

⁴The OECD 425 Up/Down Procedure, revised by OECD in December 2001, is available under docket ID number EPA–HQ–OPPT–2005–0033 at the EPA Docket Center, Rm. B102, 1301 Constitution Ave., NW., Washington, DC, from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays.

⁵The neutral red uptake basal cytotoxicity assay, which may be used to estimate the starting dose for the mammalian toxicity-acute endpoint, is available under docket ID number EPA–HQ–OPPT–2005–0033 at the EPA Docket Center, Rm. B102, 1301 Constitution Ave., NW., Washington, DC, from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays.

(k) *Effective date.* This section is effective on April 17, 2006.

[71 FR 13730, Mar. 16, 2006, as amended at 71 FR 71062, Dec. 8, 2006]

§ 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.	<p>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:</p> <ul style="list-style-type: none"> —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)). <p>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)).</p>

(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 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 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 (K_p) 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 K_p . 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 K_p 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 K_p , 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) \times hr^{-1} \times centimeters (cm)⁻²) by the concentration of the test substance (measured in $\mu\text{g} \times \text{cm}^{-3}$) applied to the skin. (For example, if the steady-state rate is 1 microgram \times hr^{-1} \times cm^{-2} and the concentration applied to the skin is 1,000 micrograms \times cm^{-3} , then the *Kp* value is calculated to be 0.001 $\text{cm} \times \text{hr}^{-1}$.) 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 ($\mu\text{g} \times \text{hr}^{-1} \times \text{cm}^{-2}$) 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]

Subpart E—Product Properties Test Guidelines

SOURCE: 65 FR 78751, Dec. 15, 2000, unless otherwise noted.

§ 799.6755 TSCA partition coefficient (n-octanol/water), shake flask method.

(a) *Scope*—(1) *Applicability.* This section is intended to meet the testing requirements of the Toxic Substances Control Act (TSCA) (15 U.S.C. 2601).

(2) *Source.* The source material used in developing this TSCA test guideline is the Office of Prevention, Pesticides and Toxics (OPPTS) harmonized test guideline 830.7550 (August 1996, final guideline). The source is available at the address in paragraph (f) of this section.

(b) *Introductory information*—(1) *Prerequisites.* Suitable analytical method, dissociation constant, water solubility, and hydrolysis (preliminary test).

(2) *Coefficient of variation.* The coefficient of variation on the mean values reported by the participants of the Organization for Economic Cooperation and Development (OECD) Laboratory Intercomparison Testing, Part I, 1979, appeared to be dependent on the chemicals tested; it ranges from 0.17 to 1.03.

(3) *Qualifying statements.* This method applies only to pure, water soluble substances which do not dissociate or associate, and which are not surface active. In order to use the partition coefficient (P) as a screening test for bioaccumulation, it should be ascertained that the impurities in the commercial product are of minor importance. Testing of P (n-octanol/water) cannot be used as a screening test in the case of organometallic compounds.

(4) *Alternative methods.* High-pressure liquid chromatography (HPLC) methods described in the references in paragraphs (f)(3), (f)(4), and (f)(5) of this section may be considered as an alternative test method.

(c) *Method*—(1) *Introduction, purpose, scope, relevance, application, and limits of test.* The P of a substance between water and a lipophilic solvent (n-octanol) is one model variable which may be used to describe the transfer of a substance from the aquatic environment into an organism and the potential bioaccumulation of the substance. Studies show a highly significant relationship between the P of different substances in the system water/n-octanol