Guidelines to the Regulatory Flexibility Act of 1980, as shown above. Further information on the initial RFA is available in the background information package (see **SUPPLEMENTARY INFORMATION** section near the beginning of this preamble).

G. Miscellaneous

In accordance with section 117 of the Act, publication of this proposal was preceded by consultation with appropriate advisory committees, independent experts, and Federal departments and agencies. The Administrator will welcome comments on all aspects of the proposed regulation, including health, economic and technical issues, and on the proposed test methods.

This regulation will be reviewed 8 years from the date of promulgation. This review will include an assessment of such factors as evaluation of the residual health and environmental risks, any overlap with other programs, the existence of alternative methods, enforceability, improvements in emission control technology and health data, and the recordkeeping and reporting requirements.

List of Subjects in 40 CFR Part 63

Environmental protection, Air pollution control, Hazardous substances, Reporting and recordkeeping requirements.

Dated: March 15, 1995.

Carol M. Browner,

Administrator.

[FR Doc. 95–7066 Filed 3–28–95; 8:45 am]

BILLING CODE 6560–50–P

40 CFR Part 180

[PP 3F4233/P609; FRL–4944–7]

RIN 2070–AC18

Bromoxynil; Pesticide Tolerance

AGENCY: Environmental Protection Agency (EPA).

ACTION: Proposed rule.

SUMMARY: This document proposes a tolerance for residues of the herbicide bromoxynil (3,5-dibromo-4-hydroxybenzonitrile), resulting from the application of its octanoic and heptanoic acid esters. The proposal would amend the tolerance in or on the raw agricultural commodity (RAC) cottonseed (transgenic BXN varieties only) at 0.04 part per million (ppm). Rhone-Poulenc AG Co. submitted petitions requesting EPA to establish the maximum permissible residue of the herbicide in or on transgenic cottonseed.

DATES: Written comments, identified by the document control number, [PP 3F4233/P609], must be received on or before April 28, 1995.

ADDRESSES: By mail, submit comments to: Public Docket and Freedom of Information Section, Field Operations Division (7506C), Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. In person bring comments to: Rm. 1132, CM #2, 1921 Jefferson Davis Hwy., Arlington, VA 22202.

Information submitted as a comment concerning this document 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 comment that does not contain CBI must be submitted for inclusion in the public record. Information not marked confidential may be disclosed publicly by EPA without prior notice. All written comments will be available for public inspection in Rm. 1132 at the address given above, from 8 a.m. to 4 p.m., Monday through Friday, excluding legal holidays.

FOR FURTHER INFORMATION CONTACT: By mail: Robert J. Taylor, Product Manager (PM) 25, Registration Division (7505C), Environmental Protection Agency, 401 M. St., SW., Washington, DC 20460. Office location and telephone number: Rm., 241, CM #2, 1921 Jefferson Davis Hwy., Arlington, VA 22202, (703)-305-6800; e-mail: Taylor.Robert@epamail.epa.gov.

SUPPLEMENTARY INFORMATION: EPA issued a notice, published in the **Federal Register** of October 21, 1993 (58 FR 54354), announcing that the Rhone-Poulenc AG Co., P.O. Box 12014, 2 T.W. Alexander Drive, Research Triangle Park, NC 27709, had submitted a pesticide petition, PP 3F4233, to EPA proposing to amend 40 CFR 180.324 by establishing a regulation to permit the residues of the herbicide bromoxynil (3,5-dibromo-4-hydroxybenzonitrile) resulting from the application of its octanoic and heptanoic acid esters in or on the raw agricultural commodity (RAC) transgenic cottonseed at 0.04 ppm. There were no comments or requests for referral to an advisory committee received in response to the notice of filing.

The data submitted in the petition and other relevant material have been evaluated. The toxicology data listed below were considered in support of this tolerance. Based on bridging studies, the Agency has determined that bromoxynil octanoate and bromoxynil heptanoate are toxicologically equivalent. For this reason, studies using the bromoxynil phenol are accepted in fulfillment of studies required for bromoxynil octanoate and bromoxynil heptanoate.

Phenol technical-grade bromoxynil

1. Several acute toxicology studies were performed, placing technical-grade bromoxynil in toxicity Category II.

2. An acute oral toxicity study in rats resulted in LD_{50} = 81 mg/kg (males) and LD_{50} = 93 mg/kg (females).

3. A 2-year combined feeding/carcinogenicity study was conducted with rats administered (oral) dosages of 0, 60, 190, or 600 ppm (0, 2.6, 8.2, or 28 mg/kg/day in males; 0, 3.3, 11.0, or 41 mg/kg/day in females) bromoxynil phenol in the diet. In males the no-observed-effect-level (NOEL) for systemic toxicity is 2.6 mg/kg/day, and the lowest-effect-level (LEL) is 8.2 mg/kg/day. In females, the NOEL is 3.3 mg/kg/day, and the lowest-effect-level (LEL) is 11.0 mg/kg/day. This study did not demonstrate any increase in tumor incidences in either male or female rats. This study has not been considered by the RfD committee. The RfD was set based on the NOEL from the supplementary rat study (see item #4).

4. A 2-year combined feeding/carcinogenicity study was conducted with rats administered bromoxynil phenol in the diet at dose levels of 0, 10, 30, or 100 ppm (0, 0.5, 1.5, or 5 mg/kg/day). In both males and females, the NOEL and LOEL for systemic toxicity was 5 mg/kg/day and >5 mg/kg/day, respectively. At the highest dose tested, increased liver weights were observed at 12 months, but not at 24 months. This study was considered negative for carcinogenicity. This study is considered supplementary. The RfD is based on this study and an uncertainty factor of 300 rather than 100 was used since the study is supplementary.

5. A 1-year oral study was conducted with dogs administered bromoxynil phenol at dose levels of 0, 0.1, 0.3, 1.5, or 7.5 mg/kg/day in capsules. The NOEL is 0.3 mg/kg/day and the LEL is 1.5 mg/kg/day in both males and females.

6. An 18-month carcinogenicity study was conducted with mice administered bromoxynil phenol at dose levels of 0, 10, 30, or 100 ppm (0, 1.3, 3.9, or 13 mg/kg/day) in the diet. For males, dose-related increases in hyperplastic nodules and liver adenomas/carcinomas were observed which were statistically significant at the 13-mg/kg/day dose level. Increased relative liver weights

were also observed. In females, increased absolute liver weights and relative liver and kidney weights were observed. The study was considered negative for carcinogenicity for females.

7. A developmental toxicity study was conducted with rats administered (orally) bromoxynil phenol at dose levels of 0, 4, 12.5, or 40 mg/kg/day. The maternal NOEL and LEL are 12.5 mg/kg/day and 40 mg/kg/day, respectively. The developmental NOEL and LEL are 4 mg/kg/day and 12.5 mg/kg/day, respectively.

8. A developmental toxicity study was conducted with rats administered (orally) bromoxynil phenol at dose levels of 0, 5, 15, or 35 mg/kg/day. The maternal NOEL and LEL are 5 mg/kg/day and 15 mg/kg/day, respectively. The fetotoxicity and developmental NOEL and LEL are less than 5 mg/kg/day and 5 mg/kg/day, respectively.

9. A developmental toxicity study was conducted with rats administered (orally) bromoxynil phenol at dose levels of 0, 1.7, 5, or 15 mg/kg/day. The maternal NOEL and LEL is 5 mg/kg/day and 15 mg/kg/day, respectively. The developmental NOEL and LEL are 5 mg/kg/day and 15 mg/kg/day, respectively.

10. A developmental toxicity study was conducted with rabbits administered (orally) bromoxynil phenol at dose levels of 0, 15, 30, or 60 mg/kg/day. The maternal NOEL and LEL are 15 mg/kg/day and 30 mg/kg/day, respectively. The developmental NOEL and LEL are less than 15 mg/kg/day and 15 mg/kg/day, respectively.

11. A developmental toxicity study was conducted with mice administered (orally) bromoxynil phenol at dose levels of 0, 11, 32, or 96 mg/kg/day. The maternal NOEL and LEL are 11 mg/kg/day and 32 mg/kg/day, respectively. The developmental NOEL and LEL are 32 mg/kg/day and 96 mg/kg/day, respectively.

12. A reproduction study was conducted with rats administered (orally) bromoxynil phenol at dose levels of 0, 0.8, 4, or 21 mg/kg/day in the diet. The systemic adult rat NOEL is 4 mg/kg/day, and the LEL is 21 mg/kg/day. The reproductive NOEL is 21 mg/kg/day, and the LEL is greater than 21 mg/kg/day. The postnatal developmental NOEL is 4 mg/kg/day, and the LEL is 21 mg/kg/day.

13. A reproduction study was conducted with rats administered (orally) bromoxynil phenol at dose levels of 0, 1.5, 5, or 15 mg/kg/day in the diet. The systemic adult rat NOEL is 1.5 mg/kg/day (tentative), and the LEL is 5 mg/kg/day (tentative). The reproductive NOEL is 15 mg/kg/day, and the LEL is greater than 15 mg/kg/day. The offspring developmental NOEL is 5 mg/kg/day, and the LEL is 15 mg/kg/day.

14. Mutagenicity data included unscheduled DNA synthesis study—rat primary hepatocytes (negative); in vitro transformation assay—mouse cells (negative); sister chromosomal exchange study—CHO cells (negative); forward mutation study—mouse lymphoma cells (negative without activation and positive with activation); DNA repair test—E. coli (positive); in vitro chromosomal aberration (negative without activation and positive with activation); two separate micronucleus assays (both negative); forward mutation—CHO cells (negative); and Ames study Salmonella typhimurium (negative with and without activation).

Heptanoate technical-grade bromoxynil

1. Several acute toxicology studies were performed, placing technical-grade bromoxynil in toxicity Category II.

2. An acute oral toxicity study in rats resulted in LD_{50} = 362 mg/kg (males) and LD_{50} = 292 mg/kg (females).

3. A general metabolism study was conducted with rats, and the results were similar when a single low dose (2 mg/kg), a single high dose (20 mg/kg) or a low dose (2 mg/kg/day) administered for 14 consecutive days were administered. Bromoxynil heptanoate is rapidly absorbed and widely distributed in most tissues. The highest concentrations were found in the blood, plasma, liver, kidney, and thyroid. Higher tissue concentrations were found in females than in males. Excretion was more rapid in males. Most of the radioactivity was excreted in the urine, mostly in the form of bromoxynil phenol. Bromoxynil phenol and bromoxynil heptanoate were present in the feces. There was no significant retention in tissues after 7 days. Essentially, bromoxynil heptanoate was metabolized to bromoxynil phenol via ester hydrolysis.

Octanoate technical-grade bromoxynil

1. Several acute toxicology studies were performed, placing technical-grade bromoxynil in toxicity Category II.

2. An acute oral toxicity study in rats resulted in LD_{50} = 400 mg/kg (males) and LD_{50} = 238 mg/kg (females).

3. A 13-week oral study was conducted with rats administered bromoxynil octanoate at dose levels of 0, 150, 600, or 1,100 ppm (0, 11, 45, or 91 mg/kg/day in males; 0, 13, 55, or 111 mg/kg/day in females) in the diet. This is equivalent to 0, 8, 31, or 63 mg/kg/day in males; 0, 9, 38, or 77 mg/kg/day in females of bromoxynil phenol. The NOEL and LEL in males are 31 mg/kg/day and 63 mg/kg/day, respectively. In females, the NOEL and LEL are 9 mg/kg/day and 38 mg/kg/day, respectively.

4. A developmental toxicity study was conducted with rats administered (orally) bromoxynil octanoate at dose levels of 0, 2.4, 7.3, or 21.8 mg/kg/day. This is equivalent to 0, 1.7, 5, or 15 mg/kg/day of bromoxynil phenol. The maternal NOEL and LEL are 5 mg/kg/day and 15 mg/kg/day, respectively. The developmental NOEL and LEL are 5 mg/kg/day and 15 mg/kg/day, respectively.

5. Mutagenicity data included the following: the Ames study—Salmonella typhimurium (negative with and without activation); micronucleus assay (negative); and unscheduled DNA synthesis—rat primary hepatocytes (negative).

Carcinogenicity Peer Review Committee/SAP

The Scientific Advisory Panel met on June 25, 1992, to review the scientific issues regarding the Carcinogenicity Peer Review Committee's classification of bromoxynil as a Group C carcinogen and recommended that a low- dose extrapolation model, applied to the experimental animal tumor data, be used for quantification (Q_1*) of human risk. The Panel felt that a Group D classification was more consistent with the existing data base. The SAP concluded that the available data did not provide sufficient evidence to classify bromoxynil as Group C and recommended a Group D classification pending completion of the ongoing mouse carcinogenicity study. The SAP further recommended that the mouse study be extended beyond 18 months (e.g., 24 months) if survival was adequate and that contemporary historical control data be made available at the time of evaluation.

After the SAP meeting the Carcinogenicity Peer Review Committee met on July 29, 1992, to further discuss and evaluate the weight-of-the-evidence on bromoxynil with particular reference to its carcinogenic potential. The Peer Review Committee (PRC) concluded that the classification of bromoxynil as a Group C, possible human carcinogen, should be maintained and recommended that for the purpose of risk characterization the Reference Dose (RfD) methodology should be used at this time. The PRC also placed a condition on the decision to defer utilization of a Q_1*. The condition was that additional uses should not be granted prior to analysis of the new mouse study. The PRC agreed that the results of the new mouse cancer study were critical to the ultimate classification and dose-response

assessment. Since the conditional registration involves a new use, HED has determined that it is prudent to apply the Q_1* to existing data.

Nature of the Residue and Analytical Method

The nature of the residue in transgenic cotton is considered to be adequately understood. The primary bromoxynil metabolite in transgenic cotton is 3,5-dibromo-4-hydroxybenzoic acid (DBHA). DBHA is only a major metabolite in/on bromoxynil treated transgenic cotton. For the purposes of a time-limited tolerance, only the parent compound will be regulated as in 40 CFR 180.324. This interim decision is based on the minimal risk resulting from total residues of the parent and metabolite in cottonseed contributing only about 1/1000th to the total dietary exposure from all registered uses of bromoxynil.

Adequate methodology is available for enforcement purposes, based upon methods for the parent compound. The method is a modified version of Method I in the Pesticide Analytical Manual (PAM), Vol. II. The method involves sample reflux in methanolic KOH, partitioning with ether/hexane, concentration of the organic phase, derivatization with diazomethane and analysis by GC. The limit of detection (LOD) for this method is 0.02 ppm.

The nature of the residue in ruminants and poultry is considered to be adequately understood. Any secondary residues occurring in the fat, meat, and meat byproducts of cattle, goats, horses, poultry, and sheep will be covered by existing tolerances.

Risk Assessment

The reference dose (RfD) (acceptable daily intake (ADI)) for bromoxynil is calculated to be 0.02 mg/kg body weight/day based on a 2-year rat chronic feeding study with a NOEL of 5.0 mg/kg bwt/day and a safety factor of 300. The theoretical maximum residue contribution (TMRC) for published tolerances is 0.450 ug/kg bwt/day or 2.25% of the RfD for the overall U.S. population. The use on transgenic cotton would contribute less than 0.0004 *u*g/kg bwt/day representing approximately 1/1000 of the total dietary exposure to bromoxynil residue. This analysis comparing the dietary exposure from bromoxynil to the noncarcinogenic chronic effects results in a negligible chronic risk.

Although the new mouse study has been received, a full review by the Agency has not been completed at this time. Therefore, an estimate of the upper-bound carcinogenic risk has been estimated based on published tolerances and the previously determined upper bound potency factor (Q_1* = 4.1 X 10^{-1} $(mg/kg/day)^{-1}$). The resulting upper-bound cancer risk was found to be 2 X 10^{-4}. An additional cancer risk as a result of the use of bromoxynil on transgenic BXN cotton would be 2 X 10^{-7}, which is incrementally insignificant. The 10^{-4} risk includes the assumption that residues were present in or on every commodity at tolerance level and that one hundred percent of the acreage for every commodity was treated with bromoxynil. Thus, this cancer risk should be viewed as an unrealistic ''worst case'' estimate. The risk resulting from the use of bromoxynil on transgenic cotton alone will be negligible.

Based on the above information cited, the Agency has determined that the establishment of the tolerance by amending 40 CFR part 180 will protect the public health. Therefore, the tolerance is established as set forth below.

The tolerance will expire on April 1, 1997. Based upon the evaluation of a mouse carcinogenicity study currently under review and submission of an analytical method, residue data and livestock metabolism study on the metabolite, the Agency will determine whether establishing permanent tolerances is appropriate. Residues remaining in or on the raw agricultural commodity after expiration of this tolerance will not be considered actionable if the pesticide is legally applied during the term, and in accordance with the provisions of the conditional registration.

Any person who has registered or submitted an application for registration of a pesticide, under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) as amended, which contains any of the ingredients listed herein, may request within 30 days after publication of this document in the **Federal Register** that this rulemaking proposal be referred to an Advisory Committee in accordance with section 408(e) of the Federal Food, Drug, and Cosmetic Act.

Interested persons are invited to submit written comments on the proposed regulation. Comments must bear a notation indicating the document control number [PP 8F3671/609]. All written comments filed in response to this petition will be available in the Public Response and Program Resources Branch, at the address given above from 8 a.m. to 4 p.m., Monday through Friday, except legal holidays.

The Office of Management and Budget has exempted this regulation from section 3 of Executive Order 12866.

Pursuant to requirements of the Regulatory Flexibility Act (Pub. L. 96-354, 94 Stat. 1164, 5 U.S.C. 601-612), the Administrator has determined that regulations establishing new tolerances or raising tolerance levels or establishing exemptions from tolerance requirements do not have a significant economic impact on a substantial number of small entities. A certification statement to this effect was published in the **Federal Register** of May 4, 1981 (46 FR 24950).

List of Subjects in 40 CFR Part 180

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

Dated: March 23, 1995.

Daniel M. Barolo,

Director, Office of Pesticide Programs.

Therefore, it is proposed that part 180 be 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. In § 180.324, by adding new paragraph (d), to read as follows:

§ 180.324 Bromoxynil; tolerances for residues.

* * * * *

(d) Tolerances are established for residues of the herbicide bromoxynil (3,5-dibromo-4-hydroxybenzonitrile) resulting from application of its octanoic and heptanoic acid esters in or on the following raw agricultural commodity:

Commodity	Parts per million	Expiration date
Cottonseed (transgenic BXN varieties only)	0.04	April 1, 1997

[FR Doc. 95–7714 Filed 3–28–95; 8:45 am]
BILLING CODE 6560–50–F