§799.18 Chemicals subject of test rules or consent orders for which the testing reimbursement period has passed.

The following table lists substances and mixtures that have been the subjects of section 4 testing actions and for which the testing reimbursement period has terminated (sunset). The Federal Register citation in the table is for the final rule/consent order that includes the particular substance for which the sunset date listed in the table below applies. Section 12(b) export notification is no longer required for these substances and mixtures. Substances that are the subjects of two or more section 4 testing actions may have section 4 reimbursement or section 12(b) export notification requirements that have not sunset; see subparts B, C, and D of this part to determine if certain other section 4 testing requirements apply. Additionally, section 12(b) export notification may also be triggered by proposed or final action under TSCA section 5, 6, or 7 (in addition to final actions under section 4); see 40 CFR part 707, subpart D for further information regarding the TSCA section 12(b) export notification requirements.

CAS No.	Chemical Name	FR cite	Sunset dates
	C-9 Aromatic Hydrocarbon Fraction[1]	50 FR 20662, 5/17/85	Aug 13, 1994
62-53-3	Aniline	53 FR 31804, 8/19/88	July 27, 1994
71-55-6	1,1,1-Trichloroethane	49 FR 39810, 10/10/84	June 29, 1992
75-56-9	Propylene oxide	50 FR 48762, 11/27/85	Dec,21, 1992
78-87-5	1,2-Dichloropropane	52 FR 37138, 10/5/87	April 17, 1995
79-94-7	Tetrabromobisphenol-A	52 FR 25219, 7/6/87	Aug 24, 1994
80-05-7	Bisphenol A	51 FR 33047, 9/18/86	April 6, 1993
84-65-1	Anthraquinone	52 FR 21018, 6/4/87	Aug 21, 1994
87-61-6	1,2,3-trichlorobenzene	51 FR 11728,4/7/86	Nov 13, 1993
88-74-4	2-nitroaniline	53 FR 31804, 8/19/88	Sept 19, 1994
92-52-4	1,1-Biphenyl	50 FR 37182, 9/12/85	March 15, 1994
95-48-7	Ortho-cresols AKA 2-methylphenol	51 FR 15771, 4/28/86	Dec. 6, 1994
95-50-1	1,2-dichlorobenzene	51 FR 24657, 7/8/86	April 27, 1994
95-51-2	2-chloroaniline	53 FR 31804, 8/19/88	Sept 6, 1994
95-76-1	3,4-dichloroaniline	53 FR 31804, 8/19/88	Oct 2, 1994
95-94-3	1,2,4,5-tetrachlorobenzene	51 FR 24657,7/8/86	April 27, 1994
97-02-9	2,4-dinitroaniline	53 FR 31804, 8/19/88	Oct 19, 1993
98-82-8	Cumene	53 FR 28195, 7/27/88	March 11, 1995
99-30-9	2,6-dichloro-4-nitroaniline	53 FR 31804, 8/19/88	Aug 6, 1994
100-01-6	4-nitroaniline	53 FR 31804, 8/19/88	Sept 19, 1994
106-44-5	Para-cresols AKA 4-methylphenol	51 FR 15771, 4/28/86	Dec. 6, 1994
106-46-7	1,4-dichlorobenzene	51 FR 24657, 7/8/86	Jan 22, 1994
106-47-8	4-chloroaniline	53 FR 31804, 8/19/88	Oct 19, 1993
108-39-4	Meta-cresols AKA 3-methylphenol	51 FR 15771, 4/28/86	Dec. 6, 1994
108-90-7	Monochlorobenzene	51 FR 24657, 7/8/86	Nov 13, 1991
112-90-3	Oleylamine	52 FR 31962, 8/24/87	Nov 28, 1994

116-14-3	Tetrafluoroethene	52 FR 21516, 6/8/87	May 19, 1993
116-15-4	Hexafluoropropene	52 FR 21516, 6/8/87	Jan 22, 1994
123-31-9	Hydroquinone	50 FR 53145, 12/30/85	Dec. 11, 1994
149-57-5	2-Ethylhexanoic Acid	51 FR 40318, 11/6/86	June 19, 1993
328-84-7	3,4-Dichlorobenzotrifluoride	52 FR 23547, 6/23/87	Dec. 5, 1993
25550-98-5	Diisodecyl Phenyl Phosphite	54 FR 8112, 2/24/89	May 21, 1995

[1] Only substances obtained from the reforming of crude petroleum.

[60 FR 31923, June 19, 1995]

§799.1053 Trichlorobenzenes.

(a) Identification of testing substance. (1) 1,2,3- and 1,2,4-trichlorobenzenes, CAS Numbers 87-61-6 and 120-82-1 respectively, shall be tested in accordance with this section.

(2) The substances identified in paragraph (a)(1) of this section shall be 99 percent pure and shall be used as the test substances in each of the tests specified.

(3) For health effects testing required under paragraph (e) of this section, the test substance shall not contain more than 0.05 percent benzene and 0.05 percent hexachlorobenzene.

(b) Persons required to submit study plans, conduct tests, and submit data. (1) All persons who manufacture or process substances identified in paragraph (a)(1) of this section, other than an impurity, from May 21, 1986, to the end of the reimbursement period, shall submit a letter of intent to test or exemption applications and shall conduct tests, in accordance with part 792 of this chapter, and submit data as specified in this section, subpart A of this part and part 790 of this chapter for two-phase rulemaking.

(2) Persons subject to this section are not subject to the requirements of §790.50(a) (2), (5), (6) and (b) and §790.87(a)(1)(ii) of this chapter.

(3) Persons who notify EPA of their intent to conduct tests in compliance with the requirements of this section must submit plans for those tests no later than 30 days before the initiation of each of those tests.

(4) In addition to the requirements of §790.87(a)(2) and (3) of this chapter, EPA will conditionally approve exemption applications for this rule if EPA has received a letter of intent to conduct the testing from which exemption is sought and EPA has adopted test standards and schedules in a final Phase II test rule.

(5) For health effects testing required under paragraph (e) of this section, all persons who manufacture (import) or process 1,2,4-trichlorobenzene, other than as an impurity, after the effective date of this rule (August 21, 1986) to the end of the reimbursement period shall submit letters of intent to conduct testing or exemption applications, submit study plans, conduct tests, and submit data as specified in this section, subpart A of this part, and parts 790 and 792 of this chapter for single-phase rulemaking.

(c) [Reserved]

(d) Environmental effects testing. 1,2,3- and 1,2,4-trichlorobenzenes shall be tested in accordance with this section.

(1) Marine invertebrate acute toxicity testing—(i) Required testing. Testing using measured concentrations, flow through or static renewal systems, and systems that control for evaporation of the test substance, shall be conducted for 1,2,3- and 1,2,4-trichlorobenzenes. Testing shall be conducted with mysid shrimp (Mysidopis bahia) to develop data on the acute toxicity of the above chlorobenzene isomers to marine invertebrates.

(ii) Test standards. The marine invertebrate (mysid shrimp, Mysidopis bahia) acute toxicity testing for 1,2,3- and 1,2,4-trichlorobenzenes shall be conducted in accordance with §797.1930 of this chapter.

(iii) Reporting requirements. (A) The acute toxicity tests on marine invertebrates shall be completed and the final report submitted to EPA within 1 year of the effective date of the final Phase II test rule.

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

(2) Marine fish acute toxicity testing—(i) Required testing. Testing using measured concentrations, flow through systems, and systems that control for evaporation of the test substance shall be conducted for 1,2,3-trichlorobenzene. Testing shall be conducted with Silversides (Menidia menidia) to develop data on the acute toxicity of 1,2,3-trichlorobenzene to saltwater fish.

(ii) Test standard. The marine fish (silverside minnow, Menida menidia) acute toxicity test shall be conducted for 1,2,3-trichlorobenzene in accordance with §797.1400 of this chapter.

(iii) Reporting requirements. (A) The marine fish (silversides minnow, Menidia menidia) acute toxicity test shall be completed and the final results submitted within 1 year of the effective date of the Phase II final test rule.

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

(3) Freshwater fish acute toxicity testing—(i) Required testing. Testing using measured concentrations, flow through systems, and systems that control evaporation of the test substance shall be conducted for 1,2,3-trichlorobenzene. A 96-hour LC50 test shall be conducted with the fathead minnow (Pimephales promelas) to develop data on the acute toxicity of 1,2,3-trichlorobenzene to freshwater fish.

(ii) Test standard. The freshwater fish (fathead minnow, Pimephales promelas) acute toxicity test shall be conducted for 1,2,3-trichlorobenzene in accordance with §797.1400 of this chapter.

(iii) Reporting requirements. (A) The freshwater fish acute toxicity study shall be completed and the final report submitted to EPA within 1 year of the effective date of the final Phase II test rule.

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

(4) Freshwater invertebrate acute toxicity testing—(i) Required testing. Testing using measured concentrations, flow through or static renewal systems, and systems that control for evaporation of the test substance shall be conducted for 1,2,3-trichlorobenzene. A 96-hour EC50 shall be conducted for one species of Grammarus to develop data on the acute toxicity of 1,2,3-trichlorobenzene to aquatic freshwater invertebrates.

(ii) Test standard. The freshwater invertebrate (Gammarus sp.) acute toxicity test shall be conducted for 1,2,3-trichlorobenzene in accordance with §795.120 of this chapter.

(iii) Reporting requirements. (A) The freshwater invertebrate acute toxicity test shall be completed and the final report submitted to EPA within 411 days of the effective date of the final Phase II rule.

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

(5) Mysid shrimp chronic toxicity testing—(i) Required testing. Testing using measured concentrations, flow through or static renewal systems, and systems that control for evaporation of the test substance shall be conducted for 1,2,4-trichlorobenzene. Testing shall be conducted with mysid shrimp (Mysidopsis bahia) to develop data on the chronic toxicity of 1,2,3-trichlorobenzene, should the acute LC50 of this chemical to mysid shrimp be determined to be less than 1 ppm.

(ii) Test standards. The mysid shrimp (Mysidopis bahia) chronic toxicity test shall be conducted for 1,2,4-trichlorobenzene in accordance with §797.1950 of this chapter. Testing shall also be conducted according to §797.1950 for 1,2,3-trichlorobenzene should the results of testing required by (d)(1)(ii) of this section yield an acute LC50 for this chemical substance of less than 1 ppm.

(iii) Reporting requirements. (A) The mysid shrimp chronic toxicity test for 1,2,4-trichlorobenzene shall be completed and the final report submitted to EPA within 1 year of the effective date of the final Phase II rule. The mysid shrimp chronic toxicity test for 1,2,3-trichlorobenzene, (required if the LC50 is less than 1 ppm), shall be completed and final report submitted to EPA within 15 months of the effective date of the final Phase II rule.

(B) Progress reports shall be submitted to EPA at 6-month intervals, beginning 6 months after of the effective date of the final Phase II rule and until the final report is submitted to EPA.

(e) Health effects testing—(1) Oncogenicity—(i) Required testing. (A) A test for oncogenic effects shall be conducted with 1,2,4-TCB in accordance with §798.3300 of this chapter.

(B) The route of administration for the oncogenicity testing for 1,2,4-TCB shall be via the animal feed.

(C) Two rodent species shall be used and one shall be the Fischer-344 rat.

(ii) Reporting requirements. (A) The oncogenicity test shall be completed and the final results submitted to EPA by June 30, 1994.

(B) Progress reports shall be submitted to the Agency every 6 months after the effective date of the final rule.

(2) [Reserved]

(f) [Reserved]

(g) Effective date. (1) The effective date of the final phase II rule is August 14, 1987, except for paragraphs (d)(4)(iii)(A) and (e)(1)(ii)(A) of this section. The effective date for paragraph (d)(4)(iii)(A) of this section is March 1, 1990. The effective date for paragraph (e)(1)(ii)(A) of this section is June 12, 1992.

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

[51 FR 11737, Apr. 7, 1986; 51 FR 18444, May 20, 1986, as amended at 51 FR 24667, July 8, 1986; 52 FR 24465, July 1, 1987; 55 FR 7327, Mar. 1, 1990; 57 FR 24960, June 12, 1992; 57 FR 27845, June 22, 1992; 58 FR 34205, June 23, 1993]

§799.1560 Diethylene glycol butyl ether and diethylene glycol butyl ether acetate.

(a) Identification of test substances. (1) Diethylene glycol butyl ether (DGBE), CAS Number 112-34-5, and diethylene glycol butyl ether acetate (DGBA), CAS Number 124-17-4, shall be tested in accordance with this section.

(2) DGBE of at least 95 percent purity and DGBA of at least 95 percent purity shall be used as the test substances.

(b) Persons required to submit study plans, conduct tests, and submit data. All persons who manufacture (including import) or process or intend to manufacture or process DGBE and/or DGBA, other than as an impurity, after April 11, 1988, to the end of the reimbursement period shall submit letters of intent to conduct testing, submit study plans and conduct tests, and submit data, or submit exemption applications as specified in this section, subpart A of this part, and parts 790 and 792 of this chapter for single-phase rulemaking. Persons who manufacture or process DGBE are subject to the requirements to test DGBE in this section. Only persons who manufacture or process DGBA are subject to the requirements to test DGBA in this section.

(c) Health effects testing—(1) Subchronic toxicity—(i) Required testing. (A) A 90-day subchronic toxicity test of DGBE shall be conducted in rats by dermal application in accordance with §798.2250 of this chapter except for the provisions in paragraphs (e)(9)(iv), (10)(i)(A) and (ii)(B), (11) (ii) and (iii), and (12)(i) of §798.2250.

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

(1) A satellite group to evaluate fertility shall be established. Control males shall be cohabited with control females, and males and females administered the high dose shall be cohabited. Endpoints to be evaluated shall include percent mated; percent pregnant; length of gestation; litter size; viability at birth, on Day 4, and weaning, on Day 21; sex of the offspring; and litter weights at birth and Days 4, 7, 14, and 21. Litters shall be standardized on day 4 in accordance with the reproductive and fertility effects guideline, §798.4700(c)(6)(iv) of this chapter. Gross examinations shall be made at least once each day and physical or behavioral anomalies in the dam or offspring

shall be recorded. At weaning, dams shall be sacrificed and examined for resorption sites indicative of post-implantation loss. An additional 20 males and 40 females will have to be added to the subchronic study for this test. If the animals in the high dose group exhibit marked toxicity (e.g. greater than 20 percent weight loss), then the fertility tests shall be conducted in the next highest dose group.

(2) Cage-side observations shall include, but not be limited to, changes in skin and fur; eyes and mucous membranes; respiratory, circulatory autonomic, and central nervous systems; somatomotor activity; and behavior pattern. In addition a daily examination for hematuria shall be done.

(3) Certain hematology determinations shall be carried out at least three times during the test period: Just prior to initiation of dosing (baseline data), after approximately 30 days on test, and just prior to terminal sacrifice at the end of the test period. Hematology determinations which are appropriate to all studies: Hematocrit, hemoglobin concentration, erythrocyte count, total and differential leucocyte count, mean corpuscular volume, and a platelet count.

(4) Urinalyses shall be done at least three times during the test period: Just prior to initiation of dosing (baseline data), after approximately 30 days into the test, and just prior to terminal sacrifice at the end of the test period. The animals shall be kept in metabolism cages, and the urine shall be examined microscopically for the presence of erythrocytes and renal tubular cells, in addition to measurement of urine volume, specific gravity, glucose, protein/albumin, and blood.

(5) The liver, kidney, adrenals, brain, gonads, prostate gland, epididymides, seminal vesicles, and pituitary gland shall be weighed wet, as soon as possible after dissection, to avoid drying.

(6) The following organs and tissues, or representative samples thereof, shall be preserved in a suitable medium for possible future histopathological examination: All gross lesions; lungs—which should be removed intact, weighed, and treated with a suitable fixative to ensure that lung structure is maintained (perfusion with the fixative is considered to be an effective procedure); nasopharyngeal tissues; brain—including sections of medulla/pons, cerebellar cortex, and cerebral cortex; pituitary; thyroid/parathyroid; thymus; trachea; heart; sternum with bone marrow; salivary glands; liver; spleen; kidneys; adrenals; pancreas; gonads; uterus; oviducts; vagina; vas deferens; accessory genital organs (epididymis, prostate, and, if present, seminal vesicles); aorta; (skin); gall bladder (if present); esophagus; stomach; duodenum; jejunum; ileum; cecum; colon; rectum; urinary bladder; representative lymph node; (mammary gland); (thigh musculature); peripheral nerve; (eyes); (femur—including articular surface); (spinal cord at three levels—cervical, midthoracic, and lumbar); and (zymbal and exorbital lachrymal glands).

(7) (i) Full histopathology on normal and treated skin and on organs and tissues listed in paragraph (c)(1)(i)(B)(6) of this section, as well as the accessory genital organs (epididymides, prostate, seminal vesicles) and the vagina, of all animals in the control and high dose groups.

(ii) The integrity of the various cell stages of spermatogenesis shall be determined, with particular attention directed toward achieving optimal quality in the fixation and embedding; preparations of testicular and associated reproductive organ samples for histology should follow the recommendations of Lamb and Chapin (1985) under paragraph (d)(1) of this section, or an equivalent procedure. Histological analyses shall include evaluations of the spermatogenic cycle, i.e., the presence and integrity of the 14 cell stages. These evaluations should follow the guidance provided by Clermont and Perey (1957) under paragraph (d)(2) of this section. Information shall also be provided regarding the nature and level of lesions observed in control animals for comparative purposes.

(iii) Data on female cyclicity shall be obtained by performing vaginal cytology over the last 2 weeks of dosing; the cell staging technique of Sadleir (1978) and the vaginal smear method in Hafez (1970) under paragraphs (d) (3) and (7) of this section or equivalent methods should be used. Data should be provided on whether the animal is cycling and the cycle length.

(iv) The ovary shall be serially sectioned with a sufficient number of sections examined to adequately detail oocyte and follicular morphology. The methods of Mattison and Thorgiersson (1979) and Pederson and Peters (1968) under paragraphs (d) (4) and (5) of this section may provide guidance. The strategy for sectioning and evaluation is left to the discretion of the investigator, but shall be described in detail in the study plan and final report. The nature and background level of lesions in control tissue shall also be noted.

(ii) Reporting requirements. (A) The subchronic test shall be completed and the final report submitted to EPA within 15 months of the effective date of the final test rule.

(B) Progress reports shall be submitted to EPA every 6 months, beginning 6 months from the effective date of the final rule until submission of the final report to EPA.

(2) Neurotoxicity/behavioral effects—(i) Required testing—(A) (1) Functional observational battery. A functional observational battery shall be performed in the rat by dermal application of DGBE for a period of 90 days according to §798.6050 of this chapter except for the provisions in paragraphs (b)(1), (d)(4)(ii), (5), and (8)(ii)(E) of §798.6050.

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

(i) Definition. Neurotoxicity is any adverse acute and/or lasting effect on the structure or function of the central and/or peripheral nervous system related to exposure to a chemical substance.

(ii) Lower doses. The data from the lower doses shall show either graded dose-dependent effects in at least two of all the doses tested including the highest dose, or no neurotoxic (behavioral) effects at any dose tested.

(iii) Duration and frequency of exposure. Animals shall be exposed for 6 hours/day, 5 days/week for a 90-day period.

(iv) Sensory function. A simple assessment of sensory function (vision, audition, pain perception) shall be made. Marshall et al. (1971) in §798.6050(f)(8) of this chapter have described a neurologic exam for this purpose; these procedures are also discussed by Deuel (1977), under §798.6050(f)(4) of this chapter. Irwin (1968) under §798.6050(f)(7) of this chapter described a number of reflex tests intended to detect gross sensory deficits. Many procedures have been developed for assessing pain perception (e.g., Ankier (1974) under §798.6050(f)(1); D'Amour and Smith (1941) under §798.6050(f)(3); and Evans (1971) under §798.6050(f)(6) of this chapter.

(B)(1) Motor activity. A motor activity test shall be conducted in the rat by dermal application of DGBE for a period of 90 days according to §798.6200 of this chapter except for the provisions in paragraphs (c), (d)(3)(ii), (4)(ii), (5), (8)(i), and (iii) of §798.6200.

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

(i) Principle of the test method. The test substance is administered to several groups of experimental animals, one dose being used per group. Measurements of motor activity are made. Where possible, the exposure levels at which significant changes in motor activity are produced are compared to those levels which produce toxic effects not originating in the central and/or peripheral nervous system.

(ii) Positive control data. Positive control data are required to document the sensitivity of the activity measuring device and testing procedure. These data should demonstrate the ability to detect increases or decreases in activity and to generate a dose-effect curve or its equivalent using three values of the dose or equivalent independent variable. A single administration of the dose (or equivalent) is sufficient. It is recommended that chemical exposure be used to collect positive control data. Positive control data shall be collected at the time of the test study unless the laboratory can demonstrate the adequacy of historical data for this purpose.

(iii) Lower doses. The data from the lower doses shall show either graded dose-dependent effects in at least two of all the doses tested including the highest dose, or no neurotoxic (behavioral) effects at any dose tested.

(iv) Duration and frequency of exposure. Animals shall be exposed for 6 hours/day, 5 days/week for a 90-day period.

(v) General. Motor activity shall be monitored by an automated activity recording apparatus. The device used shall be capable of detecting both increases and decreases in activity, i.e. baseline activity as measured by the device shall not be so low as to preclude decreases nor so high as to preclude increases. Each device shall be tested by a standard procedure to ensure, to the extent possible, reliability of operation across devices and across days for any one device. In addition, treatment groups shall be balanced across devices. Each animal shall be tested individually. The test session shall be long enough for motor activity to approach asymptotic levels by the last 20 percent of the session for most treatments and for the session control animals. All sessions should be of the same duration. Treatment groups shall be counter-balanced across test times. Effort should be made to ensure that variations in the test conditions are minimal and are not systematically related to treatment. Among the variables which can affect motor activity are sound level, size and shape of the test cage, temperature, relative humidity, lighting conditions, odors,

use of home cage or novel test cage, and environmental distractions. Tests shall be executed by an appropriately trained individual.

(vi) Subchronic. All animals shall be tested prior to initiation of exposure and at 30 ±4, 60 ±4, and 90 ±4 days during the exposure period. Testing shall occur prior to the daily exposure. Animals shall be weighed on each test day and at least once weekly during the exposure period.

(C)(1) Neuropathology. A neuropathology test shall be conducted in the rat by dermal application of DGBE for a period of 90 days according to §798.6400 of this chapter except for the provisions in paragraphs (d)(4)(ii), (5), (8)(iv)(C), and (E)(2) of §798.6400.

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

(i) Lower doses. The data from the lower doses shall show either graded dose-dependent effects in at least two of all the doses tested including the highest dose, or no neurotoxic (behavioral) effects at any dose tested.

(ii) Duration and frequency of exposure. Animals shall be exposed for 6 hours/day, 5 days/week for a 90-day period.

(iii) Clearing and embedding. After dehydration, tissue specimens shall be cleared with xylene and embedded in paraffin or paraplast except for the sural nerve which should be embedded in plastic. Multiple tissue specimens (e.g. brain, cord, ganglia) may be embedded together in one single block for sectioning. All tissue blocks shall be labeled to provide unequivocal identification. A method for plastic embedding is described by Spencer et al. in paragraph (d)(6) of this section.

(iv) Special stains. Based on the results of the general staining, selected sites and cellular components shall be further evaluated by the use of specific techniques. If hematoxylin and eosin screening does not provide such information, a battery of stains shall be used to assess the following components in all appropriate required samples: Neuronal body (e.g., Einarson's gallocyanin), axon (e.g., Bodian), myelin sheath (e.g., Kluver's Luxol Fast Blue), and neurofibrils (e.g., Bielchosky). In addition, peripheral nerve fiber teasing may be used. Detailed staining methodology is available in standard histotechnological manuals such as Armed Forces Institute of Pathology (AFIP) (1968) under §798.6400(f)(1), Ralis et al. (1973) under §798.6400(f)(5), and Chang (1979) under §798.6400(f)(2) of this chapter. The nerve fiber teasing technique is discussed in Spencer and Schaumberg (1980) under §798.6400(f)(6) of this chapter. A section of normal tissue shall be included in each staining to assure that adequate staining has occurred. Any changes shall be noted and representative photographs shall be taken. If a lesion(s) is observed, the special techniques shall be repeated in the next lower treatment group until no further lesion is detectable.

(ii) Reporting requirements. (A) The neurotoxicity/behavioral tests required under paragraph (c)(2) of this section shall be completed and the final reports submitted to EPA within 17 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 from the effective date of the final rule until submission of the applicable final report to EPA.

(3) Developmental neurotoxicity—(i) Required testing. A developmental neurotoxicity test of DGBE shall be conducted after a public program review of the Tier I data from the functional observational battery, motor activity, and neuropathology tests in paragraph (c)(2) of this section, and the reproductive tests in paragraph (c)(1) of this section, and if EPA issues a Federal Register notice or sends a certified letter to the test sponsor specifying that the testing shall be initiated. The test shall be performed in rats in accordance with §795.250 of this chapter.

(ii) Reporting requirements. (A) The developmental neurotoxicity test shall be completed and the final report submitted to EPA within 15 months of EPA's notification of the test sponsor by certified letter or Federal Register notice under paragraph (c)(3)(i) of this section that the testing shall be initiated.

(B) Progress reports shall be submitted to EPA every 6 months, beginning 6 months after the date of notification that the testing shall be initiated, until submission of the final report to EPA.

(4) Pharmacokinetics—(i) Required testing. (A) Pharmacokinetics testing of DGBE and DGBA will be conducted in rats by the dermal route of administration in accordance with §795.225 of this chapter, except for the provisions in paragraphs (b) (1)(ii) and (3)(i) of §795.225.

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

(1) Animals. Adult male and female Sprague Dawley rats shall be used. The rats shall be 7 to 8 weeks old and weigh 180 to 220 grams. Prior to testing, the animals shall be selected at random for each group. Animals showing signs of ill health shall not be used.

(2) Observation of animals—Urinary and fecal excretion. The quantities of 14C excreted in urine and feces by rats dosed as specified in paragraph (b)(2)(iv) of §795.225 shall be determined at 8, 24, 48, 72, and 96 hours after dosing, and if necessary, daily thereafter until at least 90 percent of the dose has been excreted or until 7 days after dosing (whichever occurs first). Four animals per sex per dose group shall be used for this purpose.

(ii) Reporting requirements. (A) The pharmacokinetics tests shall be completed and the final reports submitted to EPA within 8 months of the effective date of the final amendment.

(B) A progress report shall be submitted to EPA 6 months from the effective date of the final amendment.

(d) References. For additional background information the following references should be consulted:

(1) Lamb, J.C. and Chapin, R.E. “Experimental models of male reproductive toxicology.” In: “Endocrine Toxicology.” Thomas, J.A., Korach, K.S., and McLachlan, J.A., eds. New York, NY: Raven Press. pp. 85-115. (1985).

(2) Clermont, Y. and Perey, B. “Quantitative study of the cell population of the seminiferous tubules in immature rats.” American Journal of Anatomy. 100:241-267. (1957).

(3) Sadleir, R.M.F.S. “Cycles and seasons.” In: “Reproduction in Mammals: I. Germ Cells and Fertilization.” Austin, C.R. and Short, R.V., eds. New York, NY: Cambridge Press. Chapter 4. (1978).

(4) Mattison, D.R. and Thorgiersson, S.S. “Ovarian aryl hydrocarbon hydroxylase activity and primordial oocyte toxicity of polycyclic aromatic hydrocarbons in mice.” Cancer Research.39:3471-3475. (1979).

(5) Pederson, T. and Peters, H. “Proposal for classification of oocytes and follicles in the mouse ovary. Journal of Reproduction and Fertility. 17:555-557. (1968).

(6) Spencer, P.S., Bischoff, M.C., and Schaumburg, H.H. “Neuropathological methods for the detection of neurotoxic disease.” In: “Experimental and Clinical Neurotoxicology.” Spencer, P.S. and Schaumburg, H.H., eds. Baltimore, MD: Williams & Wilkins, pp. 743-757. (1980).

(7) Hafez, E.S., ed., “Reproduction and Breeding Techniques for Laboratory Animals.” Chapter 10. Philadelphia: Lea & Febiger (1970).

(e) Effective date. (1) The effective date of the final rule is April 11, 1988, except for paragraph (c)(2)(ii)(A) of this section. The effective date for paragraph (c)(2)(ii)(A) of this section is March 1, 1990. The effective date for paragraphs (c)(4)(ii)(A) and (c)(4)(ii)(B) of this section is November 27, 1989.

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

[53 FR 5950, Feb. 26, 1988, as amended at 54 FR 27357, June 29, 1989; 54 FR 41835, Oct. 12, 1989; 55 FR 7326, Mar. 1, 1990; 58 FR 34205, June 23, 1993]

§799.1575 Diethylenetriamine (DETA).

(a) Identification of chemical test substance. (1) Diethylenetriamine (CAS No. 111-40-0, also known as DETA) shall be tested in accordance with this part.

(2) Diethylenetriamine of at least 99 percent purity shall be used as the test substances in all tests.

(b) Persons required to submit study plans, conduct tests and submit data. All persons who manufacture or process diethylenetriamine from July 8, 1985, to the end of the reimbursement period shall submit letters of intent to test, exemption applications, and study plans and shall conduct tests and submit data as specified in this section, subpart A of this part and part 790 of this chapter (Test Rule Development and Exemption Procedures).

(c) Health effects testing—(1) Mutagenic effects—Gene mutation—(i) Required testing. (A) A sex-linked recessive lethal test in Drosophila melanogaster shall be conducted with DETA.

(B) A mouse specific locus assay shall be conducted with DETA, if the sex-linked recessive lethal test in Drosophila melanogaster conducted pursuant to paragraph (c)(1)(i)(A) of this section produces a positive result.

(ii) Test standards. (A) The testing for the sex-linked recessive lethal assay shall be conducted in accordance with the following revised EPA-approved modified study plan (June 19, 1986) originally submitted by the Diethylenetriamine Producers/Importers Alliance (DPIA): “Sex-linked recessive lethal test in Drosophila melanogaster,” with modifications as approved by EPA on March 9, 1987, and May 21, 1987.

(B) The testing for the mouse visible specific locus assay shall be conducted in accordance with the following revised EPA-approved modified study plan (June 19, 1986) originally submitted by the Diethylenetriamine Producers/Importers Alliance (DPIA): “Mouse specific locus test for visible markers.”

(C) These revised EPA-approved modified study plans are available for inspection in the Non-Confidential Information Center (NCIC) (7407), Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency, Room B-607 NEM, 401 M St., SW., Washington, DC 20460, between the hours of 12 p.m. and 4 p.m. weekdays excluding legal holidays.

(iii) Reporting requirements. (A) The sex-linked recessive lethal test of DETA in Drosophila melanogaster shall be completed and a final report submitted to the Agency within 14 months from the effective date of the final Phase II rule. Two interim progress reports shall be submitted at 6-month intervals, the first of which is due within 6 months of the effective date of the final Phase II rule.

(B) If required pursuant to paragraph (c)(1)(i)(B) of this section, the mouse specific locus test of DETA for visible markers shall be completed and a final report submitted to the Agency within 48 months from the designated date contained in EPA's notification of the test sponsor by certified letter or Federal Register notice that testing should be initiated. Seven interim progress reports shall be submitted at 6-month intervals, the first of which is due within 6 months of EPA's designated date.

(2) Mutagenic effects—Chromosomal aberrations—(i) Required testing. (A) An in vitro cytogenetics test shall be conducted with DETA.

(B) An in vivo cytogenetics test shall be conducted with DETA, if the in vitro cytogenetics test conducted pursuant to paragraph (c)(2)(i)(A) of this section produces a negative result.

(C) A dominant lethal assay shall be conducted with DETA, if either the in vitro cytogenetics test conducted pursuant to paragraph (c)(2)(i)(A) of this section or the in vivo cytogenetics test conducted pursuant to paragraph (c)(2)(i)(B) of this section produces a positive result.

(D) A heritable translocation assay shall be conducted with DETA, if the dominant lethal assay conducted pursuant to paragraph (c)(2)(i)(C) of this section produces a positive result.

(ii) Test standards. (A) The testing for cytogenetic effects shall be conducted in accordance with the following revised EPA-approved modified study plan (June 19, 1986) originally submitted by the Diethylenetriamine Producers/Importers Alliance (DPIA): “In vitro cytogenetics test” and “In vivo cytogenetics test,” with modifications as approved by EPA on March 9, 1987, and May 21, 1987.

(B) Other testing for cytogenetic effects shall be conducted in accordance with the following revised EPA-approved modified study plans (June 19, 1986) originally submitted by the Diethylenetriamine Producers/Importers Alliance (DPIA): “Dominant lethal assay of diethylenetriamine in CD rats,” and “Heritable translocation of diethylenetriamine in CD-1 mice.”

(C) These revised EPA-approved modified study plans are available for inspection in the Non-Confidential Information Center (NCIC) (7407), Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency, Room B-607 NEM, 401 M St., SW., Washington, DC 20460, between the hours of 12 p.m. and 4 p.m. weekdays excluding legal holidays.

(iii) Reporting requirements. (A) The in vitro cytogenetics testing of DETA shall be completed and a final report submitted to the Agency within 6 months of the effective date of the final Phase II rule.

(B) If required pursuant to paragraph (c)(2)(i)(B) of this section, the in vivo cytogenetics testing of DETA shall be completed and final report submitted to the Agency within 14 months of the effective date of the final Phase II rule. One interim progress report shall be submitted within 12 months of the final rule's effective date.

(C) If required pursuant to paragraph (c)(2)(i)(C) of this section, the dominant lethal testing of DETA shall be completed and a final report submitted to the Agency within 20 months of the effective date of the final Phase II rule.

(D) If required pursuant to paragraph (c)(2)(i)(D) of this section, the heritable translocation testing of DETA shall be completed and a final report submitted to the Agency within 18 months of the designated date contained in EPA's notification of the test sponsor by certified letter or Federal Register notice that testing should be initiated. Two interim progress reports shall be submitted at 6-month intervals, the first of which is due within 6 months of EPA's designated date.

(3) Subchronic effects—(i) Required testing. A ninety-day oral subchronic toxicity test shall be conducted with DETA in at least one mammalian species.

(ii) Test standard. The testing shall be conducted in accordance with the following revised EPA-approved modified study plans (June 19, 1986) originally submitted by the Diethylenetriamine Producers/Importers Alliance (DPIA): “Ninety-Day (subchronic) dietary toxicity study with diethylenetriamine in albino rats,” with modifications approved by EPA on March 9, 1987, and May 21, 1987. This revised EPA-approved modified study plans is available for inspection in the Non-Confidential Information Center (NCIC) (7407), Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency, Room B-607 NEM, 401 M St., SW., Washington, DC 20460, between the hours of 12 p.m. and 4 p.m. weekdays excluding legal holidays.

(iii) Reporting requirements. The testing shall be completed and a final report submitted to the Agency within 15 months of the effective date of the final Phase II rule. Two interim progress reports shall be submitted at 6-month intervals, the first of which is due within 6 months of the effective date of the final Phase II rule.

(d) Chemical fate testing—(1) Required testing. Testing to assess N-nitrosamine formation, resulting from aerobic biological and/or chemical transformation, shall be conducted with DETA using environmental samples of lake water, sewage, and soil.

(2) Test standard. The testing shall be conducted in accordance with the following revised EPA-approved modified study plan (June 7, 1990) originally submitted by the Diethylenetriamine Producers/Importers Alliance (DPIA): “Modified Final Copy (04-17-90); Diethylenetriamine: Environmental Fate in Sewage, Lake Water and Soil”. This revised EPA-approved modified study plans are available for inspection in the Non-Confidential Information Center (NCIC) (7407), Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency, Room B-607 NEM, 401 M St., SW., Washington, DC 20460, between the hours of 12 p.m. and 4 p.m. weekdays excluding legal holidays.

(3) Reporting requirements. The testing shall be completed and a final report submitted to EPA within 20 months of the effective date of the final Phase II rule. Interim progress reports shall be submitted at 6-month intervals, the first of which is due within 6 months of the effective date of the final Phase II rule.

(e) Modifications. Persons subject to this section are not subject to the requirements of §790.50(a)(2)(ii) of this chapter.

(f) Effective date. (1) The effective date of the final Phase II rule for diethylenetriamine is March 19, 1987, except for paragraphs (c)(4)(iii), (d)(2), and (d)(3) of this section. The effective date of paragraphs (c)(4)(iii), and (d)(3) of this section is March 1, 1990. The effective date for paragraph (d)(2) of this section is May 21, 1991.

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

[50 FR 21412, May 23, 1985; 50 FR 33543, Aug. 20, 1985; 51 FR 3468, Jan. 28, 1986; 51 FR 4736, Feb. 7, 1986; 52 FR 3238, Feb. 3, 1987; 54 FR 27356, June 29, 1989; 55 FR 3408, Feb. 1, 1990; 55 FR 7326, Mar. 1, 1990; 56 FR 23230, May 21, 1991; 58 FR 34205, June 23, 1993; 60 FR 34467, July 3, 1995]

Back to Top

§799.1645 2-Ethylhexanol.

(a) Identification of test substance. (1) 2-Ethylhexanol (CAS No. 104-76-7) shall be tested in accordance with this section.

(2) 2-Ethylhexanol of at least 99.0-percent purity shall be used as the test substance.

(b) Persons required to submit study plans, conduct tests, and submit data. All persons who manufacture or process, or intend to manufacture or process 2-ethylhexanol, other than as an impurity, from the effective date of this 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 exemption applications as specified in this section, subpart A of this part, and parts 790 and 792 of this chapter for single-phase rulemaking.

(c) Health effects—(1) Oncogenic effects—(i) Required testing. (A) Oncogenicity tests shall be conducted in Fisher 344 rats and B6C3Fl mice by the oral route with 2-ethylhexanol in accordance with §798.3300 of this chapter, except for the provisions in §798.3300(b)(6).

(B) For the purpose of this section, the following provisions also apply to the oncogenicity tests: (1) Administration of the test substance. 2-Ethylhexanol shall be administered either by microencapsulation before adding it to the diet or by gavage.

(2) [Reserved]

(ii) Reporting requirements. (A) The study plan for the oncogenicity test shall be submitted at least 45 days before the initiation of testing.

(B) The oncogenicity testing shall be completed and final report submitted to the Agency within 53 months of the effective date of this final rule if 2-ethylhexanol is administered by gavage or within 56 months of the effective date of this final rule if administered by microencapsulation.

(C) 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.

(2) [Reserved]

(d) Effective date. The effective date of this final rule requiring oncogenicity testing of 2-ethylhexanol is September 16, 1987.

[52 FR 28704, Aug. 3, 1987, as amended at 58 FR 34205, June 23, 1993]

Back to Top

§799.1700 Fluoroalkenes.

(a) Identification of test substances. (1) Vinyl fluoride (VF; CAS No. 75-02-5), vinylidene fluoride (VDF; CAS No. 75-38-7), tetrafluoroethene (TFE; CAS No. 116-14-3), and hexafluoropropene (HFP; CAS No. 116-15-4) shall be tested in accordance with this section.

(2) VF, VDF, TFE, and HFP of at least 99 percent purity shall be used as the test substances.

(b) Persons required to submit study plans, conduct tests and submit data. All persons who manufacture VF, VDF, TFE, or HFP, other than as an impurity, from July 22, 1987 to the end of the reimbursement period shall submit letters of intent to conduct testing or exemption applications, submit study plans, conduct tests in accordance with the TSCA Good Laboratory Practice Standards (40 CFR part 792), and submit data as specified in this section, subpart A of this part, and part 790 of this chapter for single-phase rulemaking, for the substances they manufacture.

(c) Health effects testing—(1) Mutagenic effects—Gene mutation—(i) Required testing. (A) (1) A detection of gene mutations in somatic cells in culture assay shall be conducted with TFE and HFP in accordance with §798.5300 of this chapter except for the provisions in paragraphs (c), (d)(3)(i), (4), (5) and (6) and (e).

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

(i) Reference substances. No reference substance is required.

(ii) Test method—Type of cells used in the assay. Mutation induction at the HPRT locus shall be measured in Chinese hamster ovary (CHO) cells. Cells shall be checked for Mycoplasma contamination and may also be checked for karyotype stability.

(iii) Test method—Metabolic activation. Cells shall be exposed to the test substance only in the presence of a metabolic activation system for TFE, and in both the presence and absence of a metabolic activation system for HFP. The metabolic activation system shall be derived from the post-mitochondrial fraction (S-9) of livers from rats pretreated with Aroclor 1254.

(iv) Test method—Control groups. Positive and negative controls shall be included in each experiment. In assays with metabolic activation, the positive control substance shall be known to require such activation. Nitrogen shall serve as the negative control and diluting gas.

(v) Test method—Test chemicals. The test should be designed to have a predetermined sensitivity and power. The number of cells, cultures, and concentrations of test substance used should reflect these defined parameters. The number of cells per culture is based on the expected background mutant frequency; a general guide is to use a number which is 10 times the inverse of this frequency. Several concentrations (usually at least four) of the test substance shall be used. These shall yield a concentration-related toxic effect. The highest concentration shall produce a low level of survival (approximately 10 percent), and the survival in the lowest concentration shall approximate that of the negative control. Cytotoxicity shall be determined after treatment with the test substance both in the presence and in the absence of the metabolic activation system.

(vi) Test performance. Cells in treatment medium with and without metabolic activation shall be exposed to varying concentrations of test gas-air mixtures by flushing treatment flasks (or chambers) with 10 volumes of test gas-air mixture at a rate of 500 mL/min or that rate which will allow complete flushing within 1 minute. In the case of a test chamber volume of 1.67 L, a flow rate of 10 L/min is appropriate. Each flask shall be closed with a cap with a rubber septum. Headspace samples shall be taken at the beginning and end of the exposure period and analyzed to determine the amount of test gas in each flask. Flasks shall be incubated on a rocker panel at 37 °C for 5 hours for tests with metabolic activation. For the non-activated portion of the test, the incubation time shall be 18 to 19 hours at 37 °C. At the end of the exposure period, cells treated with metabolic activation shall be washed and incubated in culture medium for 21 to 26 hours prior to subculturing the viability and expression of mutant phenotype. Cells treated without metabolic activation shall be washed and subcultured immediately to determine viability and to allow for expression of mutant phenotype. Appropriate subculture schedules (generally twice during the expression period) shall be used. At the end of the expression period, which shall be sufficient to allow near optimal phenotypic expression of induced mutants (generally 7 days for this cell system), cells shall be grown in medium with and without selective agent for determination of numbers of mutants and cloning efficiency, respectively. This last growth period is generally 7 days at 37 °C. Results of this test shall be confirmed in an independent experiment.

(B)(1) A sex-linked recessive lethal test in Drosophila melanogaster shall be conducted with VDF and VF in accordance with §798.5275 of this chapter except for the provisions in paragraph (d)(5). This test shall also be performed with TFE or HFP if the somatic cells in culture assay conducted pursuant to paragraph (c)(1)(i)(A) of this section produces a positive result.

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

(i) Test chemicals. It is sufficient to test a single dose of the test substance. This dose shall be the maximum tolerated dose or that which produces some indication of toxicity. Exposure shall be by inhalation.

(ii) [Reserved]

(C)(1) A mouse visible specific locus assay (MVSL) shall be conducted with VF, VDF, TFE, and HFP in accordance with §798.5200 of this chapter, except for the provisions of paragraph (d)(5) of §798.5200, or a mouse biochemical-specific locus assay (MBSL) shall be conducted with VF, VDF, TFE, and HFP in accordance with §798.5195 of this chapter, except for the provisions of paragraph (d)(5) of §798.5195, for whichever of these substances produces a positive test result in the sex-linked recessive lethal test in Drosophila melanogasterconducted pursuant to paragraph (c)(1)(i)(B) of this section 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.

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

(i) Test chemicals. A minimum of two dose levels shall be tested. The highest dose tested shall be the highest dose tolerated without toxic effects, provided that any temporary sterility induced due to elimination of spermatagonia is of only moderate duration, as determined by a return of males to fertility within 80 days after treatment, or shall be the highest dose attainable. Animals shall be exposed to the test substance by inhalation. Exposure shall be for 6 hours a day. Duration of exposure shall be dependent upon accumulated total dose desired for each group.

(ii) [Reserved]

(ii) Reporting requirements. (A) Mutagenic effects-gene mutation tests shall be completed and the final reports shall be submitted to EPA as follows: Somatic cells in culture assay, within 6 months after the effective date of the final rule; Drosophila sex-linked recessive lethal, within 9 months (for VF and VDF) and within 15 months (for TFE and HFP) after the effective date of the final rule; MVSL or MBSL, within 51 months after the date of EPA's notification of the test sponsor by certified letter or Federal Register notice that testing shall be initiated.

(B) Progress reports shall be submitted to the Agency every 6 months beginning 6 months after the effective date of the final rule or receipt of notice that testing shall be initiated.

(2) Mutagenic effects—Chromosomal aberrations—(i) Required testing. (A)(1) A mouse micronucleus cytogenetics test shall be conducted with VDF and TFE in accordance with §798.5395 of this chapter except for the provisions in paragraphs (d)(5) (i), (ii), and (iii).

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

(i) Test method—Vehicle. No vehicle is required.

(ii) Test method—Dose levels. Three dose levels shall be used. The highest dose tested shall be the maximum tolerated dose, that dose producing some indication of cytotoxicity (e.g., a change in the ratio of polychromatic to normochromatic erythrocytes, or the highest dose attainable).

(iii) Test method—route of administration. Animals shall be exposed by inhalation with a single 6-hour exposure, with three sampling times between 20 and 72 hours.

(B)(1) For each respective test substance, a dominant lethal assay shall be conducted with VF and HFP in accordance with §798.5450 of this chapter except for the provisions in paragraphs (d)(2)(i), (4) (i), (5) and (e). This test shall also be performed with TFE or VDF if the mouse micronucleus cytogenetics test conducted pursuant to paragraph (c)(2)(i)(A) of this section produces a positive result.

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

(i) Test method—Description. For this assay, the test substance shall be administered by inhalation for 5 consecutive days for 6 hours per day.

(ii) Test method—Concurrent controls. Concurrent positive and negative (vehicle) controls shall be included in each experiment.

(iii) Test method—Test chemicals. Exposure shall be by inhalation for 5 consecutive days for 6 hours per day. Three dose levels shall be used. The highest dose shall produce signs of toxicity (e.g., slightly reduced fertility) or shall be the highest attainable.

(iv) Test performance. Individual males shall be mated sequentially to 1 or 2 virgin females. Females shall be left with the males for at least the duration of one estrus cycle or alternatively until mating has occurred as determined by the presence of sperm in the vagina or by the presence of a vaginal plug. In any event, females shall be left with the males for no longer than 7 days. The number of matings following treatment shall ensure that germ cell maturation is adequately covered. Mating shall continue for at least 6 weeks. Females shall be sacrificed in the second half of pregnancy, and uterine contents shall be examined to determine the number of implants and live and dead embryos. The examination of ovaries to determine the number of corpora lutea is left to the discretion of the investigator.

(C)(1) A heritable translocation assay shall be conducted with VF, VDF, TFE, or HFP in accordance with §798.5460 of this chapter except for the provisions of paragraphs (d)(3)(i), (5), and (e)(1), if the dominant lethal assay conducted for that substance pursuant to paragraph (c)(2)(i)(B) 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.

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

(i) Test method—Animal selection. The mouse shall be used as the test species.

(ii) Test method. No vehicle is required. At least two dose levels shall be used. The highest dose level shall result in toxic effects (which shall not produce an incidence of fatalities which would preclude a meaningful evaluation) or shall be the highest dose attainable. Animals shall be exposed by inhalation.

(iii) Test performance—Treatment and mating. The animals shall be dosed with the test substance 6 hours per day, 7 days per week over a period of 35 days. After treatment, each male shall be caged with 2 untreated females for a period of 1 week. At the end of 1 week, females shall be separated from males and caged individually. When females give birth, the date of birth, litter size and sex of progeny shall be recorded. All male progeny shall be weaned and all female progeny shall be discarded.

(ii) Reporting requirements. (A) Mutagenic effects-chromosomal aberration testing shall be completed and final results submitted to EPA after the effective date of the rule as follows: mouse micronucleus cytogenetics for VDF by November 22, 1988, and for TFE within 10 months after the effective date of the final rule; dominant lethal assay for VF and HFP by October 22, 1988, and for VDF and TFE within 19 months after the effective date of the rule; heritable translocation assay, within 25 months after the date of EPA's notification of the test sponsor by certified letter or Federal Register notice that testing shall be initiated.

(B) Progress reports shall be submitted to the Agency every 6 months beginning 6 months after the effective date of the final rule or receipt of notice that testing shall be initiated.

(3) Subchronic toxicity—(i) Required Testing. (A) An inhalation subchronic toxicity test shall be conducted with HFP in accordance with the TSCA Test Guideline specified in §798.2450 of this chapter except for the provisions in paragraphs (d)(5), (10)(v), and (e)(3)(iv)(D).

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

(1) Test procedures—Exposure conditions. The animals shall be exposed to the test substance 6 hours per day, 5 days per week for 90 days.

(2) Test procedures—Observation of animals. Animals shall be weighted weekly, and food and water consumption shall also be measured weekly.

(3) Test report—Individual animal data. Food and water consumption data shall be reported.

(ii) Reporting requirements. (A) The required subchronic toxicity test shall be completed and final results submitted to the Agency within 18 months after the effective date of the final rule.

(B) Progress reports shall be submitted to the Agency every 6 months beginning 6 months after the effective date of the final rule.

(4) Oncogenicity—(i) Required testing. (A) (1) Oncogenicity tests shall be conducted in both rats and mice by inhalation with VF in accordance with §798.3300 of this chapter, except for the provisions in paragraph (b)(7)(vi) of §798.3300.

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

(i) Test procedures—observations of animals. All mice of test groups in which survival is approximately 25 percent of mice at risk (approximately 25 percent of 70, or approximately 18 mice) will be sacrificed near the time that 25 percent survival is achieved. All mice surviving the 18-month test period will be sacrificed and necropsied. The order of sacrifice for mice at all pathological evaluations will be random among all exposure groups within a sex. Moribund animals should be removed and sacrificed when noticed.

(ii) All rats of test groups in which survival is approximately 25 percent of rats at risk (approximately 25 percent of 60, or approximately 15 rats) will be sacrificed near the time that 25 percent survival is achieved. All rats surviving the 24-month test period will be sacrificed and necropsied. The order of sacrifice for rats at all pathological evaluations will be random among all exposure groups within a sex. Moribund animals should be removed and sacrificed when noticed.

(B) Oncogenicity testing shall be conducted in mice with VDF in accordance with §798.3300 of this chapter.

(C) [Reserved]

(D) Oncogenicity tests shall also be conducted by inhalation in both rats and mice with TFE in accordance with §798.3300 of this chapter if TFE yields a positive test result in any one of the following mutagenicity tests: The in vitro cytogenetics assay conducted pursuant to paragraph (c)(2)(i)(A) of this section, the mouse micronucleus cytogenetics assay conducted pursuant to paragraph (c)(2)(i)(B) of this section, the mammalian cells in culture assay conducted pursuant to paragraph (c)(1)(i)(A) of this section or the sex-linked recessive lethal assay in Drosophila melanogaster conducted pursuant to paragraph (c)(1)(i)(B) of this section 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. Criteria for positive test results are established in 40 CFR 798.5375, 798.5385, 798.5300 and 798.5275 of this chapter, respectively.

(ii) Reporting requirements. (A) The oncogenicity testing for VDF shall be completed and the final results submitted to the Agency by March 23, 1992. The oncogenicity testing for VF shall be completed and the final results submitted to the Agency by July 22, 1992. For TFE and HFP, the oncogenicity testing shall be completed and the final results submitted to the Agency within 56 months after the date of EPA's notification of the test sponsor by certified letter or Federal Register notice that testing shall be initiated.

(B) Progress reports shall be submitted every 6 months beginning 6 months after the effective date of the final rule for VF and VDF and beginning 6 months after notification by certified letter or Federal Register notice that testing is to begin for TFE and HFP.

(d) Effective date. (1) The effective date of the final rule is July 22, 1987, except for paragraphs (c)(1)(i)(C)(1), (c)(1)(ii)(A), (c)(4)(i) and(c)(4)(ii)(A) of this section. The effective date of paragraphs (c)(1)(i)(C)(1) and (c)(1)(ii)(A) of this section is May 21, 1990. The effective date of paragraphs (c)(4)(i)(A)(1) (c)(4)(i)(A)(2)(i), (c)(4)(i)(B) and (c)(4)(i)(D) of this section is May 21, 1991. The effective date for paragraphs (c)(4)(i)(A)(2)(ii) and (c)(4)(i)(C) of this section is June 12, 1992. The effective date of paragraph (c)(4)(ii)(A) of this section is May 28, 1993.

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

[52 FR 21530, June 8, 1987, as amended at 52 FR 43762, Nov. 16, 1987; 54 FR 27357, June 29, 1989; 54 FR 33148, Aug. 11, 1989; 55 FR 12643, Apr. 5, 1990; 56 FR 23230, May 21, 1991; 57 FR 24960, June 12, 1992; 58 FR 30992, May 28, 1993; 58 FR 34205, June 23, 1993]

Back to Top

§799.2155 Commercial hexane.

(a) Identification of test substance. (1) “Commercial hexane,” for purposes of this section, is a product obtained from crude oil, natural gas liquids, or petroleum refinery processing in accordance with the American Society for Testing and Materials Designation D 1836-83 (ASTM D 1836), consists primarily of six-carbon alkanes or cycloalkanes, and contains at least 40 liquid volume percent n-hexane (CAS No. 110-54-3) and at least 5 liquid volume percent methylcyclopentane (MCP; CAS No. 96-37-7). ASTM D 1836, formally entitled “Standard Specification for Commercial Hexanes,” is published in 1986 Annual Book of ASTM Standards: Petroleum Products and Lubricants, ASTM D 1836-83, pp. 966-967, 1986, is incorporated by reference, and is available for public inspection at the National Archives and Records Administration (NARA). For information on the availability of this material at NARA, call 202-741-6030, or go
to: http://www.archives.gov/federal_register/code_of_federal_regulations/ibr_locations.html. This incorporation by reference was approved by the Director of the Office of the Federal Register in accordance with 5 U.S.C. 522(a) and 1 CFR part 51. This material is incorporated as it exists on the date of approval, and a notice of any change in this material will be published in the Federal Register. Copies of the incorporated material may be obtained from the Director, Environmental Assistance Division (7408), Office of Pollution Prevention and Toxics, Environmental Protection Agency, Rm. E-543B, 1200 Pennsylvania Ave. NW., Washington, DC 20460-0001.

(2) The commercial hexane test substance, for purposes of this section, is a product which conforms to the specifications of ASTM D1836 and contains at least 40 liquid volume percent but no more than 55 liquid volume percent n-hexane and no less than 10 liquid volume percent MCP.

(b) Persons required to submit study plans, conduct tests, and submit data. All persons who manufacture (including import) or process or intend to manufacture or process commercial

hexane, as defined in paragraph (a)(1) of this section and 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 in accordance with part 792 of this chapter, 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. Persons who manufacture commercial hexane as a byproduct are covered by the requirements of this section. Notwithstanding §790.50(a)(1) of this chapter, persons who notify EPA of their intent to conduct neurotoxicity testing in compliance with paragraph (c)(7) of this section may submit study plans for those tests less than 45 days before beginning testing provided that EPA receives the study plans before this testing begins.

(c) Health effects testing—(1) Subchronic inhalation toxicity—(i) Required testing. (A) A subchronic inhalation toxicity test shall be conducted with commercial hexane in accordance with §798.2450 of this chapter except for the provisions in paragraphs (d)(4)(ii) and (5) of §798.2450.

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

(1) High dose level. The highest concentration should result in toxic effects but neither produce an incidence of fatalities which would prevent a meaningful evaluation nor exceed the lower explosive limit of commercial hexane.

(2) Exposure conditions. Animals shall be dosed for 6 hours/day, 5 days/week for 90 days.

(ii) Reporting requirements. (A) The subchronic inhalation toxicity test shall be completed and the final report submitted to EPA within 15 months of the effective date of the final rule.

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

(2) Oncogenicity—(i) Required testing. (A) An oncogenicity test shall be conducted with commercial hexane in accordance with §798.3300 of this chapter except for the provisions in paragraphs (b)(3)(ii) and (6) of §798.3300.

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

(1) High dose level. The high dose level should elicit signs of minimal toxicity without substantially altering the normal life span and should not exceed the lower explosive limit of commercial hexane.

(2) Administration of test substance. Animals shall be exposed to commercial hexane by inhalation.

(ii) Reporting requirements. (A) The oncogenicity test shall be completed and the final report submitted to EPA within 53 months of the effective date of the final rule. The mouse portion of the oncogenicity study shall be submitted by June 5, 1993.

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

(3) Reproduction and fertility effects—(i) Required testing. (A) A reproduction and fertility effects test shall be conducted with commercial hexane in accordance with §798.4700 of this chapter except for the provisions in paragraphs (c)(3)(ii) and (5) of §798.4700.

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

(1) High dose level. The highest dose level should induce toxicity but not high levels of mortality in the parental (P) animals. In addition, the highest dose level should not exceed the lower explosive limit of commercial hexane.

(2) Administration of test substance. Animals shall be exposed to commercial hexane by inhalation.

(ii) Reporting requirements. (A) The reproduction and fertility effects test shall be completed and the final report submitted to EPA within 29 months of the effective date of the final rule.

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

(4) Inhalation developmental toxicity—(i) Required testing. (A) An inhalation developmental toxicity test shall be conducted with commercial hexane in accordance with §795.4350 of this chapter except for the provisions in paragraph (e)(3)(iv) of §798.4350.

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

(1) High dose level. Unless limited by the physical/chemical nature or biological properties of the test substance, the highest concentration level shall induce some overt maternal toxicity such as reduced body weight or body weight gain, but not more than 10 percent maternal deaths. In addition, the highest dose level should not exceed the lower explosive limit of commercial hexane.

(2) [Reserved]

(ii) Reporting requirements. (A) The inhalation developmental toxicity test shall be completed and the final report submitted to EPA within 12 months of the effective date of the final rule.

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

(5) Mutagenic effects—gene mutations—(i) Required testing. (A)(1) A Salmonella typhimurium reverse mutation assay shall be conducted with commercial hexane in accordance with §798.5265 of this chapter except for the provisions in paragraphs (d)(4) and (e) of §798.5265.

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

(i) Metabolic activation. Bacteria shall be exposed to commercial hexane both in the presence and absence of an appropriate metabolic activation system.

(ii) Test performance. The assay shall be performed using the desiccator method described as follows: The agar overlay plates shall be placed uncovered in a 9-liter desiccator. A volume of the liquid test substance shall be added to the glass Petri dish suspended beneath the porcelain shelf of the desiccator. The highest exposure concentration should not result in a vapor concentration which exceeds the lower explosive limit of commerical hexane. A magnetic stirring bar to serve as a fan to assure rapid and even distribution of the vapor shall be placed on the bottom of the inside of the desiccator. The desiccator shall be placed on a magnetic stirrer within a 37 °C room or chamber for 7 to 10 hours. The plates shall then be removed, their lids replaced, followed by incubation for an additional 40 hours at 37 °C before counting. An appropriate selective medium with an adequate overlay agar shall be used. All plating should be done in at least triplicate.

(B)(1) A gene mutation test in mammalian cells shall be conducted with commercial hexane in accordance with §798.5300 of this chapter except for the provisions in paragraphs (d)(3)(ii) and (4) of §798.5300 if the results from the Salmonella typhimurium test conducted pursuant to paragraph (c)(5)(i)(A) of this section are negative.

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

(i) Cell growth and maintenance. Appropriate culture media and incubation conditions (culture vessels, CO2 concentrations, temperature, and humidity) shall be used. The cell culture shall be directly dosed by pipetting liquid commercial hexane mixed with liquid DMSO into the culture medium. Cells shall be exposed to test substance both in the presence and absence of an appropriate metabolic activation system.

(ii) [Reserved]

(C)(1) A sex-linked recessive lethal test in Drosophila melanogaster shall be conducted with commercial hexane in accordance with §798.5275 of this chapter except for the provisions in paragraphs (d)(5) (ii) and (iii) of §798.5275, unless the results of both the Salmonella typhimurium test conducted pursuant to paragraph (c)(5)(i)(A) of this section and the mammalian cells in the culture gene mutation test conducted pursuant to paragraph (c)(5)(i)(B) of this section, if required, are negative.

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

(i) Dose levels. For the initial assessment of mutagenicity, it is sufficient to test a single dose of the test substance for screening purposes. This dose should be the maximum tolerated dose, or that which produces some indication of toxicity or shall be the highest dose attainable and should not exceed the lower explosive limit of commercial hexane. For dose-response purposes, at least three additional dose levels should be used.

(ii) Route of administration. The route of administration shall be by exposure to commercial hexane vapors.

(D)(1) Unless the results of the sex-linked recessive lethal test in Drosophila melanogaster conducted with commercial hexane pursuant to paragraph (c)(5)(i)(C) of this section are negative, EPA shall conduct a public program review of all of the mutagenicity data available for this substance. If, after this review, EPA decides that testing of commercial hexane for causing heritable gene mutations in mammals is necessary, it shall notify the test sponsor by certified letter or Federal Register notice that testing shall be initiated in either the mouse visible specific locus test or the mouse biochemical specific locus test. The mouse visible specific locus test, if conducted, shall be performed for commercial hexane in accordance with §798.5200 of this chapter except for the provisions in paragraphs (d)(5)(ii) and (d)(5)(iii) of §798.5200. The mouse biochemical specific locus test, if conducted, shall be performed for commercial hexane in accordance with §798.5195 of this chapter except for the provisions in paragraphs (d)(5)(ii) and (d)(5)(iii) of §798.5195.

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

(i) Dose levels. A minimum of two dose levels shall be tested. The highest dose tested shall be the highest dose tolerated without toxic effects, provided that any temporary sterility induced due to elimination of spermatogonia is of only moderate duration, as determined by a return of males to fertility within 80 days of treatment, or shall be the highest dose attainable below the lower explosive limit concentration of commercial hexane. Exposure shall be for 6 hours a day. Duration of exposure shall be dependent upon the accumulated total dose desired for each group.

(ii) Route of administration. Animals shall be exposed to commercial hexane by inhalation.

(ii) Reporting requirements. (A) The gene mutation tests shall be completed and final reports submitted to EPA as follows:

(1) The Salmonella typhimurium reverse mutation assay within 8 months of the effective date of the final rule.

(2) The gene mutation in mammalian cells assay within 17 months of the effective date of the final rule.

(3) The sex-linked recessive-lethal test in Drosophila melanogaster within 24 months of the effective date of the final rule.

(4) The mouse visible specific locus test or the mouse biochemical specific locus test shall be completed and a final report shall be submitted to EPA within 51 months of the date on which the test sponsor is notified by EPA by certified letter or Federal Register notice that testing shall be initiated.

(B) Interim progress reports for each test shall be submitted to EPA for the gene mutation in mammalian cells assay and Drosophila sex-linked recessive lethal test at 6-month intervals beginning 6 months after the effective date of the final rule, until the applicable final report is submitted to EPA.

(C) Interim progress reports for either the mouse visible specific locus test or the mouse biochemical specific locus test shall be submitted to EPA at 6-month intervals, beginning 6 months after EPA's notification of the test sponsor that testing should be initiated, until the applicable final report is submitted to EPA.

(6) Mutagenic effects—chromosomal aberrations—(i) Required testing. (A)(1) An in vitro cytogenetics test shall be conducted with commercial hexane in accordance with §798.5375 of this chapter except for the provisions in paragraph (e)(3) of §798.5375.

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

(i) Treatment with test substance. The test substance shall be added in liquid form mixed with DMSO to the treatment vessels.

(ii) [Reserved]

(B)(1) An in vivo cytogenetics test shall be conducted with commercial hexane in accordance with §798.5385 of this chapter except for the provisions in paragraphs (d)(5) (ii), (iii) and (iv) of §798.5385, if the in vitro test conducted pursuant to paragraph (c)(6)(i)(A) of this section is negative.

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

(i) Dose levels. For an initial assessment, one dose level of the test substance may be used, the dose being the maximum tolerated dose (to a maximum of 5,000 mg/kg), or that producing some indication of cytotoxicity (e.g., partial inhibition of mitosis), or shall be the highest dose attainable (to a maximum of 5,000 mg/kg) and should not exceed the lower explosive limit of commercial hexane. Additional dose levels may be used. For determination of dose-response, at least three dose levels should be used.

(ii) Route of administration. Animals shall be exposed to commercial hexane by inhalation.

(iii) Treatment schedule. The duration of exposure shall be for 6 hours per day for 5 consecutive days.

(C)(1) A dominant lethal assay shall be conducted with commercial hexane in accordance with §798.5450 of this chapter except for the provisions in paragraphs (d)(5) (ii) and (iii) of §798.5450, unless both the in vitro and in vivo cytogenetics tests conducted pursuant to paragraphs (c)(6)(i) (A) and (B) of this section are negative.

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

(i) Dose levels. Normally, three dose levels shall be used. The highest dose shall produce signs of toxicity (e.g., slightly reduced fertility and slightly reduced body weight). The highest dose should not exceed the lower explosive limit of commercial hexane. However, in an initial assessment of dominant lethality, a single high dose may be sufficient. Nontoxic substances shall be tested at 5 g/kg or, if this is not practicable, then at the highest dose attainable.

(ii) Route of administration. Animals shall be exposed to commercial hexane by inhalation.

(iii) Treatment schedule. The duration of exposure shall be for 6 hours per day for 5 consecutive days.

(D)(1) A heritable translocation test shall be conducted with commercial hexane in accordance with §798.5460 of this chapter except for the provisions in paragraphs (d)(5) (ii) and (iii) of §798.5460, if the results of the dominant lethal assay conducted pursuant to paragraph (c)(6)(i)(C) of this section are positive 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.

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

(i) Dose levels. At least two dose levels shall be used. The highest dose level shall result in toxic effects (which shall not produce an incidence of fatalities which would prevent a meaningful evaluation) or shall be the highest dose attainable or 5 g/kg body weight and should not exceed the lower explosive limit of commercial hexane.

(ii) Route of administration. Animals shall be exposed to commercial hexane by inhalation.

(iii) Reporting requirements. (A) The chromosomal aberration tests shall be completed and the final reports submitted to EPA as follows:

(1) The in vitro cytogenetics test within 15 months of the effective date of the final rule.

(2) The in vivo cytogenetics test within 19 months of the effective date of the final rule.

(3) The dominant lethal assay within 28 months of the effective date of the final rule.

(4) The heritable translocation test within 25 months of the date of EPA's notification of the test sponsor by certified letter or Federal Register notice that testing shall be initiated.

(B) Interim progress reports for each test shall be submitted to EPA for the in vivo cytogenetics and the dominant lethal assays at 6-month intervals beginning 6 months after the effective date of the final rule, until the applicable final report is submitted to EPA.

(C) Interim progress reports shall be submitted to EPA for the heritable translocation assay at 6-month intervals beginning 6 months after the date of EPA's notification of the test sponsor that testing shall be initiated, until the final report is submitted to EPA.

(7) Neutrotoxicity—(i) Required testing. (A)(1) A schedule-controlled operant behavior test shall be conducted with commercial hexane in accordance with §798.6500 of this chapter except for the provisions in paragraphs (d)(5)(i), (6) and (7) of §798.6500.

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

(i) High dose level. The highest dose shall produce clear behavioral effects or life-threatening toxicity. In addition, the highest dose should not exceed the lower explosive limit of commercial hexane.

(ii) Duration and frequency of exposure. Animals shall be dosed once for 4 to 6 hours.

(iii) Route of administration. Animals shall be exposed to commercial hexane by inhalation.

(B)(1) A functional observation battery shall be conducted with commercial hexane in accordance with §798.6050 of this chapter except for the provisions in paragraphs (d)(4)(i), (5), and (6) of §798.6050.

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

(i) High dose level. The highest dose shall produce clear behavioral effects or life-threatening toxicity. In addition, the highest dose should not exceed the lower explosive limit of commercial hexane.

(ii) Duration and frequency of exposure. Animals shall be dosed for 6 hours/day, 5 days/week for 90 days.

(iii) Route of exposure. Animals shall be exposed to commercial hexane by inhalation.

(C)(1) A motor activity test shall be conducted with commercial hexane in accordance with §798.6200 of this chapter except for the provisions in paragraphs (d)(4)(i), (5), and (6) of §798.6200.

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

(i) High dose level. The highest dose shall produce clear effects on motor activity of life-threatening toxicity. In addition, the highest dose should not exceed the lower explosive limit of commercial hexane.

(ii) Duration and frequency of exposure. Animals shall be dosed for 6 hours/day, 5 days/week for 90 days.

(iii) Route of exposure. Animals shall be exposed to commercial hexane by inhalation.

(D)(1) A neuropathology test shall be conducted with commercial hexane in accordance with §798.6400 of this chapter except for the provisions in paragraphs (d)(4)(i), (5), and (6) of §798.6400.

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

(i) High dose level. The highest dose shall produce clear behavior effects or life-threatening toxicity. In addition, the highest dose should not exceed the lower explosive limit of commercial hexane.

(ii) Duration and frequency of exposure. Animals shall be dosed for 6 hours/day, 5 days/week for 90 days.

(iii) Route of exposure. Animals shall be exposed to commercial hexane by inhalation.

(ii) Reporting requirements. (A) The schedule-controlled operant behavior, functional observation battery, motor activity, and neuropathology tests shall be completed and the final reports submitted to EPA within 15 months of the effective date of the final rule.

(B) Interim progress reports for each test shall be submitted to EPA for the schedule-controlled operant behavior, functional observation battery, motor activity, and neuropathology tests at 6-month intervals beginning 6 months after the effective date of the applicable final rule, until the applicable final report is submitted to EPA.

(8) Pharmacokinetics—(i) Required testing. (A) Pharmacokinetics testing shall be conducted in rats in accordance with §795.232 of this chapter, except for paragraph (c)(1)(ii) of §795.232.

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

(1) Test animals. Adult male and female rats shall be used for testing. The rats shall be 9 to 11 weeks old and their weight range should be comparable from group to group. The animals shall be purchased from a reputable dealer and shall be permanently identified upon arrival. The animals

shall be selected at random for the testing groups, and any animal showing signs of ill health shall not be used.

(2) Species and strain. The rat strain used shall be the same as the strain used in the subchronic and chronic tests required under §§798.2450(d)(1)(i) and 798.3300(b)(1)(i).

(ii) Reporting requirements. (A) The inhalation and dermal pharmacokinetics tests shall be completed and the final report submitted to EPA by August 21, 1992.

(B) Interim progress reports shall be submitted to EPA for the inhalation and dermal pharmacokinetics tests at 6-month intervals, beginning 6 months after the effective date specified in paragraph (d)(1) of this section, until the final report is submitted to EPA.

(d) Effective date. (1) The effective date of this final rule is November 17, 1988, except for the provisions of paragraphs (c)(2)(ii)(A), (c)(5)(i)(D), (c)(5)(ii)(A)(4), (c)(5)(ii)(C), (c)(8)(i) and (c)(8)(ii)(A) of this section. The effective date for paragraphs (c)(5)(i)(D), (c)(5)(ii)(A)(4) and (c)(5)(ii)(C) of this section is May 21, 1990. The effective date for paragraphs (c)(8)(i) and (c)(8)(ii)(A) of this section is June 12, 1992. The effective date of paragraph (c)(2)(ii)(A) is September 8, 1994.

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

[53 FR 3392, Feb. 5, 1988, as amended at 53 FR 38953, Oct. 4, 1988; 55 FR 634, Jan. 8, 1990; 55 FR 7325, Mar. 1, 1990; 55 FR 12643, Apr. 5, 1990; 57 FR 24961, June 12, 1992; 58 FR 34205, June 23, 1993; 59 FR 46357, Sept. 8, 1994; 60 FR 34467, July 3, 1995; 69 FR 18803, Apr. 9, 2004; 77 FR 46293, Aug. 3, 2012]

Back to Top

§799.2325 Isopropanol.

(a) Identification of test substance. (1) Isopropanol (CAS No. 67-63-0) shall be tested in accordance with this section.

(2) Isopropanol of at least 99.8 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 or byproduct manufacture) or intend to manufacture or process isopropanol, from the effective date of this 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 parts 790 and 792 of this chapter for single-phase rulemaking.

(c) Health effects testing—(1) Subchronic inhalation toxicity—(i) Required testing. A subchronic inhalation toxicity test shall be conducted with isopropanol in accordance with §798.2450 of this chapter.

(ii) Reporting requirements. (A) The subchronic inhalation toxicity test shall be completed and the final report submitted to EPA within 15 months of the date specified in paragraph (d) of this section.

(B) Progress reports shall be submitted to EPA for the subchronic inhalation toxicity test at 6-month intervals beginning 6 months after the date specified in paragraph (d)(1) of this section until submission of the final report.

(2) Reproduction and fertility effects—(i) Required testing. A reproduction and fertility effects test shall be conducted by gavage with isopropanol in accordance with §798.4700 of this chapter.

(ii) Reporting requirements. (A) The reproduction and fertility effects test shall be completed and the final report submitted to EPA within 29 months of the date specified in paragraph (d)(1) of this section.

(B) Progress reports shall be submitted at 6-month intervals beginning 6 months after the date specified in paragraph (d)(1) of this section until submission of the final report.

(3) Developmental toxicity—(i) Required testing. A developmental toxicity test shall be conducted in two mammalian species by gavage with isopropanol in accordance with §798.4900 of this chapter.

(ii) Reporting requirements. (A) The developmental toxicity test shall be completed and the final report submitted to EPA within 12 months of the date specified in paragraph (d)(1) of this section.

(B) A progress report shall be submitted 6 months after the date specified in paragraph (d)(1) of this section.

(4) Mutagenic effects—gene mutations—(i) Required testing. (A) A gene mutation test in mammalian cells shall be conducted with isopropanol in accordance with §798.5300 of this chapter.

(B)(1) A sex-linked recessive lethal test in Drosophila melanogaster shall be conducted with isopropanol in accordance with §798.5275 of this chapter, except for the provisions in paragraphs (d)(5)(ii) and (iii) of §798.5275, unless the results of the mammalian cells in the culture gene mutation test conducted pursuant to paragraph (c)(5)(i)(A) of this section are negative.

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

(i) Route of administration. The route of administration shall be by exposure to isopropanol vapors or by injection of isopropanol.

(ii) [Reserved]

(C)(1) The mouse visible specific locus (MVSL) test shall be conducted with isopropanol by inhalation in accordance with §798.5200, except for the provisions in paragraphs (d)(5)(ii) and (iii) of §798.5200, if the results of the sex-linked recessive lethal test conducted pursuant to paragraph (c)(4)(i)(B) of this section are positive 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.

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

(i) Dose levels and duration of exposure. A minimum of 2 dose levels shall be tested. The duration of exposure shall be for 6 hours per day. Duration of exposure shall be dependent upon accumulated total dose desired for each group.

(ii) Route of administration. Animals shall be exposed to isopropanol by inhalation.

(ii) Reporting requirements. (A) The gene mutation tests shall be completed and final report submitted to EPA as follows:

(1) The gene mutation in mammalian cells assay within 6 months of the date specified in paragraph (d)(1) of this section.

(2) The sex-linked recessive-lethal test in Drosophila melanogaster within 18 months of the date specified in paragraph (d)(1) of this section.

(3) The mouse visible specific-locus test within 51 months of the date of EPA's notification of the test sponsor by certified letter or Federal Register notice under paragraph (c)(4)(i)(C) of this section that testing shall be initiated.

(B) Progress reports shall be submitted to EPA for the Drosophila sex-linked recessive lethal test at 6-month intervals beginning 6 months after the date specified in paragraph (d)(1) of this section until the submission of the final report.

(C) Progress reports shall be submitted to EPA for the mouse visible specific locus test at 6-month intervals beginning 6 months after the date of EPA's notification of the test sponsor that testing shall be initiated until submission of the final report.

(5) Mutagenic effects—chromosomal aberrations—(i) Required testing. (A)(1) The micronucleus test shall be conducted with isopropanol in accordance with §798.5395 of this chapter.

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

(i) Route of administration. Animals shall be exposed to isopropanol by either inhalation or oral gavage or inperitoneally (IP).

(ii) Duration of exposure. For inhalation, the duration of exposure shall be for 6 hours per day for 5 consecutive days with one sacrifice time or for 6 hours for 1 day with three sacrifice times.

(B)(1) A dominant lethal assay shall be conducted with isopropanol in accordance with §798.5450 of this chapter, except for the provisions in paragraphs (d)(5)(ii) and (iii) of §798.5450, unless the micronucleus test conducted pursuant to paragraphs (c)(5)(i)(A) of this section is negative.

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

(i) Route of administration. Animals shall be exposed to isopropanol by inhalation.

(ii) Duration of exposure. The duration of exposure shall be for 6 hours per day for 5 consecutive days.

(C)(1) The mouse visible specific locus test (MVSL) shall be conducted with isopropanol by inhalation in accordance with §798.5200 of this chapter, except for the provisions in paragraphs (d)(5)(ii) and (d)(5)(iii) of §798.5200, or a mouse biochemical specific locus test (MBSL) shall be conducted with isopropanol by inhalation in accordance with §798.5195 of this chapter, except for the provisions in paragraphs (d)(5)(ii) and (d)(5)(iii) of §798.5195, if the results of the sex-linked recessive lethal test conducted pursuant to paragraph (c)(4)(i)(B) of this section are positive 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.

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

(i) Route of administration. Animals shall be exposed to isopropanol by inhalation.

(ii) [Reserved]

(ii) Reporting requirements. (A) The chromosomal aberration tests shall be completed and the final reports submitted to EPA as follows:

(1) The micronucleus test within 15 months of the date specified in paragraph (d)(1) of this section.

(2) The dominant lethal assay within 27 months of the date specified in paragraph (d)(1) of this section.

(3) The MVSL or MBSL test within 51 months of the date of EPA's notification of the test sponsor by certified letter or Federal Register notice under paragraph (c)(4)(i)(C) of this section that testing shall be initiated.

(B) Progress reports shall be submitted to EPA for the micronucleus and the dominant lethal assays at 6-month intervals beginning 6 months after the date specified in paragraph (d)(1) of this section until submission of the final report.

(C) Progress reports shall be submitted to EPA for the heritable translocation assay at 6-month intervals beginning 6 months after the date of EPA's notification of the test sponsor that testing shall be initiated until submission of the final report.

(6) Neurotoxicity—(i) Required testing. (A)(1) A functional observation battery shall be conducted with isopropanol in accordance with §798.6050 of this chapter except for the provisions in paragraphs (d)(5) and (6) of §798.6050.

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

(i) Duration and frequency of exposure. For subchronic study, animals shall be dosed for 6 hours per day, 5 days per week for 90 days. For acute study, animals shall be dosed for 4 to 6 hours once.

(ii) Route of exposure. Animals shall be exposed to isopropanol by inhalation.

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

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

(i) Duration of exposure. For subchronic study, animals shall be dosed for 6 hours per day, 5 days per week for 90 days. For acute study, animals shall be dosed for 4 to 6 hours once.

(ii) Route of exposure. Animals shall be exposed to isopropanol by inhalation.

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

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

(i) Duration of exposure. Animals shall be dosed for 6 hours per day, 5 days per week for 90 days.

(ii) Route of exposure. Animals shall be exposed to isopropanol by inhalation.

(D) The developmental neurotoxicity test shall be conducted with isopropanol in accordance with §795.250 of this chapter, except for paragraph (c)(1)(iv).

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

(i) Numbers of animals. The objective is for a sufficient number of pregnant rats to be exposed to ensure that an adequate number of offspring are produced for neurotoxicity evaluation. At least 24 litters shall be used at each dose level.

(ii) [Reserved]

(2) [Reserved]

(ii) Reporting requirements. (A) The acute functional observation battery and motor activity tests shall be completed and the final report submitted to EPA within 15 months of the date specified in paragraph (d)(1) of this section. The subchronic functional observation battery, motor activity, and neuropathology tests shall be completed and the final reports submitted to EPA within 18 months of the date specified in paragraph (d)(1) of this section. The developmental neurotoxicity test shall be completed and the final report submitted to EPA within 21 months of the date specified in paragraph (d)(1) of this section.

(B) Progress reports shall be submitted to EPA for the functional observation battery, motor activity, neuropathology, and developmental neurotoxicity tests at 6-month intervals beginning 6 months after the date specified in paragraph (d)(1) of this section until submission of the applicable final report.

(7) Pharmacokinetics studies—(i) Required testing. An oral and inhalation pharmacokinetics test shall be conducted with isopropanol in accordance with §795.231 of this chapter.

(ii) Reporting requirements. (A) The pharmacokinetic test shall be completed and the final report submitted to EPA within 15 months of the date specified in paragraph (d)(1) of this section.

(B) Progress reports shall be submitted to EPA for the pharmacokinetics test at 6-month intervals beginning 6 months after the date specified in paragraph (d)(1) of this section until submission of the final report.

(8) Oncogenicity—(i) Required testing. An oncogenicity test shall be conducted by inhalation with isopropanol in accordance with §798.3300 of this chapter.

(ii) Reporting requirements. (A) The oncogenicity test shall be completed and the final report submitted to EPA by July 5, 1994.

(B) Progress reports shall be submitted at 6-month intervals beginning 6 months after the date specified in paragraph (d)(1) of this section until submission of the final report.

(d) Effective date. (1) The effective date of this final rule is December 4, 1989, except for the provisions of paragraphs (c)(5)(i)(C)(1), (c)(5)(ii)(A)(3), (c)(6)(i)(D), and (c)(8)(ii)(A), of this section. The effective date for paragraphs (c)(5)(i)(C)(1), and (c)(5)(ii)(A)(3) of this section is May 21, 1990. The effective date for paragraphs (c)(6)(i)(D) of this section is May 21, 1991. The effective date of paragraph (c)(8)(ii)(A) is September 29, 1995.

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

[54 FR 43262, Oct. 23, 1989, as amended at 55 FR 12644, Apr. 5, 1990; 56 FR 23231, May 21, 1990; 58 FR 34205, June 23, 1993; 60 FR 56956, Nov. 13, 1995]

Back to Top

§799.2475 2-Mercaptobenzothiazole.

(a) Identification of test substance. (1) 2-Mercaptobenzothiazole (MBT, CAS No. 149-30-4) shall be tested in accordance with this section.

(2) MBT of at least 97.6 percent purity (plus or minus 1.5 percent) shall be used as the test substance.

(b) Persons required to submit study plans, conduct tests, and submit data. All persons who manufacture (including byproduct manufacture, and import of MBT and MBT-containing articles) or process or intend to manufacture or process MBT, other than as an impurity, after October 21, 1988, 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 parts 790 and 792 of this chapter for single-phase rulemaking.

(c) Chemical fate—(1) Aerobic aquatic biodegradation—(i) Required testing. Aerobic aquatic biodegradation testing shall be conducted with MBT in accordance with §796.3100 of this chapter.

(ii) Reporting requirements. (A) The aerobic aquatic biodegradation test 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.

(2) Indirect photolysis-screening level test—(i) Required testing. Indirect photolysis testing shall be conducted with MBT in accordance with §795.70 of this chapter.

(ii) Reporting requirements. (A) The indirect photolysis test 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.

(3) Chemical mobility—(i) Required testing. Chemical mobility testing shall be conducted with MBT in accordance with §796.2750 of this chapter.

(ii) Reporting requirements. (A) The chemical mobility test 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 this final rule.

(d) Environmental effects—(1) Fish chronic toxicity—(i) Required testing. (A) Chronic toxicity testing of MBT shall be conducted using rainbow trout (Salmo gairdneri.) according to §797.1600 of this chapter, except for paragraphs (c)(4)(iv)(A), (c)(4)(x)(E) and (c)(4)(x)(F), (c)(6)(iv)(A), (d)(2)(vii)(A)(2), and (d)(3)(iv) of §797.1600.

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

(1) The first feeding for the fathead and sheepshead minnow fry shall begin shortly after transfer of the fry from the embryo cups to the test chambers. Silversides are fed the first day after hatch. Trout species initiate feeding at swim-up. The trout fry shall be fed trout starter mash or live newly-hatched brine shrimp nauplii (Artemia salina) three times a day ad libitum,with excess food siphoned off daily. The minnow fry shall be fed live newly-hatched brine shrimp nauplii (Artemia salina) at least three times a day.

(2) All physical abnormalities (e.g., stunted bodies, scoliosis, etc.) shall be photographed and preserved.

(3) At termination, all surviving fish shall be measured for growth. Total length measurements should be used except in cases where fin erosion occurs, then the use of standard length measurements shall be permitted. Standard length measurements should be made directly with a caliper, but may be measured photographically. Measurements shall be made to the nearest millimeter (0.1 mm is desirable). Weight measurements shall also be made for each fish alive at termination (wet, blotted dry, and to the nearest 0.01 g for the minnows and 0.1 g for the trout). If the fish exposed to the toxicant appear to be edematous compared to control fish, determination of dry, rather than wet, weight is recommended.

(4)(i) Test substance measurement. Prior to addition of the test substance to the dilution water, it is recommended that the test substance stock solution be analyzed to verify the concentration. After

addition of the test substance, the concentration of test substance shall be measured in the test substance delivery chamber prior to beginning, and during, the test. The concentration of test substance should also be measured at the beginning of the test in each test concentration (including both replicates) and control(s), and at least once a week thereafter. Equal aliquots of test solution may be removed from each replicate chamber and pooled for analysis. If a malfunction in the delivery system is discovered, water samples shall be taken from the affected test chambers immediately and analyzed.

(ii) pH. It is recommended that a pH of 7 be maintained in the test chambers.

(iii) Reporting. An analysis of the stability of the stock solution for the duration of the test shall be reported.

(5) [Reserved]

(6) For brook and rainbow trout, a 16-hour light and 8-hour dark photoperiod shall be provided.

(ii) Reporting requirements. (A) The fish chronic toxicity test 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.

(2) Daphnid chronic toxicity—(i) Required testing. (A) Daphnid chronic toxicity testing shall be conducted with MBT using Daphnia magna according to §797.1330 of this chapter.

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

(1) Test substance measurement. Test substance concentration shall be measured in the test substance delivery chamber prior to beginning, and during, the test.

(2) pH. It is recommended that a pH of 7 be maintained in the test chambers.

(3) Reporting. An analysis of the stability of the stock solution for the duration of the test shall be reported and data comparing trout starter mash with A. salina for supporting trout growth should be submitted with the final report.

(ii) Reporting requirements. (A) The daphnid chronic toxicity test 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.

(e) Health effects—(1) Developmental toxicity testing—(i) Required testing. Developmental toxicity testing shall be conducted in two mammalian species with MBT in accordance with §798.4900 of this chapter, using the oral route of administration.

(ii) Reporting requirements. (A) The developmental toxicity test 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.

(2) Reproductive toxicity—(i) Required testing. Reproductive toxicity testing shall be conducted with MBT in accordance with §798.4700 of this chapter, using the oral route of administration.

(ii) Reporting requirements. (A) The reproductive test shall be completed and the final report submitted to EPA within 29 months of the effective date of the final rule.

(B) Progress reports shall be submitted to EPA at 6-month intervals beginning 6 months after the effective date of the final rule until submission of the final report.

(3) Neurotoxicity—(i) Required testing. (A)(1) An acute and subchronic functional observation battery shall be conducted with MBT in accordance with §798.6050 of this chapter except for the provisions in paragraphs (d)(5) and (6) of §798.6050.

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

(i) Duration and frequency of exposure. For acute study, animals shall be administered MBT over a period not to exceed 24 hours. For subchronic study, animals shall be dosed daily for at least 90 days.

(ii) Route of exposure. Animals shall be exposed to MBT orally.

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

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

(i) Duration and frequency of exposure. For acute study, animals shall be administered over a period not to exceed 24 hours. For subchronic study, animals shall be dosed daily for at least 90 days.

(ii) Route of exposure. Animals shall be exposed to MBT orally.

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

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

(i) Duration and frequency of exposure. Animals shall be dosed daily for at least 90 days.

(ii) Route of exposure. Animals shall be exposed to MBT orally.

(ii) Reporting requirements. (A) The functional observation battery, motor activity, and neuropathology tests shall be completed and the final reports for each test submitted to EPA within 18 months of the effective date of the final rule.

(B) A progress report shall be submitted to EPA for the functional observation battery, motor activity, and neuropathology tests, respectively, 6 months after the effective date of the final rule.

(4) Mutagenic effects—Chromosomal aberrations—(i) Required testing. (A) A dominant lethal assay shall be conducted with MBT in accordance with §798.5450 of this chapter, using the oral route of administration.

(B) A heritable translocation assay shall be conducted with MBT in accordance with the test guideline specified in §798.5460 of this chapter if MBT produces a positive result in the dominant lethal assay conducted pursuant to paragraph (e)(4)(i)(A) of this section 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.

(ii) Reporting requirements. (A) Mutagenic effects—Chromosomal aberration testing of MBT shall be completed and the final report submitted to EPA as follows: Dominant lethal assay, within 12 months after the effective date of this rule; heritable translocation assay, within 24 months after notification under paragraph (e)(4)(i)(B) of this section that the testing shall be initiated.

(B) For the dominant lethal assay, an interim progress report shall be submitted to EPA 6 months after the effective date of the final rule; for the heritable translocation assay, progress reports shall be submitted to EPA at 6-month intervals beginning 6 months after the date of EPA's notification of the test sponsor that testing shall be initiated until submission of the final report.

(f) Effective date. (1) The effective date of this final rule is October 21, 1988, except for paragraphs (a)(2), (d)(1)(i), (d)(2)(i)(B)(3), and (e)(3)(ii)(A) of this section. The effective date for paragraphs (a)(2), (d)(1)(i), (d)(2)(i)(B)(3), and (e)(3)(ii)(A) of this section is March 1, 1990.

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

[53 FR 34530, Sept. 7, 1988; 53 FR 37393, Sept. 26, 1988, as amended at 55 FR 7326, Mar. 1, 1990; 58 FR 34205, June 23, 1993]

Back to Top

§799.2700 Methyl ethyl ketoxime.

(a) Identification of test substance. (1) Methyl ethyl ketoxime (MEKO, CAS No. 96-29-7) shall be tested in accordance with this section.

(2) MEKO 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) or process or intend to manufacture or process MEKO, including persons who manufacture or process or intend to manufacture or process MEKO as a byproduct, or who import or intend to import products which contain MEKO, after the date specified in paragraph (e) of this section 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 parts 790 and 792 of this chapter for single-phase rulemaking. Persons who manufacture, import, or process MEKO only as an impurity are not subject to these requirements.

(c) Health effects testing—(1) Pharmacokinetics testing—(i) Required testing. Pharmacokinetics testing shall be conducted with MEKO in accordance with paragraph (c)(1)(ii) of this section.

(ii) [Reserved]

(2) Oncogenicity—(i) Required testing. Oncogenicity testing shall be conducted in accordance with §798.3300 of this chapter.

(ii) Route of administration. MEKO shall be administered either orally or by inhalation.

(iii) Reporting requirements. (A) Oncogenicity testing shall be completed and a final report submitted to EPA within 53 months of the date specified in paragraph (e) of this section.

(B) Interim progress reports shall be submitted to EPA at 6-month intervals, beginning 6 months after the date specified in paragraph (e) of this section, until submission of the final report to EPA.

(3) Developmental toxicity—(i) Required testing. Developmental toxicity testing shall be conducted in a rodent and a nonrodent mammalian species in accordance with §798.4900 of this chapter.

(ii) Route of administration. MEKO shall be administered orally.

(iii) Reporting requirements. (A) Developmental toxicity testing shall be completed and a final report submitted to EPA within 15 months of the date specified in paragraph (e) of this section.

(B) Interim progress reports shall be submitted to EPA at 6-month intervals, beginning 6 months after the date specified in paragraph (e) of this section.

(4) Reproductive toxicity—(i) Required testing. (A) Reproductive toxicity testing shall be conducted orally in accordance with §798.4700 of this chapter except for the provisions in paragraphs (c)(8)(iii) and (9)(i) of §798.4700.

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

(1) The following organs and tissues, or representative samples thereof, shall be preserved in a suitable medium for possible future histopathological examination: Vagina, uterus, oviducts, ovaries, testes, epididymides, vas deferens, seminal vesicles, prostate, pituitary gland, and, target organ(s) of all P and F1 animals selected for mating.

(2)(i) Full histopathology shall be conducted on the organs and tissues listed in paragraph (c)(4)(i)(B)(1) of this section for all high dose and control P and F1 animals selected for mating.

(ii) The integrity of the various cell stages of spermatogenesis shall be determined, with particular attention directed toward achieving optimal quality in the fixation and embedding. Preparations of testicular and associated reproductive organ samples for histology should follow the recommendations of Lamb and Chapin (1985) under paragraph (d)(1) of this section, or an equivalent procedure. Histopathology of the testes shall be conducted on all P and F1 adult males at the time of sacrifice, and histological analyses shall include evaluations of the spermatogenic cycle, i.e., the presence and integrity of the 14 cell stages. These evaluations should follow the guidance provided by Clermont and Percy (1957) under paragraph (d)(2) of this section. Information shall also be provided regarding the nature and level of lesions observed in control animals for comparative purposes.

(iii) Data on female cyclicity shall be obtained by conducting vaginal cytology in P and F1 females over the last 3 weeks prior to mating; the cell staging technique of Sadleir (1978) and the vaginal smear method in Hafez (1978) under paragraphs (d)(3) and (d)(7) of this section, respectively, or equivalent methods should be used. Data shall be provided on whether the animal is cycling and the cycle length.

(iv) P and F1 females shall continue to be exposed to MEKO for at least an additional 2 weeks following weaning of offspring to permit them to begin cycling once again. They shall then be sacrificed and their ovaries shall be serially sectioned with a sufficient number of sections examined to adequately detail oocyte and follicular morphology. The methods of Mattison and Thorgiersson (1979) and Pederson and Peters (1968) under paragraphs (d) (4) and (5) of this section, respectively, may provide guidance. The strategy for sectioning and evaluation is left to the discretion of the investigators, but shall be described in detail in the study plan and final report. The nature and background level of lesions in control tissue shall also be noted.

(v) Gross and histopathologic evaluations shall be conducted on the mammary glands in F1 females and F2 pups sacrificed at weaning and in adult F1 females at the termination of the study. Any abnormalities shall be described in the final report.

(ii) Reporting requirements. (A) Reproductive toxicity testing shall be completed and a final report submitted to EPA within 29 months of the date specified in paragraph (e) of this section.

(B) Interim progress reports shall be submitted to EPA at 6-month intervals, beginning six months after the date specified in paragraph (e) of this section until submission of the final report to EPA.

(5) Mutagenic effects—gene mutations—(i) Required testing. The sex-linked recessive lethal assay in Drosophila shall be conducted with MEKO in accordance with §798.5275 of this chapter.

(ii) Reporting requirements. (A) The sex-linked recessive lethal assay in Drosophila shall be completed and a final report submitted to EPA within 18 months of the date specified in paragraph (e) of this section.

(B) Interim progress reports shall be submitted to EPA at 6-month intervals beginning 6 months after the date specified in paragraph (e) of this section.

(6) Mutagenic effects—chromosomal aberrations—(i) Required testing. (A) An in vivo mammalian bone marrow cytogenetics test shall be conducted with MEKO in accordance with either §798.5385 (chromosomal analysis) of this chapter, or §798.5395 (micronucleus assay) of this chapter except for the provisions in paragraphs (d)(5) (ii), (iii), and (iv) of §§798.5385 and 798.5395.

(B) For the purpose of this section, the following provisions also apply if §798.5385 of this chapter is used in conducting the test:

(1) Dose levels and duration of exposure. At least three dose levels shall be tested. The highest dose tested shall be the maximum tolerated dose or that dose producing some signs of cytotoxicity (e.g., partial inhibition of mitosis) or shall be the highest dose attainable. Under oral administration, animals shall be exposed once per day for 5 consecutive days. Under administration by inhalation, animals shall be exposed 6 hours per day for 5 consecutive days.

(2) Route of administration. Animals shall be exposed to MEKO either orally or by inhalation.

(C) For the purpose of this section, the following provisions also apply if §798.5395 of this chapter is used in conducting the test:

(1) Dose levels and duration of exposure. At least three-dose levels shall be tested. The highest dose tested shall be the maximum tolerated dose or that dose producing some signs of cytotoxicity (e.g., a change in the ratio of polychromatic to normochromatic erythrocytes) or shall be the highest dose attainable. Under oral administration animals shall be exposed once per day for 5 consecutive days. Under administration by inhalation, animals shall be exposed 6 hours per day for 5 consecutive days.

(2) Route of administration. Animals shall be exposed to MEKO either orally or by inhalation.

(ii) Reporting requirements. (A) The oral in vivo mammalian cytogenetics test shall be completed and a final report submitted to EPA within 14 months of the date specified in paragraph (e) of this section. The inhalation in vivo mammalian cytogenetics test shall be completed and a final report submitted to EPA within 17 months of the date specified in paragraph (e) of this section.

(B) Interim progress reports shall be submitted to EPA at 6-month intervals, beginning 6 months after the date specified in paragraph (e) of this section.

(7) Neurotoxicity—(i) Required testing—(A) Functional observational battery. (1) A functional observational battery shall be conducted with MEKO in accordance with §798.6050 of this chapter except for the provisions in paragraphs (d) (4)(ii), (5), and (6) of §798.6050.

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

(i) Route of exposure. Animals shall be exposed either orally or by inhalation.

(ii) Lower doses. The data from the lower doses shall show either graded dose-dependent effects in at least two of all the doses tested, including the highest dose, or no neurotoxic (behavioral) effects at any dose tested.

(iii) Duration and frequency of exposure. For the oral acute testing, animals shall be exposed once. For the oral subchronic testing, animals shall be exposed once per day 5 days per week for a 90-day period. For the inhalation acute testing, animals shall be exposed for 6 hours for 1 day. For the inhalation subchronic testing, animals shall be exposed 6 hours per day 5 days per week for a 90-day period.

(B) Motor activity. (1) A motor activity test shall be conducted with MEKO in accordance with §798.6200 of this chapter except for provisions in paragraphs (d) (4)(ii), (5), and (6) of §798.6200.

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

(i) Route of exposure. Animals shall be exposed either orally or by inhalation.

(ii) Lower doses. The data from the lower doses shall show either graded dose-dependent effects in at least two of all the doses tested including the highest dose, or no neurotoxic (behavioral) effects at any dose tested.

(iii) Duration and frequency of exposure. For the acute oral testing, animals shall be exposed once. For the oral subchronic testing, animals shall be exposed once per day 5 days per week for a 90-day period. For the acute inhalation testing, animals shall be exposed for 6 hours for 1 day. For the inhalation subchronic testing, the animals shall be exposed for 6 hours per day 5 days per week for a 90-day period.

(C) Neuropathology. (1) A neuropathology test shall be conducted with MEKO in accordance with §798.6400 of this chapter except for the provisions in paragraphs (d) (4)(ii), (5), (6), and (8)(iv)(C) of §798.6400.

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

(i) Route of exposure. Animals shall be exposed either orally or by inhalation.

(ii) Lower doses. The data from the lower doses shall show either graded dose-dependent effects in at least two of all the doses tested including the highest dose, or no neurotoxic (behavioral) effects at any dose tested.

(iii) Duration and frequency of exposure. Animals shall be exposed orally once per day 5 days per week for a 90-day period; or if exposed by inhalation, for 6 hours per day 5 days per week for a 90-day period.

(iv) Clearing and embedding. After dehydration, tissue specimens shall be cleared with xylene and embedded in paraffin or paraplast except for the sural nerve which should be embedded in plastic. Multiple tissue specimens (e.g., brain, cord, ganglia) may be embedded together in one single block for sectioning. All tissue blocks shall be labeled to provide unequivocal identification. A suggested method for plastic embedding is described by Spencer et al. in paragraph (d)(6) of this section.

(ii) Reporting requirements. (A) The neurotoxicity tests required under this paragraph (c)(7) and administered orally shall be completed and the final results submitted to EPA within 18 months of the date specified in paragraph (e) of this section. The neurotoxicity tests required under this paragraph (c)(7) and administered by inhalation shall be completed and the final results submitted to EPA within 21 months of the date specified in paragraph (e) of this section.

(B) Interim progress reports shall be submitted to EPA at 6-month intervals beginning 6 months after the date specified in paragraph (e) of this section until submission of the final report to EPA.

(d) References. For additional background information, the following references should be consulted.

(1) Lamb, J. and Chapin, R.E. “Experimental models of male reproductive toxicology.” In: “Endocrine Toxicity.” Thomas, J.A., Korach, K.S., and McLachlan, J.A., eds. New York, NY: Raven Press. pp. 85-115. (1985).

(2) Clermont, Y. and Percey, B. “Quantitative study of the cell population of the seminiferous tubules in immature rats.” “American Journal of Anatomy.” 100:241-267. (1957).

(3) Sadleir, R.M.F.S. “Cycles and seasons.” In: “Reproduction in Mammals: I. Germ Cells and Fertilization.” Austin, R. and Short R.V., eds. New York, NY: Cambridge Press. Chapter 4. (1978).

(4) Mattison, D.R. and Thorgiersson, S.S. “Ovarian aryl hydrocarbon hydroxylase activity and primordial oocyte toxicity of polycyclic aromatic hydrocarbons in mice.” “Cancer Research.” 39:3471-3475. (1979).

(5) Pederson, T. and Peters, H. “Proposal for classification of oocytes and follicles in the mouse ovary.” “Journal of Reproduction and Fertility.” 17:555-557. (1968).

(6) Spencer, P.S., Bischoff, M., and Schaumburg, H.H. “Neuropathological methods for the detection of neurotoxic disease.” In: “Experimental and Clinical Neurotoxicology.” Spencer, P.S. and Schaumburg, H.H., eds. Baltimore, MD: Williams and Wilkins, pp. 743-757 (1980).

(7) Hafez, E.S., ed., “Reproduction and Breeding Techniques for Laboratory Animals.” Chapter 10. Philadelphia: Lea and Febiger. (1970).

(e) Effective dates. (1) The effective date of this final rule is October 27, 1989.

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

[54 FR 37808, Sept. 13, 1989, as amended at 58 FR 34205, June 23, 1993]

Back to Top

§799.3300 Unsubstituted phenylenediamines.

(a) Identification of test substance. (1) The unsubstituted phenylenediamines (pda's), para-phenylenediamine (p-pda, CAS No. 106-50-3), or its sulfate salt (p-pda.H2SO4, CAS No. 1624-57-75), meta-phenylenediamine (m-pda, CAS No. 108-45-2), or its sulfate salt (m-pda.H2SO4, CAS No. 54-17-08), and ortho-phenylenediamine (o-pda, CAS No. 95-54-5) shall be tested in accordance with this section.

(2) p-Pda, m-pda, and o-pda of at least 98 percent purity shall be used as the test substances. Either the hydrochloride or sulfate salt of m-pda shall be used as the test substances. Either the hydrochloride or sulfate salt of m-pda shall be used as a test substance in the oncogenicity test in paragraph (c)(2) of this section if the free base proves to be unstable under the conditions of this study. Either the hydrochloride or sulfate salt of o-pda, p-pda, or m-pda shall be used as a test substance in the 90-day subchronic neurotoxicity studies in paragraph (c)(3)(B) of this section if the free base proves to be unstable under the conditions of these studies. The salt(s) shall be of at least 98 percent purity.

(b) Persons required to submit study plans, conduct tests, and submit data. (1) All persons who manufacture (including import or by-product manufacture) or process m-pda or m-pda.H2SO4, or intend to manufacture or process m-pda or m-pda.H2SO4, after the effective date of this rule to the end of the reimbursement period shall submit letters of intent to test, submit study plans, conduct tests, and submit data, or submit exemption applications as specified in paragraphs (c), (d), and (e) of this section, subpart A of this part, and parts 790 and 792 of this chapter for single-phase rulemaking.

(2) All persons who manufacture (including import or by-product manufacture) or process p-pda, or p-pda.H2SO4, or intend to manufacture or process p-pda, or p-pda H2SO4, after the effective date of this rule to the end of the reimbursement period shall submit letters of intent to test, submit study plans, conduct tests, and submit data, or submit exemption applications as specified in paragraphs (c)(3), (d), and (e) of this section, subpart A of this part and parts 790 and 792 of this chapter for single-phase rulemaking.

(3) All persons who manufacture (including import or by-product manufacture) or process o-pda, or intend to manufacture or process o-pda after the effective date of this rule to the end of the reimbursement period shall submit letters of intent to test, submit study plans, conduct tests, and submit data, or submit exemption applications as specified in paragraphs (c)(3), (d), and (e) of this section, subpart A of this part, and parts 790 and 792 of this chapter for single-phase rulemaking.

(c) Health effects testing—(1) Mutagenicity testing—(i) Required testing. (A) The sex-linked recessive lethal (SLRL) assay shall be conducted, by injection, in Drosophila melanogasterwith m-pda in accordance with § 798.5275 of this chapter.

(B) If the SLRL assay conducted pursuant to paragraph (c)(1)(i)(A) of this section is positive, either the mouse visible specific locus test (MVSL) or the mouse biochemical specific locus test (MBSL) shall be conducted for m-pda by gavage in accordance with §§798.5200 or 798.5195 of this chapter, if after public program review, EPA issues a Federal Register notice or sends a certified letter to the test sponsor(s) specifying that testing shall be initiated. The test sponsor shall notify EPA of its choice in writing in its first interim report.

(C) The mouse bone marrow cytogenetics: micronucleus (MBMC) assay shall be conducted on m-pda in accordance with § 798.5395 of this chapter.

(D) If the MBMC assay conducted pursuant to paragraph (c)(1)(i)(C) of this section is positive, the dominant lethal assay (DL) in mice shall be conducted on m-pda pursuant to § 798.5450 of this chapter.

(E) If the DL conducted pursuant to paragraph (c)(1)(i)(D) of this section is positive, heritable translocation (HT) testing in the mouse on m-pda shall be conducted pursuant to § 798.5460 of this chapter, if after a public program review, EPA issues a Federal Register notice or sends a certified letter to the test sponsor(s) specifying that testing shall be initiated.

(ii) Reporting requirements. (A) The tests shall be completed and the final reports for the MBMC assay shall be submitted to the EPA no later than January 16, 1991. The final report for the SLRL in Drosophila melanogaster shall be submitted no later than April 15, 1991.

(B) If required, the DL test shall be completed and the final report shall be received by EPA no later than 24 months after the effective date of this final rule.

(C) If required, the MVSL or the MBSL shall be completed and the final report shall be received by EPA no later than 51 months after EPA issues a Federal Register Notice or sends a certified letter to the test sponsor(s) identified under paragraph (c)(1)(i)(B) of this section specifying that testing shall be initiated.

(D) If required, the HT test shall be completed and the final report shall be submitted to EPA not later than 36 months after the date on which EPA notifies the test sponsor under paragraph (c)(1)(i)(E) of this section to begin testing.

(E) Interim reports for the SLRL assay and MBMC are required at 6-month intervals beginning 6 months after the effective date of this section. If the DL is triggered, interim reports are required at 6 month intervals beginning with the date of initiation of the study.

(F) Interim reports for the HT and either the MBSL or MVSL are required at 6-month intervals beginning 6 months after the date of notification by EPA that testing shall be initiated, and ending when the final report is submitted.

(2) Oncogenicity—(i) Required testing. A 2-year dermal oncogenicity bioassay shall be conducted with m-pda if, after public program review, EPA issues a Federal Register notice specifying that the testing shall be initiated.

(ii) [Reserved]

(iii) Reporting requirements. (A) The final results and final report for the oncogenicity bioassay shall be submitted to EPA no later than 53 months after EPA issues a Federal Registernotice or sends a certified letter to the test sponsor under paragraph (c)(2)(i) of this section specifying that the testing shall be initiated.

(B) Interim reports for the oncogenicity study are required at 6-month intervals beginning 6 months after the date of notification by EPA that testing shall be initiated and ending when the final report is submitted.

(3) Neurotoxicity—(i) Required testing. (A) Acute neurotoxicity testing in the neurotoxicity functional observational battery (FOB) in accordance with § 798.6050 of this chapter, and the motor activity test (MAT) in accordance with § 798.6200 of this chapter, shall be conducted for o-, m-, and p-pda. The test chemicals shall be administered in a single oral dose. Clinical observations shall be made at a minimum of 1, 4, 24, and 48 hours and at 7 days after dosing.

(B) If neurotoxic effects are observed at 24 hours, or longer, during the testing conducted pursuant to paragraph (c)(3)(i)(A) of this section, then 90-day subchronic neurotoxic FOB and MAT tests shall be conducted in accordance with §§ 798.6050 and 798.6200 of this chapter, respectively, for each isomer showing such effects. At the end of these tests, the animals shall be sacrificed and the nervous tissue preserved and examined as described in the neuropathology test standard, § 798.6400 of this chapter.

(ii) Reporting requirements. (A) The acute neurotoxicity tests shall be completed and the final report submitted to EPA no later than September 15, 1990. If triggered, the final report of the subchronic neurotoxicity testing and the neuropathological examination shall be submitted to EPA on the following schedules. If one isomer is triggered, the reporting deadline is July 15, 1990. If two isomers are triggered, the reporting deadline is January 15, 1992. If three isomers are triggered, the reporting deadline is July 15, 1992.

(B) [Reserved]

(d) Chemical fate testing—(1) Indirect photolysis testing—(i) Required testing. Indirect photolysis studies shall be conducted with p-, m-, and o-pda to determine the half-life in water of each of the three unsubstituted pda's in accordance with § 795.70 of this chapter.

(ii) Reporting requirements. (A) The final report shall be submitted to EPA no later than 8 months after the effective date of the final rule.

(B) The final report shall include a calculation of the predicted environmental concentration (PEC), 100 × PEC, and 1,000 × PEC for each isomer. PEC shall be calculated by using results from the indirect photolysis studies and solving the following equations for the appropriate isomer: o-pda: PECo = 0.3629 + 1.0468 log t 1/2; m-pda: PECm = 0.6830 + 1.9702 log t 1/2; p-pda: PECp = 0.0085 + 0.0024 log t 1/2, where PEC is the predicted concentration in ppb and t 1/2 is the half-life for oxidation (i.e., indirect photolysis) expressed in minutes. PEC, 100 × PEC, and 1,000 × PEC shall be used in the decision logic described in paragraph (e) of this section.

(2) [Reserved]

(e) Environmental effects testing—(1) Acute toxicity testing—(i) Required testing. (A) Flow-through fish acute toxicity tests in the rainbow trout (Salmo gairdneri) shall be conducted with o-, m-, and p-pda in accordance with § 797.1400 of this chapter.

(B) Acute flow-through studies on the freshwater invertebrate Gammarus shall be conducted with o-, m-, and p-pda in accordance with § 795.120 of this chapter.

(C) If the concentration affecting 50 percent of the population (LC50 or EC50) for any study conducted pursuant to paragraphs (e)(1)(i)(A) and (B) of this section is less than or equal to 100 × PEC, less than or equal to 1 milligram/liter (mg/L), or less than or equal to 100 mg/L and shows indications of chronicity, chronic toxicity testing shall be conducted pursuant to paragraph (e)(2) of this section. Indications of chronicity shall be the following: for fish or aquatic invertebrates, the ratio of 24 hour/96 hour LC50s is greater than or equal to 2; for gammarids, the ratio of 24 hour/48 hour EC50s is greater than or equal to 2.

(ii) Reporting requirements. The final reports for acute toxicity testing shall be submitted as follows:

(A) Testing on the rainbow trout shall be completed and submitted to EPA 9 months after the effective date of the final rule for o-pda and p-pda. Testing for m-pda shall be completed and submitted by January 15, 1991.

(B) The acute toxicity testing in freshwater Gammarus shall be completed and submitted no later than January 15, 1991.

(2) Chronic toxicity testing—(i) Required testing. (A) A fish partial life-cycle flow-through test shall be conducted in the more sensitive fish species, either Pimephales promelas or Salmo gairdneri, with each isomer, o-, m-, and p-pda, demonstrating an LC50, determined by testing of fish pursuant to paragraph (e)(1)(i)(A) of this section, equal to or less than 100 × PEC; or less than 1 mg/L; or less than 100 mg/L with indications of chronicity. Chronicity indicators are defined in paragraph (e)(1)(i)(C) of this section. Testing shall be conducted in accordance with § 797.1600 of this chapter.

(B) An invertebrate life-cycle flow-through toxicity test shall be conducted in Daphnia magna for o- and p-pda in accordance with § 797.1330 of this chapter.

(ii) Reporting requirements. (A) The fish partial life-cycle flow-through test shall be completed and final results shall be submitted to EPA no later than December 1, 1992.

(B) The invertebrate life-cycle flow-through toxicity test shall be completed and the final report submitted to EPA no later than January 15, 1993.

(C) Progress reports shall be submitted at 6 month intervals after the effective date of the final rule.

(f) Effective dates. (1) The effective date of this final rule is January 16, 1990, except for paragraphs (c)(1)(i)(B), (c)(1)(ii)(A), (c)(1)(ii)(C), (c)(1)(ii)(F), (c)(3)(ii)(A), (e)(1)(ii), (e)(2)(ii)(A), and (e)(2)(ii)(B) of this section. The effective date for paragraphs (c)(1)(i)(B), (c)(1)(ii)(C), and (c)(1)(ii)(F) of this section is May 21, 1990. The effective date for paragraphs (c)(1)(ii)(A), (c)(3)(ii)(A), and (e)(1)(ii), of this section is May 21, 1991. The effective date for paragraph (e)(2)(ii)(A) is June 12, 1992. The effective date for paragraph (e)(2)(ii)(B) is May 28, 1993.

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

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

Back to Top

§799.4360 Tributyl phosphate.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

(2) [Reserved]

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

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

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

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

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

(2) [Reserved]

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

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

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

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

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

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

(ii) [Reserved]

(iii) Reporting requirements. (A) The somatic cells in culture assay shall be completed and the final report submitted to EPA, within 10 months after the effective date of the final rule. If required, the Drosophila sex-linked recessive lethal assay shall be completed and the final report submitted to EPA within 22 months after the effective date of the final rule.

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

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

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

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

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

(ii) [Reserved]

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

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

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

(ii) [Reserved]

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

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

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

(ii) [Reserved]

(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), (b)(6)(i) and (b)(9), of §798.3300.

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

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

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

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

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

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

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

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

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

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

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

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

(ii) Reporting requirements. (A) The pharmacokinetics test required in paragraph (c)(8)(i) of this section shall be completed and the final report submitted to EPA by December 26, 1992.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

(B) For the purpose of this section, the following 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 by September 27, 1991.

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

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

≤100 mg/L and either the rainbow trout or gammarid 24 hour to 96 hour LC50 ratio ≥2, or the daphnid 24-hour to 48-hour EC50 or LC50 ratio is ≥2.

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

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

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

(B) The benthic sediment invertebrate bioassay shall be conducted according to the test procedure specified in the American Society for Testing and Materials, Special Technical Publication 854 (ASTM STP 854) entitled, “Aquatic Safety Assessment of Chemicals Sorbed 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 National Archives and Records Administration (NARA). For information on the availability of this material at NARA, call 202-741-6030, or go to: http://www.archives.gov/federal_register/code_of_federal_regulations/ibr_locations.html. Copies may be obtained from the Director, Environmental Assistance Division (7408), Office of Pollution Prevention and Toxics, Environmental Protection Agency, Rm. E-543B, 1200 Pennsylvania Ave. NW., Washington, DC 20460-0001. 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 bioassy 6 months after the initiation of the test.

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

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

(2) Sediment and soil adsorption isotherm—(i) Required testing. Sediment and soil 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 by September 27, 1990.

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

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

(2) [Reserved]

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

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

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

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

[54 FR 33413, Aug. 14, 1989; 56 FR 23231, May 21, 1991, as amended at 57 FR 24961, June 12, 1992; 58 FR 30992, May 28, 1993; 58 FR 34205, June 23, 1993; 60 FR 34467, July 3, 1995; 69 FR 18803, Apr. 9, 2004; 77 FR 46293, Aug. 3, 2012]

Back to Top

§799.4440 Triethylene glycol monomethyl ether.

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

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

(b) Persons required to submit study plans, conduct tests, and submit data. All persons who manufacture or process TGME, other than as an impurity, after May 17, 1989, 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 parts 790 and 792 of this chapter for single-phase rulemaking.

(c) Developmental neurotoxicity—(1) Required testing. Developmental neurotoxicity testing shall be performed in the Sprague-Dawley rat by gavage in accordance with §795.250 of this chapter except for the provision in paragraph (c)(3)(iii) of §795.250.

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

(i) Number of animals. The objective is for a sufficient number of pregnant rats to be exposed to ensure that an adequate number of offspring are produced for neurotoxicity evaluation. At least 24 litters are recommended at each dose level.

(ii) Dose levels and dose selection. In the absence of developmental toxicity or maternal toxicity the maximum dose shall be 5 grams/kilogram.

(3) Reporting requirements—(i) The developmental neurotoxicity test shall be completed and the final report submitted to EPA within 21 months of the initiation of the test.

(ii) Progress reports shall be submitted to EPA at 6- month intervals, beginning six months after the initiation of the test.

(d) Effective date. (1) The effective date of this final rule is May 17, 1989, except for paragraph (c)(2)(i) and (c)(3)(i) of this section. The effective date for paragraph (c)(2)(ii) and (c)(3)(i) of this section is May 21, 1991.

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

[54 FR 13477, Apr. 3, 1989; 56 FR 23232, May 21, 1991, as amended at 58 FR 34205, June 23, 1993]

Back to Top

Subpart C—Testing Consent Orders

Back to Top

§799.5000 Testing consent orders for substances and mixtures with Chemical Abstract Service Registry Numbers.

This section sets forth a list of substances and mixtures which are the subject of testing consent orders adopted under 40 CFR part 790. Listed below in Chemical Abstract Service (CAS) Registry Number order are the substances and mixtures which are the subject of these orders and the Federal Register citations providing public notice of such orders.

CAS Number	Substance or mixture name	Testing	FR Publication Date
67-64-1	Acetone	Health effects	January 23, 1995.
71-55-6	1,1,1-Trichloroethane	Health effects	August 23, 1989.
78-83-1	Isobutyl alcohol	Health effects	January 23, 1995.
79-10-7	Acrylic Acid	Health effects	March 4, 1992.
84-74-2	Di-n-butyl phthalate	Environmental effects	January 9, 1989.
84-75-3	Di-n-hexyl phthalate	Environmental effects	January 9, 1989.
		Chemical fate	January 9, 1989.
100-40-3	4-Vinylcyclohexene	Health effects	September 23, 1991.
		Chemical fate	September 23, 1991.
106-91-2	Glycidyl methacrylate	Health effects	January 26, 1995.
108-10-1	Methyl isobutyl ketone	Health effects	January 23, 1995.
109-99-9	Tetrahydrofuran	Health effects	January 23, 1995.
110-82-7	Cyclohexane	Health Effects and Environmental Releases Report	November 18, 1994.
112-35-6	Triethylene glycol monomethyl ether	Health effects	April 3, 1989.
112-50-5	Triethylene glycol monoethyl ether	Health effects	April 3, 1989.
117-81-7	Di-2-ethylhexyl phthalate	Chemical fate	January 9, 1989.
119-06-2	Ditridecyl phthalate	Chemical fate	January 9, 1989.
123-86-4	N-butyl acetate	Health effects	January 23,

			1995.
131-11-3	Dimethly phthalate	Environmental effects	January 9, 1989.
141-78-6	Ethyl acetate	Health effects	January 23, 1995.
141-79-7	Mesityl oxide	Health effects	September 5, 1991.
143-22-6	Triethylene glycol monobutyl ether	Health effects	January 9, 1989.
143-33-9	Sodium cyanide	Chemical fate	December 17, 1991.
		Terrestrial effects	December 17, 1991.
556-67-2	Octamethylcyclotetrasiloxane (D4)	Chemical fate Environmental effects Environmental testing	January 10, 1989. January 10, 1989. April 4, 2014.
628-63-7	N-amyl acetate	Health effects	January 23, 1995.
872-50-4	N- methylpyrrolidone	Health effects	November 23, 1993.
994-05-8	Tertiary-amyl methyl ether	Health effects	March 21, 1995.
1634-04-4	Methyl tert-butyl ether	Health effects	March 31, 1988.
2461-18-9	Lauryl glycidyl ether[1]	Health effects	June 11, 1996.
3618-72-2	C.I. Disperse Blue 79:1 Acetamide,N-[5-[bis[2-(acetyloxy) ethyl]amino]-2-[(2-bromo-4, 6-dinitrophenyl) azo]-4-methoxyphenyl]-	Health effects	November 21, 1989.
		Environmental effects	November 21, 1989.
3648-20-2	Diundecyl phthalate	Environmental effects	January 9, 1989.
4170-30-3	Crotonaldehyde	Environmental effects	November 9, 1989.
		Chemical fate	November 9, 1989.
4675-54-3	Bisphenol A diglycidyl ether	Health effects Exposure evaluation	August 1, 1994.
15965-99-8	Hexadecyl glycidyl ether[1]	Health effects	June 11, 1996.
16245-97-9	n-Octadecyl glycidyl ether[1]	Health effects	June 11, 1996.

26761-40-0	Diisodecyl phthalate	Chemical fate	January 9, 1989.
38954-75-5	Tetradecyl glycidyl ether[1]	Health effects	June 11, 1996.
68081-84-5	Alkyl (C10-C16) glycidyl ether[1]	Health effects	June 11, 1996.
68515-47-9	Ditridecyl phthalate (mixed isomers)	Chemical fate	January 9, 1989.
68515-49-1	Diisodecyl phthalate (mixed isomers)	Chemical fate	January 9, 1989.
68515-50-4	Dihexyl phthalate (mixed isomers)	Environmental effects	January 9, 1989.
		Chemical fate	January 9, 1989.
68609-97-2	Alkyl (C12-C14) glycidyl ether[1]	Health effects	June 11, 1996.
84852-15-3*	4-Nonylphenol, branched	Environmental effects	February 21, 1990.
		Chemical fate	February 21, 1990.
120547-52-6	Alkyl (C12-C13) glycidyl ether	Health effects	March 22, 1996.
142844-00-6	Refractory ceramic fibers	Exposure monitoring	May 14, 1993.

[1] As represented by alkyl (C12-C13) glycidyl ether (CAS No. 120547-52-6)

[57 FR 18829, May 1, 1992, as amended at 57 FR 24961, June 12, 1992; 58 FR 28520, May 14, 1993; 58 FR 34205, June 23, 1993; 58 FR 61816, Nov. 23, 1993; 59 FR 38920, Aug. 1, 1994; 59 FR 59663, Nov. 18, 1994; 60 FR 4519, Jan. 23, 1995; 60 FR 5140, Jan. 26, 1995; 60 FR 14911, Mar. 21, 1995; 60 FR 31924, June 19, 1995; 61 FR 11742, Mar. 22, 1996; 61 FR 29487, June 11, 1996; 79 FR 18825, Apr. 4, 2014]

Back to Top

§799.5025 Testing consent orders for mixtures without Chemical Abstracts Service Registry Numbers.

This section sets forth a list of mixtures (with no Chemical Abstracts Service Registry Numbers) which are the subject of testing consent orders adopted under 40 CFR part 790. Listed below are the mixtures which are the subject of these orders and the Federal Register citations providing public notice of such orders.

Mixture/substance	**Required test**	**FR citation**
Di(heptyl, nonyl, undecyl) phthalate (D711P) as a mixture of the following six substances:		
(1) diheptyl phthalate (branched and linear isomers), CAS No. 68515-44-6	Environmental effects.	January 9, 1989.
(2) dinonyl phthalate (branched and linear isomers), CAS No. 68515-45-7	.....do	Do.

(3) di(heptyl, nonyl) phthalate (branched and linear isomers), CAS No. 111381-89-6	.....do	Do.
(4) diundecyl phthalate (branched and linear isomers), CAS No. 3648-20-2	.....do	Do.
(5) di(heptyl, undecyl) phthalate (branched and linear isomers), CAS No., 111381-90-9	.....do	Do.
(6) di(nonyl, undecyl) phthalate (branched and linear isomers), CAS No. 111381-91-0)	.....do	Do.
Fluoropolymer composite substance:		
(1) For Dry Non-Melt Resin containing the following chemical substances as specified in the ECA:		
(i) Ethene, tetrafluoro-, homopolymer, CAS No. 9002-84-0	Environmental effects.	July 8, 2005.
(ii) Polytetrafluoroethylene, Document Control Number (DCN) 63040000018A	.....do	Do.
(iii) Propane, 1,1,1,2,2,3,3-heptafluoro-3-[(trifluoroethenyl)oxy]-, polymer with tetrafluoroethene, CAS No. 26655-00-5	.....do	Do.
(2) For Dry Melt Fluoropolymer Resin containing the following chemical substances as specified in the ECA:		
(i) 1-Propene, 1,1,2,3,3,3-hexafluoro-, polymer with tetrafluoroethene, CAS No. 25067-11-2	.....do	Do.
(ii) Propane, 1,1,1,2,2,3,3-heptafluoro-3-[(trifluoroethenyl)oxy]-, polymer with tetrafluoroethene, CAS No. 26655-00-5	.....do	Do.
(iii) Ethene, tetrafluoro-, polymer with trifluoro(pentafluoroethoxy)ethene, CAS No. 31784-04-0	.....do	Do.
(iv) 1-Propene, 1,1,2,3,3,3-hexafluoro-, polymer with 1,1-difluoroethene and tetrafluoroethene, CAS No. 25190-89-0	.....do	Do.
(v) ETFE, DCN 63040000026	.....do	Do.
(vi) 1-Propene, 1,1,2,3,3,3-hexafluoro-, polymer with ethene and tetrafluoroethene, CAS No. 35560-16-8	.....do	Do.
(3) For Dry Non-Melt Fluoroelastomer Resin/Gum containing the following chemical substances as specified in the ECA:		
(i) 1-Propene, 1,1,2,3,3,3-hexafluoro-, polymer with 1,1-difluoroethene, CAS No. 9011-17-0	.....do	Do.
(ii) 1-Propene, 1,1,2,3,3,3-hexafluoro-, polymer with 1,1-difluoroethene and tetrafluoroethene, CAS No. 25190-89-0	.....do	Do.
(iii) 1-Propene, polymer with 1,1- difluoroethene and tetrafluoroethene, CAS No. 54675-89-7	.....do	Do.
(iv) 1-Propene, polymer with tetrafluoroethene, CAS No. 27029-05-6	.....do	Do.
(v) Ethene, tetrafluoro-, polymer with trifluoro(trifluoromethoxy) ethene, CAS No. 26425-79-6	.....do	Do.
(vi) Ethene, chlorotrifluoro-, polymer with 1,1-	.....do	Do.

difluoroethene, CAS No. 9010-75-7		
(vii) Fluoroelastomer, DCN No. 63040000018C	.....do	Do.
(viii) Fluoroelastomer DCN 63040000018D	.....do	Do.
(ix) A low temperature fluoroelastomer, ACC No. 137678	.....do	Do.
(4) For Aqueous Fluoropolymer Dispersions containing the following chemical substances as specified in the ECA:		
(i) Ethene, tetrafluoro-, homopolymer, CAS No. 9002-84-0	.....do	Do.
(ii) 1-Propene, 1,1,2,3,3,3-hexafluoro-, polymer with tetrafluoroethene, CAS No. 25067-11-2	.....do	Do.
(iii) Propane, 1,1,1,2,2,3,3-heptafluoro-3-[(trifluoroethenyl)oxy]-, polymer with tetrafluoroethene, CAS No. 26655-00-5	.....do	Do.
(iv) 1-Propene, 1,1,2,3,3,3- hexafluoro-, polymer with 1,1-difluoroethene and tetrafluoroethene, CAS No. 25190-89-0	.....do	Do.
(v) Polytetrafluoroethylene, DCN No. 63040000018B	.....do	Do.
Fluorotelomer-based composite substance:		
(1) For Paper containing three of the following chemical substances as specified in the ECA:		
(i) Perfluoroalkylethyl acrylate copolymer, EPA-designated accession number (ACC) 171790	Environmental effects.	July 8, 2005.
(ii) Perfluoroalkyl acrylate copolymer, ACC 158022	.....do	Do.
(iii) Perfluoroalkyl methacrylate polymer, EPA document control number (DCN) 63040000037A	.....do	Do.
(iv) Substituted methacrylate, propenoic acid, perfluoroalkyl esters, DCN 63040000033B	.....do	Do.
(v) Perfluoroalkyl acrylic polymer, DCN 63040000037C	.....do	Do.
(vi) Poly-.beta.-fluoroalkylethyl acrylate and alkyl acrylate, ACC 174993	.....do	Do.
(vii) Poly(.beta.-fluoroalkylethyl acrylate and alkyl acrylate), ACC 70430	.....do	Do.
(viii) Polysubstituted acrylic copolymer, ACC 157381	.....do	Do.
(ix) Perfluoroalkyl acrylate copolymer latex, ACC No. 70907	.....do	Do.
(2) For Textile containing six of the following chemical substances as specified in the ECA:		
(i) Perfluoroalkylethyl acrylate copolymer, EPA-designated accession number (ACC) 171790	.....do	Do.
(ii) Perfluoroalkyl acrylate copolymer, ACC 158022	.....do	Do.
(iii) Perfluoroalkyl methacrylate polymer, EPA document control number (DCN) 63040000037A	.....do	Do.
(iv) Substituted methacrylate, propenoic acid, perfluoroalkyl esters, DCN 63040000033B	.....do	Do.
(v) Perfluoroalkyl acrylic polymer, DCN 63040000037C	.....do	Do.
(vi) Poly-.beta.-fluoroalkylethyl acrylate and alkyl acrylate, ACC 174993	.....do	Do.

(vii) Poly(.beta.-fluoroalkylethyl acrylate and alkyl acrylate), ACC 70430	.....do	Do.
(viii) Polysubstituted acrylic copolymer, ACC 157381	.....do	Do.
(ix) Perfluoroalkyl acrylate copolymer latex, ACC 70907	.....do	Do.

[55 FR 3059, Jan. 30, 1990, as amended at 70 FR 39629, 39636, July 8, 2005]

Back to Top

Subpart D—Multichemical Test Rules

Back to Top

§799.5055 Hazardous waste constituents subject to testing.

(a) Identification of test substances. (1) The table in paragraph (c) of this section identifies those chemical substances that shall be tested in accordance with this section.

(2) Substances of at least 98-percent purity shall be used as the test substances.

(b) Persons required to submit study plans, conduct tests, and submit data. All persons who manufacuture (including import or manufacture as a byproduct) or process or intend to manufacture or process one or more of the substances in paragraph (c) of this section, other than as an impurity, after July 29, 1988, 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 for those substances they manufacture or process, or intend to manufacture or process, as specified in this section, subpart A of this part, and parts 790 and 792 of this chapter for single-phase rulemaking.

(c) Designation of testing. The substances identified in the following table by name and CAS number shall be tested in accordance with the designated requirements under paragraphs (d) and (e) of this section. The paragraph numbers listed for a substance refer to the specific testing and reporting requirements specified in paragraphs (d) and (e) of this section.

Chemical name	**CAS No.**	**Required testing under paragraphs (d) and (e) of this section**
Acetamide, 2-fluoro	640-19-7	(e)(1)
Bis(2-chloroethoxy)methane	111-91-1	(d)(2), (e)(1)
Bis(2-chloroisopropyl)ether	108-60-1	(d)(2)
4-Bromobenzyl cyanide	16532-79-9	(d)(1), (2), (e)(1)
Bromoform	75-25-2	(d)(2)
4-Chlorobenzo-trichloride	5216-25-1	(e)(1)
2,4-D	94-75-7	(d)(2)
Dibromomethane 74-95-3 (d)(2)		
1,2-Dichlorobenzene	95-50-1	(d)(2)
1,1-Dichloroethane	75-34-3	(d)(2)
1,3-Dichloropropanol	96-23-1	(d)(1), (e)(1)
Dihydrosafrole	94-58-6	(d)(2)
Endrin	72-20-8	(d)(2)
Ethyl methacrylate	97-63-2	(d)(2)

Maleic hydrazide	123-33-1	(d)(1), (2)
Malononitrile	109-77-3	(d)(1), (e)(1)
Methanethiol	74-93-1	(d)(1)
Methyl chloride	74-87-3	(d)(2)
p- Nitrophenol	100-02-7	(e)(1)
Pentachlorobenzene	608-93-5	(d)(2)
Pentachloroethane	76-01-7	(d)(2)
1,2,4,5-Tetrachlorobenzene	95-94-3	(d)(2)
Trichloromethanethiol	75-70-7	(d)(1), (2), (e)(1)

(d) Chemical fate testing—(1) Soil adsorption—(i) Required testing. A soil adsorption isotherm test shall be conducted with the substances designated in paragraph (c) of this section in accordance with §796.2750 of this chapter except that the provisions of §796.2750 (b)(1)(vii)(A) shall not apply to 1,3-Dichloropropanol.

(ii) Reporting requirements. The sediment and soil adsorption isotherm tests shall be completed and the final results submitted to EPA within 9 months of the effective date of the final rule except that final results for testing of 1,3-Dichloropropanol and Methanethiol shall be completed and submitted to EPA within 11 months and 15 months, respectively, of the effective date of the final rule.

(2) Hydrolysis—(i) Required testing. A test of hydrolysis as a function of pH at 25 °C shall be conducted with the substances designated in paragraph (c) of this section in accordance with §796.3500 of this chapter.

(ii) Reporting requirements. The hydrolysis tests with the substances designated in paragraph (c) of this section shall be completed and the final results submitted to EPA within 6 months of the effective date of the final rule except that hydrolysis tests for Dibromomethane, Dihydrosafrole, Ethyl methacrylate, and Methyl chloride shall be completed and the final results submitted to EPA within 12 months of the effective date of the final rule; and hydrolysis tests for 1,2-Dichlorobenzene and 1,2,4,5-Tetrachlorobenzene shall be completed and final results submitted to EPA within 9 months of the effective date of the final rule.

(e) Health effects testing—(1) Subchronic toxicity—(i) Required test. (A) An oral gavage subchronic toxicity test shall be conducted in the rat with the substances designated in paragraph (c) of this section except for bis(2-chloroethoxy) methane (CAS No. 111-91-1) in accordance with §798.2650 of this chapter.

(B) For Bis(2-chloroethoxy)methane, an oral gavage subchronic toxicity test shall be conducted in the rat in accordance with §798.2650 of this chapter except for the provisions in paragraphs (e)(9)(i)(A) and (e)(9)(i)(B). For Bis(2-chloroethoxy)methane, the following provisions also apply:

(1) Hematology determinations shall be carried out at least two times during the test period: Just after dosing on day 30 and just prior to terminal sacrifice. Hematology determinations which are appropriate to all studies are: Hematocrit, hemoglobin concentration, erythrocyte count, total and differential leukocyte count, and a measure of clotting potential such as clotting time, prothrombin time, thromboplastin time, or platelet count.

(2) Certain clinical biochemistry determinations on blood shall be carried out at least two times: Just after dosing on day 30 and just prior to terminal sacrifice. Test areas which are considered appropriate to all studies are: Electrolyte balance, carbohydrate metabolism, and liver and kidney function. The selection of specific tests will be influenced by observations on the mode of action of the substance. Suggested determinations are: Calcium, phosphorus, chloride, sodium, potassium, fasting glucose (with the period of fasting appropriate to the species), serum glutamic oxaloacetic transaminase (now known as serum aspartate aminotransferase), ornithine decarboxylase, gamma glutamyl transpeptidase, urea nitrogen, albumen blood creatinine, total bilirubin and total serum protein measurements. Other determinations which may be necessary for an adequate toxicological evaluation include: Analysis of lipids, hormones, acid/base balance, methemoglobin, and cholinesterase activity. Additional clinical biochemistry may be employed, where necessary, to extend the investigation of observed effects.

(ii) Reporting requirements. (A) The oral gavage subchronic tests with the substances designated in paragraph (c) of this section shall be completed and submitted to EPA within 12 months of the effective date of the final rule except that the tests with Bis(2-chloroethoxy)methane, 1,3-

Dichloropropanol, and Malononitrile shall be completed and the results submitted to EPA within 15 months of the effective date of the final rule.

(B) Progress reports for each test shall be submitted to the Agency 6 months after the effective date of the final rule.

(2) [Reserved]

(f) Effective date. (1) The effective date of the final rule is July 29, 1988, except for paragraphs (d)(1)(i), (d)(1)(ii), (d)(2)(ii), (e)(1)(i), and (e)(1)(ii)(A) of this section. The effective date of paragraphs (d)(1)(i), (d)(1)(ii), (d)(2)(ii), (e)(1)(i)(B) and (e)(1)(ii)(A) of this section is March 1, 1990. The effective date of paragraph (e)(1)(i)(A), is May 21, 1991.

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

[53 FR 22324, June 15, 1988; 53 FR 48645, Dec. 2, 1988, as amended at 54 FR 49760, Dec. 1, 1989; 55 FR 7324, Mar. 1, 1990; 56 FR 23232, May 21, 1991; 58 FR 34205, June 23, 1993]

Back to Top

§799.5075 Drinking water contaminants subject to testing.

(a) Identification of test substance. (1) 1,1,2,2-tetrachloroethane (CAS No. 79-34-5), and 1,3,5-trimethylbenzene (CAS No. 108-67-8) shall be tested as appropriate in accordance with this section.

(2) A test substance of at least 99 percent purity shall be used for Chloroethane, 1,1-dichloroethane, and 1,3,5-trimethylbenzene. A test substance of at least 98 percent purity shall be used for 1,1,2,2-tetrachloroethane.

(b) Persons required to submit study plans, conduct tests, and submit data. All persons who manufacture (including import and by-product manufacture) or process, or who intend to manufacture or process, the substances listed in paragraph (a) of this section after the effective date of this section to the end of the reimbursement period shall submit letters of intent to test, submit study plans, conduct tests, and submit data, or submit exemption applications as specified in this section, subpart A of this part, and parts 790 and 792 of this chapter for single-phase rulemaking, for the substances they manufacture subject to exclusions contained in §790.42(a)(2), (a)(4) and (a)(5). These sections provide that processors, persons who manufacture less than 500 kg (1,100 lbs) annually, or persons who manufacture small quantities of the chemical solely for research and development as defined in §790.42(a)(5) shall not be required to submit study plans, conduct tests and submit data, or submit exemption applications as specified in this section unless directed to do so in a subsequent notice as set forth in §790.48(b).

(c) Health effects testing—(1) Subacute toxicity—(i) Required testing. (A) An oral 14-day repeated dose toxicity test shall be conducted with 1,1,2,2-tetrachloroethane, and 1,3,5-trimethylbenzene in accordance with §798.2650 of this chapter except for the provisions in §798.2650 (a), (b)(1), (c), (e)(3), (e)(4)(i), (e)(5), (e)(6), (e)(7)(i), (e)(7)(iv), (e)(7)(v), (e)(8)(vii), (e)(9)(i)(A), (e)(9)(i)(B), (e)(11)(v), and (f)(2)(i). Each substance shall be tested in one mammalian species, preferably a rodent, but a non-rodent may be used. The species and strain of animals used in this test should be the same as those used in the 90-day subchronic test required in paragraph (c)(2)(i) of this section. The tests shall be performed using drinking water. However, if, due to poor stability or palatability, a drinking water test is not feasible for a given substance, that substance shall be administered either by oral gavage, in the diet, or in capsules.

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

(1) Purpose. To assess and evaluate the toxic characteristics of a substance, the determination of subacute toxicity should be carried out after initial information on toxicity has been obtained by acute testing. The 14-day repeated dose oral study provides information on the health hazard likely to arise from repeated short-term exposure by the oral route over a very limited period of time. It has been designed to permit the determination of the no-observed-adverse-effect level and toxic effects associated with continuous or repeated exposure to a test substance for 14 days and to evaluate reversibility, persistence, and delayed occurrence of toxic effects during a 14-day

follow-up recovery period. The test is not capable of determining those effects that have a long latency period for development (e.g., carcinogenicity and life shortening). It will provide information on target organs and the possibility of accumulation, and can be used in selecting dose levels for subchronic studies and for establishing safety criteria for short-term human exposure.

(2) Definitions. Subacute oral toxicity is the manifestation of adverse effect(s) occurring as a result of the repeated daily exposure of experimental animals to a substance by the oral route for 14 days.

(3) Principle of the test method. The test substance is administered orally in graduated daily doses to several groups of experimental animals, one dose level per group, for a period of 14 days. During the period of administration the animals are observed daily to detect signs of toxicity. Animals which die during the period of administration are necropsied. At the conclusion of the test, all animals, except the satellite group, are necropsied and histopathological examinations are carried out. The satellite group is necropsied after the 14-day recovery period.

(4) Satellite group (Rodent only). A satellite group of 20 animals (10 animals per sex) shall be treated with the high dose level for 14 days and observed for reversibility, persistence, and delayed occurrence of toxic effects for a post-treatment recovery period of at least 14 days.

(5) Dose levels and dose selection. In subacute toxicity tests, it is desirable to have a dose response relationship as well as a NOAEL. Therefore, at least 3 dose levels with a control and, where appropriate, a vehicle control (corresponding to the concentration of vehicle at the highest exposure level) shall be used. Doses shall be spaced appropriately to produce test groups with a range of toxic effects. The data should be sufficient to produce a dose-response curve.

(6) Exposure conditions. The animals are dosed with the test substance every day for 14 days.

(7) Observation period. All animals shall be observed daily during the 14-day exposure period.

(8) Observation period of satellite group. Animals in the satellite group scheduled for follow-up observations shall be kept for at least 14 days further without treatment to detect recovery from, or persistence of, and delayed onset of toxic effects and shall be observed daily.

(9) Administration of test substance. For substances of low toxicity, it is important to ensure that when administered in the drinking water, by gavage, in the diet, or in capsules, the quantities of the test substance involved do not interfere with normal nutrition. When the test substance is administered in the diet, either a constant dietary concentration (ppm) or a constant dose level in terms of the animals' body weight shall be used; the alternative used shall be specified in the final test report.

(10) Time of administration of test substance. For a substance administered by gavage or capsule, the dose shall be given at approximately the same time each day, and adjusted on day 7 to maintain a constant dose level in terms of animal body weight.

(11) Observation of animals. At the end of the 14-day exposure period, all survivors, except those in the satellite group, shall be necropsied. All survivors in the satellite group shall be necropsied after a recovery period of at least 14 days.

(12) Hematology determinations. Certain hematology determinations shall be carried out at least two times during the test period: Just prior to initiation of dosing if adequate historical baseline data are not available (baseline data) and just prior to terminal sacrifice at the end of the test period. Hematology determinations which are appropriate to all studies are: Hematocrit, hemoglobin concentration, erythrocyte count, total and differential leukocyte count, and a measure of clotting potential such as clotting time, prothrombin time, thromboplastin time, or platelet count.

(13) Clinical biochemical determinations. Certain clinical biochemistry determinations on blood should be carried out at least two times: Just prior to initiation of dosing (if adequate historical baseline data are not available) and just prior to terminal sacrifice at the end of the test period. Test areas which are considered appropriate to all studies are: Electrolyte balance, carbohydrate metabolism, and liver and kidney function. The selection of specific tests will be influenced by observations on the mode of action of the substance. Suggested determinations are: Calcium, phosphorus, chloride, sodium, potassium, fasting glucose (with the period of fasting appropriate to the species), serum alanine aminotransferase, serum aspartate aminotransferase, gamma glutamyl transpeptidase, urea nitrogen, albumin, blood creatinine, and total serum protein measurements. Other determinations which may be necessary for an adequate toxicological evaluation include: analyses of lipids, hormones, acid/base balance, methemoglobin, and

cholinesterase activity. Additional clinical biochemistry may be employed, where necessary, to extend the investigation of observed effects.

(14) Histopathology. Histopathology of the lungs of all animals shall be performed. Special attention to examination of the lungs of rodents shall be made for evidence of infection since this provides a convenient assessment of the state of health of the animals.

(15) Evaluation of the study results. The findings of a subacute oral toxicity study should be evaluated in conjunction with the findings of preceding studies and considered in terms of the toxic effects and the necropsy and histopathological findings. The evaluation will include the relationship between the dose of the test substance and the presence or absence, the incidence and severity, of abnormalities, including behavioral and clinical abnormalities, gross lesions, identified target organs, body weight changes, effects on mortality and any other general or specific toxic effects. A properly conducted subacute test should provide a satisfactory estimation of a NOAEL.

(ii) Reporting requirements. (A) Each subacute test shall be completed and the final report submitted to EPA within 12 months of the date specified in paragraph (d)(1) of this section, except for 1,1,2,2-tetrachloroethane. The subacute testing for 1,1,2,2-tetrachloroethane. The subacute testing for 1,1,2,2-tetrachloroethane shall be completed and the final report submitted to EPA by February 15, 1996.

(B) Except for 1,3,5-trimethylbenzene, a progress report shall be submitted to EPA for each test beginning 6 months after the date specified in paragraph (d)(1) of this section and at 6-month intervals thereafter until the final report is submitted to EPA . The progress report for 1,3,5-trimethylbenzene shall be submitted to EPA by April 10, 1995.

(2) Subchronic toxicity—(i) Required testing. (A) An oral 90-day subchronic toxicity test shall be conducted with 1,3,5-trimethylbenzene in accordance with §798.2650 of this chapter except for the provisions in §798.2650 (e)(3), (e)(7)(i), and (e)(11)(v). The tests shall be performed using drinking water. However, if, due to poor stability or palatability, a drinking water test is not feasible for a given substance, that substance shall be administered either by oral gavage, in the diet, or in capsules.

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

(1) Satellite group (Rodent only). A satellite group of 20 animals (10 animals per sex) shall be treated with the high dose level for 90 days and observed for reversibility, persistence, and delayed occurrence of toxic effects for a post-treatment period of appropriate length, normally not less than 28 days.

(2) Histopathology. Histopathology of the lungs of all animals shall be performed. Special attention to examination of the lungs of rodents shall be made for evidence of infection since this provides a convenient assessment of the state of health of the animals.

(ii) Reporting requirements. (A) The subchronic testing for chloroethane shall be completed and the final report submitted to EPA by June 27, 1995. The subchronic testing for 1,1-dichloroethane and 1,1,2,2-tetrachlorethane shall be completed and the final report submitted to EPA by August 27, 1995. The subchronic testing for 1,3,5-trimethylbenzene shall be completed and the final report submitted to EPA by April 10, 1995.

(B) For each test, a progress report shall be submitted to EPA beginning 9 months after the date specified in paragraph (d)(1) of this section and at 6-month intervals thereafter until the final report is submitted to EPA.

(d) Effective date. (1) This section is effective on December 27, 1993, except for paragraphs (a)(1), (a)(2), (c)(1)(i)(A), (c)(1)(ii)(A), (c)(1)(ii)(B), (c)(2)(i)(A), and (c)(2)(ii)(A). The effective date for paragraphs (a)(2), (c)(1)(ii)(B), and (c)(2)(ii)(A) is September 29, 1995. The effective date for paragraphs (a)(1), (c)(1)(i)(A), and (c)(2)(i)(A) is February 27, 1996. The effective date for paragraph (c)(1)(ii)(A) is June 30, 1997.

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

[58 FR 59681, Nov. 10, 1993; 58 FR 1992, Jan. 13, 1994, as amended at 60 FR 56956, Nov. 13, 1995; 61 FR 7223, Feb. 27, 1996; 62 FR 35105, June 30, 1997]

§799.5115 Chemical testing requirements for certain chemicals of interest to the Occupational Safety and Health Administration.

(a) What substances will be tested under this section? Table 2 in paragraph (j) of this section identifies the chemical substances that must be tested under this section. For the chemical substances identified as “Class 1” substances in Table 2 in paragraph (j) of this section, the purity of each chemical substance must be 99% or greater, unless otherwise specified in this section. For the chemical substances identified as “Class 2” substances in Table 2 in paragraph (j) of this section, a representative form of each chemical substance must be tested.

(b) Am I subject to this section? (1) If you manufacture (including import) or intend to manufacture, or process or intend to process, any chemical substance listed in Table 2 in paragraph (j) of this section at any time from May 26, 2004, to the end of the test data reimbursement period as defined in 40 CFR 791.3(h), you are subject to this section with respect to that chemical substance.

(2) If you do not know or cannot reasonably ascertain that you manufacture or process a chemical substance listed in Table 2 in paragraph (j) of this section during the time period described in paragraph (b)(1) of this section (based on all information in your possession or control, as well as all information that a reasonable person similarly situated might be expected to possess, control, or know, or could obtain without an unreasonable burden), you are not subject to this section with respect to that chemical substance.

(c) If I am subject to this section, when must I comply with it? (1)(i) Persons subject to this section are divided into two groups, as set forth in Table 1 of this paragraph: Tier 1 (persons initially required to comply) and Tier 2 (persons not initially required to comply). If you are subject to this section, you must determine if you fall within Tier 1 or Tier 2, based on Table 1 of this paragraph.

Table 1—Persons Subject to the Rule: Persons in Tier 1 and Tier 2

Persons initially required to comply with this section (Tier 1)	**Persons not initially required to comply with this section (Tier 2)**
Persons not otherwise specified in column 2 of this table that manufacture (as defined at TSCA section 3(7)) or intend to manufacture a chemical substance included in this section.	A. Persons who manufacture (as defined at TSCA section 3(7)) or intend to manufacture a chemical substance included in this section solely as one or more of the following: —As a byproduct (as defined at 40 CFR 791.3(c)); —As an impurity (as defined at 40 CFR 790.3); —As a naturally occurring substance (as defined at 40 CFR 710.4(b)); —As a non-isolated intermediate (as defined at 40 CFR 704.3); —As a component of a Class 2 substance (as described at 40 CFR 720.45(a)(1)(i)); —In amounts of less than 500 kilograms (kg) (1,100 lbs) annually (as described at 40 CFR 790.42(a)(4)); or —For research and development (as described at 40 CFR 790.42(a)(5)).
	B. Persons who process (as defined at TSCA section 3(10)) or intend to process a chemical substance included in this section

	(see 40 CFR 790.42(a)(2)).

(ii) Table 1 in paragraph (c)(1)(i) of this section expands the list of persons specified in §790.42(a)(2), (a)(4), and (a)(5) of this chapter, who, while legally subject to this section, must comply with the requirements of this section only if directed to do so by EPA under the circumstances set forth in paragraphs (c)(4) through (c)(7) and (c)(10) of this section.

(2) If you are in Tier 1 with respect to a chemical substance listed in Table 2 in paragraph (j) of this section, you must, for each test required under this section for that chemical substance, either submit to EPA a letter of intent to test or apply to EPA for an exemption from testing. The letter of intent to test or the exemption application must be received by EPA no later than June 25, 2004.

(3) If you are in Tier 2 with respect to a chemical substance listed in Table 2 in paragraph (j) of this section, you are considered to have an automatic conditional exemption and you will be required to comply with this section with regard to that chemical substance only if directed to do so by EPA under paragraphs (c)(5), (c)(7), or (c)(10) of this section.

(4) If no person in Tier 1 has notified EPA of its intent to conduct one or more of the tests required by this section on any chemical substance listed in Table 2 in paragraph (j) of this section by June 25, 2004, EPA will publish a Federal Register document that would specify the test(s) and the chemical substance(s) for which no letter of intent has been submitted, and notify manufacturers in Tier 2A of their obligation to submit a letter of intent to test or to apply for an exemption from testing.

(5) If you are in Tier 2A with respect to a chemical substance listed in Table 2 in paragraph (j) of this section, and if you manufacture this chemical substance as of May 26, 2004, or within 30 days after publication of the Federal Register document described in paragraph (c)(4) of this section, you must, for each test specified for that chemical substance in the document described in paragraph (c)(4) of this section, either submit to EPA a letter of intent to test or apply to EPA for an exemption from testing. The letter of intent to test or the exemption application must be received by EPA no later than 30 days after publication of the document described in paragraph (c)(4) of this section.

(6) If no manufacturer in Tier 1 or Tier 2A has notified EPA of its intent to conduct one or more of the tests required by this section on any chemical substance listed in Table 2 in paragraph (j) of this section within 30 days after the publication of the Federal Register document described in paragraph (c)(4) of this section, EPA will publish another Federal Registerdocument that would specify the test(s) and the chemical substance(s) for which no letter of intent has been submitted, and notify processors in Tier 2B of their obligation to submit a letter of intent to test or to apply for an exemption from testing.

(7) If you are in Tier 2B with respect to a chemical substance listed in Table 2 in paragraph (j) of this section, and if you process this chemical substance as of May 26, 2004, or within 30 days after publication of the Federal Register document described in paragraph (c)(6) of this section, you must, for each test specified for that chemical substance in the document described in paragraph (c)(6) of this section, either submit to EPA a letter of intent to test or apply to EPA for an exemption from testing. The letter of intent to test or the exemption application must be received by EPA no later than 30 days after publication of the document described in paragraph (c)(6) of this section.

(8) If no manufacturer or processor has notified EPA of its intent to conduct one or more of the tests required by this section for any of the chemical substances listed in Table 2 in paragraph (j) of this section within 30 days after the publication of the Federal Register document described in paragraph (c)(6) of this section, EPA will notify all manufacturers and processors of those chemical substances of this fact by certified letter or by publishing a Federal Register document specifying the test(s) for which no letter of intent has been submitted. This letter or Federal Register document will additionally notify all manufacturers and processors that all exemption applications concerning the test(s) have been denied, and will give the manufacturers and processors of the chemical substance(s) an opportunity to take corrective action.

(9) If no manufacturer or processor has notified EPA of its intent to conduct one or more of the tests required by this section for any of the chemical substances listed in Table 2 in paragraph (j) of this section within 30 days after receipt of the certified letter or publication of the Federal Register document described in paragraph (c)(8) of this section, all manufacturers and processors subject to this section with respect to that chemical substance who are not already in violation of this section will be in violation of this section.

(10) If a problem occurs with the initiation, conduct, or completion of the required testing or the submission of the required data with respect to a chemical substance listed in Table 2 in paragraph (j) of this section, under the procedures in §§790.93 and 790.97 of this chapter, EPA may initiate termination proceedings for all testing exemptions with respect to that chemical substance and may notify persons in Tier 1 and Tier 2 that they are required to submit letters of intent to test or exemption applications within a specified period of time.

(11) If you are required to comply with this section, but your manufacturing or processing of a chemical substance listed in Table 2 in paragraph (j) of this section begins after the applicable compliance date referred to in paragraphs (c)(2), (c)(5), (c)(7), or (c)(10) of this section, you must either submit a letter of intent to test or apply to EPA for an exemption. The letter of intent to test or the exemption application must be received by EPA no later than the day you begin manufacturing or processing.

(d) What must I do to comply with this section? (1) To comply with this section you must either submit to EPA a letter of intent to test, or apply to and obtain from EPA an exemption from testing.

(2) For each test with respect to which you submit to EPA a letter of intent to test, you must conduct the testing specified in paragraph (h) of this section and submit the test data to EPA.

(3) You must also comply with the procedures governing test rule requirements in part 790 of this chapter, as modified by this section, including the submission of letters of intent to test or exemption applications, the conduct of testing, and the submission of data; Part 792—Good Laboratory Practice Standards of this chapter; and this section. The following provisions of 40 CFR part 790 do not apply to this section: Paragraphs (a), (d), (e), and (f) of §790.45; paragraph (a)(2) and paragraph (b) of §790.80; and §790.48.

(e) If I do not comply with this section, when will I be considered in violation of it? You will be considered in violation of this section as of 1 day after the date by which you are required to comply with this section.

(f) How are EPA's data reimbursement procedures affected for purposes of this section? If persons subject to this section are unable to agree on the amount or method of reimbursement for test data development for one or more chemical substances included in this section, any person may request a hearing as described in 40 CFR part 791. In the determination of fair reimbursement shares under this section, if the hearing officer chooses to use a formula based on production volume, the total production volume amount will include amounts of a chemical substance produced as an impurity.

(g) Who must comply with the export notification requirements? Any person who exports, or intends to export, a chemical substance listed in Table 2 in paragraph (j) of this section is subject to part 707, subpart D, of this chapter.

(h) How must I conduct my testing? The chemical substances identified by Chemical Abstract Service Registry Number (CAS No.) and chemical name in Table 2 in paragraph (j) of this section must be tested as follows:

(1) Applicability. This in vitro dermal absorption rate test standard must be used for all testing conducted under this section. In certain instances, modifications to the test standard may be considered. The procedures for applying for a modification to the test standard are specified in 40 CFR 790.55.

(2) Source. The test standard is based on the Protocol for In Vitro Percutaneous Absorption Rate Studies, referenced in paragraph (h)(8)(v) of this section.

(3) Purpose. In the assessment and evaluation of the characteristics of a chemical substance or mixture for which testing is required under this section (test substance), it is important to determine the rate of absorption of the test substance in cases where dermal exposure to the test substance in the workplace may result in systemic toxicity. This test standard is designed to develop data that describe the rate at which test substances are absorbed through the skin so that the body burden of a test substance resulting from dermal exposure in the workplace can be better evaluated.

(4) Principles of the test standard. This test standard describes procedures for measuring a permeability constant (Kp) and two short-term dermal absorption rates for test substances in liquid form. The test standard utilizes in vitro diffusion cell techniques which allow absorption studies to be conducted with human cadaver skin. In vitro diffusion studies are necessary for measuring a Kp. This test standard specifies the use of static or flow-through diffusion cells and non-viable human

cadaver skin. It also requires the use of radiolabeled test substances unless it can be demonstrated that procedures utilizing a non-radiolabeled test substance are able to measure the test substance with a sensitivity equivalent to the radiolabeled method.

(5) Test procedure—(i) Choice of membrane—(A) Skin selection. Human cadaver skin must be used in all testing conducted under this test standard. This test standard does not require use of live skin, or the maintenance of skin viability during the course of the experiment. However, the time elapsed between death and harvest of tissue must be reported.

(B) Number of skin samples. Data for the determination of a Kp must be obtained from a minimum of six skin samples and the skin samples must come from at least three different human subjects (two skin samples from each subject) in order to allow for biological variation between subjects. Data for the determination of each short-term (i.e., 10 minute and 60 minute) absorption rate must be obtained from a minimum of six skin samples and the skin samples must come from at least three different human subjects (two skin samples from each subject).

(C) Anatomical region. In order to minimize the variability in skin absorption measurements for these tests, samples of human cadaver skin must be obtained from the abdominal region of human subjects of known source and disease state.

(D) Validation of human cadaver skin barrier. Prior to conducting an experiment with the test substance, barrier properties of human cadaver skin must be pretested either by:

(1) Measuring the absorption of a standard compound such as tritiated water as discussed, for example, in the reference in paragraph (h)(8)(i) of this section;

(2) Determining an electrical resistance to an alternating current, at up to two volts; or

(3) Measuring trans-epidermal water loss from the stratum corneum.

(ii) Preparation of membrane. Full thickness skin must not be used. A suitable membrane must be prepared from skin either with a dermatome at a thickness of 200 to 500 micrometers (μm), or with heat separation by treating the skin at 60 °C for 45 seconds to 2 minutes after which the epidermis can be peeled from the dermis. These epidermal membranes can be stored frozen (-20 °C) for up to 3 months, if necessary, if they are frozen quickly and the barrier properties of the samples are confirmed immediately prior to commencement of the experiment.

(iii) Diffusion cell design. Either static or flow-through diffusion cells must be used in these studies. To ensure that an increase in concentration of the test substance in the receptor fluid does not alter penetration rate, the testing laboratory must verify that the concentration of the test substance in the receptor fluid is less than 10% of the initial concentration in the donor chamber. Concentration of the neat (i.e., undiluted) liquid must be taken as the density of the test substance.

(iv) Temperature. Skin must be maintained at a physiological temperature of 32 °C during the test.

(v) Testing hydrophobic chemicals. When testing hydrophobic chemicals, polyethoxyoleate (polyethylene glycol (PEG) 20 oleyl ether) must be added to the receptor fluid at a concentration of 6%.

(vi) Vehicle. If the test substance is a liquid at room temperature and does not damage the skin during the determination of Kp, it must be applied neat. If the test substance cannot be applied neat because it is a solid at room temperature or because it damages the skin when applied neat, it must be dissolved in water. If the concentration of a hydrophobic test substance in water is not high enough so that a steady-state absorption can be obtained, the test substance must be dissolved in isopropyl myristate. A sufficient volume of liquid must be used to completely cover the skin and provide the amount of test substance as described in paragraph (h)(5)(vii) of this section.

(vii) Dose—(A) Kp. A Kp must be determined for each test chemical, except for methyl isoamyl ketone (MIAK; CAS No.: 110-12-3, Chemical Abstracts (CA) Index Name: 2-Hexanone, 5-methoxy-) and dipropylene glycol methyl ether (DPGME; CAS No.: 34590-94-8, CA Index Name: Propanol, 1(or 2)-(2-methoxymethylethoxy)-). An “infinite dose” of the test substance must be applied to the skin to achieve the steady-state rate of absorption necessary for calculation of a Kp. Infinite dose is defined as the concentration of a test substance required to give an undepletable reservoir on the surface of the skin. The actual concentration required to give an undepletable reservoir on the surface of the skin depends on the rate of penetration of the test substance. Preliminary studies may be necessary to determine this concentration. Percutaneous absorption must be determined under occluded (i.e., covered) conditions unless it is demonstrated that such conditions cause leakage of material or damage to the skin membrane as a result of unrealistically

high pressures or excessive hydration. Skin barrier integrity must be verified at the end of the experiment by the methods discussed in paragraph (h)(5)(i)(D) of this section.

(B) Short-term absorption rates. Short-term absorption rates must be determined for all test chemicals. The dose of test chemical applied to the skin must be sufficient to completely cover the exposed skin surface. A minimum of four diffusion cells must be set up using skin from a single subject. Two diffusion cells must be terminated at 10 minutes. The remaining two diffusion cells must be terminated at 60 minutes. Skin absorption at each sampling time is the sum of the receptor fluid levels and the absorbed test substance that remains in the skin, as discussed, for example, in the reference in paragraph (h)(8)(iii) of this section. Unabsorbed chemical must be removed from the skin surface by washing gently with soap and water. This experiment must be repeated with skin from two additional subjects. In order to ensure reliable short-term absorption rates, percutaneous absorption must be determined under occluded conditions unless it is demonstrated that such conditions cause leakage of material or damage to the skin membrane as a result of unrealistically high pressures or excessive hydration.

(viii) Study duration—(A) Kp. The in vitro dermal absorption rate test must be performed until at least four absorption measurements per diffusion cell experiment are obtained during the steady-state absorption portion of the experiment. A preliminary study may be useful to establish time points for sampling. The required absorption measurements can be accomplished in an hour or two with fast-penetrating chemicals but may require 24 hours or longer for slow-penetrating chemicals. Unabsorbed test substance need not be removed from the surface of the skin after each experiment.

(B) Short-term absorption rates. The test substance must be applied to skin for durations of 10 and 60 minutes. At the end of the study, the unabsorbed test substance must be removed from the surface of the skin with soap and water and the amount absorbed into the skin and receptor fluid must be determined, as discussed, for example, in the reference in paragraph (h)(8)(iii) of this section.

(6) Results—(i) Kp. The Kp must be calculated by dividing the steady-state rate of absorption (measured in micrograms (µg) × hr−1 × centimeters (cm)−2) by the concentration of the test substance (measured in µg × cm−3) applied to the skin. (For example, if the steady-state rate is 1 microgram × hr−1 × cm−2 and the concentration applied to the skin is 1,000 micrograms × cm−3, then the Kp value is calculated to be 0.001 cm × hr−1.) The mean and standard deviation of the calculated Kp values for all diffusion cell experiments must be determined.

(ii) Short-term absorption rate. The absorption rates (µg × hr−1 × cm−2) must be determined from the total amount of test substance found in the receptor fluid and skin after the 10-minute and 60-minute exposures for each diffusion cell experiment. The mean and standard deviation of 10-minute short-term absorption rates from all experiments must be calculated. The mean and standard deviation of 60-minute short-term absorption rates from all experiments must also be calculated.

(7) Test report. In addition to compliance with the TSCA Good Laboratory Practice Standards (GLPS) at 40 CFR part 792, the following specific information must be collected and reported by the date in paragraph (i) of this section:

(i) Test systems and test methods. (A) A description of the date, time, and location of the test, the name(s) of the person(s) conducting the test, the location of records pertaining to the test, as well as a GLPS statement. These statements must be certified by the signatures of the individuals performing the work and their supervisors.

(B) A description of the source, identity, and purity of the test substance and the source, identity, and handling of the test skin. There must be a detailed description of the test procedure and all materials, devices used and doses tested, as well as a detailed description and illustration of static or flow-through cell design. There must also be a description of the skin preparation method, including measurements of the skin membrane thickness.

(C) A description of the analytical techniques to be used, including their accuracy, precision, and detection limits (in particular for non-radiolabeled tests), and, if a radiolabel is used, there must be a description of the radiolabel (e.g., type, location of, and radiochemical purity of the label).

(D) All data must be clearly identified as to dose and specimen. Derived values (means, permeability coefficient, graphs, charts, etc.) are not sufficient.

(ii) Conduct of study. Data must be collected and reported on the following:

(A) Monitoring of testing parameters.

(B) Temperature of chamber.

(C) Receptor fluid pH.

(D) Barrier property validation.

(E) Analysis of receptor fluid for radioactivity or test chemical

(iii) Results. The mean Kp and mean short-term absorption rates must be presented along with their standard deviations and the number of diffusion cell experiments. In addition, all raw data from each individual diffusion cell must be retained to support the calculations of permeability constants and short-term absorption rates. When a radiolabeled test substance is used, a full balance of the radioactivity must be presented, including cell rinsing and stability of the test substance in the donor compartment.

(8) References. For background information on this test standard, the following references may be consulted. These references are available under docket ID number OPPT-2003-0006 at the EPA Docket Center, Rm. B102-Reading Room, EPA West, 1301 Constitution Ave., NW., Washington, DC, from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays.

(i) Bronaugh, R.L., Stewart, R.F., and Simon, M. Methods for In Vitro Percutaneous Absorption Studies VII: Use of Excised Human Skin. Journal of Pharmaceutical Sciences. 75:1094-1097. 1986.

(ii) Bronaugh, R.L. and Stewart, R.F. Methods for In Vitro Percutaneous Absorption Studies IV: The Flow-Through Diffusion Cell. Journal of Pharmaceutical Sciences. 74:64-67. 1985.

(iii) Bronaugh, R.L., Stewart, R.F., and Storm, J.E. Extent of Cutaneous Metabolism During Percutaneous Absorption of Xenobiotics. Toxicology and Applied Pharmacology. 99:534-543. 1989.

(iv) Walker, J.D., Whittaker, C. and McDougal, J.N. Role of the TSCA Interagency Testing Committee in Meeting the U.S. Government Data Needs: Designating Chemicals for Percutaneous Absorption Rate Testing. Dermatotoxicology. F. Marzulli and H. Maibach, Eds. Taylor & Francis, Washington, DC. pp. 371-381. 1996.

(v) Bronaugh, R.L., and Collier, S.W. Protocol for In Vitro Percutaneous Absorption Studies. In Vitro Percutaneous Absorption: Principles, Fundamentals, and Applications. R.L. Bronaugh and H.I. Maibach, Eds. CRC Press, Boca Raton, FL. pp. 237-241. 1991.

(i) Reporting requirements. The reports submitted under this section must include the information specified in paragraph (h)(7) of this section. A final report for each chemical substance must be received by EPA by June 27, 2005, unless an extension is granted in writing pursuant to 40 CFR 790.55.

(j) Designation of specific chemical substances for testing. The chemical substances identified by chemical name, CAS No., and class in Table 2 of this paragraph must be tested in accordance with the testing requirements in paragraph (h) of this section and the requirements described in 40 CFR part 792.

Table 2—Chemical Substances Designated For Testing

CAS No.	Chemical name	Class
75-05-8	Acetonitrile	1
75-15-0	Carbon disulfide	1
75-35-4	Vinylidene chloride	1
77-73-6	Dicyclopentadiene	1
78-59-1	Isophorone	1
78-87-5	Propylene dichloride	1
79-20-9	Methyl acetate	1
79-46-9	2-Nitropropane	1
91-20-3	Naphthalene	1
92-52-4	Biphenyl	1

98-29-3	tert-Butylcatechol	1
100-00-5	p-Nitrochlorobenzene	1
100-01-6	p-Nitroaniline	1
100-44-7	Benzyl chloride	1
106-42-3	p-Xylene	1
106-46-7	p-Dichlorobenzene	1
107-06-2	Ethylene dichloride	1
107-31-3	Methyl formate	1
108-03-2	1-Nitropropane	1
108-90-7	Chlorobenzene	1
108-93-0	Cyclohexanol	1
109-66-0	Pentane	1
109-99-9	Tetrahydrofuran	1
110-12-3	Methyl isoamyl ketone	1
111-84-2	Nonane	1
120-80-9	Catechol	1
122-39-4	Diphenylamine	1
123-42-2	Diacetone alcohol	1
127-19-5	Dimethyl acetamide	1
142-82-5	n-Heptane	1
150-76-5	p-Methoxyphenol	1
25013-15-4	Vinyl toluene	2
34590-94-8	Dipropylene glycol methyl ether	2

(k) Effective date This section is effective on May 26, 2004.

[69 FR 22436, Apr. 26, 2004, as amended at 71 FR 18654, Apr. 12, 2006]