

4.3 Exception

[Revise 4.3 to read as follows:]

Some parcels may be successfully processed on BMC parcel sorters even though they do not conform to the general machinability criteria in 4.1. The manager, BMC Operations, USPS Headquarters (see G043 for address) may authorize a mailer to enter such parcels as machinable parcels rather than irregular parcels if the parcels are tested on BMC parcel sorters and prove to be machinable. Mailers who wish to have parcels tested for machinability on USPS parcel sorting machines must:

a. Submit a written request to BMC Operations. The request must list mailpiece characteristics for every shape, weight, and size to be considered. If the letter requesting testing describes a mailpiece that falls within the specifications of pieces that were tested previously, the mailpiece will not be tested.

b. Describe mailpiece construction, parcel weight(s), estimated number of parcels to be mailed in the coming year, and preparation level (e.g., destination BMC pallets).

c. Send 100 samples to the test facility designated by the manager, BMC Operations, at least 6 weeks prior to the first mailing date. The manager, BMC Operations, will recommend changes, to ensure machinability, of parcels that do not qualify.

\* \* \* \* \*

6.0 OUTSIDE PARCEL (NONMACHINABLE)

[Revise the first sentence to read as follows:]

An outside parcel is a parcel that exceeds any of the maximum dimensions for a machinable parcel.

\* \* \* \* \*

G General Information

G000 The USPS and Mailing Standards

\* \* \* \* \*

G040 Information Resources

\* \* \* \* \*

G043 Address List for Correspondence

[Add the following address:] BMC Operations, US Postal Service, 475 L'Enfant PLZ, SW., RM 7631, Washington, DC 20260-2806.

\* \* \* \* \*

We will publish an appropriate amendment to 39 CFR part 111 to reflect these changes.

Neva R. Watson,

Attorney, Legislative.

[FR Doc. 04-9414 Filed 4-23-04; 8:45 am]

BILLING CODE 7710-12-P

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Parts 9 and 799

[OPPT-2003-0006; FRL-7312-2]

RIN 2070-AD42

In Vitro Dermal Absorption Rate Testing of Certain Chemicals of Interest to the Occupational Safety and Health Administration

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: EPA is promulgating a final rule under the Toxic Substances Control Act (TSCA) that requires manufacturers (including importers) and processors of 34 chemicals to conduct in vitro dermal absorption rate testing. These chemicals are of interest to the Occupational Safety and Health Administration (OSHA) of the Department of Labor, and the data obtained under this testing program will be used by OSHA to evaluate the need for "skin designations" for these chemicals. Skin designations are used by OSHA to alert industrial hygienists, employers, and workers to the potentially significant contribution to the overall exposure to certain chemicals which can occur by the cutaneous route. Thus, skin designations encourage employers to consider whether changes should be made to processes involving such chemical substances in order to reduce the potential for systemic toxicity from dermal absorption of these chemicals. Persons who export or intend to export any chemical substance included in this final rule are subject to the export notification requirements in TSCA section 12(b).

DATES: This final rule is effective on May 26, 2004. For purposes of judicial review, this final rule shall be promulgated at 1 p.m. eastern daylight/standard time on May 10, 2004.

ADDRESSES: EPA has established a docket for this action under docket identification (ID) number OPPT-2003-0006. All documents in the docket are listed in the EDOCKET index at http://www.epa.gov/edocket/. Although listed in the index, some information is not

publicly available, i.e., Confidential Business Information (CBI) or other information whose disclosure is restricted by statute. Certain other material, such as copyrighted material, will not be placed on the Internet and will be publicly available only in hard copy form. Publicly available docket materials are available either electronically in EDOCKET or in hard copy at the Office of Pollution Prevention and Toxics (OPPT) Docket, EPA Docket Center (EPA/DC), EPA West, Room B102, 1301 Constitution Ave., NW., Washington, DC. The Public Reading Room is open from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays. The EPA Docket Center Reading Room telephone number is (202) 566-1744, and the telephone number for the OPPT Docket, which is located in EPA Docket Center, is (202) 566-0280.

FOR FURTHER INFORMATION CONTACT: For general information contact: Colby Lintner, Regulatory Coordinator, Environmental Assistance Division (7408M), Office of Pollution Prevention and Toxics, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001; telephone number: (202) 554-1404; e-mail address: TSCA-Hotline@epa.gov.

For technical information contact: Keith Cronin or Catherine Roman, Chemical Control Division (7405M), Office of Pollution Prevention and Toxics, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001; telephone number: (202) 564-8157 or (202) 564-8172; e-mail address: cronin.keith@epa.gov or roman.catherine@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 § 799.5115(j) of the regulatory text. Any use of the term "manufacture" in this document will encompass "import," unless otherwise stated. In addition, as described in Unit VI., any person who exports or intends to export any of the chemical substances in this final rule is subject to the export notification requirements in 40 CFR part 707, subpart D. Entities that could be subject to the requirements in this final rule may include, but are not limited to:

- Manufacturers (defined by statute to include importers) of one or more of the 34 subject chemical substances

(NAICS 325 and 324110), e.g., chemical manufacturing and petroleum refineries.

- Processors of one or more of the 34 subject chemical substances (NAICS 325 and 324110), e.g., chemical manufacturing and petroleum refineries.

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 this unit could also be affected. The North American Industry 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 may be affected by this action, you should carefully examine the applicability provisions in Unit V.E. and consult the regulatory text at 40 CFR 799.5115(b). If you have any questions regarding the applicability of this action to a particular entity, consult one of the technical persons listed under **FOR FURTHER INFORMATION CONTACT**.

#### *B. How Can I Access Electronic Copies of this Document and Other Related Information?*

In addition to EDOCKET (<http://www.epa.gov/edocket/>), you may access this **Federal Register** document electronically through the EPA Internet under the "**Federal Register**" listings at <http://www.epa.gov/fedrgrstr/>. A frequently updated electronic version of 40 CFR part 9 and part 799 is available on E-CFR Beta Site Two at <http://www.gpoaccess.gov/ecfr/>.

## II. Background

### *A. What Action is the Agency Taking?*

In this action, EPA is promulgating a test rule under TSCA section 4 (15 U.S.C. 2603) which responds to recommendations of the Interagency Testing Committee (ITC). Under TSCA section 4(e)(1), the ITC is responsible for recommending chemical substances and mixtures to the EPA Administrator for priority testing consideration. In September 1991, the ITC received a nomination from OSHA of 658 chemical substances and mixtures for ITC review. 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 (Ref. 1). OSHA indicated to the ITC that it needed quantitative measures of dermal absorption to evaluate the potential hazard of these chemicals to workers (Ref. 2). These quantitative measures are expressed as the dermal absorption rate for a particular chemical (Ref. 3, p. 35725). The results of the ITC's review

were published in the **Federal Register** (Ref. 1, p. 26900 and Ref. 2, pp. 38492–38493).

In the 31<sup>st</sup>, 32<sup>nd</sup>, and 35<sup>th</sup> ITC Reports to the EPA Administrator (Refs. 1, 2, and 4), the ITC designated for *in vitro* dermal absorption rate testing a total of 83 of the 658 chemical substances nominated by OSHA. A summary of the process by which the ITC selected the 83 chemical substances was presented in the proposal to this action (Ref. 5, p. 31077). The data reviewed by the ITC included data obtained from TSCA section 8(a) and 8(d) rules (Refs. 6, 7, and 8) which were promulgated by EPA for the 83 chemical substances included in the 31<sup>st</sup>, 32<sup>nd</sup>, and 35<sup>th</sup> ITC Reports (Refs. 1, 2, and 4). These rules required the reporting to EPA of certain production, use and exposure-related information, and unpublished health and safety data concerning the 83 chemical substances.

In reviewing the available data, the ITC determined that the data for methyl methacrylate, diethyl phthalate, and cyclohexanone would meet OSHA's data needs for these three chemicals. Accordingly, the ITC withdrew its designation for these three chemicals: Methyl methacrylate and diethyl phthalate in the 34<sup>th</sup> ITC Report (Ref. 3), and cyclohexanone in the 36<sup>th</sup> ITC Report (Ref. 9).

Eighty of the chemical substances originally 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 31<sup>st</sup>, 32<sup>nd</sup>, and 35<sup>th</sup> ITC Reports (Refs. 1, 2, and 4), EPA 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, EPA again solicited interested parties to submit proposals for ECAs (Ref. 10). On June 26, 1996, EPA received a proposal from the ARCO Chemical Company (ARCO) (Ref. 11) for *tert*-butyl alcohol. On March 26, 1998, EPA received a study from ARCO entitled [<sup>14</sup>C]-*t*-Butyl Alcohol: Topical Application: Dermal Absorption Study in the Male Rat (Refs. 12 and 12a.). This study was reviewed and found acceptable as a means of determining the dermal absorption rate for *tert*-butyl alcohol. Accordingly, EPA did not propose testing of *tert*-butyl alcohol.

On June 9, 1999, EPA responded to the ITC's designation of the remaining 79 chemicals by issuing a proposed test rule under TSCA section 4 (Ref. 5) which would require that 47 of these

chemical substances be tested with respect to *in vitro* dermal absorption rate. The Agency selected the 47 chemicals for testing because, at the time of the proposal, EPA believed that their production volumes were the highest among the 80 chemicals designated by the ITC. At the time of the proposed rule, the most current information available to EPA indicated that each of the 47 chemicals was produced in "substantial quantities," meaning that their annual production volumes ranged from one million to more than one billion pounds. These chemical substances were being used in a wide variety of applications, which resulted in potential exposures of 1,000 or more workers to each chemical substance. Based upon EPA's review of more recent production volume data, exposure data, and dermal absorption rate data, which became available after the proposal to this rule was published, EPA is now requiring testing for 34 of the 47 chemicals that had been included in the proposed rule. The rationale for EPA's decision not to finalize testing requirements for the other 13 chemicals, which were originally proposed for testing, is described in Unit VII.A. through I.

EPA is requiring that the 34 chemicals be tested according to the *in vitro* dermal absorption rate test standard set forth in § 799.5115(h) of the regulatory text. EPA has also specified reporting requirements in § 799.5115(i) of the regulatory text. EPA may pursue testing of the remaining 32 chemicals based on further analysis.

In the solicitations discussed in this unit (Refs. 1, 2, 4, and 10), EPA referenced an *in vitro* dermal absorption rate test method for review by potential submitters in developing their proposed protocols (Ref. 10, p. 14776). This method was based on the peer reviewed method of Bronaugh and Collier (Ref. 13). Some refinements of the method were made by a panel of Federal scientists from ITC member and liaison agencies (including, for example, Consumer Product Safety Commission (CPSC), Department of Defense (DoD), EPA, Food and Drug Administration (FDA), National Institute for Occupational Safety and Health (NIOSH), and OSHA). EPA received public comments on the method and entered them, along with the method itself, into the dockets for the 31<sup>st</sup>, 32<sup>nd</sup>, and 35<sup>th</sup> ITC Reports (docket control numbers OPPTS-41038, OPPTS-41039, and OPPTS-41042, respectively). In addition, the American Chemistry Council (ACC, formerly the Chemical Manufacturers Association (CMA)) submitted a proposed protocol outlining

an alternative method (Refs. 14 and 14a.). Scientists from the Federal Agencies represented on the ITC (including EPA and OSHA) reviewed the public comments and the ACC proposal. As a result of this review, the ITC and EPA scientists further refined the *in vitro* dermal absorption rate test method of Bronaugh and Collier which EPA then proposed to be the test standard required by this final rule (Ref. 5).

The test standard that will be required under this final rule describes the procedures for measuring a permeability constant (Kp) and two short-term absorption rates (10 minutes and 60 minutes) for chemical substances in liquid form. A Kp is useful in estimating skin permeation when contact with the chemical is prolonged (hours) and steady state is achieved, while a short-term absorption rate measurement is more relevant when the contact is short-term (minutes). Both measurements are required by the test standard.

This test standard makes use of established *in vitro* diffusion cell techniques that allow absorption rate studies to be conducted using human cadaver skin and either flow-through or static diffusion cells (see § 799.5115(h) in the regulatory text). This test standard also requires the use of radiolabeled chemical substances unless the test sponsor can demonstrate that procedures utilizing a non-radiolabeled test substance are able to measure the substance with equivalent sensitivity. The first six parameters that are discussed under test procedures in § 799.5115(h)(5) of the regulatory text (i.e., choice of membrane, preparation of membrane, diffusion cell design, temperature, testing of hydrophobic chemicals, and vehicle) are similar for the determination of either of the two percutaneous absorption rate values (Kp and short-term absorption rate). In contrast, the remaining two parameters (i.e., dose and study duration) are different for the two percutaneous absorption rate values.

The *in vitro* approach was chosen not only for the practical considerations that it makes efficient use of labor and materials and can easily be performed by a variety of laboratories, but also because *in vitro* diffusion cell studies are necessary for measuring a Kp. Although the *in vitro* method in § 799.5115(h) of the regulatory text will satisfy OSHA's data needs to support its skin designations, EPA does not believe the method is an adequate substitute for all dermal absorption rate testing methods.

#### *B. What is the Agency's Authority for Taking this Action?*

This final rule is being promulgated under TSCA section 4 (15 U.S.C. 2603), which authorizes EPA to require the development of data relevant to assessing the risk to health and the environment posed by exposure to chemical substances and mixtures (chemicals).

Section 2(b)(1) of TSCA (15 U.S.C. 2603(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/or 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 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 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 [.]

The purpose of this testing is to develop data about the substance's or mixture's health or 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 enters or may reasonably be anticipated to enter the environment in substantial quantities or there is or may be significant or substantial human exposure to the chemical substance), EPA may require any type of health or environmental effect 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 to reasonably predict the effects of the manufacture, distribution in commerce, processing, use, or disposal of such substance or mixture or any combination of such activities on health or the environment, 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) (Ref. 55, pp. 28738–28739).

In this final rule, EPA is using its broad TSCA section 4(a) authority to obtain dermal absorption rate data necessary for OSHA to evaluate the need for "skin designations" (see Unit III.B.3.) for the 34 chemical substances specified in Table 2 in § 799.5115(j) of the regulatory text. Following consideration of the public comments received by EPA on the proposed test rule (Ref. 5), EPA is making the following findings for these chemicals under TSCA section 4(a)(1)(B): 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.

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 (Ref. 68, p. 59673).

### III. Response to Public Comments

#### A. Summary

EPA received comments on the proposed rule (Ref. 5) from ACC, Monsanto Company, First Chemical Corporation, American Forest and Paper Association (AFPA), American Petroleum Institute (API), Biphenyl Work Group, Diethyl Ether Producers Association (DEPA), Synthetic Organic Chemical Manufacturers Association (SOCMA), Acetonitrile Task Force, Dupont Dow Elastomers, Fragranced Products Information Network, Association of Veterinarians for Animal Rights, People for the Ethical Treatment of Animals, Animal Protection Institute Midwest Regional Office, Humane Society of the United States, Doris Day Animal League, Chlorobenzene Producers Association, Tetrahydrofuran Task Force (THFTF), a private citizen, and Union Carbide Corporation (Refs. 15–33).

ACC's Naphthalene Panel, Propylene Glycol Ethers Panel, Olefins Panel (ACC/O), Hydrocarbon Solvents Panel, Ketones Panel and Oxo Process Panel (ACC/KO), and Carbon Disulfide Panel, generally supported the comments by ACC (Refs. 34–39). The Chlorobenzene Producers Association, Biphenyl Work Group, and the Acetonitrile Task Force, also endorsed the comments submitted by ACC. Comments by ACC and those comments generally supportive of ACC's comments are collectively referred to as "ACC's" hereinafter in this document. Comments submitted by these groups that are specific to a chemical are addressed, as appropriate, in Unit III.F. and in Unit VII.

A summary of the comments received by EPA on the Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of Certain Chemicals of Interest to Occupational Safety and Health Administration is included in this unit, along with EPA's responses to those comments. The comments are available in the public docket for this rulemaking (see ADDRESSES).

#### B. TSCA Section 4 Findings

1. "Substantial" human exposure, TSCA section 4(a)(1)(B)(i)(II)—a. "B" policy. ACC commented that EPA has not provided a sufficient basis for its finding of "substantial" human exposure under TSCA section 4(a)(1)(B)(i)(II), (15 U.S.C. 2603(a)(1)(B)(i)(II)), with its approach in this final rule which is based solely on numbers of people exposed (more specifically, the number of workers exposed) to each chemical. ACC asserts that a substantial human exposure finding must additionally be based on

information such as each chemical's physical, chemical, and biological properties; the manner of use and release; exposure concentrations; and duration and frequency of exposure. ACC states that neither OSHA's objective of developing skin designations, nor EPA's objectives under TSCA, are served by requiring dermal testing in circumstances where dermal exposures are at low concentrations, or are so infrequent that harm is not likely to occur.

EPA disagrees with ACC's assertion that EPA has not provided a sufficient rationale for its finding that there is or may be "substantial" human exposure to the chemical substances that are subject to this final rule as required under TSCA section 4(a)(1)(B)(i)(II). EPA also disagrees with ACC's contention that EPA must consider chemical-specific factors to make a "substantial" human exposure finding. In its policy statement that explains how EPA generally makes findings under TSCA section 4(a)(1)(B)(i) (the "B" policy), EPA articulated quantitative thresholds to serve as guidance in making findings of "substantial" production, release, and human exposure. (Ref. 55) These quantitative thresholds are based on the Agency's belief that it is reasonable to interpret the word "substantial" to mean exposure to large numbers of people. Therefore, EPA believes that, in the case of this final rule, where, based on information available to EPA (Refs. 5 and 56), 1,000 or more workers are potentially exposed to each chemical for which the final rule would require testing, it is reasonable to require the testing of each chemical. In other words, EPA's policy (as articulated in its final "B" policy statement (Ref. 55)) is that quantitative data alone can justify EPA's finding that production, potential release, or the number of people potentially exposed to a chemical are "substantial." This is consistent with TSCA's goals of ensuring that, given the exposure of humans and the environment to a large number of chemical substances and mixtures with potentially harmful effects, there is effective regulation of commerce in such substances (15 U.S.C. 2601(a)), that adequate data 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 these substances (15 U.S.C. 2601(b)). Affected entities had the opportunity to comment on the proposed rule and submit current

employee information, readily available to them, to refute EPA's finding that a substantial number of employees is exposed. In those instances when EPA agreed with information submitted by commenters which demonstrated that fewer than 1,000 employees were exposed to a chemical, that chemical was not included in this final rule (see Unit VII.D., E., and G.)

A "substantial" human exposure finding under TSCA section 4(a)(1)(B)(i)(II) requires no hazard or risk analysis (Ref. 55, p. 28742). Given the statutory framework, the legislative history, and the case law interpreting the TSCA section 4 testing provisions, EPA does not believe that it is required to consider each of the types of information described by ACC in order to make a TSCA section 4(a)(1)(B)(i)(II) "substantial" human exposure finding (Ref. 55, p. 28742).

Although EPA is not required to consider the factors mentioned by ACC in making its "substantial" human exposure findings, information of the sort described by ACC is nevertheless relevant to other decisions leading to a determination as to whether to require testing under TSCA section 4. As stated in the Agency's "B" policy:

[f]or each substance-specific rulemaking under section 4, EPA must determine whether there are sufficient 'data and experience' upon which to 'reasonably determine or predict' the health and environmental effects of a chemical substance, and whether testing of such substance is 'necessary to develop such data.' In making these determinations, the Agency has always, and will continue to examine all available and relevant information concerning the substance in question, including the physical and biological properties of the substance, the manner of its use and release, the level, frequency, and duration of exposure, and any available relevant exposure and toxicity data. It is the responsibility of interested parties to provide any information they believe may be relevant to the Agency's determination to require testing of a particular chemical substance under TSCA section 4. (Ref. 55, p. 28743).

In those instances where interested parties provided such relevant information on chemical substances prior to the publication of this final test rule, EPA and OSHA carefully reviewed the information and, based on that review, EPA in some cases decided not to require testing for those chemical substances. (See Unit VII.A. through G.)

b. *The National Occupational Exposure Survey (NOES)*. ACC commented that EPA has continued to rely on the NOES database to support its findings of "substantial" human exposure, a data base which ACC

believes to be unrepresentative, incomplete, and outdated. ACC states that the NOES estimates are greatly overstated and should not be relied upon by EPA in making its findings. ACC provided a critique of the NOES (Ref. 40) as support for its statements and added that EPA should evaluate the level, frequency, and duration of exposure to each chemical to determine if it is "substantial."

EPA disagrees with the commenter's statements regarding the adequacy of the NOES for supporting a finding of "substantial" human exposure under TSCA section 4(a)(1)(B)(i)(II). This database contains, among other things, useful information on the approximate number of workers potentially exposed to a chemical substance specified in the database. That is to say, while the survey does not provide meaningful information on the level, frequency, or duration of exposure, it is useful for providing an estimate of the potential number of workers exposed to a chemical. As noted in Unit III.B.1.a., EPA also does not agree with the comment that EPA should undertake an exhaustive analysis of exposure (i.e., level, frequency, and duration) to a chemical substance to find that there is or may be "substantial" human exposure.

For each of the chemicals for which testing is required in this final rule, estimates of the number of exposed workers were identified in the NOES. The NOES was a nationwide data gathering project conducted by NIOSH, which was designed to develop national estimates for the number of workers potentially exposed to various chemical, physical, and biological agents and describe the distribution of those potential exposures. Initiated in 1980 and completed in 1983, the survey involved a walkthrough investigation by trained surveyors of 4,490 facilities in 523 different types of industries. Surveyors recorded potential exposures when a chemical agent was likely to enter or contact a worker's body for a minimum duration. These potential exposures could be observed or inferred. Information from these representative facilities was extrapolated to generate national estimates of potentially exposed workers for more than 10,000 different chemicals (Ref. 41). The NOES survey is the most recent and comprehensive source of this kind of information.

In the critique of the NOES cited by ACC, a general conclusion of the authors was:

We conclude from reviewing the survey design that, despite some flaws, it represents

one of the soundest approaches possible, within the limited budget, for attaining national estimates of the number of workers in the proximity of potentially hazardous agents. (Ref. 40).

EPA agrees with this conclusion and believes that it is reasonable to use information provided in the NOES database to support a finding of "substantial" human exposure for a chemical substance contained within that database.

In addition, EPA agrees with the authors of the critique, Buell et al (Ref. 40), that the survey results, while potentially useful for making broad, national estimates of the number of persons in workplaces where potentially hazardous agents are also present, should not be used to gauge actual worker exposure to these agents, particularly to individual chemicals in individual industry sectors. This information was not collected in the survey. EPA has relied only on the information in the NOES database regarding the approximate number of potentially exposed workers in support of its finding of "substantial" human exposure.

Because some time has passed since the NOES was completed, EPA acknowledges that there may be instances where changes in various industrial sectors (i.e., market demand, advances in technology, and other mitigating factors) have led to a decrease in the number of workers potentially exposed to certain chemical substances. EPA's proposed test rule asked interested parties to provide any information they believed relevant to the Agency's determination to require testing of a particular chemical substance under TSCA section 4. EPA has received additional exposure information on certain chemical substances for which testing was proposed. This information has been fully considered, and for those chemical substances for which EPA believes it cannot make the "substantial" human exposure finding in light of such information, the Agency is not finalizing testing requirements. (See Units VII.D., E., and G.).

c. *The Toxic Release Inventory (TRI)*. ACC stated that it is unclear what role the TRI data played in making the TSCA section 4 findings in the proposed rule, and that EPA should clarify how environmental releases factor into a determination of occupational dermal exposures. ACC notes that TSCA section 4(a)(1)(B), makes no mention of "release," but refers to whether a substance "enters" the environment. ACC asserts that in the context of TSCA

section 4, the word "enter" connotes presence in the environment. Accordingly, ACC argues that "release" of a chemical in excess of one million pounds per year is not necessarily evidence that the compound "enters" the environment in "substantial" quantities. For example, if a substance is dispersed, degraded, or reacted rapidly upon release from manufacturing and processing facilities and is never present in significant concentrations in air, water, or soil, ACC asserts that it has not "entered" the environment in "substantial" quantities.

Moreover, ACC contends that environmental release, such as that reported under section 313 of the Emergency Planning and Community Right-to-Know Act (EPCRA), does not correlate well with dermal exposure in the workplace. ACC notes that TRI reports do not indicate the concentrations of listed substances in environmental media or the extent of their distribution in the environment. Accordingly, ACC asserts that the release quantities reported under section 313 of EPCRA are not an adequate basis to support a TSCA section 4(a)(1)(B)(i)(I) finding in the context of this final rule, and they should not be combined with other data on the number of workers potentially exposed to support such a finding.

Although EPA reviewed information contained in the TRI database to identify additional support material for the test rule (Ref. 56), EPA did not find it necessary to use TRI release data in developing its exposure findings for this final rule.

d. *TSCA sections 8(a) and 8(d)*. API commented that EPA does not present results of data gathering in the 1993, 1994, and 1995 TSCA section 8(a) and 8(d) rules (Refs. 6–8) for the proposed test rule chemicals. API objects to EPA's issuing data gathering rules and then not using the data gathered for the purposes of the test rule, particularly given that it is 10 years more current than the data that EPA used to make its TSCA section 4(a)(1)(B)(i)(II) finding i.e., NOES data (Ref. 19).

Following the EPA Administrator's receipt of the ITC Reports (Refs. 1, 2, and 4) which designated 83 chemicals for priority testing, the EPA's Office of Pollution Prevention and Toxics (OPPT) promulgated TSCA section 8(a) Preliminary Assessment Information Reporting (PAIR) and TSCA section 8(d) Health and Safety Data rules (Refs. 6–8) for the 83 chemicals designated for testing by the ITC. The TSCA section 8(a) rule required manufacturers and importers of chemicals designated for testing by the ITC to submit production

and exposure reports. The TSCA section 8(d) rule required manufacturers (including importers), and processors of chemicals designated for testing by the ITC to submit unpublished health and safety studies. These rules are automatically promulgated by EPA unless the ITC requests that EPA not do so.

The ITC reviews the TSCA section 8(a) PAIR reports, TSCA section 8(d) studies, and "other information" that become available after the ITC adds chemicals to the *Priority Testing List*. "Other information" includes TSCA section 4(a) studies, TSCA section 8(c) submissions, TSCA 8(e) "substantial risk" notices, "For Your Information" (FYI) submissions, ITC-FYI voluntary submissions, unpublished data submitted to U.S. Government organizations represented on the ITC, published papers, as well as use, exposure, effects, and persistence data that are voluntarily submitted to the ITC by manufacturers, importers, processors, and users of chemicals recommended by the ITC. The submissions are indexed and maintained by EPA. After the ITC reviews this information it determines if data needs should be revised, if chemicals should be removed from the *Priority Testing List*, or if recommendations should be changed to designations.

EPA disagrees with the comment that data gathered under TSCA section 8(a) and 8(d) rules were not considered in preparing the proposal. In fact, the proposed rule described the ITC's use of the data from the TSCA section 8(d) rules to support withdrawing its designation for three chemicals. As described in the proposal (Ref. 5, p. 31077), the ITC received dermal absorption rate data for three chemicals after EPA had promulgated TSCA section 8(d) rules for these chemicals. The ITC determined that the dermal absorption rate data for these three chemicals would meet OSHA's data needs, and accordingly, the ITC withdrew its designation for these three chemicals: Methyl methacrylate and diethyl phthalate in the 34<sup>th</sup> ITC Report (Ref. 3, p. 35725), and cyclohexanone in the 36<sup>th</sup> ITC Report (Ref. 9, p. 42987).

Furthermore, the ITC's review of the data gathered under TSCA sections 8(a) and 8(d) for the 80 remaining designated chemicals did not provide a sufficient rationale for the ITC to make a determination that the specified data needs should be revised or that its designation of chemicals for *in vitro* dermal absorption rate testing should be withdrawn and those chemicals removed from its *Priority Testing List*.

The proposed rule also described EPA's use of production data as a basis for its decision to pursue rulemaking on only 47 of the remaining 80 designated chemicals because of their greater production volumes, data which were reported under the TSCA section 8(a) rules (Ref. 5, p. 31077). Although EPA considered the information on employee exposure at manufacturing sites provided in the TSCA section 8(a) submissions, EPA also relied on NOES data as they indicate what additional employee exposure may occur at processing facilities.

Finally, for those remaining 32 chemicals designated for *in vitro* dermal absorption rate testing by the ITC which are not addressed by this final rule, EPA will present any determinations regarding data gathered from TSCA section 8(a) and 8(d), as well as any other available data in any future proposal for those chemicals.

2. "Data are insufficient," TSCA 4(a)(1)(B)(ii). DEPA (Ref. 21), the Chlorobenzene Producers Association (Ref. 31), and the Union Carbide Corporation (Ref. 47) challenged the Agency's finding that data are insufficient to determine a dermal absorption rate for ethyl ether, *o*-dichlorobenzene, and *n*-amyl acetate, respectively. These commenters provided studies to support their claims that available data are sufficient to determine dermal absorption rates. ACC (Ref. 15) commented that isobutyl alcohol and sec-butyl alcohol are structurally similar to other alcohols for which data have been generated and that a structure-activity relationship (SAR) approach could be used to predict the dermal absorption rates of these two chemicals. EPA reviewed the submitted studies and agreed that the available data are sufficient at this time to adequately determine or predict dermal absorption rates for these five chemicals. See Unit VII.A. through C. and F. for a description of the submitted studies and the basis for EPA's decision not to pursue rulemaking on these five chemicals.

3. "Testing is necessary," TSCA section 4(a)(1)(B)(iii). ACC commented that EPA failed to demonstrate that the proposed testing is necessary to develop data to predict the effects of the chemicals on human health and the environment (Ref. 15). ACC also stated that the Agency has provided no information on the need for dermal absorption data to "support chemical risk assessments at EPA as well as at other Federal agencies." As a general matter, ACC believes that EPA should not require testing when the Agency has not determined how the data will be

used, and indeed cannot conclude that testing is necessary in such a case. Similarly, API and THFTF (Refs. 19 and 32) requested that EPA explain how the Agency (or other Federal Agencies) might use the dermal test data.

EPA believes it has adequately demonstrated a need for the testing that will be conducted under this final rule. As discussed in the preamble to the proposed rule (Ref. 5, pp. 31076–31078) and in the 31<sup>st</sup>, 32<sup>nd</sup>, and 35<sup>th</sup> ITC Reports to the Administrator (Refs. 1, 2, and 4, respectively), OSHA has found that for many toxic substances to which workers are exposed via multiple routes, and specifically for the chemical substances for which testing will be required under this final rule, very little knowledge exists of the contribution of dermal exposure to the total body burden of the substance.

Dermal absorption rate data for toxic substances encountered in industrial and occupational settings are quantitative estimates of the rate (amount per specified period of time) at which substances pass through the layers of the skin to enter the systemic circulation. 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. In order to assign a skin designation for a chemical substance, OSHA requires dermal absorption rate data. OSHA requested (Refs. 1, 2, and 4) that the ITC help identify chemicals which lack sufficient data for OSHA to develop skin designations and to use its authority to recommend chemicals for priority testing consideration by EPA to obtain these data.

As described in the proposed rule, the ITC performed searches for data relating to the chemicals on the following databases: RTECS (Registry of Toxic Effects of Chemical Substances), TOXLINE (TOXicology of 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 (Ref. 2, p. 38493).

Also as described in the proposed rule, in addition to these literature searches, the ITC reviewed data from

TSCA section 8(a) and 8(d) rules (Refs. 6 through 8) which were promulgated by EPA for the chemical substances included in the 31<sup>st</sup>, 32<sup>nd</sup>, and 35<sup>th</sup> ITC Reports (Refs. 1, 2, and 4). These rules required the reporting to EPA of certain production, use and exposure-related information, and unpublished health and safety data concerning these chemicals. For the 34 chemicals for which *in vitro* dermal absorption rate testing is required under this final rule, there was either no dermal absorption rate information available or available data were insufficient to derive a dermal absorption rate.

Testing of the 34 subject chemical substances is necessary to develop dermal absorption rate data. Dermal absorption rate data derived from testing these 34 chemical substances are needed by OSHA to estimate the amount of the chemical substance absorbed after contact with the skin. Only when dermal absorption is considered along with inhalation exposure data can a more complete and accurate quantitative assessment of body burden be estimated. Accurate estimates of body burden are necessary to develop assessments of risk to worker health posed by exposures to toxic substances in the workplace. This testing is needed to determine if the manufacturing, processing, or use of these 34 chemical substances presents an unreasonable risk of injury to human health.

In addition to playing an important role in assessing body burden, dermal absorption rate data can generate useful quantitative information for making recommendations or decisions concerning engineering controls or employee use of personal protective clothing to prevent exposure by the dermal route. Such information, when considered in conjunction with toxicologic and health effects data, can be used by industrial hygienists, other occupational health professionals, employers, and workers. Dermal absorption information is useful for hazard communication and right-to-know purposes, including Material Safety Data Sheets, and product labels. Additionally, dermal absorption rate data for chemicals used or produced in particular work sites are useful in developing comprehensive safety and health programs at those facilities.

OSHA standards, including skin designations, are widely applied and referenced. Local, State, and county governments, and other Federal Agencies rely on OSHA's occupational standards, as do other national governments. It is both appropriate and necessary to require dermal absorption

rate testing of these industrial chemicals.

Although OSHA is the primary agency requesting the data that will be developed under this final rule, OSHA is not the only Federal Agency that will use the data. NIOSH is also very interested in method-related issues associated with characterizing dermal exposure and advancing improvements in occupational exposure assessments.

EPA is also interested in data that may be gathered on these chemicals. The information obtained by the testing required in this final rule may be used to inform the Agency's decisionmaking process by providing data which can be used in a preliminary estimate of the potential health risk of certain chemical exposures. The 34 chemicals for which testing is required under this final rule are part of other ongoing Agency efforts. For example, all 34 chemicals are included in EPA's High Production Volume (HPV) Initiative (<http://www.epa.gov/chemrtk.htm>.) In addition, EPA's Voluntary Children's Chemical Evaluation Program (VCCEP) (Ref. 43) is designed to provide data to enable the public to better understand the potential health risks to children associated with certain chemical exposures. Four of the 34 chemicals are included in EPA's VCCEP: Vinylidene chloride (Chemical Abstract Service Registry Number (CAS No.) 75-35-4); *p*-dichlorobenzene (CAS No. 106-46-7); ethylene dichloride (CAS No. 107-06-2); and chlorobenzene (CAS No. 108-90-7). (See <http://www.epa.gov/chemrtk/childhlt.htm>.) While *in vitro* dermal absorption rate data are not being developed under either of these Agency efforts, the data may be of benefit in preliminary risk screening, which is the purpose of data gathering in the HPV Initiative. Dermal absorption rate data may also be beneficial in further consideration of chemicals to which children may be exposed. Thus, EPA may use data obtained under this test rule in preliminary risk screenings to support its HPV Initiative and VCCEP, or for other Agency efforts to protect human health and the environment from unreasonable risks resulting from the manufacture, processing, or use of chemicals.

In summary, the data developed under this test rule will assist the Agency and others in evaluating these chemical substances for potential health or safety risk concerns. Although it is not an independent basis for supporting this final rule, as an additional benefit, the data will be publicly available, and thus will serve to further the Agency's goal of identifying and controlling human health and environmental risks

by providing greater knowledge to the public.

### C. Categories

ACC (Ref. 15) believes that EPA should consider a category approach to dermal absorption rate testing. In reviewing the list of 79 ITC-designated chemicals, ACC concludes that a great majority can be grouped into categories of similar chemical structure and that selected chemicals from each category could be tested for the purpose of obtaining sufficient data that would allow an accurate prediction of dermal absorption rate for other members of the structural group through a combination of modeling and quantitative structure activity relationship (QSAR) analysis. ACC states that for the designated chemicals, these categories would include aliphatic alcohols, ketones, aliphatic hydrocarbons, nitroaliphatics, halogenated hydrocarbons, aliphatic esters, aromatic hydrocarbons, nitroaromatics, halogenated aromatics, amides, aromatic amines, and phenols/phenol ethers. ACC suggests that the data generated from testing chemicals within categories could then be combined with existing data on other category members (including those in the larger group of 658 workplace chemicals that were originally nominated for testing by OSHA) to attempt to correlate chemical structure with dermal absorption rates.

EPA disagrees with the category approach suggested by ACC as an alternative to the approach proposed by EPA for testing these chemicals. ACC has not provided specifics on the number of chemicals in each category that would need to be tested and the reason certain chemicals would be representative so that reliable structure activity predictions could be made. Twelve different structural classes were mentioned as potential categories by ACC, but additional classes would likely be needed to categorize within the group of 79 chemicals that have been designated for testing by the ITC. EPA remains unconvinced that the approach suggested by ACC will either minimize the testing burden or more efficiently develop data on the chemicals of interest. However, the results from the dermal absorption rate testing of the chemicals in this final rule could, in appropriate cases, provide additional data for more thorough QSAR analysis and better validated models for future predictions.

### D. Use of Calculated Kps to Screen and Prioritize Chemicals

ACC commented that adequate data already exist to "reasonably determine

or predict adverse effects," according to TSCA 4(a)(1)(B), for most if not all of the chemicals included in the proposed test rule (Ref. 15). It is ACC's understanding that the ITC calculated dermal penetration rates (Kps) for all of the chemicals covered by the test rule. ACC also notes that in 1992, EPA published guidance for estimating Kps for organic chemicals (see Ref. 42). The guidance document included calculated Kps for 11 of the 47 chemicals proposed for testing. In addition, ACC indicates that EPA's 1992 methodology has been largely validated, as the calculated Kps closely approximate available experimentally determined penetration rates. As such, ACC asserts that Kps, estimated using the suggested methodology, would be of sufficient quality to be used in screening-level assessments to determine the likely influence of dermal exposure on total worker exposure (i.e., the need for OSHA skin designations).

ACC states that EPA should consider giving industry the option of using calculated Kp values in lieu of testing, and together with industry and OSHA, assess the feasibility of using such data before the final rule is promulgated. ACC also states that, at a minimum, EPA should consider using calculated Kp data in order to screen and prioritize the chemicals for the proposed dermal absorption rate testing (Ref. 15). To do this, ACC states that prior to requiring testing the available calculated Kp data should be used to screen chemicals for their potential to cause systemic toxicity as a result of dermal exposure by assessing the potential contribution of dermal exposures to total occupational exposures, and that this assessment should be used to prioritize testing needs. ACC believes that the dermal absorption rate testing should be reserved for those chemicals for which screening-level assessments indicate the dermal pathway may be of concern. ACC comments that neither OSHA nor EPA has attempted to prioritize chemicals using published EPA dermal exposure assessment guidance, including published estimated dermal penetration rates.

EPA disagrees that adequate data exist to "reasonably determine or predict adverse effects," according to TSCA 4(a)(1)(B), for the chemicals included in the final test rule. As an initial matter, EPA believes that measured Kps (i.e., those determined through well designed and conducted *in vitro* or *in vivo* testing experiments) are generally more reliable than calculated Kps, and measured Kps are not available for the 34 chemicals subject to this final rule. EPA further believes that calculated Kp data may not

be sufficiently reliable to be used in lieu of testing or in screening-level assessments to prioritize testing needs when the most relevant worker exposures involve exposure to neat compounds or compounds dissolved in organic solvents. With respect to the chemicals for which measured Kps are presented in Table 5-8 in EPA's 1992 guidance document (Ref. 42), the Kps were measured exclusively for the chemicals when they were in aqueous solutions; the table presents no measured Kps for neat liquids or chemicals in organic solvents, both of which are generally expected to be more relevant to the workplace (Ref. 62). Thus, these data are not adequate to provide the information needed for OSHA's intended purpose (Ref. 62). However, the *in vitro* testing required by this final rule, in addition to developing data needed to assess the potential risk of the 34 subject chemicals, will expand the existing data base and allow more thorough comparisons of measured Kps with calculated Kps relevant to occupational exposures.

#### *E. Comments on Proposed In Vitro Test Standard*

1. *General.* EPA received comments supporting use of the proposed test standard from several groups and individuals (Refs. 25-30). Many of these comments were similar in that they supported the standard as a means of gathering data without utilizing laboratory animals.

EPA agrees that there are instances, such as utilizing the test standard articulated in this final rule, in which sufficient data on the dermal absorption rate of a chemical substance may be gathered without using live laboratory animals. EPA considers many factors in relying upon specific test methods in its proposals under TSCA section 4. In specifying the standard for this rulemaking, the ITC and EPA considered the views of the public commenters, Federal scientists, and laboratories capable of conducting such testing. The standard articulated in this rulemaking makes efficient use of labor and materials and can be performed in a consistent, economical, and timely manner by different laboratories. The specification of the *in vitro* method as the test standard for this final rule also reflects EPA efforts to reduce the use of animals, where appropriate, in its testing programs. However, as noted previously in Unit II.A., although this *in vitro* method will satisfy OSHA's data needs to support its skin designations, EPA does not believe the method is an adequate substitute for all dermal absorption rate testing methods.

2. *Technical.* In addition to the general comments received by EPA on the proposed test standard, EPA also received technical comments from ACC, API, THFTF, DEPA, and a private citizen. In general, commenters argue that the proposed test standard was unnecessarily rigid and that several improvements would provide greater flexibility and reduce the cost of testing. EPA and OSHA agree with a number of the changes recommended by ACC, API, and THFTF, and have revised the test standard accordingly, as described in this unit.

a. ACC, API, and THFTF commented that both static and flow-through *in vitro* cells have been found acceptable in estimating dermal penetration of compounds. EPA agrees. Both static and flow-through *in vitro* cells, as described by the commenters and in the international Organization for Economic Co-operation and Development (OECD) draft guidance document (Ref. 44), are acceptable for estimating dermal penetration of compounds (Ref. 62). EPA has modified the test standard at paragraph (h)(5)(iii) to read: "Either static or flow-through diffusion cells must be used in these studies."

b. EPA received a comment from a private citizen (Ref. 33) who believes that more scientifically valid dermal absorption rates would be obtained by using the technologically more advanced flow-through type cells and viable human skin instead of the older method using static diffusion cells and cadaver skin.

EPA agrees that in some instances it may be preferable to utilize flow-through cell types and viable human skin to generate dermal absorption rate data. Based on this comment and similar comments by ACC, API, and THFTF, EPA has modified the test standard to allow the use of either flow-through cells or static diffusion cells in developing the data required under this final rule (See § 799.5115(h)(5)(iii) of the regulatory text). However, although EPA agrees that utilizing viable human skin could provide more reliable data, EPA is requiring that human cadaver skin be utilized for all testing required in this action. EPA's rationale for this decision is described in Unit III.E.2.o.ix.

c. ACC commented that heat treatment to separate epidermis from dermis is an acceptable alternative to dermatome slicing for preparing epidermal membranes. EPA agrees. The use of a dermatome prepared skin membrane of a thickness of 200 to 500 micrometers (um) is but one scientifically acceptable method of preparation. Peeling the epidermis from the dermis after heat treatment at 60° C

for 45 seconds, as recommended by ACC (Ref. 15), or 1 to 2 minutes, as specified in the draft OECD guidance document (Ref. 44), is also a scientifically accepted means of preparing the test membrane (Ref. 62). In response to this comment, EPA specified a time range of 45 seconds to 2 minutes as the time for heat treatment to include the two recommended treatment times in the ACC and OECD methods (45 seconds and 1 to 2 minutes, respectively). EPA modified the required test standard § 799.5115(h)(5)(ii) to read:

A suitable membrane must be prepared from skin either with a dermatome at a thickness of 200 to 500 micrometers (um), or with heat separation by treating the skin at 60° C for 45 seconds to 2 minutes after which the epidermis can be peeled from the dermis.

d. ACC and THFTF commented that the requirement that barrier properties of human cadaver skin must be pretested with a standard compound such as tritiated water prior to conducting the study should be expanded to include suitable alternatives to the use of tritiated water. (See Howes, et al., *Methods for Assessing Absorption*, in *ECVAM Workshop Report 13*, J.H. Fentem, ed., European Center for the Validation of Alternative Methods, 94–95 (Ispra, Italy 1996)). EPA agrees. Membrane integrity checks conducted with transepidermal water loss (TEWL) or electrical resistance, as described by the commenters and in the OECD guidance document (Ref. 44), are acceptable alternatives to dermal penetration of tritiated water for the evaluation of human cadaver skin integrity (Ref. 62). EPA has modified the test standard in § 799.5115(h)(5)(i)(D) to read:

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

- (1) measuring the movement of a standard compound such as tritiated water as discussed, for example, in the reference in § 799.5115(h)(8)(i),
- (2) determining an electrical resistance to an alternating current, at up to two volts, or
- (3) measuring trans-epidermal water loss from the stratum corneum.

e. API, THFTF, and ACC commented that human cadaver skin samples can be stored frozen for periods longer than 2 weeks, as proposed by EPA. Frozen storage, even for longer periods of time, does not adversely affect the integrity of the dermal barrier (see Ref. 45).

EPA agrees that for purposes of this test rule, the human cadaver skin samples can be stored frozen for periods longer than 2 weeks. However, EPA does not agree with ACC that skin samples can be frozen for up to 18

months without changes in penetration rates for standard compounds. EPA does not believe that a single report (Ref. 45) of acceptable skin penetration using a single substance (water) with membranes frozen for 466 days justifies extending the standard storage period to 18 months. Most of the chemicals designated for testing in this final rule are organic chemicals with chemical properties quite different from water. EPA believes it is reasonable to extend the maximum period of time during which human cadaver skin samples can be stored frozen (-20° C) to 3 months (Ref. 62). This period of time is consistent with OECD guidance (Ref. 44). In response to these comments, EPA has modified the test standard in § 799.5115(h)(5)(ii) to read:

These epidermal membranes can be stored frozen (-20° C) for up to 3 months, if necessary, if they are frozen quickly and the barrier properties of the samples are confirmed immediately prior to commencement of the experiment.

f. THFTF commented that EPA should allow a longer, though unspecified, amount of time for study completion. THFTF cited three circumstances which would make more time necessary:

- The practical ability of companies to test multiple materials.
- The availability of contracting facilities to conduct the test.
- The extra time needed to synthesize radiolabeled material.

EPA agrees. Circumstances may arise where the proposed 9 months would be an insufficient amount of time to complete testing. Therefore, EPA is extending the period of time provided to complete the required testing from 9 months to 13 months which EPA believes should accommodate the circumstances cited by THFTF.

g. ACC and THFTF noted that the test standard requires a full balance sheet to demonstrate recovery of radioactivity. (A “full balance” refers to a determination of where the radiolabel is present at the conclusion of the experiment (i.e., in the receptor fluid, skin sample, test vehicle, or diffusion cell) and that the recovery of radioactivity in the test system is nearly 100%). Commenters stated that it is unclear whether this requirement applies to Kp studies, to studies to measure short-term absorption rates, or both. They assert that full balance sheets are not necessary for studies in which Kp is being determined. Additionally, they commented that small losses of the test article do not affect the outcome of the studies because the study is, by definition, conducted with an infinite

dose. (Infinite dose is the amount of test preparation applied to the skin where a maximum absorption rate is achieved and maintained because such a volume ensures continuous excess of test preparation in the donor chamber.) (Ref. 44). Commenters requested that EPA clarify how accounting for losses affects Kp values.

EPA believes the test standard should require that a full balance of radioactivity be presented for both Kp and short-term absorption rate studies, as proposed. While EPA agrees that small losses of test compound are tolerable in the infinite dose design, it is, nevertheless, considered good laboratory procedure and does not require excessive effort to assess recovery in experiments using radiolabeled compound (Ref. 62).

h. ACC and API (Refs. 15 and 19) commented that the use of isopropyl myristate (IPM) as a solvent in the proposed test standard is inappropriate. ACC and API stated that IPM, although frequently used as a vehicle in various dermatological formulations, has questionable applicability in an occupational environment to the chemicals subject to this test rule. ACC and API also stated that IPM may not mimic workplace conditions and if used, some corrective factor should be applied to determine the rate of percutaneous absorption.

EPA disagrees. IPM is an appropriate all-purpose solvent for the rare instances in which certain water insoluble substances capable of damaging skin are being tested (Ref. 62). ACC has not provided evidence to suggest that use of IPM will generate distorted Kp values unrepresentative of occupational settings. If such evidence exists, EPA is willing to consider, via the procedures specified at 40 CFR 790.55, *in vitro* percutaneous absorption experiments with other vehicles for specific test chemicals, if the test sponsor demonstrates that their vehicle is more representative of relevant occupational exposure than IPM. EPA will not speculate on what, if any, adjustments might be made to Kp values determined by the test standard in order “to reflect realistic exposure scenarios” or to account for differences in regional absorption for skin.

i. ACC noted that the preamble to the proposed rule indicates that the parent chemical and its major metabolites are to be detected in certain cases, and requested clarification as to which of the major metabolites of the chemicals this requirement applies.

In the proposal to this action, EPA mentioned that the measurement of major metabolites in the receptor fluid

is done when viable skin is used and significant dermal metabolism is anticipated. However, EPA did not propose nor is EPA requiring that live skin be used and skin viability be maintained during performance of the required tests. Therefore, EPA is also not requiring measurement of major metabolites in the receptor fluid. (See Unit III.E.2.o.ix.).

j. ACC was unsure whether EPA's proposed test standard would require the use of 6 or 18 human cadaver skin samples per chemical. EPA is requiring a minimum of 18 human cadaver skin samples per chemical. EPA has modified the test standard at § 799.5115(h)(5)(i)(B) to clarify that data must be obtained from a minimum of six samples for each of the determinations, i.e., Kp, 10-minute short-term absorption rate, and 60-minute short-term absorption rate. Also, the samples used for the testing of a given chemical must come from at least three different human subjects, with two samples from each subject being used for each determination to allow for biological variation among subjects. (See § 799.5115(h)(5)(i)(B) of the regulatory text).

k. ACC commented that in § 799.5115(h)(5)(v) of the proposed regulatory text it is unclear whether it is necessary to demonstrate that the concentration of a test substance in the donor chamber has remained at greater than 90% of its original value, or that the concentration of the test substance in the receptor fluid is less than 10% of the initial test substance concentration in the donor chamber. Similarly, THFTF commented that § 799.5115(h)(5)(v) of the proposed regulatory text should be revised to state that physicochemical data or experimental results should be used to show that about 10 times the concentration in the receptor fluid is achievable under experimental conditions. This will ensure that back diffusion is not significant. See the OECD Guideline 1999 (Ref. 44).

EPA has removed the language in question in § 799.5115(h)(5)(v) of the regulatory text, and has inserted related text in the test standard at § 799.5115(h)(5)(iii) to read:

To ensure that an increase in concentration of the test substance in the receptor fluid does not alter penetration rate, the testing laboratory must verify that the concentration of the test substance in the receptor fluid is less than 10% of the initial concentration in the donor chamber.

This requirement applies to all chemicals to be tested, including hydrophobic chemicals.

l. ACC commented that there is some confusion created by inconsistencies

between statements in the proposed rule preamble and requirements in the proposed test standard. ACC points out that the preamble states that "the measurement of a short-term absorption rate is only required when a Kp cannot be obtained using this standard," whereas § 799.5115(h)(5)(vii)(B) of the proposed regulatory text states that "Short-term absorption rates must be determined for all chemicals." It is not clear to ACC why short-term absorption rates must be determined for all test chemicals. ACC believes that if a chemical affects the skin and a Kp value cannot be determined, determining a Kp rate is moot. Knowledge of the short-term rate is not useful in determining Kp values. API similarly commented that it is not clear why determining the short-term absorption rate for each test rule chemical is necessary.

EPA is requiring the measurement of short-term absorption rates for all chemicals included in this final rule. The panel of Federal scientists that refined the method of Bronaugh and Collier (Ref. 13) recommended that all chemicals be tested for short-term absorption in order to obtain *in vitro* dermal absorption rate measurements for brief dermal exposures that commonly occur in occupational settings, such as spills or splashes. EPA believes that the panel's rationale supporting the testing of all chemicals for short-term absorption is reasonable.

m. ACC and THFTF commented that the correct unit of measurement is micrometers, not millimeters, as stated in § 799.5115(h)(5)(ii) of the proposed regulatory text. EPA agrees that the correct unit of measurement is micrometers, not millimeters. EPA has corrected the test standard in § 799.5115(h)(5)(ii) of the regulatory text to reflect this.

n. DEPA argues that the proposed test standard is unacceptable for measuring very volatile liquids, such as ethyl ether, because efforts to prevent evaporation would lead to unrealistically high pressures, leakage of material from the cell, damage to the skin membrane, and other substantial technical difficulties. EPA disagrees. DEPA did not provide any evidence to suggest, nor is EPA aware, that any such problems have ever been reported. However, in those instances where a test sponsor can document that closed (i.e., occluded) conditions lead to leakage of material or damage to the skin membrane or similar technical difficulties, *in vitro* percutaneous dermal absorption rate experiments with the skin surfaces uncovered (unoccluded) may be substituted, via the provisions in 40 CFR 790.55, if EPA agrees that

conducting the study in such a manner is more technically feasible and appropriate.

o. THFTF suggested numerous minor changes to the test standard that EPA believes go against either the recommendations of the ITC expert panel or TSCA Good Laboratory Practice Standards (GLPS) at 40 CFR part 792, and do not enhance the validity or acceptability of the method. The suggested changes include:

i. Removing the requirement that the time elapsed between the death and harvest of human skin specimens be reported. EPA believes that all experimental parameters should be reported in accordance with TSCA GLPS, and has retained this requirement in the final rule.

ii. Removing the requirement that the thickness of the skin membrane be reported. EPA believes that all experimental parameters should be reported in accordance with TSCA GLPS, and has retained this requirement in the final rule.

iii. Requiring solids to be applied directly to the skin and determining percentage absorbed rather than dissolving solids in a vehicle and determining Kp. EPA disagrees. Although there may be instances where some of the test rule chemicals that are solids at room temperature have dermal exposures limited to the chemical in solid form, it is also possible based on common industrial practices, that there will be occupational exposures to these chemicals when they are dissolved or suspended in an aqueous or solvent medium. In addition, test solutions are more suitable for determining Kp values for chemicals that are solids at room temperature. This is because solutions in contact with the skin are uniform and have known concentrations, which is not necessarily the case with solids in contact with skin (Ref. 63). Therefore, EPA is generally requiring, as proposed, that chemicals that are solids at room temperature be dissolved in water. If the chemical is hydrophobic and its concentration in water is not high enough to obtain a steady-state absorption, the chemical must be dissolved in isopropyl myristate. However, in those instances where a test sponsor can document that occupational exposure is limited to a chemical in solid form, development of percutaneous dermal absorption rate experiments with solid material may be substituted, via the provisions contained in 40 CFR 790.55, if EPA agrees that conducting the study in such a manner is more appropriate.

iv. Specifying fixed amounts of test chemical, 10 milligrams per centimeter

squared ( $\text{mg}/\text{cm}^2$ ) for dry solid or 10 microliters per centimeter squared ( $\text{ul}/\text{cm}^2$ ) for liquids, be used in short-term absorption rate experiments rather than simply requiring the use of sufficient test chemical to cover the skin and reporting the quantity used. EPA disagrees. It is not necessary to specify that all substances be tested at the same fixed volume per skin area. The size of the diffusion chamber will partially determine the volume of required test material. The important issue is that sufficient test chemical is available to completely cover the skin. This is because the absorption rate of a chemical is reported per square centimeter of skin, thus, it is necessary to precisely ascertain the area of skin contacted (Ref. 63).

v. Requiring three rather than four absorption measurements for determination of  $K_p$ . EPA disagrees. The panel of Federal scientists that refined the Bronaugh and Collier method (Ref. 13) for use as the test standard in this final rule believes that three measurements during the steady state absorption period are inadequate to accurately determine the  $K_p$  and that an additional measurement is necessary for this purpose (Ref. 62). As a result, EPA is retaining the requirement in this final rule that four absorption measurements be taken for the determination of a  $K_p$ .

vi. Specifying that exposure time should be up to 8 hours for estimating dermal absorption of finite doses. EPA disagrees. EPA does not believe that it will be necessary to test each of the chemicals for as long as 8 hours. In fact in many instances, the study can be completed in an hour. However, there may be chemicals for which the study could require up to 24 hours to complete. Therefore, EPA believes that specifying a study duration of up to 8 hours is inappropriate (Ref. 63). However, if a test sponsor provides EPA with documentation that an alternate exposure time for a specific chemical is more relevant than the exposure time specified in this final rule, EPA may provide for the substitution of other exposure durations for the development of *in vitro* percutaneous dermal absorption rate experiments, via the provisions contained in 40 CFR 790.55, if EPA agrees that conducting the study in such a manner is more appropriate.

vii. Allowing 1:1 ethanol:water to be used as receptor fluid for hydrophobic chemicals in addition to 6% polyethylene glycol (PEG) in water. EPA agrees that a 1:1 ratio of ethanol to water is a suitable receptor fluid for hydrophobic chemicals. However, EPA is specifying that the PEG receptor solvent at a concentration of 6% be used

for testing of hydrophobic chemicals. EPA believes that specifying the use of the single PEG receptor solvent for these chemicals should ensure more uniform and consistent results. Specifying that a single receptor fluid be used for all hydrophobic chemicals will enhance the interpretability of test results for these chemicals (Ref. 63).

viii. Not expressing short-term finite absorption as a rate, i.e., micrograms per hour per centimeter squared ( $\text{ug}/\text{h}/\text{cm}^2$ ), because the true absorption rate is likely to change over the time interval during which absorption is being measured. This is to be distinguished from  $K_p$  determinations at steady state conditions under which there is little change in an absorption rate over time. The commenter suggests that cumulative amount absorbed per area, i.e., micrograms per centimeter squared ( $\text{ug}/\text{cm}^2$ ) is a more appropriate way to express the data.

EPA disagrees. EPA is aware of the distinctions between a short-term absorption rate measured under non-steady state conditions and a  $K_p$  value based on a steady state absorption rate. (See § 799.5115(h)(5)(vii)(A) of the regulatory text which states that an infinite dose must be applied to the skin to achieve a steady-state rate of absorption for calculation of a  $K_p$ .) Concerning the units to be used for short-term absorption rates, EPA does not agree that expressing short-term absorption data as cumulative amount per area rather than a rate provides any interpretive advantage. A short-term absorption rate represents the average absorption over the time interval during which it is measured. The true rate will usually be greater than the average rate early in the time interval and less than the average rate later in the time interval. A determination of cumulative amount absorbed per unit of area provides only end of the experiment information rather than information about the average rate during the course of the test. EPA is requiring that the results be expressed as a rate ( $\text{ug}/\text{h}/\text{cm}^2$ ), rather than as an amount per area ( $\text{ug}/\text{cm}^2$ ) in order to be consistent with rate units used to calculate  $K_p$  (Ref. 63).

ix. Allowing the use of human skin obtained from cosmetic surgery (breast and/or abdominal skin) as an alternative to human cadaver skin for testing. In refining the test method, the ITC and EPA considered the collective views of commenters, Federal scientists, and laboratories capable of conducting such testing. The test standard specifies the use of human cadaver skin which EPA believes makes efficient use of labor and materials and can easily be performed by many different laboratories. EPA

believes that the use of this human cadaver skin will provide the desired results in an economical and timely manner. Although EPA agrees that a method utilizing viable human skin could provide more reliable  $K_p$ s for compounds in which skin metabolism influences dermal penetration, EPA does not believe that extensive metabolism is likely, based on the physical chemical properties, for the 34 chemicals subject to this final rule. Based on the public comments received and discussions with Federal scientists and laboratories capable of conducting such testing, EPA believes that performing the study with skin from cosmetic surgery could increase test costs. As a result, the final test standard requires the use of human cadaver skin.

x. Not requiring the use of radiolabeled materials in the required testing because many chemicals subject to the final rule are unlikely to be readily available in radiolabeled form. Thus, it will take additional time to prepare an adequate supply of radiolabeled chemicals, potentially adversely affecting industry's ability to meet the regulatory deadlines established for completing the testing and submitting the test results.

EPA disagrees. This comment was in reference to a single chemical (tetrahydrofuran) and was the only comment which indicated that radiolabeled materials are not available off-the-shelf. EPA believes that radiolabeled materials are likely to be available for at least some of the other chemicals included in this final rule. In those instances where radiolabeled materials are not currently available and must be synthesized, EPA believes that the additional amount of time provided in this final rule (see Unit III.E.2.f.) is sufficient both to prepare such materials and complete the testing. Also, radiolabeling is not an uncommon analytical procedure and there are many different laboratories (Ref. 46) in the United States that are capable of preparing radiolabeled materials. Finally, the test itself is short-term, generally taking no longer than 24 hours to complete. The Agency has provided test sponsors with 13 months to complete the requirements established under this final rule. To the extent that a test sponsor does require additional time to comply with the final rule, an extension from EPA may be requested utilizing the procedures at 40 CFR 790.55.

xi. Deleting the word "live" as used in § 799.5115(h)(5)(i)(A) of the proposed regulatory text which states "the most accurate absorption rate data for regulatory concerns related to human

health would be obtained with live human skin." In the course of developing the final test rule, EPA deleted this statement from the test standard primarily for the reasons presented in Unit III.E.2.o.ix.

#### F. Chemical Specific Comments

Chemical specific comments on ethyl ether (CAS No. 60-29-7), isobutyl alcohol (CAS No. 78-83-1), *sec*-butyl alcohol (CAS No. 78-92-2), *o*-dichlorobenzene (CAS No. 95-50-1), *p*-nitrotoluene (CAS No. 99-99-0), *beta*-chloroprene (CAS No. 126-99-8), *n*-amyl acetate (CAS No. 628-63-7), *N*-isopropylaniline (CAS No. 768-52-5), and *o*-dinitrobenzene (CAS No. 528-29-0) are addressed in Unit VII.

1. *Acetonitrile*. The Acetonitrile Task Force commented that the total number of workers associated with acetonitrile (CAS No. 75-05-8) production in the United States is on the order of 500 (Ref. 23). The Task Force believes that EPA has included laboratory personnel in its larger estimate as the Agency's figure far exceeds the number of personnel involved in manufacturing the chemical. The Task Force notes that analytical laboratory personnel are well trained in safely handling hazardous materials of this type, and that these workers typically handle small volumes of acetonitrile.

EPA reviewed the Acetonitrile Task Force's estimate of the number of workers exposed to acetonitrile at manufacturing sites, but did not find that the information provided sufficient basis to conclude that there are not substantial numbers of workers potentially exposed to acetonitrile during manufacturing, processing, and use. Although EPA requested the Acetonitrile Task Force to provide documentation for its estimate of the number of workers exposed to acetonitrile, EPA did not receive any further information from the Task Force in support of its estimate. Also, the NOES data used by EPA did include laboratory personnel and EPA believes it is appropriate to include them because they are potentially exposed. EPA believes that employee training does not assure that exposure will not occur and is no basis for the assertion that laboratory employees will have no exposure. EPA also believes that the Task Force's estimate that 500 employees are potentially exposed may be low if it did not include laboratory personnel. Absent specific data indicating otherwise, EPA believes the NOES database should be used to estimate worker exposure because it is the most recent and comprehensive source of this kind of information.

Therefore, EPA is requiring the testing of acetonitrile to determine an *in vitro* dermal absorption rate.

2. *Carbon disulfide*. ACC's Carbon Disulfide Panel cited three studies summarized in an Agency for Toxic Substances and Disease Registry (ATSDR) document (*Toxicological Profile for Carbon Disulfide* (August 1996), p. 65-66) as a supporting rationale for its assertion that sufficient data exist for carbon disulfide (CAS No. 75-15-0) and that testing of carbon disulfide is therefore, unnecessary (Ref. 39). One 30-year-old study estimated dermal absorption by measuring very small changes in carbon disulfide solution before and after immersion of the hand (T. Dutkiewicz and B. Baranowska. 1967. The significance of absorption of carbon disulfide through the skin in the evaluation of exposure. *Toxicology of Carbon Disulfide. Proceedings of a Symposium, Prague, 1966*, pp. 50-51). EPA reviewed this study and considered the methodology flawed due to its indirect measurement and potential failure to control for volatilization. In the other two studies cited by the Carbon Disulfide Panel (A.E. Cohen, et al. 1958. Skin absorption of carbon disulfide vapor in rabbits. I. Associated changes in blood protein and zinc. *AMA Archives of Industrial Health*, 17:164-169; and H. Drexler, et al. 1995. Carbon disulfide. 2. Investigations on the uptake of CS<sub>2</sub> and the excretion of its metabolite 2-thiothiazolidine-4-carboxylic acid after occupational exposure. *International Archives of Occupational Environmental Health*, 67:5-10), EPA notes that a dermal absorption rate was not determined and could not be derived using the data gathered (Ref. 62).

The Carbon Disulfide Panel also cited a dermal absorption rate calculated by EPA for carbon disulfide in composted sludge at a level of 0.59 milligrams per kilogram (mg/kg) soil. EPA notes that the dermal absorption rate was not experimentally determined, but was estimated from low environmental levels in composted sludge rather than the potentially higher worker exposure to the undiluted liquid (Ref. 62). EPA and OSHA do not consider the data cited by the Carbon Disulfide Panel to be sufficient to determine a useful and reliable dermal absorption rate (Ref. 62).

The Carbon Disulfide Panel also cited ATSDR's statement that "carbon disulfide partitions immediately to the air when released to the environment, and does not therefore expose humans to carbon disulfide through oral or dermal contact" (*Toxicological Profile for Carbon Disulfide* (August 1996), pp.

134-141). EPA notes that this statement refers to dermal contact with environmental media that had been contaminated with carbon disulfide, not to occupational exposure (Ref. 62). In fact, the same document makes it clear that the main way workers are exposed to carbon disulfide is through the inhalation of vapors and dermal contact (*Toxicological Profile for Carbon Disulfide* (August 1996), pp. 9 and 63). Therefore, EPA is requiring the testing of carbon disulfide to determine an *in vitro* dermal absorption rate in this final rule.

3. *Naphthalene*. ACC's Naphthalene Panel commented that dermal toxicity data generated under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) makes the [proposed] test rule unnecessary [with respect to naphthalene] (Ref. 34). The Naphthalene Panel comments summarize four unpublished studies submitted under FIFRA to support the registration of naphthalene (CAS No. 91-20-3) as an active ingredient in moth repellants. One study reports the simulated amount of naphthalene that would be deposited on the hands of a homeowner handling mothballs. However, the study did not simulate occupational exposure and a dermal absorption rate was not measured. The other three studies were toxicity investigations in which the test compound was topically applied to animals, but none of the studies measured the rate of absorption. The toxicity endpoints examined (mortality, body/organ weights, hematology, gross tissue examination, skin lesions) related to only dermal irritation or advanced systemic effects (Ref. 62). EPA and OSHA do not consider the data cited by the Naphthalene Panel to be sufficient to determine a dermal absorption rate. Therefore, EPA is requiring the testing of naphthalene to determine an *in vitro* dermal absorption rate in this final rule.

The Naphthalene Panel also commented that EPA's proposed test rule for certain Hazardous Air Pollutants (Ref. 48) estimated that 23,092 workers are exposed to naphthalene, yet, the proposal to this final rule estimated that 112,695 workers are exposed to naphthalene. In both proposals, EPA cited the NOES as the basis for the estimates. The Naphthalene Panel argued that neither figure is correct and that an informal survey of Naphthalene Panel members, which comprise the major manufacturers and importers of naphthalene, showed that only approximately 263 workers are potentially exposed during naphthalene manufacturing activities in the United States. The Naphthalene Panel also

argued that the NOES did not obtain information on the frequency, concentration, nor duration of worker exposure to naphthalene, and therefore EPA should not rely on the NOES to find "substantial" or "significant" worker exposure. Furthermore, although the criteria stated in EPA's "B" policy for finding "substantial" human exposure may be met (Ref. 55, p. 28746), the Naphthalene Panel believes NOES does not show worker exposure to naphthalene at levels that may cause health concerns. Moreover, the Naphthalene Panel indicated (without providing further specific information) that NOES does not reflect current workplace conditions or naphthalene exposure levels.

EPA acknowledges that different estimates for the numbers of workers exposed to naphthalene were cited in the two proposed test rules indicated by the commenter and that these estimates were both from the NOES. The estimate of 23,092 workers in the Hazardous Air Pollutants proposal (Ref. 48) was based on an interim report (Ref. 49) compiled in March of 1989. The NOES database was still being updated after that time until June 1990, when the final update was completed and trade name product resolution ceased. The estimate of 112,695 potentially exposed workers cited in the proposal to this final rule was based on the final update of the NOES. The figure is still the most up-to-date NOES information EPA has related to potential worker exposure to naphthalene, which includes employee exposure information on both manufacturing and processing sites. EPA considered the results of the Naphthalene Panel's survey of its members which found that 263 workers were potentially exposed at their manufacturing sites. However, that number does not include an estimate of the number of employees potentially exposed to naphthalene at processing sites.

As stated in Unit III.B.1.a., it is EPA's belief that the "substantial" human exposure finding in TSCA section 4(a)(1)(B)(i)(II) was intended to address situations in which large numbers of people, in this instance, large numbers of workers, may be potentially exposed to a chemical substance. EPA is not required to make a finding that a chemical substance would pose an unreasonable risk of injury at some hypothetical level of toxicity and exposure in order to require testing under TSCA section 4(a)(1)(B). See *Chemical Manufacturers Association v. EPA*, 899 F.2d 344, 354-55 (5th Cir. 1990). EPA has made the necessary findings under TSCA section 4(a)(1)(B),

and EPA is therefore requiring the testing of naphthalene to determine an *in vitro* dermal absorption rate in this final rule.

4. *Biphenyl*. The Biphenyl Work Group (BWG) commented that biphenyl (CAS No. 92-52-4) currently has two primary uses. Both uses are in closed systems either as a chemical intermediate or as a component of thermal fluids in highly specialized, closed industrial heat transfer systems (Ref. 20). The BWG states that previous industrial uses of biphenyl in fruit wrappings and as a dye carrier have been phased out. Therefore they state that any exposure to biphenyl is unlikely. The BWG asserts that only very low airborne exposures of biphenyl are found in manufacturing facilities and facilities using heat transfer fluids. They state that, with reference to the biphenyl occupational exposure limit of 200 parts per billion (ppb) (29 CFR 1910.1000(a), Table Z-1), occupational airborne exposures are very low. The BWG estimated that at present, no more than 100 workers are involved in U.S. biphenyl production (including maintenance and laboratory personnel) and fewer than 100 workers have potential dermal exposure in heat transfer uses.

EPA reviewed the BWG's estimate of number of workers exposed to biphenyl, but did not agree that the information provided sufficient basis to conclude that there are not substantial numbers of workers potentially exposed to biphenyl (Ref. 67). Although EPA requested the BWG to provide documentation for its estimate of the number of workers exposed to biphenyl, EPA did not receive any further information from the BWG to support its estimate. Absent specific data indicating otherwise, EPA believes the NOES database should be used to estimate worker exposure because it is the most recent and comprehensive source of this kind of information. Therefore, EPA is requiring the testing of biphenyl to determine an *in vitro* dermal absorption rate.

5. *p-Xylene, pentane, nonane, and n-heptane*. The Hydrocarbon Solvents Panel states that EPA should be able to reliably determine dermal absorption rates for untested members of a chemical category by comparing the logarithms of their octanol-water partition coefficients (log  $K_{OW}$ ) to those of structurally similar category members which have data on dermal absorption rates (Ref. 37).

The Hydrocarbon Solvents Panel did not provide sufficient detail to evaluate its case for a category approach with these four chemicals. The Hydrocarbon Solvents Panel also did not provide any

data, nor is EPA aware of any data, which would provide EPA with a reliable estimate of the dermal absorption rate for *p*-xylene, pentane, nonane, and *n*-heptane. Therefore, EPA is requiring testing of *p*-xylene, pentane, nonane, and *n*-heptane.

6. *p-Dichlorobenzene and chlorobenzene*. The Chlorobenzene Producers Association cited a number of acute dermal toxicity studies for *p*-dichlorobenzene (CAS No. 106-46-7) and chlorobenzene (CAS No. 108-90-7) to support its position that testing of these chemicals is unnecessary (Ref. 31). In addition, the Association cited EPA's *Dermal Exposure Assessment: Principles and Applications* (Ref. 42), which described calculated Kps for chlorobenzene and *p*-dichlorobenzene.

EPA disagrees with the comment that testing chlorobenzene and *p*-dichlorobenzene is unnecessary because existing data on dermal toxicity or calculated Kp values are sufficient to reasonably predict the human health effects of dermal exposure to these chemicals. None of the studies cited by the Chlorobenzene Producers Association for chlorobenzene or *p*-dichlorobenzene specifically measure the dermal absorption rate of these chemicals or provide data by which dermal absorption rate can be determined. The Kp values cited in the 1992 EPA Dermal Exposure Assessment Report for the two chemicals are estimated from empirical models and not experimental data and, therefore, do not meet OSHA needs. Therefore, EPA is requiring testing of chlorobenzene and *p*-dichlorobenzene to determine an *in vitro* dermal absorption rate.

7. *Tetrahydrofuran*. THFTF commented that quantitative dermal absorption data for tetrahydrofuran (CAS No. 109-99-9) are not needed by OSHA to establish its skin designations because OSHA has established skin designations in the past without such data. THFTF also commented that "current MSDS warnings and product stewardship efforts" are adequately protective against harmful dermal exposure to tetrahydrofuran in the workplace (Ref. 32).

OSHA's current skin designations (29 CFR 1910.1000, Table Z-1) were originally recommendations made by the Threshold Limit Value (TLV) Committee of the American Conference of Governmental Industrial Hygienists (ACGIH) in 1970 or prior to 1970, and adopted without reservation by OSHA in 1971. It is true that OSHA was able to set the original "skin designations" without quantitative dermal absorption data. However, OSHA currently believes that now and in the future when a skin

designation is included in a standard that limits occupational exposure, it should be supported by a scientific determination of the ability or speed of the substance to be absorbed through the skin after dermal contact. Because methods are now available to provide this information for human skin, OSHA is seeking such testing.

Regarding "current MSDS warnings and product stewardship efforts," EPA agrees with THFTF that these vehicles have been important in reducing worker exposures, but they are only as good as the scientific data on which they are based. To ensure that the exposure limits endorsed by MSDSs are sufficiently protective, dermal absorption rate information is needed to better understand the contribution to total exposure from the dermal route.

8. *Dipropylene glycol methyl ether*. ACC's Propylene Glycol Ethers Panel cited a number of acute, subacute, and subchronic toxicity studies on dipropylene glycol methyl ether (CAS No. 34590-94-8), including studies via the dermal route, to support the position that testing this chemical is unnecessary (Ref. 35). None of the studies described in the Panel's comments specifically measure the dermal absorption rate of dipropylene glycol methyl ether nor can dermal absorption rates be derived from the data provided in those studies (Ref. 64). Therefore, EPA is requiring testing of dipropylene glycol methyl ether to determine an *in vitro* dermal absorption rate.

#### G. Laboratory Capacity

API and THFTF commented that EPA should consider ongoing demands for laboratory services. API noted that government and industry are currently involved in many testing projects, including the voluntary HPV Challenge Program (Ref. 51). API suggested that EPA evaluate laboratory capacity and the combined demand that multiple testing programs will create. Likewise, THFTF warned of the possibility that available laboratory expertise will be overwhelmed by the testing required in this final rule.

In specifying the *in vitro* dermal absorption rate test standard for this rulemaking, EPA concluded that the test standard uses labor and materials efficiently and can be performed in the manner described by a variety of laboratories. The Agency has conducted, in addition to the analysis (Ref. 52) described in the proposal to this rulemaking (Ref. 5), two more recent studies (Refs. 46 and 53) of laboratory capacity associated with its other chemical testing programs. These two studies provided further support to

EPA's belief that there is sufficient laboratory capacity to accommodate the testing which is required by this final rule.

The testing required under this rulemaking is not very complicated. The *in vitro* tests are of short duration, generally taking no longer than 24 hours to complete. The Agency has provided test sponsors with 13 months to complete the requirements established under this final rule. EPA does not believe that the relatively modest amount of new testing required (a total of three tests on each of 34 chemicals) will exceed the available laboratory capacity, particularly given the short-term nature of the testing, the relatively low cost of the tests, and the long time period allowed for completing the studies. Furthermore, based on the analyses developed by EPA (Refs. 46, 52, and 53), EPA does not believe the cumulative impacts associated with a variety of its existing chemical testing programs is likely to overwhelm the available laboratory expertise as suggested by API and THFTF.

#### H. Export Notification

Several issues raised in comments relate to EPA's implementation of TSCA section 12(b) (15 U.S.C. 2611(b)) export notification requirements for chemicals for which the submission of data is required under TSCA section 4. Section 12(b) of TSCA states, in part, that any person who exports or intends to export to a foreign country a chemical substance or mixture for which the submission of data is required under TSCA section 4 must notify the EPA Administrator of such export or intent to export. The Administrator in turn will notify the government of the importing country of EPA's regulatory action with respect to the substance. EPA's regulations implementing TSCA section 12(b) are at 40 CFR part 707, subpart D.

As a general matter, comments on the scope of EPA's regulations under TSCA section 12(b) are beyond the scope of this rulemaking. However, three comments associated with the requirements under TSCA section 12(b) do merit some discussion in this preamble.

1. *Application to chemical in any form*. ACC commented that EPA's statement in its proposed rule that export notification requirements would apply to exporters of the chemical substances subject to the final rule regardless of the form (e.g., byproduct, impurity) in which they are exported constitutes an unprecedented expansion of the TSCA section 12(b) notification requirements.

EPA disagrees with this comment. TSCA section 12(b) and the implementing regulations at 40 CFR part 707 apply, in part, to the export or intended export of a chemical substance for which the submission of data is required under TSCA section 4. Neither the statutory nor the regulatory language restricts this requirement to exporters of chemical substances and mixtures in particular forms, but instead generally extends export notification requirements to exporters of chemical substances and mixtures without regard to the form in which the chemical substances and mixtures are being or will be exported. The language in the proposed rule and in this final rule are not an expansion of the TSCA section 12(b) notification requirements. It is noted, however, that the Agency did not intend to change the current export notification provisions affecting articles which specify that no export notification is required for articles, except polychlorinated biphenyl articles, unless required in specific section 5, 6, or 7 rules. See 40 CFR 707.60(b).

2. *Exporters subject to notification requirement*. ACC states that TSCA section 12(b) limits the imposition of export notification requirements related to TSCA section 4 actions to persons who actually have testing obligations under TSCA section 4. EPA disagrees. TSCA section 12(b)(1) and the implementing regulations at 40 CFR part 707, subpart D apply to any person who "exports or intends to export to a foreign country a chemical substance or mixture for which the submission of data is required under [TSCA section 4]." (15 U.S.C. 2611(b)(1)). Under 40 CFR 707.65(a)(2)(ii), exporters must notify EPA of their first export or intended export to a particular country when data are required under TSCA section 4. EPA believes the language unambiguously requires notification of export by exporters of substances which are the subject of TSCA section 4 actions regardless of whether the exporters themselves are also subject to the underlying TSCA section 4 rules. Thus, exporters of a chemical substance that is covered by data submission requirements under TSCA section 4, including persons who are not otherwise subject to the TSCA section 4 rule itself as manufacturers and/or processors, are subject to export notification requirements under TSCA section 12(b).

3. *Information collection request (ICR)*. API suggests that, because this final rule will result in the requirement that export notifications are submitted to EPA for exports or intended exports

of the substances covered by the final rule, this is a new information collection activity that requires OMB review (Ref. 19). Furthermore, API believes that EPA's cost estimates for TSCA section 12(b) notification ignores the biggest costs associated with export notification, which are the internal training and systems necessary to identify exports against the export notification list, tracking of what notifications have already been submitted and to what countries, and so forth. These system costs are magnified when business operations change (e.g., sales, acquisitions, and so forth) and export notification systems need to be adjusted accordingly.

EPA disagrees that this action is a new collection of information requiring OMB review. The information collection activities related to export notification under TSCA section 12(b)(1) are approved under OMB control number 2070-0030 (EPA ICR No. 0795). The methodologies, assumptions, and estimates developed by EPA for implementation of TSCA section 12(b) have been reviewed under notice and comment procedures during the development of the ICR. EPA believes it would be more appropriate to address API's burden concerns in the context of the ICR renewal process and therefore will not respond to them in the context of this final rule.

#### *I. Persons Required to Test*

EPA stated in the proposed rule that manufacturers and processors of the chemical substances included in the final rule would be subject to the final rule. As in the past, under the procedures set forth at 40 CFR part 790, the persons subject to the final rule fall into one of two groups, designated here as Tier 1 and Tier 2. Persons in Tier 1 (those who would initially have to comply with the final rule) would be obligated either to: 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 final rule) would not need to take any action unless they are notified by EPA that they are required to do so. Persons in Tier 1 who obtain exemptions and persons in Tier 2 would nonetheless be subject to providing reimbursement to persons who actually conduct the testing.

Under 40 CFR part 790, EPA traditionally has treated the following persons as being in Tier 2 in TSCA section 4(a) test rules:

- 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)).

- Manufacturers of small quantities for research and development ("Research and Development (R&D) manufacturers") (40 CFR 790.42(a)(5)).

In the proposed test rule, EPA reconfigured the tiers in 40 CFR 790.42 by adding 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 also proposed that persons who do not know or cannot reasonably ascertain that they are manufacturing or processing the chemical substances included in the final rule would not be subject to the final rule.

EPA's proposed approach to the "persons required to test" portion of this test rule was intended to clarify subject entities' obligations under the final rule and focus the testing requirements initially on those entities whom EPA believes would be most likely to conduct testing (Ref. 5, pp. 31080-31082). EPA solicited comment on this new approach to the "persons required to test" portion of the test rule, and received a number of comments. After considering these comments, EPA has decided to finalize the approach as proposed, with the addition of provisions related to the "subtiering" of Tier 2 entities (see Ref. 5, pp. 31081-31082, and Unit III.I.3.).

1. *General agreement with EPA's "persons required to test" approach.* All the commenters on the new approach to the "persons required to test" section of the proposed rule agreed that manufacturers of byproducts and impurities and processors are appropriately placed in Tier 2. These commenters also agreed that the persons EPA has put in Tier 1 are appropriately placed in Tier 1. API stated that the approach in the proposed rule "appropriately focuses the rule, will reduce burden and complexity, and will facilitate timely accomplishment of testing." API also agreed with the Agency's rationales for tiering. AFPA stated that the new "persons required to test" approach would provide greater certainty to people about what they must do under the final rule.

ACC/O and ACC/KO additionally agreed with the inclusion of manufacturers of components of Class 2 substances in Tier 2. API agreed with the exclusion of manufacturers or processors who do not know or cannot reasonably ascertain that they are

manufacturing or processing a test rule substance.

2. *EPA should retain the ability to move Tier 2 groups to Tier 1.* AFPA, ACC/O, and ACC commented that EPA should retain the flexibility to move Tier 2 groups to Tier 1 on a case-by-case basis. For example, if certain processing activities cause special risks, then processors could be brought into Tier 1 upfront in the proposed rule. If case-specific justifications exist for moving Tier 2 entities to Tier 1, EPA should state these justifications publicly.

EPA agrees that the Agency should retain the ability to elevate Tier 2 entities to Tier 1 on a case-specific basis in future test rules, and where the Agency takes such an action, it will state its justification(s) for doing so. For example, if EPA is able to determine that a chemical is manufactured solely or primarily in the form of a byproduct, EPA may propose to include persons who manufacture that chemical as a byproduct in Tier 1, even though byproduct manufacturers of other chemicals listed in the same proposed rule might otherwise be included in Tier 2. EPA does not agree, however, that risk should be a basis for moving entities from Tier 2 to Tier 1 (see Unit III.I.4.).

EPA will continue to retain flexibility over the status of entities covered by Tier 2 consistent with EPA's flexibility over the narrower group of entities that have been included in Tier 2 in previous test rules; processors, small-quantity manufacturers (i.e., manufacturers of less than 500 kg (1,100 lbs.) of a test rule chemical), and R&D manufacturers (40 CFR 790.42(a)(2), (a)(4), and (a)(5), respectively). In the final rule which established the general Tier 2 status of small-quantity and R&D manufacturers and processors in test rules, EPA stated that it "reserves the right to differ from the general procedure in this final rule by proposing in a specific TSCA section 4 test rule to require R&D manufacturers and/or small-quantity manufacturers to submit exemption applications" (Ref. 69, p. 18882). EPA will also continue to retain the ability to elevate, on a case-specific basis, R&D manufacturers, small-quantity manufacturers, and processors, from Tier 2 to Tier 1. The concept that flexibility can be built into test rules in general is suggested by 40 CFR 790.2, which states in part that "the procedures for test rules are applicable to each test rule in part 799 of this chapter unless otherwise stated in specific test rules in part 799 of this chapter."

The Agency does not intend to specifically identify all individual Tier

2 entities. Rather, these entities would self-identify via the submission of letters of intent to test or exemption applications. EPA expects that, similar to the arrangements typically developed when Tier 1 entities are under an obligation to conduct testing, if Tier 2 entities are required to conduct testing, it would generally be to their benefit to reach agreement on who will actually conduct the testing. The Agency believes that it is unlikely that Tier 2 entities will be required to conduct testing under this final test rule, a view that is shared by ACC which stated that:

[ACC] is not aware of any substance covered by the testing proposal for which there is likely to be no Tier 1 producer who comes forward [to conduct testing]. Indeed, ACC is not aware of any instance in the past where not a single person initially required to comply with a test rule came forward, such that EPA was required to notify other persons of their obligations under the test rule.

EPA intends to follow the procedures laid out in the regulatory text if it becomes necessary for EPA to call upon persons in Tier 2 to conduct testing. In other words, if EPA does not receive a letter of intent to test from any Tier 1 entities, the Agency will publish a **Federal Register** notice to alert Tier 2 entities to the requirement that they submit letters of intent to test or exemption applications.

3. *Do not subdivide Tier 2 as a general matter, instead subdivide Tier 2 on a case-by-case basis.* In the proposed rule, EPA solicited comments on subdividing Tier 2 to enable the Agency to prioritize which persons in Tier 2 would be required to perform testing, if needed. ACC and API suggested that EPA should not subdivide Tier 2 entities as a general matter, for all test rules. They commented that, if EPA considers requiring Tier 2 entities to conduct testing, the Agency should first determine whether in fact there are no Tier 1 entities, and reevaluate whether the proposed testing is still necessary. If Tier 1 manufacturers do not conduct testing and the testing is still necessary, then EPA should identify upfront which persons in Tier 2 will be required to test. ACC suggests that subtiering the Tier 2 entities could be done on a case-by-case basis as needed, based on the activities that give rise to the need for testing. API argues that there is no basis for distinguishing processors from the various types of manufacturers included in Tier 2, therefore there is no justification for subtiering the Tier 2 entities.

Despite these comments, and although EPA does not anticipate a need for Tier 2 entities to conduct testing

under this final rule, EPA has decided to subdivide the Tier 2 entities upfront in this final rule (see Unit V.E.3.e.). Subdividing Tier 2 upfront in test rules may facilitate compliance by requiring Tier 2 manufacturers, when required to comply, to submit letters of intent to test or exemption applications before processors are called upon to do so. The Agency's expectation is that it may generally be less administratively complex for manufacturers to conduct the testing (including coordinating efforts to determine who will actually conduct testing) than for processors to do so. This is because there are generally fewer manufacturers (even as byproducts, impurities, etc.) than processors. EPA also believes that testing costs have traditionally been passed by manufacturers along to processors, and has not received evidence to the contrary. The Agency does not believe at this time that it can justify a subdivision of Tier 2 entities other than between Tier 2 manufacturers and processors. For example, EPA does not believe it would be appropriate to base a subdivision on the activities that give rise to the need for testing (see, e.g., Unit III.I.7.).

4. *Persons who solely manufacture and/or process non-isolated intermediates or naturally occurring substances should not be subject to rules under TSCA section 4.* Commenters provided several reasons for completely exempting these manufacturers from test rule coverage. Certain commenters believe that these entities have never been covered by test rules in the past, and were specifically excluded under the amended proposed rule for hazardous air pollutant (HAP) chemicals (Ref. 70). These commenters pointed out that non-isolated intermediates are exempt from Premanufacture Notification (PMN), the Inventory Update Rule (IUR), PAIR, and general TSCA section 8(a) requirements. One commenter indicated that production of non-isolated intermediates does not contribute to the need for testing or present the same concerns as do other substances introduced into commerce, thus manufacturers of non-isolated intermediates should not be considered subject to test rules. Another commenter suggested that EPA has discretion under TSCA section 4 to specify the classes of persons subject to or exempt from a test rule based on its rationale for requiring testing. The comments suggest, however, that where EPA has case-specific justification(s) (for example, chemical-specific hazard or exposure concerns related to the manufacture of

non-isolated intermediates or naturally occurring substances are demonstrated), these categories of manufacturers could be appropriately included as subject to a rule.

EPA does not believe that it would be appropriate to fully exempt manufacturers and processors of non-isolated intermediates and naturally occurring substances from rules under TSCA section 4. Instead, it is generally appropriate to include such entities as persons subject to TSCA section 4 test rules because they are considered manufacturers and processors under TSCA and should be included among those responsible for conducting testing or providing fair and equitable reimbursement to those who have conducted testing. As a general matter, however, EPA intends to place manufacturers of non-isolated intermediates and naturally occurring substances in Tier 2 in test rules unless, for example, the Agency believes such manufacturers are responsible for a disproportionate share of the production volume of a test rule substance, in which case EPA may place them in Tier 1.

The plain language of the statute indicates that testing responsibilities under TSCA section 4(b)(3)(B) are not restricted to those who manufacture or process a test rule chemical for limited uses. Nor is EPA required to demonstrate that particular types of manufacturing or processing contribute to the need for testing (i.e., that a particular type of manufacture plays a direct role in increasing risk, in the case of a rule based on a TSCA section 4(a)(1)(A) finding, or in increasing exposure, in the case of a rule based on a TSCA section 4(a)(1)(B) finding). See TSCA section 4(a). The statute indicates that if EPA finds that the effects associated with manufacture, distribution in commerce, processing, use, or disposal cannot reasonably be determined or predicted (see TSCA section 4(a)(1)(A)(ii) and 4(a)(1)(B)(ii)), then manufacturers and/or processors are generally required to test (see TSCA section 4(b)(3)(B)). For example, the final TSCA section 4 rule for biphenyl (Ref. 77, pp. 37184–37185) stated that TSCA section 4 testing responsibilities are not restricted to only those who manufacture or process a test rule chemical for certain uses. Rather, the persons who manufacture and/or process (depending on the findings made) a test rule chemical are generally subject to the requirements of a final test rule.

In order to ensure that reimbursement of the entity(ies) conducting testing is equitable, as a general matter, EPA does

not believe that it is appropriate for classes of entities otherwise potentially subject to a rule to be dropped from all rule-related obligations (with the exception of persons who do not know or cannot reasonably ascertain that they manufacture or process a test rule substance). There may be circumstances, not present here, when it would be equitable to exempt additional entities from all test rule obligations, but that determination would need to be made on a case-by-case basis.

Persons who solely manufacture a chemical in the form of a non-isolated intermediate are generally exempt from the TSCA section 5 PMN regulations (40 CFR 720.30(h)(8)), the TSCA section 8(a) IUR (40 CFR 710.30(c)), the TSCA section 8(a) PAIR (40 CFR 712.25(d)(2)), and the general TSCA section 8(a) regulations (40 CFR 704.5(d)) for reasons particular to those regulations. However, this does not preclude EPA from treating these persons as manufacturers of chemical substances for purposes of other provisions of TSCA, including TSCA section 4. For example, EPA has stated that:

chemical substances [which are not intentionally removed from the equipment in which they were manufactured] are considered to be manufactured or processed for a commercial purpose for the purposes of section 8 of the Act. (Ref. 71, p. 64588).

EPA believes it is generally appropriate to include manufacturers of non-isolated intermediates and naturally occurring substances as persons subject to TSCA section 4 test rules in order to ensure that reimbursement of those who paid the costs of testing is equitable. TSCA section 4(c)(3)(A) requires EPA to order "fair and equitable" reimbursement for test costs under the Agency's reimbursement regulations. Consistent with this purpose, EPA's current "persons required to test" approach distributes the burden of testing and reimbursement equitably among the persons who manufacture and/or process test rule substances, with an exemption for persons who do not know or cannot reasonably ascertain that they manufacture or process a test rule substance.

Even if it were relevant to the question of who is subject to a TSCA section 4 test rule, EPA disagrees with the assertion that the manufacture of non-isolated intermediates does not present any exposure-related concerns. While the amount of chemical substance released as a result of this type of production may generally be expected to be less than is released as a result of other production, manufacturing or

processing a chemical as an intermediate does not preclude exposure to that chemical. See Office of Solid Waste final test rule (Ref. 72, p. 22305). The production of non-isolated intermediates presents concerns related to acute exposures, from, e.g., spills, leaks or transfers. In addition, as EPA stated in the test rule for Office of Solid Waste chemicals:

It is common experience that process waste streams and reactor vessel residues will contain "intermediates." In many instances, these chemicals are released to the environment as fugitive emissions, liquid or solid wastes, and as unreacted feedstock (impurities) in finished products. As such, "intermediates" typically exist as chemicals to which there is potential for human exposure. (Ref. 72, p. 22305).

EPA believes that, although a person's manufacture of a chemical in the form of a non-isolated intermediate may provide a lesser exposure concern than the manufacture by other persons of the same chemical in other forms, an appropriate accounting of responsibility is provided for in the determination of fair and equitable reimbursement under TSCA, when necessary. TSCA section 4(c)(3)(A) states that "all relevant factors" must be considered by EPA in the promulgation of rules for the determination of reimbursement. Pursuant to this provision, EPA established mechanisms in its general reimbursement rule to allow, as needed, for the case-specific consideration of factors such as exposure to a chemical as a result of each subject person's manufacturing and/or processing activities. See 40 CFR 791.40(a).

Finally, manufacturers and processors of non-isolated intermediates and naturally occurring substances have been subject to test rules in the past, except as proposed in the amended proposals for the testing of certain hazardous air pollutants (HAPs). (Ref. 73, pp. 19696, 19699 and Ref. 70, pp. 67470, 67481). EPA is not adopting the approach taken in the HAPs proposals for this final rule and, as described in Unit V.E., is taking a different position here. TSCA section 4(a) requires testing if findings have been made with regard to certain activities involving chemical substances or mixtures, and, under TSCA section 4(b)(3)(B), manufacturers and/or processors must conduct such testing if findings have been made. TSCA does not distinguish among manufacturers and processors of different forms/production types of a chemical substance or mixture; all are generally subject to the requirements of TSCA section 4.

5. "Manufacturers of test substances as components of Class 2 substances" should not be included among the persons subject to the final rule. In the proposed rule, EPA stated that manufacturers of test substances as components of Class 2 substances would be among those entities that would be subject to the final rule, but not initially required to comply (i.e., Tier 2). Class 2 substances are chemical substances having a chemical composition that cannot be represented by a specific, complete chemical structure diagram, because such a substance generally contains two or more different chemical species (not including impurities) (see 40 CFR 720.45(a)(1)(i)). The Agency received a number of comments debating the appropriateness of the proposed Tier 2 status of manufacturers of components of Class 2 substances.

a. ACC and API (Refs. 15 and 19) commented that components of Class 2 substances are not considered under TSCA to have been "manufactured" in their own right unless they have been separated from the Class 2 substance.

EPA disagrees. The Agency considers a substance to be manufactured for purposes of TSCA section 4 even if it is manufactured as a component of another chemical substance, and regardless of its isolation from other components of the combination. EPA maintains that to be regulated under a TSCA section 4 action (for which findings have been made that allow EPA to cover manufacturers), a manufacturer must be a "manufacturer" as defined by TSCA section 3, and manufacture a chemical substance (or mixture) that is subject to a test rule. Under TSCA section 3(7):

[t]he term 'manufacture' means to import into the Customs territory of the United States (as defined in general headnote 2 of the Tariff Schedules of the United States), produce, or manufacture.

There are no limitations in the definition of "manufacture" or in TSCA section 4 to suggest that if a person imports, produces, or manufactures a test rule substance as part of a complex combination of substances (i.e., a Class 2 substance), as opposed to an isolated component, then the person is not a manufacturer of that test rule substance. Therefore, EPA considers a chemical substance to be manufactured and subject to coverage under TSCA section 4 even if it is manufactured as a component of another chemical substance, and regardless of its isolation from other components of the combination.

EPA has used the term "Class 2 substance" as a way to describe variable composition substances and complex combinations of substances which can separately be considered "chemical substances" under TSCA. If a Class 2 substance is a chemical substance as defined by section 3(2)(A) of TSCA, then EPA may regulate the Class 2 substance itself. Neither the designation of a particular substance as a Class 2 substance, nor EPA's authority to regulate it as a distinct chemical substance under the Act, changes the fact that it may contain any number of individual components which may also be "chemical substances" as defined by TSCA, and therefore, also be subject to EPA's regulatory authority under the Act. See, especially, TSCA section 3(2)(A), which identifies among the set of substances that are "chemical substances":

... any organic or inorganic substance of a particular molecular identity, including any combination of such substances occurring in whole or in part as a result of a chemical reaction or occurring in nature. . .

Thus, if appropriate TSCA section 4(a)(1) findings are made with regard to manufacturing, distribution in commerce, use, and/or disposal activities for a chemical substance, then manufacturers of that substance are subject to the test rule according to TSCA section 4(b)(3), regardless of whether they manufacture the substance as a component of a Class 2 substance or in some other manner.

This is consistent with the position set forth in the proposed methylcyclopentane (MCP) and commercial hexane test rule, stating that:

... manufacturers and processors of MCP or commercial hexane who do so in the course of producing gasoline or other motor or heating fuels are subject to this rule because the Agency's . . . findings are based on the manufacture, processing, and use of MCP and commercial hexane. (Ref. 75, p. 17864-17865).

Gasoline is a Class 2 substance; commercial hexane is a Class 2 component of gasoline and MCP is one of its C<sub>6</sub> isomer components. In the final rule, EPA dropped the testing requirement for MCP, but kept the requirement for manufacturers of commercial hexane, stating that "[i]f health effects are positive for commercial hexane, then EPA may consider testing the C<sub>6</sub> components individually" (Ref. 76, pp. 3387-3388).

The Agency acknowledges that it has not explicitly required persons who manufacture test substances as components of Class 2 substances to

comply with certain test rules in the past. However, the Agency does believe that these persons are manufacturers for purposes of TSCA section 4, and hence are subject to test rules where appropriate findings are made under TSCA sections 4(a)(1) and in accordance with TSCA section 4(b)(3).

b. ACC (Ref. 15) commented that EPA should clarify that it will continue to treat Class 2 substances as distinct chemical substances (with components that are not regulated under the PMN and other TSCA regulations) regardless of the "persons required to test" approaches taken in the OSHA dermal and HAPs proposed rules.

The approach to the identification of "persons required to test" that is being adopted in this final test rule, and which may be applied in other, future test rules, is not intended to modify the status of any chemical substance or entity under other existing TSCA regulations.

c. API (Ref. 19) commented that Tier 2 should include "manufacturers of Class 2 substances that contain a test rule substance" rather than "manufacturers of components of Class 2 substances."

EPA disagrees with this suggested change, and has not implemented it in this final rule. The Agency believes it has the authority under TSCA section 4 to regulate both manufacturers of Class 2 substances themselves (for example, by requiring the testing of a Class 2 substance by manufacturers of that Class 2 substance) and manufacturers of test substances as components of Class 2 substances (for example, by requiring the testing of a chemical substance by manufacturers that produce or import that chemical substance as a component of a Class 2 substance). In this final test rule, persons in the former group are included in Tier 1 of the grouping of persons required to test, whereas persons in the latter group are included in Tier 2.

d. API (Ref. 19) commented that manufacturers of Class 2 substances should not be considered manufacturers of the myriad components in the Class 2 substances unless they isolate a component chemical, for a number of reasons:

- Class 2 substances are distinct chemical substances that are complex and variable in composition, and the Class 2 nomenclature is accurate and useful for representing them.
- A Class 2 stream may contain a substance as a component at some times but not at others.
- Applying TSCA rules to Class 2 substances, rather than to their

individual components, does not compromise protection of human health and the environment.

- Because many components of Class 2 substances do not add commercial value to the products, manufacturers of Class 2 substances may not be aware of the presence of test rule substances as components.

As stated in Unit III.I.5.a., EPA does not agree that manufacturers of components of Class 2 substances should only be regulated under TSCA section 4 if they isolate a component substance that is subject to the test rule. TSCA section 4(b)(3)(B) generally provides the authority for the Agency to include all manufacturers and/or processors in the scope of test rules, regardless of whether they isolate a test rule substance from a Class 2 substance.

The inclusion of manufacturers of test substances as components of Class 2 substances as persons subject to this final test rule is not intended to reflect any finding, or determination on the part of EPA that there is a direct connection between a specific manufacturing activity and the potential human health and/or environmental hazards or risks that may be associated with the test rule substance. See also biphenyl final test rule (Ref. 77, pp. 37184-37185). Their inclusion as persons subject to the rule is intended to facilitate the fair and equitable distribution of burden of testing and reimbursement among the persons who manufacture and process test rule substances. For example, there may be cases where large quantities of a component of a Class 2 substance are manufactured, such that the quantity of a particular non-isolated component (that is the subject of a TSCA section 4 test rule) is far greater than the quantity of the same chemical substance manufactured in isolated form by other persons.

The concern that "because many components of Class 2 substances do not add commercial value to the products, manufacturers of Class 2 substances may not be aware of the presence of test rule substances as components" is addressed by the provision in this final test rule which exempts persons from testing obligations where their status as manufacturers or processors of a particular substance is not "known to or reasonably ascertainable by" them.

In response to the comment noting that persons may be aware of the presence of a component of a Class 2 substance in a stream at some times but not others, EPA believes that the reimbursement process under TSCA

section 4 and the implementing regulations at 40 CFR part 791 address the concern; under these provisions, if utilized, persons would be required to provide fair and equitable contributions to test costs. The circumstance of a substance that is known to be produced at only certain times and not others may be a consideration under that process.

e. API (Ref. 19) commented that requiring manufacturers of Class 2 substances to test components of Class 2 substances that are also test substances would be a departure from past regulatory practice under TSCA section 4.

EPA disagrees with the commenter's statement that requiring manufacturers of Class 2 substances to test components that are also test substances that the person manufactures would be a departure from past regulatory practice under TSCA section 4. EPA acknowledges that in general its past practice has not been to impose explicit obligations under TSCA section 4 on persons who manufacture a test substance as a component of a Class 2 substance, unless that person isolates the test substance from the Class 2 substance, although as discussed in Unit III.I.5.a., there have been exceptions.

However, EPA did not explicitly require testing by manufacturers of test substances as components of Class 2 substances in certain previous test rules in part because EPA had determined in light of comments received on the proposals that testing of the Class 2 substance itself would be more appropriate than requiring testing on the individual components of Class 2 substances. See the discussion of the commercial hexane test rule (Ref. 76) in Unit III.I.5.a. In another case, EPA declined to require testing by manufacturers of components of Class 2 substances in a final test rule because it believed that it had provided insufficient notice that such manufacturers would be subject to the test rule. See the clarification to the final test rule covering certain "Office of Water chemicals" (Ref. 78).

As discussed previously, however, TSCA sections 4(c)(3)(A) and 4(c)(4)(A) require EPA to order, where necessary, "fair and equitable" reimbursement from manufacturers and processors for test costs incurred by those who are developing, or who have submitted the required test data. EPA believes that fairness and equity can be best facilitated by including within the pool of persons from whom reimbursement can potentially be sought all persons who can be considered manufacturers or processors under TSCA, subject to narrow, clear exemptions. EPA believes

that persons who manufacture test substances as components of Class 2 substances are "manufacturers" under TSCA section 4, and generally should not be exempt from inclusion among those from whom reimbursement could potentially be sought.

6. *Create a de minimis exemption.* API suggests that EPA provide a de minimis exemption like the exemption provided in the amended proposed HAPs rules (Ref. 70, pp. 67470, 67481 and Ref. 73, pp. 19696, 19699) for manufacturers and processors who solely manufacture or process test rule chemicals in amounts less than 1% in a mixture.

EPA is not adopting this suggestion in this final rule. The final rule contains an exemption from all responsibilities associated with the final rule for persons who do not know or cannot reasonably ascertain that they manufacture or process a test rule substance. The final rule also provides Tier 2 status to manufacturers of small quantities (less than 500 kg/1,100 lb per year or solely for R&D), those who manufacture the test substance as a byproduct, impurity, naturally occurring substance, non-isolated intermediate, or component of a Class 2 substance, and all processors. With respect to manufacturers of small quantities who manufacture the test substance as a component of a Class 2 substance, the 500 kg/1,100 lb cutoff applies to the manufacture of the test substance, not the Class 2 substance. EPA believes that these provisions supply sufficient relief from test rule requirements to lower volume manufacturers and processors. These groups are still subject to reimbursement, however, and they would also potentially be subject to testing.

To the extent that persons who manufacture a test rule chemical in amounts less than 1% in a mixture are not covered by the "known to or reasonably ascertainable by" exemption, and are not otherwise included in Tier 2, they are initially required to comply with the final test rule. EPA believes that Tier 1 status is appropriate for these manufacturers, who produce or import at least 500 kg/1,100 lb of a test rule chemical each year, and who know (or who could reasonably ascertain) that they are manufacturing the chemical.

7. *In determining who is responsible for conducting testing, EPA should consider the data needs the rule is intended to fill and the role of specific manufacturing and processing activities in creating the exposure scenarios the rule is intended to evaluate.* ACC commented that under TSCA section

4(b)(3)(B), responsibility for conducting testing may be imposed on those manufacturers and/or processors engaged in activities for which EPA has determined that available data and experience are insufficient under TSCA section 4(a). Thus, EPA's approach to the "persons required to test" section in a given test rule should depend on the data needs the rule is intended to fill, and the role of the specific manufacturing and processing activities in creating the particular human or environmental exposure scenarios which the rule is intended to evaluate.

TSCA does not limit the persons subject to a test rule solely to specific classes of manufacturers and/or processors based on the data needs the rule is intended to fill, or based on the role of the specific manufacturing and processing activities in creating particular exposures. Rather, persons who manufacture and/or process (depending on the findings made) a test rule chemical are generally subject to the requirements of the test rule. TSCA section 4(b)(3)(B). See also biphenyl final test rule (Ref. 77, pp. 37184–37185), which states that testing responsibilities under TSCA section 4 are not restricted to only those who manufacture or process a test rule chemical for certain uses.

EPA agrees that certain limited exemptions for persons who would otherwise be subject to test rules may be appropriate. However, in order to fully exempt a group of persons otherwise covered by a test rule from responsibilities under the test rule, EPA's view is that there must be an adequate justification for doing so that is consistent with the intent of the statute, and that is applicable only to those persons who it is proposing to exempt, and not any others. For example, in this final rule EPA is exempting manufacturers and processors who "do not know or cannot reasonably ascertain" that they are manufacturing or processing a test rule chemical (see § 799.5115(b)(2) of the regulatory text).

Exempting individual entities or classes of entities from test rule requirements on the basis of a determination that their activities do not relate in some direct way to the data needs the rule is intended to fill or to the exposure scenarios addressed by the rule is not consistent with the intent of the statute. Such exemptions would likely result in the need for multiphase rulemaking, and may in most cases not be possible from a practical standpoint given that EPA often would not have enough information to make such determinations. In addition, exempting

certain individual entities or classes of entities from test rule requirements increases the potential that the burden of testing and reimbursement would be distributed in an inequitable manner among the persons who manufacture and process test rule substances. The Agency believes it is appropriate to generally require manufacturers and/or processors of a test rule chemical to be subject to a rule, rather than to fully exempt individual manufacturers or processors or certain classes of manufacturers or processors from test rule responsibilities.

8. *Tier 2 should not be subject to reimbursement.* AFPA, API, ACC/O, ACC/KO, and ACC commented that subjecting Tier 2 entities to reimbursement would, in large part, eliminate the benefit associated with having a tiered approach. EPA should only require Tier 2 entities to reimburse if they are required to conduct testing in the absence of testing commitments from Tier 1 entities.

EPA does not agree. In order to ensure that test sponsors have the ability to seek equitable reimbursement, Tier 2 entities are subject to reimbursement regardless of whether the entities included in Tier 1 complete the testing required under the rule. EPA addressed this issue in the context of its May 7, 1990 rule amending the testing procedural rule by adding certain groups of manufacturers to Tier 2. EPA stated the following in the final rule:

Some commenters suggested that chemicals produced solely for R&D [research and development] purposes should be excluded altogether from TSCA section 4 rules. Thus, rather than placing R&D manufacturers in a "second tier," they would not be legally subject unless specified in a particular test rule... EPA does not believe that it should grant a total exemption to R&D manufacturers. TSCA section 4 gives EPA authority to require testing of chemicals manufactured for R&D. Congress did not exempt R&D manufacturers from being subject to TSCA section 4, as in the case of [rules under] sections 5 or 8 of TSCA. In this rule, EPA has lifted the procedural burden imposed on R&D manufacturers by test rules, recognizing that test sponsors would rarely, if ever, seek reimbursement from R&D manufacturers. By maintaining legal authority over R&D manufacturers, however, EPA has reserved the right of a test sponsor to seek reimbursement from all persons legally subject to a test rule. (Ref. 69, p. 18883).

The final rule amending the testing procedural rule indicates that persons in Tier 2 are subject to the requirement to conduct testing under a test rule during the period from the effective date of the test rule to the end of the reimbursement period, but will not

generally be required to submit letters of intent to test or exemption applications unless no other manufacturer of the chemical submits a letter of intent to test (Ref. 69, p. 18882). In addition, persons in Tier 2 will be required to submit letters of intent to test or exemption applications 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 included in the test rule.

However, although Tier 2 entities are subject to providing reimbursement, EPA's experience under previous test rules has been that persons who manufacture the largest quantities of a test rule substance have generally found it to be in their best interest to develop cost-sharing arrangements (which typically do not include all persons subject to providing reimbursement) to cover the costs of testing, rather than attempting to reach an agreement regarding reimbursement among the broader group made up of all persons potentially subject to providing reimbursement, or soliciting the involvement of the Agency under the reimbursement regulations at 40 CFR part 791 in developing a reimbursement arrangement. The development of such private cost-sharing arrangements appears to avoid possible difficulties that could be associated with coordinating the larger group of all persons potentially subject to reimbursement under a test rule, and provides flexibility to the parties to the arrangement because it may take any form they choose. If the parties are unable to agree upon a cost-sharing arrangement, they may contact EPA and initiate formal reimbursement procedures under 40 CFR part 791. These procedures would include all persons subject to the rule, i.e., all entities from both Tier 1 and Tier 2.

Other comments related to the issue of reimbursement by Tier 2 entities are listed below:

a. Persons not initially required to comply with a test rule have never been required to reimburse before (ACC, ACC/O, API). EPA disagrees. Since 1990, EPA has included processors, small-quantity manufacturers (i.e., manufacturers of less than 500 kg (1,100 lbs.) of a test rule chemical), and R&D manufacturers in Tier 2 (See 40 CFR 790.42(a)(2), 40 CFR 790.42(a)(4), and 40 CFR 790.42(a)(5), respectively). As a result, for the last decade these entities have been considered subject to test rules, but not initially required to comply with the requirement that letters of intent to test or exemption applications be submitted to EPA.

Shifting groups of manufacturers and/or processors to Tier 2 does not "change the legal rights and obligations of persons subject to TSCA section 4 test rules, but would only eliminate some of the paperwork burden associated with compliance." (Ref. 69, p. 18882). In fact, persons included in Tier 2 "would still be subject to test rules (and export notification requirements as specified in TSCA section 12(b)), and would not be exempt from reimbursement claims." (Ref. 69, p. 18882).

The Agency shifted R&D and small-quantity manufacturers to Tier 2 based on its recognition that, in practice, the administrative costs of seeking reimbursement from these entities would likely exceed the reimbursement that might be gained by their participation. Therefore, the filing of exemption applications by R&D and small-quantity manufacturers serves no practical purpose (i.e., there is no need for them to self-identify by submitting exemption applications). As discussed in the proposed rule, processors were originally put in Tier 2 for another reason, i.e., manufacturers would not likely seek reimbursement directly from them, but would rather pass their costs on to processors indirectly via the market. In addition, the large numbers of processors would create administrative difficulties in making testing decisions (Ref. 5, p. 31081).

Persons who are subject to a test rule, but who are not initially required to comply with the test rule have always been potentially subject to reimbursement under the formal reimbursement procedures at 40 CFR part 791. For example, see the interim final rule amending the procedural rule at 40 CFR part 790 (Ref. 74, p. 20654), which states that, where manufacturers and processors are subject to a test rule, processors will automatically be given a conditional exemption from the requirement that letters of intent to test or exemption applications be submitted to EPA. This exemption is conditional because it would be lifted if none of the persons initially required to comply with the rule (i.e., manufacturers) submit a letter of intent to test. In addition, processors may be required to provide reimbursement directly to those sponsoring the testing.

Although Tier 2 entities are subject to reimbursement under this final test rule and have been subject under past test rules (see final rule amending the testing procedural rule at 40 CFR part 790 (Ref. 69)), EPA believes that they have not historically participated in reimbursement because other manufacturers have always created cost-

sharing arrangements that did not require their involvement.

b. Tier 1 manufacturers should be those persons who undertake the activities that, for the most part, give rise to the need for testing. As a result, they should be the only ones responsible for reimbursement. EPA should identify upfront in a rule the persons whose activities warrant their contribution to the cost of testing. All of these persons should be included in Tier 1, and reimbursement should only apply to those Tier 1 persons (unless EPA has to resort to requiring entities in Tier 2 to submit letters of intent to test/exemption applications, and then Tier 2 would have to reimburse also) (API). Entities in Tier 1 that obtain an exemption in lieu of testing should generally be the only persons responsible for reimbursing. EPA should retain flexibility to impose costs on Tier 2 entities when circumstances warrant (ACC, ACC/O).

Under TSCA section 4(b)(3)(B), once EPA has made the requisite regulatory findings with respect to a chemical, "each person" who manufactures (or intends to manufacture) and/or processes (or intends to process) the chemical "shall" be required to conduct tests and submit data. Tier 2 entities have "automatic conditional exemptions" from the requirement that they conduct testing (see § 799.5115(c)(3) of the regulatory text). TSCA sections 4(c)(3) and 4(c)(4) indicate that persons granted exemptions from the requirement that testing be conducted and data submitted may be required to reimburse the costs of testing under reimbursement regulations promulgated by the Agency if the persons subject to the rule do not otherwise agree on the amount and method of reimbursement. As a result, although EPA initially exempts Tier 2 entities from requirements associated with testing and the submission of data, these entities are not exempt from the requirement that they reimburse the costs of testing.

EPA does not believe TSCA provides flexibility to impose reimbursement obligations on Tier 2 entities only when it makes a determination that the circumstances warrant it, or based on determinations as to whether particular manufacturers/processors or specific groups of such entities undertake activities that relate directly to the rationale for requiring testing. TSCA section 4 indicates that testing responsibilities are not restricted to those who manufacture or process a test rule chemical in certain forms (such as restricting the requirements of the rule only to Tier 1 entities). Rather, persons

who manufacture and/or process (depending on the findings made) a test rule chemical are generally subject to the requirements of a final test rule. TSCA section 4(b)(3)(B). See also biphenyl final test rule (Ref. 77, pp. 37184–37185). EPA has created an exception to this general approach solely for persons who do not know or who cannot reasonably ascertain that they manufacture and/or process a test rule chemical.

c. Reimbursement requirements should only apply to persons who may be required to conduct tests and submit data, i.e., Tier 1 (ACC).

All persons included in either Tier 1 or Tier 2 may be required to reimburse the costs of testing because all manufacturers and processors of the chemical substances included in this final test rule are subject to the final test rule. As the reimbursement regulations (promulgated pursuant to TSCA section 4(c)(3)(A)) provide: "[p]ersons subject to a test rule have an obligation ... either to test or to obtain an exemption and pay reimbursement" (40 CFR 791.2(a)). Tier 2 entities have automatic conditional exemptions from testing requirements, as discussed earlier. Although Tier 2 entities are not as likely to be required to conduct testing as Tier 1 entities, both groups are responsible for reimbursing the person(s) who actually conduct testing.

d. EPA's proposed extension of reimbursement obligations to Tier 2 entities might complicate future efforts to conduct testing under ECAs (ACC, ACC/O).

EPA is not significantly changing the status quo with regard to reimbursement obligations established under previous TSCA section 4 regulations. Persons in Tier 2 under previous test rules have been subject to providing reimbursement. See the final rule amending the testing procedural rule at 40 CFR part 790 (Ref. 69). The primary effect of the approach to "persons required to test" that was proposed and is being adopted in this final rule is to better focus the set of persons included in Tier 1, and to expand and clarify the set of persons included in Tier 2. EPA is unaware of any reason to believe that this approach to "persons required to test" will make it more difficult to develop ECAs.

e. EPA has said that manufacturers of impurities, byproducts, and components of Class 2 substances have not historically participated in testing or reimbursement. This is true of all other entities included in Tier 2 under this final rule. Extending reimbursement to Tier 2 disregards this experience (ACC, ACC/O).

EPA agrees that manufacturers of impurities, byproducts, components of Class 2 substances, and all other entities included in Tier 2 under this final rule have probably not historically participated in testing or reimbursement. However, the likely reason they have not participated is because the costs of testing under test rules promulgated to date have been contributed to by a smaller group of entities subject to the rule (the larger manufacturers of each test rule substance), without the need for EPA's involvement. EPA anticipates that similar cost-sharing arrangements would continue to occur under this final rule and other rules using this revised approach to "persons required to test," as they offer significant advantages to the persons subject to the rule. If EPA were to become involved in reimbursement via the reimbursement procedures at 40 CFR part 791, then all Tier 1 and Tier 2 manufacturers and processors would be included in those proceedings.

9. EPA should clarify that the approaches to the "persons required to test" sections in the OSHA dermal and HAPs proposed rules will not affect the applicability of requirements under TSCA programs outside those implementing TSCA section 4. ACC/O and ACC commented that where a particular group (e.g., manufacturers of non-commercial byproducts) is currently exempt under certain TSCA regulations, it should continue to be exempt under those regulations regardless of the "persons required to test" approach taken in test rules under TSCA section 4.

The approach the Agency takes in the "persons required to test" portion of any given test rule is not intended to affect the status of persons under regulations other than those relevant to the given test rule.

#### J. Economic Impact Analysis

API noted that EPA's Economic Impact Analysis estimates administrative costs only for companies initially required to comply with the final test rule (companies in Tier 1). API believes that this analysis is inappropriate if EPA pursues imposing reimbursement obligations on Tier 2 entities. If reimbursement obligations are imposed on Tier 2 companies, API asserts there will be associated administrative, negotiation, and other costs that EPA should include in its analysis.

EPA disagrees with this comment. Although Tier 2 entities are subject to reimbursement, EPA's experience under past test rules has been that Tier 1

persons have found it to be in their best interest to develop cost-sharing arrangements among themselves to cover the cost of testing. The development of such private cost-sharing arrangements appears to avoid possible difficulties that could be associated with coordinating a larger group of persons subject to reimbursement under a test rule, and provides maximum flexibility to the parties to the arrangement. Because manufacturers in Tier 1 have been identified for each subject chemical (see discussion of economic analysis in Unit VIII. (Ref. 57)), EPA expects that at least one such person will comply with the testing requirements. EPA is not aware of any circumstances in which Tier 1 entities have sought reimbursement from Tier 2 entities either through private agreements or by soliciting the involvement of the Agency under the reimbursement regulations at 40 CFR part 791. Given this consistent experience with previous TSCA testing actions, EPA does not believe that there will be any administrative, negotiation, or any other costs associated with seeking reimbursement from Tier 2 companies.

#### K. Definition of Small Business

In the preamble of the proposal to this rule (Ref. 5), EPA requested comment on whether the Agency should establish an alternative 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.

SOCMA commented that the most appropriate definition to use in conducting small entity analyses for TSCA section 4(a) test rules is the employee-based definition established by the U.S. Small Business Administration (SBA), which for most industries classifies firms as small based on the number of employees in the firm. The SBA set the numerical threshold for what is considered small on an industry-by-industry basis. SOCMA believes that this definition provides EPA with a straightforward and appropriate distinction between small and large companies that are closely related to a company's total annual sales. SOCMA also commented that it does not believe that an alternative approach, such as the small business definition from TSCA section 8 would be appropriate for conducting impact analyses for TSCA section 4(a) test rules. However, SOCMA believes if EPA were to pursue a sales volume-based definition of "small business," an appropriate level would be, at a

minimum, a total annual sales of \$100 million.

EPA did use SBA's size criteria, which SOCMA stated it prefers, in its economic analysis for this final rule. Based on the SBA definitions, EPA has concluded that there are no significant impacts on small entities (Ref. 57). Regarding SOCMA's second comment, EPA notes that SOCMA did not provide its reasoning as to why it considers a definition of small business based on a combination of revenue and production volume inappropriate, nor did it provide any research or justification as to why an appropriate level of annual sales used in such a definition should be set at a minimum of \$100 million.

As a more general matter, EPA disagrees with SOCMA's position that the SBA small business size standards are the most appropriate to use in analyzing the impacts of TSCA section 4 testing rules. The Regulatory Flexibility Act (RFA) of 1980, as amended by the Small Business Regulatory Enforcement Act (SBREFA) of 1996, requires that special consideration be given to small businesses affected by proposed Federal regulations. The SBA size standards, which are primarily intended to determine whether a business entity is eligible for 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. Section 601(3) of 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 for each industrial sector using an employment threshold that entities in that sector may not exceed to be classified as small. (13 CFR 121.201). RFA recognizes that it may be appropriate at times to use an alternate definition of small business for the purpose of analyzing potential regulatory impacts. As such, section 601(3) of RFA 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.

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 incurring significant costs or burdens.

Therefore, EPA is currently determining what levels 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. EPA may propose, following conclusion of its analysis, that an alternative definition based on sales be established in accordance with section 601(3) of the RFA.

#### IV. Findings

##### A. What is the Basis for EPA's Final Rule to Test These Chemical Substances?

As indicated in Unit II.B., in order to promulgate a rule under TSCA section 4(a) requiring testing of chemical substances or mixtures, EPA must make certain findings for those chemical substances or mixtures regarding either hazard (TSCA section 4(a)(1)(A)(i)); or exposure (TSCA section 4(a)(1)(B)(i)). EPA is requiring testing of the chemical substances included in this final 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). The chemical substances included in this final rule are listed in § 799.5115(j) of the regulatory text along with their CAS numbers.

In EPA's policy for making findings under TSCA section 4(a)(1)(B)(i) (i.e., the "B" policy), "substantial production" of a chemical substance or mixture is generally interpreted to be aggregate production (including import) volume equaling or exceeding one million pounds per year (Ref. 55, p. 28746). The general "B" policy threshold for "substantial human exposure" of workers is the exposure of 1,000 workers annually to a chemical substance or mixture (Ref. 55, p. 28746). See EPA's "B" policy (Ref. 55) for further discussion on how EPA generally makes decisions under TSCA section 4(a)(1)(B)(i).

EPA finds that, under TSCA section 4(a)(1)(B)(i), each of the 34 chemical substances included in this final rule is produced in "substantial quantities" and there is or may be "substantial human exposure" to each chemical substance (Ref. 56). 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 manufacture, processing, or use of these chemical substances, or of any combination of such activities, on human health or the environment. In particular, as discussed

in Unit IV.D., EPA has determined that there are insufficient *in vitro* dermal absorption rate data on these chemicals. EPA also finds that testing of the 34 chemical substances is necessary to develop such data (TSCA section 4(a)(1)(B)(iii)) (see Unit IV.E.). EPA has not identified any “additional factors” as discussed in the “B” policy (Ref. 55, p. 28746) to cause the Agency to use decision making criteria other than the general thresholds described in the policy with respect to the chemicals included in this final rule.

#### *B. Are These Chemical Substances Produced and/or Imported in Substantial Quantities?*

Each of the chemical substances included in this final rule is produced and/or imported in an amount equal to or greater than one million pounds per year (Ref. 57), based on information gathered pursuant to the 2002 TSCA section 8(a) IUR (40 CFR part 710). The IUR is the most recently available compilation of TSCA Inventory data, and is contained in the TSCA Chemical Update System. 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) (Ref. 55).

#### *C. Are a Substantial Number of Workers Exposed to These Chemicals?*

EPA finds that the manufacture, processing, and use of the chemical substances included in this action result or may result in exposure to a substantial number of workers. These chemical substances are used in a wide variety of industrial applications which result in potential exposures to workers, as described in the exposure support document for this final rule (Ref. 56).

EPA defines human exposure as the contact with a chemical or agent at the visible exterior of a person (i.e., skin and openings into the body such as mouth and nostrils) (Ref. 58, p. 22891). Worker exposure is the human exposure to a chemical or agent that occurs while a person is working. Worker exposure may have various causes, with chemical releases being a common cause of exposure. Chemical manufacturing and processing plants can release chemicals from pumps as fugitive emissions, from reactor and condenser vents as stack emissions, in the form of a vapor and/or as a particulate. Diffusion and air currents may carry a chemical throughout the plant and workers may breathe air containing the chemical, resulting in exposures. Certain human activities such as manually transferring a chemical from one container to another may also cause exposures.

Each of the chemicals in this final rule was identified in the NOES as having a total worker exposure of 1,000 workers or more (Ref. 56). EPA believes that an exposure of 1,000 workers or more to a chemical substance is or may be “substantial” as that term is used with reference to “human exposure” in TSCA section 4(a)(1)(B)(i) (Ref. 55).

#### *D. Do Sufficient Data Exist for These Chemical Substances?*

As discussed in this preamble, dermal absorption rate is an important factor in ascertaining the health effects of the 34 chemicals in this final rule. EPA has determined that for the 34 chemicals for which *in vitro* dermal absorption rate testing is required under this final rule, there is either no dermal absorption rate information available or where there is some information, these data are insufficient to estimate dermal absorption rate. Therefore, existing data are insufficient to reasonably determine or predict the human health effects that may result from dermal exposures to the chemical substances included in this final rule during the 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 II.A.

#### *E. Is Testing Necessary for These Chemical Substances?*

EPA believes that the testing of these 34 subject chemical substances is necessary to determine if the manufacturing, processing, or use of these chemical substances may present an unreasonable risk of injury to human health. In particular, the testing required by this final rule will provide dermal absorption rate data which OSHA can consider together with toxicity data to evaluate the need for skin designations which are used to protect against potential health risks associated with exposures to these chemicals in the workplace. See Unit III.B.3. for a detailed description of this and other data needs that will be filled by the testing required by this final rule.

### **V. Final Rule**

#### *A. What Testing is Required by this Action?*

EPA is specifying testing and reporting requirements for the chemical substances listed in Table 2 in § 799.5115(j) of the regulatory text according to the *in vitro* dermal absorption rate test standard set forth in § 799.5115(h) of the regulatory text.

The test standard that will be used under this final rule was refined as described in Unit III.B. of the proposed rule (Ref. 5). In addition, certain modifications which added flexibility to the test standard have been made in response to comments submitted to EPA and addressed in Unit III.E.2. of this final rule.

#### *B. When Will the Testing Imposed by this Final Rule Begin?*

Once this final rule is effective, which will be 30 days after its publication in the **Federal Register**, the required testing must be initiated at a time sufficient to allow the final report to be submitted by the deadline indicated in § 799.5115(i) of the regulatory text, i.e., 13 months after the effective date of the final rule.

#### *C. How Must the Studies Required Under this Test Rule be Conducted?*

Persons required to comply with this final rule must conduct the necessary testing in accordance with the testing and reporting requirements described in the regulatory text, and with the TSCA Good Laboratory Practice Standards (GLPS) (40 CFR part 792). Clarification was provided in the test standard concerning how data should be reported. The clarification indicates that means and standard deviations must be used when reporting the required determinations. Although the test standard in the proposed rule would have required three separate determinations for each chemical (i.e., one each for Kp, 10-minute, and 60-minute short-term dermal absorption rates), reporting each as a mean and standard deviation was not specified. However, good scientific practice would suggest that the determinations be reported in this way, and EPA believes that this clarification does not substantively change the reporting requirements or their burden and costs (Ref. 57).

#### *D. What Substances Will be Tested Under this Final Rule?*

The “Class 1” chemical substances listed in Table 2 in § 799.5115(j) of the regulatory text (i.e., 32 of the 34 chemical substances included in this final rule) must be tested at a purity of at least 99%. The term Class 1 chemical substance refers to a chemical substance having a chemical composition that consists of a single chemical species (not including impurities) that can be represented by a specific, complete structure diagram. In those instances in which the test sponsor(s) believes that a 99% level of purity is unattainable for a given chemical, the sponsor may

request a modification under the procedures described in 40 CFR 790.55.

For the "Class 2" chemical substances listed in Table 2 in § 799.5115(j) of the regulatory text (i.e., 2 of the 34 chemical substances included in this final rule), EPA is requiring that the substance to be tested be any representative form of the chemical substance.

In providing a different approach for identifying the substance to be tested with regard to Class 2 substances, EPA recognizes two characteristics which further distinguish Class 2 from Class 1 chemical substances. First, unlike Class 1 substances, knowledge of the composition of commercial Class 2 substances can vary in quality and specificity from substance to substance. The composition of the chemical species which comprise a Class 2 substance may be:

- Well characterized in terms of molecular formulae, structural diagrams, and compositional percentages of all species present (for example, methyl phenol);
- Less well-characterized, for example, characterized only by molecular formulae, nonspecific structural diagrams, and/or by incomplete or unknown compositional percentages of the species present (for example C<sub>12</sub>-C<sub>14</sub> tert-alkyl amines); or
- Poorly characterized because all that is known is the identity of only some of the chemical species present and their percentages of composition, or of only the feedstock and method used to manufacture the substance (for example, nut shell liquors of cashews).

Second, the composition of some Class 2 substances may vary from one manufacturer to another, or, for a single manufacturer, from production run to production run, because of small variations in feedstock, manufacturing methods, or other production variables. A "Class 2" designation most frequently applies to a substance consisting of a combination of different chemical species that are either structurally similar or related by being formed together when a certain chemical reaction or process is carried out on a certain chemical feedstock. Small variations in the feedstock or in chemical production methods or

conditions can account for the types of small variations in composition typically allowable within a given Class 2 Inventory listing. By contrast, a "Class 1" designation generally applies to a substance which is an individual chemical whose only variables are its impurities and byproducts.

EPA believes that, for purposes of this final rule which would require the determination of a Kp and two *in vitro* short-term dermal absorption rates, the testing of any representative form of a subject Class 2 substance would be relevant to a determination of whether the chemical substance would or would not present an unreasonable risk to human health. However, EPA would encourage the selection of representative forms of the test substances that meet industry or consensus standards, where they exist. In accordance with TSCA GLPS at 40 CFR part 792, the final study report must include test substance identification information, including name, CAS No., strength, purity, and composition, or other appropriate characteristics. (See 40 CFR 792.185).

#### *E. Am I Required to Test Under this Final Rule?*

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

1. *Am I subject to this final rule?* You are subject to this final 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 Table 2 in § 799.5115(j) of the regulatory text during the time period discussed in Unit V.E.2. 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 an unreasonable burden), you are not subject to the final rule for that listed substance.

2. *When will my manufacture or processing (or my intent to do so) cause me to be subject to this final rule?* You are subject to this final rule if you manufacture or process, or intend to manufacture or process, a substance listed in Table 2 in § 799.5115(j) of the regulatory text at any time from the effective date of the final test rule to the end of the test cost 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.E.4.).

3. *Will I be required to test if I am subject to the final rule?* It depends on the nature of your activities. All persons who are subject to this TSCA section 4(a) test rule, which, unless otherwise noted in the regulatory text, incorporates EPA's generic procedures applicable to TSCA section 4(a) test rules (contained within 40 CFR part 790), fall into one of two groups, designated here as Tier 1 and Tier 2. Persons in Tier 1 (those who must initially comply with the final 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 do not have to initially comply with the final rule) need not take any action unless they are notified by EPA that they are required to do so, as described in Unit V.E.3.d. Note that persons in Tier 1 who obtain exemptions and persons in Tier 2 are nonetheless subject to providing reimbursement to persons who actually conduct the testing, as described in Unit V.E.4.

a. *Who is in Tier 1 and Tier 2?* All persons subject to this final rule are 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 1.—PERSONS SUBJECT TO THE FINAL RULE: PERSONS IN TIER 1 AND TIER 2

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

b. *When is it appropriate for a person required to comply with the rule 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)). You can find procedures relating to exemptions in 40 CFR 790.80 through 790.99, and § 799.5115(c)(2), (c)(5), (c)(7), and (c)(11) of the regulatory text. In this final rule, EPA will not require the submission of 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. Therefore, 40 CFR 790.82(e)(1) and 40 CFR 790.85 do not apply to this final test rule.

c. *What will happen if I submit an exemption application?* EPA believes that requiring the collection of duplicative data is unnecessarily burdensome. As a result, if EPA receives a letter of intent to test from another source or has received (or expects to receive) the test data that are required under this final rule, the Agency will conditionally approve your exemption application under 40 CFR 790.87. The Agency will terminate conditional exemptions if a problem occurs with the initiation, conduct, or completion of the required testing, or with the submission of the required data to EPA. EPA may then require you to submit a letter of intent to test or an exemption application. See 40 CFR 790.93 and § 799.5115(c)(10) of the regulatory text. Persons who obtain exemptions or receive them automatically will nonetheless be subject to providing reimbursement to persons who actually conduct the testing, as described in Unit V.E.4.

d. *What are my obligations if I am in Tier 2?* If you are in Tier 2, you are

subject to the final rule and you are responsible for providing reimbursement to persons in Tier 1, as described in Unit V.E.4. You are considered to have an automatic conditional exemption. You do not need to submit a letter of intent to test or an exemption application 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 letter of intent to test or an exemption application. See 40 CFR 790.93 and § 799.5115(c)(10) of the regulatory text. In addition, you will need to submit a letter of intent to test or an exemption application if:

- No manufacturer in Tier 1 has notified EPA of its intent to conduct testing.
- EPA has published a **Federal Register** document directing persons in Tier 2 to submit to EPA letters of intent to conduct testing or exemption applications. (See § 799.5115(c)(4), (c)(5), (c)(6), and (c)(7) of the regulatory text.)

The Agency will 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 final rule.

e. *Subdivision of Tier 2 entities.* In the proposed rule that preceded this final rule, EPA solicited comment on the issue of whether the Agency should prioritize which persons in Tier 2 would be required to perform testing, if needed (Ref. 5, p. 31082). Specifically, the Agency suggested that it could subdivide Tier 2 entities into:

- *Tier 2A.* Tier 2 manufacturers, i.e., 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.

- *Tier 2B.* Tier 2 processors, i.e., those who process, or intend to process, a test rule substance (in any form). The terms "process" and "processor" are defined by TSCA section 3(10) and (11), respectively.

After consideration of comments received by the Agency (see Unit III.I.3.), EPA has decided that it will subdivide Tier 2 in the suggested manner, and the final rule regulatory text is structured to reflect this. If the Agency needs testing from persons in Tier 2, EPA will seek testing from persons in Tier 2A before proceeding to Tier 2B. It is appropriate to require manufacturers in Tier 2A to submit letters of intent to test or exemption applications before processors are called upon because the Agency believes that testing costs are traditionally passed by manufacturers along to processors, enabling them to share in the costs of testing (Ref. 74, p. 20654). In addition, "[t]here are [typically] so many processors [of a given test rule chemical] 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" (Ref. 79, p. 31789).

f. *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 test rules in 40 CFR part 790. For the purposes of this final rule, EPA is setting forth certain requirements

that differ from those under 40 CFR part 790.

In this 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 rule. EPA believes that those persons in Tier 1 who will conduct testing under this final rule will 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 historically have not themselves participated in testing or contributed to the reimbursement of those persons who have conducted testing. EPA understands that these manufacturers 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 disproportionate to the additional benefits of including these persons in Tier 1. Therefore, EPA does not believe that the likelihood of the persons who are being added to Tier 2 actually conducting 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, are subject to reimbursement obligations to persons who actually conduct the testing, as described in Unit V.E.4.

TSCA section 4(b)(3)(B) 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 final rule, e.g., manufacturers or processors of the substances as trace contaminants who

are not aware of these activities, are not subject to the final rule. (See Unit V.E.1. and § 799.5115(b)(2) of the regulatory text.)

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.
- 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 final rule, amounts manufactured as impurities will 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).

#### *F. What are the Reporting Requirements Under this Final Rule?*

A final report must be submitted for each chemical 13 months after the effective date of the final rule, i.e., by the deadline indicated in § 799.5115(i) of the regulatory text. Although EPA originally proposed a deadline of 9 months after the effective date, EPA extended the reporting deadline to 13 months after the effective date in response to public comments. (See Unit III.E.2.f.) EPA is not requiring the submission of interim progress reports for the *in vitro* dermal absorption rate testing required in this final rule. For the short-term studies required by this final rule, interim progress reports would likely yield little useful information. Furthermore, by not requiring interim progress reports for these short-term studies, the overall burden of the final rule will be somewhat reduced.

#### *G. What Would I Need to Do if I Cannot Complete the Testing?*

A company that submits a letter of intent to test under this final rule and that subsequently anticipates difficulties in completing the testing by the deadline may submit a request to the Agency to modify the test schedule, pursuant to 40 CFR 790.55. EPA will determine whether modification of the test schedule is appropriate, and may first seek public comment on the modification.

#### *H. Will There be Sufficient Test Facilities and Personnel to Undertake the Testing in this Test Rule?*

Various surveys of the availability of test facilities and personnel to handle the additional demand for testing services created by TSCA section 4(a) test rules indicate that available test facilities and personnel will adequately accommodate the testing specified in this final rule (Refs. 46, 52, and 53) (see also Unit III.G.).

#### *I. Might EPA Seek Further Testing of the Chemicals in this Final Rule?*

If EPA determines that it needs additional data regarding any of the chemical substances included in this final rule, the Agency might seek further health and/or environmental effects testing for these chemical substances. Should the Agency decide to seek such additional testing, EPA would initiate a separate action under TSCA section 4 for that purpose.

## **VI. Export Notification**

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

## **VII. Decision to Terminate Rulemaking**

EPA is withdrawing the *in vitro* dermal absorption rate testing proposed on June 9, 1999 (64 FR 31074) for 13 chemicals: Ethyl ether, isobutyl alcohol, *sec*-butyl alcohol, *o*-dichlorobenzene, *p*-nitrotoluene, *beta*-chloroprene, *n*-amyl acetate, *N*-isopropylaniline, *o*-dinitrobenzene, ethyl bromide, *o*-chlorotoluene, disulfiram, and *N,N*-dimethylaniline. The rationale for the decision to withdraw this proposed testing is presented in this unit.

#### *A. Ethyl Ether*

DEPA commented that ethyl ether (CAS No. 60-29-7) should be removed from the rule, in part, because dermal

absorption rate data had previously been developed and because the high volatility of ethyl ether would not allow a dermal absorption rate to be adequately determined under the proposed standard (Ref. 21).

EPA and OSHA have reviewed the dermal absorption rate study by Blank et al., 1967 (*Journal of Investigative Dermatology*, 49:582–589), submitted by DEPA as an attachment to its comments (Ref. 21). The study measured a Kp for an aqueous solution of ethyl ether through a human abdominal epidermal membrane using an *in vitro* static diffusion cell. Barrier function was maintained as verified by measuring penetration of tritiated water. Most other experimental parameters conformed with the standard proposed by EPA for determining an *in vitro* dermal absorption rate. A sensitive gas chromatographic method was used to analyze the receptor fluid in place of radiolabeled compound. It is unclear whether absorption was determined under occluded or unoccluded conditions, but the Kp values are close to theoretical calculations, indicating that ethyl ether evaporation likely did not confound absorption measurements under these experimental conditions. Skin penetration of the neat liquid was not reported, but EPA and OSHA believe this can be estimated using the aqueous Kp value and data on water solubility and liquid density. Therefore, EPA and OSHA believe that this study provides sufficient data for an adequate determination of the dermal absorption rate information sought in this rulemaking and testing of ethyl ether is not required at this time (Ref. 62).

#### B. Isobutyl Alcohol and Sec-Butyl Alcohol

ACC, in its comment proposing a category approach when testing chemical substances to determine *in vitro* dermal absorption rates, noted that in its suggested aliphatic alcohol category, three of the four possible isomers for butyl alcohol were included in the proposed rule (Ref. 15). ACC stated that given their same molecular weight and functionality, and taking into consideration the likelihood of there being existing dermal absorption rate data for other three-, four-, and five-carbon alcohols, evaluating the three isomers using a structure activity relationship (SAR) approach would appear reasonable, in lieu of testing these chemicals under this rule.

The three butyl alcohols referred to by ACC are isobutyl alcohol (CAS No. 78–83–1), *sec*-butyl alcohol (CAS No. 78–92–2), and *tert*-butyl alcohol (CAS No. 75–65–0). The first two were included

in the proposed rule. The third substance, *tert*-butyl alcohol was cited in the proposed rule (Ref. 5) as a chemical substance that was removed from the test list as a result of a 1998 study. The fourth butyl alcohol, not included in the proposed test rule, is *n*-butyl alcohol (CAS No. 71–36–3) which the ITC found to have sufficient dermal absorption rate data.

EPA agrees with ACC that sufficient data on *in vitro* dermal absorption rates have been generated on three, four, and five carbon aliphatic alcohols to adequately predict Kps for isobutyl alcohol and *sec*-butyl alcohol (Ref. 62). *In vitro* dermal absorption rates and Kps using human skin have already been measured for a series of homologous two [ethanol], three [propanol], four [*n*-butanol], and five [pentanol] carbon aliphatic alcohols (Ref. 65). This provides adequate structure activity information to predict the dermal absorption rates for the closely related branched chain alcohols, isobutyl alcohol and *sec*-butyl alcohol, with reasonable accuracy. Therefore, EPA is not requiring the testing of isobutyl alcohol and *sec*-butyl alcohol under this final rule.

#### C. *o*-Dichlorobenzene

The Chlorobenzene Producers Association cited two documents to support its position that testing of *o*-dichlorobenzene (CAS No. 95–50–1) is unnecessary (Ref. 31). The Association cited EPA's *Dermal Exposure Assessment: Principles and Applications* (Ref. 42), which described a calculated Kp for *o*-dichlorobenzene. The Association also noted that a study conducted at the North Carolina State University at Raleigh entitled *Percutaneous Absorption of Volatile Compounds* (Ref. 50) analyzed the relative absorption and penetration of *o*-dichlorobenzene on the skin surface in the context of evaluating volatile organic compounds.

The Kp value for *o*-dichlorobenzene cited in the 1992 EPA Report on dermal exposure assessment is estimated from empirical models rather than experimental data and, therefore, does not meet OSHA needs. However, the data developed for *o*-dichlorobenzene in the context of evaluating percutaneous absorption of volatile organic compounds does provide a measure of the dermal absorption rate of *o*-dichlorobenzene. Therefore, testing of *o*-dichlorobenzene is not required in this final rule.

#### D. *p*-Nitrotoluene

First Chemical Corporation provided EPA with biological monitoring

information (Ref. 17a.), toxicity studies (Ref. 17b.), and specific information on the numbers of workers exposed to *p*-nitrotoluene (CAS No. 99–99–0) (Ref. 17). First Chemical Corporation concluded from the submitted information that *p*-nitrotoluene does not present a significant hazard from dermal contact and proposed that this chemical be removed from the test list. One study (Ref. 17a.) discussed biological monitoring in workers but did not measure dermal absorption. An acute toxicity study with short-term dermal administration to experimental animals was negative (Ref. 17b.). This study also did not attempt to measure dermal absorption, and, therefore is not adequate to eliminate the testing requirement. A submission under section 8(d) of TSCA “found no evidence of skin absorption when a dermal dose of 1.0 g/kg was applied to rabbits” (Ref. 17) but further review by EPA finds no mention of the methodology or data that support this statement in the submission. EPA does not consider the data cited by First Chemical Corporation to be sufficient to determine a dermal absorption rate for *p*-nitrotoluene (Ref. 62).

First Chemical Corporation also submitted data relevant to EPA's finding of substantial human exposure. First Chemical Corporation is the only domestic manufacturer of *p*-nitrotoluene and accounts for the vast majority of the total quantity on the U.S. market. The company provided information on handling procedures, onsite operations, and a summary of the number of workers with potential exposure to the chemical. This summary was based on a survey of onsite operations and inquiries to each offsite company known to handle *p*-nitrotoluene. EPA has reviewed these data and agrees with First Chemical Corporation that the number of workers exposed to *p*-nitrotoluene at its facilities and those of its customers (processors) do not meet the general worker threshold for substantial human exposure that EPA has established to require testing under TSCA section 4(a)(1)(B). EPA has also reviewed the information submitted in response to the TSCA section 8(a) PAIR for *p*-nitrotoluene (Ref. 8). PAIR information for 1994 revealed that another company in the *p*-nitrotoluene market did not use *p*-nitrotoluene in its processes, sell it to its customers, or report any worker exposure, thus making the number of exposed workers reported by First Chemical Corp. the total of the reported worker exposures in the United States. Therefore, EPA is

not requiring testing of *p*-nitrotoluene under this final rule.

#### E. *beta*-Chloroprene

DuPont Dow Elastomers (DDE) provided EPA with specific information on production and worker exposure to *beta*-chloroprene (CAS No. 126-99-8) during production and use (Ref. 24). According to DDE, domestic production of *beta*-chloroprene occurs only at DDE's facility in LaPlace, Louisiana. DDE also states that no *beta*-chloroprene is imported. DDE acknowledges that *beta*-chloroprene is manufactured in quantities in excess of one million pounds per year which satisfies the "substantial production" TSCA section 4(a)(1)(B) finding. However, the company maintains that the number of workers exposed to *beta*-chloroprene does not meet the general "substantial human exposure" TSCA section 4(a)(1)(B) finding.

According to DDE, more than 90% of *beta*-chloroprene produced annually is used for the production of dry polychloroprene. Most of the remaining *beta*-chloroprene is used to produce polychloroprene latex, a colloidal suspension of polychloroprene in water. A small portion is used to manufacture a comonomer, subsequently incorporated in polychloroprene polymerization. DDE states that polymer manufacture is the only commercial use of *beta*-chloroprene. From its sole *beta*-chloroprene production facility in Louisiana, DDE produces *beta*-chloroprene monomer to supply its polychloroprene manufacturing operations. DDE, the only domestic producer of *beta*-chloroprene or polychloroprene, handles *beta*-chloroprene at only two of its facilities and the total number of DDE employees at these sites is approximately 500. DDE states that the actual number of the workers exposed via the dermal route is significantly less than the total number of DDE employees at the two facilities that manufacture or handle *beta*-chloroprene. DDE has determined that the total number of workers potentially exposed to *beta*-chloroprene vapor is less than 200. Due to the nature of the *beta*-chloroprene and polychloroprene manufacturing processes, the number of workers with potential exposure to liquid *beta*-chloroprene is apparently significantly less than those potentially exposed to *beta*-chloroprene vapor.

EPA has reviewed the production and worker exposure information submitted by DDE and concurs with DDE in its assessment of the potential number of workers exposed to *beta*-chloroprene. Because the potential number of workers exposed to *beta*-chloroprene

does not appear to meet the threshold that EPA generally relies upon in making the TSCA section 4(a)(1)(B) "substantial human exposure" finding on the basis of worker exposure, testing of *beta*-chloroprene is not required under this final rule.

#### F. *n*-Amyl acetate

EPA and OSHA have reviewed a dermal absorption study for *n*-amyl acetate (CAS No. 628-63-7) submitted by Union Carbide Corporation (Ref. 47). A Kp and 6-24 hours dermal absorption rates for *n*-amyl acetate were determined. Absorption data were also collected at earlier time points of 10 minutes and 1 hour. The method used an *in vitro* static diffusion cell technique with human cadaver skin and was similar, but not identical, to the test standard for the study required in this final rule. The test substance was a mixed isomer of primary amyl acetate applied neat (65% *n*-amyl acetate) rather than as a pure compound. A sensitive (non-radiolabeled) gas chromatographic technique specific to *n*-amyl acetate was used as a detection method. The anatomical region of the skin and membrane thickness were not stated, although variability in the results and the method of epidermal membrane preparation were found to be acceptable. The receptor fluid was ethanol in water instead of the PEG solution required in the test standard for this final rule; however, it is unlikely that this influenced the results of the study because ethanol in water, as stated previously in Unit III.E.2.o.vii., is generally a suitable receptor fluid. This is the case despite the fact that under this final rule EPA is requiring the use of a PEG solution as the receptor fluid for all hydrophobic chemicals for purposes of consistency. Therefore, EPA and OSHA believe that this study provides sufficient data for an adequate determination of dermal absorption rate and further testing of *n*-amyl acetate is not required under this final rule (Ref. 64).

#### G. *N*-Isopropylaniline

Monsanto Company provided EPA with specific information on production and worker exposure to *N*-isopropylaniline (CAS No. 768-52-5) during production and use (Ref. 16). Monsanto Company stated that *N*-isopropylaniline is an intermediate in the production of the pesticide propachlor, the active ingredient in Ramrod branded herbicides, and is produced and consumed at the Monsanto plant in Muscatine, Iowa. No *N*-isopropylaniline is sold or used domestically for any other purpose.

Propachlor, which was introduced on the market in 1965, is nearing the end of its commercial life cycle and production of *N*-isopropylaniline has fallen accordingly. Thus, it is anticipated that *N*-isopropylaniline will be produced in amounts far less than the Agency's general "substantial production" threshold of one million pounds per year.

Monsanto Company also provided EPA with a detailed description of the number of workers exposed to *N*-isopropylaniline during production and use. *N*-isopropylaniline is produced and consumed in enclosed systems. Monsanto Company projected a maximum of 35 workers are potentially exposed to *N*-isopropylaniline.

EPA has reviewed the production and worker exposure information submitted by Monsanto Company for *N*-isopropylaniline. EPA has confirmed, via 1998 and 2002 IUR data (see 40 CFR part 710), that manufacture (including import) of *N*-isopropylaniline is below the one million pounds per year threshold which EPA generally relies upon as "substantial production" under TSCA section 4(a)(1)(B). In addition, the potential number of workers exposed to *N*-isopropylaniline does not appear to meet the "substantial human exposure" threshold of exposure equal to or greater than 1,000 workers which EPA generally relies upon in making the TSCA section 4(a)(1)(B) "substantial human exposure" finding on the basis of worker exposure. As a result, testing of *N*-isopropylaniline is not required under this final rule.

#### H. *o*-Dinitrobenzene

EPA received no comments in response to its proposal to require that *o*-dinitrobenzene (CAS No. 528-29-0) be tested to determine an *in vitro* dermal absorption rate. In developing a finding for the final rule of "substantial production" under TSCA section 4(a)(1)(B) for this chemical, EPA found that according to 1998 IUR data (see 40 CFR part 710), *o*-dinitrobenzene is no longer produced or imported in amounts equal to or greater than one million pounds per year. The 1998 IUR data became available after the publication of the proposed rule, which made a finding for substantial production based on 1994 IUR data. Also, there were no 2002 IUR data reported for *o*-dinitrobenzene. Because the 1998 IUR data and the lack of 2002 IUR data do not support a finding of substantial production as required under TSCA section 4(a)(1)(B)(i), testing of *o*-dinitrobenzene to determine an *in vitro* absorption rate is not required at this time.

*I. Ethyl Bromide, o-Chlorotoluene, Disulfiram, and N,N-Dimethylaniline*

In developing findings for the final rule of "substantial production" under TSCA section 4(a)(1)(B) for ethyl bromide (CAS. No. 74-96-4), *o*-chlorotoluene (CAS No. 95-49-8), disulfiram (CAS No. 97-77-8), and *N,N*-dimethylaniline (CAS No. 121-69-7), EPA found that according to 2002 IUR data (see 40 CFR part 710), these four chemical substances are no longer manufactured or imported in amounts equal to or greater than one million pounds per year. Because the 2002 IUR data show manufacture (including import) below the one million pounds per year threshold which EPA generally relies upon as "substantial production" under TSCA section 4(a)(1)(B)(i), testing of ethyl bromide, *o*-chlorotoluene, disulfiram, and *N,N*-dimethylaniline to determine *in vitro* dermal absorption rates is not required at this time.

#### VIII. Economic Impacts

EPA has prepared an economic assessment entitled *Economic Impact Analysis and Small Entity Impact Analysis of the TSCA Section 4(a) Test Rule for 34 Chemicals Targeted for In Vitro Dermal Absorption Rate Testing* (Ref. 57), a copy of which has been placed in the official public docket. This economic assessment evaluates the potential for significant economic impacts as a result of the testing that would be required by this final rule. The total cost of providing test data on the 34 chemicals that were evaluated in this economic analysis is estimated to be a total of \$1.16 million for all 34 chemicals, or \$33,987 per chemical (Ref. 57).

While legally subject to this test rule, Tier 2 manufacturers and all processors of a subject chemical would only be required to comply with the requirements of the final rule if they are directed to do so by EPA as described in § 799.5115(c)(5), (c)(7) and (c)(10) of the regulatory text. EPA would require Tier 2 manufacturers or processors to test only if no Tier 1 manufacturer has submitted a letter 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 expects that, for each chemical in this final rule, at least one such person will submit a letter of intent to conduct the required testing and that person will conduct such testing and will submit the test data to EPA. EPA

believes, therefore, that there will not be any costs to Tier 2 manufacturers or processors for conducting the testing required by the final rule. In addition, as explained in Unit III.J., EPA is not aware of any circumstances in which Tier 1 entities have sought reimbursement from Tier 2 entities either through private agreements or by soliciting the involvement of the Agency under the reimbursement regulations at 40 CFR part 791. Given this consistent experience with previous test rules, EPA does not believe that there will be any administrative, negotiation, or any other costs associated with seeking reimbursement from Tier 2 companies.

To evaluate the potential for an adverse economic impact of testing on manufacturers of the chemical substances in this final rule, EPA employed a screening approach that compares the annual revenues from the sale of a chemical to the annualized testing costs for that chemical and expresses the testing costs as a percent of revenues generated from each chemical. Annualized testing costs divide testing expenditures into an equivalent, constant yearly expenditure over a longer period of time. To calculate the percent price impact, testing costs (including laboratory and administrative expenditures) are annualized over 15 years using a 7% discount rate. Annualized testing costs are then divided by the estimated annual revenue of the chemical to derive the cost-to-sales ratio.

EPA estimates the annualized cost of testing the 34 chemicals evaluated in the economic analysis to be \$3,732 per chemical or a total annualized cost of \$126,888 for all 34 chemicals (34 x \$3,732) (Ref. 57). In addition, the TSCA section 12(b) export notification that is required for the first export to a particular country of a chemical subject to the final rule, is estimated to be \$61.31 for the first time that an exporter must comply with TSCA section 12(b) export notification requirements, and \$18.07 for each subsequent export notification submitted by an exporter (Ref. 57). The Agency's estimated total costs of testing (including both laboratory and administrative costs), annualized testing costs, price impacts, and public reporting burden hours for this final rule are presented in the economic impact analysis (Ref. 57).

Price data were available for 26 of the 34 chemicals, with an average cost of \$.88 per pound for those 26 chemicals. The price impact of the test costs is a function of the chemical's price per pound and the production volume. For 21 of the 26 chemicals (80.8%) for which price data were available, the

price impact is less than 1.0% when the production volume for each chemical is assumed to be one million pounds, which is the threshold for substantial production. The average test cost impact for all 26 chemicals with price data was 0.68%. This means that the testing costs represent, on average, 0.68% of revenues generated from each chemical. The actual impacts are likely to be lower, however, because all of the subject chemicals are produced in volumes of at least one million pounds per year. With a price impact of less than 1.0%, EPA concludes that for these 21 chemicals the potential for adverse economic impacts is low.

For five of the twenty-six chemicals (19.2%) with price data, the price impact is in excess of 1.0%. The average price impact for these five chemicals is 1.96% and the maximum is 3.7%. Again, these impacts occur when the production volumes are assumed to be one million pounds. The actual impacts decline in direct proportion to a chemical's actual production volume above one million pounds. Thus, if the actual production volume is two million pounds, the impact is reduced by 50%. The Agency verified production volumes for these five chemicals based on the 2002 reports to the TSCA Chemical Update System Database, and has found that the actual production volume in each case exceeds 10 million pounds per year. Therefore, the Agency believes that the impact for all five of these chemicals is below 1.0%.

The Agency computed "critical prices" for the remaining eight chemicals for which price data were not available. The "critical price" is the price per pound below which there would be an impact of 1.0% or greater. Assuming a minimum production volume of one million pounds per year and annualized testing costs of \$3,732 per chemical, the critical price is \$0.37 per pound. Below that price, the testing costs would represent more than 1.0% of the revenues from the chemical at a one million pound production volume level. The average price for the 26 chemicals with actual price data available is \$0.88 per pound. Thus, the critical price is substantially below this average. While it cannot be shown conclusively that the price impacts will be less than or greater than 1.0% of the sales for these chemicals, the Agency believes that adverse impacts are unlikely, given that both the chemicals' prices would have to be below \$.37 per pound, and the production volume would have to meet the worst-case assumption of one million pounds per year.

On the basis of these calculations, EPA believes that the required chemical testing presents a low potential for adverse economic impact for the majority of the chemicals subject to the final rule. Because the subject chemical substances have relatively large production volumes, the annualized costs of testing, expressed as a percentage of annual revenues, are very small for most chemicals. There are, however, eight chemicals for which it cannot conclusively be shown that the price impact will be below 1.0% of the revenue for these chemicals. For these eight chemicals, companies may choose to use revenue sources other than profits from the individual chemicals to pay for testing. To account for this, the Agency also compared the costs of compliance to company sales data. These calculations were made as part of the Agency's small entity impact analysis (Ref. 57), conducted in accordance with the requirements of the Regulatory Flexibility Act, as amended by the Small Business Regulatory Enforcement Fairness Act. These results are presented in Unit X.B.

#### IX. Materials in the Docket

An official docket was established under docket ID number OPPT-2003-0006. The official public docket includes information considered by EPA in developing this final rule, such as the documents specifically referenced in this action, any public comments received, and other information related to this action. In addition, interested parties should consult documents that are referenced in the documents that EPA has placed in the docket, regardless of whether these referenced documents are physically located in the docket. For assistance in locating documents that are referenced in documents that EPA has placed in the docket, but that are not physically located in the docket, please consult one of the technical persons listed under **FOR FURTHER INFORMATION CONTACT**. The official public docket is available for review as specified in **ADDRESSES**. The following is a listing of the documents referenced in this preamble that have been placed in the official docket for this final rule:

##### A. Supporting Documentation

1. U.S. Census Bureau. Bridge between NAICS and SIC. 1997 Economic Census. Core Business Statistics Series. Issued June 2000.
2. United States Environmental Protection Agency (USEPA). Laboratory Cost Estimate for *In Vitro* Dermal Absorption Rate Testing—Short-term Absorption Rate. Prepared by Economic and Policy Analysis Branch (EPAB),

Economics, Exposure and Technology Division (EETD), OPPT. February 20, 2003.

3. USEPA. Laboratory Cost Estimate for *In Vitro* Dermal Absorption Rate Testing—Long-term Absorption Rate. Prepared by EPAB, EETD, OPPT. March 26, 2003.

4. Background information listed in § 799.5115(h)(8) of the regulatory text:
  - a. Bronaugh, R.L., Stewart, R.F., and Simon, M. Methods for *in vitro* Percutaneous Absorption Studies VII: Use of Excised Human Skin. *Journal of Pharmaceutical Sciences*. 75:1094–1097. 1986.

- b. Bronaugh, R.L. and Stewart, R.F. Methods for *in vitro* Percutaneous Absorption Studies IV: The Flow-Through Diffusion Cell. *Journal of Pharmaceutical Sciences*. 74:64–67. 1985.

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

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

- e. 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.

##### B. References

1. Interagency Testing Committee (ITC). Thirty-First Report of the TSCA Interagency Testing Committee to the Administrator; Receipt of Report, Request for Comments, Opportunity to Initiate Negotiations for TSCA Section 4 Testing Consent Agreements. **Federal Register** (58 FR 26898, May 5, 1993) (FRL-4583-4).

2. ITC. Thirty-Second Report of the TSCA Interagency Testing Committee to the Administrator; Receipt of Report, Request for Comments, Notice of Opportunity to Initiate Negotiations for TSCA section 4 Testing Consent Agreements. **Federal Register** (58 FR 38490, July 16, 1993) (FRL-4630-2).

3. ITC. Thirty-Fourth Report of the TSCA Interagency Testing Committee to the Administrator; Receipt of Report and Request for Comments. **Federal**

**Register** (59 FR 35720, July 13, 1994) (FRL-4870-4).

4. ITC. Thirty-Fifth Report of the TSCA Interagency Testing Committee to the Administrator; Receipt of Report, Request for Comments, Solicitation of Interested Parties in Developing Testing Consent Agreement. **Federal Register** (59 FR 67596, December 29, 1994) (FRL-4923-2).

5. USEPA. Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of Certain Chemicals of Interest to Occupational Safety and Health Administration. **Federal Register** (64 FR 31074, June 9, 1999) (FRL-5760-3).

6. USEPA. Preliminary Assessment Information and Health and Safety Data Reporting; Addition of Chemicals. (TSCA Sections 8(a) and 8(d) Final Rules for Chemicals contained in the ITC's 31<sup>st</sup> Report to the EPA Administrator). **Federal Register** (58 FR 68311, December 27, 1993) (FRL-4644-1).

7. USEPA. Preliminary Assessment Information and Health and Safety Data Reporting; Addition of Chemicals. (TSCA sections 8(a) and 8(d) Final Rules for Chemicals contained in the ITC's 32<sup>nd</sup> Report to the EPA Administrator). **Federal Register** (59 FR 5956, February 9, 1994) (FRL-4745-5).

8. USEPA. Preliminary Assessment Information and Health and Safety Data Reporting; Addition of Chemicals. (TSCA Sections 8(a) and 8(d) Final Rules for Chemicals contained in the ITC's 35<sup>th</sup> Report to the EPA Administrator). **Federal Register** (60 FR 34879, July 5, 1995) (FRL-4954-9).

9. USEPA. Thirty-Sixth Report of the TSCA Interagency Testing Committee to the Administrator; Receipt of Report, Request for Comments, Solicitation of Use and Exposure Data. **Federal Register** (60 FR 42982, August 17, 1995) (FRL-4965-6).

10. USEPA. Request for Proposals for Enforceable Consent Agreements; Dermal Absorption Rate Testing of Eighty OSHA Chemicals; Solicitation of Interested Parties; Text of Test Protocol. **Federal Register** (61 FR 14773, April 3, 1996) (FRL-5359-3).

11. ARCO Chemical Company. Proposal to conduct *in vivo* dermal absorption rate testing for *tert*-butyl alcohol under an enforceable consent agreement (ECA). Letter from Joan McCuen to Charles M. Auer, OPPT, USEPA. June 26, 1996.

12. ARCO Chemical Company. A letter from Joan McCuen to Keith Cronin, OPPT, USEPA transmitting a dermal absorption rate study (Ref. 12a.). March 23, 1998.

- 12a. Huntington Life Sciences Ltd., Suffolk, England. [14C]-*t*-Butyl Alcohol:

Topical Application: Dermal Absorption Study in the Male Rat; Final Report. Prepared for ARCO Chemical Company. January 7, 1998.

13. 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. Chapter 19, pp. 237-241. 1991.

14. Chemical Manufacturers Association (CMA). Comments on ITC proposal for dermal penetration testing and protocol (Ref. 14a.) proposed by CMA. Letter from Sarah Doelp to Charles M. Auer, USEPA. October 21, 1994.

14a. CMA, Existing Chemicals Testing Task Group. Proposed Protocol for *In Vitro* Percutaneous Absorption Studies. October 4, 1994.

15. ACC. Comments on EPA's TSCA section 4(a)(1)(B) Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of Certain Chemicals of Interest to OSHA submitted to the TSCA Public Docket Office, USEPA. August 10, 1999.

16. Monsanto Company. Comments on EPA's TSCA section 4(a)(1)(B) Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of Certain Chemicals of Interest to OSHA submitted to the TSCA Public Docket Office, USEPA. July 19, 1999.

17. First Chemical Company. Comments on EPA's TSCA section 4(a)(1)(B) Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of Certain Chemicals of Interest to OSHA submitted to the TSCA Public Docket Office, USEPA. August 4, 1999.

17a. Linch, A.L. Biological monitoring for industrial exposure to cyanogenic aromatic nitro and amino compounds. *American Industrial Hygiene Association Journal*. 35:426-432. 1974.

17b. Kinkead, E.R., MacEwen, J.D., Haun, C.C., Vernot, E.H., and Dacre, J.C. Toxic hazards evaluation of five atmospheric pollutants from Army ammunition plants. Prepared by University of California, Irvine for Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, OH. Report number AMRL-TR-77-25. June 1977.

18. American Forest & Paper Association. Comments on EPA's TSCA section 4(a)(1)(B) Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of Certain Chemicals of Interest to OSHA submitted to the TSCA Public Docket Office, USEPA. August 9, 1999.

19. American Petroleum Institute. Comments on EPA's TSCA section 4(a)(1)(B) Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of

Certain Chemicals of Interest to OSHA submitted to the TSCA Public Docket Office, USEPA. August 9, 1999.

20. Biphenyl Work Group, Washington, DC. Comments on EPA's TSCA section 4(a)(1)(B) Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of Certain Chemicals of Interest to OSHA submitted to the TSCA Public Docket Office, USEPA. August 6, 1999.

21. Diethyl Ether Producers Association, Inc. Comments on EPA's TSCA section 4(a)(1)(B) Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of Certain Chemicals of Interest to OSHA submitted to the TSCA Public Docket Office, USEPA. August 9, 1999.

22. Synthetic Organic Chemical Manufacturers Association, Inc. Comments on EPA's TSCA section 4(a)(1)(B) Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of Certain Chemicals of Interest to OSHA submitted to the TSCA Public Docket Office, USEPA. August 9, 1999.

23. Acetonitrile Task Force. Comments on EPA's TSCA section 4(a)(1)(B) Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of Certain Chemicals of Interest to OSHA submitted to the TSCA Public Docket Office, USEPA. August 9, 1999.

24. DuPont Dow Elastomers. Comments on EPA's TSCA section 4(a)(1)(B) Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of Certain Chemicals of Interest to OSHA submitted to the TSCA Public Docket Office, USEPA. August 9, 1999.

25. Fragranced Products Information Network. Comments on EPA's TSCA section 4(a)(1)(B) Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of Certain Chemicals of Interest to OSHA submitted to the TSCA Public Docket Office, USEPA. July 6, 1999.

26. Association of Veterinarians for Animal Rights. Comments on EPA's TSCA section 4(a)(1)(B) Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of Certain Chemicals of Interest to OSHA submitted to the TSCA Public Docket Office, USEPA. July 17, 1999.

27. People for the Ethical Treatment of Animals. Comments on EPA's TSCA section 4(a)(1)(B) Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of Certain Chemicals of Interest to OSHA submitted to the TSCA Public Docket Office, USEPA. July 30, 1999.

28. Animal Protection Institute, Midwest Regional Office. Comments on EPA's TSCA section 4(a)(1)(B) Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of Certain Chemicals of Interest to OSHA

submitted to the TSCA Public Docket Office, USEPA. August 4, 1999.

29. Humane Society of the United States. Comments on EPA's TSCA section 4(a)(1)(B) Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of Certain Chemicals of Interest to OSHA submitted to the TSCA Public Docket Office, USEPA. August 9, 1999.

30. Doris Day Animal League. Comments on EPA's TSCA section 4(a)(1)(B) Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of Certain Chemicals of Interest to OSHA submitted to the TSCA Public Docket Office, USEPA. August 9, 1999.

31. Chlorobenzene Producers Association. Comments on EPA's TSCA section 4(a)(1)(B) Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of Certain Chemicals of Interest to OSHA submitted to the TSCA Public Docket Office, USEPA. August 9, 1999.

32. Tetrahydrofuran Task Force. Comments on EPA's TSCA section 4(a)(1)(B) Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of Certain Chemicals of Interest to OSHA submitted to the TSCA Public Docket Office, USEPA. August 9, 1999.

33. Private Citizen. Comments on EPA's TSCA section 4(a)(1)(B) Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of Certain Chemicals of Interest to OSHA submitted to the TSCA Public Docket Office, USEPA. June 15, 1999.

34. ACC Naphthalene Panel. Comments on EPA's TSCA section 4(a)(1)(B) Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of Certain Chemicals of Interest to OSHA submitted to the TSCA Public Docket Office, USEPA. August 9, 1999.

35. ACC Propylene Glycol Ethers Panel. Comments on EPA's TSCA section 4(a)(1)(B) Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of Certain Chemicals of Interest to OSHA submitted to the TSCA Public Docket Office, USEPA. August 6, 1999.

36. ACC Olefins Panel. Comments on EPA's TSCA section 4(a)(1)(B) Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of Certain Chemicals of Interest to OSHA submitted to the TSCA Public Docket Office, USEPA. August 9, 1999.

37. ACC Hydrocarbon Solvents Panel. Comments on EPA's TSCA section 4(a)(1)(B) Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of Certain Chemicals of Interest to OSHA submitted to the TSCA Public Docket Office, USEPA. August 9, 1999.

38. ACC Ketones Panel and Oxo Process Panel. Comments on EPA's TSCA section 4(a)(1)(B) Proposed Test Rule for *In Vitro* Dermal Absorption

Rate Testing of Certain Chemicals of Interest to OSHA submitted to the TSCA Public Docket Office, USEPA. August 9, 1999.

39. ACC Carbon Disulfide Panel. Comments on EPA's TSCA section 4(a)(1)(B) Proposed Test Rule for *In Vitro* Dermal Absorption Rate Testing of Certain Chemicals of Interest to OSHA submitted to the TSCA Public Docket Office, USEPA. August 9, 1999.

40. Buell, D.A., Blaustein, M.B., and Lynch, J.R. An Assessment of the National Occupational Exposure Survey. Prepared by Temple, Barker & Sloane, Inc. and Exxon Corp. Undated.

41. Seta, J.A., Sundin, D.S., and Pedersen, D.H. *National Occupational Exposure Survey Field Guidelines*. National Institute for Occupational Safety and Health, Cincinnati, OH. DHHS (NIOSH) Publication No. 88-106. 1988.

42. USEPA, Office of Research and Development. *Dermal Exposure Assessment: Principles and Applications*. EPA/600/8-91/011B. January 1992.

43. USEPA. Voluntary Children's Chemical Evaluation Program. **Federal Register** (65 FR 81699, December 26, 2000) (FRL-6758-5).

44. OECD, Paris. Guidance Document for the Conduct of *In Vitro* Skin Absorption Studies. (Draft). April 1999.

45. Harrison, S.M., Barry, B.W., and Dugard, P.H. Effects of freezing on human skin permeability. *Journal of Pharmacy and Pharmacology*. 36: 261. 1984.

46. USEPA. Laboratory Capacity and the HPV Challenge Program. OPPT/EETD/EPAB, Washington, DC. October 14, 1999.

47. Union Carbide Corporation (now Dow Corporation). A letter from Dr. Imogene Treble to Frank Kover, USEPA transmitting a study entitled *Primary Amyl Acetate, Mixed Isomers: In Vitro Percutaneous Absorption Study in Human Skin*. July 5, 2000.

48. USEPA. Proposed Test Rule for Hazardous Air Pollutants. **Federal Register** (61 FR 33178, June 26, 1996) (FRL-4869-1).

49. National Institute for Occupational Safety and Health. National Occupational Exposure Survey. March 29, 1989.

50. Riviere, J.E., Brooks, J.D., Qiao, G.L., and Monteiro-Riviere, N.A. *Percutaneous Absorption of Volatile Chemicals*. Prepared by North Carolina State University, Raleigh, NC for AFSOR/NL, Bolling AFB, Washington, DC. NTIS number ADA332910. November 1997.

51. USEPA. Data Collection and Development on High Production

Volume (HPV) Chemicals. **Federal Register** (65 FR 81686, December 26, 2000) (FRL-6754-6).

52. USEPA. EPA Census of TSCA Testing Laboratories. Prepared by OPPT, EETD, EPAB, Washington, DC. October 10, 1996.

53. USEPA. Analysis of U.S. Laboratory Capacity for Developmental and Reproductive Toxicity Testing and the Impact of Expanded TSCA Test Rules. Prepared by OPPT/EETD/EPAB, Washington, DC. May 28, 1999.

54. USEPA. ChemRTK, HPV Challenge Program Chemical List. Prepared by OPPT. (This list is updated periodically, and is available electronically at <http://www.epa.gov/chemrtk/hpvchmlt.htm>)

55. USEPA. TSCA section 4(a)(1)(B) Final Statement of Policy. **Federal Register** (58 FR 28736, May 14, 1993) (FRL-4059-9).

56. USEPA. Information on OSHA Dermal Test Rule Chemicals: TRI Release Data and Number of Workers Exposed. Prepared by OPPT/EETD/Chemical Engineering Branch (CEB), Washington, DC. April 24, 2001 and March 1998.

57. USEPA. Economic Impact Analysis and Small Entity Impact Analysis of the TSCA Section 4(a) Test Rule for 34 Chemicals Targeted for *In Vitro* Dermal Absorption Rate Testing. Prepared by OPPT/EETD/EPAB, Washington, DC. February 3, 2004.

58. USEPA. Guidelines for Exposure Assessment. **Federal Register** (57 FR 22888, May 29, 1992) (FRL-4129-5).

59. Small Business Administration, Office of Size Standards. Small Business Size Standards matched to North American Industry Classification System (NAICS). On website: <http://www.sba.gov/size/sizetable2002.html>.

60. USEPA. Treatment of 12(b) Export Notification Unit Costs for section 4 Test Rule Analyses. Prepared by Lynne Blake-Hedges OPPT/EETD/EPAB, Washington, DC. April 1, 1999.

61. USEPA. Economic Analysis in Support of the TSCA 12(b) Information Collection Request. Prepared by Joseph Callahan OPPT/EETD/EPAB, Washington, DC. October 30, 1998.

62. OSHA. OSHA dermal test rule. Electronic mail from Val Schaeffer to Keith Cronin, USEPA. May 22, 2000.

63. OSHA. Dermal rule. Electronic mail from Val Schaeffer to Keith Cronin, USEPA. March 20, 2002.

64. OSHA. Dermal rule. Electronic mail from Val Schaeffer to Keith Cronin, USEPA. August 25, 2000.

65. Scheuplein, R.J. and Blank, I.H. Mechanism of percutaneous absorption. IV. Penetration of nonelectrolytes (alcohols) from aqueous solutions and

from pure liquids. *Journal of Investigative Dermatology*. 60:286-296. 1973.

66. USEPA. Wage Rates for Economic Analysis of the Toxics Release Inventory Program. Prepared by Cody Rice, Analytical Support Branch, Environmental Analysis Division, Office of Environmental Information. April 11, 2002.

67. USEPA. Review of comments received on proposed dermal absorption test rule. Memorandum from Greg Macek, CEB to Keith Cronin, Chemical Control Division. October 8, 1999.

68. USEPA. Office of Water Chemicals; Final Test Rule. **Federal Register** (58 FR 59667, November 10, 1993) (FRL-4047-2).

69. USEPA. Testing Consent Agreements and Test Rules; Final Rule. **Federal Register** (55 FR 18881, May 7, 1990) (FRL-3687-6).

70. USEPA. Amended Proposed Test Rule for Hazardous Air Pollutants; Extension of Comment Period. **Federal Register** (62 FR 67465, December 24, 1997) (FRL-5742-2).

71. USEPA. Inventory Reporting Requirements; Final Rule. **Federal Register** (42 FR 64571, December 23, 1977) (FRL-817-1).

72. USEPA. Office of Solid Waste Chemicals; Final Test Rule. **Federal Register** (53 FR 22300, June 15, 1988) (FRL-3396-8).

73. USEPA. Amended Proposed Test Rule for Hazardous Air Pollutants; Extension of Comment Period. **Federal Register** (63 FR 19694, April 21, 1998) (FRL-5780-6).

74. USEPA. Toxic Substances; Test Rule Development and Exemption Procedures. **Federal Register** (50 FR 20652, May 17, 1985) (FRL-2809-7).

75. USEPA. Methylcyclopentane and Commercial Hexane; Proposed Test Rule. **Federal Register** (51 FR 17854, May 15, 1986) (FRL-3008-8).

76. USEPA. Commercial Hexane and Methylcyclopentane; Final Test Rule. **Federal Register** (53 FR 3382, February 5, 1988) (FRL-3325-1).

77. USEPA. Toxic Substances; Biphenyl; Final Test Rule. **Federal Register** (50 FR 37182, September 12, 1985) (FRL-2871-5).

78. USEPA. Office of Water Chemicals, Final Test Rule; Clarification. **Federal Register** (59 FR 45629, September 2, 1994) (FRL-4047-2).

79. USEPA. Toxic Substances Control Act; Data Reimbursement. **Federal Register** (48 FR 31785 July 11, 1983) (FRL-2349-8).

## X. Statutory and Executive Order Reviews

### A. Paperwork Reduction Act

The information collection requirements contained in TSCA section 4 test rules have already been approved by OMB under the provisions of the Paperwork Reduction Act, 44 U.S.C. 3501 *et seq.*, and have been assigned OMB control number 2070-0033 (EPA ICR No. 1139). 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 No. 0795). This final rule does not contain any new or amended requirements that would require additional review and/or approval by OMB.

The standard chemical testing program involves the submission of letters of intent to test (or exemption applications), study plans, progress reports, and test results. EPA estimates that the information collection activities related to chemical testing for all chemicals in this final rule (representing the submission of letters of intent or exemption applications, study plans, and the final reports; progress reports are not required by this final rule because testing will be completed within about 1 year) would result in an annual public reporting burden of 165 hours per chemical or a total of 5,610 hours for the 34 chemicals (Ref. 57).

The annual public reporting burden related to export notification is estimated to be 0.5 to 1.5 burden hours for each chemical/country combination (Ref. 57). 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 (Refs. 57, 60, and 61).

For each manufacturer of the 34 chemicals identified in the economic analysis, the parent company (ultimate corporate entity, or UCE) was also identified. The economic analysis identified a total of 84 UCEs that EPA believes would be the likely respondents to the final rule. The public reporting burden for this collection of information is estimated to average 165 hours per chemical. Multiplying by 34 chemicals (34 x 165 = 5,610 hours total), and dividing by 84 UCEs, results in a per respondent estimated burden of 66.8 hours. This burden estimate includes time for reviewing instructions, searching existing data sources, gathering and maintaining the data

needed, and completing and reviewing the collection of information.

As defined by 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 which have subsequently changed; 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.

Under PRA, an agency may not conduct or sponsor, and a person is not required to respond to, an information collection request unless it displays a currently valid OMB control number. The OMB control numbers for EPA's regulations are listed in 40 CFR part 9 and included on the related collection instrument. EPA is amending the table in 40 CFR part 9 to list the OMB approval number for the information collection requirements contained in this final rule. This listing of the OMB control numbers and their subsequent codification in the CFR satisfies the display requirements of PRA and OMB's implementing regulations at 5 CFR part 1320. This ICR was previously subject to public notice and comment prior to OMB approval, and given the technical nature of the table, EPA finds that further notice and comment to amend it is unnecessary. As a result, EPA finds that there is "good cause" under section 553(b)(1)(B) of the Administrative Procedure Act, 5 U.S.C. 553(b)(1)(B), to amend this table without further notice and comment.

### B. Regulatory Flexibility Act (RFA)

Pursuant to section 605(b) of the Regulatory Flexibility Act (RFA), 5 U.S.C. 601 *et seq.*, the Agency hereby certifies that this final rule will not have a significant adverse 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 final rule (Ref. 57), and is briefly summarized here.

Three factors are examined in EPA's small entity assessment (Ref. 57) in

order to characterize the potential small entity impacts of this final rule:

- The size of the adverse impact (measured as the ratio of the cost to sales or revenue).
- The total number of small entities that experience the adverse impact.
- The percentage of the total number of small entities that experience the adverse impact.

Section 601(3) of 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 for each industry sector. (13 CFR 121.201). For this final rule, EPA has analyzed the potential small business impacts using the size standards established under this default definition. The SBA size standards, which are primarily intended to determine whether a business entity is eligible for 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. Industrial sectors are identified by a NAICS code. In most cases, SBA has specified an employee size standard (100; 500; 750; 1,000; or 1,500 employees) or, in some cases, a sales-based, or other industry-specific indicator, cut-off below which an entity in that particular NAICS code would be considered small (Ref. 59).

The SBA employee size standards that apply to most of the NAICS codes that are potentially impacted (Ref. 57) by this final rule range from 500 to 1,500 employees. Size standards for three potentially affected non-manufacturing NAICS are defined in terms of sales, and in each case the standards are \$5 million in annual sales, while the standards for the set of possible NAICS where another entity is likely to fail, are expressed in terms of electricity generating capacity (4 million megawatt hours).

Sales and employment data were obtained for the 84 UCEs that manufacture the 34 chemicals subject to this final rule to identify those UCEs that qualify for "small business" status, where data were available. Based on the SBA size standards for the NAICS codes that applied to those UCEs, 25 of the 84 UCEs (30%) were identified as small. The significance of this final rule's impact on these small businesses was analyzed by examining the number of small entities that experienced different levels of costs as a percentage of their sales. In such an analysis, small businesses are placed in the following

categories on the basis of cost-to-sales ratios: less than 1.0%, 1.0% but less than 3.0%, and 3.0% or greater. Of the 25 companies that qualified for small business status according to the SBA size standards, none had a cost-to-sales ratio that exceeded 1.0%. Given these results, EPA concludes that there is not a significant economic impact on these small entities as a result of this final rule.

There were an additional seven UCEs for which the NAICS code, sales, and employment data were not available. Because of this, EPA could not determine whether they are small businesses or assess the potential impacts of the test rule on them. However, it is very unlikely that all seven of these UCEs are small entities. Moreover, given the Agency's analysis for the identified small businesses, which concluded that there is not a significant economic impact on any of them, EPA believes it is reasonable to conclude that even if some of these seven UCEs are small entities, they will not experience a significant economic impact. Consequently, EPA concludes that there will not be a significant economic impact on a substantial number of small entities as a result of this final rule.

In analyzing potential impacts on small entities, RFA recognizes that it may be appropriate at times to use an alternate definition of small business. As such, section 601(3) of RFA 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 final rule, EPA does not believe that the SBA size standards are generally the best standards to use in assessing potential impacts of TSCA section 4(a) test rules on small entities. EPA believes that a standard based on total annual sales, such as the definition found in TSCA (40 CFR 704.3), may provide a more appropriate means to determine the ability of a chemical manufacturing firm to support testing without significant costs or burdens. EPA is 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. Therefore, as previously stated in this unit, the RFA determination for this final rule is based on an analysis using the default SBA size standards. In the proposal to

this rule, EPA requested comment on whether the Agency should establish an alternate small business definition to use in small entity impact analyses for future TSCA section 4(a) test rules, and what size cutoff may be appropriate. The comment received on this subject and the Agency's response are in Unit III.K.

Although EPA has not yet pursued the establishment of an alternate definition for use in the analysis conducted for this final rule, the analysis does present the results of calculations using a standard based on total annual sales. Under the TSCA definition at 40 CFR 704.3, a firm is classified as small if it has either total annual sales below \$40 million and annual production or importation volume less than or equal to 100,000 pounds, or, annual sales below \$4 million. Of the 84 UCEs subject to the final rule, a maximum of 9 can be classified as small under the TSCA definition, with data unavailable for an additional 7 firms. None of those 9 firms will be affected at the level of 1.0% or greater. Impacts could not be determined for the 7 firms whose size was unknown, but as with the analysis conducted using the SBA size standards, the Agency believes it is reasonable to conclude that under the referenced TSCA definition of small, the 7 UCEs will not experience significant economic impacts as a result of the final rule.

The estimated costs of the TSCA section 12(b) export notification, which, as a result of this final rule, would be required for the first export to a particular country of a chemical subject to the rule, is estimated to be \$61.31 for the first time that an exporter must comply with TSCA section 12(b) export notification requirements, and \$18.07 for each subsequent export notification submitted by that exporter (Refs. 57, 60, and 61). EPA has concluded that the costs of TSCA section 12(b) export notification would have a negligible impact on exporters of the chemicals in this final rule, regardless of the size of the exporter.

Therefore, the Agency certifies that this final rule will not have a significant adverse economic impact on a substantial number of small entities.

#### C. Unfunded Mandates Reform Act

Pursuant to Title II of the Unfunded Mandates Reform Act of 1995 (Public Law 104-4), EPA has determined that this regulatory action 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 for the private sector in any 1 year. The analysis of the costs

associated with this action are described in Unit VIII. In addition, since EPA does not have any information to indicate that any State, local, or tribal government manufactures or processes the chemicals covered by this action such that this final rule would apply directly to State, local, or tribal governments, EPA has determined that this final rule does not significantly or uniquely affect small governments. Accordingly, this final rule is not subject to the requirements of sections 202, 203, 204, and 205 of UMRA.

#### D. Executive Order 13132

Executive Order 13132, entitled *Federalism* (64 FR 43255, August 10, 1999), requires EPA to develop an accountable process to ensure "meaningful and timely input by State and local officials in the development of regulatory policies that have federalism implications." "Policies that have federalism implications" is defined in the Executive order to include regulations that have "substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government."

This final rule does not have federalism implications. It will not have substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government, as specified in Executive Order 13132. This final rule establishes testing and recordkeeping requirements that apply to manufacturers (including importers) and processors of certain chemicals. Because EPA has no information to indicate that any State or local government manufactures or processes the chemical substances covered by this action, this final rule does not apply directly to States and localities and will not affect State and local governments. Thus, Executive Order 13132 does not apply to this final rule. Although Executive Order 13132 was not yet in effect when EPA developed the proposed rule, its predecessor, Executive Order 12875, was and EPA's conclusions under Executive Order 13132 are consistent with EPA's considerations under Executive Order 12875.

#### E. Executive Order 13175

Under Executive Order 13175, entitled *Consultation and Coordination with Indian Tribal Governments* (65 FR 67249, November 6, 2000), this final rule does not have tribal implications

because it will not have substantial direct effects on tribal governments, on the relationship between the Federal Government and the Indian tribes, or on the distribution of power and responsibilities between the Federal Government and Indian tribes, as specified in the Order. As indicated above, EPA has no information to indicate that any tribal government manufactures or processes the chemical substances covered by this action. Thus, Executive Order 13175 does not apply to this final rule. Although Executive Order 13175 was not yet in effect when EPA developed the proposed rule, its predecessor, Executive Order 13084, was and EPA's conclusions under Executive Order 13175 are consistent with EPA's considerations under Executive Order 13084.

F. Executive Order 13045

This final rule does not require special consideration pursuant to the terms of Executive Order 13045, entitled Protection of Children from Environmental Health Risks and Safety Risks (62 FR 19885, April 23, 1997), because it is not likely to have an annual effect on the economy of \$100 million or more and it does not have a potential effect or impact on children. This final rule establishes testing and recordkeeping requirements that apply to manufacturers (including importers) and processors of certain chemicals, and will result in the production of information that will assist the Agency and others in determining whether the chemical substances in this final rule present potential risks, allowing the Agency and others to take appropriate action to investigate and mitigate those risks.

G. Executive Order 13211

This final rule is not a "significant energy action" as defined in Executive Order 13211, Actions Concerning Regulations That Significantly Affect Energy Supply, Distribution, or Use (66 FR 28355, May 22, 2001) because it is not likely to have a significant adverse effect on the supply, distribution, or use of energy. As such, the Agency has concluded that this final rule is not likely to have adverse energy effects.

H. National Technology Transfer and Advancement Act

As noted in the proposed rule, section 12(d) of the National Technology Transfer and Advancement Act of 1995 (NTTAA), Public Law 104-113 section 12(d) (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.

Because this final rule involves technical standards, the Agency conducted a search to identify potentially applicable voluntary consensus standards. No such standards were identified and none were brought to the Agency's attention in comments. Therefore, EPA has decided to use the in vitro dermal absorption rate test standard finalized in this document. This standard was based on the peer reviewed method of Bronaugh and Collier which was published in 1991 (Ref. 13) and refined by a panel of Federal scientists from ITC member and liaison agencies (including, for example, CPSC, DoD, EPA, FDA, NIOSH, and OSHA). The method was further refined by this panel in response to public comments.

I. Executive Order 12898

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), the Agency has considered environmental justice-related issues with regard to the potential impacts of this action on the environmental and health conditions in minority and low-income populations. The Agency believes that the information collected under this final rule will assist EPA and others in determining the hazards and risks associated with the chemicals covered by the final rule. Although not directly impacting environmental justice-related concerns, this information will better enable the Agency to protect human health and the environment.

J. Congressional Review Act

The Congressional Review Act, 5 U.S.C. 801 et seq., generally provides that before a rule may take effect, the Agency promulgating the rule must submit a rule report to each House of the Congress and the Comptroller General of the United States. EPA will submit a report containing this rule and other required information to the U.S. Senate, the U.S. House of Representatives, and the Comptroller General of the United States prior to publication of the rule in the Federal

Register. This rule is not a "major rule" as defined by 5 U.S.C. 804(2).

List of Subjects

40 CFR Part 9

Environmental protection, Reporting and recordkeeping requirements.

40 CFR Part 799

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

Dated: April 4, 2004.

Susan B. Hazen,

Acting Assistant Administrator, Office of Prevention, Pesticides and Toxic Substances.

Therefore, 40 CFR chapter I is amended as follows:

1. By amending part 9 as follows:

PART 9—[AMENDED]

a. The authority citation for part 9 continues to read as follows:

Authority: 7 U.S.C. 135 et seq., 136-136y; 15 U.S.C. 2001, 2003, 2005, 2006, 2601-2671; 21 U.S.C. 331j, 346a, 348; 31 U.S.C. 9701; 33 U.S.C. 1251 et seq., 1311, 1313d, 1314, 1318, 1321, 1326, 1330, 1342, 1344, 1345 (d) and (e), 1361; E.O. 11735, 38 FR 21243, 3 CFR, 1971-1975 Comp. p. 973; 42 U.S.C. 241, 242b, 243, 246, 300f, 300g, 300g-1, 300g-2, 300g-3, 300g-4, 300g-5, 300g-6, 300j-1, 300j-2, 300j-3, 300j-4, 300j-9, 1857 et seq., 6901-6992k, 7401-7671q, 7542, 9601-9657, 11023, 11048.

b. In § 9.1, the table is amended by adding an entry for § 799.5115 in numerical order under the indicated heading to read as follows:

§ 9.1 OMB approvals under the Paperwork Reduction Act.

40 CFR citation	OMB control No.
* * * * *	* * * * *
Identification of Specific Chemical Substance and Mixture Testing Requirements	
* * * * *	* * * * *
799.5115 .....	2070-0033
* * * * *	* * * * *

2. By amending part 799 as follows:

PART 799—[AMENDED]

a. The authority citation for part 799 continues to read as follows:

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

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

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

(2) If you do not know or cannot reasonably ascertain that you manufacture or process a chemical substance listed in Table 2 in paragraph (j) of this section during the time period described in paragraph (b)(1) of this section (based on all information in your possession or control, as well as all

information that a reasonable person similarly situated might be expected to possess, control, or know, or could obtain without an unreasonable burden), you are not subject to this section with respect to that chemical substance.

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

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

Persons initially required to comply with this section (Tier 1)	Persons not initially required to comply with this section (Tier 2)
Persons not otherwise specified in column 2 of this table that manufacture (as defined at TSCA section 3(7)) or intend to manufacture a chemical substance included in this section.	<p>A. Persons who manufacture (as defined at TSCA section 3(7)) or intend to manufacture a chemical substance included in this section solely as one or more of the following:</p> <ul style="list-style-type: none"> <li>—As a byproduct (as defined at 40 CFR 791.3(c));</li> <li>—As an impurity (as defined at 40 CFR 790.3);</li> <li>—As a naturally occurring substance (as defined at 40 CFR 710.4(b));</li> <li>—As a non-isolated intermediate (as defined at 40 CFR 704.3);</li> <li>—As a component of a Class 2 substance (as described at 40 CFR 720.45(a)(1)(i));</li> <li>—In amounts of less than 500 kilograms (kg) (1,100 lbs) annually (as described at 40 CFR 790.42(a)(4)); or</li> <li>—For research and development (as described at 40 CFR 790.42(a)(5)).</li> </ul> <p>B. Persons who process (as defined at TSCA section 3(10)) or intend to process a chemical substance included in this section (see 40 CFR 790.42(a)(2)).</p>

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

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

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

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

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

the document described in paragraph (c)(4) of this section.

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

(7) If you are in Tier 2B with respect to a chemical substance listed in Table 2 in paragraph (j) of this section, and if you process this chemical substance as of May 26, 2004, or within 30 days after publication of the **Federal Register** document described in paragraph (c)(6) of this section, you must, for each test specified for that chemical substance in the document described in paragraph (c)(6) of this section, either submit to EPA a letter of intent to test or apply to EPA for an exemption from testing. The

letter of intent to test or the exemption application must be received by EPA no later than 30 days after publication of the document described in paragraph (c)(6) of this section.

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

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

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

(11) If you are required to comply with this section, but your manufacturing or processing of a chemical substance listed in Table 2 in paragraph (j) of this section begins after the applicable compliance date referred to in paragraphs (c)(2), (c)(5), (c)(7), or (c)(10) of this section, you must either submit a letter of intent to test or apply to EPA for an exemption. The letter of intent to test or the exemption

application must be received by EPA no later than the day you begin manufacturing or processing.

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

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

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

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

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

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

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

(1) *Applicability.* This *in vitro* dermal absorption rate test standard must be used for all testing conducted under this section. In certain instances, modifications to the test standard may be considered. The procedures for

applying for a modification to the test standard are specified in 40 CFR 790.55.

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

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

(4) *Principles of the test standard.* This test standard describes procedures for measuring a permeability constant ( $K_p$ ) and two short-term dermal absorption rates for test substances in liquid form. The test standard utilizes *in vitro* diffusion cell techniques which allow absorption studies to be conducted with human cadaver skin. *In vitro* diffusion studies are necessary for measuring a  $K_p$ . This test standard specifies the use of static or flow-through diffusion cells and non-viable human cadaver skin. It also requires the use of radiolabeled test substances unless it can be demonstrated that procedures utilizing a non-radiolabeled test substance are able to measure the test substance with a sensitivity equivalent to the radiolabeled method.

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

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

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

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

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

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

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

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

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

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

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

(vi) *Vehicle.* If the test substance is a liquid at room temperature and does not damage the skin during the determination of K<sub>p</sub>, it must be applied neat. If the test substance cannot be applied neat because it is a solid at room temperature or because it damages the skin when applied neat, it must be dissolved in water. If the concentration of a hydrophobic test substance in water

is not high enough so that a steady-state absorption can be obtained, the test substance must be dissolved in isopropyl myristate. A sufficient volume of liquid must be used to completely cover the skin and provide the amount of test substance as described in paragraph (h)(5)(vii) of this section.

(vii) *Dose—(A) K<sub>p</sub>.* A K<sub>p</sub> must be determined for each test chemical. An “infinite dose” of the test substance must be applied to the skin to achieve the steady-state rate of absorption necessary for calculation of a K<sub>p</sub>. Infinite dose is defined as the concentration of a test substance required to give an undepletable reservoir on the surface of the skin. The actual concentration required to give an undepletable reservoir on the surface of the skin depends on the rate of penetration of the test substance. Preliminary studies may be necessary to determine this concentration. Percutaneous absorption must be determined under occluded (i.e., covered) conditions unless it is demonstrated that such conditions cause leakage of material or damage to the skin membrane as a result of unrealistically high pressures or excessive hydration. Skin barrier integrity must be verified at the end of the experiment by the methods discussed in paragraph (h)(5)(i)(D) of this section.

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

(viii) *Study duration—(A) K<sub>p</sub>.* The *in vitro* dermal absorption rate test must be performed until at least four absorption

measurements per diffusion cell experiment are obtained during the steady-state absorption portion of the experiment. A preliminary study may be useful to establish time points for sampling. The required absorption measurements can be accomplished in an hour or two with fast-penetrating chemicals but may require 24 hours or longer for slow-penetrating chemicals. Unabsorbed test substance need not be removed from the surface of the skin after each experiment.

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

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

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

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

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

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

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

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

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

(A) Monitoring of testing parameters.

(B) Temperature of chamber.

(C) Receptor fluid pH.

(D) Barrier property validation.

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

(iii) *Results.* The mean Kp and mean short-term absorption rates must be presented along with their standard deviations and the number of diffusion cell experiments. In addition, all raw

data from each individual diffusion cell must be retained to support the calculations of permeability constants and short-term absorption rates. When a radiolabeled test substance is used, a full balance of the radioactivity must be presented, including cell rinsing and stability of the test substance in the donor compartment.

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

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

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

(iii) Bronaugh, R.L., Stewart, R.F., and Storm, J.E. Extent of Cutaneous Metabolism During Percutaneous Absorption of Xenobiotics. *Toxicology*

and *Applied Pharmacology*. 99:534-543. 1989.

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

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

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

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

TABLE 2.—CHEMICAL SUBSTANCES DESIGNATED FOR TESTING

CAS No.	Chemical name	Class
75-05-8	Acetonitrile	1
75-15-0	Carbon disulfide	1
75-35-4	Vinylidene chloride	1
77-73-6	Dicyclopentadiene	1
77-78-1	Dimethyl sulfate	1
78-59-1	Isophorone	1
78-87-5	Propylene dichloride	1
79-20-9	Methyl acetate	1
79-46-9	2-Nitropropane	1
91-20-3	Naphthalene	1
92-52-4	Biphenyl	1
98-29-3	<i>tert</i> -Butylcatechol	1
100-00-5	<i>p</i> -Nitrochlorobenzene	1
100-01-6	<i>p</i> -Nitroaniline	1
100-44-7	Benzyl chloride	1

TABLE 2.—CHEMICAL SUBSTANCES DESIGNATED FOR TESTING—Continued

CAS No.	Chemical name	Class
106-42-3	<i>p</i> -Xylene	1
106-46-7	<i>p</i> -Dichlorobenzene	1
107-06-2	Ethylene dichloride	1
107-31-3	Methyl formate	1
108-03-2	1-Nitropropane	1
108-90-7	Chlorobenzene	1
108-93-0	Cyclohexanol	1
109-66-0	Pentane	1
109-99-9	Tetrahydrofuran	1
110-12-3	Methyl isoamyl ketone	1
111-84-2	Nonane	1
120-80-9	Catechol	1
122-39-4	Diphenylamine	1
123-42-2	Diacetone alcohol	1
127-19-5	Dimethyl acetamide	1
142-82-5	<i>n</i> -Heptane	1
150-76-5	<i>p</i> -Methoxyphenol	1
25013-15-4	Vinyl toluene	2
34590-94-8	Dipropylene glycol methyl ether	2

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

[FR Doc. 04-9409 Filed 4-23-04; 8:45 am]

BILLING CODE 6560-50-S

## ENVIRONMENTAL PROTECTION AGENCY

### 40 CFR Part 52

[CA 083-0436a; FRL-7650-4]

#### Revisions to the California State Implementation Plan, San Joaquin Valley Unified Air Pollution Control District

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

**ACTION:** Direct final rule.

**SUMMARY:** EPA is taking direct final action to approve revisions to the San Joaquin Valley Unified Air Pollution Control District (SJVUAPCD) portion of the California State Implementation Plan (SIP). The revisions concern stack monitoring, source sampling, and the emission of volatile organic compounds from bakery ovens. We are approving

local rules that are administrative or regulate this emission source under the Clean Air Act as amended in 1990 (CAA or the Act).

**DATES:** This rule is effective on June 25, 2004 without further notice, unless EPA receives adverse comments by May 26, 2004. If we receive such comments, we will publish a timely withdrawal in the **Federal Register** to notify the public that this rule will not take effect.

**ADDRESSES:** Send comments to Andy Steckel, Rulemaking Office Chief (AIR-4), U.S. Environmental Protection Agency, Region IX, 75 Hawthorne Street, San Francisco, CA 94105, or e-mail to [steckel.andrew@epa.gov](mailto:steckel.andrew@epa.gov), or submit comments at <http://www.regulations.gov>.

You can inspect a copy of the submitted rule or rule revisions and EPA's technical support document (TSD) at our Region IX office during normal business hours. You may also see a copy of the submitted rule or rule revisions and TSD at the following locations:

Environmental Protection Agency, Air Docket (6102), Ariel Rios Building,

1200 Pennsylvania Avenue, NW., Washington DC 20460  
California Air Resources Board, Stationary Source Division, Rule Evaluation Section, 1001 "I" Street, Sacramento, CA 95814

San Joaquin Valley Unified Air Pollution Control District, 1990 East Gettysburg Street, Fresno, CA 93726

A copy of the rule may also be available via the Internet at <http://www.arb.ca.gov/drdb/drdbtxt.htm>. Please be advised that this is not an EPA Web site and may not contain the same version of the rule that was submitted to EPA.

**FOR FURTHER INFORMATION CONTACT:** Al Petersen, Rulemaking Office (AIR-4), U.S. Environmental Protection Agency, Region IX, (415) 947-4118, [petersen.alfred@epa.gov](mailto:petersen.alfred@epa.gov).

**SUPPLEMENTARY INFORMATION:** Throughout this document, "we," "us" and "our" refer to EPA.

#### Table of Contents

- I. The State's Submittal
  - A. What rules did the State submit?
  - B. Are there other versions of these rules?