ENVIRONMENTAL PROTECTION AGENCY

40 CFR Parts 795 and 799

[OPTS-42100B; FRL-3627-4]

Tributyl Phosphate; Final Test Rule

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: EPA is issuing a final test rule under section 4 of the Toxic Substances Control Act (TSCA) requiring manufacturers and processors of tributyl phosphate (TBP, CAS No. 126-73-3) to perform testing for health effects (oncogenicity, neurotoxicity, reproductive and developmental toxicity, mutagenicity, dermal sensitization, and oral/dermal pharmacokinetics), environmental effects (acute effects on algae, fish and aquatic invertebrates, and triggered chronic effects on fish and aquatic invertebrates and sediment bioassay), and chemical fate (vapor pressure, Koc, and hydrolysis rate). This rule is in response to the TSCA Interagency Testing Committee's (ITC) designation of TBP for priority health effects, chemical fate, and environmental effects testing.

DATES: This rule shall become effective on September 27, 1989. For purposes of judicial review, in accordance with 40 CFR 23.5, this rule shall be promulgated at 1 p.m. eastern (standard or daylight as appropriate) time on August 28, 1989. The incorporation by reference in this rule is approved by the Director of the Federal Register as of September 27, 1989.

FOR FURTHER INFORMATION CONTACT: Michael M. Stahl, Director, TSCA Assistance Office (TS-799), Office of Toxic Substances, Room EB-44, 401 M Street SW., Washington, DC 20460, (202) 554-1404, TDD (202) 554-0551.

SUPPLEMENTARY INFORMATION: EPA is promulgating a final test rule under section 4(a) of TSCA requiring health effects, environmental effects and chemical fate testing of TBP.

I. Introduction

A. Test Rule Development Under TSCA

This final rule is part of the overall implementation of section 4 of TSCA (Pub. L. 94-469, 90 Stat. 2003 et seq., 15 U.S.C. 2601 et seq.), which authorizes EPA to require the development of data relevant to assessing the risk to health and the environment posed by exposure to particular chemical substances or mixtures (chemicals).

Under section 4(a) of TSCA, EPA must require testing of a chemical to develop data if the Administrator makes certain findings as described in TSCA under section 4(a)(1)(A) or (B). Detailed discussions of the statutory section 4 findings are provided in the EPA's first and second proposed test rules published in the Federal Register's of July 18, 1980 (45 FR 48510) and June 5, 1981 (46 FR 30300).

B. Regulatory History

The ITC recommended TBP with intent-to-designate in its eighteenth report published in the Federal Register of May 19, 1986 (51 FR 18368), and designated TBP for priority testing consideration in its nineteenth report published in the Federal Register of November 16, 1986 (51 FR 41417). In response to this designation, EPA issued a proposed test rule in the Federal Register of November 12, 1987 (52 FR 43346) which would require that manufacturers and processors of TBP test the chemical for various health and environmental effects, under sections 4(a)(1)(A) and (B) of TSCA.

II. Response to Comments

EPA received written comments on the TBP proposed test rule from the Tributyl Phosphate Task Force (TBPTF) of the Synthetic Organic Chemical Manufacturers Association (SOCMA) on January 12, 1988 (Ref. 1). The TBPTF also requested a public meeting on their comments which was held on April 7, 1988. The comments received by EPA in response to the proposed rule for TBP are given below.

A. Exposure

1. *TBPTF exposure survey.* The TBPTF commented that the exposure information available to EPA was insufficient to support a finding of significant or substantial human exposure since the data were merely suggestive. The TBPTF proposed to do an industry-wide survey of U.S. sites distributing, processing, and using TBP and products containing TBP to determine the uses, use conditions, and potential worker exposure associated with TBP. EPA agreed to consider the study results in its deliberations for a final rule. TBPTF commissioned Temple, Barker, Sloane, Inc., to conduct and validate the survey. On April 7, 1988, the TBPTF presented EPA with the first part of a report, "1987 U.S. Survey of Tributyl Phosphate Users, Potential Exposure and Safety Procedures" (Ref. 2). The report did not contain an estimate of the number of workers potentially exposed to aircraft hydraulic fluid, a product that accounts for a major part of TBP usage (89 percent by volume). After a public meeting with the TBPTF, EPA granted TBPTF a brief period to estimate the numbers and extent of potential worker exposure to aircraft hydraulic fluid containing TBP from survey and additional data. On July 11, 1988, TBPTF submitted a report to EPA on estimated exposure to TBP-containing aircraft hydraulic fluid (Ref. 3).

The TBPTF reported that the greatest number of workers potentially exposed was in the use of aircraft hydraulic fluid. The three primary uses include aircraft manufacturing, hydraulic system component manufacturing, and commercial airline operations (passenger and freight). The TBPTF reported each type of user exposure in terms of estimated numbers of employees potentially exposed on an infrequent basis (less than once per week for less than one hour) and on a more frequent or routine basis. On the basis of confidential discussions with two major aircraft manufacturers, TBPTF estimates that 740 workers in this industry may be infrequently exposed to fluid, and 241 workers may be frequently exposed to hydraulic fluid containing TBP. On the basis of survey responses from aircraft component manufacturers, the TBPTF estimates that 176 employees in this industry may be frequently exposed to aircraft hydraulic fluid containing TBP, and 411 employees may be infrequently exposed. On the basis of confidential estimates by one of the major airlines, TBPTF estimates that 2,200 employees in this industry are routinely exposed to aircraft hydraulic fluid containing TBP and approximately 43,000 aircraft mechanics at some time could be exposed to aircraft hydraulic fluid. The activities potentially causing exposure include: Venting of pressurized systems at service sites, removal and repair of components, and testing and inspection of components. Aircraft manufacturers report that they require mechanics to use protective equipment (gloves, aprons, sleeve shields, goggles/face shields).

In the survey, the other two types of hydraulic fluid users report these and other methods of protection. However, the survey report indicates that in practice, aircraft mechanics only take minimal precautions to prevent contact even though they are aware of the irritating properties of hydraulic fluid. Also, according to the survey, aircraft mechanics do not wear protective gloves.

Survey respondents reported that 100 distributor workers for 296 worker-hours per year and 200 processor workers for

T2

108,358 worker-hours per year have direct exposure to TBP.

An estimated total of 245 distributer workers (estimated from survey respondents and non-respondents) are potentially exposed for 502 worker-hours per year according to the survey. An estimated total of 345 processor workers (estimated from survey respondents and non-respondents) are potentially exposed for 183,382 worker-hours per year.

Other uses of TBP involve partially enclosed or open operations, and the concentration of TBP in these products is under 10 percent. Of these miscellaneous uses, paint spraying operations represent the most likely exposure potential, but spray booths are often used and the paint is used only by original equipment manufacturers, suggesting that exposure is limited to manufacturing use.

2. *EPA's response to TBPTF's exposure survey.* EPA reviewed the exposure survey performed by the TBPTF and finds the conclusions regarding potential occupational exposure to TBP to be reasonable. EPA has concerns about the completeness and accuracy of the survey but these do not interfere with the adequacy of the study for present purposes (Refs. 4 and 5). The survey results simply confirm EPA's earlier conclusion that potential human exposure to TBP is substantial.

B. Testing

1. *Genotoxicity.* The TBPTF commented that studies of gene mutation in mammalian cells in culture and in vivo cytogenetics, specifically the mouse micronucleus test, should be conducted to determine potential clastogenic effects, and that a program review of the entire genotoxicity data base should precede any considerations for further genotoxicity testing.

EPA agrees that a study of gene mutation in somatic cells in culture is necessary as an early tier teset for gene mutation effects of TBP. However, EPA believes that an in vitro mammalian cytogenetics test and in vivo mammalian bone marrow cytogenetics chromosomal analysis test are necessary early tier tests for cytogenetics effects. EPA is reviewing the mouse micronucleus test as a potential alternative test for cytogenetic effects in future test rules.

2. *Pharmacokinetics.* The TBPTF commented that the rat oral and dermal absorption, distribution and excretion pharmacokinetics, and oral metabolism studies should be performed as proposed. However, the TBPTF recommended dermal absorption testing in the pig (mini-pig or weanling swine) rather than the guinea pig, because pig skin is a better model for human skin than guinea pig skin.

EPA has reviewed the evidence the TBPTF has submitted to support testing the pig over the guinea pig and EPA agrees that the pig (mini-pig or weanling pig) is an acceptable substitute testing model for the guinea pig for dermal absorprtion testing (Refs. 6 through 9).

3. *Oncogenicity.* The TBPTF commented that, because potential worker exposure is significant only by the dermal route as indicated by the exposure survey, a pilot 28-day dermal study in the rat should be conducted first to evaluate the feasibility of performing chronic efforts and oncogenicity studies by that route. The TBPTF believes that a decision regarding oncogenicity studies should be deferred pending results of the proposed pilot dermal studies and the completion of pharmacokinetics studies.

EPA reported in the proposed rule that the available data suggest TBP may have oncogenic potential. EPA is requiring an oncogenicity study by the oral route because the comparative oral/dermal pharmacokinetics data will allow analysis of effects related to differences in route of administration. Protocol design for dermal bioassays present many problems including: Selection of appropriate species; estimation and demonstration of absorbed versus applied dose; criteria for defining the maximum tolerated dose, e.g., whether based on skin or systemic effects. EPA is assessing the literature on this subject and has sponsored a workshop on dermal carcinogenesis bioassay problems and protocol development. In the near future EPA hopes to publish a generic protocol for dermal bioassays and publish guidelines on when testing should be done by that route.

4. *Dermal sensitization.* TBPTF commented that additional dermal sensitization testing is unnecessary because a mixture containing TBP has been tested in a human study and no sensitization occurred. TBPTF believes that if TBP were a sensitizer, some reaction would have occurred and results of (any) human study should take precedence over those obtained in animal (guinea pig) studies (Ref. 1).

EPA is requiring a dermal sensitization study because photosensitization was not evaluated in the available human study, and the exact TBP concentration in the test mixture was unknown and may have been too low (reported as "less than 25 percent") to have elicited a reaction.

5. *Developmental toxicity.* TBPTF comments that because the exposure survey indicates there is insignificant exposure potential for women of child-bearing age and because of irritant warning properties and low exposure levels, developmental toxicity testing should not be required.

For purposes of requiring testing under section 4 of TSCA, EPA is not required to take into account gender-specific exposure patterns in its deliberations. EPA does not assume that gender-specific exposure patters will persist. Because there is a potential for substantial human exposure to TBP, developmental toxicity testing is required.

6. *Reproductive toxicity.* TBPTF comments that reproductive testing should be triggered by more general indications of reproductive toxicity such as in vivo genotoxicity tests (*Drosophila* and in vivo cytogenetics) because there are very low levels of exposure of both males and females to TBP. In addition, two long-term studies, an 18-week study by Laham et al. and a 13-week study by FMC, showed no effect on gonadal tissues.

While EPA recognizes that there are situations where short-term tests may be appropriate to screen for reproductive effects, EPA does not agree that in the present situation the in vivo genotoxicity tests are adequate to screen for the reproductive toxicity of TBP. And although the two studies mentioned by TBPTF do not show reproductive effects, they are not adequate by themselves to determine whether TBP has reproductive toxicity. It is well documented that there are effects on reproduction that are not detectable by simple histopathological analysis, i.e. effects on reproductive performance, hormones, outcomes of pregnancy, growth and maturation of offspring postnatally. Therefore testing specific for reprodactive toxicity is required.

7. *Neurotoxicity.* The TBPTF suggested a tiered approach consisting of an acute functional observational battery and motor activity screen to be followed by a subchronic behavioral evaluation if required after program reveiw. The TBPTF commented that neurotoxicity testing should be by the dermal route if this route proves feasible from the results of the 28-day study. The TBPTF believes that because available studies conclusively show that TBP is not a delayed neurotoxicant (organophosphorus induced delayed neurotoxicity (OPIDN) is the primary mechanism by which organophosphates act directly on the nerves) a further concern for neuropathy is unwarranted

and requirements for in situ perfusion should be removed from the test rule.

EPA does not agree with TBPTF's tiered approach. Both acute and subchronic tests are necessary because EPA is concerned about acute effects as well as the potential effects following repeated exposure. EPA encourages use of the relevant route of administration when possible. Although the dermal route of administration is theoretically acceptable, there are a number of practical problems which must be addressed before a dermal study would be acceptable. First, there must be a demonstration that a sufficient dose of the compound can be absorbed to produce neurobehavioral changes. Without such a high dose level effect, negative results would not be conclusive. Second, dermal application may interefere with satisfactory interpretation of neurobehavioral information. Dermal application can serve as a stress inducer and produce alterations in various neurobehavioral parameters. To account for this possible confounding effect it would be necessary to use a positive control which can also be applied dermally (e.g., acrylamide). Because these problems have not been addressed, neurotoxicity testing by the oral route is required.

EPA believes that, although available studies indicate that under the conditions tested, TBP does not produce organophosphorus-induced delayed neuropathy (OPIDN), other available literature provides evidence of neurobehavioral changes following exposure to TBP, and a standard battery of tests is still indicated (Refs. 10 through 13).

8. *Environmental effects.* The TBPTF commented that EPA's proposed environmental effects testing is generally reasonable and supportable. TBPTF raised the following points. First, TBP argued that the chronicity ratio of 24- to 96-hour LC50 for fish and certain aquatic invertebrates (e.g., *Gammarus*) or the ratio of the 24- to 48-hour LC50 for daphnid of 2 or greater is extremely stringent and should be modified. Second, TBPTF believes there is no clear need for plant translocation tests because there is no or low level exposure for this environment, as TBP is shown to be readily biodegradable in the OECD screening test, by semi-continuous activated sludge, in a river die-away test and in ultimate biodegradation. Third, with respect to specific guidelines, the TBPTF believes that ascertaining whether the test material is in solution does not require analysis of both the total and filtered concentrations of the test material. The concentration in only a filtered sample should be required except in the algal test, where measurements of the amount of test material associated with the algal cells is required. Centrifuging the samples is better because filtration may trap TBP in the filter medium. Requiring analysis of both total and filtered or centrifuged test medium will double analysis costs without any real need. Fourth, the time allotted (9 months) for the completion of the flow-through acute tests may not be adequate. Flow-through tests with analytical measurement of test solutions tend to experience more problems than simple static tests; 12 months from official notification to final report would be a more reasonable estimate.

EPA does not agree with the TBPTF that the chronicity ratio for fish and invertebrates is too stringent because historical data confirm the predictive capability of this decision criterion. EPA agrees with TBPTF that the plant translocation test is unnecessary and EPA is not requiring this test because human exposure from plant dietary uptake does not appear to be of concern. EPA is considering whether it should propose the early seedling growth test to determine the toxicity of TBP to plants. EPA does not agree that only the filtered sample should require analysis and supports the testing guidelines which require analysis of both total and filtered samples. Testing both the total and filtered samples is necessary to know how much dissolved test substance is available during aquatic toxicity tests. EPA is not requiring that both the total and dissolved chemical be measured for every sample. If the dissolved test substance being measured is consistently greater than or equal to 80 percent of total measured test substance, for all test substance concentrations, then it is necessary to measure only the dissolved or total test substance not both. EPA does not agree with TBPTF that 9 months is inadequate to conduct acute flow-though testing because the TBPTF does not provide adequate evidence to the contrary.

C. Economic Issues

1. *Comment:* The TBPTF has estimated the cost of the testing program at about $2.4 million. The information to be developed by the testing program is not a capital asset; and therefore the cost involved must be treated as current expenses. Using the EPA estimated production volume range of 6 to 9 million pounds during an approximate 2-year test program, the cost of the testing proposed per pound would be $0.15 and $0.20 per pound of TBP produced. TBPTF does not believe this is an inconsequential amount.

Response: EPA's estimate of the test cost is between $1.3 million and $1.7 million. TBPTF's estimate of the oncogenicity test is roughly double EPA's estimate, and accounts for the largest portion of the difference. Some of the other estimates submitted by the TBPTF range from 2 to almost 10 times greater than EPA's estimates.

EPA has developed detailed test cost information for each test included in the rule. TBPTF has provided no such information nor any documentation regarding their test cost estimates. In addition, TBPTF has not addressed the method used by EPA to estimate test cost or any of the detailed estimates. Without any such information, EPA cannot address the estimates provided by TBPTF.

Also, TBPTF confuses the procedures used to determine reimbursement for testing costs under section 4 of TSCA with the analysis used to determine economic impacts of the rule. TBPTF looks at the accounting method used to pay for the costs associated with testing, while EPA's economic analysis employs cost recovery analysis to estimate the likelihood of adverse economic impact. In the economic analysis, test costs are annualized over the assumed market life of the product to estimate the amount which firms will have to increase price of the product to recover the costs associated with testing. This estimate of product price increase, as explained in the economic analysis, is used as an indicator of the potential for adverse economic impact. EPA's analysis method is fully explained in the economic analysis document accompanying the proposed rule.

2. *Comment:* Domestic TBP, and TBP-based end-use products, effectively compete in the international market. Aircraft hydraulic fluids containing TBP are used by every major airline in the free world, and more than one-half of the fluid produced domestically is exported. While these fluids are currently only available from domestic sources, excessive testing requirements and associated costs can only encourage the entry of non-domestic suppliers, thus placing an unfair competitive burden on domestic manufacturers and processors of TBP.

Response: As the TBPTF has indicated, fluids containing TBP are used by every major commercial airline in the free world and there are only U.S. sources of these fluids. TBPTF has not demonstrated that a price increase of 1.4 percent to 2.0 percent to cover the costs of testing will be a great enough

incentive for companies outside of the U.S. to begin production of TBP. In addition, any person who begins to import TBP from the effective date of the rule through the reimbursement period would also be subject to the test rule and therefore would be subject to reimbursement of the test costs.

3. *Comment:* TBPTF comments further that conclusions regarding the burden of testing, which are based on fixed assumptions in the inexact field of economic theory, must be seriously and thoroughly evaluated. The ability to pass through costs under conditions of inelastic demand and stable market conditions may be true, but dramatically increased costs at only some producers or processors creates unstable conditions from both supply and consumption dynamics. In a world-wide market, domestic producers and processors of TBP could be placed at an unfair disadvantage. Even if domestic suppliers were able to pass through costs to domestic customers, it is less likely that such pass-through could be successful in foreign markets, putting a double burden on the domestic marketplace. It is economically more prudent and more realistic to assume demand for TBP to be elastic with little probability of increasing price enough to cover costs of testing in a reasonable time. These increased costs, under such assumptions, will directly impact the profitability of TBP production and may ultimately eliminate one or more producers, or even the product, from the market.

Response: TBPTF has not demonstrated that an increase in price of 1.4 percent to 2.0 percent qualifies as "dramatically increased costs". Moreover, as the TBPTF has indicated, there are no foreign sources of TBP-containing fluids. As a result, all producers of TBP would incur these increased costs. EPA has not been able to identify any viable substitutes for TBP in its largest use. Producers of TBP should be able to pass along the cost of testing to all of these customers and not just to domestic customers.

III. Final Test Rule

EPA is basing its final health and environmental effects testing for TBP on the authority of sections 4(a)(1) (A) and (B) of TSCA.

A. Findings

Under section 4(a)(1)(A), EPA finds that the manufacturing, processing, distribution, use, and disposal of TBP in aircraft hydraulic fluid and other uses may present an unreasonable risk of adverse oncogenic effects, neurotoxic effects, and dermal sensitization. These findings are based on the available toxicity data discussed in Unit II of this preamble and in Unit II.F. of the preamble to the proposed rule (52 FR 43346).

Under section 4(a)(1)(B), EPA finds that TBP is produced in substantial quantities and that there is or may be substantial human exposure to TBP in its manufacture, processing, distribution, use, and disposal. The estimated 1985 production capacity of TBP is 6 to 9 million pounds per year (Ref. 14). Potentially 43,000 aircraft mechanics and another roughly 3000 aircraft industry employees at some time could be exposed to aircraft hydraulic fluid containing TBP (Ref. 3). The exposure of mechanics is mainly dermal exposure from removing and repairing components, venting pressurized systems at service sites, and the testing and visual and manual inspection of components. There is also potential of mainly dermal exposure to TBP of approximately 500 TBP manufacturing, processing, and distribution workers from such operations as handling, transfer and packaging of products, equipment repair, cleaning equipment and spill cleanups. There is also potential limited dermal exposure to users of other TBP-containing products (less than 10 percent concentration representing in total 28 percent of TBP volume) including use in original equipment, paints and coatings, inks, leather finishing, liquid fluorescent penetrant, sewage treatment, vinyl floor finish for commercial and industrial applications, and stripping agents.

Under section 4(a)(1)(B), EPA finds that TBP is produced in substantial quantities, and that it enters or may reasonably be anticipated to enter the environment in substantial quantities as a result of its manufacture, processing, distribution, use, and disposal as indicated by its presence in surface water, sediment and groundwater. As stated in the proposed rule, TBP is expected to enter the environment as a result of wastewater release from sites where it is made or used and from leachate releases from landfills (see Unit II.D. of the proposed rule). EPA believes that the low concentrations of TBP detected in or released to the environment at numerous and widely dispersed locations suggest that the total release is substantial under section 4(a)(1)(B) of TSCA.

1. *Health effects.* EPA finds that the available data for insufficient to reasonably determine or predict the oncogenicity, neurotoxicity, dermal sensitization, developmental toxicity, reproductive and fertility effects, mutagenicity, and oral/dermal pharmacokinetics of TBP resulting from exposure during manufacturing, processing, distribution, use, and disposal. EPA finds that testing is necessary to develop these data. EPA believes that the data resulting from this testing will be relevant to a determination as to whether the manufacturing, processing, distribution, use, or disposal of TBP does or does not present an unreasonable risk of injury to human health.

2. *Environmental effects and chemical fate.* EPA believes that, for chemicals that have substantial production and substantial environmental release, reliable data should be developed to assess their toxicity and persistence. Available data are insufficient to reasonably determine or predict TBP's acute toxicity to algae, fish, and aquatic invertebrates, and chronic toxicity to fish and aquatic invertebrates (free swimming and in sediment). Available data are insufficient to reasonably determine or predict TBP's vapor pressure data at 25°C, Koc, and hydrolysis rate. Vapor pressure data at 25°C are needed to estimate a reliable Henry's Law Constant (He) for TBP. Data on Koc are needed to estimate the sorption of TBP to soil and sediments. Finally, hydrolysis rate data, which complement the available biodegradation data, are needed to estimate the persistence of TPB in aquatic systems. EPA finds that testing is necessary to develop environmental effects data and chemical fate data, and believes that the data resulting from these test requirements will be relevant to a determination that the manufacturing, processing, use and disposal of TBP does or does not present an unreasonable risk of injury to the environment.

B. Required Testing, Test Standards and Reporting Requirements

On the basis of these findings EPA is requiring that chemical fate, environmental effects and health effects testing be conducted for TBP in accordance with specific test guidelines set forth in 40 CFR parts 796, 797 and 798, or other published test methods as specified in this test rule as listed in the following table.

REQUIRED TESTING, TEST STANDARDS, AND REPORTING REQUIREMENTS FOR TRIBUTYL PHOSPHATE

Test	Test standard 40 CFR citation	Reporting deadline for final rule [1]	Number interim (6-mo) reports required
Chemical fate:			
Vapor pressure	§ 796.1950	6	0
Hydrolysis rate at 25 °C	§ 796.3500	6	0
Sediment and soil adsorption isotherm	§ 796.2750	9	0
Environmental effects:			
Gammarid acute toxity	§ 795.120	9	0
Selenastrum acute toxicity	§ 797.1050	9	0
Rainbow trout acute toxicity	§ 797.1400	9	0
Daphnid acute toxicity	§ 797.1300	9	0
Daphnid chronic toxicity	§ 797.1330	21	1
Fish early life stage	§ 797.1600	21	1
Sediment invertebrate bioassay	Adams et al. (Ref. 15)	21	1
Health effects:			
Oral/dermal pharmacokinetics	§ 798.228	12	1
Oncogenicity	§ 798.3300	53	8
Reproduction and fertility effects (oral)	§ 798.4700	29	4
Developmental toxicity (oral)	§ 798.4900	12	1
Dermal sensitization	§ 798.4100	6	0
Functional observation battery (acute and subchronic)	§ 798.6050	18	2
Motor activity (acute and subchronic)	§ 798.6200	18	2
Neuropathology	§ 798.6400	18	2
Mammalian cells in culture	§ 798.5300	10	1
Drosophila sex-linked recessive lethal	§ 798.5275	22	1
In vitro cytogenetics	§ 798.5375	10	1
In vivo cytogenetics	§ 798.5385	24	1
Dominant lethal assay	§ 798.5450	36	5
Heritable translocation assay	§ 798.5460	[2] 25	3

[1] Number of months after effective date, except as indicated.
[2] Figure indicates the reporting deadline, in months, calculated from the date of notification of the test sponsor by certified letter or FEDERAL REGISTER notice that following public review of all the existing data for TBP, the Agency has determined that required testing must be performed.

Although the major occupational exposure route for TBP is dermal, EPA is requiring that testing for oncogenicity, neurotoxicity, development toxicity, reproductive and fertility effects shall be by the oral route because (1) the skin irritating effects of TBP could confound the results of dermal testing, (2) existing supporting studies have been done by the oral route, and (3) there are technical problems conducting dermal tests. EPA is also requiring oral/dermal pharmacokinetics. EPA is specifying that the Sprague-Dawley rat be used for both oncogenicity and pharmacokinetics testing because existing data presented in the proposed rule show this species to be sensitive to TBP.

EPA requires that all data developed under this rule be reported in accordance with its TSCA Good Laboratory Practice (GLP) Standards, in 40 CFR part 792.

In accordance with 40 CFR part 790, under single-phase rulemaking procedures, test sponsors are required to submit individual study plans at least 45 days before initiation of each test.

EPA is required by TSCA section 4(b)(1)(C) to specify the time period during which persons subject to a test rule must submit test data. Final testing requirements, test standards and reporting requirements for this TBP test rule are summarized in the preceding table. Interim progress reports for the tests shall be provided to EPA at 6-month intervals after the effective date of this rule until the final report is submitted to EPA.

TSCA section 14(b) governs EPA disclosure of all test data submitted pursuant to section 4 of TSCA. Upon receipt of data required by this rule, EPA will publish a notice of receipt in the **Federal Register** as required by section 4(d).

Persons who export a chemical which is subject to a section 4 test rule are subject to the export reporting requirements of section 12(b) of TSCA. Final regulations interpreting the requirements of section 12(b) are in 40 CFR part 707. In brief, as of the effective date of this test rule, an exporter of TBP must report to EPA the first annual export or intended export of TBP to each country. EPA will notify the foreign country concerning the test rule for TPB.

For the purpose of this test rule, these guidelines are the test standards that must be met by the test sponsors. The route of administration of TBP for all tests shall be oral unless otherwise specified. Data resulting from these tests will assist EPA in conducting health and environmental risk assessments for TBP. The TSCA test guidelines, proposed modifications, and other cited test guidelines discussed in the following paragraphs in III.B. specify generally accepted minimal conditions for determining toxicities and properties of substances such as TBP to which human and aquatic life are expected to be exposed. Conducting the required studies in accordance with these TSCA guidelines will help ensure that the test results are reliable and adequate.

The oral/dermal pharmacokinetics test guideline in the proposed rule has been revised based upon public comments and is promulgated as § 795.228 Oral/dermal pharmacokinetics test.

EPA periodically reviews the TSCA Test Guidelines, according to the process described at 47 FR 41857 (September 22, 1982).

1. *Health effects.* The neurotoxicity testing required will consist of an acute and subchronic functional observation battery specified in § 798.6050, as modified in § 799.4360(c)(1)(i)(A)(*2*), an acute and subchronic motor activity test specified in § 798.6200, as modified in § 799.4360(c)(1)(i)(B)(*2*), and a subchronic neuropathologic evaluation of tissues perfused in situ specified in § 798.6400, as modified in § 799.4360(c)(1)(i)(C)(*2*).

To assess the developmental effects of TBP, EPA is requiring that testing be conducted by gavage according to § 798.4900, as modified in § 799.4360(c)(2)(i)(B).

To assess the reproductive and fertility effects of TBP, EPA is requiring that testing be conducted according to § 798.4700, as modified in § 799.4360(c)(3)(i)(B) (i)(B).

To assess the mutagenic effects of TBP, EPA is requring that testing be conducted in tiers. First-tier testing will consist of the detection of gene mutation in somatic cells in culture using the test guideline § 798.5300, an in vitro mammalian cytogenetics test using the test guideline in § 798.5375, and an in vivo mammalian bone marrow cytogenetics chromosomal analysis test using the test guideline in § 798.5385, as modified in § 799.4360(c)(5)(i)(B)(*2*). Unless the results of the gene mutation in somatic cells in culture are negative, a sex-linked recessive lethal test in *Drosophila melanogaster* will be required. Second-tier testing will consist of a sex-linked recessive lethal assay in *Drosophila melanogaster* using the test guideline in § 798.5275, as modified in § 799.4360(c)(4)(i)(B)(*2*), and a rodent dominant lethal test using the test guideline in § 798.5450; third-tier testing will consist of a rodent heritable translocation test using the test guidelines in § 798.5460, and as modified in § 799.4360(c)(5)(i)(D)(*2*).

In the proposed rule, EPA would have required third-tier testing consisting of a mouse visible specific locus test using the test guideline in § 798.5200 as modified. Positive results in the sex-linked recessive lethal test may have triggered the requirement for conducting a mouse visible specific locus (MVSL) test. EPA believes that the MVSL may be necessary, when these lower-tier tests are positive, to establish definitively whether a substance is capable of eliciting heritable gene mutations. Under the approach proposed, EPA would have considered the positive results in the lower-tier tests in a public program review, together with other relevant information, during which interested persons would be able to give their views to EPA. If, after the review, EPA had determined that the MVSL was still appropriate, EPA would have notified the test sponsors by letter or **Federal Register** notice that they must conduct the test. If EPA had determined that the test was no longer necessary, EPA would have amended the rule to delete the test requirement.

The final test rule for TBP includes requirements to conduct the lower-tier tests for gene mutation. However, EPA is not promulgating the requirement for the MVSL for TBP at this time. EPA has based its proposal to require the MVSL, in part, on information and assumptions about the cost of conducting the test and the availability of laboratories capable of performing the test. The information and assumptions have since proven to be incorrect. Accordingly, EPA is in the process of reexamining the MVSL requirement for all those chemical substances for which the MVSL has been required or proposed to be required. In particular, EPA is reviewing whether any laboratories are available to perform the MVSL for industry in accordance with the TSCA Good Laboratory Practice Standards at 40 CFR part 792 and the cost of such testing. EPA is also reviewing possible alternative tests to the MVSL for which costs may be lower or laboratory availability may be more certain.

EPA has published a notice in the **Federal Register** concerning the MVSL for TBP and other substances subject to proposed and final TSCA section 4 test rules (53 FR 51897). This notice provides up-to-date information on the cost of MVSL testing, availability of laboratories to perform the MVSL, and possible alternative tests to the MVSL together with their costs and laboratory availability. The notice also addresses EPA's intentions about any changes to the MVSL requirements in the various test rules and provides an opportunity for public comment. If, after this proposed rule is finalized and if after lower tier mutagenicity testing of TBP, EPA concludes that the MVSL is appropriate for TBP, EPA will amend this rule to include the MVSL requirements with any appropriate modifications.

Should the gene mutation in somatic cells test prove negative, no further gene-mutation tests will be required. If the sex-linked recessive lethal test is negative, no further gene-mutation test will be required of TBP.

If the results of the in vitro mammalian cytogenetics test are negative, an in vivo mammalian bone marrow cytogenetics, chromosomal analysis test will be required. Unless the results of the in vivo test are negative, a rodent dominant lethal test will be required. A positive result in the rodent dominant lethal test will trigger the requirement that a heritable translocation test be conducted. Should the in vivo mammalian cytogenetics test results prove negative, no further chromosomal effects testing will be required. If the dominant lethal test is negative, no further chromosomal effects testing will be required for TBP.

Under this final rule, if the result of the second-tier rodent dominant lethal test is positive, EPA will hold a public program review before industry will be required to initiate the third-tier heritable translocation test. The public will participate in this program review either by submitting written comments or commenting during a public meeting. A request for public comment or notification of public meeting will be published in the **Federal Register**. Should EPA determine, from the available weight of evidence, that proceeding to the heritable translocation test is no longer warranted, EPA will propose to repeal this testing requirement and, after public comment, issue a final amendment to rescind this requirement. EPA will notify the test sponsors by certified letter or **Federal Register** notice, following the public program review of all the then-existing data for TBP, if the heritable translocation test must be performed. EPA will also conduct internal program reviews of the reports of the gene mutations in somatic cells in culture assay, the in vitro mammalian bone marrow cytogenetics test, and the in vivo mammalian bone marrow cytogenetics test and other available mutagenicity data to evaluate whether the sex-linked recessive lethal and the rodent dominant lethal tests have been triggered.

For a more detailed discussion of mutagenicity tiered testing and public program review procedures, see EPA's final test rule for the C9 aromatic hydrocarbon fraction published in the **Federal Register** of May 17, 1985 (50 FR 20662).

To assess the oncogenic effects of TBP, EPA is requiring that testing be conducted according to § 798.3300 in Sprague-Dawley rats and in mice via the oral route of administration.

To assess the dermal sensitization effects of TBP, EPA is requiring that testing be conducted according to § 798.4100.

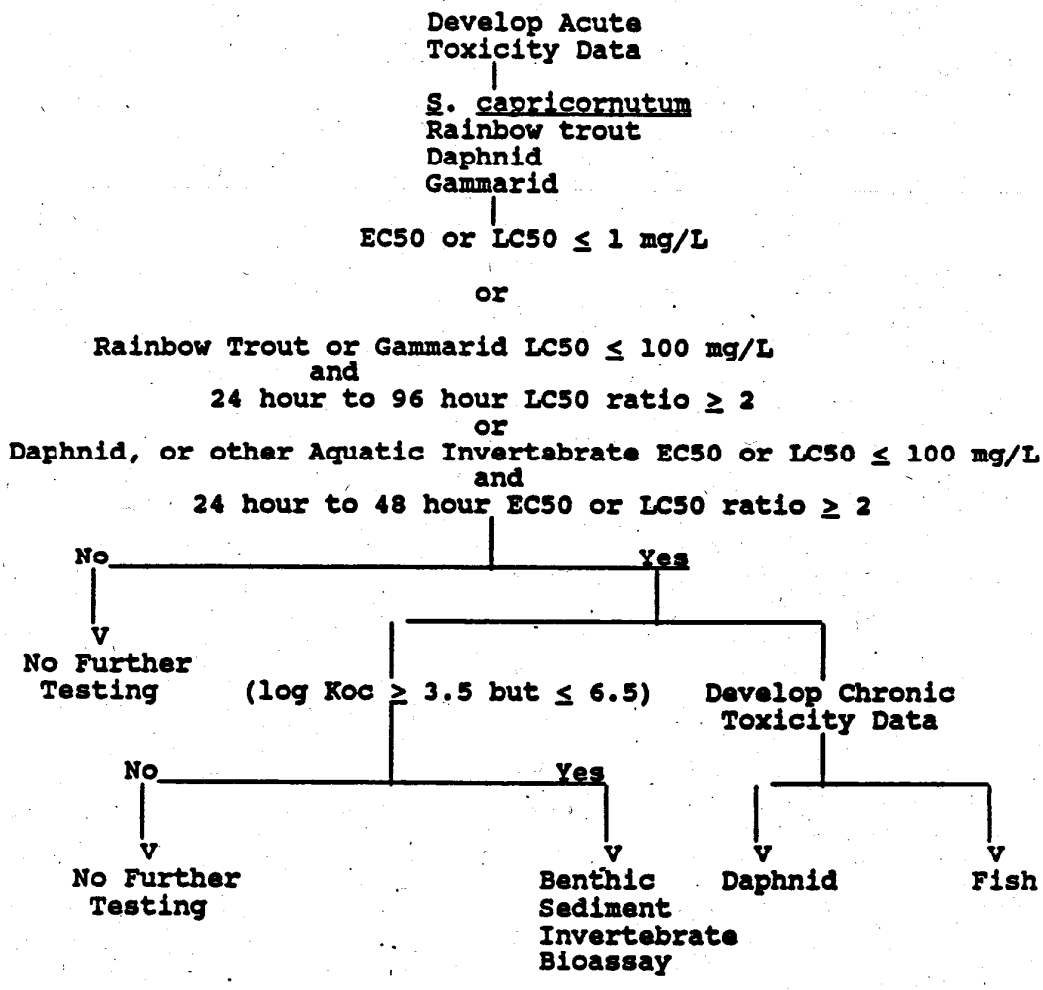
To compare the oral route of administration of TBP in § 798.3300 and the dermal route, in § 798.4100 which is thought to be a primary route of human exposure, EPA is requiring an oral/dermal pharmacokinetic test with TBP to examine absorption, distribution, metabolism, and excretion. EPA is requiring that testing be conducted according to § 798.7485. The decision to require most testing of TBP by the oral route is based on the results of dermal irritation tests showing TBP effects to range from irritating to corrosive (Unit II.F.1. of preamble to proposed rule). Moreover, dermal application of the corrosive TBP could stress the test animals, which may distort test results. TBP is well tolerated by the oral route (Unit II.F. of preamble to proposed rule).

EPA is not requiring the renal effects test recommended by the ITC. Acute and subacute oral studies by Mitomo et al. (Ref. 16) showed kidney tubule damage in rats and mice. However, two oral subchronic rats studies of 90 days and 126 days showed no kidney damage even at dosages higher than the Mitomo studies (Refs. 17 and 18). EPA believes that there are adequate data available to assess the effects of TBP on kidney tubules.

2. *Environmental effects.* EPA is requiring the following environmental effects testing to determine the toxicity of TBP to an alga, a fish, and aquatic invertebrates: (1) *Selenastrum capricornutum*, in accordance with § 797.1050 as modified in § 799.4300(d)(1)(i)(B); (2) rainbow trout in accordance with § 797.1400, as modified in § 799.4360(d)(2)(i)(B); (3) daphnids in accordance with § 797.1300, and as modified in § 799.4360(d)(3)(i)(B); and (4) gammarids in accordance with § 795.120, as modified in § 799.4360(d)(4)(i)(B). Only one test species, rainbow trout, is required for the fish acute toxicity test because an acute test for the fathead minnow is available and adequate in combination with the testing required for the rainbow trout for purposes of assessing the acute toxicity of TBP of fish (see Unit II.C.). All the acute aquatic toxicity data from these tests will be used to determine whether chronic aquatic testing is necessary according to the testing scheme presented in the following figure:

BILLING CODE [illegible]

Figure--DECISION LOGIC FOR DEVELOPING ENVIRONMENTAL EFFECTS DATA



BILLING CODE 6560-50-C

T9

EPA believes that, for chemicals with substantial production and ubiquitous environmental distribution, reliable data should be developed to assess their toxicity and persistence. EPA also believes that, for widely distributed chemicals such as TBP, hazard-based decision criteria should be applied to the data to determine the need to conduct further testing (see Figure). EPA believes it is inappropriate to use integrated decision criteria (i.e., criteria based on predicted environmental concentrations) for these chemicals because the widespread occurrence of these chemicals may make it very difficult to calculate reliable predicted environmental concentrations.

Therefore, if any of the results of acute aquatic toxicity tests satisfy the criteria specified in the Figure, the following chronic tests shall be conducted: (1) The invertebrate *Daphnia* life-cycle test in accordance with § 797.1330, as modified in § 799.4360(d)(5)(i)(B): (2) early-life stage toxicity to fish using the fish with the lower LC50 value in accordance with § 797.1600, as modified in § 799.4360(d)(6)(i)(B); and (3) a benthic sediment invertebrate bioassay with the midge, *Chironomous tentans* (if TBP's measured log Koc satisifies the log Koc criterion in Figure), using three different TBP—containing clean, freshwater sediments having low, medium, and high organic carbon content, using the benthic sediment bioassay method by Adams et al. (Ref. 16) as specified in § 799.4360(d)(7)(i)(B). This incorporation by reference is approved by the Director of the Federal Register. The log Koc criterion is TBP-specific.

3. *Chemical fate.* EPA is requiring measuring the vapor pressure of TBP at 25° C in accordance with § 796.1950, measuring the sediment and soil adsorption isotherm and calculating log Koc in accordance with § 796.2750 (EPA will provide two soil and two sediment samples), and measuring the hydrolysis rate in accordance with § 796.3500.

C. Test Substance

EPA is requiring that TBP of at least 99 percent purity shall be used as the test substance. TBP of such purity is commercially available.

D. Persons Required to Test

Section 4(b)(3)(B) specifies that the activities for which EPA makes section 4(a) findings (manufacture, proceeding, distribution in commerce, use, and/or disposal) determine who bears the responsibility for testing a chemical. Manufacturers and persons who intend to manufacture the chemical are required to test if the findings are based on manufacturing ("manufacture" is defined in section 3(7) of TSCA to include "import"). Processors and persons who intend to process the chemical are required to test if the findings are based on processing. Manufacturers and processors and persons who intend to manufacture and process the chemical are required to test if the exposures giving rise to the potential risk occur during distribution in commerce, use, or disposal of the chemical.

Because EPA has found that there are insufficient data and experience to reasonably determine or predict the effects resulting from manufacturing, processing, distribution, use and disposal of TBP, EPA is requiring that persons who manufacture or process, or who intend to manufacture to process TBP, other than as an impurity, at any time from the effective date of the final test rule to the end of the reimbursement period are subject to the testing requirements contained in this final rule. The end of the reimbursement period will be 5 years after the last final report is submitted or an amount of time equal to that which was required to develop data, whichever is later.

Because TSCA contains provisions to avoid duplicative testing, not every person subject to this rule must individually conduct testing. Section 4(b)(3)(A) of TSCA provides that EPA may permit two or more manufacturers or processors who are subject to the rule to designate one such person or a qualified third person to conduct the test and submit data on their behalf. Section 4(c) provides that any persons required to test may apply to EPA for an exemption from the requirement. EPA promulgated procedures for applying for TSCA section 4(c) exemptions in 40 CFR part 790.

Manufacturers (including importers) subject to this rule are required to submit either a letter of intent to perform testing or an exemption application within 30 days after the effective date of the final test rule or if manufacture commences 30 days after the effective date of the rule but before the end of the reimbursement period, by the date manufacture begins. The required procedures for submitting such letters and applications are described in 40 CFR part 790. Although EPA has not identified any individuals who manufacture TBP as a byproduct, such persons will be subject to the requirements of this test rule.

Processors rule to this subject, unless they are also manufacturers, will not be required to submit letters of intent or exemption applications, or to conduct testing, unless manufacturers fail to submit notices of intent to test or later fail to sponsor the required tests. EPA expects that the manufacturers will pass an appropriate portion of the costs of testing on to processors through the pricing of their products or other reimbursement mechanisms. If manufacturers perform all the required tests, processors will be granted exemptions automatically. If manufacturers fail to submit notices of intent to test or fail to sponsor all the required tests, EPA will publish a separate notice in the Federal Register to notify processors to respond; this procedure is described in 40 CFR part 790.

EPA is not requiring the submission or equivalence data as a condition for exemption from the required testing for TBP. As noted in Unit III.C, EPA is interested in evaluating the effects attributable to TBP and has specified a relatively pure substance for testing.

Manufacturers and processors subject to this test rule must comply with the test rule development and exemption procedures in 40 CFR Part 790 for single-phase rulemaking.

E. Enforcement Provisions

EPA considers failure to comply with any aspect of a section 4 rule to be a violation of section 15 of TSCA. Section 15(1) of TSCA makes it unlawful for any person to fail or refuse to comply with any rule or order issued under section 4. Section 15(3) of TSCA makes it unlawful for any person to fail or refuse to: (1) Establish or maintain records, (2) submit reports, notices, or other information, or (3) permit access to or copying of records required by TSCA or any regulation or rule issued under TSCA.

Additionally, TSCA section 15(4) makes it unlawful for any person to fail or refuse to permit entry or inspection as required by TSCA section 11. Section 11 applies to any "establishment, facility, or other premises in which chemical substances or mixtures are manufactured, processed, stored, or held before or after their distribution in commerce * * *" EPA considers a testing facility to be a place where the chemical is held or stored and, therefore, subject to inspection. Laboratory inspections and data audits will be conducted periodically in accordance with the authority and procedures outlined in TSCA section 11 by designated representatives of EPA for the purpose of determining compliance with the final rule for TBP. These inspections may be conducted for purposes which include verification that testing has begun, schedules are being met, and reports accurately reflect the

T10

underlying raw data, interpretations, and evaluations, and to determine compliance with TSCA GLP standards and the test standards established in this rule.

EPA's authority to inspect a testing facility also derives from section 4(b)(1) of TSCA, which directs EPA to promulgate standards for the development of test data. These standards are defined in section 3(12)(B) of TSCA to include those requirements necessary to assure that data developed under testing rules are reliable and adequate, and to include such other requirements as are necessary to provide such assurance. EPA maintains that laboratory inspections are necessary to provide this assurance.

Violators of TSCA are subject to criminal and civil liability. Persons who submit materially misleading or false information in connection with the requirement of any provision of this rule may be subject to penalties which may be calculated as if they never submitted their data. Under the penalty provisions of section 16 of TSCA, any person who violates section 15 of TSCA could be subject to a civil penalty of up to $25,000 for each violation with each day of operation in violation constituting a separate violation. This provision would be applicable primarily to manufacturers that fail to submit a letter of intent or an exemption request and that continue manufacturing after the deadlines for such submissions. This provision would also apply to processors that fail to submit a letter of intent or an exemption application and continue processing after EPA has notified them of their obligation to submit such documents (see 40 CFR 790.28(b)). Knowing or willful violations could lead to the imposition of criminal penalties of up to $25,000 for each day of violation, imprisonment for up to 1 year, or both. In determining the amount of penalty, EPA will take into account the seriousness of the violation and the degree of culpability of the violator as well as the other factors listed in TSCA section 16. Other remedies are available to EPA under section 17 of TSCA, such as seeking an injunction to restrain violations of TSCA section 4.

Individuals as well as corporations could be subject to enforcement actions. Sections 15 and 16 of TSCA apply to "any person" who violates provisions of TSCA. EPA may, at its discretion, proceed against individuals as well as companies themselves. In particular, this includes individuals who report false information or who cause it to be reported. In addition, the submission of false, fictitious, or fraudulent statements is a violation under 18 U.S.C. 1001.

IV. Economic Analysis of Final Rule

To assess the potential economic impact of this final rule, EPA has prepared an economic analysis that evaluates the potential for significant economic impacts on the industry as a result of the required testing. The economic analysis estimates the costs of conducting the required testing and evaluates the potential costs by examining four market characteristics of TBP: (1) Price sensitivity of demand, (2) industry cost characteristics, (3) industry structure, and (4) market expectations. If these indications are negative, no further economic analysis is performed. However, if the first level of analysis indicates a potential for significant economic impact, a more comprehensive and detailed analysis is conducted which more precisely predicts the magnitude and distribution of the expected impact.

Total testing costs for the testing of TBP are estimated to range from $1.3 to $1.7 million. To predict the financial decision-making practices of manufacturing firms, these costs have been annualized. Annualized costs are compared with annual revenue as an indication of potential impact. The annualized costs represent equivalent constant costs which would have to be recouped each year of the payback period to finance the testing expenditure in the first year.

The annualized test costs (using a cost of capital of 7 percent over a period of 15 years) range from $140,400 to $186,700. Based on 1986 production of 6 million pounds, the unit test costs range from $0.02 to $0.03 per pound. In relation to the selling price of $1.00 per pound for TBP, these costs are equivalent to 1.46 to 1.95 percent of the price.

Though the annualized unit costs of the tests relative to the product price of TBP appear to be high, EPA believes that the potential for adverse economic impact is low. This conclusion is based on the following observations:

1. The demand for TBP appears to be inelastic with respect to price in its largest use, primarily because of the current lack of viable substitutes.

2. The market for TBP appears to be stable.

Refer to the economic analysis which is contained in the public record for this rulemaking for a complete discussion of test costs estimation and potential for economic impact resulting from these costs.

V. Availability of Test Facilities and Personnel

Section 4(b)(1) of TSCA requires E to consider "the reasonably foreseea availability of the facilities and personnel needed to perform the testing required under the rule". Therefore, EPA conducted a study to assess the availability of test facilities and personnel to handle the additional demand for testing services created by this section 4 test rule (Ref. 19). Copies of the study, Chemical Testing Industry: Profile of Toxicological Testing, can be obtained through the National Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, VA 22161 (PB-82-140773). On the basis of this study, EPA believes that there will be available test facilities and personnel to perform the testing specified in this rule.

EPA has reviewed the availability of contract laboratory facilities to conduct the required neurotoxicity tests (Ref. 20) and believes that facilities will be available for the tests. The laboratory review indicates that few laboratories are currently conducting these tests according to the TSCA test guidelines and TSCA GLP Standards. However, the barriers faced by testing laboratories to conduct these tests are not formidable. Laboratories will have to invest in testing equipment and personnel training but EPA believes that these investments will be recovered as the neurotoxicity testing program under TSCA section 4 continues. EPA's expectations of laboratory availability were borne out under the testing requirements of the C9 aromatic hydrocarbon fraction test rule (50 FR 20675; May 17, 1985). Pursuant to that rule, manufacturers were able to contract with a laboratory to conduct the testing according to TSCA test guidelines and TSCA GLP Standards.

VI. Rulemaking Record

EPA has established a record for this rulemaking (Docket Number OPTS-42100B). This record contains the basic information considered by EPA in developing this proposal and appropriate Federal Register notices.

This record includes:

A. Supporting Documentation

(1) Federal Register notices pertaining to this rule consisting of:

(a) Notice containing the ITC's intent to designate TBP to the Priority List (51 FR 18368; May 19, 1986), and the designation of TBP to the Priority List (51 FR 41417; November 14, 1986).

(b) Rules requiring TSCA section 8(a) and 8(d) reporting on TBP (51 FR 18323; May 19, 1986).

(c) TSCA test guidelines cited as test standards for this rule.

(2) Economic Impact Analysis of Proposed Test Rule for Tributyl Phosphate.

(3) Communications consisting of: (a) Written public comments and letters.

(b) Contact reports of telephone conversations.

(c) Meeting summaries.

(4) Reports—published and unpublished factual materials.

B. References

(1) TBPTF. Tributyl Phosphate Task Force of the Synthetic Organic Chemicals Manufacturers Association. Washington, DC. Comments on EPA's proposed test rule for tributyl phosphate. (January 11, 1988).

(2) TBPTF. 1987 U.S. Survey of Tributyl Phosphate Users, Potential Exposure and Safety Procedures, conducted by Temple, Barker, Sloan Inc. (1987).

(3) TBPTF. Letter from J. Kneiss, Managing Director of the Tributyl Phosphate Task Force to M. McCommas, Office of Toxic Substances, U.S. Environmental Protection Agency, July 11, 1988.

(4) USEPA. U.S. Environmental Protection Agency. Exposure Tech Team notes on TBPTF's exposure survey from S. Shapley to M. McCommas, Office of Toxic Substances (1988).

(5) USEPA. Tributyl Phosphate (TBP) task force exposure estimates for populations handling aircraft hydraulic fluids containing TBP. Memo from V. Rodriguez to M. McCommas. Office of Toxic Substances (1988).

(6) Ainsworth, M. "Methods for measuring percutaneous absorption." *Journal of the Society of Cosmetic Chemistry* 11:69–78 (1960).

(7) Marzulli, F.N., Callahan, J.F., and Brown, D.W.C. "Chemical structure and skin penetrating capacity of a short series of organo phosphates and phosphoric acid." *Journal of Investigative Dermatology* 44:339–344 (1965).

(8) Tregar, R. "The permeability of mammalian skin to ions." *Journal of Investigative Dermatology* 46:16–23 (1966).

(9) Marzulli, F.N. et al. "Techniques for studying skin penetration." *Toxicology and Applied Pharmacology* Supplement 2, 3:76–83 (1969).

(10) Robertson, D.G., Mattson, A.M., Bestervelt, L.L., Richardson, and R.J., Anderson, R.J., "Time course of electrophysiological effects induced by di-n-butyl-2,2-dichlorovinyl phosphate (DBCV) in the adult hen." *Journal of Toxicology and Environmental Health* 23:283–294 (1988).

(11) Roberts, D.V. "A longitudinal electromyographic study of six men occupationally exposed to organophosphorus compounds." *International Archives of Occupational and Environmental Health* 38:221–229 (1977).

(12) Brown, D.R. and Murphy, S.D. "Factors influencing dimethoate and trimethyl phosphate-induced narcosis in rats and mice." *Toxicology and Applied Pharmacology* 18:895–906 (1971).

(13) Deichmann, W.B. and Witherup, S. "Observations on the effects of trimethyl phosphate upon experimental animals." *Journal of Pharmacology and Experimental Therapeutics* 88:338–347 (1946).

(14) USEPA. Aggregated production volume for CASRN 126–73–8, 1985. U.S. Environmental Protection Agency, Confidential Data Branch, Office of Toxic Substances, Washington, DC (1987).

(15) Adams, W.J., Kimmerle, R.A., and Mosher, R.G. "Aquatic safety assessment of chemicals sorbed to sediments." Published in Aquatic Toxicology and Hazard Assessment Seventh Symposium. ASTM STP 854. American Society for Testing and Materials, Philadelphia, PA pp. 429–453 (1985).

(16) Mitomo, L., Ito, T., Ueno, Y., and Terao, K. "Toxicological studies on tributyl phosphate. I. Acute and Subacute Toxicities." *Journal of Toxicological Services* 5:270–271 (1969).

(17) Laham, S., Long, G., and Broxup, B. "Induction of urinary bladder hyperplasia in Sprague–Dawley rats orally administered tri-n-butyl phosphate." *Archives of Environmental Health* 40:301–306 (1985).

(18) FMC Corporation. TSCA 8(d) submission 88800000106, Thirteen week feeding study of tributyl phosphate in rats. Office of Toxic Substances, U.S. EPA, Washington, DC (1988).

(19) NTIS. National Technical Information Service. Chemical Testing Industry: Profile of Toxicological Testing (PB 82–140773). Springfield, VA (1986).

(20) USEPA. Evaluation of TSCA test guidelines for neurotoxicity testing. Mathtech, Inc. Contract Number 68–02–4235. Regulatory Impact Branch. Office of Toxic Substances, Washington, DC. (April 4, 1987).

Confidential Business Information (CBI), while part of the record, is not available for public review. A public version of the record, from which CBI has been deleted, is available for inspection in the OPTS Reading Room G–004, NE Mall, 401 M Street, SW., Washington, DC, from 8 a.m. to 4 p.m., Monday through Friday except legal holidays.

VII. Other Regulatory Requirements

A. Executive Order 12291

Under Executive Order 12291, EPA must judge whether a regulation is "major" and therefore subject to the requirement of a Regulatory Impact Analysis. EPA has determined that this test rule is not major because it does not meet any of the criteria set forth in section 1(b) of the Order; i.e., it will not have an annual effect on the economy of at least $100 million, will not cause a major increase in costs or prices, and will not have a significant adverse effect on competition or the ability of U.S. enterprise to compete with foreign enterprises.

This regulation was submitted to the Office of Management and Budget (OMB) for review as required by Executive Order 12291. Any written comments from OMB to EPA, and any EPA responses to those comments, are included in the rulemaking record.

B. Regulatory Flexibility Act

Under the Regulatory Flexibility Act (5 U.S.C. 601 *et seq.*, Pub. L. 96–354, September 19, 1980), EPA is certifying that this test rule will not have a significant impact on a substantial number of small businesses because: (1) They are not likely to perform testing themselves, or to participate in the organization of the testing effort; (2) they will experience only very minor costs, if any, in securing exemption from testing requirements; and (3) they are unlikely to be affected by reimbursement requirements.

C. Paperwork Reduction Act

The information collection requirements contained in this rule have been approved by the OMB under the provisions of the Paperwork Reduction Act, 44 U.S.C. 3502 *et seq.* and have been assigned OMB control number 2070–0033.

Public reporting burden for this collection of information is estimated to average 486 hours per response including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information.

Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Chief, Information Policy Branch, PM–223, U.S. Environmental Protection Agency, 401 M St., SW., Washington, DC 20460; and to the Office of Information and Regulatory Affairs, Office of Management and Budget, Washington, DC 20503, marked "Attention: Desk Officer for EPA."

List of Subjects in 40 CFR Parts 795 and 799

Chemicals, Environmental protection, Hazardous substances, Testing, Laboratories, Recordkeeping and reporting requirements, Incorporation by reference.

Dated: August 3, 1989.

Victor J. Kimm,

Acting Assistant Administrator for Pesticides and Toxic Substances.

Therefore, 40 CFR Chapter I, Subchapter R is amended as follows:

PART 795—[AMENDED]

1. In part 795:

a. The authority citation continues to read as follows:

Authority: 15 U.S.C. 2603.

b. Section 795.228 is added to subpart D, to read as follows:

§ 795.228 Oral/dermal pharmacokinetics.

(a) *Purpose.* The purpose of these studies are to: (1) Ascertain whether the pharmacokinetics and metabolism of a chemical substance or mixture ("test substance") are similar after oral and dermal administration.

(2) Determine bioavailability of a test substance after oral and dermal administration.

(3) Examine the effects of repeated dosing on the pharmacokinetics and metabolism of the test substance.

(b) *Definitions.* (1) "Bioavailability" refers to the rate and relative amount of administered test substance which reaches the systemic circulation.

(2) "Metabolism" means the study of the sum of the processes by which a particular substance is handled in the body and includes absorption, tissue distribution, biotransformation, and excretion.

(3) "Percent absorption" means 100 times the ratio between total excretion of radioactivity following oral or dermal administration and total excretion following intravenous administration of test substance.

(4) "Pharmacokinetics" means the study of the rates of absorption, tissue distribution, biotransformation, and excretion.

(c) *Test procedures.*—(1) *Animal selection.*—(i) *Species.* The rat shall be used for pharmacokinetics testing because it has been used extensively for metabolic and toxicological studies. For dermal bioavailability studies, the rat and the mini-pig shall be used.

(ii) *Test animals.* For pharmacokinetics testing and dermal studies, adult male and female Sprague-Dawley rats, 7 to 9 weeks of age, shall be used. For dermal studies, young adult mini-pigs shall also be used. The animals should be purchased from a reputable dealer and shall be identified upon arrival at the testing laboratory. The animals shall be selected at random for the test groups and any animal showing signs of ill health shall not be used. In all studies, unless otherwise specified, each test group shall contain at least 4 animals of each sex for a total of at least 8 animals.

(iii) *Animal care.* (A) The animals shall be housed in environmentally controlled rooms with at least 10 air changes per hour. The rooms shall be maintained at a temperature of 24 ± 2 °C and humidity of 50 ± 20 percent with a 12-hour light/dark cycle per day. The animals shall be kept in a quarantine facility for at least 7 days prior to use and shall be acclimated to the experimental environment for a minimum of 48 hours prior to administration of the test substance.

(B) 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*. The mini-pig diet shall be supplemented with adequate amounts of ascorbic acid in the drinking water.

(2) *Administration of test substance.*—(i) *Test substance.* The use of a radioactive test substance is required for all studies. Ideally, the purity, radioactive and nonradioactive, is greater than 99 percent. The radioactive and nonradioactive test substances shall be chromatographed separately and together to establish purity and identity. If the purity is less than 99 percent or if the chromatograms differ significantly, EPA should be consulted.

(ii) *Dosage and treatment.*—(A) *Intravenous.* The low dose of test substance, in an appropriate vehicle, shall be administered intravenously to groups of rats and mini-pigs of each sex. If feasible, the same low dose should be used for intravenous, oral, and dermal studies.

(B) *Oral.* Two doses of test substance shall be used in the oral study, a low dose and a high dose. The high dose should ideally induce some overt toxicity, such as weight loss. The low dose should correspond to a no-observed effect level. The oral dosing shall be accomplished by gavage or by administering the encapsulated test substance. If feasible, the same high and low doses should be used for oral and dermal studies.

(C) *Dermal.* (*1*) 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 shaved with an electric clipper 24 hours before treatment. The test substance shall be applied to the intact shaven skin (approximately 2 cm^2 for rats, 5 cm^2 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.

(*2*) Washing efficacy study. Before initiation of the dermal absorption studies, an initial washing efficacy experiment shall be conducted to assess the removal of the applied low dose of the test substance by washing the exposed skin area with soap and water and an appropriate organic solvent. The low dose shall be applied to 4 rats and 4 mini-pigs in accordance with paragraph (c)(2)(ii)(C)(*1*) of this section. After application (5 to 10 minutes), the treated areas of 2 rats and 2 mini-pigs shall be washed with soap and water and the treated areas of the remaining rats and pigs shall be washed with an appropriate solvent. The amounts of test substance recovered in the washings shall be determined to assess efficacy of its removal by washing.

(iii) *Dosing and sampling schedule.*—(A) *Rat studies.* After administration of the test substance, each rat shall be placed in a metabolic unit to facilitate collection of excreta. For the dermal studies, excreta from the rats shall also be collected during the 6 hour exposure periods. At the end of each collection period, the metabolic units shall be cleaned to recover any excreta that might adhere to them. All studies, except the repeated dosing study, shall be terminated at 7 days or after at least 90 percent of the radioactivity has been recovered in the excreta, whichever occurs first.

(*1*) *Intravenous study.* Group A shall be dosed once intravenously at the low dose of test substance.

(*2*) *Oral study.* (*i*) Group B shall be dosed once per os with the low dose of test substance.

(*ii*) Group C shall be dosed once per os with the high dose of test substance.

(*3*) *Dermal studies.* Unless precluded by corrosivity, the test substance shall be applied and kept on the skin for a minimum of 6 hours. At the time of removal of the porous covering, the treated area shall be washed with an appropriate solvent to remove any test substance that may be on the skin surface. Both the covering and the washing shall be assayed to recover residual radioactivity. At the termination of the studies, each animal shall be sacrificed and the exposed skin area removed. An appropriate section of the skin shall be solubilized and assayed for radio-activity to ascertain if the skin acts as a reservoir for the test substance. Studies on the dermal absorption of corrosive test substances should be discussed with EPA prior to initiation.

(*i*) Group D shall be dosed once dermally with the low dose of test compound.

(*ii*) Group E shall be dosed once dermally with the high dose of the test substance.

(*4*) *Repeated dosing study.* Group F shall receive a series of single daily oral low doses of nonradioactive test substance over a period of at least 7 days. Twenty-four hours after the last nonradioactive dose, a single oral low dose of radioactive test substance shall be administered. Following dosing with

the radioactive substance, the rats shall be placed in individual metabolic units as described in paragraph (c)(2)(iii) of this section. The study shall be terminated at 7 days after the last dose, or after at least 90 percent of the radioactivity has been recovered in the excreta, whichever occurs first.

(B) *Mini-Pig studies.* For all mini-pig studies, the test groups shall consist of four young adult animals. After administration of the test substance, each mini-pig shall be kept in a metabolic unit to facilitate collection of excreta. At the end of each collection period, the metabolic units are to be cleaned to recover any excreta that might adhere to them. All studies shall be terminated at 7 days, or after at least 90 percent of the radio-activity has been recovered in the excreta, whichever occurs first.

(1) *Intravenous study.* Group G is to be dosed once intravenously at the low dose of the test substance.

(2) *Dermal studies.* Following the experimental guidance described in (c)(2)(iii)(A)(*3*) of this section:

(*i*) Group H shall be dosed once dermally with the low dose of test substance.

(*ii*) Group I shall be dosed once dermally with the high dose of the test substance.

(3) *Types of studies*—(i) *Pharmacokinetics studies*—(A) *Rat studies.* Groups A through F shall be used to determine the kinetics of absorption of the test substance. In the group administered the test substance by intravenous routes, (i.e., Group A), the concentration of radioactivity in blood and excreta shall be measured following administration. In groups administered the test substance by the oral and dermal route (i.e., Groups B, C, D, E and F), the concentration of radioactivity in blood and excreta shall be measured at selected time intervals during and following the exposure period.

(B) *Mini-Pig studies.* Groups G, H, and I shall be used to determine the extent of dermal absorption of the test substance. The amount of radioactivity in excreta shall be determined at selected time intervals.

(ii) *Metabolism studies—Rat studies.* Groups A through F shall be used to determine the metabolism of the test substance. Urine, feces, and expired air shall be collected for identification and quantification of the test substance and metabolites.

(4) *Measurements*—(i) *Pharmacokinetics.* Four animals from each group shall be used for these purposes.

(A) *Rat studies*—(*1*) *Bioavailability.* The levels of radioactivity shall be determined in whole blood, blood plasma or blood serum at 15 and 30 minutes and at 1, 2, 8, 24, 48, and 96 hours after initiation of dosing.

(*2*) *Extent of absorption.* The total quantities of radioactivity shall be determined for excerta collected daily for 7 days or until at least 90 percent of the radioactivity has been recovered in the excreta.

(*3*) *Excretion.* The quantities of radioactivity eliminated in the urine, feces, and expired air shall be determined separately at appropriate time intervals. The collection of carbon dioxide may be discontinued when less than one percent of the dose is found to be exhaled as radioactive carbon dioxide in 24 hours.

(*4*) *Tissue distribution.* At the termination of each study, the quantities of radioactivity in blood and in various tissues, including bone, brain, fat, gastrointestinal tract, gonads, heart, kidney, liver, lungs, muscle, skin, and residual carcass of each animal shall be determined.

(*5*) *Changes in pharmacokinetics.* Results of pharmacokinetics measurements (i.e., bioavailability and extent of absorption, tissue distribution, and excretion) obtained in rats receiving the single low oral dose of the test substance (Groups B and C) shall be compared to the corresponding results obtained in rats receiving repeated oral doses of the test substance (Group F).

(B) *Mini-Pig studies—Extent of absorption.* The total quantities of radioactivity shall be determined for excreta daily for 7 days or until at least 90 percent of the test substance has been excreted.

(ii) *Metabolism.* Four animals from each group shall be used for these purposes.

(A) *Rat studies*—(*1*) *Biotransformation.* Appropriate qualitative and quantitative methods shall be used to assay urine, feces, and expired air collected from rats. Efforts shall be made to identify any metabolite which comprises 5 percent or more of the administered dose and the major radioactive components of blood.

(*2*) *Changes in biotransformation.* Appropriate qualitative and quantitative assay methodology shall be used to compare the composition of radioactive compounds in excreta from rats receiving a single oral dose (Groups B and C) with those in the excreta from rats receiving repeated oral doses (Group H).

(d) *Data and reporting.* The final test report shall include the following:

(1) *Presentation of results.* Numerical data shall be summarized in tabular form. Pharmacokinetic data shall also be presented in graphical form. Qualitative observations shall also be reported.

(2) *Evaluation of results.* All quantitative results shall be evaluated by an appropriate statistical method.

(3) *Reporting results.* In addition to the reporting requirements as specified in 40 CFR part 792, the following specific information shall be reported:

(i) Species and strains of laboratory animals.

(ii) Chemical characterization of the test substance, including:

(A) For the radioactive test substances, information on the site(s) and degree of radiolabeling, including type of label, specific activity, chemical purity, and radiochemical purity.

(B) For the nonradioactive compound, information on chemical purity.

(C) Results of chromatography.

(iii) A full description of the sensitivity, precision, and accuracy of all procedures used to generate the data.

(iv) Percent of absorption of test substance after oral and dermal exposures to rats and dermal exposure to mini-pigs.

(v) Quantity and percent recovery of radioactivity in feces, urine, expired air, and blood. In dermal studies on rats and mini-pigs, include recovery data for skin, skin washings, and residual radioactivity in the covering as well as results of the washing efficacy study.

(vi) Tissue distribution reported as quantity of radioactivity in blood and in various tissues, including bone, brain, fat, gastrointestinal tract, gonads, heart, kidney, liver, lung, muscle, skin and in residual carcass of rats.

(vii) Materials balance developed from each study involving the assay of body tissues and excreta.

(viii) Biotransformation pathways and quantities of test substance and metabolites in excreta collected after administering single high and low doses to rats.

(ix) Biotransformation pathways and quantities of the test substance and metabolites in excreta collected after administering repeated low doses to rats.

(x) Pharmacokinetics model(s) developed from the experimental data.

PART 799—[AMENDED]

2. In part 799:

a. The authority citation continues to read as follows:

Authority: 15 U.S.C. 2603, 2611, 2625.

b. Section 799.4360 is added to subpart B to read as follows:

§ 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 within 12 months of the effective date of the final rule.

(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 within 29 months of the effective date of the final rule.

(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 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 § 798.5400 of this chapter except for the provisions of paragraph (d)(5)(iii) of § 798.5400.

(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*]

(ii) *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) and (6)(i) 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.

(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 pharmacokinetics test shall be conducted with TBP in accordance with § 795.228 of this chapter.

(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 within 12 months of the effective date of the final rule.

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

(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 provisons 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 dissovled 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 within 21 months of the effective date of the final rule.

(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 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 within 21 months of the effective date of the final rule.

(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 to 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, Room 8301, 1100 L St., NW., Washington, DC 20408, and copies may be obtained from the EPA TSCA Public Docket Office in Rm. G–004, NE Mall, 401 M St., SW., Washington, DC 20460. 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 within 6 months of the effective date of the final rule.

(2) *Sediment and soil adsorption isotherm.*—(i) *Required testing.* Sediment and soil absorption 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 absorption isotherm test required under paragraph (d)(2) of this section shall be completed and the final report submitted to EPA within 6 months of the effective date of the final rule.

(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) of this section shall be completed and the final report submitted to EPA within 6 months of the effective date of the final rule.

(f) *Effective date.* (1) The effective date of the final rule is September 27, 1989.

(2) The guidelines and other test methods cited in this section are referenced here as they exist on September 27, 1989.

(Information collection requirements have been approved by the Office of Management and Budget under Control Number 2070–0033.)

[FR Doc. 89–18850 Filed 8–11–89; 8:45 am]
BILLING CODE 6560–50–M

111