**ENVIRONMENTAL PROTECTION AGENCY**

**40 CFR Part 799**

**[OPPTS–42196; FRL–5760–3]**

**RIN 2070–AB07**

## Proposed Test Rule for In Vitro Dermal Absorption Rate Testing of Certain Chemicals of Interest to Occupational Safety and Health Administration

**AGENCY:** Environmental Protection Agency (EPA).

**ACTION:** Proposed rule.

**SUMMARY:** EPA is proposing a test rule under section 4(a) of the Toxic Substances Control Act (TSCA) to require manufacturers, importers, and processors of 47 chemical substances of interest to the Occupational Safety and Health Administration (OSHA) to conduct *in vitro* dermal absorption rate testing. These chemicals, and others, were designated for *in vitro* dermal absorption rate testing in the 31st, 32nd, and 35th Reports of the TSCA Section 4(e) Interagency Testing Committee (ITC) to the EPA Administrator. The dermal absorption rate data obtained under this testing program would be used to support OSHA's development of ''skin designations'' for the chemical substances included in this proposed rule. Skin designations are used by OSHA to provide specific guidance to employers concerning whether changes should be made to processes involving chemical substances in order to reduce the hazard of systemic toxicity from dermal absorption of these chemicals. Changes to a process might include changes in engineering controls or changes in the use of or type of personal protective equipment. Skin designations alert industrial hygienists, employers, and workers to potential adverse health effects resulting from dermal exposure to chemicals in the workplace. Persons who export or intend to export any chemical substance included in the final rule based on this proposed rule will be subject to the export notification requirements in TSCA section 12(b)(1).

**DATES:** Comments, identified by docket control number OPPTS–42196, must be received by EPA on or before August 9, 1999. Your request to present oral comments must be in writing and must be received by EPA on or before July 9, 1999.

**ADDRESSES:** Comments may be submitted by mail, electronically, or in person. Follow the detailed instructions for each method as provided in Unit I.C. of the ''SUPPLEMENTARY INFORMATION'' section of this preamble. To ensure proper receipt by EPA, your comments must identify docket control number OPPTS–42196 in the subject line on the first page of your response.

**FOR FURTHER INFORMATION CONTACT:** *For general information*: Christine Augustyniak, Associate Director, Environmental Assistance Division (7408), Office of Pollution Prevention and Toxics, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460; telephone number: (202) 554–1404; TDD: (202) 554–0551; e-mail address: TSCA-Hotline@epa.gov.

*For technical information*: Keith Cronin, Project Manager, Chemical Control Division (7405), Office of Pollution Prevention and Toxics, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460; telephone number: (202) 260–8157; fax number: (202) 260–1096; e-mail address: cronin.keith@epa.gov.

**SUPPLEMENTARY INFORMATION:**

### I. General Information

*A. Does This Action Apply To Me?*

You may be affected by this action, if you manufacture (defined by statute to include import) or process any of the chemical substances that are listed in Table 2 of this unit. Use of the term ''manufacture'' in this preamble will encompass ''import,'' unless otherwise stated. In addition, as described in Unit VI. of this preamble, once the Agency issues the final rule, any person who exports, or intends to export, one of these chemical substances will be subject to the export notification requirements in 40 CFR part 707, subpart D. The export notification requirements do not apply until the Agency issues a final test rule, and then, only apply to exports of the chemical substances that are contained in the final test rule. Therefore, entities potentially affected by this proposed rule may include, but are not limited to:

TABLE 1.— ENTITIES POTENTIALLY AFFECTED BY THE PROPOSED TESTING REQUIREMENTS

| Type of entity | SIC | NAICS | Examples of potentially affected entities |
|---|---|---|---|
| Chemical manufacturers and importers | 28, 2911 | 325, 32411 | Persons who manufacture (defined by statute to include import) one or more of the subject chemical substances |
| Chemical processors | 28, 2911 | 325, 32411 | Persons who process one or more of the subject chemical substances. |

This listing is not intended to be exhaustive, but rather provides a guide for readers regarding entities likely to be affected by this action. Other types of entities not listed in Table 1 of this unit could also be affected. The Standard Industrial Classification (SIC) codes and the North American Industrial Classification System (NAICS) codes have been provided to assist you and others in determining whether this action might apply to certain entities. To determine whether you or your business is affected by this action, you should carefully examine the applicability provisions in Unit V.C. of this preamble entitled ''Would I Be Required To Test Under This Rule?'' and consult the proposed regulatory text in § 799.5115. If you have any questions regarding the applicability of this action to a particular entity, consult the technical person listed in ''FOR FURTHER INFORMATION CONTACT'' at the beginning of the preamble.

If you are an entity identified in Table 1 of this unit, you would only be subject to the testing requirements contained in this proposed rule if you manufacture or process any of the 47 chemical substances that are listed in Table 2 of this unit.

TABLE 2.—LIST OF CHEMICAL SUBSTANCES PROPOSED FOR TESTING

| CAS No. | Chemical substance |
|---|---|
| 60–29–7 | Ethyl ether |
| 74–96–4 | Ethyl bromide |
| 75–05–8 | Acetonitrile |
| 75–15–0 | Carbon disulfide |
| 75–35–4 | Vinylidene chloride |
| 77–73–6 | Dicyclopentadiene |
| 77–78–1 | Dimethyl sulfate |
| 78–59–1 | Isophorone |
| 78–83–1 | Isobutyl alcohol |
| 78–87–5 | Propylene dichloride |
| 78–92–2 | *sec*-Butyl alcohol |
| 79–20–9 | Methyl acetate |
| 79–46–9 | 2-Nitropropane |
| 91–20–3 | Naphthalene |

TABLE 2.—LIST OF CHEMICAL SUBSTANCES PROPOSED FOR TESTING—Continued

| CAS No. | Chemical substance |
|---|---|
| 92–52–4 | Biphenyl |
| 95–49–8 | *o*-Chlorotoluene |
| 95–50–1 | *o*-Dichlorobenzene |
| 97–77–8 | Disulfiram |
| 98–29–3 | *tert*-Butylcatechol |
| 99–99–0 | *p*-Nitrotoluene |
| 100–00–5 | *p*-Nitrochlorobenzene |
| 100–01–6 | *p*-Nitroaniline |
| 100–44–7 | Benzyl chloride |
| 106–42–3 | *p*-Xylene |
| 106–46–7 | *p*-Dichlorobenzene |
| 107–06–2 | Ethylene dichloride |
| 107–31–3 | Methyl formate |
| 108–03–2 | 1-Nitropropane |
| 108–90–7 | Chlorobenzene |
| 108–93–0 | Cyclohexanol |
| 109–66–0 | Pentane |
| 109–99–9 | Tetrahydrofuran |
| 110–12–3 | Methyl isoamyl ketone |
| 111–84–2 | Nonane |
| 120–80–9 | Catechol |
| 121–69–7 | Dimethylaniline |
| 122–39–4 | Diphenylamine |
| 123–42–2 | Diacetone alcohol |
| 126–99–8 | *beta*-Chloroprene |
| 127–19–5 | Dimethyl acetamide |
| 142–82–5 | *n*–Heptane |
| 150–76–5 | *p*-Methoxyphenol |
| 528–29–0 | *o*-Dinitrobenzene |
| 628–63–7 | *n*-Amyl acetate |
| 768–52–5 | *N*-Isopropylaniline |
| 25013–15–4 | Vinyl toluene |
| 34590–94–8 | Dipropylene glycol methyl ether |

*B. How Can I Get Additional Information or Copies of This Document or Other Documents?*

1. *Electronically*. You may obtain electronic copies of this document and other documents from the EPA Internet EPA Home Page at http://www.epa.gov/ . On the Home Page select ''Law and Regulations'' and then look up the entry for this document under ''**Federal Register**—Environmental Documents.'' You can also go directly to the **Federal Register** listings at http://www.epa.gov/fedrgstr/.

2. *In person* . The official record for this proposed rule, which includes the public version, has been established under docket control number OPPTS–42196. The official record consists of the documents referenced in this preamble (see Unit VIII. of this preamble), as well as the public comments that will be received during the comment period, and other information related to this rulemaking, including information claimed as Confidential Business Information (CBI). This official record includes the documents that are physically located in the docket, as well as all documents that are referenced in those documents. The public version of the offical record does not include any information claimed as CBI. The public version of the official record, which includes printed, paper versions of any electronic comments that may be submitted as described in Unit I.C. and D. of this preamble, is available for inspection in the TSCA Nonconfidential Information Center, Rm. NE B–607, 401 M St., SW., Washington, DC. The Center is open from 12 noon to 4 p.m., Monday through Friday, excluding legal holidays. The telephone number of the Center is (202) 260–7099.

*C. How and To Whom Do I Submit Comments?*

You may submit comments through the mail, in person, or electronically. To ensure proper receipt by EPA, your comments must identify docket control number OPPTS–42196 in the subject line on the first page of your response.

1. *By mail*. Submit comments to: Document Control Office (7407), Office of Pollution Prevention and Toxics, Environmental Protection Agency, 401 M St., SW., East Tower, Rm. G–099, Washington, DC 20460.

2. *In person or by courier*. Deliver comments to: Document Control Office, Office of Pollution Prevention and Toxics, Environmental Protection Agency, 401 M St., SW., East Tower, Rm. G–099, Washington, DC. The telephone number for the OPPT Document Control Office is (202) 260–7093.

3. *Electronically*. Submit your comments electronically by e-mail to: oppt.ncic@epa.gov, or you may mail or deliver your computer disk to the addresses identified in Units I.C.1. or 2. of this preamble. Do not submit any information electronically that you consider to be CBI. Submit comments as an ASCII file, avoiding the use of special characters and any form of encryption. Comments will also be accepted on standard disks in WordPerfect 5.1/6.1 or ASCII file format. All copies of electronic comments must be identified by docket control number OPPTS–42196. Electronic comments may be filed online at many Federal Depository Libraries.

*D. How Should I Handle CBI Information That I Want To Submit To The Agency?*

Do not submit any information electronically that you consider to be CBI. You may claim information that you submit in response to this document as CBI by marking any part or all of that information as CBI. Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR part 2. In addition to one complete version of the comments that include any information claimed as CBI, a copy of the comments that does not contain the information claimed as CBI must be submitted for inclusion in the public version of the official record. Information not marked confidential will be included in the public version of the official record by EPA without prior notice. If you have any questions about CBI or the procedures for claiming CBI, consult the technical person identified in ''FOR FURTHER INFORMATION CONTACT''at the beginning of this preamble.

*E. Can I Request An Opportunity To Present Oral Comments To The Agency?*

You may submit a request for an opportunity to present oral comments. This request must be in writing. If such a request is received on or before July 9, 1999, EPA will hold a public meeting on this proposed rule in Washington, DC. This written request must be submitted to the address provided in Unit I.C. of this preamble. If such a request is received, EPA will announce the scheduling of the public meeting in a subsequent **Federal Register** document. If a public meeting is announced, and if you are interested in attending or presenting oral and/or written comments at the public meeting, you should follow the instructions provided in the subsequent **Federal Register** document announcing the public meeting.

*F. What Should I Consider as I Prepare My Comments For EPA?*

We invite you to provide your views on the various options we propose, new approaches we have not considered, the potential impacts of the various options (including possible unintended consequences), and any data or information that you would like the Agency to consider during the development of the final rule. You may find the following suggestions helpful for preparing your comments:

- Explain your views as clearly as possible.
- Describe any assumptions that you used.
- Provide copies of any technical information and/or data you used that support your views.
- If you estimate potential burden or costs, explain how you arrived at the estimate.
- Provide specific examples to illustrate your concerns.
- Offer alternative ways to improve the rule or collection activity.

•Make sure to submit your comments by the deadline in this document.

•At the beginning of your comments, be sure to properly identify the document you are commenting on. To ensure proper receipt by EPA, your comments must identify the docket control number assigned to this action in the subject line on the first page of your response. You may also provide the name, date, and **Federal Register** citation.

*G. Are There Issues On Which EPA Is Particularly Interested In Receiving Comment?*

EPA invites comment on any aspect of this proposed rule. EPA is particularly interested in specific comments on the approach discussed in Unit V.C. of this preamble, entitled ''Would I Be Required To Test Under This Rule?''

## II. Authority

This document proposes a test rule under TSCA section 4(a) (15 U.S.C 2603(a)) that would require an *in vitro* dermal absorption rate test for 47 of the chemical substances designated by the ITC for this testing.

Section 2(b)(1) of TSCA (15 U.S.C. 2601(b)(1)) states that it is the policy of the United States that ''adequate data should be developed with respect to the effect of chemical substances and mixtures on health and the environment and that the development of such data should be the responsibility of those who manufacture and those who process such chemical substances and mixtures [.]'' To implement this policy, TSCA section 4(a) mandates that EPA require by rule that manufacturers and processors of chemical substances and mixtures conduct testing if the Administrator finds that:

(1)(A)(i) the manufacture, distribution in commerce, processing, use, or disposal of a chemical substance or mixture, or that any combination of such activities, may present an unreasonable risk of injury to health or the environment,

(ii) there are insufficient data and experience upon which the effects of such manufacture, distribution in commerce, processing, use, or disposal of such substance or mixture or of any combination of such activities on health or the environment can reasonably be determined or predicted, and

(iii) testing of such substance or mixture with respect to such effects is necessary to develop such data; or

(B)(i) a chemical substance or mixture is or will be produced in substantial quantities, and (I) it enters or may reasonably be anticipated to enter the environment in substantial quantities or (II) there is or may be significant or substantial human exposure to such substance or mixture,

(ii) there are insufficient data and experience upon which the effects of the manufacture, distribution in commerce, processing, use, or disposal of such substance or mixture or of any combination of such activities on health or the environment can reasonably be determined or predicted, and

(iii) testing of such substance or mixture with respect to such effects is necessary to develop such data [.]

If EPA makes these findings for a chemical substance or mixture, the Administrator must require by rule that testing be conducted on that chemical substance or mixture. The purpose of the testing would be to develop data about the substance or mixture's health and environmental effects for which there is an insufficiency of data and experience, and which are relevant to a determination that the manufacture, distribution in commerce, processing, use, or disposal of the substance or mixture, or any combination of such activities, does or does not present an unreasonable risk of injury to health or the environment.

Once the Administrator has made a finding under TSCA section 4(a)(1)(A)(i) (i.e., a finding that a chemical substance may present an unreasonable risk of injury to health or the environment) or a finding under TSCA section 4(a)(1)(B)(i) (i.e., a finding that a chemical substance is or will be produced in substantial quantities and either it may enter the environment in substantial quantities or there may be significant or substantial human exposure to the chemical substance), EPA may require any type of health or environmental effects testing necessary to address unanswered questions about the effects of the chemical substance. EPA need not limit the scope of testing required to the factual basis for the TSCA section 4(a)(1)(A)(i) or (B)(i) findings, as long as EPA also finds that there are insufficient data and experience upon which the effects of the manufacture, distribution in commerce, processing, use, or disposal of such substance or mixture or of any combination of such activities on health or the environment can reasonably be determined or predicted, and that testing is necessary to develop such data. This approach is explained in more detail in EPA's statement of policy for making findings under TSCA section 4(a)(1)(B) (frequently described as the ''B'' policy) in the **Federal Register** of May 14, 1993 (58 FR 28736, 28738–28739).

In this proposed rule, EPA intends to use its broad TSCA section 4(a) authority to obtain dermal absorption rate data necessary to support OSHA's development of ''skin designations'' (see Unit III.C. of this preamble) for the 47 chemical substances included in the proposed rule. EPA has made preliminary findings for these chemicals under TSCA section 4(a)(1)(B) that: They are produced in substantial quantities; there is or may be substantial human exposure to them; existing data are insufficient to determine or predict their health effects; and testing is necessary to develop such data.

Under TSCA section 10(b), EPA is responsible, through an interagency committee, for collecting data and disseminating the data to other Federal agencies, such as OSHA, as the Agency is proposing in this document. EPA has used its TSCA section 4(a) authority in the past to support regulatory programs of other EPA offices as well as other Federal agencies needing health and/or environmental effects test data. See, e.g., the final test rule for the Office of Water Chemicals (58 FR 59667, 59673 November 10, 1993).

## III. Background

*A. Why Is EPA Proposing To Take This Action?*

Under TSCA section 4(e)(1), the ITC is responsible for recommending chemical substances and mixtures to the EPA Administrator for priority testing consideration. The chemical substances and mixtures so designated by the ITC comprise a list called the *Priority Testing List*. OSHA nominated 658 chemical substances and mixtures for ITC review in September 1991. The results of the ITC's review were published in the **Federal Register** issues of May 5, 1993 (58 FR 26898, 26900) and July 16, 1993 (58 FR 38490, 38492–38493). OSHA requested that the ITC assess the availability of data relevant to dermal absorption for these chemical substances and mixtures and determine the need for further testing (58 FR 26898, 26900, May 5, 1993). OSHA indicated to the ITC that it needed quantitative measures of dermal absorption to evaluate the potential hazard of these chemicals to workers (58 FR 38490, 38492, July 16, 1993). These quantitative measures are expressed as the dermal absorption rate for a particular chemical (59 FR 35720, 35725, July 13, 1994).

In its 31st, 32nd, and 35th ITC Reports to the EPA Administrator (58 FR 26898, May 5, 1993; 58 FR 38490, July 16, 1993; and 59 FR 67596, December 29, 1994, respectively), the ITC designated for *in vitro* dermal absorption rate testing a total of 83 of the chemical substances nominated by OSHA. In reducing OSHA's list of 658 chemicals to 83 chemicals, the ITC

grouped the nominated chemicals into categories as a means of prioritizing the chemicals for consideration. Chemicals that were assigned to categories such as polymers, pesticides, and chloroflurocarbons were eliminated from consideration by the ITC. They were eliminated because, among other reasons, they are regulated under other Federal authorities or because EPA, under TSCA, does not have the authority to require the testing of certain chemicals (58 FR 26898, 26900–26902 and 58 FR 38490, 38493). The remaining chemicals were then grouped by production volume, and literature searches were performed.

The ITC performed searches for data relating to the chemicals on the following data bases: RTECS (Registry of Toxic Effects of Chemical Substances), TOXLINE (TOXicology information onLINE), MEDLINE (MEDlars onLINE), TOXLIT (TOXicology LITerature from special sources), CECATS (OPPT/Risk Assessment Division/Chemical Screening Branch's Existing Chemical Assessment Tracking System), TSCATS (Toxic Substances Control Act Test Submissions), and INDEX MEDICUS. The search strategy was designed to identify any toxicological tests that used the dermal route of exposure. The information from the searches was collected and the chemicals were subcategorized based on the number of postings (58 FR 38490, 38493).

The 83 chemicals designated by the ITC were identified as follows: The ITC first ascertained those chemicals having no dermal information postings in any of the data bases searched, and, in its 31st ITC Report, the ITC designated this group of 24 chemicals for priority testing consideration (58 FR 26898, 26900). A second group of chemicals with limited dermal toxicity or dermal absorption data (as determined by the searches described in this unit) from which dermal absorption rate could not be estimated was then identified by the ITC, which designated this group of 34 chemicals in its 32nd ITC Report (Ref. 1) (58 FR 38490, 38492, 38494). Another 25 chemicals were designated in the 35th ITC Report, after the ITC reviewed the dermal data of 63 high production volume chemicals with slightly larger information bases (59 FR 67596, 67598). These data were insufficient to estimate dermal absorption rate because dermal absorption rate could not be calculated on the basis of the dermal absorption data which were available to the ITC.

The ITC then reviewed data from TSCA section 8(a) and 8(d) rules which were promulgated by EPA for these 83 chemical substances included in the 31st, 32nd, and 35th ITC Reports (40 CFR 712.30(e) (58 FR 68311, December 27, 1993; 59 FR 5956, February 9, 1994; 60 FR 34879, July 5, 1995)). These rules required the reporting to EPA of certain production, use and exposure-related information, and unpublished health and safety data concerning these 83 chemicals.

In reviewing the available data relating to these 83 chemicals, the ITC determined that the dermal absorption rate data for methyl methacrylate (Ref. 2), diethyl phthalate (Ref. 3), and cyclohexanone (Ref. 4) would meet OSHA's data needs for the chemicals (59 FR 35720, 35722, July 13, 1994; 60 FR 42982, 42985, August 17, 1995). Accordingly, the ITC withdrew its designation for these 3 chemicals: Methyl methacrylate and diethyl phthalate in the 34th ITC Report (59 FR 35720, 35725, July 13, 1994), and cyclohexanone in the 36th ITC Report (60 FR 42982, 42987, August 17, 1995).

Eighty of the chemical substances nominated by OSHA are thus currently designated by the ITC for *in vitro* dermal absorption rate testing under TSCA. In the **Federal Register** notices containing the 31st, 32nd, and 35th ITC Reports, EPA additionally solicited proposals for TSCA section 4 enforceable consent agreements (ECAs) for dermal absorption rate testing of the 80 chemical substances. EPA received no proposals for ECAs for dermal absorption rate testing in response to these solicitations.

On April 3, 1996 (61 FR 14773), EPA again solicited interested parties to submit proposals for ECAs. On June 26, 1996, EPA received a proposal for the development of an ECA for *tert*-butyl alcohol from the ARCO Chemical Company (ARCO). On March 26, 1998, EPA received a study entitled ''[$^{14}$C]-*t*-Butyl Alcohol: Topical Application: Dermal Absorption Study in the Male Rat,'' from ARCO (Ref. 5). This study was reviewed and found acceptable as a means of determining the dermal absorption rate for *tert*-butyl alcohol (Ref. 6). Accordingly, this action does not propose testing of *tert*-butyl alcohol.

In this action, EPA is proposing *in vitro* dermal absorption rate testing of 47 chemical substances of interest to OSHA. These chemical substances are listed in Table 2 of Unit I.A. of this preamble, entitled ''List of Chemical Substances Proposed for Testing,'' and in Table 2 of § 799.5115(i) of the proposed regulatory text, entitled ''Required Testing: Chemical Substances Designated for *In Vitro* Dermal Absorption Rate Testing.'' EPA has selected these 47 chemicals for testing because the Agency believes that the production volumes of these chemicals are higher than the production volumes of the 32 chemicals remaining out of the 80 chemicals currently designated by the ITC. Testing of the latter chemicals for dermal absorption rate will be addressed at a later date.

### *B. How Was the Test Standard Developed For EPA's Use in This Proposed Rule?*

In the solicitations discussed in Unit III.A. of this preamble, EPA referenced an *in vitro* dermal absorption rate test protocol for review by potential submitters in developing their proposed protocols (Ref. 7). The draft protocol was developed by a group of scientists from EPA in conjunction with ITC member and liaison agencies (Consumer Product Safety Commission (CPSC), Department of Defense (DoD), Food and Drug Administration (FDA), National Institute for Occupational Safety and Health (NIOSH), and OSHA) and consisted of the methods of Bronaugh and Collier (Ref. 7). EPA received public comments on the proposed protocol and entered them, along with the protocol itself, into the dockets for the 31st, 32nd, and 35th ITC Reports, as appropriate (docket control numbers OPPTS–41038, OPPTS–41039, and OPPTS–41042, respectively). In addition, the Chemical Manufacturers Association (CMA) submitted a proposed protocol outlining an alternative method (Ref. 8). Scientists from EPA and other Federal agencies represented on the ITC (including OSHA) reviewed the public comments and the CMA proposal. Based on their review of the Bronaugh and Collier protocol, public comments, and the CMA proposal, EPA and ITC scientists developed the *in vitro* dermal absorption rate test method which is the test standard used in this proposed rule.

### *C. How Will The Data Developed Under This Test Rule Be Used?*

This proposed rule would require the development of quantitative measures of dermal absorption rate to assist in evaluating the potential contribution of dermal absorption of the chemical substances proposed for testing to total exposures to workers from chemicals in the workplace. The dermal absorption rate data obtained under this testing program would be used to support OSHA's development of ''skin designations'' for the chemical substances included in this proposed rule.

OSHA assigns a skin designation to a chemical if it determines that cutaneous exposure (through the skin, eyes, and mucous membranes) to the chemical may result in systemic toxicity. Skin

designations are used by OSHA to provide specific guidance to employers concerning whether changes should be made to processes involving chemical substances in order to reduce the hazard of systemic toxicity from dermal absorption of these chemicals. Changes to a process might include changes in engineering controls or changes in the use or type of personal protective equipment. Skin designations alert industrial hygienists, employers, and workers to potential adverse health effects resulting from dermal exposure to chemicals in the workplace.

The information that would be developed under this test rule would not only support OSHA's activities, but also would support chemical risk assessment activities at EPA as well as at other Federal agencies. In particular, these data would provide input for chemical risk assessments involving environmental exposure scenarios which include intentional or incidental skin contact.

## IV. EPA Findings

### *A. What Is The Basis For EPA's Proposal To Test These Chemical Substances?*

As indicated in Unit II. of this preamble, in order to develop a rule under TSCA section 4(a) requiring the testing of chemical substances or mixtures, EPA must make certain findings for those chemicals regarding either:

1. Hazard (TSCA section 4(a)(1)(A)(i)); or

2. Production and either chemical release or human exposure (TSCA section 4(a)(1)(B)(i)).

EPA is proposing to require testing of the chemical substances included in this test rule based on its findings under TSCA section 4(a)(1)(B)(i) relating to ''substantial'' production and ''substantial human exposure,'' as well as findings under TSCA sections 4(a)(1)(B)(ii) and (iii).

In EPA's ''B'' policy, discussed in Unit II. of this preamble, ''substantial'' production of a chemical substance or mixture is generally interpreted to be aggregate production (including import) volume equaling or exceeding one million pounds (lbs) per year of that chemical substance or mixture (58 FR 28736, 28746, May 14, 1993). The ''B'' policy sets out the numeric threshold for ''substantial human exposure'' of workers to a chemical substance or mixture of 1,000 workers annually being exposed to that chemical substance or mixture. *Id.* See EPA's ''B'' policy (58 FR 28736, May 14, 1993) for further discussion on how EPA makes decisions under TSCA section 4(a)(1)(B)(i).

EPA has found preliminarily that, under TSCA section 4(a)(1)(B)(i), each of the 47 chemical substances proposed for dermal absorption rate testing is produced in ''substantial quantities'' and there is or may be ''substantial human exposure'' to each chemical substance. In addition, under TSCA section 4(a)(1)(B)(ii), EPA believes that there are insufficient data and experience to reasonably determine or predict the effects of the manufacturing, processing, or use of these chemical substances, or of any combination of such activities, on human health. In particular, as discussed in Unit IV.D. of this preamble, EPA has determined that there are insufficient data relating to dermal absorption rate resulting from human exposure to these chemicals. EPA also finds that testing the substances identified in this document is necessary to develop such data (TSCA section 4(a)(1)(B)(iii)). EPA has not identified any ''additional factors'' as discussed in the ''B'' policy (58 FR 28736, 28746, May 14, 1993) to cause the Agency to use decisionmaking criteria other than those described in the policy.

The specific chemical substances included in this proposed test rule are listed in Table 2 of Unit I.A. of this preamble, and in § 799.5115(i) of the proposed regulatory text.

### *B. Are These Chemical Substances Produced in Substantial Quantities?*

Each of the chemical substances included in this proposal is produced in an amount equal to or greater than one million lbs per year (Ref. 9), based on information gathered pursuant to the 1994 TSCA section 8(a) Inventory Update Rule (40 CFR part 710) and contained in the TSCA Chemical Update System. Their production volumes range from over one million to well over one billion lbs annually. Assuming the continued accuracy of these figures, EPA believes that these annual production volumes are ''substantial'' as that term is used with reference to production in TSCA section 4(a)(1)(B)(i). See 58 FR 28736, 28746, May 14, 1993.

### *C. Are a Substantial Number Of Workers Exposed To These Chemicals?*

EPA finds that the manufacturing, processing, and use of the chemical substances included in this document result or may result in exposure of a substantial number of workers. Table 3, entitled ''Exposure Information for Chemical Substances Included in This Proposed Test Rule,'' in Unit IV.C. of this preamble contains an estimate of the actual and potential worker exposure to these chemical substances (Ref. 10). These chemical substances are used in a wide variety of applications as industrial solvents, which result in potential exposures of workers as described in the exposure support document for this proposed rule (Ref. 10). EPA believes that the exposure to each chemical substance of 1,000 workers or more (Table 3 of this unit) is or may be ''substantial'' as that term is used with reference to ''human exposure'' in TSCA section 4(a)(1)(B)(i). See 58 FR 28376, 28746, May 14, 1993.

TABLE 3.—EXPOSURE INFORMATION FOR CHEMICAL SUBSTANCES INCLUDED IN THIS PROPOSED TEST RULE

| CAS No. | Chemical name | Number of workers exposed[1] |
|---|---|---|
| 60–29–7 | Ethyl ether | 272,746 |
| 74–96–4 | Ethyl bromide | 12,285 |
| 75–05–8 | Acetonitrile | 31,341 |
| 75–15–0 | Carbon disulfide | 45,761 |
| 75–35–4 | Vinylidene chloride | 2,679 |
| 77–73–6 | Dicyclopentadiene | 6,247 |
| 77–78–1 | Dimethyl sulfate | 10,482 |
| 78–59–1 | Isophorone | 47,097 |
| 78–83–1 | Isobutyl alcohol | 256,975 |
| 78–87–5 | Propylene dichloride | 2,944 |
| 78–92–2 | *sec*-Butyl alcohol | 126,200 |
| 79–20–9 | Methyl acetate | 20,455 |
| 79–46–9 | 2-Nitropropane | 9,817 |
| 91–20–3 | Naphthalene | 112,695 |
| 92–52–4 | Biphenyl | 32,000 |

TABLE 3.—EXPOSURE INFORMATION FOR CHEMICAL SUBSTANCES INCLUDED IN THIS PROPOSED TEST RULE—Continued

| CAS No. | Chemical name | Number of workers exposed[1] |
|---|---|---|
| 95–49–8 | *o*-Chlorotoluene | 11,617 |
| 95–50–1 | *o*-Dichlorobenzene | 92,248 |
| 97–77–8 | Disulfiram | 53,525 |
| 98–29–3 | *tert*-Butylcatechol | 27,528 |
| 99–99–0 | *p*-Nitrotoluene | 4,354 |
| 100–00–5 | *p*-Nitrochlorobenzene | 2,949 |
| 100–01–6 | *p*-Nitroaniline | 1,448 |
| 100–44–7 | Benzyl chloride | 41,075 |
| 106–42–3 | *p*-Xylene | 20,367 |
| 106–46–7 | *p*-Dichlorobenzene | 33,980 |
| 107–06–2 | Ethylene dichloride | 83,245 |
| 107–31–3 | Methyl formate | 7,739 |
| 108–03–2 | 1-Nitropropane | 21,535 |
| 108–90–7 | Chlorobenzene | 18,049 |
| 108–93–0 | Cyclohexanol | 112,366 |
| 109–66–0 | Pentane | 38,464 |
| 109–99–9 | Tetrahydrofuran | 356,041 |
| 110–12–3 | Methyl isoamyl ketone | 18,835 |
| 111–84–2 | Nonane | 7,277 |
| 120–80–9 | Catechol | 13,517 |
| 121–69–7 | Dimethylaniline | 30,479 |
| 122–39–4 | Diphenylamine | 155,673 |
| 123–42–2 | Diacetone alcohol | 264,660 |
| 126–99–8 | *beta*-Chloroprene | 17,752 |
| 127–19–5 | Dimethyl acetamide | 28,944 |
| 142–82–5 | *n*-Heptane | 449,487 |
| 150–76–5 | *p*-Methoxyphenol | 250,088 |
| 528–29–0 | *o*-Dinitrobenzene | 1,358 |
| 628–63–7 | *n*-Amyl acetate | 265,435 |
| 768–52–5 | *N*-Isopropylaniline | >1,000[2] |
| 25013–15–4 | Vinyl toluene | 25,353 |
| 34590–94–8 | Dipropylene glycol methyl ether | 210,735 |

[1]National Occupational Exposure Survey (NOES) conducted by the NIOSH (1981–1983), unless otherwise indicated. These data are the most recent available to the Agency (Ref. 10).

[2]Not listed in NOES data base. The exposure analysis for this chemical is attached to Reference 10.

*D. Do Sufficient Data Exist For These Chemical Substances?*

As discussed in this preamble, dermal absorption rate is an important factor in ascertaining the effects of the 47 chemicals in this proposed rule on human health. EPA has determined that there are no dermal absorption rate data for the chemicals in this proposed rule and, therefore, existing data are insufficient to reasonably determine or predict the human health effects relating to dermal absorption rate that result from manufacturing, processing, or use of the subject chemical substances. This finding is based on the review and analysis of relevant data by the ITC (which included EPA participation), as described in Unit III.A. of this preamble.

*E. Is Testing Necessary For These Chemical Substances?*

EPA believes that the proposed testing of the 47 subject chemical substances is necessary to develop dermal absorption rate data. This testing is needed to determine if the manufacturing, processing, or use of these chemical substances presents an unreasonable risk of injury to human health.

## V. Proposed Rule

*A. How Would the Studies Proposed Under This Test Rule Be Conducted?*

EPA is proposing specific testing and reporting requirements for the chemical substances specified in Table 2 in § 799.5115(i) of the proposed regulatory text according to the *in vitro* dermal absorption rate test standard set forth at § 799.5115(h) of the proposed regulatory text.

The test standard that would be required under this rule was developed as described in Unit III.B. of this preamble. This standard describes the procedures for measuring a permeability constant (Kp) and a short-term absorption rate for chemicals in liquid form. Measurement of short-term absorption rates is only required when a Kp cannot be obtained using this test standard. For most chemicals, a Kp is useful in estimating skin permeation. However, for ''harsh'' chemicals, i.e., those that may damage the skin more severely with prolonged contact, it is more appropriate to obtain a short-term absorption rate measurement.

This test standard utilizes established *in vitro* diffusion cell techniques that allow absorption rate studies to be conducted using human skin (see the proposed regulatory text at § 799.5115(h)). The *in vitro* approach was chosen for practical considerations because it is efficient in terms of labor and materials and can be performed easily by a variety of laboratories. In addition, *in vitro* diffusion cell studies are necessary for measuring a Kp (Ref. 7).

The *in vitro* dermal absorption rate test standard allows use of cadaver skin and static diffusion cells to maintain the viability of the skin, thus more closely simulating *in vivo* conditions. This test method also requires the use of radiolabelled chemical substances unless the test sponsor can demonstrate that alternative, non-radiolabelled methods provide sensitivity sufficient to detect the parent chemical (and its major metabolites in those cases in which skin viability is maintained). The first six parameters that are discussed (choice of membrane, preparation of membrane, diffusion cell design, temperature, testing hydrophobic chemicals, and vehicle) are similar for determination of either of the two percutaneous absorption rate values. In

contrast, the remaining two parameters (i.e., dose and study duration) are different for the two percutaneous absorption rate values.

Testing under this proposed rule must be conducted in accordance with TSCA Good Laboratory Practice (GLP) Standards (40 CFR part 792).

*B. What Substances Would Be Tested Under This Rule?*

EPA is proposing that the chemical substances listed in Table 2 in § 799.5115(i) of the proposed regulatory text be tested at a purity of at least 99%.

*C. Would I Be Required To Test Under This Rule?*

Under TSCA section 4(a)(1)(B), EPA has made preliminary findings that there are insufficient data and experience to reasonably determine or predict health effects resulting from the manufacturing, processing, or use of the chemical substances listed in this proposed rule. As a result, under TSCA section 4(b)(3)(B), manufacturers and processors of these substances would be subject to the rule with regard to those listed chemicals which they manufacture or process.

1. *Would I be subject to this rule?* You would be subject to this rule and may be required to test if you manufacture (which is defined by statute to include import) or process, or intend to manufacture or process, one or more chemical substances listed in this proposed rule during the time period discussed in Unit V.C.2. of this preamble, entitled ''When would my manufacturing or processing (or my intent to do so) cause me to be subject to this rule?'' However, if you do not know or cannot reasonably ascertain that you manufacture or process a listed test substance (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 would not be subject to the rule.

2. *When would my manufacturing or processing (or my intent to do so) cause me to be subject to this rule?* You would be subject to this rule if you manufacture or process, or intend to manufacture or process, a substance listed in the rule at any time from the effective date of the final test rule to the end of the test data reimbursement period.

The term *reimbursement period* is defined at 40 CFR 791.3(h) and may vary in length for each substance to be tested under a final TSCA section 4(a) test rule, depending on what testing is required and when testing is completed. See Unit V.C.4. of this preamble, entitled ''How do the reimbursement procedures work?''

3. *Would I be required to test if I were subject to the rule?* It depends on the nature of your activities. All persons who would be subject to this TSCA section 4(a) test rule, which incorporates EPA's generic procedures applicable to TSCA section 4(a) test rules (contained within 40 CFR part 790), would fall into one of two groups, designated here as Tier 1 and Tier 2. Persons in Tier 1 (those who would have to initially comply with the rule) must either: Submit to EPA letters of intent to conduct testing, conduct this testing, and submit the test data to EPA or apply to and obtain from EPA exemptions from testing. Persons in Tier 2 (those who would not have to initially comply with the rule) need not take any action unless they are notified by EPA that they are required to do so, as described in Unit V.C.3.d. of this preamble, entitled ''What would my obligations be if I were in Tier 2?'' Note that persons in Tier 1 who obtain exemptions and persons in Tier 2 would nonetheless be subject to providing reimbursement to persons who do actually conduct the testing, as described in Unit V.C.4. of this preamble, entitled ''How do the reimbursement procedures work?''

a. *Who would be in Tier 1 and Tier 2?* All persons subject to this rule would be considered to be in Tier 1 unless they fall within Tier 2. The following table describes who is in Tier 1 and Tier 2.

TABLE 4.— PERSONS SUBJECT TO THE RULE: PERSONS IN TIER 1 AND TIER 2

| Tier 1 (Persons initially required to comply) | Tier 2 (Persons not initially required to comply) |
|---|---|
| •Persons that manufacture (as defined at TSCA section 3(7)), or intend to manufacture, a test rule substance who are not listed under Tier 2 | •Persons that manufacture (as defined at TSCA section 3(7)) or intend to manufacture a test rule substance solely as one or more of the following:<br>—As a byproduct (as defined at 40 CFR 791.3(c));<br>—As an impurity (as defined at 40 CFR 790.3);<br>—As a naturally occurring substance (as defined at 40 CFR 710.4(b));<br>—As a non-isolated intermediate (as defined at 40 CFR 704.3);<br>—As a component of a Class 2 substance (as described at 40 CFR 720.45(a)(1)(i));<br>—In amounts of less than 500 kilograms (kg) (1,100 lbs) annually (as described at 40 CFR 790.42(a)(4)); or<br>—In small quantities solely for research and development (as described at 40 CFR 790.42(a)(5)).<br>•Persons that process (as defined at TSCA section 3(10)) or intend to process a test rule substance (see 40 CFR 790.42(a)(2)) |

b. *When would it be appropriate for a person in Tier 1 to apply for an exemption rather than to submit a letter of intent to conduct testing?* You may apply for an exemption if you believe that the required testing will be performed by another person (or a consortium of persons formed under TSCA section 4(b)(3)(A)) in Tier 1. You can find procedures relating to exemptions in 40 CFR 790.80 through 790.99, and in the proposed regulatory text at § 799.5115(c)(2), (c)(5), and (c)(7). In this rule, EPA would not require equivalence data (i.e., data demonstrating that your substance is equivalent to the substance actually being tested) as a condition for approval of your exemption. EPA is interested in evaluating the effects attributable to each listed substance itself and has specified almost pure substances for testing.

c. *What would happen if I were in Tier 1 and I submitted an exemption application?* EPA believes that requiring the collection of duplicative data is unnecessarily burdensome. As a result, if EPA has received a letter of intent to test from another source or has received (or expects to receive) the test data that would be required under this rule, the Agency would conditionally approve your exemption application under 40 CFR 790.87. The Agency would

terminate conditional exemptions, if a problem occurs with the initiation, conduct, or completion of the required testing or the submission of the required data to EPA. EPA may then require you to submit a notice of intent to test or an exemption application. See 40 CFR 790.93 and the proposed regulatory text at § 799.5115(c)(6). Persons in Tier 1 who obtain exemptions and persons in Tier 2 would nonetheless be subject to providing reimbursement to persons who do actually conduct the testing, as described in Unit V.C.4. of this preamble, entitled ''How do the reimbursement procedures work?.''

d. *What would my obligations be if I were in Tier 2?* If you are in Tier 2, you would be subject to the rule and you would be responsible for providing reimbursement to persons in Tier 1, as described in Unit V.C.4. of this preamble. You are considered to have an automatic conditional exemption. You would not need to take any action unless you are notified by EPA that you are required to do so.

If a problem occurs with the initiation, conduct, or completion of the required testing, or the submission of the required data to EPA, the Agency may require you to submit a notice of intent to test or an exemption application. See 40 CFR 790.93 and the proposed regulatory text at § 799.5115(c)(6).

In addition, you would need to submit a notice of intent to test or an exemption application if:

i. No manufacturer in Tier 1 has notified EPA of its intent to conduct testing and

ii. EPA has published a **Federal Register** document directing all persons in Tier 2 to submit to EPA letters of intent to conduct testing or exemption applications. See 40 CFR 790.48(b) and the proposed regulatory text at § 799.5115(c)(4) and (c)(5).

The Agency would conditionally approve an exemption application under 40 CFR 790.87, if EPA has received a letter of intent to test or has received (or expects to receive) the test data required under this rule.

e. *How did EPA decide who would be in Tier 1 and Tier 2 and who would be excluded from the rule?* Under 40 CFR 790.2, EPA may establish procedures applying to specific test rules that differ from the generic procedures governing TSCA section 4(a) test rules in 40 CFR part 790. For purposes of this proposed rule, EPA is proposing to set forth certain requirements that differ from those under 40 CFR part 790.

Under 40 CFR part 790, in TSCA section 4(a) test rules EPA traditionally has treated the following persons as being in Tier 2. (These rules are found at 40 CFR part 799, subparts B and D).

- Processors (40 CFR 790.42(a)(2));
- Manufacturers of less than 500 kg (1,100 lbs) per year (''small-volume manufacturers'') (40 CFR 790.42(a)(4)); and
- Manufacturers of small quantities for research and development (''R&D manufacturers'') (40 CFR 790.42(a)(5)).

EPA has historically placed processors in Tier 2 because the Agency ''expected that, in most cases, testing will be performed by the manufacturers and that part of the cost of testing will be passed on to processors through the pricing mechanism, thereby enabling them to share in the costs of testing'' (50 FR 20652, 20654, May 17, 1985). In addition, ''[t]here are so many processors that it would be difficult to include them all in the technical decisions about the tests and in the financial decisions about how to allocate the costs'' (48 FR 31786, 31789, July 11, 1983).

EPA has historically placed small-volume manufacturers and R&D manufacturers in Tier 2 because this type of manufacturing ''normally represents a small percentage of the overall production volume [and] test sponsors are not expected to expend the administrative resources to recover the small proportional amounts of the testing costs from these manufacturers'' (55 FR 18881, May 7, 1990).

In this proposed test rule, EPA has reconfigured the tiers in 40 CFR 790.42. EPA has added the following persons to Tier 2: Byproduct manufacturers; impurity manufacturers; manufacturers of naturally occurring substances; manufacturers of non-isolated intermediates; and manufacturers of components of Class 2 substances. The Agency took administrative burden and complexity into account in determining who was to be in Tier 1 in this proposed rule. EPA believes that those persons in Tier 1 who would conduct testing under this rule, when finalized, would generally be large chemical manufacturers who, in the experience of the Agency, have traditionally conducted testing or participated in testing consortia under previous TSCA section 4(a) test rules.

The Agency also believes that byproduct manufacturers, impurity manufacturers, manufacturers of naturally occurring substances, manufacturers of non-isolated intermediates, and manufacturers of components of Class 2 substances have not themselves historically participated in testing or contributed to reimbursement of those persons who have conducted testing. EPA understands that these may include persons for whom the marginal transaction costs involved in negotiating and administering testing arrangements are deemed likely to raise the expense and burden of testing to a level that is disproportional to the additional benefits of including these persons in Tier 1. Therefore, EPA does not believe that the likelihood of the persons proposed to be added to Tier 2 actually doing the testing is sufficiently high to justify burdening these persons with Tier 1 requirements (e.g., submitting requests for exemptions). Nevertheless, these persons, along with all other persons in Tier 2, would be subject to providing reimbursement to persons who do actually conduct the testing, as described in Unit V.C.4. of this preamble, entitled ''How do the reimbursement procedures work?''

Section 4(b)(3)(B) of TSCA requires all manufacturers and processors of a chemical substance to test that chemical substance if EPA has made findings for that chemical substance, and therefore issued a TSCA section 4(a) test rule requiring testing. However, practicality must be a factor in determining who is subject to a particular test rule. Thus, persons who do not know or cannot reasonably ascertain that they are manufacturing or processing the substances subject to this proposed rule, e.g., manufacturers or processors of the substances as trace contaminants who are not aware of these activities, would not be subject to the rule. See Unit V.C.1 of this preamble and § 799.5115(b)(2) of the proposed regulatory text.

EPA is soliciting comment on who should be included in Tier 1 and Tier 2. The Agency may define these categories differently in response to comments received. EPA is also soliciting comment on who should not be subject to the rule. The latter persons are described at Unit V.C.1 of this preamble and § 799.5115(b)(2) of the proposed regulatory text.

f. *Should EPA prioritize which persons in Tier 2 would be required to perform testing?* EPA is considering subdividing Tier 2 to enable the Agency to prioritize which persons in Tier 2 would be required to perform testing, if needed. This would involve subdividing Tier 2 into:

i. *Tier 2A*. Those who manufacture, or intend to manufacture, a test rule substance solely as one or more of the following: A byproduct; an impurity; a naturally occurring substance; a non-isolated intermediate; a component of a Class 2 substance; in amounts less than 1,100 lbs. annually; or in small quantities solely for research and development.

ii. *Tier 2B.* Those who process, or intend to process, a test rule substance. If the Agency needed testing from persons in Tier 2, EPA would seek testing from persons in Tier 2A before proceeding to Tier 2B. EPA believes that, if the Agency were to subdivide Tier 2, persons in Tier 2A should be required to submit letters of intent to test or exemption applications before processors are called upon because testing costs are traditionally passed by manufacturers along to processors.

EPA is soliciting comment on whether this subtiering scheme should be applied in the final rule.

4. *How do the reimbursement procedures work?* In the past, persons subject to test rules have independently worked out among themselves their respective financial contributions to those persons who have actually conducted the testing. However, if persons are unable to agree privately on reimbursement, they may take advantage of EPA's reimbursement procedures at 40 CFR part 791, promulgated under the authority of TSCA section 4(c). These procedures include: The opportunity for a hearing with the American Arbitration Association; publication by EPA of a **Federal Register** document concerning the request for a hearing; and the appointment of a hearing officer to propose an order for fair and equitable reimbursement. The hearing officer may base his or her proposed order on the production volume formula set out at 40 CFR 791.48, but is not obligated to do so. Under this proposed rule, amounts manufactured as impurities would be included in production volume (40 CFR 791.48(b)), subject to the discretion of the hearing officer (40 CFR 791.40(a)). The hearing officer's proposed order may become the Agency's final order, which is reviewable in Federal court (40 CFR 791.60).

### *D. What Are the Reporting Requirements Proposed Under This Test Rule?*

You would be required to submit interim progress reports for each test every 6 months, beginning 6 months after the effective date of the final rule. You would be required to submit a final report for a specific test by the deadline indicated as the number of months after the effective date that would be shown in Table 2 in § 799.5115(i) of the proposed regulatory text.

### *E. Would There Be Sufficient Test Facilities and Personnel To Undertake the Testing in This Test Rule?*

EPA has conducted a study to assess the availability of test facilities and personnel to handle the additional demand for testing services created by TSCA section 4(a) test rules and has found that test facilities and personnel would adequately accommodate the testing specified in this proposed rule (Ref. 11).

### *F. Might EPA Seek Further Testing of the Chemicals in This Proposed Test Rule?*

If EPA determines that it needs additional data regarding any of the chemical substances included in this proposed rule, the Agency might seek further health and/or environmental effects testing for these chemicals. Should the Agency decide to seek such additional testing, EPA would initiate a separate action for this purpose.

## VI. Export Notification

Any person who exports, or intends to export, one of the chemical substances contained in this proposed rule in any form will be subject to the export notification requirements in TSCA section 12(b)(1) and 40 CFR part 707, subpart D, but only after the final rule is issued and only if the chemical is contained in the final rule. However, notification of export would generally not be required for articles, as provided by 40 CFR 707.60(b).

## VII. Materials in the Official Record

The official record for this proposed rule has been established under docket control number OPPTS–42196. The following is a listing of the documents that have already been placed in the official record for this proposed rule:

### *A. Supporting Documentation*

1. **Federal Register** documents:

a. Notice containing the 31st ITC Report to the EPA Administrator (58 FR 26898, May 5, 1993 (FRL–4583–4)).

b. Notice containing the TSCA section 4(a)(1)(B) Final Statement of Policy (58 FR 28736, May 14, 1993 (FRL–4059–9)).

c. Notice containing the 32nd ITC Report to the EPA Administrator (58 FR 38490, July 16, 1993 (FRL–4630–2)).

d. TSCA Sections 8(a) and 8(d) Final Rules for Chemicals Contained in the 31st ITC Report to the EPA Administrator (58 FR 68311, December 27, 1993 (FRL–4644–1)).

e. TSCA Sections 8(a) and 8(d) Final Rules for Chemicals Contained in the 32nd ITC Report to the EPA Administrator (59 FR 5956, February 9, 1994 (FRL–4745–5)).

f. Notice containing the 34th ITC Report to the EPA Administrator (59 FR 35720, July 13, 1994 (FRL–4870–4)).

g. Notice containing the 35th ITC Report to the EPA Administrator (59 FR 67596, December 29, 1994 (FRL–4923–2)).

h. TSCA Sections 8(a) and 8(d) Final Rules for Chemicals Contained in the 35th ITC Report to the EPA Administrator (60 FR 34879, July 5, 1995 (FRL–4954–9)).

i. Notice containing the 36th ITC Report to the EPA Administrator (60 FR 42982, August 17, 1995 (FRL–4965–6)).

j. Small Business Size Standards; Final Rule, issued by the Small Business Administration (SBA) (61 FR 3280, January 31, 1996).

k. Notice containing EPA's Solicitation of Interested Parties for Proposals for Enforceable Consent Agreements for Testing of 80 Chemicals of Interest to OSHA (61 FR 14773, April 3, 1996 (FRL–5359–3)).

2. Correspondence:

a. ARCO Chemical Company. Letter to Charles M. Auer, USEPA. Proposal for Development of ECA for *Tert*-Butyl Alcohol (June 26, 1996).

b. ARCO Chemical Company. Letter to Keith Cronin, USEPA. Letter transmitting a Dermal Absorption Rate Study in the Male Rat for *Tert*-Butyl Alcohol (March 23, 1998).

3. Other support documentation:

EPA. ''EPA Interim Guidance for Implementing the Small Business Regulatory Enforcement Fairness Act and Related Provisions of the Regulatory Flexibility Act.'' EPA SBREFA Task Force (February 5, 1997).

### *B. References*

1. ITC. Chemicals Under Consideration for the 32nd ITC Report; Summary of Skin Absorption Data on OSHA Tier 2 Chemicals (September 22, 1993).

2. Zeneca. Methyl Methacrylate: *In Vitro* Absorption through Human Epidermis. Zeneca Central Toxicology Report No. CTL/P/4025 provided by the Methacrylate Producers Association, Washington, D.C. (1993).

3. Scott, R.C., Dugard, P.H., Ramsey, J.D., and Rhodes, C. *In Vitro* Absorption of Some *o*-Phthalate Diesters through Human and Rat Skin. *Environmental Health Perspectives*. 74:223–227 (1987).

4. Mraz, J., Galova, E., Nohova, H., and Vitkova, D. Uptake, Metabolism and Elimination of Cyclohexanone in Humans. *International Archives of Occupational Environmental Health*. 66:203–208 (1994).

5. ARCO Chemical Company. [$^{14}$C]-*t*-Butyl Alcohol: Topical Application: Dermal Absorption Study in the Male Rat. *Huntington Life Sciences* (January 7, 1998).

6. OSHA. Review of [$^{14}$C]-*t*-Butyl Alcohol: Topical Application: Dermal Absorption Study in the Male Rat. (June 24, 1998).

7. 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).

8. Chemical Manufacturers Association (CMA). Letter to Charles M. Auer, USEPA. (October 21, 1994).

9. EPA. Economic Impact Analysis and Small Entity Impact Analysis of Proposed TSCA Section 4(a) Test Rule for 47 Chemicals Targeted for *In Vitro* Dermal Absorption Rate Testing. OPPT/EETD/EPAB, Washington, DC (May 5, 1999).

10. EPA. CEB Support to the OSHA Chemicals Test Rule—Number of Workers Exposed and TRI Release Data. OPPT/EETD/CEB, Washington, DC (March 1998).

11. EPA. EPA Census of TSCA Testing Laboratories. Washington, DC (October 10, 1996).

12. EPA. Laboratory Cost Estimate for *In Vitro* Dermal Absorption Rate Testing. OPPT/EETD/EPAB, Washington, DC (April 14, 1999).

13. EPA. ''Treatment of 12(b) Export Notification Unit Costs for Section 4 Test Rule Analyses.'' OPPT/EETD/EPAB, Washington, DC (April 1, 1999).

14. EPA. ''Economic Analysis in Support of the TSCA 12(b) Information Collection Request.'' OPPT/EETD/EPAB, Washington, DC (October 30, 1998).

## VIII. Regulatory Assessment Requirements

### *A. Executive Order 12866*

Under Executive Order 12866, entitled *Regulatory Planning and Review* (58 FR 51735, October 4, 1993), this is not a ''significant regulatory action'' subject to review by the Office of Management and Budget (OMB), because this action is not likely to result in a rule that meets any of the criteria for a ''significant regulatory action'' provided in section 3(f) of the Executive Order.

EPA has prepared an economic analysis of the potential impact of this proposed rule, which is contained in a document entitled ''Economic Impact Analysis and Small Entity Impact Analysis of Proposed TSCA Section 4(a) Test Rule for 47 Chemicals Targeted for *In Vitro* Dermal Absorption Rate Testing'' (Ref. 9). This document is available as a part of the public version of the official record for this action (instructions for accessing this document are contained in Unit I.B. of this preamble), and is briefly summarized here. The costs developed in the economic impact analysis are based on laboratory test cost estimates that have been placed in the docket for this proposed rule (Ref. 12).

While legally subject to this test rule, processors of a subject chemical would only be required to comply with the requirements of the rule if they are directed to do so by EPA as described in § 799.5115(c)(5) and (c)(6) of the proposed regulatory text. EPA would only require processors to test if no person in Tier 1 has submitted a notice of its intent to conduct testing, or if, under 40 CFR 790.93, a problem occurs with the initiation, conduct, or completion of the required testing, or the submission of the required data to EPA. Because EPA has identified at least one manufacturer in Tier 1 for each subject chemical, the Agency assumes that, for each chemical in this proposed rule, at least one such person will submit a letter of intent to conduct the required testing and that that person will conduct such testing and will submit the test data to EPA. Because processors would not need to comply with the rule initially, the economic analysis does not address processors.

To evaluate the potential economic impact of testing on manufacturers of the chemical substances in this proposed rule, EPA estimated the impact of testing requirements as a percentage of each chemical's sale price. This measure compares the annualized testing costs per pound (based on the conservative assumption that all chemicals are produced in volumes of one million lbs), to the price per pound for each chemical. First, annualized testing costs (including laboratory and administrative expenditures) are calculated by converting the total testing costs in the first year into an equivalent series of expenditures over 15 years using a 7% discount rate. Second, annualized testing costs are divided by one million lbs (the assumed production volume per chemical) to derive the annualized unit (per pound) testing cost. The price impacts—testing costs as a percentage of each chemical's price—are calculated by dividing the annualized unit testing cost by each unit price and multiplying by 100. The Agency's estimated total costs of testing (including both laboratory and administrative costs), annualized testing cost, price impacts, and public reporting burden hours for the chemicals are presented in the economic analysis (Ref. 9).

Based on the economic analysis, the total one-time cost of this action, if finalized as proposed, is estimated to be $1.55 million. When this cost is annualized over 15 years using a 7% discount rate, the total annualized cost is estimated to be $170,576, with an estimated annualized cost of $3,628 per chemical. In addition, the estimated cost of the TSCA section 12(b)(1) export notification, which, in the final rule, would be required for the first export to a particular country of a chemical subject to the rule, is estimated to be $83.38 for the first time that an exporter must comply with TSCA section 12(b)(1) export notification requirements, and $19.08 for each subsequent export notification submitted by that exporter (Ref. 9, 13, and 14).

The economic impacts of the testing, expressed as a percentage of each chemical's sale price, range from 0.09% to 3.3%, with an average impact of 0.64%. EPA estimates that 5 of the 35 chemicals for which price data are available will experience an adverse impact of 1% or greater under the assumption that production volumes for these chemicals are one million lbs. In fact, these chemicals are all manufactured or imported in excess of 10 million lbs, reducing the estimated impact by a factor of 10 to less than 1%. For the remaining 12 chemicals without price data, EPA estimates that with annualized testing costs of $3,628 per chemical and one million lbs production volumes each, an economic impact of 1% or greater would occur only at a sales price below $0.36 per lb. Given that the average price for the other 35 chemicals is $0.97 per lb (prices range from $0.11 to $3.96 per lb), that the unavailability of price data for these 12 chemicals may indicate that they are higher priced specialty chemicals, and that their production volumes are likely to be higher than the one million lbs minimum, the likelihood of an adverse impact is low.

### *B. Executive Order 12898*

This proposed rule does not involve special considerations of environmental-justice related issues pursuant to Executive Order 12898, entitled *Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations* (59 FR 7629, February 16, 1994).

### *C. Executive Order 13045*

Executive Order 13045, entitled *Protection of Children from Environmental Health Risks and Safety Risks* (62 FR 19885, April 23, 1997), does not apply to this proposed rule, because it is not ''economically significant'' as defined under Executive Order 12866; and does not concern an

environmental health or safety risk that may have a disproportionate effect on children. This proposed rule would require the development of quantitative measures of dermal absorption rate to assist in evaluating the potential contribution of the chemical substances proposed for testing to total exposures to adult workers. The public is invited, however, to submit or identify peer-reviewed studies and data, of which EPA may not be aware, that assess results of early life exposure to the 47 chemicals proposed for testing in this document.

*D. Regulatory Flexibility Act*

Pursuant to section 605(b) of the Regulatory Flexibility Act (RFA), 5 U.S.C. 601 *et seq*., the Agency hereby certifies that this rule, if promulgated as proposed, will not have a significant economic impact on a substantial number of small entities. The factual basis for the Agency's determination is presented in the small entity impact analysis prepared as part of the economic analysis for this proposed rule (Ref. 9), and is briefly summarized here. The costs developed in the small entity impact analysis are based on the laboratory test cost estimates that have been placed in the docket for this proposed rule (Ref. 12).

For the purpose of analyzing potential impacts on small entities, EPA used the RFA definition of small entities in RFA section 601(6). Under this section, a small entity may be a small government, a small non-profit organization, or a small business. Because EPA does not believe that governments or non-profit organizations are likely to be burdened by testing requirements under this proposed rule, EPA's analysis presents only the estimated potential impacts on small businesses.

Section 601(3) of the RFA establishes as the default definition of small business the definition used in section 3 of the Small Business Act (15 U.S.C. 632) under which the SBA establishes small business size standards (13 CFR 121.201). For this proposed rule, EPA has analyzed the potential small business impacts using the size standards established under the RFA section 601(3) definition.

In addition, in analyzing potential impacts, the RFA recognizes that it may be appropriate at times for Federal agencies to use an alternate definition of small business. As such, RFA section 601(3) also provides that an agency may establish a different definition of small business after consultation with the SBA Office of Advocacy and after notice and an opportunity for public comment. Even though the Agency has used the default SBA definition of small business to conduct its analysis of potential small entity impacts for this proposed rule, EPA does not believe that the SBA size standards are generally the best size standards to use in assessing potential small entity impacts with regard to TSCA section 4(a) test rules.

The SBA size standards, which are primarily intended to define whether a business entity is eligible for Federal government programs and preferences reserved for small businesses (13 CFR 121.101), ''seek to ensure that a concern that meets a specific size standard is not dominant in its field of operation'' (13 CFR 121.102(b)). See section 632(a)(1) of the Small Business Act. The SBA size standard is generally based on the number of employees an entity in a particular industrial sector may have. For example, in the chemical manufacturing industrial sector (i.e., SIC 28 and SIC 29), approximately 98% of the industries would be classified as small businesses under the default SBA definition. The SBA size standard for 75% of this industry sector is 500 employees, and the size standards for 23% of this industry sector are 750, 1,000, or 1,500 employees. As a result, when assessing the potential impacts of test rules on chemical manufacturers, EPA believes that a standard based on total annual sales may provide a more appropriate means to judge the ability of a chemical manufacturing firm to support chemical testing without significant costs or burdens.

EPA is currently determining what level of annual sales would provide the most appropriate size cutoff with regard to various segments of the chemical industry usually impacted by TSCA section 4(a) test rules, but has not yet reached a determination. As stated in this unit, therefore, the factual basis for the RFA determination for this proposed rule is based on an analysis using the default SBA size standards. Although EPA is not proposing to establish an alternate small business definition in the small entity impact analysis conducted for this proposed rule, the analysis includes the results of calculations using a size standard based on total annual sales. EPA is interested in receiving comments on whether the Agency should consider establishing an alternate small business definition to use in the small entity impact analyses for future TSCA section 4(a) test rules, and what size cutoff may be appropriate.

Based on the Agency's estimated total costs for this proposed rule, which are summarized in Unit VIII.A. of this preamble, EPA estimates that the annualized cost for the testing in this proposed rule will be $3,628 per chemical. As discussed previously, EPA was unable to obtain any price information on 12 of the 47 chemicals in this proposed test rule. Nevertheless, EPA provides an estimate of the price of these chemicals in the economic analysis, and concludes that the total cost of testing these 47 chemicals as proposed, will not result in a significant impact on the chemical manufacturers subject to the proposed rule, regardless of their size. EPA identified a total of 102 ultimate corporate entities (UCEs) that would be potentially impacted by the proposed test rule. None of these manufacturers would experience a significant impact as a result of the rule.

In addition, the estimated cost of the TSCA section 12(b)(1) export notification, which, as a result of the final rule, would be required for the first export to a particular country of a chemical subject to the rule, is estimated to be $83.38 for the first time that an exporter must comply with TSCA section 12(b)(1) export notification requirements, and $19.08 for each subsequent export notification submitted by that exporter (Ref. 9, 13, and 14). EPA has concluded that the costs of TSCA section 12(b)(1) export notification would have a negligible impact on exporters of the chemicals in the final rule, regardless of the size of the exporter.

The Agency has also examined the standard practices that industry uses in carrying out chemical testing in response to test rules, such as this one. Based on that examination, EPA believes that:

1. Small businesses do not perform the testing themselves, nor do they participate in the organization of the testing effort, because health effects testing of chemical substances is generally carried out by consortia of the large manufacturers or importers of the chemical substances;

2. A small business would experience only very minor costs, if any, in securing an exemption from testing requirements, because exemption request requirements, described generally at 40 CFR 790.80 through 790.99 and the proposed regulatory text at § 799.5115(c)(2), (c)(5), and (c)(7), are minimal and EPA does not charge a fee for filing such a request; and

3. Small businesses are unlikely to be affected by the reimbursement requirements because under the reimbursement provisions described in 40 CFR part 791, manufacturers and importers with a significant share of production or importation are the entities that will likely pay the highest share of testing costs, and the marginal

benefit of securing reimbursement from small contributors may not be worth the cost.

Information relating to this determination has been included in the public version of the official record for the proposed rule. This information will also be provided to the SBA Chief Counsel for Advocacy upon request. Any comments regarding the impacts that this action may impose on small entities, or regarding whether the Agency should consider establishing an alternate definition of small business to be used for analytical purposes for future test rules and what size cutoff may be appropriate, should be submitted to the Agency in the manner specified in Unit I.C. of this preamble.

*E. Paperwork Reduction Act*

Pursuant to the Paperwork Reduction Act (PRA) (44 U.S.C. 3501 *et seq.*), an Agency may not conduct or sponsor, and a person is not required to respond to, a collection of information that is subject to approval under the PRA, unless it displays a currently valid OMB control number. The OMB control numbers for EPA's regulations, after appearing in the preamble of the final rule, are listed in 40 CFR part 9, and included on the related collection instrument. The information collection activities related to chemical testing under TSCA section 4(a) have already been approved under OMB control number 2070–0033 (EPA ICR# 1139), and the information collection activities related to export notification under TSCA section 12(b)(1) are already approved under OMB control number 2070–0030 (EPA ICR# 0795). Since this proposed rule does not contain any new information collection activities, additional review and approval of these activities by OMB under the PRA is not necessary.

Although the information collection activities contained in this proposed rule have already been approved by OMB, the total burden hours currently approved for the information collection activities related to chemical testing in general include an average burden estimate to cover future test rules. As described in the information collection instrument for chemical testing, the Agency's total burden estimate specifically accounts for the potential issuance of approximately 7 final test rules during the approval period, with an estimated burden of less than 20,000 burden hours each. EPA believes that the existing approval includes a sufficient burden hour allocation to cover the estimated burden related to this proposed rule, if finalized as proposed. When the final rule is issued, EPA will verify that the approved burden hours will cover the estimated burden for the final rule, or request that the total approved burden hour allocation be increased accordingly.

The standard chemical testing program involves the submission of letters of intent to test (or exemption applications), study plans, semi-annual progress reports, and test results. For this proposed rule, EPA estimates that the information collection activities related to chemical testing would result in 105.4 burden hours for each chemical, for a total estimated burden increase of 4,954 hours (Ref. 9). The estimated burden of the information collection activities related to export notification is 0.5–1.5 burden hours for each chemical/country combination (Ref. 9). In estimating the total burden hours approved for the information collection activities related to export notification, the Agency has included sufficient burden hours to accommodate any export notifications that may be required by the Agency's issuance of final chemical test rules (Ref. 9, 13, and 14). As such, EPA does not expect to need to request an increase in the total burden hours approved by OMB for export notifications.

As defined by the PRA and 5 CFR 1320.3(b), *burden* means the total time, effort, or financial resources expended by persons to generate, maintain, retain, or disclose or provide information to or for a Federal agency. This includes the time needed to review instructions; develop, acquire, install, and utilize technology and systems for the purposes of collecting, validating, and verifying information, processing and maintaining information, and disclosing and providing information; adjust the existing ways to comply with any previously applicable instructions and requirements; train personnel to be able to respond to a collection of information; search data sources; complete and review the collection of information; and transmit or otherwise disclose the information.

Comments are requested on the Agency's need for this information, the accuracy of the provided burden estimates, and any suggested methods for minimizing respondent burden, including through the use of automated collection techniques. Send comments to EPA as part of your overall comments on this proposed action in the manner specified in Unit I.C. of this preamble. In the final rule, the Agency will address any comments received regarding the information collection requirements contained in this proposal.

*F. Unfunded Mandates Reform Act*

Pursuant to Title II of the Unfunded Mandates Reform Act of 1995 (UMRA), Pub. L. 104–4, EPA has determined that this proposed rule does not contain a Federal mandate that may result in expenditures of $100 million or more for State, local, and tribal governments, in the aggregate, or the private sector in any 1 year. It is estimated that the total one-time cost of the rule, which is summarized in Unit VIII.A. of this preamble, is $1.55 million, with the total annualized cost estimated to be $170,576, and the estimated annual cost per chemical to be $3,628. In addition, EPA has determined that this proposed rule does not significantly or uniquely affect small governments. Accordingly, today's proposed rule is not subject to the requirements of UMRA sections 202, 203, 204, or 205.

*G. Executive Order 12875*

Under Executive Order 12875, entitled *Enhancing the Intergovernmental Partnership* (58 FR 58093, October 28, 1993), EPA may not issue a regulation that is not required by statute and that creates a mandate upon a State, local, or tribal government, unless the Federal government provides the funds necessary to pay the direct compliance costs incurred by those governments, or EPA consults with those governments. If EPA complies by consulting, Executive Order 12875 requires EPA to provide to OMB a description of the extent of EPA's prior consultation with representatives of affected State, local, and tribal governments, the nature of their concerns, any written communications from the governments, and a statement supporting the need to issue the regulation. In addition, Executive Order 12875 requires EPA to develop an effective process permitting elected officials and other representatives of State, local, and tribal governments ''to provide meaningful and timely input in the development of regulatory proposals containing significant unfunded mandates.''

EPA does not believe the today's proposed rule under TSCA section 4(a) creates a Federal mandate on State, local, or tribal governments, and thus, EPA does not believe that the requirements of section 1(a) of Executive Order 12875 apply to this rule. The Agency does not know of any State, local, or tribal governments that would be subject to the requirements of the rule if it were promulgated as proposed. In the history of the TSCA section 4(a) testing program, the Agency has never received a letter of intent to

test or an exemption application from a State, local, or tribal government. EPA is requesting comment on whether any State, local, or tribal government would be subject to the requirements of the proposed rule. If, on the basis of these comments, EPA determines that the rule would create a Federal mandate, the Agency will consult with representatives of affected State, local, or tribal governments in accordance with the Executive Order prior to promulgating the final rule.

*H. Executive Order 13084*

Under Executive Order 13084, entitled *Consultation and Coordination with Indian Tribal Governments* (63 FR 27655, May 19, 1998), EPA has determined that this proposed rule does not significantly or uniquely affect the communities of Indian tribal governments. This determination is based on the Agency's belief that, as a practical matter, the burden of chemical testing under TSCA section 4(a) rules has traditionally fallen on large, private sector manufacturers rather than on tribal governments. Accordingly, the requirements of section 3(b) of Executive Order 13084 do not apply to this proposed rule.

*I. National Technology Transfer and Advancement Act*

Section 12(d) of the National Technology Transfer and Advancement Act of 1995 (NTTAA) (15 U.S.C. 272 note), directs EPA to use voluntary consensus standards in its regulatory activities unless to do so would be inconsistent with applicable law or otherwise impractical. Voluntary consensus standards are technical standards (e.g., materials specifications, test methods, sampling procedures, and business practices) that are developed or adopted by voluntary consensus standards bodies. The NTTAA directs EPA to provide Congress, through OMB, explanations when the Agency decides not to use available and applicable voluntary consensus standards.

If the Agency has made findings under TSCA section 4(a), EPA is required by TSCA section 4(b) to include specific standards for the development of data in test rules. The testing that would be required under this rule would be conducted according to the enforceable *in vitro* dermal absorption rate test standard proposed in this document. This test standard was developed by EPA in conjunction with ITC member and liaison agencies (CPSC, DoD, FDA, NIOSH, and OSHA). It was based on the methods of Bronaugh and Collier (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)) (Ref. 7) , and modified in response to public comments. The group of scientists that developed this test standard did so based on their experience with the methodologies available for conducting this type of testing. As a result of their collective expertise in these methodologies, they considered the method developed for this testing program to be an effective and efficient method for testing a large number of chemicals to determine an *in vitro* dermal absorption rate using human cadaver skin.

EPA is not aware of any potentially applicable voluntary consensus standards which needed to be considered in lieu of the *in vitro* dermal absorption rate test standard included in this proposed rule. The Agency invites comment on the potential use of voluntary consensus standards in this proposed rule, and, specifically, invites the public to identify potentially applicable voluntary consensus standard(s) and to explain why such standard(s) should be used here.

**List of Subjects in 40 CFR Part 799**

Environmental protection, Chemicals, Hazardous substances, Reporting and recordkeeping requirements, Laboratories.

Dated: June 1, 1999.

**Susan H. Wayland,**

*Acting Assistant Administrator for Prevention, Pesticides and Toxic Substances.*

Therefore, it is proposed that 40 CFR chapter I, subchapter R, be amended as follows:

## PART 799—[AMENDED]

1. The authority citation for part 799 would continue to read as follows:

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

2. By adding § 799.5115 to subpart D to read as follows:

### § 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 (i) of this section identifies the chemical substances that must be tested under this section. The purity of each test substance must be 99% or greater unless otherwise specified in this section.

(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 of paragraph (i) of this section at any time from the effective date specified in Table 2 of paragraph (i) of this section 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 of paragraph (i) 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)(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. | •Persons that 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:<br>—As a byproduct (as defined at 40 CFR 791.3(c));<br>—As an impurity (as defined at 40 CFR 790.3);<br>—As a naturally occurring substance (as defined at 40 CFR 710.4(b));<br>—As a non-isolated intermediate (as defined at 40 CFR 704.3);<br>—As a component of a Class 2 substance (as described at 40 CFR 720.45(a)(1)(i));<br>—In amounts of less than 500 kilograms (kg) (1,100 lbs) annually (as described at 40 CFR 790.42(a)(4)); or<br>—For research and development (as described at 40 CFR 790.42(a)(5)).<br>•Persons that 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 of 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) and (c)(5) of this section.

(2) If you are in Tier 1 with respect to a chemical substance listed in Table 2 of paragraph (i) of this section, you will be required to comply with this section with regard to that chemical substance, as described in paragraph (d) of this section, no later than 30 days after the effective date specified in Table 2 of paragraph (i) of this section for that chemical substance. Sections 790.45(a) and 790.80(b)(1) of this chapter do not apply to this section.

(3) If you are in Tier 2 with respect to a chemical substance listed in Table 2 of paragraph (i) 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) or (c)(6) 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 of paragraph (i) of this section within 30 days after the effective date in Table 2 of paragraph (i) of this section, EPA will publish a **Federal Register** document that will specify the test and the chemical substance for which no letter of intent has been submitted. Section 790.48(b)(2) of this chapter does not apply to this section.

(5) If you are in Tier 2 with respect to a chemical substance listed in Table 2 of paragraph (i) of this section, and if you manufacture or process this chemical as of the effective date specified in Table 2 of paragraph (i) of this section, or within 30 days after publication of the **Federal Register** document described in paragraph (c)(4) of this section, you must do the following: For each test on that chemical specified in the **Federal Register** document described in paragraph (c)(4) of this section, either notify EPA by letter of your intent to test or submit to EPA an exemption application. You must comply within 30 days after the date of publication of the **Federal Register** document described in paragraph (c)(4) of this section. Sections 790.48(b)(3), and 790.80(a)(2) and (b)(1) of this chapter do not apply to this section.

(6) 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 of paragraph (i) of this section, under the procedures in 40 CFR 790.93 and 790.97, EPA will terminate all testing exemptions with respect to that 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. A notification will be given by certified letter or by publication of a **Federal Register** document.

(7) If you are required to comply with this section, but your manufacturing or processing of a chemical substance listed in Table 2 of paragraph (i) 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 comply by submitting a letter of intent to test or an exemption application as of the day you begin manufacturing or processing. Sections 790.45(d)(1) and (d)(2), and 790.80(b)(2) and (b)(3) of this chapter do not apply to this section.

(d) *What must I do to comply with this section?* (1) To comply with this section you must either:

(i) Submit to EPA a letter of intent to test, conduct the testing specified in Table 2 of paragraph (i) of this section, and submit the test data to EPA; or

(ii) Apply to and obtain from EPA an exemption from testing.

(2) You must also comply with the procedures governing test rule requirements in part 790 of this chapter, including the submission of letters of intent to test or exemption applications, the conduct of testing, and the submission of data; part 792 of this chapter; and this section.

(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. Sections 790.45(e) and (f) of this chapter do not apply to 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 of paragraph (i) of this section is subject to part 707, subpart D, of this chapter.

(h) *What test standard must I follow?* The chemical substances identified by Chemical Abstract Service (CAS) registry number and chemical name in Table 2 of paragraph (i) 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.

(2) *Source*. The source used to develop this test standard is the ''Protocol for *In Vitro* Percutaneous Absorption Studies,'' (Referenced in paragraph (h)(8)(i)(A) of this section).

(3) *Purpose*. In the assessment and evaluation of the characteristics of a chemical substance or mixture (test substance), determination of the rate of absorption of the chemical substance where dermal exposure to the chemical substance in the workplace may result in systemic toxicity is important. This test standard is designed to develop data on the rate at which chemicals are absorbed through the skin so that the body burden of chemical resulting from dermal exposure in the workplace can be better evaluated.

(4) *Principles of the test method*. This test standard describes procedures for measuring a permeability constant (Kp) and a short-term *in vitro* absorption rate for chemical substances in liquid form. The test standard utilizes *in vitro* diffusion cell techniques which allow absorption studies to be conducted with human skin. *In vitro* diffusion studies are necessary for measuring a Kp. This test standard specifies the use of cadaver skin and static diffusion cells to maintain the viability of the skin, thus, more closely simulating *in vivo* conditions. It also requires the use of radiolabeled test chemicals unless it can be demonstrated that procedures utilizing a non-radiolabeled test substance are able to measure the 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. The most accurate absorption-rate data for regulatory concerns related to human health would be obtained with live human skin. Because this test standard requires the use of static diffusion cells, maintenance of skin viability is not necessary. However, the time elapsed between death and harvest of the tissue must be reported.

(B) *Number of samples*. Data from a total of at least six samples obtained from at least three human subjects must be averaged to allow for biological variation among subjects.

(C) *Anatomical region*. In order to minimize the variability in skin absorption measurements for these tests, samples of human skin must be obtained from the abdominal region of human subjects of known source and disease state. Variability in skin permeation is well known to occur in different anatomical regions. The trunk and its extremities have reasonably similar barrier properties (less than 2-fold differences). Enhanced absorption can be observed in regions of the face (4-fold) and the scrotum (20-fold). Small differences in regional absorption may not be significant compared to intersubject variability

(D) *Validation of human skin barrier*. Barrier properties of human skin must be pretested with a standard compound such as tritiated water prior to conducting an experiment with the test chemical because barrier alteration can result from surgery or topical scrubbing, as discussed in the reference in paragraph (h)(8)(i)(B) of this section.

(ii) *Preparation of membrane*. Full thickness skin must not be used. Because chemicals are taken up by blood vessels directly beneath the epidermis *in vivo*, this *in vitro* test standard must be conducted using a membrane with most of the dermis removed. This is particularly important for hydrophobic chemicals that diffuse slowly through the dermis. A suitable membrane must be prepared from skin with a dermatome at a thickness of 200 to 500 millimeters (mm). The microtomed skin samples can be stored frozen for up to 2 weeks, if necessary, provided that they are frozen quickly and the barrier properties of the samples are confirmed.

(iii) *Diffusion cell design*. Static diffusion cells must be used in these studies. The testing laboratory must verify that the difference in the concentration of the test compound across the skin membrane does not decrease by more than 10% during the experiment. This will ensure that the test compound concentration in the receptor fluid does not alter the penetration rate. Concentration of the neat liquid must be taken as the density of the compound.

(iv) *Temperature*. Skin must be maintained at a physiological temperature of 32° Celsius.

(v) *Testing hydrophobic chemicals*. Chemicals with water solubility less than about 10 milligrams/liter do not freely partition from skin into aqueous receptor fluid. To increase the water solubility of such hydrophobic chemicals, polyethoxyoleate (polyethylene glycol (PEG) 20 oleyl ether) must be added to the receptor fluid at a concentration of 6%. To ensure that an increase in concentration of the chemical in the receptor fluid does not alter penetration rate, the concentration difference across the membrane must not decrease by more than 10% during the experiment.

(vi) *Vehicle*. If the test chemical is a liquid at room temperature and does not damage the skin during the determination of Kp, it must be applied neat. If the chemical 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 chemical in water is not high enough so that a steady-state absorption can be obtained, the chemical 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 chemical needed as described in paragraph (h)(5)(vii) of this section.

(vii) *Dose*--(A) *Kp*. An ''infinite dose'' of the test chemical must be applied to the skin to achieve the steady-state rate of absorption necessary for calculation of a Kp. The actual concentration required to give an undepletable reservoir on the surface of the skin depends on the rate of penetration of the test chemical. Preliminary studies may be necessary to determine this concentration. The diffusion cell tops must be covered with a stopper or with parafilm 7 to ensure that significant evaporation of the vehicle or test chemical does not occur. The skin barrier integrity must be verified at the end of the experiment by measuring the absorption of a standard compound such as tritiated water, as discussed in the reference in paragraph (h)(8)(i)(B) of this section.

(B) *Short-term absorption rate*. 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 to six diffusion cells must be set up using skin from a single subject and two to three of these shall be terminated at 10 and 60 minutes. Skin absorption at each sampling time is the sum of the receptor-fluid levels and the absorbed chemical that remains in the skin, as discussed in the reference in paragraph (h)(8)(i)(C) of this section. Unabsorbed chemical must be removed from the skin surface by washing gently with soap and water. This procedure must be repeated with skin from two additional subjects. In order to ensure reliable short-term absorption rates, the diffusion cell tops must be covered with a stopper or with parafilm 7 to prevent evaporation of the test chemical.

(viii) *Study duration*—(A) *Kp*. This *in vitro* dermal absorption rate test must be performed until at least four absorption measurements are obtained during the steady state absorption portion of the procedure. 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 require 24 hours or longer for slow-penetrating chemicals. Unabsorbed material need not be removed from the surface of the skin.

(B) *Short-term exposure rate*. The test chemical must be applied to skin for durations of at least 10 and 60 minutes. At the end of the study, the unabsorbed material 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 in the reference in paragraph (h)(8)(i)(C) of this section.

(6) *Results*--(i) *Kp*. The Kp must be calculated by dividing the steady-state rate of penetration (measured in micrograms x $hr^{-1}$ x centimeters $(cm)^{-2}$) by the concentration of the test chemical (measured in micrograms x $cm^{-3}$) applied to the skin. For example, if the steady-state rate is 1 microgram x $hr^{-1}$ x $cm^{-2}$ and the concentration applied to the skin is 1,000 micrograms x $cm^{-3}$, then the Kp value is calculated to be 0.001 cm x $hr^{-1}$.

(ii) *Short-term exposure rate*. The rates of penetration (micrograms x $hr^{-1}$ x $cm^{-2}$ ) must be determined from the total amount of test chemical found in the receptor fluid and skin after the 10- and 60-minute exposures.

(7) *Test reports*. In addition to compliance with the TSCA Good Laboratory Practice (GLP) Standards at 40 CFR part 792, the following specific information must be collected and reported under 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 GLP 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 chemical 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 flow-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 Kp or short-term absorption rate must be presented. In addition, all raw data from each individual diffusion cell must be maintained to support the calculations of Kp and short-term exposure rates. When radiolabeled compounds are 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*. (i) For background information on this test standard, the following references should be consulted. These references are available at the TSCA Nonconfidential Information Center, Rm. NE B–607, Environmental Protection Agency, 401 M St., SW., Washington, DC, 12 noon to 4 p.m., Monday through Friday, except legal holidays.

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

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

(C) Bronaugh, R.L., Stewart, R.F., and Storm, J.E. Extent of Cutaneous Metabolism during Percutaneous Absorption of Xenobiotics. *Toxicology and Applied Pharmacology*. Vol. 99, pp. 534–543 (1989).

(ii) Two additional documents consulted in developing this test standard are:

(A)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. *Dermatoxicology*. F. Marzulli and H. Maibach, Eds. Taylor & Francis, Washington, DC. pp. 371–381 (1996).

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

(i) *Reporting requirements*. The reports submitted under this section must include the information specified in paragraph (h)(7) of this section. Interim progress reports for each test must be submitted every 6 months, beginning 6 months after the effective date of any specific test listed in Table 2 of this paragraph. A final report for a specific test must be submitted by the deadline indicated as the number of months after the effective date shown in Table 2 of this paragraph.

TABLE 2.—REQUIRED TESTING: CHEMICAL SUBSTANCES DESIGNATED FOR IN VITRO DERMAL ABSORPTION RATE TESTING

| CAS No. | Chemical name | Deadline for final report | Number of Interim (6 month) reports required | Effective date |
|---|---|---|---|---|
| 60–29–7 | Ethyl ether | 9 | 1 | |
| 74–96–4 | Ethyl bromide | 9 | 1 | |
| 75–05–8 | Acetonitrile | 9 | 1 | |
| 75–15–0 | Carbon disulfide | 9 | 1 | |
| 75–35–4 | Vinylidene chloride | 9 | 1 | |
| 77–73–6 | Dicyclopentadiene | 9 | 1 | |
| 77–78–1 | Dimethyl sulfate | 9 | 1 | |
| 78–59–1 | Isophorone | 9 | 1 | |
| 78–83–1 | Isobutyl alcohol | 9 | 1 | |
| 78–87–5 | Propylene dichloride | 9 | 1 | |
| 78–92–2 | *sec*-Butyl alcohol | 9 | 1 | |

TABLE 2.—REQUIRED TESTING: CHEMICAL SUBSTANCES DESIGNATED FOR IN VITRO DERMAL ABSORPTION RATE TESTING—Continued

| CAS No. | Chemical name | Deadline for final report | Number of Interim (6 month) reports required | Effective date |
|---|---|---|---|---|
| 79–20–9 | Methyl acetate | 9 | 1 | |
| 79–46–9 | 2-Nitropropane | 9 | 1 | |
| 91–20–3 | Naphthalene | 9 | 1 | |
| 92–52–4 | Biphenyl | 9 | 1 | |
| 95–49–8 | *o*-Chlorotoluene | 9 | 1 | |
| 95–50–1 | *o*-Dichlorobenzene | 9 | 1 | |
| 97–77–8 | Disulfiram | 9 | 1 | |
| 98–29–3 | *tert*-Butylcatechol | 9 | 1 | |
| 99–99–0 | *p*-Nitrotoluene | 9 | 1 | |
| 100–00–5 | *p*-Nitrochlorobenzene | 9 | 1 | |
| 100–01–6 | *p*-Nitroaniline | 9 | 1 | |
| 100–44–7 | Benzyl chloride | 9 | 1 | |
| 106–42–3 | *p*-Xylene | 9 | 1 | |
| 106–46–7 | *p*-Dichlorobenzene | 9 | 1 | |
| 107–06–2 | Ethylene dichloride | 9 | 1 | |
| 107–31–3 | Methyl formate | 9 | 1 | |
| 108–03–2 | 1-Nitropropane | 9 | 1 | |
| 108–90–7 | Chlorobenzene | 9 | 1 | |
| 108–93–0 | Cyclohexanol | 9 | 1 | |
| 109–66–0 | Pentane | 9 | 1 | |
| 109–99–9 | Tetrahydrofuran | 9 | 1 | |
| 110–12–3 | Methyl isoamyl ketone | 9 | 1 | |
| 111–84–2 | Nonane | 9 | 1 | |
| 120–80–9 | Catechol | 9 | 1 | |
| 121–69–7 | Dimethylaniline | 9 | 1 | |
| 122–39–4 | Diphenylamine | 9 | 1 | |
| 123–42–2 | Diacetone alcohol | 9 | 1 | |
| 126–99–8 | *beta*-Chloroprene | 9 | 1 | |
| 127–19–5 | Dimethyl acetamide | 9 | 1 | |
| 142–82–5 | *n*-Heptane | 9 | 1 | |
| 150–76–5 | *p*-Methoxyphenol | 9 | 1 | |
| 528–29–0 | *o*-Dinitrobenzene | 9 | 1 | |
| 628–63–7 | *n*-Amyl acetate | 9 | 1 | |
| 768–52–5 | *N*-Isopropylaniline | 9 | 1 | |
| 25013–15–4 | Vinyl toluene | 9 | 1 | |
| 34590–94–8 | Dipropylene glycol methyl ether | 9 | 1 | |

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