Dated: December 21, 1998.

David A. Ullrich,

Acting Regional Administrator, Region 5.

For the reasons stated in the preamble, part 52, chapter I, title 40 of the Code of Federal Regulations is amended as follows:

PART 52—[AMENDED]

1. The authority citation for part 52 continues to read as follows:

Authority: 42 U.S.C. 7401 *et seq.*

Subpart O—Illinois

2. Section 52.726 is amended by adding paragraphs (u) and (v) to read as follows:

§ 52.726 Control strategy: Ozone.

* * * * *

(u) Negative declaration—Industrial wastewater category. On October 2, 1998, the State of Illinois certified to the satisfaction of the United States Environmental Protection Agency that no major sources categorized as part of the Industrial wastewater category are located in the Metro-East ozone nonattainment area (Metro-East). The Metro-East area is comprised of Madison, Monroe and St. Clair Counties which are located in southwest Illinois, adjacent to St. Louis, Missouri.

(v) Negative declaration—Industrial cleaning solvents category. On October 2, 1998, the State of Illinois certified to the satisfaction of the United States Environmental Protection Agency that no major sources categorized as part of the Industrial cleaning solvents category are located in the Metro-East ozone nonattainment area (Metro-East). The Metro-East area is comprised of Madison, Monroe and St. Clair Counties which are located in southwest Illinois, adjacent to St. Louis, Missouri.

[FR Doc. 99–227 Filed 1–5–99; 8:45 am]

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ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[OPP–300767; FRL–6049–2]

RIN 2070–AB78

Dicamba (3,6-dichloro-o-anisic acid); Pesticide Tolerance

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This regulation establishes, revises and revokes tolerances for combined residues of Dicamba in or on various raw agricultural commodities. BASF Corporation requested this tolerance under the Federal Food, Drug and Cosmetic Act (FFDCA), as amended by the Food Quality Protection Act of 1996 (Pub. L. 104–170).

DATES: This regulation is effective January 6, 1999. Objections and requests for hearings must be received by EPA on or before March 8, 1999.

ADDRESSES: Written objections and hearing requests, identified by the docket control number, [OPP–300767], must be submitted to: Hearing Clerk (1900), Environmental Protection Agency, Rm. M3708, 401 M St., SW., Washington, DC 20460. Fees accompanying objections and hearing requests shall be labeled ''Tolerance Petition Fees'' and forwarded to: EPA Headquarters Accounting Operations Branch, OPP (Tolerance Fees), P.O. Box 360277M, Pittsburgh, PA 15251. A copy of any objections and hearing requests filed with the Hearing Clerk identified by the docket control number, [OPP–300767], must also be submitted to: Public Information and Records Integrity Branch, Information Resources and Services Division (7502C), Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. In person, bring a copy of objections and hearing requests to Rm. 119, Crystal Mall #2, 1921 Jefferson Davis Hwy., Arlington, VA.

A copy of objections and hearing requests filed with the Hearing Clerk may also be submitted electronically by sending electronic mail (e-mail) to: opp-docket@epamail.epa.gov. Copies of objections and hearing requests must be submitted as an ASCII file avoiding the use of special characters and any form of encryption. Copies of objections and hearing requests will also be accepted on disks in WordPerfect 5.1/6.1 file format or ASCII file format. All copies of objections and hearing requests in electronic form must be identified by the docket control number [OPP–300767]. No Confidential Business Information (CBI) should be submitted through e-mail. Electronic copies of objections and hearing requests on this rule may be filed online at many Federal Depository Libraries.

FOR FURTHER INFORMATION CONTACT: By mail: Joanne I. Miller, Registration Division (7505C), Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. Office location, telephone number, and e-mail address: Crystal Mall #2, 1921 Jefferson Davis Hwy., Arlington, VA, (703) 305–6224, e-mail: miller.joanne@epamail.epa.gov.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of November 20, 1998 (63 FR 64481)(FRL–6043–9), EPA issued a notice pursuant to section 408 of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 346a(e) announcing the filing of pesticide petitions (PP 6F4604, 4F3041 and FAP 4H5428) for tolerances by BASF Corporation. This notice included a summary of the petitions prepared by BASF. There were no comments received in response to the notice of filing.

These petitions requested that 40 CFR 180.40 CFR part 180.227 be amended by establishing, revising and revoking tolerances for combined residues of the herbicide dicamba (3,6-dichloro-*o*-anisic acid) and its metabolites 3,6-dichloro-5-hydroxy-*o*-anisic acid and 3,6-dichloro-2-hydroxybenzoic acid in or on the commodities listed in the summary of this Final Rule

I. Risk Assessment and Statutory Findings

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

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

II. Aggregate Risk Assessment and Determination of Safety

Consistent with section 408(b)(2)(D), 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 Dicamba (3,6-dichloro-*o*-anisic acid) and to make a determination on aggregate exposure, consistent with section 408(b)(2), for revising and establishing tolerances for combined residues of Dicamba as described as follows:

1. Establishing new tolerances for residues of dicamba and its metabolite 3,6-dichloro-5-hydroxy-*o*-anisic acid in or on: barley hay at 2 ppm, corn, field, forage at 3 ppm; corn, field, stover at 3 ppm, corn, pop, stover at 3 ppm; cottonseed meal at 5 ppm; Crop Group 17 (grass forage, fodder, and hay) forage at 125 ppm and hay at 200 ppm; oats forage at 80 ppm, oats hay at 20 ppm; wheat forage at 80 ppm, wheat hay at 20 ppm.

2. Establishing new tolerances for residues of dicamba and its metabolites 3,6-dichloro-2-hydroxybenzoic acid and 3,6-dichloro-5-dichloro-5-hydroxy-*o*-anisic acid in or on aspirated grain fractions at 5100 ppm, and soybean hulls at 13 ppm.

3. Revising tolerances for residues of dicamba (3,6-dichloro-*o*-anisic acid) and its metabolite 3,6-dichloro-5-hydroxy-*o*-anisic acid in or on: barley grain to 6 ppm, barley straw at 15 ppm; cottonseed to 3 ppm; wheat grain to 2 ppm, wheat straw to 30 ppm.

4. Revising tolerances for residues of dicamba and its metabolite 3,6-dichloro-2-hydroxybenzoic acid in or on: asparagus to 4 ppm.

5. Revise tolerances for residues of dicamba and its metabolites 3,6-dichloro-2-hydroxybenzoic acid and 3,6-dichloro-5-hydroxy-*o*-anisic acid in or on soybeans seed to 10 ppm, changing the name of the commodity from soybean grain to soybean seed.

6. Revoking the following tolerances: grasses, hay at 40 ppm; grasses, pasture at 40 ppm and grasses, rangeland at 40 ppm as these tolerances are being replaced by Crop Group 17.

EPA's assessment of the dietary 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 Dicamba (3,6-dichloro-*o*-anisic acid) are discussed below.

1. *Acute toxicity*. The following acute toxicity studies with technical dicamba were submitted in support of this regulatory action:

- Acute oral in rats with an LD_{50} 2,740 mg/kg
- Acute dermal in rabbits with an LD_{50} > 2,000 mg/kg
- Acute inhalation in rats with an LD_{50} > 5.3 mg/L
- Acute eye irritation in rabbits with mild to moderate eye irritation
- Acute dermal irritation in rabbits with irritation
- Dermal Sensitization in guinea pigs with no dermal sensitization

The results from the eye irritation study and the dermal irritation study placed technical in category II as an acute toxicant.

2. In a 13-week oral toxicity study, Charles River CD rats were exposed to dicamba (86.8% a.i.) at 0, 5,000, 10,000, 12,500 or 15,000 ppm (approximately 500, 1,000, 1,250 or 1,500 mg/kg/day). At 10,000 ppm and above, a reduction of cytoplasmic vacuolization of hepatocyte was observed, along with slight decreases in body weight and food consumption. The NOAEL = approximately 500 mg/kg/day, the LOAEL = approximately 1,000 mg/kg/day based on body weight changes and liver effects.

3. In a 21-day dermal study Dicamba was administered to New Zealand white rabbits (5/sex/group) at levels of 0, 40, 200, or 1,000 mg/kg/day for 3 weeks. Administration was 6 hr/day to an area approximately 10 x 15 cm (10% of body surface area). No systemic toxicity was observed at any dose level. Dose-related dermal irritation was observed at the application sites. Desquamation was seen predominantly in the 1,000 mg/kg/day group while moderate erythema, moderate edema and atonia were observed exclusively in the 1,000 mg/kg/day group. A dose-related incidence of fissuring was noted in the 200 and 1,000 mg/kg/day groups. The severity of acanthosis and the incidence of hyperkeratosis was increased at these sites among rabbits in the 200 and 1,000 mg/kg groups. Based on these findings, the systemic NOAEL for males and females is 1,000 mg/kg/day. A systemic LOAEL could not be established. The NOAEL for dermal irritation is 40 mg/kg/day and the LOAEL is 200 mg/kg/day.

4. In the combined chronic toxicity/carcinogenicity study in rats, Dicamba 86.8% a.i. was administered to 50 Charles River CD rats/sex/dose via the diet at dose levels of 0, 50, 250 or 2,500 ppm/day (approximately 2.5, 12.5, or 125 mg/kg/day) for 24 months. There were no effects of dosing on clinical signs of toxicity, survival, mean body weights or weight gains, food consumption, and hematologic, clinical chemistry, or urinary parameters. Organ weights, macroscopic findings, and non-neoplastic histologic findings were similar among dosed and control groups.The NOAEL is approximately 125 mg/kg/day, the highest dose level tested. A LOAEL was not established. As an effect level was not achieved, it is possible that the animals may have tolerated a higher dose.

5. In the carcinogenicity study in mice, dicamba 86.8% a.i. was administered to 52 CD-1 mice/sex/dose via the diet at dose levels of 0, 50, 150, 1,000, and 3,000 ppm (approximately 0, 6, 18, 115 or 361 mg/kg/day) for 24 months. There was no significant biological evidence of oncogenicity from ingestion of dicamba. A statistically significant increase ($p<0.05$) in the mortality rate (-31%) in 3,000 ppm males could not clearly be associated with treatment because a statistically significant increase was also observed in males at 150 ppm. Also, decreased body weight gain and an increased ratio of lymphocytes to neutrophils in high-dose females could not be related to treatment with any degree of certainty.The LOAEL is 3,000 ppm (approximately 360 mg/kg/day) based on increased mortalities in males and decreased body weight gain in females. The NOAEL is 1,000 ppm (approximately 115 mg/kg/day. There was no evidence of a treatment related oncogenic response.

6. In a 1-year chronic feeding study, dicamba 86.8% a.i. was administered to Beagle dogs (4/sex/group) in the diet at 0, 10, 500 or 2,500 ppm (0, 2, 11 or 52 mg/kg/day) for 12 months. No adverse effects were observed at any dose level. No abnormalities in clinical signs, hematology, clinical chemistry or urinalysis were reported. No abnormal findings were made at necropsy, nor were there any significant changes in food consumption or body weight. The NOAEL for this study is 52 mg/kg/day, the highest dose level tested. The LOAEL could not be established.

7. In a developmental toxicity study CD (Charles River) pregnant rats (25/dose group) were administered dicamba (85.8% a.i.) at oral dose levels of 0, 64, 160 or 400 mg/kg/day in corn oil on days 6 through 19 of gestation. Maternal toxicity, limited to the high-dose group, was characterized by mortality in three gravid and one non-gravid dams that exhibited neurotoxic signs prior to death; clinical signs of nervous system toxicity that included ataxia, salivation, stiffening of the body when held, and decreased motor activity; statistically

significant (p≤0.05) decreases in body weight gain during the dosing period (days 0 to 20); and concomitant decreases in food consumption. Dicamba had no effect on any of the cesarean parameters. The maternal LOAEL is 400 mg/kg/day, based on mortality, clinical signs, body weight changes and decreases in food consumption. The maternal NOAEL is 160 mg/kg/day. No treatment-related fetal gross external, skeletal or visceral anomalies (malformations or variations) were seen at any dose level. The developmental LOAEL is not established. The developmental NOAEL is > 400 mg/kg/day, the highest dose level tested.

8. In a developmental toxicity study inseminated New Zealand White rabbits (19 or 20/dose group) were administered dicamba (90.5% a.i.) at oral (capsule) dose levels of 0, 30, 150, or 300 mg/kg/day on days 6 through 18 of gestation.No maternal toxicity was observed at 30 mg/kg/day. At 150 mg/kg/day maternal toxicity was characterized by abortion (5%) and clinical signs such as ataxia, rales, decreased motor activity. At 300 mg/kg/day maternal toxicity was manifested by abortions, clinical signs, decreased body.

9. In a 2-generation reproduction study, Sprague-Dawley rats (32 or 28/group) received dicamba technical (86.5% a.i.) in the diet at dose levels of 0, 500, 1,500, or 5,000 ppm (0, 40, 122, or 419 mg/kg/day (male) and 0, 45, 136 or 450 mg/kg/day (female). Systemic toxicity was observed at 5,000 ppm, manifested as clinical signs in dams from both generations during lactation (tense/stiff body tone and slow righting reflex) and significantly increased relative liver to body weights ratios (112% of control) in both generations and sexes, adults as well as weanlings. Relative kidney to body weights (107%) at 1,500 and/or 5,000 ppm were not considered to be toxicologically relevant since there were no gross or histopathological findings. Based on these results, the NOAEL for systemic toxicity was 1,500 ppm (122 and 136 mg/kg/day for males and females (M/F), respectively). The LOAEL was 5,000 ppm (M/F: 419/450 mg/kg/day) based on clinical signs of neurotoxicity. Reproductive and/or offspring toxicity was observed at 1,500 and 5,000 ppm, manifested as significantly decreased pup growth (decreased body weight gain) in all generations and matings at 1,500 ppm (86 - 90% of control) and at 5,000 ppm (74 - 94% of control). In addition, delayed sexual maturation was noted in F1 males at 5,000 ppm. Based on these results, the NOAEL for reproductive toxicity was 500 ppm (45 mg/kg/day) and the LOAEL was 1,500 ppm (136 mg/kg/day based on decreased pup growth. Lastly, the NOAEL for offspring toxicity was 45 mg/kg/day and the LOAEL was 136 mg/kg/day, based on significantly decreased pup growth.

10. In an acute neurotoxicity study in rats, Dicamba was administered by gavage in a single dose to Crl: CD BR rats at doses of 0, 300, 600, or 1,200 mg/kg. Vehicle controls received corn oil only. Positive controls received acrylamide at 50 mg/kg/day by i.p. injection on seven consecutive days. At 300 mg/kg, transiently impaired respiration; rigidity upon handling, prodding or dropping; freezing of movement when touched; decreased arousal and fewer rears/minute compared to controls; impaired of gait and righting reflex were observed in both sexes. In addition, males showed decreased forelimb grip strength. With the exception of the decrease in forelimb grip strength, which persisted until day seven, these effects were observed only on the day of dosing. In addition, at 600 mg/kg, both sexes showed decreases in locomotor activity and males showed significant decreases in tail flick reflex and a raised posture when placed in an open field. These effects were also observed only on the day of dosing. At the highest dose level tested (1,200 mg/kg), both males and females showed an impaired startle response to an auditory stimulus. The effect was significant in males on day seven and in females on the day of dosing. In addition, males showed decreases in body weight (5 - 9%), body weight gain (24%) and food consumption (13% between days 0 and 7. The LOAEL for this study was 300 mg/kg based on the several neurologic signs listed above; the NOAEL was < 300 mg/kg/day.

11. In a subchronic neurotoxicity study Sprague-Dawley rats (10/sex/dose) were fed test diets containing 0, 3,000, 6,000, or 12,000 ppm (0, 197.1, 401.4, 767.9 mg/kg/d (M) and 0, 253.4, 472.0 or 1,028.9 mg/kg/day (F)) Dicamba (86.9% a.i.) for 13 weeks. Neurobehavioral evaluations, consisting of FOB, locomotor activity, and auditory startle response, were conducted at prestudy and during Weeks 4, 8 and 13. No toxicologically significant differences were noted in either the mean body weights or food consumption of the treated animals. Neurobehavioral evaluations at the 4-, 8-, and 13–week evaluations revealed abnormal FOB observations consisting of rigid body tone, slightly impaired righting reflex and impaired gait. At Week 13 the incidences of these findings were decreased. Rigid body tone was also noted during evaluation of the righting reflex and landing foot splay. The NOAEL is 401.4/472.0 mg/kg/day (M/F), and the LOAEL is 767.9/1,028.9 mg/kg/day (M/F) based on rigid body tone, slightly impaired righting reflex and impaired gait.

12. In a microbial mutagenicity assay, *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, or TA1538 were exposed to the dimethylamine (DMA) salt of dicamba (40.3% a.i.) in deionized distilled water at concentrations of 100, 333, 1,000, 3,333, or 5,000 µg/plate in the presence and absence of mammalian metabolic activation. Preparations for metabolic activation were made from induced rat livers. The DMA salt of dicamba was tested up to the limit concentration of 5,000 µg/plate and no cytotoxicity was observed. The positive controls induced the appropriate responses in the corresponding strains. There was no evidence of induced mutant colonies over background (reversion to prototrophy).

13. In a microbial mutagenicity assay, *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, or TA1538 were exposed to the diglycolamine (DGA) salt of dicamba (39.7% a.i.) in deionized distilled water at concentrations of 100, 333, 1,000, 3,333, or 5,000 µg/plate in the presence and absence of mammalian metabolic activation. Preparations for metabolic activation were made from induced rat livers. The DGA salt of dicamba was tested up to the limit concentration of 5,000 µg/plate, but no cytotoxicity was observed. The positive controls induced the appropriate responses in the corresponding corresponding strains. There was no evidence of induced mutant colonies over background (reversion to prototrophy).

14. In a microbial mutagenicity assay, *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, or TA1538 were exposed to the isopropylamine (IPA) salt of dicamba (32.3% a.i.) in deionized distilled water at concentrations of 100, 333, 1,000, 3,333, or 5,000 µg/plate in the presence and absence of mammalian metabolic activation. Preparations for metabolic activation were made from induced rat livers. The IPA salt of dicamba was tested up to the limit concentration of 5,000 µg/plate and no cytotoxicity was observed. The positive controls induced the appropriate responses in the corresponding strains. There was no evidence of induced mutant colonies over background (reversion to prototrophy).

15. In a mammalian cell gene mutation assay at the thymidine kinase locus, L5178Y mouse lymphoma cells cultured *in vitro* were exposed to dicamba dimethylamine (DMA) salt (40.3% a.i.) in distilled water at concentrations of 900, 1,000, 1,500, 2,000, 2,500, 3,000, 3,500, 4,000, 4,500, and 5,000 µg/mL in the presence and absence of S9 mammalian metabolic activation. Dicamba DMA salt was tested up to the limit dose. Under nonactivation conditions, the percent total growth values over the evaluated dose range were from 69-109% (initial assay) and 65-111% (confirmatory assay). The mutation frequencies (MFs) for all of the treated cultures were <2x the solvent controls; the exception was the 4,500 µg/mL dose, which had a MF of approximately 2x background in the confirmatory trial. However, the 4,500 µg/mL response was not reproducible. The S9-activation assay confirmed the findings of the nonactivation assay. The percent total growth values were 26-109% (initial assay) and 23-113% (confirmatory assay). The MFs for all of the treated cultures were <2x the solvent controls with the exception of the 3,000 µg/mL dose in the confirmatory trial which had a MF of approximately 2x background; this result was not reproducible. It was determined that dicamba DMA salt was not mutagenic under either nonactivation or S9-activation conditions. In both the nonactivated and activated conditions, the positive controls induced the appropriate response.

16. In a mammalian cell gene mutation assay at the thymidine kinase locus (MRID 43310305), L5178Y mouse lymphoma cells cultured *in vitro* were exposed to dicamba diglycolamine (DGA) salt (39.7% a.i.) in distilled water at concentrations of 900, 1,000, 1,500, 2,000, 2,500, 3,000, 3,500, 4,000, 4,500, and 5,000 µg/mL in the presence and absence of S9 mammalian metabolic activation. Dicamba DGA salt was tested up to the limit dose. Under nonactivation conditions, the percent total growth values over the evaluated dose range were from 68-116% (initial assay) and 72-105% (confirmatory assay). The mutation frequencies (MFs) forall of the treated cultures were <2x the solvent controls. The S9-activation assay confirmed the findings of the nonactivation assay. The percent total growth values were 43-102% (initial assay) and 46-99% (confirmatory assay). The MFs for all of the treated cultures were <2x the solvent controls with the exception of the 4,500 µg/mL dose in the initial trial, which had a MF of approximately 2x background. However, this result was not reproducible. Therefore, it was determined that dicamba DGA salt was not mutagenic under either nonactivation or S9-activation conditions. In both the nonactivated and activated conditions, the positive controls induced the appropriate response.

17. In a mammalian cell gene mutation assay at the thymidine kinase locus, L5178Y mouse lymphoma cells cultured *in vitro* were exposed to dicamba isopropyl amine (IPA) salt (32.3% a.i.) in distilled water at concentrations of 900, 1,000, 1,500, 2,000, 2,500, 3,000, 3,500, 4,000, 4,500, and 5,000 µg/mL in the presence and absence of S9 mammalian metabolic activation. Dicamba IPA salt was tested up to the limit dose. Under nonactivation conditions, the percent total growth values over the evaluated dose range were from 92-101% (initial assay) and 51-107% (confirmatory assay). The mutation frequencies (MFs) for all of the treated cultures were <2x the solvent controls. The S9-activation assay confirmed the findings of the nonactivation assay. The percent total growth values were 75-126% (initial assay) and 49-114% (confirmatory assay). The MFs for all of the treated cultures were <2x the solvent controls. Therefore, it was determined that dicamba IPA salt was not mutagenic under either nonactivation or S9-activation conditions. In both the nonactivated and activated conditions, the positive controls induced the appropriate response.

18. In an *in vivo* mouse bone marrow micronucleus assay, groups of five ICR mice/sex received a single IP injection of 525, 1,050, or 2,100 mg/kg of the diglycolamine DGA salt formulation of dicamba (39.7% a.i.). Bone marrow cells were harvested at 24, 48, or 72 hours post treatment and scored for micronucleated polychromatic erythrocytes (MPCEs). Mortality occurred in 3/20 male and 1/20 female mice dosed at 2,100 mg/kg. Lethargy was observed in male and female mice at all dose levels. Cytotoxicity by the DGA salt formulation was observed by a reduction in the ratio of PCEs to total erythrocytes in males dosed at 2,100 mg/kg 48 and 72 hours following dosing. The positive control induced significant increases in MPCEs in both sexes. The DGA salt of dicamba was non-mutagenic. There was no significant increase in the frequency of MPCEs in bone marrow after any treatment time.

19. In an *in vivo* mouse bone marrow micronucleus assay, groups of five ICR mice/sex received a single IP injection of 500, 1,000, or 2,000 mg/kg of the isopropylamine (IPA) salt formulation of dicamba (32.3% a.i.). Bone marrow cells were harvested at 24, 48, or 72 hours post-treatment and scored for micronucleated polychromatic erythrocytes (MPCEs). Mortality occurred in 2/20 male and 0/20 female mice dosed at 2,000 mg/kg. Lethargy was observed in male and female mice at all dose levels. The IPA salt formulation of dicamba was not cytotoxic to the target cell. The positive control induced significant increases in MPCEs in both sexes. The IPA salt of dicamba was non-mutagenic. There was no significant increase in the frequency of MPCEs in bone marrow after any treatment time.

20. In a metabolism, distribution and excretion study, (1) groups of four males and eight females per dose of Charles River CD rats received a single oral dose (0.1 or 0.93 gm/kg) in peanut oil by esophageal intubation. The rats were sacrificed at intervals ranging from one hour to 72 hours after dosing. Tissues, urine and blood were retained for subsequent analysis. (2) One male and one female each received a single injection subcutaneously of C_{14} labeled dicamba. The rats were sacrificed at 72 hours. (3) Groups of five male and five female rates per dose housed in individual metabolic cages were fed C_{14} labeled dicamba at 10, 100, 1,000, 10,000 and 20,000 ppm for 24 days. Rats were sacrificed at 1, 3, 6, 13 and 24 days. Dietary ingestion resulted in 96% urinary excretion in 48 hours and 4% via the feces. Fairly equal tissue distribution occurred initially but tissue levels did not persist beyond a few hours, indicating no bioaccumulation. It was concluded that when administered orally to rats, C_{14} labeled dicamba is rapidly absorbed and excreted. Over 95% is excreted in the urine and the compound is not metabolized or appreciable accumulated by the tissues. A fraction of the dicamba in the urine (ca. 13%) is conjugated to the glucuronide.

B. Toxicological Endpoints

1. *Acute dietary (1–day).* In an acute neurotoxicity study in rats groups of Crl: CD BR rats (10/sex/dose) received a single oral (gavage) administration of Dicamba (86.9%) in corn oil at doses of 0, 300, 600, or 1,200 mg/kg. Vehicle controls received corn oil only. Positive controls received Acrylamide at 50 mg/kg/day by intra peritoneal injection on seven consecutive days. At 300 mg/kg, transiently impaired respiration; rigidity upon handling, prodding or dropping; freezing of movement when touched; decreased arousal and fewer rears/

minute compared to controls; impairment of gait and righting reflex were observed in both sexes. In addition, males showed decreased forelimb grip strength. With the exception of the decrease in forelimb grip strength, which persisted until day seven, these effects were observed only on the day of dosing. In addition, at 600 mg/kg, both sexes showed decreases in locomotor activity and males showed significant decreases in tail flick reflex and a raised posture when placed in an open field. These effects were also observed only on the day of dosing. At the highest dose level tested (1,200 mg/kg), both males and females showed an impaired startle response to an auditory stimulus. The effect was significant in males on day seven and in females on the day of dosing. In addition, males showed decreases in body weight (5 - 9%), body weight gain (24%) and food consumption (13% between days 0 and 7). The LOAEL was 300 mg/kg based on the several neurologic signs listed above; a NOAEL was not established.

i. *Dose and Endpoint for Risk Assessment*: LOAEL=300 mg/kg/day based on severe neurologic signs described above.

ii. *Comments about Study and Endpoint*: Neurotoxicity was seen in both sexes at the lowest dose tested. With the exception of the decrease in forelimb grip strength, which persisted until day seven, the other neurologic signs were seen only on the day of dosing. The Acute Dietary RfD is 0.10 mg/kg/day, based on the LOAEL of 300 mg/kg/day and an uncertainty factor of 3,000 for infants and children (10x for intra species variations, 10x for inter species variations, 10x because a LOAEL was used instead of a NOAEL, and 3x for FQPA considerations). The EPA used 10x because a LOAEL was used, not 3x, because of the severity of neurotoxic signs exhibited by all animals in both sexes at the lowest dose level used.

2. *Chronic dietary Reference Dose (RfD).* In a 2-generation reproduction study, Sprague-Dawley rats (32 or 28/group) received Dicamba technical (86.5%) in the diet at dose levels of 0, 500, 1,500, or 5,000 ppm (0, 40, 122, or 419 mg/kg/day for males and 0, 45, 136 or 450 mg/kg/day for females, respectively) for two generations. Systemic toxicity was observed at 5,000 ppm, manifested as clinical signs in dams from both generations during lactation (tense/stiff body tone and slow righting reflex) and significantly increased relative liver to body weights (112% of control) in both generations and sexes, adults as well as weanlings. The increase (107%) in relative kidney weights observed at 1,500 and/or 5,000 ppm were not considered to be toxicologically significant due to lack of corroborative gross or histopathological lesions in the kidneys. For parental systemic toxicity, the NOAEL was 122 and 136 mg/kg/day for males and females, respectively and the LOAEL was 419 and 450 mg/kg/day in males and females based on clinical signs of neurotoxicity. Reproductive toxicity at 1,500 and 5,000 ppm, manifested as significantly decreased pup growth in all generations and matings at 1,500 ppm (86 - 90% of control) and at 5,000 ppm (74 - 94% of control). In addition, delayed sexual maturation was noted in F1 males at 5,000 ppm. For offspring toxicity, the NOAEL was 45 mg/kg/day and the LOAEL was 136 mg/kg/day based on significantly decreased pup growth.

i. *Dose and endpoint for establishing the RfD.* NOAEL = 45 mg/kg/day based on significant decreases in pup growth in all generations and mating at 136 mg/kg/day (LOAEL).

ii. *Comments about study and endpoint.* The NOAEL/LOAEL in the two-generation study is supported by the maternal NOAEL of 30 mg/kg/day and the LOAEL of 150 mg/kg/day established in the developmental toxicity study in rabbits; the maternal LOAEL was based on abortions (5%) and clinical signs of neurotoxicity (ataxia, rales, and decreased motor activity) Uncertainty Factor (UF): An UF of 1,000 was applied to account for inter (10x)-and intra-(10x) species variation and 10 for F PA.

RfD = 45 mg/kg/day (NOAEL)/1,000 (UF) = 0.045 mg/kg/day

3. *Occupational and residential exposure (dermal).* Short-Term (1 - 7 days) Dermal In a 21-day dermal study (MRID No. 40547901) New Zealand white rabbits (5/sex/group) received 15 repeated dermal applications of dicamba in deionized water at dose levels of 0, 40, 200, or 1,000 mg/kg/day, 6 hours/day, 5 days/week over a 3-week period. No systemic toxicity was observed at any dose level. Dose-related dermal irritation was observed at the application sites. Desquamation was seen predominantly in the 1,000 mg/kg/day group while moderate erythema, moderate edema and atonia were observed exclusively in the 1,000 mg/kg/day group. A dose-related incidence of fissuring was noted in the 200 and 1,000 mg/kg/day groups. The severity of acanthosis and the incidence of hyperkeratosis was increased at these sites in rabbits at 200 and 1,000 mg/kg. For systemic toxicity, the NOAEL was 1,000 mg/kg/day (HDT); a systemic LOAEL was not established. For dermal irritation, the NOAEL was 40 mg/kg/day and the LOAEL was 200 mg/kg/day.

i. *Dose and endpoint for risk assessment.* Systemic NOAEL = 1,000 mg/kg/day, the highest dose tested.

ii. *Comments about study and endpoint.* Although no systemic toxicity was observed at the Limit-Dose, the EPA recommended this dose for risk assessment because:

a. Dicamba is used in residential lawns and thus there is potential exposure by children and infants.

b. Increased sensitivity to offspring was demonstrated in the 2-generation reproduction study. A systemic toxicological end point was not determined from the study; however, for the risk assessment for the exposures involving these tolerance actions, a conservative default NOAEL of 1,000 was used.

4. *Intermediate-term (7 days to several months) dermal.* Summarized under short term in Unit above. Dose and Endpoint for Risk Assessment: Systemic NOAEL = 1,000 mg/kg/day, the highest dose tested. Comments about Study and Endpoint: Although no systemic toxicity was observed at the Limit-Dose, the EPA recommended this dose for risk assessment because (1) Dicamba is used in residential lawns and thus there is potential exposure by children and infants and (2) increased sensitivity to offspring was demonstrated in the 2-generation reproduction study.

5. *Long term (Several months to lifetime) dermal.* Based on the current use pattern, long-term dermal exposure is not anticipated. Therefore, a dose and endpoint was not identified.

6. *Inhalation exposure (Any-time period).* Based on the LC_{50} of >5.3 mg/L, Dicamba is placed in Toxicity Category IV. The EPA determined that a risk assessment via the inhalation route is not required because of the low acute inhalation toxicity and the use pattern/application method does not indicate high exposure via this route.

7. *Margin of exposure for residential exposures.* For Short-and Intermediate Term dermal exposures a MOE of 300 is required for residential exposures because: (a) Although developmental toxicity studies showed no increased sensitivity in fetuses as compared to maternal animals following in utero exposures in rats and rabbits, increased sensitivity to offspring, however, was demonstrated in the 2-generation reproduction toxicity study in rats (See Section III.2).

(b) There is evidence of neurotoxicity in the following studies: acute and subchronic neurotoxicity, combined chronic toxicity/carcinogenicity,

developmental toxicity (rats and rabbits) and the 2-generation reproduction (See Section III.1).

(c) A weight-of-the-evidence evaluation of the data base indicates the need for a developmental neurotoxicity study.

C. Exposures and Risks

1. *Food and feed.* Tolerances have been established (40 CFR 180.227) for the combined residues of Dicamba, in or on a variety of raw agricultural commodities, including meat, milk and poultry and eggs. Risk assessments were conducted by EPA to assessed dietary exposures from Dicamba (3,6-dichloro-*o*-anisic acid) as follows:

i. *Acute exposure and risk.* 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 endpoint selected by EPA for assessment of acute dietary risk is severe neurological effects in both sexes at 300 mg/kg/day (LOAEL, a NOAEL was not established) in a rat acute neurotoxicity study. Thus, this risk assessment is required for all population subgroups. This acute dietary (food) risk assessment used the Dietary Exposure Evaluation Model (DEEM). This program utilizes individual food consumption as reported by respondents in the USDA 1989-1991 nationwide Continuing Surveys for Food Intake by Individuals (CSFII) and food residue levels to estimate possible exposure levels of various population subgroups. Regulating at the 95th percentile, acute dietary exposure values and percent of the acute RfD are shown in following table:

Acute Dietary Exposure and Risks

Population Subgroup	Acute RfD[1] (mg/kg/day)	High-end Exposure (mg/kg/day)	% Acute RfD
US Population	0.1	0.02860	28.6
Nursing Infants (<1 yr old)	0.1	0.02610	26.1
Non-nursing Infants (<1 yr old)	0.1	0.06315	63.2
Children (1-6)	0.1	0.04581	45.8
Children (7-12)	0.1	0.03116	31.2

[1] Based on LOAEL of 300 mg/kg/day and an uncertainty factor of 3,000. Adjusted for FQPA.

These estimates indicate that risks from acute dietary exposures to dicamba do not exceed EPA's level of concern.

ii. *Chronic exposure and risk.* The chronic dietary exposure analysis from food sources was conducted using the reference dose (RfD) of 0.045 mg/kg/day. The RfD is based on the NOAEL of 45 mg/kg/day, which in turn is based on reduced pup weights in all generations and matings at 136 mg/kg/day in a multi-generation reproduction study in rats; and an uncertainty factor of 1,000 applicable to all populations which include infants and children. In conducting this chronic dietary risk assessment, EPA has made very conservative assumptions: 100% of RACs having dicamba tolerances will contain dicamba residues and those residues will be at the level of the established tolerance. This results in an overestimate of human dietary exposure. Thus, in making a safety determination for this tolerance, EPA is taking into account this conservative exposure assessment.

The Dietary Exposure Evaluation Model (DEEM) analysis evaluated the individual food consumption as reported by respondents in the USDA 1989-91 nationwide Continuing Surveys for Food Intake by Individuals (CSFII) and accumulated exposure to the chemical for each commodity. The chronic DEEM analysis used mean consumption (3 day average) data and gave the results listed below:

Subgroups	%RfD
U.S. Population (48 states)	23.9
Nursing Infants (< 1 year old)	16.5
Non-Nursing Infants (< 1 year old)	71.1
Children (6 years old)	54.8
Children (7-12 years old)	36.8
Non-Hispanic Whites	24.1
Males (13-19 years old)	25.6

The subgroups listed above are: (1) the U.S. population (48 states); (2) those for infants and children; and (3) the other subgroups for which the percentage of the RfD occupied is greater than that occupied by the subgroup U.S. population (48 states). These estimates indicate that risks from chronic dietary exposures to dicamba do not exceed EPA's level of concern.

iii. *Carcinogenic risk.* In the chronic toxicity/carcinogenicity study in rats there were no observed clinical signs of toxicity, including survival, mean body weights or body gains, food consumption, hematologic clinical chemistry, urinary parameters, organ weights, macroscopic findings, and non-neoplastic histology findings at 125 mg/kg/day, the highest dose tested. A LOAEL was not established. In the mouse carcinogenicity study at the highest dose tested, 361 mg/kg/day, there were no clinical signs of carcinogenicity. A NOAEL of 115 mg/kg/day was determined for increased mortalities in males and decreased body weight gains in females. Based on these studies, a finding of carcinogenicity in rats or mice would not change the Rfd previously stated.

In accordance with the EPA Proposed Guidelines for Carcinogen Risk Assessment (10-APR-1996), the EPA classified dicamba as a ''not classifiable'' human carcinogen. This was based on the mouse carcinogenicity study and the rat combined chronic toxicity/carcinogenicity study, being classified as supplemental because an MTD was not achieved in both studies. However, these studies were adequate to indicate that dicamba has either a low or no cancer potential in mammals. A pharmacokinetics study pending EPA review indicates that the MTD for both the rat and mouse studies was reached. If this is corroborated by EPA's review, a quantitative cancer risk will not be made for dicamba and its metabolites, on the other hand, if the review does not corroborate this indication, replacement studies will be required.

2. *From drinking water.* EPA does not have monitoring data available to perform a quantitative drinking water risk assessment for dicamba at this time. A Tier 1 drinking water assessment of dicamba is given below.. This assessment utilized the GENEEC and SCI-GROW screening models to provide estimates of ground and surface water contamination from dicamba and its metabolite, 3,6-dichlorosalicylic acid (DCSA). Concentrations of the 5-hydroxy metabolite of dicamba (3,6-

dichloro-5-hydroxy-*o*-anisic acid) in surface and ground water could not be estimated; however, based on the available environmental fate data, it is not likely that this metabolite would be found in surface and ground water.

EPA followed an Interim Approach for Addressing Drinking Water Exposure in Tolerance Decision making issued on 17-NOV-1997. Thus, the GENEEC model and the SCI-GROW model were run to produce estimates of dicamba concentrations in surface and ground water respectively. The primary use of these models is to provide a coarse screen for sorting out pesticides for which OPP has a high degree of confidence that the true levels of the pesticide in drinking water will be less than the human health drinking water levels of concern (DWLOCs). A human health DWLOC is the concentration of a pesticide in drinking water which would result in unacceptable aggregate risk, after having already factored in all food exposures and other non-occupational exposures.

$DWLOC_{acute}$ = [acute water exposure (mg/kg/day) x (body weight)]/[consumption (L) x 10^{-3} mg/µg]

where acute water exposure (mg/kg/day) = acute RfD - acute food exposure (mg/kg/day)

$DWLOC_{chronic}$ = [chronic water exposure (mg/kg/day) x (body weight)]/[consumption (L) x 10^{-3} mg/µg]

where chronic water exposure (mg/kg/day) = [RfD - (chronic food exposure + chronic residential exposure) (mg/kg/day)].

There is no chronic residential exposure for dicamba. The $DWLOC_{chronic}$ is the concentration in drinking water as part of the aggregate chronic exposure that results in a negligible cancer risk. The Agency's default body weights and consumption values used to calculate DWLOCs are as follows: 70 kg/2L (adult male), 60 kg/2L (adult female), and 10 kg/1L (child).

Population Subgroup[1]	Acute Scenario				Chronic Scenario			
	Acute RfD[2] mg/kg/day	DWLOC µg/L	Ground Water SCI-GROW2 EEC in µg/L	Surface Water GENEEC EEC in µg/L	RfD2 mg/kg/day	DWLOC µg/L	SCI-GROW2 EEC in µg/L	GENEEC EEC in µg/L
U.S. Population	0.10	25000	0.013	98	0.045	1200	0.013	66
Children (1-6 yrs)	0.10	540	0.013	98	0.045	200	0.013	66

[1] DEEM TMRCs in mg/kg/day: U.S. Population = 0.01075, children (1-6 yrs) = 0.02465
[2] Adjusted for FQPA

For chronic (non-cancer) exposure to dicamba in surface and ground water, the drinking water levels of concern are 1,200 µg/L for U.S. population, and 200 µg/L for children (1-6 yrs). To calculate the DWLOC for chronic (non-cancer) exposure relative to a chronic toxicity endpoint, the chronic dietary food exposure (from DEEM) was subtracted from the RfD to obtain the acceptable chronic (non-cancer) exposure to dicamba in drinking water. DWLOCs were then calculated using default body weights and drinking consumption figures.

Estimated maximum concentrations of dicamba in surface and ground water are 98 and 0.013 ppb, respectively. The estimated concentrations of dicamba in surface and ground water are less than OPP's level of concern for dicamba in drinking water as a contribution to chronic aggregate exposure. Therefore, taking into account present uses and uses proposed in this action, EPA concludes with reasonable certainty that residues of dicamba in drinking water (when considered along with other sources of exposure for which there are reliable data) would not result in unacceptable levels of aggregate human health risk at this time.

The dietary (food and water) exposure database for dicamba is adequate to assess infants' and children's exposure.

3. *From non-dietary exposure.* Dicamba (3,6-dichloro-*o*-anisic acid) is currently registered for use on outdoor residential and recreational turf. Application is made by both homeowners and professional applicators. There is a potential oral, inhalation, eye and dermal exposure to infants and children to dicamba from the registered uses for lawn and turfgrass weed control These exposures are considered to be very low. Currently there are no inhalation or eye exposure data required for post-application of pesticides to lawns and turf. As inhalation exposure for mixer/loaders is acceptable, the risk to infants and children from inhalation exposure under a much lower exposure scenario is characterized qualitatively as being extremely low. Exposure data are required for hand to mouth movements of infants and children. As there are no chemical-specific or site-specific data available to determine the potential risks associated with residential exposures, the EPA has determined that residential exposure and risk are acceptable for dosages of 0.5 lb/A, based on a dermal NOAEL of 1,000 mg/kg/day and exposures of 0.051 mg/kg/day for low pressure hand wand, liquid formulations; and 0.079 mg/kg/day for granular formulations. For residential post-application exposure and risk assessment, EPA determined that the potential residential post-application risks for short-term and intermediate exposures did not exceed their level of concern. In this analysis both oral and dermal exposures and risks for adults and infants from post-applications were determined. This analysis was based on assumptions and generic data from the Draft HED Standard Operating Procedures (SOPs) for Residential Exposure Assessments (December 18, l997. These SOPs rely on what are considered to be upper-percentile assumptions and intended to represent Tier 1 assessments.

4. *Cumulative exposure to substances with common mechanism of toxicity.* Section 408(b)(2)(D)(v) requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider ''available information'' concerning the cumulative effects of a particular pesticide's residues and ''other substances that have a common mechanism of toxicity.'' The Agency believes that ''available information'' in this context might include not only toxicity, chemistry, and exposure data, but also scientific policies and methodologies for understanding common mechanisms of toxicity and conducting cumulative risk assessments. For most pesticides, although the Agency has some information in its files that may turn out to be helpful in eventually determining whether a pesticide shares a common mechanism of toxicity with any other substances, EPA does not at this time have the methodologies to resolve the complex scientific issues concerning common mechanism of toxicity in a meaningful way. EPA has begun a pilot process to study this issue further through the examination of particular classes of pesticides. The Agency hopes that the results of this pilot process will increase the Agency's scientific understanding of this question such that

EPA will be able to develop and apply scientific principles for better determining which chemicals have a common mechanism of toxicity and evaluating the cumulative effects of such chemicals. The Agency anticipates, however, that even as its understanding of the science of common mechanisms increases, decisions on specific classes of chemicals will be heavily dependent on chemical specific data, much of which may not be presently available.

Although at present the Agency does not know how to apply the information in its files concerning common mechanism issues to most risk assessments, there are pesticides as to which the common mechanism issues can be resolved. These pesticides include pesticides that are toxicologically dissimilar to existing chemical substances (in which case the Agency can conclude that it is unlikely that a pesticide shares a common mechanism of activity with other substances) and pesticides that produce a common toxic metabolite (in which case common mechanism of activity will be assumed).

EPA does not have, at this time, available data to determine whether dicamba and its metabolites (3,6-dichloro-5-hydroxy-*o*-anisic acid and 3,6-dichloro-*o*-2-hydroxybenzoic acid) have a common mechanism of toxicity with other substances or how to include this pesticide or its metabolites in a cumulative risk assessment. For the purposes of this tolerance action, therefore, EPA has not assumed that dicamba and its metabolites have a common mechanism of toxicity with other substances.

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

1. *Acute risk.* Under Unit II.C.1.i of this preamble an acute risk assessment using a high-end exposure estimate for dicamba was determined for the general U.S. population, infants (<1 year), children (1-6 years), children (7 -12) years). None of the population subgroups yielded percent RfDs (adjusted for FQPA) above 100.

Based on the drinking water risk assessment under Unit II.C.2 of this preamble, the maximum estimated concentrations of dicamba in surface and ground water are less than levels of concern in drinking water as a contribution to acute aggregate exposure.

2. *Chronic risk.* Using the exposure assumptions described Unit II.C.1.ii of this preamble, EPA has concluded that aggregate exposure to dicamba from food will utilize 23.9% of the RfD for the U.S. population. The major identifiable subgroup with the highest aggregate exposure is children (1-6 years old). The percent of the RfD utilized by this subgroup was determined to be 71.1%. EPA generally has no concern for exposures below 100% of the RfD because the RfD represents the level at or below which daily aggregate dietary exposure over a lifetime will not pose appreciable risks to human health. Despite the potential for exposure to dicamba in drinking water and from non-dietary, non-occupational exposure, EPA does not expect the aggregate exposure to exceed 100% of the RfD.

3. *Short and intermediate-term aggregate risk.* Dicamba is currently registered for use on turfgrass including sod production, commercial and residential turf. Short- or intermediate-term dermal toxicity endpoints have been identified for dicamba, and was quantified at 1,000 mg/kg/day. Using EPA Standard Operating Procedures for Residential Exposure Assessments, including post-application exposures and risk assessments; the Margin of Exposure (MOE) did not exceed 300 the level of concern.

4. *Aggregate cancer risk for U.S. population.* EPA has classified dicamba as a ''not classifiable'' human carcinogen. Available oncogenicity studies have been classified as supplemental because the studies did not achieve an MTD. However, the studies indicate no carcinogenicity potential at the highest dose tested, 2,500 ppm (rat) and 3,000 ppm (mice). A quantitative cancer risk can not be made based on the supplemental rat and mouse carcinogenicity studies. However, these studies were adequate to indicate that dicamba has either a low cancer risk or no cancer risk. A pharmacokinetics study presently pending review by EPA indicates that the MTD of these carcinogenicity studies was reached, thus changing these carcinogenicity studies to be acceptable studies. No quantitative cancer risk will be made for dicamba and its metabolites if the pending study is corroborated by EPA's review. Alternatively, if the study is not corroborated, replacement carcinogenicity studies will be required.

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

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

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

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

ii. *Pre- and post-natal sensitivity.* There was evidence of increased susceptibility to the offspring following pre- and/or postnatal exposure in the 2-generation reproduction study in rat. In this study, offspring toxicity was manifested as significantly decreased pup growth in all generations and mating at a dose lower than that which caused parental systemic toxicity(abortions and clinical signs of neurotoxicity). Available studies indicated no increase susceptibility of rats or rabbits in *in utero* exposure to dicamba. In a prenatal developmental toxicity study in rats, there was no evidence of developmental toxicity at the highest dose tested. In a prenatal developmental toxicity study in rabbits, developmental toxicity (irregular ossification of internasal bones) were only seen at the dose that caused maternal toxicity (abortions and neurotoxic clinical signs).

iii. *Conclusion.* There is a adequate toxicity database for dicamba and exposure data is complete or is estimated based on data that reasonably accounts for potential exposures. A ten-

fold safety factor for increased susceptibility of infants and children was applied for chronic (long-term) exposure, and a three-fold safety factor was applied for acute (short- and intermediate-term) exposures to dicamba, due to evidence of increased susceptibility to the offspring following pre- and/or postnatal exposure in the 2-generation reproduction study in rats. The uncertainty factor (FQPA Safety Factor) of ten-fold was reduced for acute dietary and short- and Intermediate-term residential exposures because the increased susceptibility was only observed in the reproduction study and not in the prenatal developmental studies. The FQPA Safety Factor was reduced to 3x for acute dietary risk assessment for all populations, including infants and children, because: (1) the endpoint of concern is clinical signs of neurotoxicity (in the absence of neuropathology) observed following a single oral exposure in an acute neurotoxicity study; (2) the increased susceptibility was seen in the offspring of parental animals receiving repeated oral exposures in a 2-generation reproduction toxicity study; (3) no increased susceptibility was observed following in utero exposures to rats or rabbits in the developmental studies; and (4) a developmental neurotoxicity study in rats is required.

2. *Acute risk.* Acute dietary risks were discussed under B_1 above. As stated there, an acute dietary RfD was determined to be 0.10 mg/kg/day, based on the LOAEL of 300 mg/kg/day and and uncertainty factor of 3,000 for infants and children. The assessment made by EPA included only exposure from food. Based on high-end exposures, the percent of the RfD occupied for the U.S population, Nursing Infants, Non-nursing Infants, Children (ages 1-6 years) and Children (ages 7-12 years) were less than 100%. The subgroup with the highest exposure was the Non-nursing Infants which occupied 63.2% of the RfD. The EPA concluded that with reasonable certainty the residues of dicamba in food and water do not contribute significantly to the aggregate acute human health risk at the present time considering the present uses and uses proposed in this Final Rule.

3. *Chronic risk.* Using the exposure assumptions described above, EPA has concluded that aggregate exposure to dicamba from food will utilize 16.5% of the RfD for nursing infants, 71.1% for non-nursing infants, 54.8% for children (1-6 years old), and 36.8% for children (7-12 years old). EPA generally has no concern for exposures below 100% of the RfD because the RfD represents the level at or below which daily aggregate dietary exposure over a lifetime will not pose appreciable risks to human health. Despite the potential for exposure to dicamba.... in drinking water and from non-dietary, non-occupational exposure, EPA does not expect the aggregate exposure to exceed 100% of the RfD

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

III. Other Considerations

A. Endocrine Disrupter Effects

EPA is required to develop a screening program to determine whether certain substances (including all pesticides and inerts) ''may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect....'' The Agency is currently working with interested stakeholders, including other government agencies, public interest groups, industry and research scientists in developing a screening and testing program and a priority setting scheme to implement this program. Congress has allowed 3 years from the passage of FQPA (August 3, l999) to implement this program. At that time, EPA may require further testing of this active ingredient and end use products for endocrine disrupter effects.

B. Analytical Enforcement Methodology.

An adequate analytical method for determining the magnitude of residues in the raw agricultural commodities listed in this Final Rule has been evaluated by EPA and is published in the Pesticide Analytical Manual (PAM II). The method may be requested from: Calvin Furlow, Public Information Branch, Field Operations Division (7502C), Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. Office location and telephone number: Room 1130A, CM #2, 1921 Jefferson Davis Highway, Arlington, VA 22202, (703–305–5937).

C. Magnitude of Residues.

The nature of the residue in plants is adequately understood for the purposes of this time-limited tolerance.

D. International Residue Limits

No CODEX Maximum Residue Levels (MRLs) have been established for dicamba in or on wheat, barley, soybeans, corn, cotton or asparagus. Compatibility cannot be achieved with the Canadian, Mexican, German or Australian tolerances because their levels are expressed in terms of parent compound only.

IV. Conclusion

The scientific evaluation of data supporting dicamba using 100% crop treated and anticipated residues for all population subgroups examined by EPA shows the use on the raw agricultural commodities for which tolerances are established or revised by this Final Rule will not cause exposure at which the Agency believes there is an appreciable risk and thus EPA concludes there is a reasonable certainty of no harm from aggregate exposure to dicamba. Based on the information cited above, EPA has determined that the tolerances for residues of dicamba in the raw agricultural commodities listed in this Final Rule will be safe; therefore, the tolerances are established as set forth below.

V. Objections and Hearing Requests

The new FFDCA section 408(g) provides essentially the same process for persons to ''object'' to a tolerance regulation issued by EPA under new section 408(e) and (l)(6) as was provided in the old section 408 and in section 409. However, the period for filing objections is 60 days, rather than 30 days. EPA currently has procedural regulations which govern the submission of objections and hearing requests. These regulations will require some modification to reflect the new law. However, until those modifications can be made, EPA will continue to use those procedural regulations with appropriate adjustments to reflect the new law.

Any person may, by March 8, 1999, file written objections to any aspect of this regulation and may also request a hearing on those objections. Objections and hearing requests must be filed with the Hearing Clerk, at the address given above (40 CFR 178.20). A copy of the objections and/or hearing requests filed with the Hearing Clerk should be submitted to the OPP docket for this rulemaking. The objections submitted must specify the provisions of the regulation deemed objectionable and the grounds for the objections (40 CFR 178.25). Each objection must be accompanied by the fee prescribed by 40 CFR 180.33(i). If a hearing is requested, the objections must include a statement of the factual issues on which a hearing is requested, the requestor's contentions on such issues, and a summary of any evidence relied upon by the requestor (40 CFR 178.27). A request for a hearing will be granted if the Administrator determines that the

material submitted shows the following: There is genuine and substantial issue of fact; there is a reasonable possibility that available evidence identified by the requestor would, if established, resolve one or more of such issues in favor of the requestor, taking into account uncontested claims or facts to the contrary; and resolution of the factual issues in the manner sought by the requestor would be adequate to justify the action requested (40 CFR 178.32). Information submitted in connection with an objection or hearing request may be claimed confidential by marking any part or all of that information as Confidential Business Information (CBI). Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR part 2. A copy of the information that does not contain CBI must be submitted for inclusion in the public record. Information not marked confidential may be disclosed publicly by EPA without prior notice.

VI. Public Record and Electronic Submissions

EPA has established a record for this rulemaking under docket control number [OPP–300767] (including any comments and data submitted electronically). A public version of this record, including printed, paper versions of electronic comments, which does not include any information claimed as CBI, is available for inspection from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The public record is located in Room 119 of the Public Information and Records Integrity Branch, Information Resources and Services Division (7502C), Office of Pesticide Programs, Environmental Protection Agency, Crystal Mall #2, 1921 Jefferson Davis Hwy., Arlington, VA.

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

VII. Regulatory Assessment Requirements

A. Certain Acts and Executive Orders

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

In addition, since tolerances and exemptions that are established on the basis of a petition under FFDCA section 408(d), such as the tolerances in this final rule, do not require the issuance of a proposed rule, the requirements of the Regulatory Flexibility Act (RFA) (5 U.S.C. 601 *et seq.*) do not apply. Nevertheless, the Agency has previously assessed whether establishing tolerances, exemptions from tolerances, raising tolerance levels or expanding exemptions might adversely impact small entities and concluded, as a generic matter, that there is no adverse economic impact. The factual basis for the Agency's generic certification for tolerance actions published on May 4, 1981 (46 FR 24950) and was provided to the Chief Counsel for Advocacy of the Small Business Administration.

B. Executive Order 12875

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

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

C. Executive Order 13084

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

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

VIII. Submission to Congress and the Comptroller General

The Congressional Review Act, 5 U.S.C. 801 *et seq.*, as added by the Small Business Regulatory Enforcement

Fairness Act of 1996, generally provides that before a rule may take effect, the agency promulgating the rule must submit a rule report, which includes a copy of the rule, to each House of the Congress and 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 the rule in the **Federal Register**. This rule is not a ''major rule'' as defined by 5 U.S.C. 804(2).

List of Subjects in 40 CFR Part 180

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

Dated: December 22, 1998.

James Jones,

Director, Registration Division, Office of Pesticide Programs.

Therefore, 40 CFR chapter I is amended as follows:

PART 180–[AMENDED]

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

Authority: 21 U.S.C. 346a and 371.

2. Section 180.227 is amended by adding a paragraph heading to paragraph (a), designating the text following the paragraph heading as paragraph (a)(1), redesignating paragraphs (b) and (c) as paragraphs (a)(2) and (a)(3), respectively, and by adding and reserving with paragraph headings new paragraphs (b), (c) and (d).

3. Section 180.227 is further amended as follows:

i. In newly designated paragraph (a)(1), by revising the entries for the following commodities: barley, grain; barley, straw; wheat, grain; and wheat, straw; by adding alphabetically entries for barley, hay; corn, field, forage; corn, field, stover; corn, pop stover; cottonseed; cottonseed, meal; crop Group 17 (grass, forage, fodder and hay); grass, forage; grass, hay; oats, forage; oats, hay; wheat, forage; and wheat, hay; and by removing the entries for asparagus; grasses, pasture; and grasses, rangeland.

ii. In newly designated paragraph (a)(2) by removing the entries for soybeans; soybeans, forage; and soybeans, hay; and by adding an entry in alphabetical order for asparagus.

iii. By revising newly designated paragraph (a)(3).

The added and revised text reads as follows:

§ 180.227 Dicamba; tolerances for residues.

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

Commodity	Parts per million
Barley, grain	6.0
Barley, hay	2.0
Barley, straw	15.0
* * *	* *
Corn, field, forage	3.0
Corn, field, stover	3.0
* * *	* *
Corn, pop, stover	3.0
Cottonseed	3.0
Cottonseed, meal	5.0
Crop Group 17 (grass, forage, fodder and hay).	
Grass, forage	125.0
Grass, hay	200.0
* * *	* *
Oats, forage	80.0
* * *	* *
Oats, hay	20.0
* * *	* *
Wheat, forage	80.0
Wheat, grain	2.0
Wheat, hay	20.0
Wheat, straw	30.0

(2) * * *

Commodity	Parts Per million
Asparagus	4.0
* * *	* *

(3) Tolerances are established for the combined residues of dicamba (3,6-dichloro-*o*-anisic and its metablites 3,6-dichloro-5-hydroxy-*o*-anisic acid and 3,6-dichloro-*o*-2-hydroxy-benzoic acid in or on the raw agricultural commodities as follows:

Commodity	Parts Per million
Aspirated grain fractions	5100.0
Soybean, hulls	13.0
Soybean, seed	10.0

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

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

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

[FR Doc. 99–109 Filed 1–5–99; 8:45 am]

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DEPARTMENT OF THE INTERIOR

Fish and Wildlife Service

50 CFR Part 23

RIN 1018–AF23

Export of River Otters Taken in Missouri in the 1998–1999 and Subsequent Seasons

AGENCY: Fish and Wildlife Service, Interior.

ACTION: Final rule.

SUMMARY: This document announces final findings by the CITES Scientific and Management Authorities of the United States that approve the addition of Missouri to the list of States and Indian Nations approved for the export of river otter skins. This approval is on a multi-year basis. The Service intends to apply these findings to river otters taken in Missouri during the 1998–1999 season and subsequent seasons, subject to the same conditions applying to other States previously approved.

DATES: This rule is effective on January 6, 1999.

FOR FURTHER INFORMATION CONTACT: Scientific Authority finding: Dr. Susan Lieberman, Chief, Office of Scientific Authority; phone: 703–358–1708; fax: 703–358–2276; E-mail: r9osa@mail.fws.gov. Management Authority finding: Ms. Teiko Saito, Chief, Office of Management Authority; U.S. Fish and Wildlife Service; Mail Stop ARLSQ 700; 1849 C Street, NW; Washington, DC 20240; phone: 703–358–2095; fax: 703–358–2280.

SUPPLEMENTARY INFORMATION: The Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES) is a treaty that regulates international trade in certain species of animals and plants. Exports of specimens (live, dead, or parts and products thereof) of animals and plants listed in Appendix II of CITES require an export permit from the country of origin. Export permits for specimens of species listed in CITES Appendix II are issued by a country's CITES Management Authority after two conditions are met: first, the country's CITES Scientific Authority must determine that the exports will not be detrimental to the survival of the species. This is known as a ''non-detriment finding''. Second, the CITES Management Authority must determine that the specimens were not obtained in violation of laws for their protection. Live animals or plants require additional findings. For exports from the United States, the U.S. Fish and