40 CFR 799.5087 - Chemical testing requirements for second group of high production volume chemicals (HPV2).

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§ 799.5087
Chemical testing requirements for second group of high production volume chemicals (HPV2).

(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" chemical 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" chemical substances in Table 2 in paragraph (j), a representative form of each chemical substance must be tested. The representative form selected for a given Class 2 chemical substance should meet industry or consensus standards where they exist.

(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 February 7, 2011 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 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) 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	Tier 2A. 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 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)).
Note: kg—kilogram, TSCA—Toxic Substances Control Act.	

(ii) Table 1 of paragraph (c)(1)(i) of this section expands the list of persons in Tier 2, that is, those persons specified in 40 CFR 790.42(a)(2), (a)(4), and (a)(5), 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), (c)(5), (c)(6), (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 March 9, 2011.

(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 on or before March 9, 2011, 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 (as specified in Table 1 in paragraph (c) of this section) with respect to a chemical substance listed in Table 2 in paragraph (j) of this section, and if you manufacture, or intend to manufacture, this chemical substance as of February 7, 2011, 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 Register document 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 (as specified in Table 1 in paragraph (c) of this section) with respect to a chemical substance listed in Table 2 in paragraph (j) of this section, and if you process, or intend to process, this chemical substance as of February 7, 2011, 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 40 CFR 790.93 and 790.97, 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 manufacture or processing of, or intent to manufacture or process, 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), or (c)(6) 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 manufacture 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 40 CFR part 790 (except for those requirements listed in this paragraph as not applicable to this section), including the submission of letters of intent to test or exemption applications, the conduct of testing, and the submission of data; 40 CFR Part 792 — Good Laboratory Practice Standards; 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; § 790.82(e)(1); § 790.85; 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 40 CFR part 707, subpart D.

(h) How must I conduct my testing? (1) The tests that are required for each chemical substance are indicated in Table 2 in paragraph (j) of this section. The test methods that must be followed are provided in Table 3 in paragraph (j) of this section. You must proceed in accordance with these test methods as required according to Table 3 in paragraph (j) of this section, or as appropriate if more than one alternative is allowed

according to Table 3 in paragraph (j) of this section. Included in Table 3 in paragraph (j) of this section are the following 18 test methods which are incorporated by reference:

(i) Standard Test Method for Relative Initial and Final Melting Points and the Melting Range of Organic Chemicals, ASTM E 324–99, approved September 10, 1999.

(ii) Standard Test Method for Partition Coefficient (N –Octanol/Water) Estimation by Liquid Chromatography, ASTM E 1147–92 (Reapproved 2005), approved August 1, 2005.

(iii) Standard Guide for Conducting Acute Toxicity Tests on Test Materials with Fishes, Macroinvertebrates, and Amphibians, ASTM E 729–96 (Reapproved 2007), approved October 1, 2007.

(iv) Standard Test Method for Measurements of Aqueous Solubility, ASTM E 1148–02 (Reapproved 2008), approved February 1, 2008.

(v) Standard Test Method for Estimating Acute Oral Toxicity in Rats, ASTM E 1163–98 (Reapproved 2002), approved October 10, 2002.

(vi) Standard Guide for Conducting Daphnia Magna Life-Cycle Toxicity Tests, ASTM E 1193–97 (Reapproved 2004), approved April 1, 2004.

(vii) Standard Guide for Conducting Static Toxicity Tests with Microalgae, ASTM E 1218–04 e1, approved April 1, 2004.

(viii) Standard Test Method for Vapor Pressure of Liquids by Ebulliometry, ASTM E 1719–05, approved March 1, 2005.

(ix) Standard Test Method for Determining Ready, Ultimate, Biodegradability of Organic Chemicals in a Sealed Vessel CO2 Production Test. ASTM E 1720–01 (Reapproved 2008), approved February 1, 2008.

(x) Standard Test Method for Determining Vapor Pressure by Thermal Analysis, ASTM E 1782–08, approved March 1, 2008.

(xi) Water Quality—Evaluation of Ultimate Aerobic Biodegradability of Organic Compounds in Aqueous Medium—Method by Analysis of Inorganic Carbon in Sealed Vessels (CO2 Headspace Test). First Edition, March 15, 1999. ISO 14593:1999(E).

(xii) Water Quality—Evaluation in an Aqueous Medium of the “Ultimate” Aerobic Biodegradability of Organic Compounds—Method by Analysis of Dissolved Organic Carbon (DOC). Second Edition, September 15, 1994. ISO 7827:1994(E).

(xiii) Water Quality—Evaluation of Ultimate Aerobic Biodegradability of Organic Compounds in Aqueous Medium by Determination of Oxygen Demand in a Closed Respirometer. Second Edition, August 1, 1999. ISO 9408:1999(E).

(xiv) Water Quality—Evaluation of Ultimate Aerobic Biodegradability of Organic Compounds in Aqueous Medium—Carbon Dioxide Evolution Test. Second Edition, March 1, 1999. ISO 9439:1999(E).

(xv) Water Quality—Evaluation in an Aqueous Medium of The “Ultimate” Aerobic Biodegradability of Organic Compounds—Method by Analysis of Biochemical Oxygen Demand (Closed Bottle Test). First Edition, October 15, 1994. ISO 10707:1994(E).

(xvi) Water Quality—Evaluation in an Aqueous Medium of the Ultimate Aerobic Biodegradability of Organic Compounds—Determination of Biochemical Oxygen Demand in a Two-Phase Closed Bottle Test. First Edition, February 1, 1997. ISO 10708:1997(E).

(xvii) Water Quality—Guidance for the Preparation and Treatment of Poorly Water-Soluble Organic Compounds for the Subsequent Evaluation of Their Biodegradability in an Aqueous Medium. First Edition, August 15, 1995. ISO 10634:1995(E).

(xviii) Guideline for the Testing of Chemicals: Melting Point/Melting Range. OECD 102. July 27, 1995.

(2) The Director of the Federal Register approved this incorporation by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. You may obtain copies of the ASTM test methods from the American Society for Testing and Materials, 100 Bar Harbor Dr., P.O. Box C700, West Conshohocken, PA 19428–2959, telephone number: (610) 832–9585, web address: http://www.astm.org; copies of the ISO test methods from the International Organization for Standardization, 1, ch. de la Voie-Creuse, Case postale, 56 CH–1211 Geneve 20 Switzerland, telephone number: 41 22 749 01 11, web address: http://www.iso.org; and a copy of the OECD guideline from the Organization

for Economic Cooperation and Development, 2, rue André Pascal,75775 Paris Cedex 16 France, telephone number: 33 1 45 24 82 00, web address: http://www.oecd.org. You may inspect each test method and guideline at the EPA Docket Center, EPA West, Rm. B102, 1301 Constitution Ave., NW., Washington, DC 20004, telephone number: (202) 566-1744, or 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/cfr/ibr-locations.html.

(i) Reporting requirements. A final report for each specific test for each subject chemical substance must be received by EPA by March 7, 2012, unless an extension is granted in writing pursuant to 40 CFR 790.55. A robust summary of the final report for each specific test should be submitted in addition to and at the same time as the final report. The term "robust summary" is used to describe the technical information necessary to adequately describe an experiment or study and includes the objectives, methods, results, and conclusions of the full study report which can be either an experiment or in some cases an estimation or prediction method. Guidance for the compilation of robust summaries is described in a document entitled "Draft Guidance on Developing Robust Summaries" which is available on-line: http://www.epa.gov/chemrtk/pubs/general/robsumgd.htm.

(j) Designation of specific chemical substances and testing requirements. The chemical substances identified by chemical name, Chemical Abstract Service Registry Number (CASRN), and class in Table 2 of this paragraph must be tested in accordance with the requirements designated in Tables 2 and 3 of this paragraph, and the requirements described in 40 CFR part 792 —Good Laboratory Practice Standards:

Table 2—Chemical Substances and Testing Requirements

CASRN	Chemical name	Class	Required tests/(See table 3 of this section)
75-07-0	Acetaldehyde	1	C2, F2.
78-11-5	1,3-Propanediol, 2,2-bis[(nitrooxy)methyl]-, dinitrate (ester)	1	C4.
84-65-1	9,10-Anthracenedione	1	C6.
89-32-7	1H,3H-Benzo[1,2-c:4,5-c']difuran-1,3,5,7-tetrone	1	A3, A4, A5, B, C1, D, E1, F1.
110-44-1	2,4-Hexadienoic acid, (E,E)-	1	C6.
118-82-1	Phenol, 4,4'-methylenebis[2,6-bis(1,1-dimethylethyl)-	1	C1.
119-61-9	Methanone, diphenyl-	1	B, C2.
144-62-7	Ethanedioic acid	1	A1, A2, A3, A5, B, C1, E2.
149-44-0	Methanesulfinic acid,hydroxy-, monosodium salt	1	E1.
2524-04-1	Phosphorochloridothioic acid, O,O-diethyl ester	1	A1, A2, A3, A4, A5, B, C1, E1, E2, F2.
4719-04-4	1,3,5-Triazine-1,3,5(2H,4H,6H)-triethanol	1	C6.
6381-77-7	D-erythro-hex-2-enonic acid, gamma.-lactone, monosodium salt	1	A4, B, C1.
31138-65-5	D-gluco-heptonic acid, monosodium salt, (2.xi.)-	1	A1, A2, A4, A5, B, C1, D, E1, E2, F1.
66241-11-0	C.I. Leuco Sulphur Black 1	2	A1, A2, A3, A4, A5, B, C1, D, E1, E2, F1.
68187-76-8	Castor oil, sulfated, sodium salt	2	A1, A2, C1, D, E1, E2, F1.

68187-84-8	Castor oil, oxidized	2	A1, A2, B, E1, E2, F1.
68479-98-1	Benzenediamine, ar,ar-diethyl-ar-methyl-	1	A1, A3, A4, A5, C1, E1, E2, F1.
68527-02-6	Alkenes, C12-24, chloro	2	A1, A2, A3, A4, A5, B, C1, E2, F2.
68647-60-9	Hydrocarbons, C > 4	2	A2, A3, A5, B, C1, D, E1, E2, F1.
Note: CASRN = Chemical Abstract Service Registry Number.			

Table 3—Key to the Test Requirements Denoted by Alphanumeric Symbols in Table 2 of this Paragraph

[Note: The ASTM and ISO test methods and the OECD guideline required in this paragraph are incorporated by reference; see paragraph (h) of this section.]			
Testingcategory	Testsymbol	Test requirements and references	Special conditions
Physical/chemical properties	A	1. Melting Point: American Society for Testing and Materials (ASTM) E 324-99 (capillary tube), if a Freezing Point: Organization for Economic Cooperation and Development (OECD) 102 (melting point/melting range)2. Boiling Point: ASTM E 1719-05 (ebulliometry) 3. Vapor Pressure: ASTM E 1782-08 (thermal analysis) 4. n-Octanol/Water Partition Coefficient (log 10 basis) or log KOW: (See Special Conditions for the log KOW test requirement and select the appropriate method to use, if any, from those listed in this column.) Method A: 40 CFR 799.6755 (shake flask) Method B: ASTM E 1147-92 (Reapproved 2005) (liquid chromatography) Method C: 40 CFR 799.6756 (generator column) 5. Water Solubility: (See Special Conditions for the water solubility test requirement and select the appropriate method to use, if any, from those listed in this column.) Method A: ASTM E 1148-02 (Reapproved 2008) (shake flask) Method B: 40 CFR 799.6784 (shake flask) Method C: 40 CFR 799.6784 (column elution) Method D: 40 CFR 799.6786 (generator column)	n-Octanol/water Partition Coefficient (log 10 basis) or log KOW:Which method is required, if any, is determined by the test substance's estimated i log KOW as follows: log KOW < 0: No testing required. log KOW range 0-1: Method A or B. log KOW range > 1-4: Method A, B, or C. log KOW range > 4-6: Method B or C. log KOW > 6: Method C. Test sponsors must provide in the final study report the underlying rationale for the method and pH selected. In order to ensure environmental relevance, EPA highly recommends that the selected study be conducted at pH 7. Water Solubility: Which method is required, if any, is determined by the test substance's estimated ii water solubility. Test sponsors must provide in the final study report the underlying rationale for the method and pH selected. In order to ensure environmental relevance, EPA highly recommends that the selected study be conducted starting at pH 7. > 5,000 milligram/Liter (mg/L): Method A or B. > 10 mg/L-5,000 mg/L: Method A, B, C, or D. > 0.001 mg/L-10 mg/L: Method C or D. ≤ 0.001 mg/L: No testing required.
Environmental fate and pathways —ready biodegradation	B	For B, consult International Organization for Standardization (ISO) 10634:1995(E) for guidance, and choose one of the methods listed in this	Which method is required, if any, is determined by the test substance's physical and chemical properties, including its water solubility. ISO 10634:1995(E) provides guidance for selection of an appropriate test

		column:1. ASTM E 1720-01 (Reapproved 2008) (sealed vessel CO2 production test) OR 2. ISO 14593:1999(E) (CO2 headspace test) OR 3. ISO 7827:1994(E) (analysis of DOC) OR 4. ISO 9408:1999(E) (determination of oxygen demand in a closed respirometer) OR	method for a given test substance. Test sponsors must provide in the final study report the underlying rationale for the method selected.
		5. ISO 9439:1999(E) (CO2 evolution test) OR	
		6. ISO 10707:1994(E) (closed bottle test) OR	
		7. ISO 10708:1997(E) (two-phase closed bottle test)	
Aquatic toxicity	C1	For C1, Test Group 1 or Test Group 2 listed in this column must be used to fulfill the testing requirements—See Special Conditions.Test Group 1 for C1: 1. Acute Toxicity to Fish: ASTM E 729-96 (Reapproved 2007) 2. Acute Toxicity to Daphnia: ASTM E 729-96 (Reapproved 2007) 3. Toxicity to Plants (Algae): ASTM E 1218-04 e1 Test Group 2 for C1: 1. Chronic Toxicity to Daphnia: ASTM E 1193-97 (Reapproved 2004) 2. Toxicity to Plants (Algae): ASTM E 1218—04 e1	The following are the special conditions for C1, C2, C3, C4, C5, and C7 testing; there are no special conditions for C6.Which test group is required is determined by the test substance's measured log KOW as obtained under Test Category A, or using an existing measured log KOW. iii If log KOW < 4.2: Test Group 1 is required. If log KOW ≥ 4.2: Test Group 2 is required
	C2	For C2, Test Group 1 or Test Group 2 listed in this column must be used to fulfill the testing requirements—See Special Conditions.	
		Test Group 1 for C2:	
		1. Acute Toxicity to Daphnia: ASTM E 729-96 (Reapproved 2007)	
		2. Toxicity to Plants (Algae): ASTM E 1218-04 e1	
		Test Group 2 for C2:	
		1. Chronic Toxicity to Daphnia: ASTM E 1193-97 (Reapproved 2004)	
		2. Toxicity to Plants (Algae): ASTM E 1218-04 e1	
	C3	For C3, Test Group 1 or Test Group 2 listed in this column must be used to fulfill the testing requirements—See Special Conditions.	
		Test Group 1 for C3:	
		1. Acute Toxicity to Fish:	

		ASTM E 729–96 (Reapproved 2007)
		2. Toxicity to Plants (Algae): ASTM E 1218–04 e1
		Test Group 2 for C3:
		1. Chronic Toxicity to Daphnia: ASTM E 1193–97 (Reapproved 2004)
		2. Toxicity to Plants (Algae): ASTM E 1218–04 e1
	C4	For C4, Test Group 1 or Test Group 2 listed in this column must be used to fulfill the testing requirements—See Special Conditions.
		Test Group 1 for C4:
		1. Acute Toxicity to Fish: ASTM E 729–96 (Reapproved 2007)
		2. Acute Toxicity to Daphnia: ASTM E 729–96 (Reapproved 2007)
		Test Group 2 for C4:
		1. Chronic Toxicity to Daphnia: ASTM E 1193–97 (Reapproved 2004)
	C5	For C5, Test Group 1 or Test Group 2 listed in this column must be used to fulfill the testing requirements—See Special Conditions.
		Test Group 1 for C5:
		1. Acute Toxicity to Daphnia: ASTM E 729–96 (Reapproved 2007)
		Test Group 2 for C5:
		1. Chronic Toxicity to Daphnia: ASTM E 1193–97 (Reapproved 2004)
	C6	Toxicity to Plants (Algae): ASTM E 1218–04 e1
	C7	For C7, Test Group 1 or Test Group 2 listed in this column must be used to fulfill the testing requirements—See Special Conditions.
		Test Group 1 for C7:
		1. Acute Toxicity to Fish: ASTM E 729–96 (Reapproved 2007)
		Test Group 2 for C7:
		1. Chronic Toxicity to Daphnia: ASTM E 1193–97

		(Reapproved 2004)	
Mammalian toxicity—acute	D	See special conditions for this test requirement and select the method that must be used from those listed in this column.Method A: Acute Inhalation Toxicity (rat): 40 CFR 799.9130 Method B: EITHER: 1. Acute (Up/Down) Oral Toxicity (rat): ASTM E 1163–98 (Reapproved 2002) OR 2. Acute (Up/Down) Oral Toxicity (rat): 40 CFR 799.9110(d)(1)(i)(A)	Which testing method is required is determined by the test substance's physical state at room temperature (25 °C). For those test substances that are gases at room temperature, Method A is required; otherwise, use either of the two methods listed under Method B.In Method B, 40 CFR 799.9110(d)(1)(i)(A) refers to the OECD 425 Up/Down Procedure.iv Estimating starting dose for Method B: Data from the neutral red uptake basal cytotoxicity assay v using normal human keratinocytes or mouse BALB/c 3T3 cells may be used to estimate the starting dose.
Mammalian toxicity—genotoxicity	E1	Bacterial Reverse Mutation Test (in vitro): 40 CFR 799.9510	None
	E2	Conduct any one of the following three tests for chromosomal damage: In vitro Mammalian Chromosome Aberration Test: 40 CFR 799.9537 OR Mammalian Bone Marrow Chromosomal Aberration Test (in vivo in rodents: mouse (preferred species), rat, or Chinese hamster): 40 CFR 799.9538 OR Mammalian Erythrocyte Micronucleus Test [sampled in bone marrow] (in vivo in rodents: Mouse (preferred species), rat, or Chinese hamster): 40 CFR 799.9539	Persons required to conduct testing for chromosomal damage are encouraged to use the in vitro Mammalian Chromosome Aberration Test (40 CFR 799.9537) to generate the needed data unless known chemical properties (e.g., physical/chemical properties, chemical class characteristics) preclude its use. A subject person who uses one of the in vivo methods instead of the in vitro method to address a chromosomal damage test requirement must submit to EPA a rationale for conducting that alternate test in the final study report.
Mammalian toxicity—repeated dose/reproduction/developmental	F1	Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test: 40 CFR 799.9365 OR Reproduction/Developmental Toxicity Screening Test: 40 CFR 799.9355 AND Repeated Dose 28-Day Oral Toxicity Study in rodents: 40 CFR 799.9305	Where F1 is required, EPA recommends use of the Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (40 CFR 799.9365). However, there may be valid reasons to test a particular chemical using both 40 CFR 799.9355 and 40 CFR 799.9305 to fill Mammalian Toxicity—Repeated Dose/Reproduction/Developmental data needs. A subject person who uses the combination of 40 CFR 799.9355 and 40 CFR 799.9305 in place of 40 CFR 799.9365 must submit to EPA a rationale for conducting these alternate tests in the final study reports. Where F2 or F3 is required, no rationale for conducting the required test need be provided in the final study report.
	F2	Reproduction/Developmental Toxicity Screening Test: 40	

		CFR 799.9355
	F3	Repeated Dose 28-Day Oral Toxicity Study in rodents: 40 CFR 799.9305

i EPA recommends, but does not require, that log KOW be quantitatively estimated prior to initiating this study. One method, among many similar methods, for estimating log KOW is described in the article entitled "Atom/Fragment Contribution Method for Estimating Octanol-Water Partition Coefficients" by W.M. Meylan and P.H. Howard in the Journal of Pharmaceutical Sciences. 84(1):83-92. January 1992. This reference is available in docket ID number EPA-HQ-OPPT-2007-0531 at the EPA Docket Center, Rm. 3334, EPA West Bldg., 1301 Constitution Ave., NW., Washington, DC 20004, telephone number: (202) 566-1744, from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays.

ii EPA recommends, but does not require, that water solubility be quantitatively estimated prior to initiating this study. One method, among many similar methods, for estimating water solubility is described in the article entitled "Improved Method for Estimating Water Solubility From Octanol/Water Partition Coefficient" by W.M. Meylan, P.H. Howard, and R.S. Boethling in Environmental Toxicology and Chemistry. 15(2):100-106. 1996. This reference is available in docket ID number EPA-HQ-OPPT-2007-0531 at the EPA Docket Center, Rm. 3334, EPA West Bldg., 1301 Constitution Ave., NW., Washington, DC 20004, telephone number: (202) 566-1744, from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays.

iii Chemical substances that are dispersible in water may have log KOW values greater than 4.2 and may still be acutely toxic to aquatic organisms. Test sponsors who wish to conduct Test Group 1 studies on such chemicals may request a modification to the test standard as described in 40 CFR 790.55 . Based upon the supporting rationale provided by the test sponsor, EPA may allow an alternative threshold or method be used for determining whether acute or chronic aquatic toxicity testing be performed for a specific substance.

iv The OECD 425 Up/Down Procedure, revised by OECD in December 2001, is available in docket ID number EPA-HQ-OPPT-2007-0531 at the EPA Docket Center, Rm. 3334, EPA West Bldg., 1301 Constitution Ave., NW., Washington, DC 20004, telephone number: (202) 566-1744, from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays.

v The neutral red uptake basal cytotoxicity assay, which may be used to estimate the starting dose for the mammalian toxicity-acute endpoint, is available in docket ID number EPA-HQ-OPPT-2007-0531 at the EPA Docket Center, Rm. 3334, EPA West Bldg., 1301 Constitution Ave., NW., Washington, DC 20004, telephone number: (202) 566-1744, from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays.

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