

1990, except for paragraphs (c)(1)(i)(B), (c)(1)(ii)(A), (c)(1)(ii)(C), (c)(1)(ii)(F), (c)(3)(ii)(A), (e)(1)(ii), (e)(2)(ii)(A), and (e)(2)(ii)(B) of this section. The effective date for paragraphs (c)(1)(i)(B), (c)(1)(ii)(C), and (c)(1)(ii)(F) of this section is May 21, 1990. The effective date for paragraphs (c)(1)(ii)(A), (c)(3)(ii)(A), and (e)(1)(ii), of this section is May 21, 1991. The effective date for paragraph (e)(2)(ii)(A) is June 12, 1992. The effective date for paragraph (e)(2)(ii)(B) is May 28, 1993.

(2) The guidelines and other test methods cited in this rule are referenced as they exist on the effective date of the final rule.

[54 FR 49294, Nov. 30, 1989, as amended at 55 FR 12644, Apr. 5, 1990; 56 FR 23231, May 21, 1991; 57 FR 24961, June 12, 1992; 58 FR 30992, May 28, 1993; 58 FR 34205, June 23, 1993]

§ 799.4360 Tributyl phosphate.

(a) *Identification of test substance.* (1) Tributyl phosphate (TBP, CAS No. 126-73-8) shall be tested in accordance with this section.

(2) TBP of at least 99 percent purity shall be used as the test substance.

(b) *Persons required to submit study plans, conduct tests, and submit data.* All persons who manufacture (including import and byproduct manufacture) or process or intend to manufacture or process TBP, other than as an impurity, from the effective date of the final rule to the end of the reimbursement period shall submit letters of intent to conduct testing, submit study plans, conduct tests, and submit data, or submit exemption applications as specified in this section, subpart A of this part, and part 790 of this chapter for single-phase rulemaking.

(c) *Health effects testing*—(1) *Neurotoxicity*—(i) *Required testing.* (A)(1) An acute and subchronic functional observational battery shall be conducted with TBP in accordance with § 798.6050 of this chapter except for the provisions of paragraphs (d) (5) and (6) of § 798.6050.

(2) For the purpose of this section, the following provisions also apply:

(i) *Animal selection.* Testing shall be performed in laboratory rats.

(ii) *Duration of testing.* For the acute testing, the substance shall be administered over a period not to exceed 24

hours; for the subchronic testing, test species shall be exposed daily for at least 90 days.

(iii) *Route of exposure.* Animals shall be exposed to TBP orally.

(B)(1) An acute and subchronic motor activity test shall be conducted with TBP in accordance with § 798.6200 of this chapter except for the provisions of paragraphs (d) (5) and (6) of § 798.6200.

(2) For the purpose of this section, the following provisions also apply:

(i) *Animal selection.* Testing shall be performed in laboratory rats.

(ii) *Duration of testing.* For the acute testing, the substance shall be administered over a period not to exceed 24 hours; for the subchronic testing, test species shall be exposed daily for at least 90 days.

(iii) *Route of administration.* Animals shall be exposed to TBP orally.

(C)(1) A neuropathology test shall be conducted with TBP in accordance with § 798.6400 of this chapter except for the provision of paragraphs (d)(1)(i) (5) and (6) of § 798.6400.

(2) For the purpose of this section, the following provisions also apply:

(i) *Animal selection.* Testing shall be performed in laboratory rats.

(ii) *Duration of testing.* Animals shall be exposed for at least a 90-day period.

(iii) *Route of administration.* Animals shall be exposed to TBP orally.

(ii) *Reporting requirements*—(A) The neurotoxicity tests required under paragraph (c)(1)(i) (A), (B), and (C) of this section shall be completed and final reports submitted to EPA within 18 months of the effective date of the final rule.

(B) An interim progress report for these neurotoxicity tests shall be submitted to EPA 6 months after the effective date of the final rule.

(2) *Developmental toxicity*—(i) *Required testing.* (A) A developmental toxicity study shall be conducted with TBP in accordance with § 798.4900 of this chapter, except for the provisions of paragraph (e)(5) of § 798.4900.

(B) for the purpose of this section, the following provision also applies:

(1) *Route of administration.* The animals shall be exposed to TBP by gavage.

(2) [Reserved]

(ii) *Reporting requirements.* (A) The developmental toxicity study required under paragraph (c)(2) of this section shall be completed and a final report submitted to EPA by January 27, 1991.

(B) An interim progress report shall be submitted to EPA 6 months after the effective date of the final rule.

(3) *Reproductive and fertility*—(i) *Required testing.* (A) A reproduction and fertility study shall be conducted with TBP in accordance with § 798.4700 of this chapter, except for the provisions of paragraph (c)(5)(i)(A) of § 798.4700.

(B) for the purpose of this section, the following provisions also apply:

(1) *Route of administration.* Animals should be exposed to TBP by gavage.

(2) [Reserved]

(ii) *Reporting requirements.* (A) The reproduction and fertility effects study required under paragraph (c)(3) of this section shall be completed and a final report submitted to EPA by August 17, 1992.

(B) Interim program reports shall be submitted to EPA at 6 month intervals, beginning 6 months after the effective date of the final rule, until the final report is submitted to EPA.

(4) *Mutagenic effects—Gene mutation*—(i) *Required testing.* (A) A detection of gene mutation in somatic cells in culture test shall be conducted with TBP in accordance with § 798.5300 of this chapter.

(B)(1) If TBP produces a positive result in the assay conducted pursuant to paragraph (c)(4)(i)(A) of this section, a sex-linked recessive lethal test in *Drosophila melanogaster* shall be conducted with TBP in accordance with § 798.5275 of this chapter, except for the provisions of paragraph (d)(5)(iii) of § 798.5275.

(2) For the purpose of this section, the following provisions also apply:

(i) *Route of administration.* Animals shall be exposed to TBP orally.

(ii) [Reserved]

(iii) *Reporting requirements.* (A) The somatic cells in culture assay shall be completed and the final report submitted to EPA, within 10 months after the effective date of the final rule. If required, the *Drosophila* sex-linked recessive lethal assay shall be completed and the final report submitted to EPA

within 22 months after the effective date of the final rule.

(B) Interim progress reports shall be submitted to EPA at 6 month intervals beginning 6 months after initiation of the sex-linked recessive lethal test in *Drosophila* until the applicable final reports are submitted to EPA.

(5) *Mutagenic effects—Chromosomal aberration*—(i) *Required testing.* (A) An in vitro mammalian cytogenetics test shall be conducted with TBP in accordance with § 798.5375 of this chapter.

(B)(1) If TBP produces a negative result in the in vitro cytogenetics test conducted pursuant to paragraph (c)(5)(i)(A) of this section, an in vivo mammalian bone marrow cytogenetics test shall be conducted with TBP in accordance with § 798.5385 of this chapter, except for the provisions of paragraph (d)(5)(iii) of § 798.5385.

(2) For the purpose of this section, the following provisions also apply:

(i) *Route of administration.* Animals shall be exposed to TBP orally.

(ii) [Reserved]

(C)(1) If TBP produces a positive result in either the in vitro or the in vivo cytogenetics test conducted pursuant to paragraphs (c)(5)(i) (A) and (B) of this section, a rodent dominant-lethal assay shall be conducted with TBP in accordance with § 798.5450 of this chapter, except for the provisions of paragraph (d)(5)(iii) of § 798.5450.

(2) For the purpose of this section, the following provisions also apply:

(i) *Route of administration.* Animals shall be exposed orally to TBP.

(ii) [Reserved]

(D)(1) A rodent heritable translocation assay shall be conducted with TBP if the dominant-lethal assay conducted for TBP pursuant to paragraph (c)(5)(i)(C) of this section produces a positive result, and if, after a public program review, EPA issues a FEDERAL REGISTER notice or sends a certified letter to the test sponsor specifying that the testing shall be initiated. This test shall be conducted in accordance with § 798.5460 of this chapter except for the provisions of paragraph (d)(5)(iii) of § 798.5460.

(2) For the purpose of this section, the following provisions also apply:

(i) *Route of administration.* Animals shall be exposed to TBP orally.

(ii) [Reserved]

(i) *Reporting requirements.* (A)(1) The in vitro mammalian cytogenetics test shall be completed and the final report submitted to EPA within 10 months after the effective date of the final rule.

(2) If required, the in vivo mammalian bone-marrow cytogenetics test shall be completed and the final report submitted to EPA within 24 months after the effective date of the final rule.

(3) If required, the dominant lethal assay shall be completed and the final report submitted to EPA within 36 months after the effective date of the final rule.

(4) If required, the heritable translocation assay shall be completed and the final report submitted to EPA within 25 months after the date of EPA's notification of the test sponsor under paragraph (c)(5)(i)(D) of this section that testing shall be initiated.

(B) Interim progress reports shall be submitted to EPA at 6 month intervals beginning 6 months after initiation of the rodent dominant lethal assay and the rodent heritable translocation assay respectively, if required, until the applicable final reports are submitted to EPA.

(6) *Oncogenicity*—(i) *Required testing.* (A) An oncogenicity test shall be conducted with TBP in accordance with § 798.3300 of this chapter except for the provisions of paragraphs (b)(1)(i), (b)(6)(i) and (b)(9), of § 798.3300.

(B) For the purpose of this section, the following provisions also apply:

(1) *Animal selection.* TBP shall be tested in Sprague-Dawley rats and in mice.

(2) *Route of administration.* Animals shall be exposed to TBP orally.

(3) *Clinical examinations.* At 12 months, 18 months and during month 24, a blood smear shall be obtained from all animals. A differential blood count shall be performed on blood smears from those animals in the highest dosage group and the controls. If these data, or data from the pathological examination indicate a need, then the 12- and 18-month blood smears from other dose levels shall also be examined. Differential blood counts shall be performed for the next lower group(s) if there is a major discrepancy

between the highest group and the controls. If clinical observations suggest a deterioration in health of the animals during the study, a differential blood count of the affected animals shall be performed.

(ii) *Reporting requirements.* (A) The oncogenicity test required under paragraph (c)(6) of this section shall be completed and a final report submitted to EPA within 53 months of the effective date of the final rule.

(B) Interim progress reports shall be submitted to EPA at 6 month intervals beginning 6 months after the effective date of the final rule, until the final report is submitted to EPA.

(7) *Dermal sensitization*—(i) *Required testing.* A dermal sensitization test shall be conducted with TBP in accordance with § 798.4100 for this chapter.

(ii) *Reporting requirements.* The dermal sensitization test shall be completed and the final report submitted to EPA within 6 months of the effective date of the final rule.

(8) *Oral/Dermal Pharmacokinetics*—(i) *Required testing.* (A) A pharmacokinetics test shall be conducted with TBP in accordance with § 795.228 of this chapter, except for the provisions of paragraphs (c)(1)(iii)(B), (c)(2)(ii)(C)(1) and (c)(2)(ii)(C)(2) of § 795.228.

(B) For the purposes of this section, the following provisions also apply:

(1) *Animal care.* During the acclimatization period, the animals shall be housed in suitable cages. All animals shall be provided with certified feed and tap water *ad libitum*.

(2) *Dermal treatment.* For dermal treatment, two doses, comparable to the low and high oral doses, shall be dissolved in a suitable vehicle and applied in volumes adequate to deliver comparable doses. The backs of the animals should be lightly clipped with an electric clipper 24 hours before treatment. The test substance shall be applied to the intact clipped skin (approximately 2 cm² for rats, 40 cm² for mini-pigs). The dosed areas shall be protected with a suitable porous covering which is secured in place, and the animals shall be housed separately.

(ii) *Reporting requirements.* (A) The pharmacokinetics test required in paragraph (c)(8)(i) of this section shall

be completed and the final report submitted to EPA by December 26, 1992.

(B) Interim 6 month progress reports shall be submitted to EPA beginning at 6 months after the effective date of the final rule and continuing until submission of the final report.

(d) *Environmental effects testing*—(1) *Algal acute toxicity*—(i) *Required testing.* (A) Algal acute toxicity testing shall be conducted with TBP using *Selenastrum capricornutum* in accordance with § 797.1050 of this chapter except for the provisions of paragraphs (c)(6)(i)(A),(B), and (ii) of § 797.1050.

(B) For the purpose of this section, the following provisions also apply:

(1) *Summary of the test.* The algal cells at the end of 24, 48, and 72 hours shall be enumerated.

(2) *Chemical measurement.* The final separation of the algal cells from the test solution shall be done using an ultrafiltration (e.g., 0.45 micrometer pore size) technique. The total and dissolved (e.g., filtered) concentrations of the test substance shall be measured in each test chamber and the delivery chamber before the test and in each test chamber at 0 and 96 hours.

(ii) *Reporting requirements.* The algal acute toxicity test required in paragraph (d)(1) of this section shall be completed and the final report submitted to EPA within 9 months of effective date of the final rule.

(2) *Fish acute toxicity*—(i) *Required testing.* (A) Fish acute toxicity testing shall be conducted with TBP using *Salmo gairdneri* (rainbow trout) in accordance with § 797.1400 of this chapter.

(B) For the purpose of this section, the following provisions also apply:

(1) *Chemical measurement.* The total and dissolved (e.g., filtered) concentrations of the test substance shall be measured in each test chamber delivery chamber before the test. If the dissolved test substance concentration is greater than 80 percent of total test substance concentration, then only total or dissolved test concentration shall be measured in each chamber at 0, 48, and 96 hours. If the dissolved test substance concentration is less than or equal to 80 percent of total test substance, then total and dissolved test substance concentration shall be measured at 0, 48 and 96 hours.

(2) *Test procedures.* The test shall be performed under flow-through conditions.

(ii) *Reporting requirements.* The fish acute toxicity test shall be completed and the final report submitted to EPA within 9 months of the effective date of the final rule.

(3) *Daphnid acute toxicity*—(i) *Required testing.* (A) Daphnid acute toxicity testing shall be conducted with TBP using *Daphnia magna* or *D. pulex* in accordance with § 797.1300 of this chapter.

(B) For the purpose of this section, the following provisions also apply:

(1) *Chemical measurement.* The total and dissolved (e.g., filtered) concentrations of the test substance shall be measured in each test chamber and the delivery chamber before the test. If the dissolved test substance concentration is greater than 80 percent of total test substance concentration, then only total or dissolved test concentration shall be measured in each chamber at 0, 24, and 48 hours. If the dissolved test substance concentration is less than or equal to 80 percent of total test substance, then total and dissolved test substance concentration shall be measured at 0, 29, and 48 hours.

(2) *Test procedures.* The test shall be performed under flow-through conditions.

(ii) *Reporting requirements.* The daphnid acute toxicity test shall be completed and the final report submitted to EPA within 9 months of the effective date of the final rule.

(4) *Gammarid acute toxicity*—(i) *Required testing.* (A) *Gammarid* acute toxicity testing shall be conducted with TBP using *Gammarus lacustris*, *G. fasciatus*, or *G. pseudolimnaeus* in accordance with § 795.120 of this chapter.

(B) For the purpose of this section, the following provisions also apply:

(1) *Chemical measurement.* The total and dissolved (e.g., filtered) concentrations of the test substance shall be measured in each test chamber and the delivery chamber before the test. If the dissolved test substance concentration is greater than 80 percent of total test substance concentration, then only total or dissolved test concentration shall be measured in each chamber at 0, 48, and 96 hours. If the dissolved test substance concentration is less than or

equal to 80 percent of total test substance, then total and dissolved test substance concentration shall be measured at 0, 48, and 96 hours.

(2) *Test procedures.* The test shall be performed under flow-through conditions.

(ii) *Reporting requirements.* The *Gammarid* acute toxicity test shall be completed and the final report submitted to EPA within 9 months of the effective date of the final rule.

(5) *Daphnid chronic toxicity*—(i) *Required testing.* (A) Daphnid chronic toxicity testing shall be conducted with TBP using *Daphnia magna* or *D. pulex* in accordance with §797.1330 of this chapter, if the algal EC50, the rainbow trout LC50, the daphnid EC50, or the gammarid LC50 determined in accordance with paragraphs (d)(1), (2), (3) and (4) of this section satisfy the following criteria: Any such value is ≤ 1 mg/L; or any fish or aquatic invertebrate EC50 or LC50 is ≤ 100 mg/L and either the rainbow trout or gammarid 24-hour to 96-hour LC50 ratio ≥ 2 , or the daphnid 24-hour to 48-hour EC50 or LC50 ratio is ≥ 2 .

(B) For the purpose of this section, the following provisions also apply:

(1) *Chemical measurement.* The total and dissolved (e.g., filtered) concentrations of the test substance shall be measured in each test chamber and the delivery chamber before the test. If the dissolved test substance concentration is greater than 80 percent of total test substance concentration, then only total or dissolved test substance concentration shall be measured in each test chamber at 0, 7, 14, and 21 days. If the dissolved test substance concentration is less than or equal to 80 percent of total test substance concentration, then total and dissolved test substance concentration shall be measured at 0, 7, 14, and 21 days.

(2) *Test procedures.* The test shall be performed under flow-through conditions.

(ii) *Reporting requirements.* (A) The daphnid chronic toxicity test, if required, shall be completed and the final report submitted to EPA by September 27, 1991.

(B) An interim progress report shall be submitted to EPA 6 months after the initiation of the test.

(6) *Fish early-life stage toxicity*—(i) *Required testing.* A fish early-life stage toxicity test shall be conducted with TBP in accordance with §797.1600 of this chapter, using the fish with the lower LC50 value (either the rainbow trout (*Salmo gairdneri*) or the fathead minnow (*Pimephales promelas*)), if the algal EC50, the rainbow trout LC50, the gammarid LC50 or the daphnid EC50 determined in accordance with paragraphs (d)(1), (2), (3), and (4) of this section satisfy the following criteria: Any such value is ≤ 1 mg/L; or any fish or aquatic invertebrate EC50 or LC50 is ≤ 100 mg/L and either the rainbow trout or gammarid 24 hour to 96 hour LC50 ratio ≥ 2 , or the daphnid 24-hour to 48-hour EC50 or LC50 ratio is ≥ 2 .

(ii) *Reporting requirements.* (A) The fish early-life stage flow-through toxicity test shall be completed and the final report submitted to EPA by December 27, 1991.

(B) An interim progress report shall be submitted to EPA 6 months after the initiation of the test.

(7) *Benthic sediment invertebrate bioassay*—(i) *Required testing.* (A) A benthic sediment invertebrate bioassay shall be conducted on TBP with the midge (*Chironomus tentans*) if chronic toxicity testing is required pursuant to paragraph (d)(5) of this section and if the log Koc calculated according to paragraph (e)(2)(B)(1) of this section is greater than or equal to 3.5 but less than or equal to 6.5. The total aqueous sediment concentrations and interstitial water concentrations of the test substance shall be measured in each test chamber at 0, 4, 7, 10, and 14 days. The aqueous concentrations of the test substance in the delivery chamber shall be measured at 0, 4, 7, 10, and 14 days. TBP-spiked clean freshwater sediments containing low, medium, and high organic carbon content shall be used.

(B) The benthic sediment invertebrate bioassay shall be conducted according to the test procedure specified in the American Society for Testing and Materials, Special Technical Publication 854 (ASTM STP 854) entitled, "Aquatic Safety Assessment of Chemicals Sorbed by Sediments," by W.J. Adams, R.A. Kimerle, and R.G. Mosher,

published in *Aquatic Toxicity and Hazard Assessment: Seventh Symposium*, ASTM STP 854, pp. 429-453, R.D. Caldwell, R. Purdy, and R.C. Bahner, Eds., 1985 which is incorporated by reference. This published procedure is available for public inspection at the Office of Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408, and copies may be obtained from the Non-Confidential Information Center (NCIC) (7407), Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency, Room B-607 NEM, 401 M St., SW., Washington, DC 20460, between the hours of 12 p.m. and 4 p.m. weekdays excluding legal holidays. This incorporation by reference was approved by the Director of the Federal Register in accordance with 5 U.S.C. 522(a) and 1 CFR part 51. The method is incorporated as it exists on the effective date of this rule and a notice of any change to the method will be published in the FEDERAL REGISTER.

(ii) *Reporting requirements.* (A) The benthic sediment invertebrate bioassay, if required, shall be completed and the final report submitted to EPA within 21 months of the effective date of the final rule.

(B) An interim progress report shall be submitted to EPA for the benthic sediment invertebrate bioassay 6 months after the initiation of the test.

(e) *Chemical fate testing*—(1) *Vapor pressure*—(i) *Required testing.* Vapor pressure testing shall be conducted with TBP in accordance with § 796.1950 of this chapter.

(ii) *Reporting requirements.* The vapor pressure test required in paragraph (d)(1) of this section shall be completed and the final report submitted to EPA by September 27, 1990.

(2) *Sediment and soil adsorption isotherm*—(i) *Required testing.* Sediment and soil adsorption isotherm testing shall be conducted with TBP in accordance with § 796.2750 of this chapter and EPA will provide two soil and two sediment samples.

(ii) *Reporting requirements.* (A) The sediment and soil adsorption isotherm test required under paragraph (d)(2) of this section shall be completed and the

final report submitted to EPA by September 27, 1990.

(B) For the purpose of this section, the following provisions also apply:

(1) A Koc value shall be calculated for each test sediment using the equation $Koc=K/$ (percent of organic carbon in test sediment).

(2) [Reserved]

(3) *Hydrolysis as a function of pH at 25 °C*—(i) *Required testing.* Hydrolysis testing shall be completed with TBP in accordance with § 796.3500 of this chapter.

(ii) *Reporting requirements.* The hydrolysis test required under paragraph (e)(3)(i) of this section shall be completed and the final report submitted to EPA by September 27, 1990.

(f) *Effective date.* (1) The effective date of this final rule is September 27, 1989, except for paragraphs (c)(2)(ii)(A), (c)(3)(ii)(A), (c)(6)(i)(A), (c)(6)(i)(B)(3), (c)(8)(i), (c)(8)(ii)(A), (d)(5)(ii)(A), (d)(6)(ii)(A), (e)(1)(ii), (e)(2)(ii)(A), and (e)(3)(ii) of this section. The effective date for paragraphs (c)(2)(ii)(A), (c)(3)(ii)(A), (c)(8)(i), (e)(1)(ii), (e)(2)(ii)(A), and (e)(3)(ii) of this section is May 21, 1991. The effective date for (c)(8)(ii)(A), (d)(5)(ii)(A), and (d)(6)(ii)(A) of this section is June 12, 1992. The effective date for (c)(6)(i)(A), (c)(6)(i)(B)(3), and (c)(8)(ii)(A) is May 28, 1993.

(2) The guidelines and other test methods cited in this rule are referenced as they exist on the effective date of the final rule.

[54 FR 33413, Aug. 14, 1989; 56 FR 23231, May 21, 1991, as amended at 57 FR 24961, June 12, 1992; 58 FR 30992, May 28, 1993; 58 FR 34205, June 23, 1993; 60 FR 34467, July 3, 1995]

§ 799.4440 Triethylene glycol monomethyl ether.

(a) *Identification of test substance.* (1) Triethylene glycol monomethyl ether (TGME, CAS No. 112-35-6) shall be tested in accordance with this section.

(2) TGME of at least 90 percent purity shall be used as the test substance.

(b) *Persons required to submit study plans, conduct tests, and submit data.* All persons who manufacture or process TGME, other than as an impurity,