Dated:September 22, 2003.

Debra Edwards,

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), 346(a) and 371.

■ 2. Section 180.493 is amended by removing the entries ''tomato'' and ''tomato, paste'' and by alphabetically adding the following commodities to the table in paragraph (a) to read follows:

§ 180.493 Dimethomorph; tolerances for residues.

(a) * * *

Commodity	Parts per million
Brassica, leafy greens, subgroup 5B	20.0
* * * * *	
Taro, corm	0.5
Taro, leaves	6.0
* * * * *	
Vegetable, fruiting, group 8	1.5

* * * * * *

[FR Doc. 03–24564 Filed 9–26–03; 8:45 am]

BILLING CODE 6560–50–S

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[OPP–2003–0058; FRL–7327–9]

Glufosinate Ammonium; Pesticide Tolerance

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This regulation establishes a tolerance for combined residues of glufosinate ammonium and its metabolites in or on certain raw agricultural commodities. Aventis CropScience USA, now Bayer CropScience, and Interregional Research Project Number 4 (IR-4) requested these tolerances under the Federal Food, Drug, and Cosmetic Act (FFDCA), as amended by the Food Quality Protection Act of 1996 (FQPA).

DATES: This regulation is effective September 29, 2003. Objections and requests for hearings, identified by docket ID number OPP–2003–0058, must be received on or before November 28, 2003.

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: Joanne I. Miller, Registration Division (7505C), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW.,Washington, DC 20460–0001; telephone number: 703–305–6224; e-mail address: *miller.joanne@epamail.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 categories and 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 the table could also be affected. The North American Industrial Classification System (NAICS) codes have been provided to assist you and others in determining whether or not this action might apply to certain entities. If you have questions regarding the applicability of this action to a particular entity, consult the person listed under **FOR FURTHER INFORMATION CONTACT**.

B. How Can I Get 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–2003–0058. 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 May 19, 2000 (65 FR 31904) (FRL–6558–2), 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 0F6140) by Aventis CropScience USA, now Bayer CropScience, PO Box 12014, 2 T. W. Alexander Drive, Research Triangle Park, NC 27709. That notice included a summary of the petition prepared by Bayer CropScience, the registrant. There were no comments received in response to the notice of filing.

In the **Federal Register** of July 24, 2002 (67 FR 48465) (FRL–7184–6), 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 OF6210) by Aventis CropScience USA, now Bayer CropScience, PO Box 12014, 2 T. W. Alexander Drive, Research Triangle Park, NC 27709. That notice included a summary of the petition prepared by Bayer CropScience, the registrant. Comments on the petition were filed by Neil J. Carman, Ph.D. of the Sierra Club

Genetic Engineering Committee. A response to these comments is provided in Unit VI.

In the **Federal Register** of August 21, 2002 (67 FR 54196) (FRL–7190–9), 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 2E6404) by Interregional Research Project Number 4 (IR-4), 681 US Highway #1 South, North Brunswick, NJ 08902–3390. That notice included a summary of the petition prepared by IR-4, the petitioner. There were no comments received in response to the notice of filing.

In the **Federal Register** of August 15, 2003 (68 FR 48908) (FRL–7322–9), 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 amended pesticide petitions (PP 0F6140 and PP OF6210) by Bayer CropScience, PO Box 12014, 2 T. W. Alexander Drive, Research Triangle Park, NC 27709. That notice included a summary of the petition prepared by Bayer CropScience. Two hundred and sixty five comments were filed. A response to these comments is provided in Unit VI.

The petitions requested that 40 CFR 180.473(a)(1) be amended by establishing tolerances for residues of the herbicide glufosinate ammonium (butanoic acid, 2-amino-4-(hydroxymethylphosphinyl)-, monoammonium salt) and its metabolite, 3-methylphosphinico-propionic acid, expressed as 2-amino-4-(hydroxymethylphosphinyl)butanoic acid equivalents in or on the raw agricultural commodities derived from cotton, undelinted seed at 3.5 parts per million (ppm) and gin byproducts at 12.0 ppm; and blueberry, lingonberry, juneberry and salal at 0.10 ppm and that 40 CFR 180.473(a)(2) be amended by establishing tolerances for residues of the herbicide glufosinate ammonium (butanoic acid, 2-amino-4-(hydroxymethylphosphinyl)-, monoammonium salt) and its metabolites, 3-methylphosphinico-propionic acid, and 2-acetamido-4-methylphosphinico-butanoic acid expressed as 2-amino-4-(hydroxymethylphosphinyl)butanoic acid equivalents in or on the raw agricultural commodities derived from transgenic cotton tolerant to glufosinate ammonium: undelinted seed at 3.5 ppm and gin byproducts at 12.0 ppm and transgenic rice tolerant to glufosinate ammonium: grain at 1.0 ppm, straw at 1.6 ppm.

IR-4 and Bayer CropScience subsequently amended the petitions to request that 40 CFR 180.473(a)(1) be amended by establishing tolerances for residues of the herbicide glufosinate ammonium (butanoic acid, 2-amino-4-(hydroxymethylphosphinyl)-, monoammonium salt) and its metabolites, 2-acetamido-4-methylphosphinico-butanoic acid and 3-methylphosphinico-propionic acid, expressed as 2-amino-4-(hydroxymethylphosphinyl)butanoic acid equivalents, in or on the following food commodities: Bushberry subgroup, lingonberry, juneberry and salal at 0.15 ppm, cattle, fat at 0.40 ppm, cattle, meat at 0.15 ppm, cattle, meat byproducts at 6.0 ppm, cotton, gin byproducts at 15 ppm, cotton, undelinted seed at 4.0 ppm, egg at 0.15 ppm, goat, fat at 0.40 ppm, goat, meat at 0.15 ppm, goat, meat byproducts at 6.0 ppm, hog, fat at 0.40 ppm, hog, meat at 0.15 ppm, hog, meat byproducts at 6.0 ppm, horse, fat at 0.40 ppm, horse, meat at 0.15 ppm, horse, meat byproducts at 6.0 ppm, Milk at 0.15 ppm, poultry, fat at 0.15 ppm, poultry, meat at 0.15 ppm, poultry, meat byproducts 0.6 ppm, sheep, fat at 0.40 ppm, sheep, meat at 0.15 ppm, and sheep, meat byproducts at 6.0 ppm.

Bayer CropScience subsequently amended the petitions to request that 40 CFR 180.473(a)(2) be amended by establishing tolerances for residues of the herbicide glufosinate ammonium (butanoic acid, 2-amino-4-(hydroxymethylphosphinyl)-, monoammonium salt) and its metabolites, 2-acetamido-4-methylphosphinico-butanoic acid and 3-methylphosphinico-propionic acid, expressed as 2-amino-4-(hydroxymethylphosphinyl)butanoic acid equivalents, in or on the following raw agricultural and processed commodities derived from transgenic cotton and rice that are tolerant to glufosinate ammonium: Cotton, gin byproducts at 15 ppm, cotton, undelinted seed at 4.0 ppm, rice, grain at 1.0 ppm, rice, straw at 2.0 ppm, and rice, hull at 2.0 ppm. These amendments were included in the August 15, 2003 notice of filing.

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 glufosinate ammonium and its metabolites on bushberry subgroup, lingonberry, juneberry and salal at 0.15 ppm, cattle, fat at 0.40 ppm, cattle, meat at 0.15 ppm, cattle, meat byproducts at 6.0 ppm, cotton, gin byproducts at 15 ppm, cotton, undelinted seed at 4.0 ppm, egg at 0.15 ppm, goat, fat at 0.40 ppm, goat, meat at 0.15 ppm, goat, meat byproducts at 6.0 ppm, hog, fat at 0.40 ppm, hog, meat at 0.15 ppm, hog, meat byproducts at 6.0 ppm, horse, fat at 0.40 ppm, horse, meat at 0.15 ppm, horse, meat byproducts at 6.0 ppm, milk at 0.15 ppm, poultry, fat at 0.15 ppm, poultry, meat at 0.15 ppm, poultry, meat byproducts at 0.60 ppm, sheep, fat at 0.40 ppm, sheep, meat at 0.15 ppm, and sheep, meat byproducts at 6.0 ppm, cotton, gin byproducts at 15 ppm, rice, grain at 1.0 ppm, rice, straw at 2.0 ppm, and rice, hull at 2.0 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 glufosinate ammonium and its metabolites are discussed in Tables 1, 2 and 3 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.—GLUFOSIANTE-AMMONIUM: ACUTE, SUBCHRONIC, CHRONIC, AND OTHER TOXICITY

Guideline No.	Study Type	Results
81–1	Acute oral	LD_{50} = 4,010 mg/kg (milligram/kilogram) in males LD_{50} = 3,030 mg/kg in females
870.3100	90–Day oral toxicity in rats (males only)	NOAEL = 6.2–8.8 mg/kg/day in males LOAEL = 64–90 mg/kg/day in males, based on glutamine synthetase inhibition in the brains
870.3100	*N*-acetyl-L-glufosinate disodium 90–Day oral toxicity in rats (males only)	NOAEL = 65–90 mg/kg/day in males LOAEL = 657–935 mg/kg/day in males, based on glutamine synthetase inhibition in the brains
870.3100	90–Day oral toxicity in mouse	NOAEL = 48 mg/kg/day in males, 192 mg/kg/day in females Highest Dose Tested (HDT) LOAEL = 192 mg/kg/day in males based on the changes in clinical biochemistry and liver weights in males
870.3200	21/28–Day dermal toxicity in rat	NOAEL = 100 mg/kg/day LOAEL = 300 mg/kg/day based on clinical observations (aggressive behavior, piloerection, and a high startle response)
870.3700	Prenatal developmental in rats (three studies combined)	Maternal: NOAEL = 10 mg/kg/day LOAEL = 50 mg/kg/day based on vaginal bleeding and hyperactivity Developmental: NOAEL = 50 mg/kg/day LOAEL =250 mg/kg/day based on dilated renal pelvis
870.3700	Prenatal developmental in rabbit	Maternal: NOAEL = 6.3 mg/kg/day LOAEL = 20.0 mg/kg/day based on reduced food consumption, body weight and weight gains Developmental: NOAEL = 6.3 mg/kg/day LOAEL = 20.0 based on decreased body weights and fetal death
870.3800	Reproduction and fertility effects in rat	Parental/Systemic NOAEL = 18.0 mg/kg/day (HDT) LOAEL = not established Reproductive NOAEL = 6.0 mg/kg/day LOAEL = 18.0 mg/kg/day based on decreased number of viable pups Offspring NOAEL = 6.0 mg/kg/day LOAEL = 18.0 mg/kg/day based on decreased number of viable pups
870.4100	Chronic toxicity in dogs	NOAEL = 5.0 mg/kg/day LOAEL = 8.5 mg/kg/day based on mortality (week 2) and alterations in the electrocardiogram at 6 months
870.4200	Carcinogenicity in rats	NOAEL = 45.4 mg/kg/day in males, 57.1 mg/kg/day in females LOAEL = 228.9 mg/kg/day in males and 281.5 based on increased incidences of retinal atrophy. No evidence of carcinogenicity
870.4300	Chronic Feeding / Carcinogenicity in rats	NOAEL = 24.4 mg/kg/day in males, 8.2 mg/kg/day in females LOAEL = not achieved in males and 28.7 based on inhibition of brain glutamate synthetase in females at 130 weeks No evidence of carcinogenicity
870.4300	Carcinogenicity mice	NOAEL = 10.82 mg/kg/day in males, 16.19 mg/kg/day in females LOAEL = 22.60 mg/kg/day in males, 63.96 mg/kg/day in females based on increased mortality and glucose levels and consistent changes in glutathione levels in males, increased glucose levels and decreased albumin and total proteins No evidence of carcinogenicity
870.5265	Reverse Mutation Assay	Glufosinate ammonium failed to cause reverse mutations in bacteria with and without metabolic activation.
870.5300	Detection of gene mutations in somatic cells in culture	Glufosinate ammonium did not increase the mutation frequency at the thymidine kinase locus
870.5395	*In vivo* mammalian cytogenetic tests	The results indicated glufosinate ammonium had no effect on micronucleus formation

TABLE 1.—GLUFOSIANTE-AMMONIUM: ACUTE, SUBCHRONIC, CHRONIC, AND OTHER TOXICITY—Continued

Guideline No.	Study Type	Results
870.5500	Bacterial DNA damage or repair test	glufosinate ammonium failed to cause damage to DNA that could be detected by this repair assay
870.5550	Unscheduled DNA synthesis in mammalian cells in culture	There was no evidence that unscheduled DNA synthesis was induced by glufosinate ammonium.
870.6200	Acute neurotoxicity in rat (2 studies)	NOAEL = 500 mg/kg in males and females (HDT) LOAEL = Not established in both sexes
870.6200	Repeat Dose Neurotoxicity in rat	NOAEL = 1.5 mg/kg/day in males, 1.8 mg/kg/day in females LOAEL = 14.9 mg/kg/day in males, 17.1 mg/kg/day in females, based on the inhibition of glutamate synthetase in the brain
870.7485	Metabolism and pharmacokinetics in rat	The majority of the radioactivity (95–98% of the dose) was eliminated during the first 24 hrs after dosing. The parent compound, glufosinate ammonium, accounted for most of the eliminated radioactivity in the urine and feces of both males (80% of the dose) and females (73% of the dose). The metabolite, 3-methylphosphinico-propionic acid, was consistently found in both urine and feces of both sexes.
870.7485	Metabolism and pharmacokinetics in rat	The majority of the radioactivity was eliminated during the first 24 to 48 hrs after dosing. The parent compound, glufosinate ammonium, accounted for the majority of the radioactivity eliminated in the excreta of both males (≈80% of the dose) and females (88% of the dose). The metabolite, 3-methylphosphinico-propionic acid, was consistently found in both urine (0.22–1.20% of the dose) and feces (0.44–1.36% of the dose) of both sexes. 2-acetamido-4-methylphosphinico-butanoic acid was found in feces (0.28–1.72% of the dose) of both male and female rats and barely above or at the level of the detection in the urine of both sexes (0.02–0.04% of the dose). Very little if any of administered glufosinate ammonium was sequestered in any tissues examined.
870.7485	Metabolism and pharmacokinetics in rat	The major route of excretion was via feces (88% and 84% of the administered radioactivity for males and females, respectively). Within 7 days of post dosing, greater than 94% of the dose was eliminated. Kinetics analysis indicated that the process of excretion was a two-phase process. The tissue radioactivity level for kidneys, liver and gonads was just above the background level.
870.7485	Metabolism and pharmacokinetics in rat	The majority of the radioactivity was excreted within 24 hrs after the last dose. The major route of elimination was via feces. There was also a two-phased elimination process. More radioactivity was found in the tissues of animals dosed repeatedly than that of animals receiving a single dose.
870.7600	Dermal penetration	The results indicate that at the low dose (0.1 mg) 42.5 to 50.8% of the applied radioactivity was absorbed whereas at the high dose (10 mg) 26% was absorbed. After removal and washing of the treated skin a substantial amount of the radioactivity still remained in the skin, and it was gradually absorbed and eliminated. Radioactivity was found in both feces and urine samples, but the majority of glufosinate ammonium was eliminated in the urine. In all organs/tissues examined, radioactivity was found to reach a maximum level either at 4 or 10 hrs after exposure. Subsequently, the radioactivity dropped rapidly. The amount of radioactivity found in the brain was very minimal relative to that of kidneys and liver.

TABLE 2.—3-METHYLPHOSPHINICO-PROPIONIC ACID: SUBCHRONIC TOXICITY

Guideline No.	Study Type	Results
870.3100	90–Day dermal toxicity in rats	NOAEL = 102 mg/kg/day in males, 113 mg/kg/day in females LOAEL = 420 mg/kg/day in males, 439 mg/kg/day in females based on increased reticulocytes and increased absolute and relative liver weights in males
870.3100	90–Day dermal toxicity in mice	NOAEL = 1,121 mg/kg/day in males, 1,340 mg/kg/day in females LOAEL = Not established

TABLE 2.—3-METHYLPHOSPHINICO-PROPIONIC ACID: SUBCHRONIC TOXICITY—Continued

Guideline No.	Study Type	Results
870.3700	Prenatal developmental in rodents in rats	Maternal: NOAEL = 300 mg/kg/day Maternal: LOAEL = 900 mg/kg/day based on one death and clinical findings (persistent piloerection and/or increased urinary output) Developmental: NOAEL = 300 mg/kg/day Developmental: LOAEL = 900 mg/kg/day based on increases in the incidences of total litter loss and in the fetal and litter incidences of wavy and/or thickened ribs.
870.3700	Prenatal developmental in rabbits	Maternal: NOAEL = 50 mg/kg/day Maternal: LOAEL = 100 mg/kg/day based on increased abortions, mortality, and reductions in food and water consumption, body weight gain, and fecal output Developmental: NOAEL = 200 mg/kg/day Developmental: LOAEL = Not observed

TABLE 3.—METABOLITE, 2-ACETOMIDO-4-METHYLPHOSPHINICO-BUTANOIC: SUBCHRONIC AND OTHER TOXICITY

Guideline No.	Study Type	Results
870.3100	90–Day oral toxicity rodents in rats	NOAEL = 147 mg/kg/day in males, 162 mg/kg/day in females LOAEL = 738 mg/kg/day in males, 800 mg/kg/day in females based on glutamine synthetase inhibition in the brain
870.3100	90–Day oral toxicity rodents in mice	NOAEL = Not established for males, 110 mg/kg/day in females LOAEL = 83 mg/kg/day in males, 436 mg/kg/day in females based on glutamine synthetase inhibition in the brain
870.3150	Subchronic Nonrodent Oral Toxicity in dogs	NOAEL = 19 mg/kg/day in males, 21 mg/kg/day in females LOAEL = 72 mg/kg/day in males, 79 mg/kg/day in females based on glutamine synthetase inhibition in the brain
870.3700	Prenatal developmental in rodents-rat	Maternal: NOAEL = 1,000 mg/kg/day Maternal: LOAEL = Not observed Developmental: NOAEL = 1,000 mg/kg/day Developmental: LOAEL = Not observed
870.3700	Prenatal developmental in rabbits	Maternal: NOAEL = 64 mg/kg/day Maternal: LOAEL = 160 mg/kg/day based on reduced feed consumption Developmental: NOAEL = 64 mg/kg/day Developmental: LOAEL = 160 based on uni- or bilateral extra at the 13th thoracic vertebra
870.6200	Acute Neurotoxicity in rats	NOAEL = 1,000 mg/kg in males and females LOAEL = 2,000 mg/kg in males and females based on clinical signs of toxicity including sedation, ruffled fur, and diarrhea
870.6200	Acute Neurotoxicity in rats	NOAEL = 100 mg/kg in males and females LOAEL = 1,000 mg/kg in males and females based on decreased body weight gain
870.6200	Repeat Dose Neurotoxicity in rats	NOAEL = 158.9 mg/kg/day in males, 179.4 mg/kg/day in females LOAEL = Not established in males and females

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. A 10x data base uncertainty factor, due to the lack of a developmental neurotoxicity study, was applied to all dietary and residential dermal, inhalation, and incidental oral exposure assessments. For residential inhalation exposure assessments an additional 10x data base uncertainty factor was applied due to the lack of an adequate inhalation study and high concern for exposure via the inhalation route (10,000). Agency policy limits the total uncertainty factor applied for any particular chemical to no more than 3,000 (see EPA report ''A Review of the Reference Dose and Reference Concentration Processes:'' EPA/630/P–02/022F, December 2002; a Notice of Availability of the Final Report was published in the **Federal Register** of

May 21, 2003 (68 FR 27805) (FRL–7501–8).

For dietary risk assessment (other than cancer) the Agency uses the 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 factors (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 glufosinate ammonium and its metabolite used for human risk assessment is shown in Table 4 of this unit:

TABLE 4.—SUMMARY OF TOXICOLOGICAL DOSE AND ENDPOINTS FOR GLUFOSINATE AMMONIUM AND ITS METABOLITES FOR USE IN HUMAN RISK ASSESSMENT

Exposure Scenario	Dose Used in Risk Assessment, UF	FQPA SF* and Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (Females 13–50 years of age)	NOAEL = 6.3 mg/kg/day UF = 1,000 Acute RfD = 0.0063 mg/kg/day.	FQPA SF = 1 aPAD = acute RfD ÷ FQPA SF = 0.0063 mg/kg/day.	Prenatal Developmental Toxicity Study in non-rodents - rabbit LOAEL = 20.0 mg/kg/day based on decreased body weights and fetal death
Chronic Dietary (All populations)	NOAEL = 6.0 mg/kg/day UF = 1,000 Chronic RfD = 0.006 mg/kg/day.	FQPA SF = 1 cPAD = chronic RfD ÷ FQPA SF = 0.006 mg/kg/day	''Weight-of-evidence'' approach from several studies; NOAEL = 6.0 mg/kg/day; brain glutamine synthetase inhibition and alterations in the electrocardiogram.
Short-Term Dermal (1 to 30 days) (Residential)	Oral study NOAEL = 6.3 mg/kg/day (dermal absorption rate = 50%)	LOC for MOE = 1,000 (Residential)	Prenatal Developmental Toxicity Study in non-rodents - rabbits LOAEL = 20 mg/kg/day based on reduced fetal body weights, increased fetal mortality, reduced food consumption, body weight, and body weight gain
Short-Term Inhalation (1 to 30 days) (Residential)	Oral study NOAEL = 6.3 mg/kg/day (inhalation absorption rate = 100%)	LOC for MOE = 3,000 (Residential)	Prenatal Developmental Toxicity Study in non-rodents - rabbits LOAEL = 20 mg/kg/day based on reduced fetal body weights, increased fetal mortality, reduced food consumption, body weight, and body weight gain

*The reference to the FQPA SF refers to any additional SF retained due to concerns unique to the FQPA.

C. Exposure Assessment

1. *Dietary exposure from food and feed uses.* Tolerances have been established (40 CFR 180.473) for the combined residues of glufosinate ammonium and its metabolites, in or on almond hulls, apples, bananas, meat, milk, fat, meat byproducts, eggs, grapes, potatoes, tree nuts and food commodities derived from transgenic canola, transgenic field corn, transgenic soybean and transgenic sugar beets. Risk assessments were conducted by EPA to assess dietary exposures from combined residues of glufosinate ammonium and its metabolites 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-Food Consumption Intake Database (DEEM-FCID®) 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: 100% crop treated for all registered and proposed commodities (Tier 1 analysis) and, depending on the level of blending of a commodity, tolerance level residues, highest field trial, or average field trial.

ii. *Chronic exposure.* In conducting this chronic dietary risk assessment the DEEM-FCID® 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: 100% crop treated for all registered and proposed commodities (Tier 1 analysis) excluding apple, canola, corn and grape, where 3 year weighted average percent crop treated was used, and, depending

on the level of blending of a commodity, tolerance level residues or average field trial.

iii. *Cancer*. No evidence of carcinogenicity at doses tested were observed in the mouse and rat carcinogenicity studies. A quantitative cancer risk assessment was not performed for glufosinate ammonium.

iv. *Anticipated residue and percent crop treated (PCT) information*. Section 408(b)(2)(F) of the FFDCA states that the Agency may use data on the actual percent of food treated for assessing chronic dietary risk only if the Agency can make the following findings: Condition 1, that the data used are reliable and provide a valid basis to show what percentage of the food derived from such crop is likely to contain such pesticide residue; Condition 2, that the exposure estimate does not underestimate exposure for any significant subpopulation group; and Condition 3, if data are available on pesticide use and food consumption in a particular area, the exposure estimate does not understate exposure for the population in such area. In addition, the Agency must provide for periodic evaluation of any estimates used. To provide for the periodic evaluation of the estimate of PCT as required by section 408(b)(2)(F) of the FFDCA, EPA may require registrants to submit data on PCT.

The Agency believes that the three conditions listed in Unit IV. have been met. With respect to Condition 1, PCT estimates are derived from Federal and private market survey data, which are reliable and have a valid basis. EPA uses a weighted average PCT for chronic dietary exposure estimates. This weighted average PCT figure is derived by averaging State-level data for a period of up to 3 years, and weighting for the more robust and recent data. A weighted average of the PCT reasonably represents a person's dietary exposure over a lifetime, and is unlikely to underestimate exposure to an individual because of the fact that pesticide use patterns (both regionally and nationally) tend to change continuously over time, such that an individual is unlikely to be exposed to more than the average PCT over a lifetime. For acute dietary exposure estimates, EPA uses an estimated maximum PCT. The exposure estimates resulting from this approach reasonably represent the highest levels to which an individual could be exposed, and are unlikely to underestimate an individual's acute dietary exposure. The Agency is reasonably certain that the percentage of the food treated is not likely to be an underestimation. As to Conditions 2 and 3, regional consumption information and consumption information for significant subpopulations is taken into account through EPA's computer-based model for evaluating the exposure of significant subpopulations, including several regional groups. Use of this consumption information in EPA's risk assessment process ensures that EPA's exposure estimate does not understate exposure for any significant subpopulation group and allows the Agency to be reasonably certain that no regional population is exposed to residue levels higher than those estimated by the Agency. Other than the data available through national food consumption surveys, EPA does not have available information on the regional consumption of food to which glufosinate ammonium may be applied in a particular area.

2. *Dietary exposure from drinking water*. The Agency lacks sufficient monitoring exposure data to complete a comprehensive dietary exposure analysis and risk assessment for glufosinate ammonium 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 glufosinate ammonium. Based on environmental fate data the residues of concern in drinking water are glufosinate ammonium, 3-methylphosphinico-propionic acid, 2-methylphosphinico-acetic acid and *N*-acetyl-glufosinate.

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 SCI-GROW model is used to predict pesticide concentrations in shallow groundwater. 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 glufosinate ammonium they are further discussed in the aggregate risk sections in Unit III.E.

Based on the PRZM-EXAMS and SCI-GROW models the EECs of glufosinate ammonium and its degradates for acute exposures are estimated to be 94 µg/liter for surface water and 9 µg/liter for ground water. The EECs for chronic exposures are estimated to be 43 µg/liter for surface water and 9 µg/liter for ground water.

3. 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).

Glufosinate ammonium is currently registered for use on the following residential non-dietary sites: Home use for spot treatment of weeds, grass, bushes and vines. The risk assessment was conducted using the following residential exposure assumptions: Application rate of 0.0312 lb active ingredient (ai) per 1,000 ft^2, dermal unit exposure of 11 mg/lb and inhalation exposure of 0.016 mg/lb from hose end application and dermal unit exposure of 56 mg/lb and inhalation exposure of 0.0065 mg/lb from low pressure hand wand application.

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.''

EPA does not have, at this time, available data to determine whether glufosinate ammonium has a common mechanism of toxicity with other substances. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding for glufosinate ammonium and any other substances and glufosinate ammonium 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 glufosinate ammonium 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 policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at *http://www.epa.gov/pesticides/cumulative/*.

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*. The studies examining prenatal and postnatal toxicity showed:

a. No quantitative or qualitative evidence of increased susceptibility following *in utero* exposure in the prenatal developmental study in rats.

b. Qualitative evidence of increased susceptibility in the prenatal developmental study in rabbits and quantitative evidence of increased susceptibility in the 2-generation reproduction study in rats. In this study, a decrease in the number of viable pups was observed in the absence of parental toxicity at any dose.

Since there is qualitative evidence of increased susceptibility of the young following exposure to glufosinate ammonium, EPA performed a degree of concern analysis to: Determine the level of concern for the effects observed when considered in the context of all available toxicity data; and identify any residual uncertainties after establishing toxicity endpoints and traditional uncertainty factors to be used in the risk assessment of this chemical. In the rabbit developmental study the degree of concern observed as low noting that the fetal effects of concern occurred only at the highest dose tested and that a clear NOAEL for effects was established. In the 2-generation reproduction study the degree of concern for the effects observed as low noting that clear NOAELs and LOAELs were identified for the offspring effects of concern and the dose-response well-characterized.

3. *Conclusion*. There is not an adequate toxicity data base for glufosinate ammonium and its metabolites although the exposure data are complete or are estimated based on data that reasonably account for potential exposures. EPA identified the following data gaps:

a. Acute neurotoxicity study conducted in the rat which includes glutamine synthetase activity measurement in the liver, kidneys, and brain.

b. A developmental neurotoxicity (DNT) study conducted in the rat which includes comparative glutamine synthetase activity measurement in the liver, kidneys, and brain of the pups and mothers.

c. A 28–day inhalation toxicity study in rats with glutamine synthetase activity measurements in brain, kidney, liver and lung.

EPA is also requesting additional data to confirm that liver and kidney changes, observed in the absence of histopathological changes, are an adaptive response and not an adverse effect. These studies are required because the glutamine synthetase measurements are not available in young and adult animals. Therefore, EPA has applied additional data base uncertainty factors in this risk assessment. The results of these studies are expected to eliminate any uncertainty that may be associated in characterizing the toxicity of glufosinate ammonium.

For dietary risk assessment, an FQPA additional 10X safety factor, retained as a data base uncertainty factor due to the lack of a developmental neurotoxicity (DNT) study that measures glutamine synthetase activity in the young and adult animals, was applied to all dietary and residential dermal, inhalation, and incidental oral exposure assessments. For residential inhalation exposure assessments an additional 10x data base uncertainty factor was applied due to the lack of an adequate inhalation study and high concern for exposure via the inhalation route with a total uncertainty factor of 3,000 applied based on EPA policy cited in Unit III.B.

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 groundwater 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 glufosinate ammonium will occupy 48% of the aPAD for females 13 years and older. In addition, there is potential for acute dietary exposure to glufosinate ammonium in drinking water. After calculating DWLOCs and comparing them to the EECs for surface water and groundwater, EPA does not expect the aggregate exposure to exceed 100% of the aPAD, as shown in Table 5 of this unit:

TABLE 5.—AGGREGATE RISK ASSESSMENT FOR ACUTE EXPOSURE TO GLUFOSINATE AMMONIUM

Population Subgroup	aPAD (mg/kg)	% aPAD (Food)	Surface Water EEC (µg/liter)	Ground Water EEC (µg/liter)	Acute DWLOC (µg/liter)
Females (13–50 years old)	0.0063	48	94	9	98

2. *Chronic risk*. Using the exposure assumptions described in this unit for chronic exposure, EPA has concluded that exposure to glufosinate ammonium from food will utilize 10% of the cPAD for the U.S. population, 20% of the cPAD for all infants and 27% of the cPAD for children (1–2 years old). Based on the use pattern, chronic residential exposure to residues of glufosinate ammonium is not expected. In addition, there is potential for chronic dietary exposure to glufosinate ammonium in drinking water. After calculating DWLOCs and comparing them to the EECs for surface water and groundwater, EPA does not expect the aggregate exposure to exceed 100% of the cPAD, as shown in Table 6 of this unit:

TABLE 6.—AGGREGATE RISK ASSESSMENT FOR CHRONIC (NON-CANCER) EXPOSURE TO GLUFOSINATE AMMONIUM

Population Subgroup	cPAD mg/kg/day	% cPAD (Food)	Surface Water EEC (µg/liter)	Ground Water EEC (µg/liter)	Chronic DWLOC (µg/liter)
U.S. Population	0.006	10	43	9	189
Youth (13–19 years old)	0.006	9	43	9	164
Females (13–50 years old)	0.006	7	43	9	167
Adults (20–49)	0.006	8	43	9	194

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).

Glufosinate ammonium is currently registered for use that could result in short-term residential exposure and the Agency has determined that it is appropriate to aggregate chronic food and water and short-term exposures.

Using the exposure assumptions described in this unit for short-term exposures, EPA has concluded that food and residential exposures aggregated result in aggregate risk index (ARI) of 5.42 for the U.S. population, 6.35 for females (13–49 years old) and 5.75 for youth (13–19 years old). The registered spot treatment of weeds is expected to result in residential exposure only to adults. Therefore, short-term aggregate assessments were not conducted for infants and children. These aggregate ARIs do not exceed the Agency's level of concern of less than 1 for aggregate exposure to food and residential uses. In addition, short-term DWLOCs were calculated and compared to the EECs for chronic exposure of glufosinate ammonium in groundwater and surface water. After calculating DWLOCs and comparing them to the EECs for surface and ground water, EPA does not expect short-term aggregate exposure to exceed the Agency's level of concern, as shown in Table 7 of this unit:

TABLE 7.—AGGREGATE RISK ASSESSMENT FOR SHORT-TERM EXPOSURE TO GLUFOSINATE AMMONIUM

Population Subgroup	Aggregate ARI[1] (Food + Residential)	Surface Water EEC (ppb)	Ground Water EEC (ppb)	Short-Term DWLOC (ppb)
U.S. Population	5.42	43	9	180
Females (13–49 years old)	6.35	43	9	159
Youths (13–19 years old)	5.75	43	9	156

[1] $ARI = MOE_{calculated\ (\ i.e.,\ food,\ dermal,\ inhalation)} \div MOE_{acceptable}$

4. *Aggregate cancer risk for U.S. population*. No evidence of carcinogenicity at doses tested were observed in the mouse and rat carcinogenicity studies. Therefore, no cancer risk is expected.

5. *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 glufosinate ammonium residues.

IV. Other Considerations

A. Analytical Enforcement Methodology

Adequate enforcement methodology (example—gas chromatography) 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

Codex and Mexico do not have maximum residue limits (MRLs) for glufosinate ammonium and its metabolites for the proposed crops or livestock commodities. Canada does not have MRLs for glufosinate ammonium and its metabolites for the proposed crops, poultry commodities or milk, but does have a MRL of 1 ppm for ruminant liver and kidney.

V. Conclusion

Therefore, the tolerance is established for combined residues of glufosinate ammonium and its metabolites in or on bushberry subgroup, Lingonberry, juneberry and salal at 0.15 ppm, cattle, fat at 0.40 ppm, cattle, meat at 0.15 ppm, cattle, meat byproducts at 6.0 ppm, cotton, gin byproducts at 15 ppm, cotton, undelinted seed at 4.0 ppm, egg at 0.15 ppm, goat, fat at 0.40 ppm, goat, meat at 0.15 ppm, goat, meat byproducts at 6.0 ppm, hog, fat at 0.40 ppm, hog, meat at 0.15 ppm, hog, meat byproducts at 6.0 ppm, horse, fat at 0.40 ppm, horse, meat at 0.15 ppm, horse, meat byproducts 6.0 ppm, Milk at 0.15 ppm, poultry, fat at 0.15 ppm, poultry, meat at 0.15 ppm, poultry, meat byproducts 0.60 ppm, sheep, fat at 0.40 ppm, sheep, meat at 0.15 ppm, and sheep, meat byproducts 6.0 ppm, cotton, gin byproducts at 15 ppm, rice, grain at 1.0 ppm, rice, straw at 2.0 ppm, and rice, hull at 2.0 ppm.

VI. Response to Comments

The overall thrust of the comments from the Sierra Club was that ''large quantities of glufosinate ammonium herbicide will be utilized on transgenic rice crops in the United States and abroad . . . even though the herbicide may have side effects on humans, farm animals and beneficial insects.'' The testing of pesticides will often reveal that a pesticide has the potential to create adverse effects in animals and/or insects; those risks are addressed via registration under FIFRA. The critical issue addressed by FFDCA is whether there is an adequate margin of safety between the aggregate exposure level of humans to the pesticide and the level that potentially may be harmful. As EPA described in Unit III.E. above, EPA's risk assessment showed that an adequate margin was available for EPA to conclude that there is a reasonable certainty of no harm for the general population including infants and children.

EPA has reprinted each of Sierra Club's more specific comments below and responded to each individually.

1. *Comment—plant metabolism of glufosinate.* A concern is other plant metabolites of glufosinate ammonium may occur in addition to the two primary metabolites identified in the grain and straw, since the two substances did not appear to account for 100% of the total radioactive residues in the two plant tissues tested. While more than 80% appeared to be accounted for, Aventis needs to identify whether additional metabolites were produced. The two primary metabolites identified as being typical of plant metabolism in the grain at harvest were 3-methylphosphinicopropionic acid, being—70% of the total radioactive residues (TRR). Another residue in the grain was *N*-acetyl-L-glufosinate (2-acetamido-4-methylphosphinicobutanoic acid), at about 11% of the TRR and parent at 5–6% of the TRR. In the straw, 3-methylphosphinicopropionic acid was the major metabolite comprising approximately 60% of the TRR. Lesser amounts of the parent (about 17% of the TRR) and *N*-acetylglufosinate (10–13% of TRR) were found in the straw fraction.

Agency response. The transgenic rice metabolism study was conducted according to the regulatory guideline requirements (OPPTS 860.1500) and conformed to EPA Good Laboratory Practice (GLP) Standards (the % TRR figures given below are averages of four samples). The study indicated that glufosinate ammonium, *N*-acetyl-glufosinate, and 3-MP accounted for 88% and 91% of the total radioactive residue (TRR) found in rice grain and rice straw, respectively (grain and straw are the only rice raw agricultural commodities (RACs)). The remainder of the radioactivity was identified as 2-methylphosphinico-acetic acid (grain—1% TRR; straw—2% TRR), several unknowns when combined accounted for 2% TRR (rice grain) and 3% TRR (rice straw), and fiber bound residues (grain—8% TRR; straw—5% TRR). The petitioner identified/characterized 99% and 101% of the TRR in rice grain and rice straw, respectively. In previously submitted transgenic canola and non-transgenic apple, corn, lettuce, soybeans, and wheat metabolism studies, the petitioner demonstrated the incorporation of radioactivity into nature plant constituents. On the basis of the transgenic rice metabolism study and the previously submitted metabolism studies, EPA concluded that the residue identification/characterization procedures performed were adequate and the residues of concern in transgenic rice, for purposes of tolerance enforcement and risk assessment, are glufosinate ammonium, *N*-acetyl-glufosinate, and 3-methylphosphinico-propionic acid (3-MP).

2. *Comment—analytical method.* We ask EPA if any independent sampling and gas chromatography analyses were conducted besides that performed by Aventis and its contractors. We request that an independent sampling and G.C. analysis program be carried out if Aventis has not had a third party independent contractor, since we are skeptical of Aventis' sampling data and analyses. We generally agree that the enforcement analytical method of utilizing gas chromatography appears to be acceptable for detecting and measuring levels of glufosinate ammonium and metabolites with a general limit of quantification of 0.05 ppm to allow detection of glufosinate residues at or above the proposed tolerances. We wonder if glufosinate residues might have been found between 0.01 ppm and 0.05 ppm, and that due to its toxicity, EPA should have required a lower detectability limit be utilized to demonstrate if glufosinate residues were missed below 0.05 ppm or 50 parts per billion (ppb) concentration down to 1 ppb.

Agency response. The rice magnitude of the residue study was conducted according to the regulatory guideline requirements (OPPTS 860.1500) and conformed to EPA GLP Standards. The rice grain and straw samples were analyzed using a method similar to that previously validated by an independent laboratory and by the EPA. Based on these validation procedures and the validation and concurrent recovery data submitted with the transgenic rice field trials, EPA concluded that the method was appropriate for data collection purposes.

EPA understands that residues below the level of quantification (< LOQ) does not mean that residues are not present. The dietary analyses assumed average field trial residues for rice commodities. When calculating the average, half LOQ residues were assumed for residues < LOQ. Therefore, the dietary risk assessment took into account the possibility of residues between 0.01 and

0.05 ppm. For further information on EPA's rationale for assuming half LOQ residues see ''Values to Non-Detectable/Non-Quantifiable Residues in Human Health Food Exposure Assessments'' (faxed upon request; telephone: (202) 401–0527; item: 6047).

3. *Comment—magnitude of glufosinate residues.* The reason that we are requesting independent sampling and gas chromatography analyses be conducted besides that performed by Aventis and its contractors is the potential for higher glufosinate residue concentrations to be confirmed above the 0.74 ppm level in rice grain and 1.48 ppm level in rice straw when sampled at 70 days or more after the last treatment. We are concerned that Aventis' sampling protocol may have been biased in some unidentified manner and that samples above the 0.74 ppm level in rice grain and 1.48 ppm level in rice straw were missed in the field residue trials. While EPA emphasizes that the treatment regime was selected to represent the use pattern that is the most likely to result in the highest residues, we are concerned that sampling bias may have transpired and resulted in bias in the G.C. analyses. We are also concerned that glufosinate treatment may have occurred closer to the sampling period than is the case and higher glufosinate concentrations were missed. After all, a higher concentration factor of approximately 2.3 was found for rice hulls compared to the grain and straw. We also question that the finding that no detectable concentration of the residues occurred when rice whole grain was processed into polished grain and bran, whereas a glufosinate residue concentration may have been present at less than the 0.05 ppm (50 ppb) detection limit.

Agency response. The rice magnitude of the residue (15 field trials conducted throughout the rice growing regions in the United States; 2 composite samples collected at each site) and processing studies were conducted according to the regulatory guideline requirements (OPPTS 860.1500 and 860.1520) and conformed to EPA GLP Standards. It is difficult to further address the potential for bias since the comment gave no specific criteria for the concern. The comment does make reference to the processing study and the concentration of residues in rice hull and the lack of concentration of residues in rice bran and polished rice. The following paragraph is a summary of the rice processing study.

Processing studies are required to determine if residues reduce or concentrate during food processing (processing factor = concentration in processed commodity ÷ concentration in unprocessed commodity). Processing factors are dependent on several factors including the location of the residues (surface or translocated residues), loss of water as in dried commodities, and/or the physical chemical properties of the residues. The rice processing study (conducted at 5x the proposed rate) resulted in quantifiable concentrations of glufosinate ammonium, *N*-acetyl-glufosinate, and 3-MP in/on all commodities excluding glufosinate ammonium and *N*-acetyl-glufosinate in/on rice hull (residues at the LOQ assumed for calculation of processing factor). Based on the combined glufosinate ammonium, *N*-acetyl-glufosinate, and 3-MP residues in/on the processed and unprocessed commodities, the following processing factors were calculated: rice hull—2.8x, rice bran—0.9x, and polished rice—1.3x. The dietary analyses assumed average field trial residues and a processing factor of 1.3 for all rice commodities excluding rice bran where a processing factor of 0.9 was assumed (rice hull is not a human food commodity).

4. *Comment—acute toxicity.* EPA states that glufosinate ammonium has been classified as toxicity category III for acute oral, dermal, and inhalation toxicity; and for eye irritation. EPA finds that glufosinate ammonium is not a dermal irritant (toxicity category IV) nor is it a dermal sensitizer. The oral LD_{50} is 2 g/kg in male rats, and 1.62 g/kg in female rats. But we are concerned about acute toxicity because of the published finding that glufosinate causes convulsions in humans and experimental rodents by brain cell glutamate receptor activation (glufosinate and glutamate are structurally similar) according to Matsumura et al. Has EPA considered the structural similarities between glufosinate and glutamate receptor activation. We request that EPA review all of the relevant toxicological literature on human and rat brain cell glutamate receptor activation and speak with scientists who performed this research as to the significance of glufosinate tampering with glutamate receptors. Evidence also exists that glufosinate stimulates nitric oxide production in the brain through *N*-methyDaspartate (NMDA) receptors. We request that EPA investigate this published finding to determine if the requested herbicide tolerance concentrations are set too high which, is a possibility.

Agency response. EPA has evaluated both the published and petitioner submitted toxicity studies. The oral, dermal, and inhalation toxicity categories assigned by EPA are based on studies conducted according to the EPA toxicity testing guidelines and were conducted in compliance with EPA GLP. In an acute oral toxicity study in rats, the oral LD_{50} was found to be 1,620 and 2,000 mg/kg/day in female and male rats, respectively. In this study, no effects were seen in rats at doses up to 630 mg/kg/day.

The commenter cites two acute exposure studies. Matsumura et al. have shown that an acute dose of 80 mg/kg injected intraperitoneally into mice was convulsive and that this effect was partially antagonized by NMDA antagonists, suggesting that NMDA receptors may mediate this effect. Nakaki et al. found that injection of glufosinate ammonium directly into the brain stimulated nitric oxide production as a result of stimulation of NMDA receptors in rat brain, another neurochemical effect. But neither of these published studies provide sufficient appropriate evidence to establish an acute endpoint for risk assessment from oral, dermal, or inhalation exposures because the routes that they used, intraperitoneal injection or direct injection into the brain, are not directly relevant to potential routes of human exposure to pesticides, i.e., oral, dermal, or inhalation exposure.

The herbicidal mechanism of action of glufosinate ammonium is inhibition of the enzyme glutamine synthetase. This enzyme is also present in mammalian systems. In mammals, glutamine synthetase facilitates the conversion of glutamate and ammonia to glutamine and is therefore involved in the metabolism of nitrogen and ammonia. In addition, glutamate is a major excitatory neurotransmitter in the nervous system; inhibition of glutamine synthetase has been shown to impair its ability to serve as a neuroprotectant by controlling glutamate concentrations in neurons. More generally in the body, ammonia is buffered for extracellular transport through its interaction with glutamate to form glutamine by glutamine synthetase.

EPA also reviewed mechanistic studies submitted by the petitioner as well as the published studies, and, where applicable and appropriate, incorporated findings from these studies in the human health risk assessment. In fact, the intermediate-term and long-term incidental oral endpoints and the chronic dietary endpoint are based on brain glutamine synthetase inhibition, the most sensitive indicator of glufosinate ammonium toxicity in humans and experimental animals.

After reviewing all of the submitted data, EPA confirms that the tolerances, as proposed, are safe.

5. *Comment—genotoxicity.* EPA claims that ... based on results of a complete genotoxicity data base, there is no evidence of mutagenic activity in a battery of studies, including: *Salmonella spp., E. coli, in vitro* mammalian cell gene mutation assays, mammalian cell chromosome aberration assays, *in vivo* mouse bone marrow micronucleus assays, and unscheduled DNA synthesis assays. EPA needs to inquire with the FDA, USDA, ATSDR, medical doctors and scientists as to whether there are reports of glufosinate induced mutations and gene toxicity which appear to be glossed over in the Aventis petition.

Agency response. Glufosinate ammonium was clearly negative in the acceptable guideline mutagenicity studies. The test battery included: a *Salmonella typhimurium* and *Escherichia coli* reverse gene mutation assay, *in vitro* mammalian cell gene mutation and chromosome aberration assays, *in vivo* mouse bone marrow micronucleus assay and an *in vitro* unscheduled DNA synthesis assay. All studies were performed in accordance with the specified Office of Prevention, Pesticides, and Toxic Substances (OPPTS) Harmonized Mutagenicity Test Guidelines Series 870 and satisfied the testing requirements of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), the Toxic Substances Control Act (TSCA), and the Organization for Economic Cooperation and Development (OECD). Further, each study meets the requirement of 40 CFR part 160, Good Laboratory Practice (GLP) and was subjected to a Quality Assurance(QA) inspection. Based on the negative responses observed in these assays, EPA concluded that there is no concern for mutagenicity from exposure to glufosinate ammonium. In addition, no evidence of carcinogenicity was observed in mice and rats in acceptable guideline carcinogenicity studies. As indicated previously, EPA evaluated both petitioner submitted guideline studies and published scientific studies. In addition, the petitioner is required by law under FIFRA (6)(a)2) to report any adverse finding to EPA.

No mutagenicity studies were found in the open literature and the Agency for Toxic Substances and Disease Registry (ATSDR) has no finalized, draft, or ''under development'' toxicological profile for glufosinate ammonium. Finally, FDA has evaluated the human safety of multiple crops with resistance to glufosinate ammonium and has no concerns for human safety but has no mutagenicity or toxicity data in the Biotechnology Notification Files on this herbicide.

6. *Comment—reproductive and developmental toxicity.* We are skeptical of EPA's findings because, based on peer-reviewed studies in the published literature, birth defects have been caused by exposure of the human father to the herbicide. EPA needs to thoroughly investigate these findings and reconsider the glufosinate herbicide tolerance limits requested by Aventis as entirely unsafe and unacceptably high. It is rather distressing to note that there does not seem to be peer reviewed studies on the metabolism of the high levels of acetyl glufosinate in harvested GM crops to highly neurotoxic and teratogenic glufosinate. Certainly, gut bacteria are well known to contain enzymes that remove acetyl groups from glufosinate and mammalian enzymes may also be capable of removing the acetyl group from glufosinate. Even though glufosinate is being used widely with GM crops in North America its safety is far from proven and its impact on humans and farm animals is difficult to trace because the GM products are not labeled for consumption. We request that EPA obtain more technical data and information to better define the neurotoxicity and teratogenicity of glufosinate and its metabolites, especially in humans. Glufosinate, for example, was found to trigger apoptosis (programmed cell suicide) in the developing brain of the embryonic mouse. Numerous, well established studies showing brain damage and birth defects seem to have been ignored by those regulating use of the herbicide. We request that the EPA conduct a more comprehensive investigation of available literature on glufosinate and make requests for unpublished information from independent scientists such as their expert opinions on the adverse health effects of glufosinate and its metabolites.

We request the same under subchronic, chronic, animal metabolism, and metabolite toxicology as requested for Reproductive and Developmental toxicity.

Agency response. The study authors (cited study by Garcia et al) state in their conclusion that ''these findings warrant further investigation.'' In this study, only 16 individuals out of 261 referenced glufosinate ammonium. The results of this study indicated that there was a marginally significant increased risk of paternally related developmental toxicity. However, in this study various contributing factors such as smoking, work habits etc. were not evaluated and therefore, this epidemiological evaluation does not establish a causal definitive link to paternally related developmental toxicity. The potential for glufosinate ammonium to cause developmental or reproductive effects due to exposure (male or female) has been evaluated in acceptable guideline studies in rats and rabbits. Based on these studies, glufosinate ammonium is not teratogenic in rats and rabbits.

The petitioner has submitted acute, subchronic, chronic, developmental, and reproductive toxicity studies conducted with glufosinate ammonium. The petitioner has also submitted developmental toxicity studies (rat and rabbit) and subchronic studies (rat, mouse, and dog) with *N*-acetyl-glufosinate and 3-MP. All of these studies were conducted according to the regulatory guideline requirements (OPPTS 870 series) and conformed to EPA GLP Standards. EPA has reviewed all of these studies and selected the most sensitive endpoints. Based on a comparison of the common studies conducted with the parent and metabolites, the metabolites exhibited toxic effects at doses equal to or greater than the parent and EPA concluded that *N*-acetyl-glufosinate and 3-MP are not likely to be more toxic than glufosinate ammonium. In regards to the enzyme that can remove acetyl groups from substrates, these enzymes are present in the toxicology test systems used to evaluate the parent and metabolites.

In the cited study by Watanabe, mouse embryo cultures were exposed to glufosinate ammonium. This is an *in vitro* experiments which indicate apoptosis in the developing brain of cultured mouse embryos. It should be noted that apoptosis is a normal part of the brain development process. This experiments did not use whole animals and the current scientific knowledge is not sufficient to allow extrapolation of *in vitro* results to whole animals.

7. *Comment—endocrine disruption.* We find EPA's statements on the potential of glufosinate to function as an endocrine-disrupting substance in humans and animals as not founded on logical information or peer-reviewed studies. In fact EPA states that no special studies have been conducted to investigate the potential of glufosinate ammonium to induce estrogenic or other endocrine effects. Given the enormous complexities of mammalian hormonal regulatory systems and the current uncertainties existing in this field of knowledge as revealed by EPA's Endocrine Disruptor Advisory Committee several years ago about how to screen for potential endocrine-disrupting substances, we feel it's totally premature for EPA at this time to dismiss all concerns about glufosinate

as an endocrine-disrupting substance. EPA stresses that no evidence of estrogenic or other endocrine effects have been noted in any of the toxicology studies that have been conducted with this product and there is no reason to suspect that any such effects would be likely. Due to the millions of Americans and their children exposed to glufosinate and its metabolites, EPA needs to conclusively determine if this herbicide has endocrine-disrupting potential.

Agency response. EPA is required under the FFDCA, as amended by the FQPA, to develop a screening program to determine whether certain substances, including all pesticide active and other ingredients, ''may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate.'' Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was scientific bases for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA has authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

When the appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, glufosinate ammonium may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption. The studies submitted as guideline studies as well as the data reviewed in the open literature did not provide any obvious indications that glufosinate ammonium and/or its metabolites have specific endocrine disruptive effects.

8. *Comment—dietary exposure.* EPA states that tolerances have been established (40 CFR 180.473) for the combined residues of glufosinate ammonium and metabolites in or on a variety of RACs. EPA further maintains that no appropriate toxicological endpoint attributable to a single exposure was identified in the available toxicity studies. This is why EPA has not established an acute RfD for the general population including infants and children. An acute RfD of 0.063 mg/kg/day was established, however, for the females 13+ subgroup. Therefore, an acute dietary analysis was conducted for this sub-population; whereas, chronic dietary analysis was conducted for the usual populations. We request that EPA reconsider and reevaluate the health information finding that no appropriate toxicological endpoint attributable to a single exposure was identified in the available toxicity studies as too being limited and erroneous.

Agency response. EPA has evaluated the published toxicity studies and considered the relevant petitioner submitted studies. On the basis of these studies, no appropriate endpoint of concern attributable to a single exposure was identified. EPA has asked the petitioner to conduct a study to evaluate potential effects of glufosinate ammonium following a single exposure (acute effects) with glutamate synthetase measurements. Until such data are available, EPA has applied additional data base UF to account or allow for uncertainty about those potential effects of acute exposure.

9. *Comment—infants and children.* We are very concerned that EPA finds that the toxicological data base is sufficient for evaluating prenatal and postnatal toxicity for glufosinate ammonium in human infants and children using exclusively results from rats and rabbits. Although EPA states that there are no prenatal or postnatal susceptibility concerns for infants and children, based on the results of the rat and rabbit developmental toxicity studies and the 2-generation reproduction study, we are concerned that human infants and children may possess genetic predispositions, biochemical individualities and behavioral patterns very different from rats and rabbits. EPA needs to do a more thorough literature review and interview scientists and medical doctors who may have relevant information on the prenatal and postnatal toxicity for glufosinate ammonium in human infants and children.

As EPA notes, Based on clinical signs of neurological toxicity in short and intermediate dermal toxicity studies with rats, the agency has determined that an added FQPA safety factor of 3x is appropriate for assessing the risk of glufosinate ammonium derived residues in crop commodities. Using the conservative assumptions described in the exposure section above, the percent of the chronic RfD that will be used for exposure to residues of glufosinate ammonium in food for children 1–6 (the most highly exposed sub-group) is 61%. Infants utilize 37% of the chronic RfD. As in the adult situation, drinking water levels of comparison are higher than the worst case DWECs and are expected to use well below 100% of the RfD, if they occur at all. Therefore, there is a reasonable certainty that no harm will occur to infants and children from aggregate exposure to residues of glufosinate ammonium.

Agency response. The short-term (dermal, inhalation, and incidental oral) and acute dietary (females 13–50 years) endpoints are based on reduced fetal body weight and increased fetal death seen in the rabbit developmental toxicity study (6.3 mg/kg/day). An acute dietary endpoint for the general population, including infants and children, could not be identified due to no adverse effects seen in the relevant studies. The chronic dietary endpoint is based on a weight-of-evidence approach from several studies which demonstrated brain glutamine synthetase inhibition and alterations in the electrocardiogram (6.0 mg/kg/day). EPA concluded that the toxicological data base for glufosinate ammonium was not complete and requested the submission of the following studies: (1) Acute neurotoxicity study conducted in the rat which includes glutamine synthetase activity measurement in the liver, kidneys, and brain; (2) a developmental neurotoxicity (DNT) study conducted in the rat which includes comparative glutamine synthetase activity measurement in the liver, kidneys, and brain of the pups and mothers; and (3) a 28–day inhalation toxicity study in rats with glutamine synthetase activity measurements in brain, kidney, liver and lung. EPA also requested additional data to confirm that liver and kidney changes, observed in the absence of histopathological changes, are an adaptive response and not an adverse effect. Kidney and liver function assays should be performed in addition to glutamine synthetase activity measurements. Pending the submission of the requested data, a 10x data base uncertainty factor was applied to all oral and dermal risk assessments and a 100x uncertainty factor was applied to all inhalation risk assessments. These uncertainty factors combined with the traditional 100x inter/intra species uncertainty factor, resulted in a total uncertainty factor of 1,000x for dermal and oral exposure assessments and 3,000x for inhalation exposure assessments (10,000x uncertainty factor reduced to 3,000x based on Agency policy cited in Unit III.B.).

EPA concluded that there is no qualitative or quantitative evidence of increased susceptibility in the developmental toxicity study conducted in rats. Qualitative evidence of increased susceptibility is demonstrated in the rabbit developmental toxicity study since fetal deaths were observed in the presence of lesser maternal toxicity at the same dose. There is also quantitative evidence of increased susceptibility in the rat 2-generation reproduction study. In this study, a decrease in the number of viable pups was observed in the absence of parental toxicity at any dose. Since there is qualitative evidence of increased susceptibility of the young following exposure to glufosinate ammonium, EPA performed a degree of concern analysis to: (1) Determine the level of concern for the effects observed when considered in the context of all available toxicity data; and (2) identify any residual uncertainties after establishing toxicity endpoints and traditional uncertainty factors to be used in the risk assessment of this chemical. Based on the data gaps listed above, the EPA did not identify any other residual uncertainties. The established endpoints are protective of pre-/postnatal toxicity following acute and chronic exposures.

The Notice of Filing (NOF) published in the **Federal Register** of July 24, 2002 (67 FR 48465)(FRL–7184–6) represents a summary of the petition prepared by the petitioner and represents the views of the petitioner. As such, and in this case, discrepancies may arise between what is stated in the NOF and the procedures/conclusions employed by EPA when assessing human health risk. For instance, the toxicological data base for glufosinate ammonium has been reevaluated by EPA since July 2002, and some of the conclusions presented in the NOF concerning the toxicity of glufosinate ammonium do not reflect current EPA conclusions.

10. *Comment—cumulative effects section 408(b)(2)(D)(v).* We are deeply concerned about the potential for cumulative effects of glufosinate and its metabolites, and therefore request that EPA not approve the Aventis tolerance petition unless or until peer-reviewed confirming scientific evidence is available that glufosinate and its metabolites do not cause any cumulative effects. It is not acceptable public health policy to dismiss cumulative effects of glufosinate and its metabolites because of lack of scientific evidence and lack of any studies. Law requires that, when considering whether to establish, modify, or revoke a tolerance, the EPA must consider ''available information'' concerning the cumulative effects of a particular pesticide's residues and ''other substances that have a common mechanism of toxicity.'' EPA has indicated that, at this time, the Agency does not have available data to determine whether glufosinate ammonium 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, EPA suggests that glufosinate ammonium does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance petition, therefore, it has not been assumed that glufosinate ammonium has a common mechanism of toxicity with other substances. We disagree with EPA's illogical and unscientific assumption that glufosinate ammonium has a common mechanism of toxicity with other substances. We propose that further study is necessary to conclusively confirm such an assumption.

Agency response. 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.''

EPA does not have, at this time, sufficient data to determine whether glufosinate ammonium has a common mechanism of toxicity with other substances. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity (i.e., organophosphates), EPA has not made a common mechanism of toxicity finding as to glufosinate ammonium and any other substances and glufosinate ammonium 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 glufosinate ammonium 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 policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at *http://www.epa.gov/pesticides/cumulative/.*

11. *Comment—safety determination U.S. population.* We believe that EPA has not done an adequate scientific job with respect to its safety determination for the U.S. population. By using what EPA claims (and may be a flawed set of assumptions) are the conservative assumptions described above and based on the completeness and reliability of the toxicity data, it is concluded that chronic dietary exposure to the registered and proposed uses of glufosinate ammonium will utilize at most 25% of the chronic RfD for the U.S. population. We disagree with EPA's assumption that the actual exposure is likely to be significantly less than predicted by this analysis as data and models that are more realistic are developed. We disagree with EPA's assumption that exposures below 100% of the reference dose (RfD) are generally assumed to be of no concern because the RfD represents the level at or below which daily aggregate exposure over a lifetime will not pose appreciable risk to human health. We dispute that the acute population of concern, female 13+ utilizes 34% of the acute RfD. We disagree with EPA's assumption that this is a Tier One highly conservative assessment and actual exposure is likely to be far less. Drinking water levels of comparison based on dietary exposures are greater than highly conservative estimated levels, and would be expected to be well below the 100% level of the RfD, if they occur at all, assuming that EPA's set of assumptions are reasonably accurate which they may not be. We believe that EPA has erroneously concluded that it is not appropriate to aggregate non-dietary exposures with dietary exposures in a risk assessment because the toxicity end-points are different. We strongly dispute EPA's concluding assumption that there is a reasonable certainty that no harm will occur to the U.S. population from aggregate exposure (food, drinking water and nonresidential) to residues of glufosinate ammonium and metabolites.

Agency response. Contrary to what was written in the Notice of Filing prepared by the petitioner, EPA did aggregate dietary (food + drinking water) and residential exposures. Glufosinate ammonium is currently registered for application in the residential setting for lawn renovation and spot treatment purposes. Since the lawn renovation use resulted in exposures greater than EPA's level of concern, revocation of this use was recommended. Therefore, aggregate exposures were conducted by combining dietary exposure and residential exposure resulting from the spot treatment use. The resulting

combined exposures were subtracted from the appropriate dose and drinking water levels of comparison (DWLOCs) were calculated and compared to EECs in groundwater and surface water. The EECs were generated using SCIGROW (groundwater) and PRZM-EXAMS (surface water). SCIGROW is a regression model designed to estimate a screening level of a pesticide concentration at an agricultural site which is highly vulnerable to leaching due to permeable soil overlaying shallow ground water. PRZM-EXAMS is used to estimate concentration that might occur in vulnerable surface water (assumes 87% of the basin is cropped and entire cropped area is treated). Both models assumed 3 applications at 1.5 lbs ai/acre (highest registered/proposed rate). The resulting EECs were less than the DWLOCs indicating aggregate exposures are less than EPA's level of concern.

12. *Comment.* Additional issues not apparently being addressed by EPA such as negative impacts on beneficial insects. Bystander or beneficial insects have been detrimentally effected by the herbicide. Kutlesa and Caveny found that the herbicide had a number of neurotoxic impacts on the skipper butterfly at levels of herbicide experienced in the field. Ahn et al found that glufosinate was toxic to some but not all predatory insects at levels of the herbicide experienced in the field. Studies showing that helpful predatory insects or bystander insects are poisoned by the herbicide seem to have been ignored by regulators of the herbicide.

Agency response. This comment raises an issue concerning the pesticide's registrability under FIFRA and is not directly relevant to the safety determination under FFDCA. For registrations of a pesticide under FIFRA, EPA requires non-target insect data if the proposed use will result in exposure to honey bees (40 CFR 158.590). Two studies on the toxicity of glufosinate ammonium to bees indicates that the herbicide (technical and a formulated product) is practically non-toxic to bees via contact and oral routes. The cited studies suggest that glufosinate ammonium may cause mortality to insects, other than bees, and mites may also be affected. The issues of the hazard to non-target insects will be addressed via registration under FIFRA.

13. *Comment.* Additional issues not apparently being addressed by EPA such as glufosinate residues in other crop varieties. Muller et al studied glufosinate metabolites in transgenic and unmodified sugar beet, carrot, purple foxglove and thorn apple, and they found that unmodified (i.e., non-genetically engineered) crops contained glufosinate mainly while GM crops contained higher levels of glufosinate and acetyl glufosinate. Beriault et al studied phloem transport of glufosinate and acetylglufosinate in canola in GM canola and unmodified canola and found that both chemicals were highly mobile.

Agency response. Common toxicity studies conducted with glufosinate ammonium, *N*-acetyl-glufosinate, and 3-MP indicate that *N*-acetyl-glufosinate and 3-MP exhibit toxic effects at doses equal to or greater than glufosinate ammonium. Based on these toxicity studies, EPA concluded that *N*-acetyl-glufosinate, and 3-MP are not likely to be more toxic than glufosinate ammonium (risk assessment assumes they are of equal toxicity to parent). The field trial data were submitted for the transgenic crops monitored for residues of glufosinate ammonium, *N*-acetyl-glufosinate, and 3-MP in/on all food/feed commodities. Therefore, the higher residues in transgenic crops and/or greater mobility of the residues of concern has been taken into consideration.

14. *Comment.* Two hundred and twenty four comments were received that were opposed to establishing tolerances for glufosinate ammonium in genetically engineered (GE) rice and cotton. They included some or all of the following comments from the campaign to halt the introduction of GE Crops:

I am writing in reference to Bayer CropScience's August 15th petition to establish a tolerance for Glufosinate in or on Rice and cotton. I believe that by approving the residues requested by Bayer you will be exposing the public to unnecessary health risks, potentially increasing use of toxic herbicides on rice and cotton, and endangering the livelihoods of farmers by shutting off valuable export markets that are rejecting transgenic crops. I am concerned about the loss of overseas markets for farmers growing transgenic crops and for farmers whose own ability to market their crops is threatened by genetic pollution. Many countries throughout the world are refusing transgenic crops and USDA organic standards strictly prohibit the use of transgenic seeds. Glufosinate tolerance levels have not been established by the international food standards commission, Codex Alimentarius. Events such as StarLink and last year's ProdiGene incident highlight the inadequacies of our current system in keeping transgenic crops segregated. In Canada, farmers growing transgenic crops have detected triple herbicide resistance in weeds and volunteer canola plants as a result of gene transfer, rendering the herbicides useless. If Bayer's petition is approved, it will only be a matter of time before red rice, which is the same species as cultivated rice and also one of the most virulent weeds on rice farms, becomes resistant to Glufosinate. Similar gene transfer in rice will lead to the need for new, more toxic herbicides. Peer-reviewed scientific studies have shown Glufosinate to be ''highly toxic'' to aquatic animals such as clams, oysters, water fleas, fish and birds at doses as low as 0.5 ppm. As rice is grown in an aquatic environment, the adoption of Glufosinate tolerant rice will have tragic impacts for the ecosystems of rice growing areas. The EPA classifies Glufosinate as ''persistent'' and it has been found in the edible parts of spinach, wheat and radishes more than 120 days after being sprayed with the chemical. The approval of Glufosinate tolerant rice and cotton will send us a step backward in our efforts toward a more sustainable agriculture. Please take action to ensure that our current system of agriculture moves toward one that is less reliant on chemicals, and ensures our farmers a prosperous livelihood. I strongly urge you to deny Bayer's request for approval of Glufosinate tolerance and to work with other government agencies to enact a more rigorous approval and testing process for transgenic crops.

Forty one comments were in favor of establishing the tolerances for glufosinate ammonium. They stated that growers need the new technology to control weed species.

Agency Response. EPA has concluded that there is a reasonable certainty that no harm will result to the general population, and to infants and children from aggregate exposure to glufosinate-ammonium and its metabolites from established and proposed tolerances. The issues of the hazard to non-target organisms and crop resistance will be addressed via registration under FIFRA. The growing of Herbicide Tolerant crops and potential effects on shipment of crops overseas is addressed by USDA and FDA in their pre-marketing review of Plant-Incorporated Protectant Seeds. EPA is responsile for the safety of the pesticide to be applied to the growing crop.

VII. 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–2003–0058 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 November 28, 2003.

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 VII.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–2003–0058, 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).

VIII. 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.

IX. 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:September 23, 2003.

Debra Edwards,

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), 346(a) and 371.

■ 2. Section 180.473 is revised to read as follows:

§ 180.473 Glufosinate ammonium; tolerances for residues.

(a) *General.* (1) Tolerances are established for residues of the herbicide glufosinate ammonium (butanoic acid, 2-amino-4-(hydroxymethylphosphinyl)-, monoammonium salt) and its metabolites, 2-acetamido-4-methylphosphinico-butanoic acid and 3-methylphosphinico-propionic acid, expressed as 2-amino-4-(hydroxymethylphosphinyl)butanoic acid equivalents, in or on the following food commodities:

Commodity	Parts per million
Almond, hulls	0.50
Apple	0.05
Banana	0.30
Banana, pulp	0.20
Bushberry subgroup 13B	0.15
Cattle, fat	0.40
Cattle, meat	0.15
Cattle, meat byproducts	6.0
Cotton, gin byproducts	15
Cotton, undelinted seed	4.0
Egg	0.15
Goat, fat	0.40
Goat, meat	0.15
Goat, meat byproducts	6.0
Grape	0.05
Hog, fat	0.40
Hog, meat	0.15
Hog, meat byproducts	6.0
Horse, fat	0.40
Horse, meat	0.15
Horse, meat byproducts	6.0
Juneberry	0.10
Lingonberry	0.10
Milk	0.15
Nut, tree, group 14	0.10
Potato	0.80
Potato, chips	1.60
Potato granules and flakes	2.00
Poultry, fat	0.15
Poultry, meat	0.15
Poultry, meat byproducts	0.60
Salal	0.10
Sheep, fat	0.40
Sheep, meat	0.15
Sheep, meat byproducts	6.0

(2) Tolerances are established for residues of the herbicide glufosinate ammonium (butanoic acid, 2-amino-4-(hydroxymethylphosphinyl)-, monoammonium salt) and its metabolites, 2-acetamido-4-methylphosphinico-butanoic acid and 3-methylphosphinico-propionic acid, expressed as 2-amino-4-(hydroxymethylphosphinyl)butanoic acid equivalents, in or on the following food commodities derived from transgenic canola, transgenic cotton, transgenic field corn, transgenic rice, transgenic soybean and transgenic sugar beet that are tolerant to glufosinate ammonium:

Commodity	Parts per million
Aspirated grain fractions	25.0
Beet, sugar, molasses	5.0
Beet, sugar, roots	0.9
Beet, sugar, tops (leaves)	1.5
Canola, meal	1.1
Canola, seed	0.4
Corn, field, forage	4.0
Corn, field, grain	0.2
Corn, field, stover	6.0
Cotton, gin byproducts	15
Cotton, undelinted seed	4.0
Rice, grain	1.0
Rice, hull	2.0
Rice, straw	2.0
Soybean	2.0
Soybean, hulls	5.0

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

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

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

[FR Doc. 03–24565 Filed 9–26–03; 8:45 am]

BILLING CODE 6560–50–S

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[OPP–2003–0218; FRL–7318–2]

Quinoxyfen; Pesticide Tolerance

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.