 ppm, rice grain at 4 ppm, rice hulls at 20 ppm, rice straw at 10 ppm, and potatoes at 0.03 ppm. Risk assessments were conducted by EPA to assess dietary exposures from azoxystrobin as follows:

i. *Acute exposure and risk*. The Agency did not conduct an acute risk assessment because no toxicological endpoint of concern was identified during review of available data.

ii. *Chronic exposure and risk*. The Dietary Exposure Evaluation Model (DEEM), a chronic exposure analysis, was used in conducting this chronic dietary risk assessment. EPA has made very conservative assumptions -- 100% of all commodities having azoxystrobin residues at the level of the tolerance with the exception of raisins and grape juice which are expected to result in an over estimation of human dietary exposure. Thus, in making a safety determination for this tolerance, the Agency is taking into account these conservative exposure assessments. The following percentages of the RfD from dietary exposure were calculated: U.S. population (48 states, all seasons), 2%; all infants (< 1 year old), 7%; nursing infants (< 1 year old), 2%; non-nursing infants (< 1 year old), 9%; children (1–6 years old), 5%; children (7–12 years old), 3% and non-Hispanic (other than black or white), 4%. The subgroups listed are infants/children and other subgroups for which the percentage of the RfD occupied is greater than the group U.S. population (48 states).

2. *From drinking water.* In the absence of reliable, available monitoring data, EPA uses models to estimate concentrations of pesticides in ground and surface water. For azoxystrobin, modeling was used to estimate surface water concentrations because of very limited surface water monitoring data. However, EPA does not use these model estimates to quantify risk. Currently, EPA uses drinking water levels of comparison (DWLOC's) as a surrogate to capture risk associated with exposure to pesticides in drinking water. A DWLOC is the concentration of a pesticide in drinking water that would be acceptable as an upper limit in light of total aggregate exposure to that pesticide from food, water, and residential uses. A DWLOC will vary depending on the residue level in foods, the toxicity endpoint and with drinking water consumption patterns and body weight for specific subpopulations. EPA believes model estimates to be overestimations of concentrations of azoxystrobin expected in drinking water. Azoxystrobin is moderately persistent in soil in the absence of light and one of its metabolites is potentially moderately mobile in coarse textured soils. The potential mobility and persistence of some degradates based on batch equilibrium studies, aerobic soil metabolism and some field dissipation studies are similar to pesticides with a potential to leach into ground water under some conditions. There is no established Maximum Contaminant Level for residues of azoxystrobin in drinking water. No health advisory levels for azoxystrobin in drinking water have been established.

i. *Acute exposure and risk*. An assessment was not conducted because no toxicological end-point of concern was identified.

ii. *Chronic exposure and risk*. Based on the chronic dietary (food) exposure estimates, chronic DWLOC's for azoxystrobin were calculated and are summarized as follows: U. S. Population (48 states) 6,200 µg/L; females (13+) (using the highest TMRC for the 5 subgroups of females), 5,200 µg/L; infants/children (using the highest TMRC for the 5 subgroups of infants/children) 1,600 µg/L and non-Hispanic (other than black or white), 6,100 µg/L. The highest EEC for azoxystrobin in surface water is from the application of azoxystrobin on grapes (39 µg/L) and is substantially lower than the DWLOCs

calculated. Therefore, chronic exposure to azoxystrobin residues in drinking water does not exceed EPA's level of concern.

3. *From non-dietary exposure.* The only registered indoor/outdoor residential use for azoxystrobin is residential turf. The Agency evaluated the existing toxicology database and determined that there are no toxicological end points of concern.

4. *Cumulative exposure to substances with common mechanism of toxicity.* Section 408(b)(2)(D)(v) requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider ''available information'' concerning the cumulative effects of a particular pesticide's residues and ''other substances that have a common mechanism of toxicity.''

EPA does not have, at this time, available data to determine whether azoxystrobin has a common mechanism of toxicity with other substances or how to include this pesticide in a cumulative risk assessment. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, azoxystrobin does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that azoxystrobin has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the final rule for Bifenthrin Pesticide Tolerances (62 FR 62961, November 26, 1997).

D. Aggregate Risks and Determination of Safety for U.S. Population

1. *Acute risk.* There were no effects of concern attributable to a single dose (exposure) in oral toxicological studies including developmental toxicity studies in rat and rabbit and an acute neurotoxicity study in rats. Accordingly, EPA concludes that azoxystrobin does not pose an acute risk.

2. *Chronic risk.* Using the exposure assumptions described in this unit, EPA has concluded that aggregate exposure to azoxystrobin from food will utilize from 2% to 9% of the RfD for the U.S. population. The major identifiable subgroup with the highest aggregate exposure is non-nursing infants (<1 year old). 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. Based on the chronic (food only) exposure, chronic DWLOC's were calculated. The lowest DWLOC of 1,600 µg/L was for infants/children (using the highest TMRC for the five subgroups of infants/children listed in the DEEM analysis). The highest Estimated Environmental Concentration (EEC) in surface water is from application to grapes (39 µg/L) and is substantially lower than the calculated DWLOC. The EEC's as a result of application to the proposed uses are no higher than those calculated for grapes. Therefore chronic exposure in drinking water does not exceed the Agency's level of concern.

3. *Short- and intermediate-term risk.* Short- and intermediate-term risk. No dermal or systemic effects were seen in the repeated dose dermal study at the limit dose. The only indoor or outdoor residential use currently registered for azoxystrobin is residential turf. EPA concluded that azoxystrobin does not pose a short- or intermediate-term risk.

4. *Aggregate cancer risk for U.S. population.* The Agency determined that azoxystrobin should be classified as ''Not Likely'' to be a human carcinogen according to the proposed revised Cancer Guidelines because there was no evidence of carcinogenicity in valid chronic toxicity studies using two species of mammals. The Agency has therefore concluded that azoxystrobin does not pose a cancer risk.

5. *Determination of safety.* Based on these risk assessments, EPA concludes that there is a reasonable certainty that no harm will result from aggregate exposure to azoxystrobin residues as a result of current use patterns.

E. Aggregate Risks and Determination of Safety for Infants and Children

1. *Safety factor for infants and children*—i. *In general.* In assessing the potential for additional sensitivity of infants and children to residues of azoxystrobin, EPA considered data from developmental toxicity studies in the rat and rabbit and a 2-generation reproduction study in the rat. The developmental toxicity studies are designed to evaluate adverse effects on the developing organism resulting from maternal pesticide exposure during gestation. Reproduction studies provide information relating to effects from exposure to the pesticide on the reproductive capability of mating animals and data on systemic toxicity.

FFDCA section 408 provides that EPA shall apply an additional tenfold margin of safety for infants and children in the case of threshold effects to account for pre- and post-natal toxicity and the completeness of the database unless EPA determines that a different margin of safety will be safe for infants and children. Margins of safety are incorporated into EPA risk assessments either directly through use of a margin of exposure (MOE) analysis or through using uncertainty (safety) factors in calculating a dose level that poses no appreciable risk to humans. EPA believes that reliable data support using the standard MOE and uncertainty factor (usually 100 for combined inter- and intra species variability) and not the additional tenfold MOE/uncertainty factor when EPA has a complete data base under existing guidelines and when the severity of the effect in infants or children or the potency or unusual toxic properties of a compound do not raise concerns regarding the adequacy of the standard MOE/safety factor.

ii. *Developmental toxicity studies*— a. *Rabbit.* In the developmental toxicity study in rabbits, developmental NOAEL was 500 mg/kg/day, at the highest dose tested (HDT). Because there were no treatment-related effects, the developmental LOAEL was greater than 500 mg/kg/day. The maternal NOAEL was 150 mg/kg/day. The maternal LOAEL of 500 mg/kg/day was based on decreased body weight gain during dosing.

b. *Rat.* In the developmental toxicity study in rats, the maternal (systemic) NOAEL was not established. The maternal LOAEL of 25 mg/kg/day at the lowest dose tested (LDT) was based on increased salivation. The developmental (fetal) NOAEL was 100 mg/kg/day (HDT).

iii. *Reproductive toxicity study. Rat.* In the 2-generation reproductive toxicity study in rats, the parental (systemic) NOAEL was 32.3 mg/kg/day. The parental LOAEL of 165.4 mg/kg/day was based on decreased body weights in males and females, decreased food consumption and increased adjusted liver weights in females, and cholangitis. The reproductive NOAEL was 32.3 mg/kg/day. The reproductive LOAEL of 165.4 mg/kg/day was based on increased weanling liver weights and decreased body weights for pups of both generations.

iv. *Pre- and post-natal sensitivity.* The pre- and post-natal toxicology data base for azoxystrobin is complete with respect to current toxicological data requirements. The results of these studies indicate that infants and children are no more sensitive to exposure than adults, based on the results of the rat and rabbit developmental toxicity studies and the 2-generation reproductive toxicity study in rats. There are no developmental effects in the rat and rabbit developmental studies and the effects

observed in the offspring in the reproduction study occur at the same dose levels in which toxicity was observed in the parents. The effects in the young are not more severe than those observed with the parents (decreased body weights in both parents and pups).

v. *Conclusion*. There is a complete toxicity database for azoxystrobin and exposure data are complete or are estimated based on data that reasonably account for potential exposures. Accordingly, EPA has determined that the standard margin of safety of infants and children and the additional tenfold safety factor can be removed.

2. *Chronic risk*. Using the exposure assumptions described in this unit, EPA has concluded that aggregate exposure to azoxystrobin from food will utilize from 2% to 9% of the RfD for infants and children. 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. Despite the potential for exposure to azoxystrobin in drinking water and from non-dietary, non-occupational exposure, EPA does not expect the aggregate exposure to exceed 100% of the RfD.

3. *Determination of safety*. Based on these risk assessments, EPA concludes that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to azoxystrobin residues.

III. Other Considerations

A. Metabolism In Plants and Animals

The qualitative nature of the residue in plants is adequately understood. A grape metabolism study was evaluated by the Agency in December, 1995 and it was determined that the residues of concern in grapes were the parent and its Z isomer. In peanut and wheat metabolism studies the major residues were also azoxystrobin and its Z isomer. Azoxystrobin does not accumulate in crop seeds or fruits. Metabolism of azoxystrobin in plants is complex, with more than 15 metabolites identified. However, these metabolites are present at low levels, typically much less than 5% of the total radioactive residue level. Based on parent being the predominant residue in the grape, wheat and peanut metabolism studies, the Agency concludes that the residues of concern in all directly treated crops are the parent and its Z isomer.

The nature of the residue in animals is adequately understood. The Agency has determined that the residue of concern in livestock is parent azoxystrobin only. This determination was based on the results of metabolism studies performed on goats and poultry. The goat metabolism study was reviewed in conjunction with PP 5F4541. The poultry metabolism study was reviewed in conjunction with PP 6F4762. Azoxystrobin and one metabolite (compound 28) were identified in egg yolk and compound 28 alone was found in liver. Residues in extracts of egg whites, muscle, and skin with underlying peritoneal fat were less than 0.01 ppm. Residues of azoxystrobin were less than 0.01 ppm at a feeding level of 1.4x in the radiolabeled study and also less than 0.01 ppm in a feeding study at 60 ppm (about 7x). As a result, there is no reasonable expectation of finite residues of azoxystrobin in poultry commodities.

The registrant submitted three analytical methods for the analysis of the subject commodities.

1. The first method, RAM 243, is a gas chromatography with nitrogen-phosphorus detection (GC/NPD) method which can be used for the analysis of cereals, processed cereals, dried beans, peas, leafy crops, bananas, soft fruits, processed soft fruits, citrus, fruiting vegetables, root crops, stone fruits, wine, and citrus juice. This method has been reviewed and validated by the Agency, and will be submitted to the Food and Drug Administration (FDA) for inclusion in PAM II.

2. The second method, RAM 260, is a GC/NPD method for the analysis of azoxystrobin and its Z isomer in crops of high lipid content. The registrant has used it for analysis of peanut kernel and hull, processed peanut, pecan kernel, coffee bean, citrus skin, and canola oil. This method has been validated by the Agency and will be submitted to the FDA for inclusion in PAM II.

3. The third method, RAM 255, uses gas chromatography with thermionic detection, nitrogen mode, for analysis of animal commodities. It has been validated by the Agency for analysis of milk and animal tissues. The laboratory will issue a written report shortly and the method will be submitted to FDA for inclusion in PAM II.

Therefore, adequate analytical methodology is available to enforce the tolerance expression. The method may be requested from: Calvin Furlow, PIRIB, IRSD (7502C), Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. Office and telephone number: Rm. 101FF, Crystal Mall #2, 1921 Jefferson Davis Hwy., Arlington, VA, (703) 305–5229.

B. Magnitude of Residues

Azoxystrobin has been subjected to FDA's multiresidue protocols. It could not be recovered through application of any protocol. Residues of azoxystrobin and its Z isomer are not expected to exceed the proposed tolerance levels and the submitted data support tolerance levels for combined residues of azoxystrobin (methyl(*E*)-2-(2-(6-(2-cyanophenoxy)pyrimidin-4-yloxy)phenyl)-3-methoxyacrylate) and its Z isomer (methyl(*Z*)-2-(2-(6-(2-cyanophenoxy)pyrimidin-4-yloxy)phenyl)-3-methoxyacrylate) in or on almond hulls at 4.0 ppm, aspirated grain fractions at 10 ppm, bananas (pre-harvest and postharvest) at 2.0 ppm (of which not more than 0.1 ppm is contained in the pulp), canola at 1.0 ppm, cucurbits at 0.3 ppm, peanut hay at 2.0 ppm, pistachios at 0.01 ppm, potatoes at 0.03 ppm, rice grain at 5.0 ppm, rice straw at 12 ppm, rice hulls at 20 ppm, stone fruits at 1.5 ppm, tree nuts at 0.010 ppm, wheat grain at 0.10 ppm, wheat bran at 0.20 ppm, wheat hay at 15 ppm, wheat straw at 4.0 ppm, and for the residues of azoxystrobin (only) in fat of cattle, goats, hogs, horses, and sheep at 0.010 ppm; meat of cattle, goats, hogs, horses, and sheep at 0.01 ppm; meat byproducts of cattle, goats, hogs, horses, and sheep at 0.010 ppm; and milk at 0.006 ppm. The submitted residue data support a tolerance level of 2.0 ppm for residues of azoxystrobin in or on whole bananas and a tolerance level of 0.1 ppm in or on banana pulp. The tolerance for bananas must be listed as 2.0 ppm for the combined residues of azoxystrobin and its Z isomer in/on bananas (whole fruit) and residues in banana pulp must not exceed 0.1 ppm.

C. International Residue Limits

There are no Codex, Canadian or Mexican Maximum Residue Limits (MRL) established for azoxystrobin for bananas, curcurbits, potatoes, or stone fruits.

D. Rotational Crop Restrictions

Rotational crop data were previously submitted. Based on this information, a 45–day plantback interval is appropriate for all crops other than those having tolerances for azoxystrobin and its Z isomer.

IV. Conclusion

Therefore, tolerances are established for combined residues of azoxystrobin (methyl(*E*)-2-(2-(6-(2-cyanophenoxy)pyrimidin-4-yloxy)phenyl)-3-methoxyacrylate) and its Z isomer (methyl(*Z*)-2-(2-(6-(2-cyanophenoxy)pyrimidin-4-yloxy)phenyl)-3-methoxyacrylate) in or

on almond hulls at 4.0 ppm, aspirated grain fractions at 10 ppm, bananas (pre-harvest and postharvest) at 2.0 ppm (of which not more than 0.1 ppm is contained in the pulp), canola at 1.0 ppm, cucurbits at 0.3 ppm, peanut hay at 2.0 ppm, pistachios at 0.01 ppm, potatoes at 0.03 ppm, rice grain at 5.0 ppm, rice straw at 12 ppm, rice hulls at 20 ppm, stone fruits at 1.5 ppm, tree nuts at 0.010 ppm, wheat grain at 0.10 ppm, wheat bran at 0.20 ppm, wheat hay at 15 ppm, wheat straw at 4.0 ppm, and for the residues of azoxystrobin (only) in fat of cattle, goats, hogs, horses, and sheep at 0.010 ppm; meat of cattle, goats, hogs, horses, and sheep at 0.01 ppm; meat byproducts of cattle, goats, hogs, horses, and sheep at 0.010 ppm; and milk at 0.006 ppm.

V. Objections and Hearing Requests

The new FFDCA section 408(g) provides essentially the same process for persons to ''object'' to a tolerance regulation as was provided in the old section 408 and in section 409. However, the period for filing objections is 60 days, rather than 30 days. EPA currently has procedural regulations which govern the submission of objections and hearing requests. These regulations will require some modification to reflect the new law. However, until those modifications can be made, EPA will continue to use those procedural regulations with appropriate adjustments to reflect the new law.

Any person may, by May 17, 1999, file written objections to any aspect of this regulation and may also request a hearing on those objections. Objections and hearing requests must be filed with the Hearing Clerk, at the address given under the ''ADDRESSES'' section (40 CFR 178.20). A copy of the objections and/or hearing requests filed with the Hearing Clerk should be submitted to the OPP docket for this regulation. The objections submitted must specify the provisions of the regulation deemed objectionable and the grounds for the objections (40 CFR 178.25). Each objection must be accompanied by the fee prescribed by 40 CFR 180.33(i). EPA is authorized to waive any fee requirement ''when in the judgement of the Administrator such a waiver or refund is equitable and not contrary to the purpose of this subsection.'' For additional information regarding tolerance objection fee waivers, contact James Tompkins, 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: Rm. 239, Crystal Mall #2, 1921 Jefferson Davis Hwy., Arlington, VA, (703) 305-5697, tompkins.jim@epa.gov. Requests for waiver of tolerance objection fees should be sent to James Hollins, Information Resources and Services Division (7502C), Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460.

If a hearing is requested, the objections must include a statement of the factual issues on which a hearing is requested, the requestor's contentions on such issues, and a summary of any evidence relied upon by the requestor (40 CFR 178.27). A request for a hearing will be granted if the Administrator determines that the material submitted shows the following: There is genuine and substantial issue of fact; there is a reasonable possibility that available evidence identified by the requestor would, if established, resolve one or more of such issues in favor of the requestor, taking into account uncontested claims or facts to the contrary; and resolution of the factual issues in the manner sought by the requestor would be adequate to justify the action requested (40 CFR 178.32). Information submitted in connection with an objection or hearing request may be claimed confidential by marking any part or all of that information as CBI. Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR part 2. A copy of the information 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.

VI. Public Record and Electronic Submissions

EPA has established a record for this regulation under docket control number [OPP–300801] (including any comments and data submitted electronically). 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 119 of the Public Information and Records Integrity Branch, Information Resources and Services Division (7502C), Office of Pesticide Programs, Environmental Protection Agency, Crystal Mall #2, 1921 Jefferson Davis Hwy., Arlington, VA.

Objections and hearing requests may be sent by e-mail directly to EPA at:
opp-docket@epa.gov.

E-mailed objections and hearing requests must be submitted as an ASCII file avoiding the use of special characters and any form of encryption.

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

VII. Regulatory Assessment Requirements

A. Certain Acts and Executive Orders

This final rule establishes a tolerance under section 408(d) of the FFDCA in response to a petition submitted to the Agency. The Office of Management and Budget (OMB) has exempted these types of actions from review under Executive Order 12866, entitled *Regulatory Planning and Review* (58 FR 51735, October 4, 1993). This final rule does not contain any information collections subject to OMB approval under the Paperwork Reduction Act (PRA), 44 U.S.C. 3501 *et seq.*, or impose any enforceable duty or contain any unfunded mandate as described under Title II of the Unfunded Mandates Reform Act of 1995 (UMRA) (Pub. L. 104–4). Nor does it require any prior consultation as specified by Executive Order 12875, entitled *Enhancing the Intergovernmental Partnership* (58 FR 58093, October 28, 1993), or special considerations as required by Executive Order 12898, entitled *Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations* (59 FR 7629, February 16, 1994), or require OMB review in accordance with Executive Order 13045, entitled *Protection of Children from Environmental Health Risks and Safety Risks* (62 FR 19885, April 23, 1997).

In addition, since tolerances and exemptions that are established on the basis of a petition under FFDCA section 408(d), such as the tolerances in this final rule, do not require the issuance of a proposed rule, the requirements of the Regulatory Flexibility Act (RFA) (5 U.S.C. 601 *et seq.*) do not apply. Nevertheless, the Agency previously assessed whether establishing tolerances, exemptions from tolerances, raising tolerance levels or expanding exemptions might adversely impact small entities and concluded, as a generic matter, that there is no adverse economic impact. The factual basis for

the Agency's generic certification for tolerance actions published on May 4, 1981 (46 FR 24950), and was provided to the Chief Counsel for Advocacy of the Small Business Administration.

B. Executive Order 12875

Under Executive Order 12875, entitled *Enhancing the Intergovernmental Partnership* (58 FR 58093, October 28, 1993), EPA may not issue a regulation that is not required by statute and that creates a mandate upon a State, local or tribal government, unless the Federal government provides the funds necessary to pay the direct compliance costs incurred by those governments. If the mandate is unfunded, EPA must provide to OMB a description of the extent of EPA's prior consultation with representatives of affected State, local, and tribal governments, the nature of their concerns, copies of any written communications from the governments, and a statement supporting the need to issue the regulation. In addition, Executive Order 12875 requires EPA to develop an effective process permitting elected officials and other representatives of State, local, and tribal governments ''to provide meaningful and timely input in the development of regulatory proposals containing significant unfunded mandates.''

Today's rule does not create an unfunded Federal mandate on State, local, or tribal governments. The rule does not impose any enforceable duties on these entities. Accordingly, the requirements of section 1(a) of Executive Order 12875 do not apply to this rule.

C. Executive Order 13084

Under Executive Order 13084, entitled *Consultation and Coordination with Indian Tribal Governments* (63 FR 27655, May 19, 1998), EPA may not issue a regulation that is not required by statute, that significantly or uniquely affects the communities of Indian tribal governments, and that imposes substantial direct compliance costs on those communities, unless the Federal government provides the funds necessary to pay the direct compliance costs incurred by the tribal governments. If the mandate is unfunded, EPA must provide OMB, in a separately identified section of the preamble to the rule, a description of the extent of EPA's prior consultation with representatives of affected tribal governments, a summary of the nature of their concerns, and a statement supporting the need to issue the regulation. In addition, Executive Order 13084 requires EPA to develop an effective process permitting elected officials and other representatives of Indian tribal governments ''to provide meaningful and timely input in the development of regulatory policies on matters that significantly or uniquely affect their communities.''

Today's rule does not significantly or uniquely affect the communities of Indian tribal governments. This action does not involve or impose any requirements that affect Indian tribes. Accordingly, the requirements of section 3(b) of Executive Order 13084 do not apply to this rule.

VIII. Submission to Congress and the Comptroller General

The Congressional Review Act, 5 U.S.C. 801 *et seq.*, as added by the Small Business Regulatory Enforcement Fairness Act of 1996, generally provides that before a rule may take effect, the Agency promulgating the rule must submit a rule report, which includes a copy of the rule, to each House of the Congress and the Comptroller General of the United States. EPA will submit a report containing this rule and other required information to the U.S. Senate, the U.S. House of Representatives and the Comptroller General of the United States prior to publication of the rule in the **Federal Register**. This rule is not a ''major rule'' as defined by 5 U.S.C. 804(2).

List of Subjects in 40 CFR Part 180

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

Dated: March 5, 1999.

James Jones,

Director, Registration Division, Office of Pesticide Programs.

Therefore, 40 CFR chapter I is amended as follows:

PART 180—[AMENDED]

1. The authority citation for part 180 continues to read as follows:

Authority: 21 U.S.C. 321(q), 346a and 371.

§ 180.507 [Amended]

2. In § 180.507, paragraph (a)(1), by removing from the table the commodities ''Bananas'', and ''Peaches''.

3. Section 180.507 is further amended in paragraph (a)(1) by changing the words ''raw agricultural commodities'' to read ''food commodities'', by alphabetically adding the following commodities to the table in paragraph (a)(1), by redesignating paragraph (a)(2) as paragraph (a)(3), and by adding a new paragraph (a)(2) to read as follows:

§ 180.507 Azoxystrobin; tolerances for residues General.

(a) *General.* (1) * * *

Commodity	Parts per million
Almond hulls	4.0
Aspirated grain fractions.	10
Bananas (pre-harvest and post harvest).	2.0 (of which not more than 0.1 is contained in the pulp)
Canola	1.0
Cucurbits	0.3
* * * * *	
Peanut hay	2.0
Pistachios	0.010
Potatoes	0.03
Rice grain	5.0
Rice hulls	20
Rice straw	12
Stone fruits	1.5
* * * * *	
Tree nuts	0.010
Wheat bran	0.20
Wheat grain	0.10
Wheat hay	15
Wheat straw	4.0

(2) Tolerances are established for residues of the fungicide, azoxystrobin [methyl(*E*)-2-(2-(6-(2-cyanophenoxy)pyrimidin-4-yloxy)phenyl)-3-methoxyacrylate] in or on the following food commodities.

Commodity	Parts per million
Cattle, fat	0.010
Cattle, meat	0.01
Cattle, meat byproducts	0.010
Goats, fat	0.010
Goats, meat	0.01
Goats, meat byproducts	0.010
Hogs, fat	0.010
Hogs, meat	0.01
Hogs, meat byproducts	0.010
Horses, fat	0.010
Horses, meat	0.01
Horses, meat byproducts	0.010
Milk.	0.006
Sheep, fat	0.010
Sheep, meat	0.01
Sheep, meat byproducts	0.010

* * * * *

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