VII. Statutory and Executive Order Reviews

This final rule establishes a tolerance under section 408(d) of 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). Because this rule has been exempted from review under Executive Order 12866 due to its lack of significance, this rule is not subject to Executive Order 13211, *Actions Concerning Regulations That Significantly Affect Energy Supply, Distribution, or Use* (66 FR 28355, May 22, 2001). 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) (Public Law 104–4). Nor does it require any special considerations under Executive Order 12898, entitled *Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations* (59 FR 7629, February 16, 1994); or OMB review or any Agency action under Executive Order 13045, entitled *Protection of Children from Environmental Health Risks and Safety Risks* (62 FR 19885, April 23, 1997). This action does not involve any technical standards that would require Agency consideration of voluntary consensus standards pursuant to section 12(d) of the National Technology Transfer and Advancement Act of 1995 (NTTAA), Public Law 104–113, section 12(d) (15 U.S.C. 272 note). Since tolerances and exemptions that are established on the basis of a petition under section 408(d) of FFDCA, such as the tolerance 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. In addition, the Agency has determined that this action will not have a substantial direct effect on States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government, as specified in Executive Order 13132, entitled *Federalism* (64 FR 43255, August 10, 1999). Executive Order 13132 requires EPA to develop an accountable process to ensure ''meaningful and timely input by State and local officials in the development of regulatory policies that have federalism implications.'' ''Policies that have federalism implications'' is defined in the Executive order to include regulations that have ''substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government.'' This final rule directly regulates growers, food processors, food handlers and food retailers, not States. This action does not alter the relationships or distribution of power and responsibilities established by Congress in the preemption provisions of section 408(n)(4) of FFDCA. For these same reasons, the Agency has determined that this rule does not have any ''tribal implications'' as described in Executive Order 13175, entitled *Consultation and Coordination with Indian Tribal Governments* (65 FR 67249, November 6, 2000). Executive Order 13175, requires EPA to develop an accountable process to ensure ''meaningful and timely input by tribal officials in the development of regulatory policies that have tribal implications.'' ''Policies that have tribal implications'' is defined in the Executive order to include regulations that have ''substantial direct effects on one or more Indian tribes, on the relationship between the Federal Government and the Indian tribes, or on the distribution of power and responsibilities between the Federal Government and Indian tribes.'' This rule will not have substantial direct effects on tribal governments, on the relationship between the Federal Government and Indian tribes, or on the distribution of power and responsibilities between the Federal Government and Indian tribes, as specified in Executive Order 13175. Thus, Executive Order 13175 does not apply to this rule.

VIII. Congressional Review Act

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 to 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 this final rule in the **Federal Register**. This final 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 26, 2004.

James Jones,

Director, 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.

■ 2. Section 180.597 is added to read as follows:

§ 180.597 Mesosulfuron-methyl; tolerances for residues.

(a) *General.* Tolerances are established for residues of the herbicide mesosulfuron-methyl, (methyl 2-[[[[(4,6-dimethoxy-2-pyrimidinyl) amino]carbonyl]amino]sulfonyl] -4-[[(methylsulfonyl)amino] methyl]benzoate]) in or on the following raw agricultural commodities:

Commodity	Parts per million
Cattle, meat byproducts	0.01
Goat, meat byproducts	0.01
Grain, aspirated fractions	0.60
Horse, meat byproducts	0.01
Sheep, meat byproducts	0.01
Wheat, forage	0.60
Wheat, germ	0.10
Wheat, grain	0.03
Wheat, hay	0.06
Wheat, straw	0.30

(b) *Section 18 emergency exemptions.* [Reserved]

(c) *Tolerances with regional registrations.* [Reserved]

(d) *Indirect or inadvertent residues.* [Reserved]

[FR Doc. 04–7781 Filed 4–6–04; 8:45 am]

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ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[OPP–2003–0296; FRL–7339–4]

Fosthiazate; Pesticide Tolerance

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This regulation establishes a tolerance for combined residues of

fosthiazate (*O*-ethyl *S*-(1-methylpropyl)(2-oxo-3-thiazolidinyl)phosphonothioate and its metabolite *O*-ethyl *S*-(1-methylpropyl)[2-(methylsulfonyl)ethyl] phosphoramidothioate (ASC–67131) in or on tomato. ISK Biosciences requested this tolerance under the Federal Food, Drug, and Cosmetic Act (FFDCA), as amended by the Food Quality Protection Act of 1996 (FQPA). This tolerance will support the use of fosthiazate on tomatoes as a replacement for methyl bromide for the control of nematodes.

DATES: This regulation is effective April 7, 2004. Objections and requests for hearings, identified by docket ID number OPP–2003–0296, must be received on or before June 7, 2004.

ADDRESSES: Written objections and hearing requests may be submitted electronically, by mail, or through hand delivery/courier. Follow the detailed instructions as provided in Unit VI. of the **SUPPLEMENTARY INFORMATION**.

FOR FURTHER INFORMATION CONTACT: Rita Kumar, Registration Division (7505C), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001; telephone number: (703) 308–8291; e-mail address: *kumar.rita@epa.gov*.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

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

- Crop production (NAICS 111)
- Animal production (NAICS 112)
- Food manufacturing (NAICS 311)
- Pesticide manufacturing (NAICS 32532)

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

B. How Can I Get Copies of this Document and Other Related Information?

1. *Docket*. EPA has established an official public docket for this action under docket identification (ID) number OPP–2003–0296. The official public docket consists of the documents specifically referenced in this action, any public comments received, and other information related to this action. Although a part of the official docket, the public docket does not include Confidential Business Information (CBI) or other information whose disclosure is restricted by statute. The official public docket is the collection of materials that is available for public viewing at the Public Information and Records Integrity Branch (PIRIB), Rm. 119, Crystal Mall #2, 1921 Jefferson Davis Hwy., Arlington, VA. This docket facility is open from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The docket telephone number is (703) 305–5805.

2. *Electronic access*. You may access this **Federal Register** document electronically through the EPA Internet under the "**Federal Register**'' listings at *http://www.epa.gov/fedrgstr/*. A frequently updated electronic version of 40 CFR part 180 is available at *http://www.access.gpo.gov/nara/cfr/cfrhtml_00/Title_40/40cfr180_00.html*, a beta site currently under development. To access the OPPTS Harmonized Guidelines referenced in this document, go directly to the guidelines at *http://www.epa.gov/opptsfrs/home/guidelin.htm*.

An electronic version of the public docket is available through EPA's electronic public docket and comment system, EPA Dockets. You may use EPA Dockets at *http://www.epa.gov/edocket/* to submit or view public comments, access the index listing of the contents of the official public docket, and to access those documents in the public docket that are available electronically. Although not all docket materials may be available electronically, you may still access any of the publicly available docket materials through the docket facility identified in Unit I.B.1. Once in the system, select "search,'' then key in the appropriate docket ID number.

II. Background and Statutory Findings

In the **Federal Register** of November 21 2001 (66 FR 58477) (FRL–6799–1), EPA issued a notice pursuant to section 408 of FFDCA, 21 U.S.C. 346a, as amended by FQPA (Public Law 104–170), announcing the filing of a pesticide petition (PP 6F4662) by ISK Biosciences Corporation, 7470 Auburn Road, Suite A, Concord, OH 44077. That notice included a summary of the petition prepared by ISK Biosciences, the registrant. There were no comments received in response to the notice of filing.

The petition requested that 40 CFR part 180 be amended by establishing a tolerance for combined residues of the insecticide fosthiazate, (*O*-ethyl *S*-(1-methylpropyl)(2-oxo-3-thiazolidinyl)phosphonothioate) and its metabolite ASC-67131 (*O*-ethyl *S*-(1-methylpropyl)[2-(methylsulfonyl)ethyl] phosphoramidothioate), in or on tomatoes at 0.02 parts per million (ppm). Fosthiazate is a new organophosphate (OP) active ingredient (a.i.), that controls a broad spectrum of nematode species. It may be applied through drip (trickle) irrigation systems, as a band application under plastic mulch. Application is made once per season, either prior to or at planting/transplanting of tomatoes. The United States Department of Agriculture's Interregional Research Project No. 4 has identified fosthiazate as a viable alternative to the use of methyl bromide for control of nematodes infesting tomato fields. Methyl bromide has been identified as a chemical that depletes the earth's ozone layer, and thus its use is being phased out. The United States is in the process of implementing a methyl bromide use reduction strategy leading to a complete ban for soil fumigation uses by the year 2005. Fosthiazate will provide growers with a pest management tool for use against nematode pest pressure.

Section 408(b)(2)(A)(i) of the FFDCA allows EPA to establish a tolerance (the legal 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) of the FFDCA 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) of the FFDCA 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 of the FFDCA 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).

III. 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 and to make a determination on aggregate exposure, consistent with section 408(b)(2) of the FFDCA, for a tolerance for combined residues of the insecticide fosthiazate, (*O*-ethyl *S*-(1-methylpropyl)(2-oxo-3-thiazolidinyl)phosphonothioate) and its metabolite ASC-67131 (*O*-ethyl *S*-(1-methylpropyl)[2-(methylsulfonyl)ethyl] phosphoramidothioate) on tomatoes at 0.02 ppm. EPA's assessment of exposures and risks associated with establishing the tolerance 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 fosthiazate are discussed in Table 1 of this unit as well as the no observed adverse effect level (NOAEL) and the lowest observed adverse effect level (LOAEL) from the toxicity studies reviewed.

TABLE 1.—SUBCHRONIC, CHRONIC, AND OTHER TOXICITY

Guideline No.	Study Type	Results
870.3100	13–Week feeding study-rat	Systemic Toxicity LOAEL: 0.08 and 0.09 mg/kg/day for males and females, respectively, based on microscopic lesions in the adrenals (males) and increased ALT (females) levels. No NOAEL was established. At higher doses, the severity of vacuolation of cells in zona fasciculata (≥1.07 ppm) and zona glomerulosa (≥53.6 ppm) of the adrenals increased in a dose-dependent manner; at ≥53.6 ppm, the brain cholinesterase inhibition (ChEI) was also noted. In addition, there was increase in adrenal gland weight at 429 ppm LOAEL for ChEI: 10.7 ppm (0.77 and 0.89 mg/kg/day for males and females, respectively) based on plasma and RBC ChEI. NOAEL: 1.07 ppm (0.08 and 0.09 mg/kg/day for males and females, respectively)
--	4–Week range-finding feeding study-rat	Systemic LOAEL: 400 ppm (equivalent to 40.87 mg/kg/day in males and 43.52 mg/kg/day in females) based on fur loss, muscle tremor, enlarged pale spongiocytes in the adrenals, increased adrenal weights, and increased alkaline phosphatase and alanine aminotransferase levels. Systemic NOAEL: 100 ppm (equivalent to 9.69 mg/kg/day in males and 10.67 mg/kg/day in females) LOAEL for ChEI: 5 ppm (equivalent to 0.48 mg/kg/day in males and 0.5 mg/kg/day in females) based on decreased plasma butyryl- and acetyl-cholinesterase, and brain acetyl-cholinesterase in females, and erythrocyte acetyl-cholinesterase in males NOAEL: 1 ppm (equivalent to 0.10 mg/kg/day in males and females
--	28–Day feeding study-rat with 2-butanesulfonic acid (BSA)	NOAEL: 1,000 mg/kg/day, the highest dose tested.
--	4–Week range-finding feeding study-mice	LOAEL: 400 ppm (males: 68.99 and females: 82.38 mg/kg/day) based on increased tubular basophilia in the kidney NOAEL: 100 ppm (equivalent to 17.59 mg/kg/day in males and 21.43 mg/kg/day in females)
870.3150	13-Weeks subchronic toxicity-dog	Systemic Toxicity LOAEL: 0.11 mg/kg/day, based on histopathological changes in the adrenal glands NOAEL: 0.054 mg/kg/day LOAEL for plasma ChEI: 0.11 mg/kg/day in females and 0.54 mg/kg/day in males NOAEL: 0.054 mg/kg/day in females and 0.11 mg/kg/day in males.

TABLE 1.—SUBCHRONIC, CHRONIC, AND OTHER TOXICITY—Continued

Guideline No.	Study Type	Results
870.3200	21–Day repeated dermal toxicity-rat	Systemic LOAEL: 250 mg/kg/day for males and females based on mortality, clinical signs (emaciation, torpor lethargy or dullness, tremor, hunched posture, hypothermia, gasping, hypersensitivity to noise, pallor paleness, tachypnea labored breathing, and piloerection), decreased body weight gains, and histopathology of the adrenal cortex observed in both sexes; increased food conversion factor and hematology findings were observed in males only Systemic NOAEL: 25 mg/kg/day LOAEL for ChEI: 25 mg/kg/day in males and 2.5 mg/kg/day in females based on inhibition of plasma, erythrocyte, and brain cholinesterase (ChE) in both sexes NOAEL for ChEI: 2.5 mg/kg/day in males and 0.5 mg/kg/day in females
870.3700	Developmental toxicity-rat	Maternal Toxicity LOAEL = 10 mg/kg/day, based on reduced body weight gain NOAEL = 5 mg/kg/day Developmental Toxicity LOAEL = Not determined NOAEL = 10 mg/kg/day Although data were not provided on clinical signs in the dams during or after dosing no cholinergic signs were seen in neurotoxicity studies at the same dose. Therefore, the study classification is upgraded to acceptable/guideline
870.3700	Developmental toxicity-rabbit	Maternal LOAEL: 2 mg/kg/day based on weight loss, abortion, and cholinergic clinical signs noted in the range finding study (MRID 41381110) NOAEL: 1.5 mg/kg/day. Developmental toxicity LOAEL: Not determined NOAEL: 2 mg/kg/day No developmental toxicity was observed at any dose tested in the definitive prenatal developmental toxicity study. No developmental toxicity was observed at doses up to 2.5 mg/kg in a range-finding study
870.3800	2–Generation reproduction-rat	Parental Toxicity LOAEL = 100 ppm (equivalent to 9.32 and 7.21 mg/kg/day in females, and males, respectively) based on increased incidences of adrenal zona glomerulosa hypertrophy, centriacinar hepatocytic vacuolation and liver inflammation in F_0 females and periacinar hepatocytic hypertrophy in F_0 males NOAEL: 30 ppm (equivalent to 2.6 and 2.09 mg/kg/day) in females and males, respectively). in F_0 females and in males Reproductive Toxicity LOAEL = >100 ppm NOAEL = 100 ppm Offspring Toxicity LOAEL = 30 ppm based on decreased litter size and decreased pup weight and viability index during lactation NOAEL = 10 ppm
870.4100	1–Year chronic oral toxicity-dog	Systemic LOAEL: 0.5 mg/kg/day in males based on increased alanine aminotransferase and 5 mg/kg/day in females based on microscopic lesions in the adrenal gland NOAEL: 0.1 mg/kg/day in males and 0.5 mg/kg/day in females LOAEL for ChEI: 0.5 mg/kg/day based on plasma acetyl- and butyryl-cholinesterase activity in males/females NOAEL: 0.1 mg/kg/day based on plasma acetyl- and butyryl-cholinesterase activity The erythrocyte and brain ChE activity LOAELs were not observed. The erythrocyte and brain cholinesterase NOAELs are 5 mg/kg/day

TABLE 1.—SUBCHRONIC, CHRONIC, AND OTHER TOXICITY—Continued

Guideline No.	Study Type	Results
870.4200	Carcinogenicity-mouse	Systemic LOAEL: 10.43 mg/kg/day (100 ppm) for females, based on increased adrenal cortico-medullary pigmentation and 30.51 mg/kg/day (300 ppm) for males, based on decreased body weights and non-neoplastic lesions in the adrenals, pituitary and kidney. At 300 ppm, increase in cholinergic signs (ataxia, hunched posture, tremors) was observed NOAEL: 3.20 mg/kg/day (30 ppm) and 10.32 mg/kg/day (100 ppm) for females and males, respectively. The test material was not carcinogenic at the doses tested
870.4300	Combined chronic/carcinogenicity-rat	Systemic LOAEL: 50 ppm (2.45 mg/kg/day) for females, based on decreased RBC parameters (packed cell volume, hemoglobin, and RBC count), and increased incidence of atrophy and foamy interstitial cells in the ovaries and 200 ppm (8.34 mg/kg/day) for males, based on increased incidences of retinal atrophy, skeletal degenerative myopathy and non-neoplastic lesions in the adrenal and pituitary glands NOAEL: 10 ppm (0.50 mg/kg/day) and 50 ppm (1.94 mg/kg/day) for female and male rats, respectively. The test material was not carcinogenic at the doses tested LOAEL for ChEI: 10 ppm for male rats (0.38 mg/kg/day) and 1 ppm for female rats (0.051 mg/kg/day) based on inhibition of plasma and RBC ChE activity NOAEL: 1 ppm for male rats (0.039 mg/kg/day) and a NOAEL was not established for female rats
870.5100	Gene mutation *salmonella*/mammalian activation gene mutation assay with BSA	Negative in *salmonella* strains with or without S-9 activation. No cytotoxicity response up to the limit dose
870.5265	Gene mutation *salmonella*/mammalian activation gene mutation assay	Negative for mutagenic effects at dose levels up to 5,000 μg/plate with or without metabolic activation
870.5300	*In vitro* gene mutation-mouse lymphoma assay	No evidence of increased mutation frequency at the thymidine locus in cells treated upto cytotoxic concentration with or without S-9. Cytotoxicity was evident at ≥640 μg/ml (-S9) and ≥160 μg/mL (+S9)
870.5300	*In vitro* mammalian gene mutation - mouse lymphoma assay with BSA	No evidence of increased mutation frequency in cells treated up to the limit dose with or without S-9
870.5375	*In vitro* cytogenetics (CHO) assay	No effects at concentrations up to 200 μg/ml (without S9) or 750 μg/mL (with S9). Cytotoxicity was evident at ≥50 μg/mL (-S9)and ≥93.75 μg/mL (+S9)
870.5395	*In vivo* mammalian cytogenetics assay	No evidence of clastogenic or aneugenic effect at doses tested. Negative for induction of micronuclei at a dose approaching oral MTD, 50 mg/kg
870.5395	*In vivo* mammalian cytogenetics micronucleus assay with BSA	No evidence of clastogenic or aneugenic effect at doses tested. Negative for induction of micronuclei
870.5500	*In vitro* DNA repair test	Negative in the DNA repair test. Fosthiazate did not induce any clear differences in the diameter of growth inhibitory zones between H17 (rec+) and M 45 (rec-), either in the presence or absence of metabolic activation
870.6100	Acute delayed neurotoxicity (ADNT) study-hen	Six hens treated with IKI-1145 (fosthiazate technical) died within 6 days; 2 had relapses and progressed to moribundity on days 13 and 26; 9 hens survived. No abnormal neuropathological changes were observed except for a minimal case of focal gliosis in the lumbar sacral area of one of the two relapsing hens. IKI-1145 did not cause ADNT

TABLE 1.—SUBCHRONIC, CHRONIC, AND OTHER TOXICITY—Continued

Guideline No.	Study Type	Results
870.6200	Acute neurotoxicity screening battery	Neurotoxicity LOAEL: 10 mg/kg/day based on decreased forelimb grip strength in females. No abnormal neuropathological changes were observed NOAEL: 0.4 mg/kg/day LOAEL for ChEI: 10 mg/kg/day based on inhibition of plasma. Erythrocyte, and brain 3 hrs postdosing (plasma ChEI was reversible) NOAEL: 0.4 mg/kg/day
--	Special cholinesterase inhibition study-rat	LOAEL: 4.0 mg/kg/day based on plasma ChEI NOAEL: 0.4 mg/kg/day Decrease plasma ChE activity was noted in the male and female rats 3 hours after a single dose at 4.0 mg/kg body weight. Brain and RBC ChE activities were unaffected
870.6200	Subchronic neurotoxicity screening battery	Systemic LOAEL: 2.5 mg/kg/day based on decreased hind limb grip strength (21%; $p<0.01$) in females. No abnormal neuropathological changes were observed NOAEL: 0.5 mg/kg/day. LOAEL for ChEI: 0.5 mg/kg/day based on significant inhibition of plasma, erythrocyte and brain ChE in females at weeks 5 and/or 9 and 14 NOAEL: 0.05 mg/kg/day
870.7485	Metabolism-rat	IKI-1145 (fosthiazate technical) was rapidly absorbed and widely distributed with only >5% detected in the tissues. No sex-related differences noted in the absorption and distribution; absorption was not dose dependent. Peak concentration in the blood was at 0.33 hr in both sexes. Only one metabolite, BESxP, represented >10% of the administered dose. Test material was rapidly eliminated primarily in the urine (57%-72%) within 24 hrs. Unacceptable/Guideline due to lack of identification of metabolites in fecal radioactivity (accounted for 9-15% of the administered dose). Mean recovery was 95%-99%. IKI-1145 was metabolized by multiple processes including hydrolysis, oxidation, methylation and glutathione conjugation
870.7485	Metabolism-rat	IKI-1145 was rapidly and extensively absorbed independent of dose; rapidly metabolized and excreted in the urine (>65%), expired air (>10%) and in feces (<9%). Elimination was biphasic with first phase elimination half-life (t1/2) of 5-6 hrs and second phase of 85-112 hrs. Metabolism and excretion was rapid within 24 hrs. IKI-1145 was metabolized by multiple processes including hydrolysis, oxidation, methylation and glutathione conjugation. Female rats tended to excrete a metabolite containing a methylsulfinylethyl group while male rats excreted more containing a sulfoethyl group
870.7485	Metabolism-rat with BSA	Recovery was 100-108%. BSA was rapidly eliminated unchanged following dosing via the iv (approx. 100% in the urine) or oral (63%-89% in the urine and 10%-28% in feces) routes. Tissue burden was low

B. Toxicological Endpoints

The dose at which no adverse effects are observed (the NOAEL) from the toxicology study identified as appropriate for use in risk assessment is used to estimate the toxicological level of concern (LOC). However, the lowest dose at which adverse effects of concern are identified (the LOAEL) is sometimes used for risk assessment if no NOAEL was achieved in the toxicology study selected. An uncertainty factor (UF) is applied to reflect uncertainties inherent in the extrapolation from laboratory animal data to humans and in the variations in sensitivity among members of the human population as well as other unknowns. An UF of 100 is routinely used, 10X to account for interspecies differences and 10X for intraspecies differences. Based on the weight of evidence presented, the Agency concluded that a developmental neurotoxicity (DNT) study with comparative cholinestrase (ChE) measurements in adults and pups is required for fosthiazate. The available data base confirms that fosthiazate is a ChE inhibitor and the increased sensitivity for this effect cannot be confirmed until the results of DNT study are known. Based on the lack of a DNT study, the Agency also concluded that a Database Uncertainty Factor (UFdb) is necessary. The available data suggest that results of a DNT study, as well as additional ChE data, could potentially impact the doses selected for risk assessment. Therefore, a 10X UFdb is required for acute dietary risk assessment and a 3X UFdb is required for chronic dietary risk assessment. Refer to Unit III.D.3 of this document for a detailed discussion of these uncertainty factors.

For dietary risk assessment (other than cancer) the Agency uses UF to calculate an acute or chronic reference dose (acute RfD or chronic RfD) where the RfD is equal to the NOAEL divided by the appropriate UF (RfD = NOAEL/UF). Where an additional safety factor (SF) is retained due to concerns unique to the FQPA, this additional factor is applied to the RfD by dividing the RfD by such additional factor. The acute or

chronic Population Adjusted Dose (aPAD or cPAD) is a modification of the RfD to accommodate this type of FQPA SF.

For non-dietary risk assessments (other than cancer) the UF is used to determine the LOC. For example, when 100 is the appropriate UF (10X to account for interspecies differences and 10X for intraspecies differences) the LOC is 100. To estimate risk, a ratio of the NOAEL to exposures (margin of exposure (MOE) = NOAEL/exposure) is calculated and compared to the LOC.

The linear default risk methodology (Q*) is the primary method currently used by the Agency to quantify carcinogenic risk. The Q* approach assumes that any amount of exposure will lead to some degree of cancer risk. A Q* is calculated and used to estimate risk which represents a probability of occurrence of additional cancer cases (e.g., risk is expressed as 1 x 10^{-6} or one in a million). Under certain specific circumstances, MOE calculations will be used for the carcinogenic risk assessment. In this non-linear approach, a "point of departure'' is identified below which carcinogenic effects are not expected. The point of departure is typically a NOAEL based on an endpoint related to cancer effects though it may be a different value derived from the dose response curve. To estimate risk, a ratio of the point of departure to exposure (MOE_{cancer} = point of departure/exposures) is calculated. A summary of the toxicological endpoints for fosthiazate used for human risk assessment is shown in Table 2 of this unit:

TABLE 2.—SUMMARY OF TOXICOLOGICAL DOSE AND ENDPOINTS FOR FOSTHIAZATE FOR USE IN HUMAN RISK ASSESSMENT

Exposure Scenario	Dose (mg/kg/day) UF/ MOE	Hazard and Exposure Based Special FQPA Safety Factor	Study and Toxicological Effects
	Dietary risk assessments		
Acute dietary (general population including infants and children)	NOAEL = 0.4 UF = 100 UFdb* = 10	1X	Acute oral neurotoxicity/rat LOAEL = 10 mg/kg/day based on inhibition of RBC ChE in males within 3 hrs post dosing
	Acute RfD and Acute PAD = 0.0004 mg/kg/day		
Chronic dietary	NOAEL = 0.05 UF = 100 UFdb* = 3	1X	Chronic oral toxicity/rat LOAEL= 0.38 mg/kg/day based on inhibition of plasma and RBC ChE in males
	Chronic RfD and Chronic PAD = 0.00017 mg/kg/day		

* UFdb = database uncertainty factors of 10X and 3X are applied for lack of a DNT study and ChE data

C. Exposure Assessment

1. *Dietary exposure from food and feed uses.* Currently there are no tolerances established for fosthiazate on any commodity. Risk assessments were conducted by EPA to assess dietary exposures from fosthiazate in food as follows:

i. *Acute exposure.* Acute dietary risk assessments are performed for a food-use pesticide if a toxicological study has indicated the possibility of an effect of concern occurring as a result of a one day or single exposure. The Dietary Exposure Evaluation Model (DEEM™) analysis evaluated the individual food consumption as reported by respondents in the USDA 1994–1996 and 1998 nationwide Continuing Surveys of Food Intake by Individuals (CSFII) and accumulated exposure to the chemical for each commodity. The following assumptions were made for the acute exposure assessments: The acute dietary risk assessment was based on field trial residues in tomato (½ limit of quantitation (LOQ) parent + ½ LOQ ASC-67131) and 100% crop treated (CT). Risks of concern were considered at the 95th percentile because field trial data with 1.3X application rate, minimum preharvest interval (PHI) and 100% CT were used, which are considered conservative inputs. No detectable residues of either the parent or its metabolite of concern were found in the edible portion during these field trials at a limit of detection (LOD) of 0.01 ppm using gas chromatograph/flame photometric detector (GC/FPD) (phosphorus) as an analytical method.

The Agency believes that the default assumption of ½ LOD of the GC/FPD (phosphorus) analytical method for each of the parent and metabolite significantly exaggerates actual exposures. Radiolabeled tomato metabolism studies were done at a 1.3X rate and using an analytical method GC/FPD (phosphorus) with a much lower LOD of 0.001 ppm (an order of magnitude lower). No residues were found in the edible fruit following the radiolabel studies. This means that residues, if present, would be present at <0.001 ppm at this application rate. Thus, the use of ½ LOD of the GC/FPD (phosphorus) analytical method for both parent and metabolite is a conservative estimate of exposure (compounded by a 100% CT assumption): Radiolabel metabolism studies suggest that residues are at least five times lower than the ½ LOD of the GC/FPD (phosphorus) analytical method assumed in the assessment, and even more if one were to take into account the 1.3X application rate.

ii. *Chronic exposure.* In conducting this chronic dietary risk assessment, the DEEM™ analysis evaluated the individual food consumption as reported by respondents in the USDA 1994–1996 and 1998 nationwide CSFII and accumulated exposure to the chemical for each commodity. The following assumptions were made for the chronic exposure assessments: The chronic dietary risk assessment was based on field trial residues in tomatoes, 100% CT, and average daily consumption estimates for each food/food form.

iii. *Cancer.* In accordance with the EPA Draft Guidelines for Carcinogen Risk Assessment (July 1999), the Agency has classified fosthiazate as "not likely to be carcinogenic to humans.'' This classification is based on the lack of evidence for carcinogenicity in studies with mice and rats; therefore, a quantitative cancer dietary assessment has not been conducted.

2. *Dietary exposure from drinking water*. The Agency lacks sufficient monitoring exposure data to complete a comprehensive dietary exposure analysis and risk assessment for fosthiazate in drinking water. Because the Agency does not have comprehensive monitoring data, drinking water concentration estimates are made by reliance on simulation or modeling taking into account data on the physical characteristics of fosthiazate.

The Agency uses the First Index Reservoir Screening Tool (FIRST) or the Pesticide Root Zone/Exposure Analysis Modeling System (PRZM/EXAMS), to produce estimates of pesticide concentrations in an index reservoir. The Screening Concentrations in Groundwater (SCI-GROW) model is used to predict pesticide concentrations in shallow ground water. For a screening-level assessment for surface water EPA will use FIRST (a Tier 1 model) before using PRZM/EXAMS (a Tier 2 model). The FIRST model is a subset of the PRZM/EXAMS model that uses a specific high-end runoff scenario for pesticides. While both FIRST and PRZM/EXAMS incorporate an index reservoir environment, the PRZM/EXAMS model includes a percent crop area factor as an adjustment to account for the maximum percent crop coverage within a watershed or drainage basin.

None of these models include consideration of the impact processing (mixing, dilution, or treatment) of raw water for distribution as drinking water would likely have on the removal of pesticides from the source water. The primary use of these models by the Agency at this stage is to provide a coarse screen for sorting out pesticides for which it is highly unlikely that drinking water concentrations would ever exceed human health levels of concern.

Since the models used are considered to be screening tools in the risk assessment process, the Agency does not use estimated environmental concentrations (EECs) from these models to quantify drinking water exposure and risk as a %RfD or %PAD. Instead drinking water levels of comparison (DWLOCs) are calculated and used as a point of comparison against the model estimates of a pesticide's concentration in water. DWLOCs are theoretical upper limits on a pesticide's concentration in drinking water in light of total aggregate exposure to a pesticide in food, and from residential uses. Since DWLOCs address total aggregate exposure to fosthiazate, they are further discussed in the aggregate risk sections in Unit E.

Based on the PRZM/EXAMS and SCI-GROW models, the EECs of fosthiazate for acute exposures are estimated to be 2.1 parts per billion (ppb) for surface water and 2.4 ppb for ground water. The EECs for chronic exposures are estimated to be 0.6 ppb for surface water and 2.4 ppb for ground water. These estimates are based on the assumption that application will be made by drip irrigation in bands with plastic mulch. Runoff as a result of this use may be unlikely from the day of application until the day of harvest (approximately 90 days) when the field is covered by the plastic mulch, unless an extremely heavy amount of rain falls immediately after application and causes runoff from under the mulch into the uncovered area. For this reason, application is prohibited when heavy rainfall is predicted. Runoff after the removal of the plastic cover may be possible, however the amount of fosthiazate remaining in soil and available for runoff would be much less than the amount applied, due to chemical degradation and dissipation in soil and to chemical uptake into plants. Assuming that half of the amount applied is absorbed by plants and the remaining half dissipates in soil at a rate of 45 days (based on laboratory and field studies), it is expected that only about one eighth of what was originally applied would be available for runoff after the cover is removed (90 days postapplication). Maximum application rate is 1.5 lbs a.i. per acre with only one application per season. Therefore, the Agency predicts that the peak estimated drinking water concentrations (EDWC) would be roughly 2.1 µg/L and the chronic EDWC would be 0.6 µg/L for the maximum application rate. These concentrations were modeled under the most conservative scenarios and likely exceed the actual level of contamination in the environment. In actual practice, the same plastic mulch is left in the field for rotated crops, thus making the EEC calculations based on the mulch being removed after 90 days even more conservative.

SCI-GROW assumes the pesticide is applied above ground without cover and the subsequent and heavy amount of water (140% of yearly average amount of rainfall) leaches some of the pesticide down to ground water. The plastic mulch cover would minimize volatilization and runoff, therefore increasing the amount of the chemical available for leaching. However, with the drip irrigation method, a small amount of water is slowly dripped into soils precisely where it is needed, thus lessening the amount of water flowing down through the soil past the root zone where it cannot be used by the crop. This should greatly reduce the potential for the chemical to reach ground water systems. For this reason, the Agency does not expect ground water contamination from the drip irrigation method under plastic mulch to exceed the levels calculated by the SCI-GROW model. Terrestrial field dissipation studies indicate no leaching of fosthiazate residues below the top (0-15 cm) soil layer.

3. *From non-dietary exposure*. The term "residential exposure'' is used in this document to refer to non-occupational, non-dietary exposure (e.g., for lawn and garden pest control, indoor pest control, termiticides, and flea and tick control on pets).

Fosthiazate is not registered for use on any sites that would result in residential exposure.

4. *Cumulative exposure to substances with a common mechanism of toxicity*. Section 408(b)(2)(D)(v) of the FFDCA 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.''

Fosthiazate is an OP pesticide, and has a common mechanism of toxicity with other OPs. The Agency has completed a Revised Cumulative Risk Assessment (CRA) for OPs, which can be found on the Agency's web site *www.epa.gov/pesticides/cumulative*. This assessment examined the cumulative effects of exposure to the OP pesticides considering monitoring values for OPs in food and water, and potential residential exposures. The relative potency factor (RPF) for fosthiazate was determined using the estimated benchmark dose (BMD)10 for female brain ChE data from feeding toxicity studies in the rat. The BMD10 is the estimated dose at which ChE is inhibited 10% compared to background inhibition. Although fosthiazate was considered in the cumulative hazard and dose-response assessment, it was not included in the OP cumulative exposure assessment since this OP pesticide (i) is not monitored by the USDA's Pesticide Data Program (PDP) or other monitoring data sets used in the cumulative OP assessment and is not expected to be present in food as a result of its use on tomatoes at levels that would be detectable by monitoring; (ii) is not expected to be present in surface water or ground water to a degree that would have any impact on the data on drinking water residues of

OPs used in the cumulative risk assessment; and (iii) has no residential uses. Residue data are available for fosthiazate from crop field trials conducted with tomatoes in which maximum (label) application rates and minimum (label) preharvest intervals were used. No residues were detected in these field trials (<0.01 ppm). Thus, EPA concludes that there is reasonable expectation that fosthiazate residues would not be detected in monitoring data from use on tomato. Further, fosthiazate would not contribute to the total estimated cumulative dietary risk in the OP cumulative risk assessment since non-detectable residues in monitoring data were considered to have a residue value of "zero.'' None of the OPs in the CRA made a significant contribution to overall exposure via the drinking water pathway, and fosthiazate does not look as though it makes a significant exposure by the water pathway from the use on tomato because of the low application rate, only one application per season, application method of drip irrigation under plastic mulch, and no leaching of the compound below the top soil layer. Accordingly, after considering the cumulative effects of the OPs, EPA concludes that the overall cumulative risk has a limited bearing on this tolerance action because fosthiazate exposure will have no impact on the estimate of cumulative risk for OPs.

D. Safety Factor for Infants and Children

1.*In general.* Section 408 of the FFDCA provides that EPA shall apply an additional tenfold margin of safety for infants and children in the case of threshold effects to account for prenatal and postnatal toxicity and the completeness of the data base on toxicity and exposure 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 MOE analysis or through using uncertainty (safety) factors in calculating a dose level that poses no appreciable risk to humans.

2. *Prenatal and postnatal sensitivity.* In a 2–generation reproduction study, there is qualitative and quantitative evidence of increased susceptibility in offspring following prenatal and postnatal exposure to fosthiazate since the effects on pups are considered to be severe and occurred at a lower dose than those on parental animals.

Since there is evidence of increased susceptibility of the young following prenatal and postnatal exposure to fosthiazate in the rat reproduction study, the Agency performed a Degree of Concern Analysis to: (i) Determine the level of concern for the effects observed when considered in the context of all available toxicity data; and (ii) identify any residual uncertainties after establishing toxicity endpoints and traditional uncertainty factors to be used in the risk assessment of this chemical.

In determining the degree of concern for these findings in the reproduction study, the Agency considered the overall quality of the study; the dose levels at which the pup effects were observed; the dose response of the pup effects; and the comparative severity of the effects seen. It was determined that there is a low degree of concern and no residual uncertainties for the susceptibility since: (i) The study was well conducted; (ii) the dose-response in the offspring is well characterized; (iii) clear NOAEL and LOAEL were established for the effects on the offspring; (iv) although the decrease in pup survival seen at the LOAEL is severe, this could be attributed to exposure to higher levels of the chemical since the mortalities occurred during early lactation; and (v) although cholinesterase activity was not measured in this study, cholinergic signs and cholinesterase inhibition were seen at comparable doses in other studies and thus could have been a cause for the pup mortality.

3. *Conclusion.* The toxicological data base for fosthiazate is not complete and therefore, EPA has retained the FQPA safety factor, in the form of a UFdb, at the level of 10X for acute risk and 3X for chronic risk. A 28–day inhalation study in rats is required, in order to better characterize exposure via the inhalation route. A DNT study in rats with comparative ChE measurements in adults and pups is also required, and is currently being conducted by the registrant. The available data base confirms that fosthiazate is a ChE inhibitor and the increased sensitivity for this effect cannot be confirmed until the results of a DNT study are known.

A FQPA safety factor, in the form of a Ufdb, was retained because the available data suggest that results of a DNT study could potentially impact the doses selected for risk assessment. ChEI has been shown to be the most sensitive endpoint for fosthiazate in adults; it can also be assumed that ChEI may potentially be the most sensitive endpoint for pups. The regulatory dose level for acute dietary risk assessment is the NOAEL of 0.4 mg/kg/day selected from the acute neurotoxicity study in adult rats. The regulatory dose level for chronic dietary risk assessment is the NOAEL of 0.05 mg/kg/day from the 2–year chronic/carcinogenicity toxicity study in rats. The dose levels in the reproductive toxicity study are estimated to be 0, 0.21, 0.69, 2.09, and 7.21 mg/kg/day. The offspring NOAEL and LOAEL are 0.69 mg/kg/day and 2.09 mg/kg/day, respectively, based on decreased pup weight, viability index, and litter size in the F_1 pups.

It can be assumed that doses used in a DNT study may be similar to those used in the reproductive toxicity study. Although it is not likely given the effects seen to date in the fosthiazate data base, the results from the DNT may show severe effects at the lowest dose tested (estimated at 0.21 mg/kg/day). In such circumstances, EPA may impose up to a 10X safety factor to project a NOAEL for the DNT which would mean a projected NOAEL of 0.02 mg/kg/day. Thus, the DNT may result in an acute ChE NOAEL for pups that is greater than 10X lower than the established offspring NOAEL of 0.69 mg/kg/day and the NOAEL of 0.4 mg/kg/day currently used for establishing the acute RfD. Given that the DNT could impact the level chosen for estimating the acute RfD by 10X or greater, EPA concludes that reliable data do not support removing the 10X children's safety factor and thus have retained that factor in the form of a 10X UFdb for acute dietary risk assessment.

As to the chronic RfD, the projected multi-dosing ChE NOAEL for pups from the DNT may be lower than the established chronic ChE NOAEL of 0.05 mg/kg/day from the 2–year chronic/carcinogenicity study and could be as low as 0.02 mg/kg/day (i.e., 10X lower than the lowest dose in the reproductive toxicity study). Although the DNT may possibly impact the level chosen for estimating the chronic RfD, there is reliable data supporting use of a 3X additional factor for chronic dietary risk assessment, because, the 0.05 mg/kg/day NOAEL currently used for risk assessment is approximately 3X higher than the potential lower NOAEL (0.02 mg/kg/day) that could be attained in the DNT. Therefore, EPA has chosen a 3X safety factor for the protection of infants and children, in the form of a 3X UFdb for chronic dietary risk assessment.

In absence of the 28–day inhalation study, the Agency is assuming 100% absorption for the route to route extrapolation. As the Acute Toxicity Category for the oral route is II and the Acute Toxicity Category for the inhalation route is III, it is unlikely that an inhalation NOAEL would be lower than the oral NOAEL being used currently. However, in order to better characterize exposure via the inhalation

route specifically, this study would provide information on portal of entry effects specific to the nasal passages and pulmonary tract.

The dietary food exposure assessment is conservative, using field trial level residues and assuming 100% CT. Dietary drinking water exposure is based on conservative modeling estimates and there are no residential uses. These assessments will not underestimate the exposure and risks posed by fosthiazate.

E. Aggregate Risks and Determination of Safety

To estimate total aggregate exposure to a pesticide from food, drinking water, and residential uses, the Agency calculates DWLOCs which are used as a point of comparison against the model estimates of a pesticide's concentration in water (EECs). DWLOC values are not regulatory standards for drinking water. DWLOCs are theoretical upper limits on a pesticide's concentration in drinking water in light of total aggregate exposure to a pesticide in food and residential uses. In calculating a DWLOC, the Agency determines how much of the acceptable exposure (i.e., the PAD) is available for exposure through drinking water (e.g., allowable chronic water exposure (mg/kg/day) = cPAD - (average food + residential exposure)). This allowable exposure through drinking water is used to calculate a DWLOC.

A DWLOC will vary depending on the toxic endpoint, drinking water consumption, and body weights. Default body weights and consumption values as used by the USEPA Office of Water are used to calculate DWLOCs: 2 liter (L)/70 kg (adult male), 2L/60 kg (adult female), and 1L/10 kg (child). Default body weights and drinking water consumption values vary on an individual basis. This variation will be taken into account in more refined screening-level and quantitative drinking water exposure assessments. Different populations will have different DWLOCs. Generally, a DWLOC is calculated for each type of risk assessment used: Acute, short-term, intermediate-term, chronic, and cancer.

When EECs for surface water and ground water are less than the calculated DWLOCs, EPA concludes with reasonable certainty that exposures to the pesticide in drinking water (when considered along with other sources of exposure for which EPA has reliable data) would not result in unacceptable levels of aggregate human health risk at this time. Because EPA considers the aggregate risk resulting from multiple exposure pathways associated with a pesticide's uses, levels of comparison in drinking water may vary as those uses change. If new uses are added in the future, EPA will reassess the potential impacts of residues of the pesticide in drinking water as a part of the aggregate risk assessment process.

1. *Acute risk.* Using the exposure assumptions discussed in this unit for acute exposure, the acute dietary exposure from food to fosthiazate will occupy 12% of the aPAD for the U.S. population, 10% of the aPAD for females 13–49 years of age, 11% of the aPAD for all infants <1 year of age and 29% of the aPAD for children 1–2 years of age. In addition, there is potential for acute dietary exposure to fosthiazate in drinking water. After calculating DWLOCs and comparing them to the EECs for surface water and ground water, EPA does not expect the aggregate exposure to exceed 100% of the aPAD, as shown in Table 3 of this unit:

TABLE 3.—AGGREGATE RISK ASSESSMENT FOR ACUTE EXPOSURE TO FOSTHIAZATE

Population Subgroup	aPAD (mg/kg)	% aPAD (Food)	Surface Water EEC (ppb)	Ground Water EEC (ppb)	Acute DWLOC (ppb)
U.S. population	0.0004	12	2.1	2.4	12
Infants (<1 year)	0.0004	11	2.1	2.4	4
Children (1–2 years)	0.0004	29	2.1	2.4	3
Females (13–49 years)	0.0004	10	2.1	2.4	11

2. *Chronic risk.* Using the exposure assumptions described in this unit for chronic exposure, EPA has concluded that exposure to fosthiazate from food will utilize 7% of the cPAD for the U.S. population; 4% of the cPAD for all infants <1 year; 15% of the cPAD for children 1–2 years; and 6% of the cPAD for females 13–49 years. There are no residential uses for fosthiazate that result in chronic residential exposure to fosthiazate. In addition, there is potential for chronic dietary exposure to fosthiazate in drinking water. After calculating DWLOCs and comparing them to the EECs for surface water and ground water, it is noted that the DWLOCs are slightly exceeded by the estimated ground water EECs for two population subgroups. However, these concentrations were modeled under the most conservative scenarios and likely exceed the actual level of contamination in the environment. SCI-GROW, used to model ground water exposures, is a Tier 1 unrefined assessment and therefore, highly conservative. Importantly, pesticide-specific aspects to this use of fosthiazate are likely to significantly exaggerate the conservativeness of the SCI-GROW estimates. SCI-GROW assumes the pesticide is applied above ground without cover and a subsequent and heavy amount of water (140% of yearly average amount of rainfall) leaches some of the pesticide down to ground water. However, with the proposed registration using the drip irrigation method, a small amount of water is slowly dripped into soils precisely where it is needed, thus lessening the amount of water containing pesticide residues flowing down through the soil past the root zone where it cannot be used by the crop. This is expected to reduce the potential for the chemical to reach into ground water systems, and the actual ground water EECs would be less than what SCI-GROW predicted. Further, fosthiazate is required to be applied in fields using plastic mulch which significantly decreases the effect of rainfall on pesticide leaching. Finally, terrestrial field dissipation studies submitted to the Agency indicate no leaching of fosthiazate residues below the top (0-15 cm) soil layer. Therefore, EPA does not expect the aggregate exposure to exceed 100% of the cPAD, as shown in Table 4 of this unit:

TABLE 4.—AGGREGATE RISK ASSESSMENT FOR CHRONIC (NON-CANCER) EXPOSURE TO FOSTHIAZATE

Population Subgroup	cPAD (mg/kg/day)	% cPAD (Food)	Surface Water EEC (ppb)	Ground Water EEC (ppb)	Chronic DWLOC (ppb)
U.S. population	0.00017	7	0.6	2.4	6
Infants (< 1 year)	0.00017	4	0.6	2.4	2
Children (1–2 years)	0.00017	15	0.6	2.4	2
Females (13–49 years)	0.00017	6	0.6	2.4	5

3. *Short-term risk*. Short-term aggregate exposure takes into account residential exposure plus chronic exposure to food and water (considered to be a background exposure level).

Fosthiazate is not registered for use on any sites that would result in residential exposure. Therefore, the aggregate risk is the sum of the risk from food and water, which do not exceed the Agency's level of concern.

4. *Intermediate-term risk*. Intermediate-term aggregate exposure takes into account residential exposure plus chronic exposure to food and water (considered to be a background exposure level).

Fosthiazate is not registered for use on any sites that would result in residential exposure. Therefore, the aggregate risk is the sum of the risk from food and water, which do not exceed the Agency's level of concern.

5. *Aggregate cancer risk for U.S. population*. Fosthiazate has been classified into the category "Not likely to be carcinogenic to humans.'' This classification is based on the lack of evidence for carcinogenicity in mice and rats. Therefore, fosthiazate is not expected to pose a cancer risk.

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

IV. Other Considerations

A. Analytical Enforcement Methodology

Adequate enforcement methodology is available to enforce the tolerance expression. The method may be requested from: Chief, Analytical Chemistry Branch, Environmental Science Center, 701 Mapes Rd., Ft. Meade, MD 20755–5350; telephone number: (410) 305–2905; e-mail address: *residuemethods@epa.gov*.

B. International Residue Limits

There are currently no established Codex, Canadian, or Mexican maximum residue limits (MRLs) for residues of fosthiazate in/on plant or livestock commodities.

V. Conclusion

Therefore, the tolerance is established for combined residues of fosthiazate, (*O*-ethyl *S*-(1-methylpropyl)(2-oxo-3-thiazolidinyl)phosphonothioate) and its metabolite ASC-67131 ((*RS*)-*S*-sec-Butyl *O*-ethyl *N*-[2-(methylsulfonyl)ethyl] phosphoramidothioate), in or on tomato at 0.02 ppm.

VI. Objections and Hearing Requests

Under section 408(g) of the FFDCA, as amended by the FQPA, any person may file an objection to any aspect of this regulation and may also request a hearing on those objections. The EPA procedural regulations which govern the submission of objections and requests for hearings appear in 40 CFR part 178. Although the procedures in those regulations require some modification to reflect the amendments made to the FFDCA by the FQPA, EPA will continue to use those procedures, with appropriate adjustments, until the necessary modifications can be made. The new section 408(g) of the FFDCA provides essentially the same process for persons to "object'' to a regulation for an exemption from the requirement of a tolerance issued by EPA under new section 408(d) of FFDCA, as was provided in the old sections 408 and 409 of the FFDCA. However, the period for filing objections is now 60 days, rather than 30 days.

A. What Do I Need to Do to File an Objection or Request a Hearing?

You must file your objection or request a hearing on this regulation in accordance with the instructions provided in this unit and in 40 CFR part 178. To ensure proper receipt by EPA, you must identify docket ID number OPP–2003–0296 in the subject line on the first page of your submission. All requests must be in writing, and must be mailed or delivered to the Hearing Clerk on or before June 7, 2004.

1. *Filing the request*. Your objection must specify the specific provisions in the regulation that you object to, and the grounds for the objections (40 CFR 178.25). If a hearing is requested, the objections must include a statement of the factual issues(s) on which a hearing is requested, the requestor's contentions on such issues, and a summary of any evidence relied upon by the objector (40 CFR 178.27). 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.

Mail your written request to: Office of the Hearing Clerk (1900C), Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001. You may also deliver your request to the Office of the Hearing Clerk in Rm. 104, Crystal Mall #2, 1921 Jefferson Davis Hwy., Arlington, VA. The Office of the Hearing Clerk is open from 8 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The telephone number for the Office of the Hearing Clerk is (703) 603–0061.

2. *Tolerance fee payment*. If you file an objection or request a hearing, you must also pay the fee prescribed by 40 CFR 180.33(i) or request a waiver of that fee pursuant to 40 CFR 180.33(m). You must mail the fee to: EPA Headquarters Accounting Operations Branch, Office of Pesticide Programs, P.O. Box 360277M, Pittsburgh, PA 15251. Please identify the fee submission by labeling it "Tolerance Petition Fees.''

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 the waiver of these fees, you may contact

James Tompkins by phone at (703) 305–5697, by e-mail at *tompkins.jim@epa.gov*, or by mailing a request for information to Mr. Tompkins at Registration Division (7505C), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001.

If you would like to request a waiver of the tolerance objection fees, you must mail your request for such a waiver to: James Hollins, Information Resources and Services Division (7502C), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001.

3. *Copies for the Docket*. In addition to filing an objection or hearing request with the Hearing Clerk as described in Unit VI.A., you should also send a copy of your request to the PIRIB for its inclusion in the official record that is described in Unit I.B.1. Mail your copies, identified by docket ID number OPP–2003–0296, to: Public Information and Records Integrity Branch, Information Resources and Services Division (7502C), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001. In person or by courier, bring a copy to the location of the PIRIB described in Unit I.B.1. You may also send an electronic copy of your request via e-mail to: *opp-docket@epa.gov*. Please use an ASCII file format and avoid the use of special characters and any form of encryption. Copies of electronic objections and hearing requests will also be accepted on disks in WordPerfect 6.1/8.0 or ASCII file format. Do not include any CBI in your electronic copy. You may also submit an electronic copy of your request at many Federal Depository Libraries.

B. When Will the Agency Grant a Request for a Hearing?

A request for a hearing will be granted if the Administrator determines that the material submitted shows the following: There is a 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(s) in the manner sought by the requestor would be adequate to justify the action requested (40 CFR 178.32).

VII. Statutory and Executive Order Reviews

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). Because this rule has been exempted from review under Executive Order 12866 due to its lack of significance, this rule is not subject to Executive Order 13211, *Actions Concerning Regulations That Significantly Affect Energy Supply, Distribution, or Use* (66 FR 28355, May 22, 2001). 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) (Public Law 104–4). Nor does it require any special considerations under Executive Order 12898, entitled *Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations* (59 FR 7629, February 16, 1994); or OMB review or any Agency action under Executive Order 13045, entitled *Protection of Children from Environmental Health Risks and Safety Risks* (62 FR 19885, April 23, 1997). This action does not involve any technical standards that would require Agency consideration of voluntary consensus standards pursuant to section 12(d) of the National Technology Transfer and Advancement Act of 1995 (NTTAA), Public Law 104–113, section 12(d) (15 U.S.C. 272 note). Since tolerances and exemptions that are established on the basis of a petition under section 408(d) of the FFDCA, such as the tolerance 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. In addition, the Agency has determined that this action will not have a substantial direct effect on States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government, as specified in Executive Order 13132, entitled *Federalism* (64 FR 43255, August 10, 1999). Executive Order 13132 requires EPA to develop an accountable process to ensure "meaningful and timely input by State and local officials in the development of regulatory policies that have federalism implications.'' "Policies that have federalism implications'' is defined in the Executive Order to include regulations that have "substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government.'' This final rule directly regulates growers, food processors, food handlers and food retailers, not States. This action does not alter the relationships or distribution of power and responsibilities established by Congress in the preemption provisions of section 408(n)(4) of the FFDCA. For these same reasons, the Agency has determined that this rule does not have any "tribal implications'' as described in Executive Order 13175, entitled *Consultation and Coordination with Indian Tribal Governments* (65 FR 67249, November 6, 2000). Executive Order 13175, requires EPA to develop an accountable process to ensure "meaningful and timely input by tribal officials in the development of regulatory policies that have tribal implications.'' "Policies that have tribal implications'' is defined in the Executive Order to include regulations that have "substantial direct effects on one or more Indian tribes, on the relationship between the Federal Government and the Indian tribes, or on the distribution of power and responsibilities between the Federal Government and Indian tribes.'' This rule will not have substantial direct effects on tribal governments, on the relationship between the Federal Government and Indian tribes, or on the distribution of power and responsibilities between the Federal Government and Indian tribes, as specified in Executive Order 13175. Thus, Executive Order 13175 does not apply to this rule.

VIII. Congressional Review Act

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 to 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 this final rule in the **Federal Register**. This final

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 26, 2004.

James Jones,

Director, 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), 346(a) and 371.

■ 2. Section 180.596 is added to subpart C to read as follows:

§ 180.596 Fosthiazate; tolerances for residues.

(a) *General.* Tolerances are established for the combined residues of Fosthiazate (*O*-ethyl *S*-(1-methylpropyl)(2-oxo-3-thiazolidinyl)phosphonothioate and its metabolite *O*-ethyl *S*-(1-methylpropyl)[2-(methylsulfonyl)ethyl] phosphoramidothioate) (ASC–67131).

Commodity	Parts per million
Tomato	0.02

(b) *Section 18 emergency exemptions.* [Reserved]

(c) *Tolerances with regional registrations.* [Reserved]

(d) *Indirect or inadvertent residues.* [Reserved]

[FR Doc. 04–7864 Filed 4–6–04; 8:45 am]

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ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[OPP–2004–0036; FRL–7352–8]

Hygromycin B phosphotransferase; Exemption from the Requirement of a Tolerance

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This regulation establishes an exemption from the requirement of a tolerance for residues of the hygromycin B phosphotransferase (APH4) marker protein on cotton when applied/used as an inert ingredient in plant-incorporated protectants. Syngenta Seeds submitted a petition to EPA under the Federal Food, Drug, and Cosmetic Act (FFDCA), as amended by the Food Quality Protection Act of 1996 (FQPA), requesting an exemption from the requirement of a tolerance. This regulation eliminates the need to establish a maximum permissible level for residues of hygromycin B phosphotransferase (APH4) marker protein when used as a plant-incorporated protectant formulation inert ingredient.

DATES: This regulation is effective April 7, 2004. Objections and requests for hearings, identified by docket ID number OPP–2004–0036, must be received on or before June 7, 2004.

ADDRESSES: Written objections and hearing requests may be submitted electronically, by mail, or through hand delivery/courier. Follow the detailed instructions as provided in Unit VIII. of the **SUPPLEMENTARY INFORMATION**.

FOR FURTHER INFORMATION CONTACT: Leonard Cole, Biopesticides and Pollution Prevention Division (7511C), Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001; telephone number: (703) 305–5412; e-mail address: *cole.leonard@epa.gov*.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

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

- Crop production (NAICS 111)
- Animal production (NAICS 112)
- Food manufacturing (NAICS 311)
- Pesticide manufacturing (NAICS 32532)

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

B. How Can I Get Copies of this Document and Other Related Information?

1. *Docket.* EPA has established an official public docket for this action under docket identification (ID) number OPP–2004–0036. The official public docket consists of the documents specifically referenced in this action, any public comments received, and other information related to this action. Although a part of the official docket, the public docket does not include Confidential Business Information (CBI) or other information whose disclosure is restricted by statute. The official public docket is the collection of materials that is available for public viewing at the Public Information and Records Integrity Branch (PIRIB), Rm. 119, Crystal Mall #2, 1921 Jefferson Davis Hwy., Arlington, VA. This docket facility is open from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The docket telephone number is (703) 305–5805.

2. *Electronic access.* You may access this **Federal Register** document electronically through the EPA Internet under the "**Federal Register**'' listings at *http://www.epa.gov/fedrgstr/*. A frequently updated electronic version of 40 CFR part 180 is available at *E-CFR Beta Site Two at http://www.gpoaccess.gov/ecfr/*.

An electronic version of the public docket is available through EPA's electronic public docket and comment system, EPA Dockets. You may use EPA Dockets at *http://www.epa.gov/edocket/* to submit or view public comments, access the index listing of the contents of the official public docket, and to access those documents in the public docket that are available electronically. Once in the system, select "search,'' then key in the appropriate docket ID number.

II. Background and Statutory Findings

In the **Federal Register** of December 10, 2003 (FR 68 2371) (FRL–7332–7), EPA issued a notice pursuant to section 408(d)(3) of the Federal Food, Drug, Cosmetic Act (FFDCA), 21 U.S.C. 346a(d)(3), announcing the filing of a pesticide tolerance petition (3F6761) by Syngenta Seeds, 3054 Cornwallis Road, Research Triangle Park, North Carolina 27709–2257. This notice included a summary of the petition prepared by the petitioner Syngenta Seeds. Comments were received from grower groups and the National Cotton Council supporting this petition.

The petition requested that 40 CFR part 180 be amended by establishing a temporary exemption from the