

Response to Public Comments

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A. Introduction

This document contains a summary of the comments received by EPA in response to the TSCA section 4 proposed test rule entitled “Testing of Certain High Production Volume chemicals” (EPA, 2000b) along with EPA’s responses to those comments. The comments are available in EPA’s public docket and e-docket for the final test rule under Docket No. OPPT-2005-0033. EPA received comments from the American Chemistry Council (ACC), American Petroleum Institute (API), Synthetic Organic Chemical Manufacturers Association (SOCMA), Center for Regulatory Effectiveness (CRE), Environmental Defense (ED), American Coke and Coal Chemicals Institute (ACCCI), Color Pigments Manufacturers Association, Inc. (CPMA), Ecological and Toxicological Association of Dyes and Organic Pigments Manufacturers (ETAD), Merisol USA LLC (Merisol), Ashland Distribution Company (Ashland), Dow Chemical Company (Dow), ExxonMobil Chemical Company (EMCC), Lonza Group, Dyno Nobel, Inc. (Dyno Nobel), Sciences International Inc.(SII), Institute of Makers of Explosives (IME), People for the Ethical Treatment of Animals (PETA), Physicians Committee for Responsible Medicine (PCRM), Doris Day Animal League (DDAL), The Humane Society of the United States (HSUS), Alternative Research & Development Foundation (ARDF), American Anti-Vivisection Society (AAVS), New England Anti-Vivisection Society (NEAVS), Silicones Environmental, Health and Safety Council (SEHSC), and numerous private citizens.

Many commenters expressed support for this test rule. ACC (ACC 2001) and SOCMA commended the Agency for its willingness to explore new and creative approaches in exercising its authority under TSCA. Although ED (ED 2001) supports the proposed test rule, it noted with concern that the proposed test rule covered only 37 chemicals (only 5% of the chemicals that were unsponsored at the time of the proposal), and that EPA would have to accelerate its efforts to develop test rules for the remaining HPV chemicals that have not been sponsored in the voluntary HPV Challenge Program to assure the availability of data on these chemicals.

ED (ED 2001), PETA, PCRM, DDAL, HSUS, and NEAVS appreciated EPA’s effort to include in the proposed test rule (EPA 2000c) the basic animal protection principles that were set forth in EPA’s October 14, 1999, letter (EPA 1999d) to the participants in the voluntary HPV Challenge Program. In addition, ACC stated it supports the principles articulated in the October 14, 1999 letter to reduce the number of test animals where possible, replace methods when acceptable alternatives are available, and refine existing methods. However, ACC believes that the single most important step in actually reducing the number of animals used is to maximize the use of existing data.

B. Use of Existing Data

Comment. ARDF commented that manufacturers must release in-house test results for the chemicals in the final test rule (EPA 2005b) rather than repeat already completed tests. ACC (ACC 2001) acknowledged that the proposal encourages companies subject to the final rule “to

make maximum use of scientifically adequate existing data” and recognizes that further testing in these cases would be unnecessary and duplicative. ACC believes that EPA should establish a scientifically grounded, weight-of-the-evidence approach that considers all types of data and information, including *in vitro*, epidemiological, non-traditional data, or other data not necessarily listed as among the SIDS data elements. ACC (ACC 2001), DDAL, and HSUS agree with EPA that, in analyzing the adequacy of existing data, companies subject to the rule should conduct thoughtful, qualitative analysis rather than use a rote checklist approach. ACC and PETA comment that the same approach should be used by EPA when evaluating existing data submitted in conjunction with rulemaking.

Response. EPA intends to make maximum use of scientifically adequate existing data. In the proposal to the final test rule, EPA urged companies to identify and make publicly available all relevant existing data, thereby avoiding unnecessary and duplicative testing as well as reducing the overall cost of testing. Also, after the rule is finalized, but prior to the initiation of testing under the rule, if the Agency receives adequate existing data that fulfill a specific data need, EPA will ensure that unnecessary testing is not required by withdrawing the portion of the rule relevant to the data need. Studies that have been conducted as specified in appropriate OECD test guidelines (as noted in the *Manual for Investigation of HPV Chemicals* (OECD 2003)) or comparable EPA test guidelines (such as the OPPTS Harmonized Guidelines available at <http://www.epa.gov/opptsfrs/home/guidelin.html> or the TSCA Test Guidelines in 40 CFR parts 795-798, and 799, subparts E and H), and appropriate Good Laboratory Practice Standards (GLPS) like those for TSCA (40 CFR part 792), consistently generate data adequate to fulfill the testing needs identified by EPA in the final test rule (EPA 2005b). Existing studies submitted in response to the proposal for the final rule were individually evaluated. Older studies that did not strictly follow the specified guidelines were not always considered adequate to satisfy the test requirements of the final rule. In evaluating submitted studies, EPA reviewers used the same guidance document on data adequacy that EPA made available on the voluntary HPV Challenge Program website (EPA 1999a) and urged participants in the voluntary HPV Challenge Program to use.

Comment. PETA, DDAL, and HSUS commented that EPA should play a more active role in obtaining existing data prior to initiating rulemaking under TSCA section 4. PETA also requested that EPA make a company’s test plans available in advance of any testing being conducted in response to the final test rule to give PETA and others the opportunity to search for existing data that matches those testing plans and thereby prevent unnecessary testing.

Response. EPA did not propose that every test in the SIDS battery be conducted for each of the 37 chemicals in the proposal. Instead, EPA identified specific tests for each chemical which EPA considered necessary to meet its data needs. In determining which tests are needed for each chemical, not only did EPA conduct a search for available existing data, but it also requested access to and utilized a data availability study conducted by ACC (ACC 1998) (See the proposed test rule (EPA 2000c) for discussion of EPA’s and ACC’s data availability studies). Concerning PETA’s request to make testing plans available in advance, EPA’s designation in the proposed

test rule of the tests and test methods to be required for each chemical is, in essence, the test plan for each chemical. At any time following the publication of the proposed test rule, the public had the opportunity to submit existing data of which it believed EPA was unaware. The public also had the opportunity during that time period to comment on the proposed tests and test methods and suggest alternatives. In general, EPA would alter tests laid out in a proposed test rule in the final test rule only if the public submitted studies that are adequate to meet the needs identified in the proposed test rule or EPA obtained newly released studies which are adequate to satisfy the data need, or EPA accepted any recommendation(s) to modify the testing requirements or test methods. For the proposed rule, EPA allowed a 120-day comment period (twice the usual 60-day comment period) to mirror the 120-day public comment period for the review of test plans under the voluntary HPV Challenge Program. EPA believes the 120-day comment period provided ample opportunity for the public to monitor whether such studies have been submitted by checking the public docket for the proposed test rule. Such studies, as with all comments on the proposed test rule, were placed in the public docket (identified under **ADDRESSES**) within a few days of receipt and are available for public viewing and copying, and are also available electronically as specified under **ADDRESSES**. The final test rule (EPA 2005b) announces whether any studies recently obtained by EPA have been found adequate to satisfy a data need and if any of the proposed testing is not being required. The final test rule (EPA 2005b) announces the final testing requirements for each chemical and its publication generally precedes the initiation of testing by several months. The rulemaking process provided the public with ample notice of chemical testing requirements sufficiently in advance of the initiation of testing to allow the public to conduct searches for existing data, submit data to EPA, comment on testing requirements and methods, and prevent unnecessary and duplicative testing. Providing additional time for the public to comment on testing plans would unnecessarily prolong an already lengthy rulemaking process.

C. Chemical Selection Process

Comment. SOCMA commented that the proposed test rule did not provide reasons why the particular 37 chemicals proposed for testing were selected. SOCMA argued that there are several hundred chemicals on the original list of 2,800 HPV chemicals that satisfy EPA's selection criteria of high production and significant worker exposure, and urged EPA to provide a basis on which the particular 37 chemicals were selected instead of a different 37.

Response. SOCMA is correct in stating that EPA selected the 37 chemicals proposed for testing based on high production volume as was described in Unit IV.B. of the proposed test rule (EPA 2000c, p. 81667); however, EPA selected the chemicals because of substantial, not significant, worker exposure as described in Unit IV.C. of the proposed test rule (EPA 2000c, p. 81667). In addition to those two factors, EPA selected those chemicals for which there was a lack of publicly available data for some or all of the SIDS testing endpoints as was noted in Unit IV.D. of the proposed test rule (EPA 2000c, p. 81667). This lack of available data compromises EPA's and others' ability to determine whether these HPV chemicals pose potential risks to human health or the environment. Another factor used was whether a chemical was "generally regarded

as safe” (GRAS) and thus exempt from the premarket approval requirements of the Federal Food, Drug, and Cosmetic Act for a particular use(s) in human food or in animal feed. GRAS chemicals were not included in the proposal to the final test rule . The final factor used to select these 37 chemicals was the lack of a commitment to sponsor the collection and/or development of needed data on these chemicals in the voluntary HPV Challenge Program. Using these factors, 37 chemicals were included in the proposal to the final test rule . Subsequent to the publication of the proposal to the final test rule , more recent production volume data became available, and additional commitments to the voluntary HPV Challenge Program were made. Because some of the more recent production volume data no longer supported the substantial production findings for certain chemicals, and the additional commitments to the voluntary HPV Challenge Program obviated the need to require testing for other chemicals, EPA is now requiring testing of only 17 of the 37 chemicals originally proposed for testing.

D. Data Availability Studies

Comment. ACC (ACC 2001) commented that the data availability studies (EPA 1998a, ACC 1998, and ED 1997), credited with initiating the voluntary HPV Challenge Program, are frequently misrepresented as indicating that little is known about the hazards of HPV chemicals. ACC believes that this is not the case as evidenced by the data already provided under the voluntary HPV Challenge Program and the demonstrable history of ACC’s member companies making chemical testing and other information available to government agencies, voluntarily and by regulation. ACC noted that each data availability study considered only electronically searchable databases and then only for specific animal test data. ACC opines that what the data availability studies do reveal is that publicly available databases cannot currently provide a complete picture of hazards of a particular chemical. PETA also expressed its concern that the data availability studies overestimated the lack of data and believes, as a result, that many redundant tests on animals will be conducted under the voluntary HPV Challenge Program and any related TSCA section 4 HPV SIDS test rules. ED commented that the separate studies conducted by EPA, ACC, and ED (EPA 1998a, ACC 1998, and ED 1997) indicated there is a surprising and disturbing paucity of screening-level data on HPV chemicals in the public record and that public availability of toxicity data is fundamental to providing the public with a reasonable assurance of chemical safety.

Response. EPA agrees with ACC that publicly available databases cannot currently provide a complete picture of the hazards of a particular chemical and EPA believes that one reason this is so is because the databases do not provide access to all the data that exist. EPA believes that the final test rule will not only cause data to be developed, which will provide critical information about the environmental fate and potential hazards associated with the 17 chemicals in the final test rule , but it should also cause manufacturers to release any in-house testing results and other existing data of which they are aware which fulfill the data needs identified by the final test rule . EPA believes the cost savings to the manufacturer of providing existing data instead of repeating already completed tests will result in such existing data being brought forward. In the event that the data availability studies have indeed overestimated the lack of available data on the 17

chemicals in the final test rule, the release of any additional existing data by manufacturers, which one would expect judging from the experience with the voluntary HPV Challenge Program, should correct any misimpressions concerning the scope of what is known about the hazards of HPV chemicals. Also, the provision by manufacturers of any existing data of which they are aware should prevent the redundant testing that PETA is concerned will occur. EPA notes that it did not rely on any general characteristics about the availability of information on HPV chemicals in the final test rule; rather the testing in the final test rule is tailored to obtaining necessary information for 17 specific chemicals based on the information that EPA is aware of for these chemicals. Finally, as noted in the proposal to the final test rule (EPA 2000c, p. 81665), at any time anyone may provide any relevant information to EPA that indicates that certain endpoints need not be tested.

E. Categories and Structure Activity Relationships (SAR)

In the proposal to the final test rule (EPA 2000c, p. 81663), EPA requested suggestions for procedures which might allow for the efficient and effective handling of category and SAR approaches in TSCA section 4 HPV SIDS rulemaking.

Comment. SOCMA commended EPA for seeking ways to incorporate category and SAR approaches into a regulatory framework. ACC (ACC 2001), API, SOCMA, PETA, PCRM, and AAVS commented that EPA should permit the use of categories and SAR modeling to fulfill the data requirements for HPV chemicals subject to this and future TSCA section 4 HPV SIDS test rules. SOCMA stated that these approaches, when justified in a transparent fashion, are scientifically sound and will result in several benefits.

Response. EPA agrees with the commenters that developing categories and SAR approaches for testing can be scientifically sound and can result in a number of benefits. First, the public would be informed earlier about potential hazards of HPV chemicals if category testing can be completed sooner than individual tests for each chemical. Second, there may be an economic savings because less testing may be needed for chemicals considered as a category or when applying SAR principles to extrapolate from appropriate existing data to predict effects on a specific endpoint. Third, a reduction in testing resulting from a combination of SAR and category approaches should result in fewer laboratory animals used. Comments involving specific proposals regarding categories and SAR are discussed in Unit E. of this document.

Comment. SOCMA suggested that decisions on categories, SAR, and surrogates be handled on a chemical-by-chemical basis in the rulemaking context in a process analogous to that which is provided under the voluntary HPV Challenge Program. That is, a sponsor could propose the case to EPA to use SAR to predict a chemical's effects on toxicity endpoints by extrapolating data from a surrogate chemical, and have that proposal placed in the public record for comment. Once comments are received, EPA could publish its decision. Only in the instance of using SAR arguments to use surrogate data would a sponsor provide a test plan. SOCMA notes, however, that this approach could lead to multi-phase rulemaking. ACC (ACC 2001) suggested that if

EPA receives a viable commitment under the voluntary HPV Challenge Program for a chemical which involves a proposal to use category or SAR approaches, then any proposed TSCA section 4 HPV SIDS test rule that includes the chemical should be left open for that particular chemical (and later, if necessary, severed from the initial proposal) until the appropriateness of the approach for that chemical can be determined. If the proposed category/SAR approach is deemed appropriate, the sponsor could submit for EPA approval a revised approach in an Enforceable Consent Agreement (ECA) under TSCA section 4. If the proposed category/SAR approach is not deemed appropriate, a final rule could require testing for that chemical as it was originally proposed. In ACC's view, this would avoid an unnecessarily complicated modification process and eliminate unfair treatment of chemicals that are candidates for category or SAR approaches (as compared with chemicals that are not candidates for such approaches).

Response. EPA believes that under SOCMA's suggested procedure, multi-phase rulemaking would be necessary and would involve publication of potentially numerous **Federal Register** document(s) in order to provide sufficient notice and comment opportunities. The procedure suggested by ACC to include category or SAR approaches in test rules would require either the issuance of two final rules or the rescinding of at least a portion of a proposal and the issuance of one or more ECA solicitation notices (and successful completion of the ECA process) and one or more final rules. These suggested procedures would substantially add to the time and effort necessary to obtain test data. As a result, EPA is not incorporating these suggestions into the final test rule. The use of SAR and category approaches continue to be available to sponsors under the voluntary HPV Challenge Program, however. Furthermore, EPA has not identified any opportunities that will allow inclusion of a category and SAR approach for any specific chemicals included in the final test rule, and commenters did not identify any. Therefore, EPA is not requiring the use of categories or SAR approaches for the chemicals in the final test rule.

Comment. PETA, DDAL, and ARDF suggested general approaches for developing categories and using SAR to achieve the goal of limiting testing in TSCA section 4 HPV SIDS test rules to a single or reduced number of chemicals. PETA suggested that SAR should be used to group test chemicals into categories. In contrast, ARDF commented that EPA should require the submission of SAR data for the test rule and then use SAR data in combination with categories so that, in general, only one representative chemical from each category would need to be tested. PETA and DDAL commented that EPA should also consider data-rich chemicals that are outside the rule or that are not HPV to form categories for use in TSCA section 4 HPV SIDS test rules.

Response. EPA notes that the approaches recommended by the commenters (i.e., use of SAR and "data-rich" chemicals) employ principles that are commonly used to develop categories or identify possible surrogates within a category for the chemical with data needs. EPA has advocated the use of categories and SAR in the voluntary HPV Challenge Program and has provided support for their use by developing guidance documents to assist industry participants and others in constructing scientifically defensible categories (EPA 1999b) and SAR (EPA 1999c). EPA did not include such approaches in the proposed test rule (EPA 2000c) because EPA had not identified any possibilities that would allow inclusion of the category and SAR

approaches for any chemical in the proposed test rule and because EPA believed that the incorporation of categories or SAR approaches in this test rule would require complex, time consuming, and resource intensive procedural steps, such as multi-phase rulemaking. Consequently, in the proposed test rule (EPA 2000c), EPA specifically solicited comments and suggestions on simplifies procedures that would allow inclusion of such approaches in TSCA section 4 HPV SIDS test rules. The recommendations by PETA, DDAL, and ARDF, however, do not address the issue of how, procedurally, the Agency might incorporate category and SAR approaches in the context of TSCA section 4 HPV SIDS test rules.

Also in the proposed test rule (EPA 2000c), EPA stated that it believed that none of the chemicals appeared to be candidates for these approaches but EPA encouraged persons who believed that a chemical under the proposed test rule can be dealt with by a category or SAR approach to submit to EPA appropriate information that substantiates this belief. The development of the proposals and rationales needed to construct scientifically defensible categories or SARs can be technically difficult determinations and should be based on a careful technical evaluation of the available literature such as the available category and SAR guidance in EPA's voluntary HPV Challenge Program (EPA 1999b and EPA 1999c). The general information provided by the commenters does not provide the scientifically defensible category and/or SAR proposals and supporting technical rationales that would support a determination by EPA that any of the 17 chemicals subject to the final test rule is appropriately included under a category or SAR approach.

Comment. PETA, PCRM, and DDAL commented that EPA should take the lead in creating categories and work as a liaison between industries developing categories. Specifically, PETA and PCRM suggested that a category approach be used for dibromomethane (CAS No. 74-95-3) and 1-chlorododecane (CAS No. 112-52-7) by including them with other halogenated solvents, and that coke oven light oil (from coal) (CAS No. 65996-78-3) could potentially be incorporated into one of the categories being developed by API. PETA also commented that EPA require the use of categories in test rules. HSUS commented that, although EPA supports category and SAR approaches in the voluntary HPV Challenge Program, they are not available in the proposed test rule in part because they require, as discussed in the proposed test rule, complex, time-consuming, and resource intensive procedural steps. HSUS suggested that the use of categories and SAR in this test rule may not be as difficult and time consuming as the proposed test rule contends because only the 37 chemicals in the proposal to the final test rule would be involved in the process.

Response. Although EPA believes that the incorporation of categories or SAR approaches in this test rule would require complex, time consuming, and resource intensive procedural steps, such as multi-phase rulemaking, EPA notes that the primary reason the final test rule does not include category and SAR approaches is because EPA has not identified, nor have the public commenters brought to EPA's attention, any possibilities that will allow inclusion of a category or SAR approach within the final test rule for any specific chemicals included in the final test rule. Also, although EPA has advocated the use of categories and SAR in the voluntary HPV Challenge Program and has provided support for their use by developing guidance documents to

assist industry participants and others in constructing scientifically defensible categories (EPA 1999b) and SAR (EPA 1999c), unfortunately no one has volunteered to sponsor in the voluntary HPV Challenge Program the three chemicals identified by PETA and PCRM.

F. Persons Required to Test

EPA stated in the proposed test 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 to either submit to EPA letters of intent to conduct testing, conduct this testing, and submit the test data to EPA, or apply to and obtain from EPA exemptions from testing. Persons in Tier 2 (those who would not have to initially comply with the final rule) would not need to take any action unless they are notified by EPA that they are required to do so because, for example, no letter of intent has been submitted by someone in Tier 1 for a given chemical. Persons in Tier 1 who obtain exemptions and persons in Tier 2 would nonetheless be subject to providing reimbursement for testing costs 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, reduce administrative burden and complexity, and focus the testing requirements initially on those entities whom EPA believes would be most likely to conduct testing (EPA 2000c, pp. 81673-81674). EPA solicited comment on this approach to the “persons required to test” portion of the test rule, and received a number of comments in response. After considering these comments, EPA has decided to finalize the approach as proposed.

1. *General agreement with EPA’s “persons required to test” approach.*

Comment. API indicated its general support for the proposed tiered classification of persons subject to the test rule, and stated that the proposed approach appropriately focuses the testing

requirements on the primary manufacturers of test rule substances. API additionally commented that EPA provided good reasons for placing byproduct manufacturers, manufacturers of naturally occurring substances, and manufacturers of non-isolated intermediates in Tier 2. ACC (ACC 2001) agreed with the placement of processors in Tier 2, as this has been consistent practice in previous TSCA section 4 test rules.

Response. No response to this comment is necessary.

2. EPA should retain the ability to move Tier 2 groups to Tier 1.

Comment. ACC (ACC 2001) suggested that, although the proposed placement of certain groups of manufacturers in Tiers 1 and 2 may be appropriate for most chemicals, if the activities of Tier 2 entities contribute in a significant way to the need for test data or the rationale for requiring testing, then EPA should elevate those Tier 2 entities to Tier 1 for that substance. For example, if air emissions are a primary reason for requiring testing and the activities of Tier 2 manufacturers contribute significantly to air emissions, then those persons should be moved to Tier 1. Further, ACC notes that should EPA want to establishing threshold triggers for moving persons to Tier 1, such as a production volume threshold or a concentration-based cut-off, EPA should be careful not to set any triggers that undermine the goal of placing in Tier 1 all persons whose activities contribute significantly to the need for testing. In ACC's view, EPA need not take the same approach for every chemical, nor in every test rule. ACC suggests that such information should be collected early or prior to a proposed rulemaking, and also that manufacturers that have been included in Tier 1 (presumably in a proposed or final rule) should be able to demonstrate that Tier 2 entities contribute significantly to the need for testing. ACC's position is that TSCA provides the Agency discretion to specify the classes of manufacturers and processors subject to a test rule based on its rationale for requiring testing. ACC believes the Agency's approach to tiering should be flexible and equitable.

Response. If EPA determines that it is appropriate for a particular group of entities to be moved as a group from Tier 2 to Tier 1 on a case-specific basis, the Agency will conduct its rulemaking in accordance with this determination. 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.

The principle of flexibility over the status of entities included in Tier 2 is already reflected in 40 CFR part 790 provisions pertaining to entities that have been included in Tier 2 in past test rules: processors, small-quantity manufacturers, and manufacturers of a test rule chemical for R&D purposes (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 the final test 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” (EPA 1990, 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 “[t]he 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.”

In the Agency’s view, however, a determination that the activities of particular persons (or groups) within Tier 2 contribute in a significant way to the need for test data or the rationale for requiring testing should not be a basis for determining whether certain manufacturers and/or processors are subject to a test rule or for moving entities from Tier 2 to Tier 1. EPA is not required to demonstrate that particular types of manufacturing or processing contribute to the need for testing (i.e., that a particular type of manufacturing 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) in order to require that those that engage in the particular types of activities are subject to the rule, or to require that certain groups initially comply with the rule by submitting a letter of intent to test or an exemption application. See TSCA section 4(a). As EPA noted in a response to a similar comment on a recently promulgated test rule, EPA would not, in most cases, have enough information to make these types of determinations (EPA 2004a, p. 22420). 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, without further justification (see TSCA section 4(b)(3)(B)).

For example, the final TSCA section 4 rule for biphenyl (EPA 1985b, 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. The Agency’s decision in the final test rule to move additional groups of manufacturers (i.e. persons who manufacture a test rule substance solely as one or more of the following: as a byproduct, as an impurity, as a naturally occurring substance, as a non-isolated intermediate, and as a component of a Class 2 substance) to Tier 2 was based on the same rationale used in the past to place small-quantity and R&D manufacturers in Tier 2, i.e. these types of manufacture normally represent a small percentage of the overall production volume and test sponsors are not expected to expend the administrative resources to recover the small proportional amounts of the testing costs from these manufacturers (EPA 1990). Similarly, where a test rule chemical is manufactured solely or primarily in a form that is generally included in Tier 2, the Agency has flexibility to elevate manufacturers of that form of the chemical from Tier 2 to Tier 1. Also, while EPA may want to consider establishing threshold triggers for moving groups of persons to Tier 1, such as a production volume threshold or a concentration-based cut-off, EPA does not want to set any such triggers in a way that might undermine the goal of ensuring that a letter of intent to test is received from the group of Tier 1 entities.

3. *Tier 2 should not be subject to reimbursement.*

Comment. API commented that Tier 2 entities should not be subject to reimbursement obligations. API contended that Tier 2 entities have not historically participated in testing, or contributed to the reimbursement of those persons conducting testing. API believes that reimbursement obligations should be limited to Tier 1 manufacturers, unless Tier 2 entities are required to sponsor testing because no Tier 1 manufacturer is identified.

Response. EPA does not agree. EPA responded at length to this comment and a number of related issues in the preamble to a recently promulgated test rule which includes virtually identical provisions with regards to persons required to test (EPA 2004a, pp. 22421-22422). Interested parties should refer to that rule for a more comprehensive discussion regarding reimbursement issues. To summarize, under TSCA section 4(b)(3)(B), once EPA makes 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. TSCA section 4(c) provides for exemptions from testing. Tier 2 entities have “automatic conditional exemptions” from the requirement that they conduct testing (see §799.5085(c)(3) of the regulatory text of the final test rule (EPA 2005b)). 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 submission of data, these entities are not exempt from the requirement that they reimburse the costs of testing.

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 (EPA 1990) 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 the final test 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. (EPA 1990, 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 (EPA 1990, 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. Thus, 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.” (EPA 1990, p. 18882).

It may be true that the entities included in Tier 2 under the final test rule have not historically participated in testing or reimbursement under test rules; however, the likely reason they have not participated is because the costs of testing have been contributed by a smaller subset of the group of entities that are 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 the final test 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. The development of such private cost-sharing arrangements appears to avoid 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 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.

4. Definition of small quantity manufacturers. Small-quantity manufacturers (i.e., manufacturers of chemicals in amounts of less than 1,100 lbs. (500 kg) annually) have generally been included in Tier 2 as persons who are subject to test rules, but who are not initially required to comply with the rules (40 CFR 790.42(a)(4)). In the proposed test rule, EPA solicited comment regarding whether it should raise the production volume threshold defining small-quantity manufacture in the final rule (EPA 2000c, p. 81674).

Comment. In response to EPA’s comment solicitation, SOCMA recommended that EPA raise the threshold from less than 1,100 lbs. annually to less than 25,000 lbs. annually, unless a consortium of companies can demonstrate that the exclusion of companies below the threshold from Tier 1 places other companies at a competitive disadvantage. ACC (ACC 2001) supported raising the threshold to 10,000 lbs. because, in its view:

- This threshold was the same as was used for Inventory Update Reporting under 40 CFR part 710 at the time ACC’s comment was made.
- The activities of smaller manufacturers will rarely be a significant factor in EPA’s decisions to require testing.
- Test sponsors are generally unlikely to seek reimbursement from small-quantity manufacturers.

- EPA would be spared the burden of processing exemption requests from these manufacturers.

ACC suggested that it may be appropriate at a later date to consider an even higher small-quantity threshold, however it also warned EPA against setting triggers for moving persons to Tier 1, such as a production volume threshold or concentration-based cutoff, such that Tier 1 is limited inappropriately.

Response. EPA does not agree with commenters that the small quantity threshold should be raised from 1,100 pounds for the final test rule. In the comment solicitation in the proposal (EPA 2000c, p. 81674), EPA requested comments on the appropriate annual production amount at which test sponsors would not be expected to seek reimbursement such that the reason for requiring an exemption application to be filed by these manufacturers would not exist. EPA also asked commenters to provide a rationale and supporting information for any specific threshold suggested. However, the commenters did not indicate whether, at the higher thresholds they suggested, test sponsors would not be expected to seek reimbursement from persons manufacturing less than the threshold amount. They also did not provide supported rationales for the specific thresholds suggested. As ACC suggests, it would be inappropriate for EPA to create triggers for moving groups of persons to Tier 1 in a way that might undermine the goal of ensuring that a letter of intent to test is received from the group of Tier 1 entities.

5. *Status of manufacturers of components of Class 2 substances.* EPA proposed that manufacturers of test rule 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 with the rule (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 comments from API concerning the appropriateness of the proposed Tier 2 status of manufacturers of components of Class 2 substances. Many of the issues raised by API were also addressed in EPA's responses to comments on another recently promulgated test rule which includes virtually identical provisions with regard to persons required to test (EPA 2004a, pp. 22418-22420). Interested parties should refer to that discussion for additional information regarding the status of manufacturers of components of Class 2 substances under TSCA section 4.

Comment. API 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. API asserted 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:

- The Class 2 nomenclature is accurate for representing substances with compositions that cannot be represented by definite, complete structural diagrams that are often derived from natural sources or complex chemical reactions.
- Health and environmental assessment and regulation of chemicals are facilitated by the

distinction between Class 1 and Class 2 substances because the nomenclature reflects differences in chemistry and the form in which they are produced and distributed in commerce.

- The Class 2 nomenclature is consistent with commercial intent and the form of the substances, given that manufacturers of Class 1 substances produce and market such substances *per se*, while manufacturers of Class 2 substances produce and market the complex streams and not their components, many of which do not add commercial value to the Class 2 substance.

Response. 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. 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.

This broad definition of “manufacture” is not limited to the manufacture of an isolated substance.

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. A Class 2 substance is a chemical substance as defined by section 3(2)(A) of TSCA, thus 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, where all manufacturers and processors of MCP would have been subject to the rule even though the substance was produced entirely in nonisolated form. MCP is a C₆ isomer that, at the time the rule was proposed, was typically manufactured in nonisolated form as a component of commercial hexane and gasoline. 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 C₆ components individually” (EPA 1998, pp. 3387-3388).

The Agency acknowledges that it has not explicitly required persons who manufacture test rule 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). The approach to the identification of subject persons (including manufacturers of components of Class 2 substances) that is being adopted in this TSCA section 4 rule, and that may be applied in other, future TSCA section 4 rules, is not intended to modify the status of any chemical substance or entity under other existing TSCA regulations.

While EPA agrees that the Class 2 nomenclature is useful for certain purposes, this nomenclature does not restrict the Agency's authority to include manufacturers and processors of test rule substances that are components of Class 2 substances as persons subject to that test rule. In addition, the applicability of TSCA section 4 is not limited to persons who manufacture or process a chemical for commercial purposes (compare with TSCA section 5(i), for example), or, as stated previously in this Unit F.5, to persons that manufacture the test substance in an isolated form. 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.

Also, the inclusion of manufacturers of test rule substances as components of Class 2 substances as persons subject to the 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 (EPA 1985b, pp. 37184-37185). The inclusion of manufacturers of test rule substances in the form of components of Class 2 substances 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 (if any). The commenter's approach would impair EPA's authority under the statute to effectively require the development of information about the substance under these circumstances.

Comment. API 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" because manufacturers of substances like petroleum streams manufacture Class 2 chemical substances rather than their components.

Response. EPA has not included this suggested change in the final test 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 rule 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 either case, the company is manufacturing the subject chemical (whereupon it is

subject to the TSCA section 4 rule), regardless of whether the subject chemical is isolated. In the final test rule (EPA 2005b), persons in the former group are included in Tier 1, whereas persons in the latter group are included in Tier 2. This stance is appropriate because considering manufacturers of components of Class 2 chemical substances not to be subject to TSCA section 4 testing could frustrate the ability of EPA to obtain necessary testing in some cases, e.g., if a substance were solely or primarily manufactured as a component of a Class 2 chemical substance.

Comment. API asserted that EPA has required refiners to test petroleum streams only when the Class 2 streams themselves are subject to test rules. API stated that the Agency has not required testing from manufacturers of Class 2 substances when the test substance is only a non-isolated component of a Class 2 substance.

Response: API's comments on this TSCA section 4 HPV SIDS rule were submitted to the Agency prior to finalization of another recent TSCA section 4 test rule related to certain chemicals of interest to the Occupational Safety and Health Administration (OSHA) which explicitly indicates that manufacturers and processors of the test rule substances as components of Class 2 substances are subject to the rule, regardless of whether the test rule substances are isolated from the Class 2 substances of which they are components. However, such manufacturers and processors are not initially required to comply with that rule (EPA 2004a).

In two other past test rules cited by API, certain substances that were manufactured primarily or solely as non-isolated components of Class 2 substances were not included as substances subject to the final test rules (EPA 1985a and EPA 1988). The decision not to include these chemicals as substances subject to the rules was not based on any conclusion on the part of EPA that it did not have authority under TSCA section 4 to require manufacturers of the substances in the form of components of Class 2 substances to test the substances, or that such manufacturers should be excluded from test rule coverage as a general matter, but because the Agency determined that the testing of other substances would be more appropriate (see EPA 1988, p. 3387; EPA 1985a, p. 20663). In both cases, the substances were dropped from the rules in their entirety, i.e., with respect to all manufacturers and processors of the substances and not just specific groups of entities such as manufacturers of the substances in the form of components of Class 2 substances. And in both cases, the Agency did not rule out the possibility of including the substances in future test rules, as necessary and appropriate, despite the fact that certain of the chemicals were manufactured primarily or solely in non-isolated form as components of Class 2 substances (EPA 1998, pp. 3387-3388; EPA 1983, p. 23089-23090).

In another past test rule cited by API, EPA declined to require testing by manufacturers of the test rule substances as components of Class 2 substances because it believed that there was some question as to whether these manufacturers had sufficient notice that they would be subject to the test rule (EPA 1994). The Agency did not subsequently provide notice to these manufacturers because it was notified that another manufacturer would be conducting the required testing. Again, the Agency did not base its decision on any judgment that the Agency does not have the authority to include manufacturers and processors of components of Class 2 substances as persons subject to TSCA section 4 test rules, or that they should be excluded from

test rule coverage as a general matter.

The Agency acknowledges that past test rules have not always explicitly indicated that persons who manufacture or process a test rule substance as a component of a Class 2 substance are subject to such rules regardless of whether the test rule substance component is isolated from the Class 2 substance. EPA's approach to the "persons required to test" portion of the final test rule concerning certain chemicals of interest to OSHA and this HPV SIDs final test rule is intended, in part, to clarify the regulatory obligations of entities such as manufacturers and processors of test rule substances as components of Class 2 substances. As explained above, EPA believes that under a straightforward reading of the statute, persons who manufacture a test rule substance as a component of a Class 2 substance are "manufacturers" under TSCA section 4 and are thus generally subject to test rules to which manufacturers are subject. In addition, 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.

G. Approaches for Selecting the Test Substance for Class 1 and Class 2 Chemicals

In the proposed test rule preceding the final test rule, EPA proposed that for each "Class 1" chemical substance included in the rule, i.e. a 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, the test substance would be at least 99% pure. Additionally, EPA proposed that for the "Class 2" chemical substances included in the rule, the test substance would be any representative form of the substance. EPA suggested that the representative form chosen should meet industry or consensus standards, where they exist. A variety of alternatives to the proposed approach were described, and the Agency solicited comments on the topic (EPA 2000c, p. 81675). After consideration of the comments, EPA has decided to utilize the proposed approach in the final test rule (see § 799.5085(a) of the regulatory text of the final test rule (EPA 2005b)).

1. Class 1 chemicals.

Comment. Merisol suggests that the rule should specify that the test substance for Class 1 chemicals may be less than 99% pure where it can be shown that a purity level of 99% or greater is unattainable.

Response. EPA agrees that there may be instances where attaining a 99% pure chemical substance is not feasible. Where EPA is aware of this difficulty prior to finalization of a test rule, EPA could specify in the rule that the purity of the test substance be other than 99%. After finalization of a test rule, where test sponsors believe that a 99% level of purity is inappropriate for a chemical, they may request a rule modification (40 CFR 790.55). Unless otherwise

specified in the final test rule (see § 799.5085(a) of the regulatory text of the final test rule (EPA 2005b)), the Agency is requiring that all of the Class 1 chemical substances included in the final test rule be tested at a purity of 99% or greater.

Comment. SOCMA suggested that the person(s) conducting the testing should be allowed to make the case to EPA that a given Class 1 chemical be treated as a Class 2 substance for purposes of test substance selection and vice versa. For example, there may be circumstances that make generating a 99% pure sample of a Class 1 substance difficult or unsafe, thereby warranting the selection of a representative sample.

Response. Again, where EPA is aware of problems associated with requiring the use of a test substance with a 99% or greater purity level prior to finalization of a test rule, it may ensure that the rule requires use of a lower purity level or the testing of a representative sample, as necessary and as appropriate. Where EPA is not aware of such problems until after a rule is finalized, a modification to the rule may be made via the procedures at 40 CFR 790.55.

2. Class 2 chemicals.

Comment. SOCMA commented that the proposed approach for the testing of Class 2 chemicals which allows the sponsor(s) to use professional judgment in selecting an appropriate representative test substance is the most prudent of the options provided in the proposed test rule. SOCMA commented that such an approach is consistent with the approach used for the testing of Class 2 substances in the voluntary HPV Challenge Program. Especially because both the voluntary HPV Challenge Program and the test rule are focused on screening level information, industry is in the best position to determine which samples meet industry and consensus standards, and are thus the most representative.

Response. EPA agrees and has included this approach in the final test rule (EPA 2005b) at § 799.5085(a) of the regulatory text. The persons conducting the testing must designate the representative forms that will be the test substances for the five Class 2 chemicals in the final test rule. For purposes of the final test rule which seeks screening-level information, the testing of any representative form of a subject Class 2 chemical would be relevant to a determination of whether the chemical would or would not present an unreasonable risk to human health or the environment. However, EPA encourages the selection of representative forms of the substances that meet industry or consensus standards, where they exist. In accordance with TSCA Good Laboratory Practice Standards at 40 CFR part 792, the final study report must include test substance identification information, including name, CAS number, strength, purity, and composition, or other appropriate characteristics. See 40 CFR 792.185.

Comment. SOCMA advised against requiring the testing of more than one representative form of any subject Class 2 substance, as this would increase testing costs yet would produce data of little value. In SOCMA's view, testing one sample is sufficient, particularly for purposes of obtaining screening-level information.

Response. EPA agrees that the testing of one representative form of each subject Class 2 substance is sufficient for purposes of the final test rule . Because the final test rule requires testing of a single representative form of each subject Class 2 substance, EPA will consider all forms of a Class 2 substance subject to the rule to be equivalent and will not require the submission of equivalence data.

Comment. PETA suggested that EPA should require the testing of the representative form of a Class 2 chemical that most people are exposed to and/or that is released into the environment in the largest quantity.

Response. Data that indicate which specific form of a Class 2 chemical results in the greatest exposures are often not available. For example, exposure surveys generally do not distinguish between closely related forms of a Class 2 chemical that are present together at a site being evaluated. In addition, selecting the test substance using the suggested approach might be more burdensome than is appropriate for purposes of the final test rule , which seeks solely to fill screening-level data gaps.

Comment. SOCMA commented that requiring the test substances for Class 2 chemicals be at least 99% pure may not be technically feasible. Any decision to use a Class 1 approach for Class 2 chemicals should be made on a chemical-by-chemical basis, and should be left to the discretion of the test sponsor.

Response. The final test rule does not require that the test substance for Class 2 chemicals included in the rule must be at least 99% pure, rather it requires that a representative sample be selected. The Agency is not allowing test sponsors to determine whether a Class 1 approach will be used for a Class 2 chemical or vice versa, as this does not appear to be necessary for purposes of conducting the testing included in the rule, and may in fact be confusing to test sponsors. In the event a test sponsor sees the need for using a Class 1 approach for a Class 2 chemical or vice versa, a modification to the final test rule (EPA 2005b) may be sought (see 40 CFR 790.55).

H. Test Battery: Adoption of SIDS Endpoints

Comment. SOCMA commended EPA for basing the screening-level tests required in the final test rule on the SIDS test battery. SOCMA commented that harmonization of test protocols (those required by the final test rule and those used in the OECD SIDS Program) will lead to overall reduction in the use of animals and savings in resources.

Response. No response to this comment is necessary.

Comment. In contrast, PETA commented that EPA has never before issued a rule requiring the generation of data on the six basic SIDS test endpoints for all HPV chemicals, and EPA should explain why these particular six endpoints are needed in order to accurately assess the hazards of the chemicals subject to the final test rule . In a similar comment, ARDF stated that use of each

SIDS test for the HPV chemicals in the final test rule should be individually justified rather than simply conducted as a part of a standardized checklist approach to testing and assessment.

Response. The availability of hazard information on individual chemicals is fundamental to EPA's ability to accomplish its mission of environmental protection— risk assessment, risk management, safeguarding children's health, expanding the public's right-to-know, and promoting the pollution prevention ethic. Activities to ensure the availability of basic hazard information on HPV chemicals are an integral part of meeting these objectives. The information that EPA believes is relevant to understanding the basic health and environmental hazards of HPV chemicals is derived from a battery of tests agreed upon by the international community through the OECD, of which the United States is a member country, as appropriate for screening international HPV chemical substances for toxicity. The six basic testing endpoints comprising this battery of tests, known as the Screening Information Data Set (SIDS), have been adopted by the OECD as the minimum required to screen international HPV chemical substances for toxicity and environmental fate. The content of the SIDS battery was agreed upon at the 13th Joint Meeting of the OECD Chemicals Group and Management Committee of the Special Programme on the Control of Chemicals (OECD 1989 and OECD 1990).

The testing required for the 17 chemicals in the final test rule is essentially identical in scope and applicability to the SIDS battery as agreed to by the OECD. While SIDS and the set of tests required by the final test rule do not fully measure a chemical's toxicity, EPA believes that the tests do provide a consistent minimum set of information that can be used to determine the relative hazards and risks of chemicals to humans and the environment and to judge if additional testing or assessment is necessary. Each test assesses the toxic effect on a different endpoint or the toxic effect due to a different duration of exposure. The physical/chemical property tests and the environmental fate test required in the final test rule will provide data which can be used to predict how a chemical will behave and the extent to which it may persist in the environment. The required aquatic toxicity tests using algae, fish, and daphnids (i.e., taxa that are accepted by EPA as representative of aquatic flora and fauna for hazard identification) will provide a base set of tests that will enable a preliminary assessment of both acute and chronic hazards to aquatic organisms to be performed. Although the required tests for mammalian toxicity do not provide complete information on all aspects of possible acute, subchronic and chronic toxicity, the combined set of tests will provide a basic set of information on the range of toxic effects that are associated with three likely exposure durations. The acute toxicity test will provide information on health hazards likely to arise from short-term exposures and may provide initial information on the mode of toxic action of a substance. The required mammalian genetic toxicity testing may provide presumptive evidence of cancer risk. The required repeated dose/reproduction testing will provide limited information on systemic toxicity, neurotoxicity, and immunotoxicity, as well as provide indications of a chemical's ability to affect fertility and to cause damage to the developing organism. Thus, the required testing under the final test rule (EPA 2005b) will enable EPA and others to support development of preliminary hazard and risk assessments for these 17 HPV chemicals and to set priorities for further testing that will produce more definitive hazard information, where needed, on these chemicals. In addition, because the tests required under the final test rule are consistent with the

internationally accepted SIDS battery, the data generated by the testing under the final test rule will be of a sort that can readily contribute to the SIDS process.

Comment. PCRMR commented that, as in the OECD SIDS Program, EPA should have incorporated in the test rule that general information be submitted for each chemical, such as general use pattern, use in consumer products, occupational exposure limits, and sources of exposure. PCRMR believes this basic information would provide significant insight into how to prioritize the HPV chemicals for further work. PCRMR also strongly recommended that EPA incorporate and place greater emphasis on human data in the test rule, including epidemiological, human toxicity, and exposure studies. PETA also asked why EPA did not propose the collection of human toxicity and exposure data.

Response. EPA agrees that information on uses, sources and extent of exposure, and human toxicity (including epidemiological studies) is important in understanding the potential risk associated with exposure to chemicals. To that end, EPA continues to welcome the submission of any additional adequate existing data on these 17 chemicals that are relevant to their hazard characterization. Basic exposure information including general and occupational use patterns, and sources and levels of exposure, can be submitted to help place the hazard information into an appropriate context. EPA is confident that data developed under the final test rule will provide critical information about the environmental fate and potential health and environmental hazards associated with these chemicals that, when combined with information about exposure and uses, will allow the Agency and others to evaluate potential health and environmental risks and take appropriate action.

I. Test Methods

I. Test Methods

1. Test guidelines.

Comment. PETA noted that EPA is proposing that testing be conducted in part according to guidelines published on December 15, 2000 (EPA 2000b), and asserted that the **Federal Register** notice containing the guidelines was a final rule that should have been preceded by an opportunity for public comment. PETA also contends that the December 15, 2000 guidelines that call for the use of animals had not undergone the rigorous validation procedures that all non-animal tests must undergo. PETA believes animal tests should undergo the same scientific scrutiny that non-animal tests receive and must be validated for reproducibility, reliability, and relevance prior to being required by a Federal agency.

Response. EPA properly found that there was good cause not to provide an opportunity for comment on its guidelines published on December 15, 2000, and adequately explained its reasons therefor in the preamble to that **Federal Register** document (see EPA 2000b, pp. 78747 and 78750).

The methods that are being used as the test standards in the final test rule have been sufficiently validated for purposes of the final test rule. Test method validation serves the

purpose of establishing the reliability and relevance of a test method in support of regulatory use. Relevance is the extent to which the test predicts or measures the biological effect of concern. Reliability is a measure of the method's intra- and inter-laboratory reproducibility. A test is considered validated when its performance characteristics, advantages, and limitations have been determined for the regulatory purpose to which it will be applied (NIEHS 1997). Use of test methods that are standardized in terms of animal breeding and handling contributes to validation by providing for reproducibility in laboratory tests. In addition, laboratory personnel are trained in animal management, test chemical administration, and measurement and observation techniques, further enhancing reproducibility and reliability.

PETA did not state any specific objections to the test standards included in the final test rule, nor did it indicate any specific reasons why it believes the guidelines published on December 15, 2000 have not been sufficiently validated. However, in answer to PETA's general comment, the guidelines published on December 15, 2000 were developed with broad public participation and extensive involvement of the scientific community, and have been validated over time as a result of their long history of use. In 1991, EPA undertook an effort to "harmonize" the testing guidance and requirements that existed in the Office of Pollution Prevention and Toxics (OPPT), the Office of Pesticides Programs (OPP) guidelines, and the guidelines published by the OECD. The product of this effort, which included opportunities for public involvement, is one set of harmonized guidelines. The Agency used its harmonized guidelines to create the TSCA specific guidelines used in the final test rule. The OPPTS harmonized guidelines were first drafted by EPA scientists, then reviewed by other EPA experts and, in some instances, presented at domestic and international colloquia in order to solicit the views of recognized experts and the regulated community. They were made available on the Internet as public drafts and a notice was published announcing the availability of the draft guidelines and soliciting public comment (EPA 1996a). After review of the public comments, the final harmonized guidelines were published on the Internet (EPA 1998b). The OPPTS harmonized guidelines and associated TSCA guidelines included in the final test rule are internationally recognized standards which were designed to, when followed, produce data which are accurate, reliable, and reproducible. As such, the TSCA guidelines are appropriate for developing the needed information on the health and environmental effects of the chemicals in the final test rule. The long history of successful use of these guidelines, in addition to their scrutiny during the harmonization process, adequately demonstrates their validation.

For some of the toxicity testing that is required under the final test rule, EPA is requiring, or provides as an alternative, the use of voluntary consensus standards issued by the American Society for Testing and Materials International (ASTM International). ASTM International is a not-for-profit organization that provides a forum for the development and publication of voluntary consensus standards for materials, products, systems, and services. ASTM has over 30,000 members from more than 100 countries. These members are producers, users, consumers, and general interest parties, such as academicians and government representatives. The members write ASTM standards through their service on ASTM's technical committees. ASTM's consensus-based method of developing standards ensures that interested individuals and organizations representing academia, industry, product users, and governments all concur in determining a standard's content. Thus, ASTM standards, like the TSCA guidelines, are

internationally accepted standards developed using a process that includes broad public participation and extensive involvement of the scientific community.

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. To comply with NTTAA, EPA has specified ten ASTM guidelines and one International Organization for Standardization (ISO) guideline in Table 2 in § 799.5085(j) of the regulatory text of the final test rule (EPA 2005b) which can be used as test standards in the final test rule ; three of the ten ASTM guidelines can be used as alternatives to the specified TSCA test guidelines published in part 799 of the CFR. Persons required to comply with the final test rule may choose either ASTM, ISO, or TSCA test guidelines as their test standards when they are presented as alternatives. EPA believes that the ASTM, ISO, and TSCA guidelines specified in the final test rule conserve labor, materials, and animal lives.

2. Acute toxicity.

Comment. PCR/M commented that the *in vitro* basal cytotoxicity test evaluated by the Multicenter Evaluation of *In vitro* Cytotoxicity (MEIC), which PCR/M referred to as the “MEIC test,” is a better predictor of lethal toxicity and is less cruel to animals than the *in vivo* LD₅₀ test (i.e., lethal dose for 50% of the animals tested) and should be the required test for acute toxicity in the final test rule . The MEIC program was an extensive evaluation of *in vitro* methods for acute toxicity initiated by the Scandinavian Society for Cell Toxicology in 1989 under the direction of Dr. Bjorn Ekwall (NIEHS 2001a). NEAVS commented that it supports the work of Dr. Bjorn Ekwall and the MEIC Program to replace the LD₅₀ test.

Response. EPA does not agree that the *in vitro* cytotoxicity test referenced by the commenter is an adequate replacement for the *in vivo* acute toxicity test; however, as discussed in this response, EPA believes the *in vitro* cytotoxicity test is a useful supplement to the *in vivo* acute toxicity test that can potentially reduce the number of animals that need to be tested. In October 2000, a workshop, organized by the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) and the National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) and co-sponsored by EPA, the National Institute for Occupational Safety and Health (NIOSH), and the National Institute for Environmental Health Sciences (NIEHS) was convened to ascertain the status of certain *in vitro* tests and the possibility of their use to replace *in vivo* tests for assessing acute systemic toxicity. The findings of this workshop were intended to provide information on these test methods to the Federal agencies that generate, use, or provide information from toxicity test methods for risk assessment purposes (NIEHS 2001a). Among the *in vitro* tests reviewed at the workshop was the

neutral red uptake (NRU) assay using either normal human keratinocytes (NHK) or BALB/c 3T3 mouse fibroblasts; this is the test PCRM referred to as the “MEIC test.” The report on that workshop (NIEHS 2001a), made available in August 2001, concluded that none of the available *in vitro* methods had been adequately evaluated for implementation to reduce and/or replace animal use for acute systemic toxicity testing. However, the report stated that the NRU assay could be useful in estimating starting doses for *in vivo* acute toxicity testing and included a recommendation to all Agencies participating in ICCVAM to consider the use of this *in vitro* test as a supplement to the current *in vivo* acute oral toxicity test. Based on the workshop’s evaluation of the NRU assay, EPA announced on its website (<http://www.epa.gov/chemrtk/toxprtcl.html>) that data from the NRU assay using either normal human keratinocytes (NHK) or BALB/c 3T3 mouse fibroblasts can be used to estimate the starting dose for the *in vivo* acute oral toxicity test conducted for the voluntary HPV Challenge Program. In December 2002, EPA announced the availability of the revised Acute Oral Toxicity test guideline, OPPTS 870.1100 (EPA 2002c). This revised test guideline encourages the use of the cytotoxicity *in vitro* methods as a supplemental component to the *in vivo* acute oral study to estimate a starting dose.

Although EPA has not yet accepted the NRU assay as a replacement for an *in vivo* acute oral toxicity test, the final test rule will accept data from the NRU assay to estimate a starting dose for the *in vivo* acute oral toxicity test when the substance being tested is not a gas at room temperature. Consistent with the approach taken under the voluntary HPV Challenge Program, EPA is requiring in the final test rule that for test substances that are gases at room temperatures (25° C), the acute mammalian toxicity test be conducted using the inhalation exposure route rather than the oral exposure route (See the entry in the Special Conditions column for mammalian acute toxicity in Table 3 in § 799.5085(j) of the regulatory text of the final test rule (EPA 2005b)). A document has been developed by NIH/NIEHS which provides guidance on how to use the NRU assay to estimate a starting dose for an acute oral toxicity test (NIEHS 2001b). The most recent versions of the standardized protocols for the NRU assay protocols are available at the NIEHS/ICCVAM website (<http://iccvam.niehs.nih.gov/methods/invitro.htm?>) (NIEHS 2003a, NIEHS 2003b, and NIEHS 2003c).

Comment. PCRM and HSUS commented that mammalian acute toxicity testing should be delayed until the median lethal dose (LD₅₀) test can be replaced with a non-animal test.

Response. EPA’s response to this comment is in Unit M.3. of this document.

Comment. PETA and HSUS commented that if EPA does require *in vivo* acute toxicity testing, EPA should accept data not only from the Up/Down Procedure adopted by the OECD as test guideline 425 (i.e., OECD 425) (OECD 2001d), but also from other acute toxicity tests adopted by the OECD, namely the Fixed Dose Procedure (OECD 420) (OECD 2001b) and the Acute Toxic Class Method (OECD 423) (OECD 2001c).

Response. Although the revision of all three guidelines was completed by the OECD in the fall of 2001, EPA believes the Up/Down Procedure (OECD 425) and the ASTM 1163 method are the

most appropriate procedures for new mammalian acute toxicity testing conducted under the final test rule for substances that are not gases at room temperature. While all three guidelines significantly reduce the number of animals used in comparison to the traditional LD₅₀ test, and allow the observation of signs of toxicity and the use of OECD guidance for humane endpoints which should reduce the overall suffering of animals in this type of test, only the Up/Down Procedure was designed to provide a point estimate of lethality, a confidence interval around the LD₅₀, and a dose-effect curve. The OECD 420 and OECD 423 methods only provide a general estimate of the LD₅₀ within a dose range (EPA 2002c and OECD 2001a). Finally, OECD 425 is the guideline referred to for mammalian acute toxicity testing in the voluntary HPV Challenge Program and EPA's Voluntary Children's Chemical Evaluation Program (VCCEP). Requiring the use of the same guideline for the testing of a particular endpoint allows greater comparability of the resulting data on different chemicals, which facilitates use of the data in the prioritization of chemicals by potential hazard.

3. Aquatic toxicity -

a. *Log K_{OW} value as selection criterion for acute vs. chronic aquatic toxicity testing.* In the proposed test rule preceding the final test rule, EPA proposed that the determination as to whether acute (Test Group 1) versus chronic (Test Group 2) aquatic toxicity testing is required for a given test rule chemical be based on the substance's n-octanol/water partition coefficient (log K_{OW}). Substances for which aquatic toxicity testing would be required that have log K_{OW}s of less than 4.2 would generally undergo acute aquatic toxicity testing, while substances for which aquatic toxicity testing would be required that have log K_{OW}s of 4.2 or more would generally undergo chronic aquatic toxicity testing. In addition, EPA proposed that any substance for which aquatic toxicity testing would be required would undergo a toxicity to plants (algae) study (EPA 2000c, pp. 81669-81670 and 81683-81684).

EPA solicited comment as to whether, for substances that may have log K_{OW} values of 4.2 or greater and that may still be acutely toxic to aquatic organisms, the Agency should include in the final rule provisions to allow test sponsors who wish to conduct acute aquatic toxicity testing rather than chronic testing to submit a written request to EPA for approval. The Agency suggested that such a request would need to include the rationale for the request, and would need to be approved by EPA prior to initiating the acute studies.

Comment. No comments were submitted in response to the Agency's suggestion; however, ACC (ACC 2001) commented that a cutoff value of 4.2 will not necessarily be appropriate for all chemicals in the context of an HPV screening program. ACC urges EPA not to set specific log K_{OW} criteria, but rather to allow industry the flexibility to propose aquatic toxicity test plans that consider the potential for long-term effects on a chemical-by-chemical basis.

Response. As stated in the proposed test rule (EPA 2000c, p. 81670), use of the 4.2 threshold is based on EPA's policy statement on the category of persistent, bioaccumulative and toxic (PBT) new chemical substances (EPA 1998c and EPA 1999f). That policy statement was developed based on EPA experience reviewing accumulated, available data on PBT and similar substances. EPA agrees with ACC that there may be instances in which the 4.2 threshold could be

inappropriate for a specific chemical substance; however, ACC did not specify, nor has EPA determined, that the threshold is inappropriate for any of the chemicals for which testing is required under the final test rule. In an instance in which a test sponsor believes that an alternative to the 4.2 threshold is appropriate, the test sponsor may request a modification as described in 40 CFR 790.55. Based upon the supporting rationale provided by the test sponsor, EPA may allow that an alternative threshold or method be used for determining whether acute or chronic aquatic toxicity testing be performed for a specific substance.

b. *Require in vitro Tetrahymena test instead of an in vivo fish acute toxicity test.*

Comment. PETA and PCRM commented that EPA's requirement of aquatic toxicity tests on fish is unnecessary given the understanding of aquatic microorganisms and the availability of *in vitro* test methods. PETA and PCRM stated that the *in vitro Tetrahymena* test, also known as the TETRATOX test (Schultz), should be used instead of the *in vivo* fish acute toxicity test.

Response. EPA does not agree that the TETRATOX test is a valid substitute for the fish acute test because of the following reasons:

- The two test organisms (fish and *Tetrahymena*) represent two entirely unrelated Phyla (LeBlanc). Extrapolating from such a wide phylogenetic gap raises considerable uncertainty in EPA's ecological effect assessments (EPA 2004j).
- The endpoints are different. The acute fish test evaluates mortality whereas the TETRATOX test evaluates cell proliferation (EPA 2004j).
- The TETRATOX test contains substances which may mitigate or mask toxicity (Larsen, et al. and EPA 2004j).
- Although the TETRATOX test correlates well with fish acute toxicity tests for neutral organic chemicals, it does not correlate as well with other classes of chemicals (EPA 2004j).
- Unlike results from the fish acute test, those from the TETRATOX test do not enable EPA to extrapolate to chronic effects nor do they permit EPA to identify toxicity caused by metabolic activation or other mechanisms (EPA 2004j; EPA 2004j).

For these reasons, EPA believes that the TETRATOX test is not an adequate substitute for the fish acute toxicity test.

J. Reporting Requirements

Comment. SOCMA commented that EPA's survey of laboratory capacity in 1996 (EPA 1996b) predicted an expansion in testing capacity to accommodate demand, but SOCMA doubts that has occurred to the extent necessary to meet the anticipated demands of the voluntary HPV Challenge Program and the testing to be required by the final test rule. As a result, SOCMA requested that EPA extend the deadline for the submission of final test reports from 13 months to 18 months after the effective date of the final test rule. SOCMA contends that this extension would still provide information in a timely manner, and would also prevent the unnecessary

burden of filing modification requests to extend the test schedule pursuant to 40 CFR 790.55. CPMA commented that the 13 months EPA has proposed for completion of all required tests is not an adequate period of time to identify all manufacturers and importers, reach agreements on testing, and conduct testing. CPMA stated that, at a minimum, several years should be allocated for completion of the testing.

Response. EPA expects that there will be sufficient laboratory capacity available (EPA 1996b and EPA 1999e) to complete the required testing in the time proposed by EPA. As noted in the EPA report entitled *Status and Future Directions of the High Production Volume Challenge Program* (EPA 2004k) and the Economic Analysis for the final test rule (EPA 2005a), only a relatively minimal amount of new testing (i.e., fewer than 10% of the endpoints for sponsored chemicals) has been proposed for sponsored chemicals in the voluntary HPV Challenge Program because a large number of the sponsored chemicals had existing data available. In consideration of the duration of time required to conduct each of the required tests and the fact that the tests can generally be conducted concurrently rather than sequentially, it is EPA's judgement that all the required testing can be planned, initiated, and completed within 13 months from the effective date of the final rule, particularly given that the final test rule seeks basic screening level information rather than requiring that complex studies be conducted. Therefore, the deadline for the submission of final test reports required under the final test rule is 13 months after the effective date of the final rule. (See Unit V.F. of the final test rule (EPA 2005b) and § 799.5085(i) of its regulatory text). If a company submits a letter of intent to test under the final rule and subsequently anticipates difficulties in completing the testing by the deadline set forth in the final test rule, then that company may submit a modification request to the Agency, 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.

K. Chemical-Specific Comments

In addition to the chemical specific comments addressed in this Unit K., EPA also received comments on many of the 20 chemicals for which EPA has decided not to pursue rulemaking. The basis for that decision for each chemical is discussed in Unit VII of the final test rule (EPA 2005b).

1. Methane, dibromo-

Comment. PETA and PCRМ commented that dibromomethane (CAS No. 74-95-3) should be included with other halogenated solvents and tested as a category.

Response. EPA has advocated the use of categories in the voluntary HPV Challenge Program and has provided support for their use by developing documents that provide step-by-step guidance to assist industry participants and others in constructing scientifically defensible categories (EPA 1999b). Although nine other chemicals in the proposed test rule that were identified by PETA and PCRМ as possible candidates for inclusion in categories have subsequently been sponsored

either directly in the voluntary HPV Challenge Program or indirectly through the ICCA HPV Initiative, unfortunately no one has volunteered to sponsor dibromomethane. A technical rationale to construct a scientifically defensible category approach for this chemical has not been developed. See also Unit E. of this document for general responses to comments related to the use of SAR and category approaches in the context of TSCA section 4 HPV SIDS test rules.

2. 1,3-Propanediol, 2,2-bis[(nitrooxy)methyl]-, dinitrate (ester).

Comment. SII, on behalf of a confidential manufacturer, and Dyno Nobel submitted comments on 1,3-propanediol, 2,2-bis[(nitrooxy)methyl]-, dinitrate (ester) (CAS No. 78-11-5), also known as pentaerythritol tetranitrate (PETN). IME stated that it supports the comments of SII and those of Dyno Nobel. The commenters claimed the NOES data used by EPA to support its finding that 1,000 or more workers may be exposed to PETN are outdated and unrepresentative of actual exposure.

Response. EPA disagrees that the NOES data are unrepresentative. The NOES, which was a nationwide data gathering project conducted by NIOSH, was designed to develop national estimates for the number of workers potentially exposed to various chemical, physical, and biological agents and to describe the distribution of those potential exposures. The NOES database and associated reports can be accessed electronically at: <http://www.cdc.gov/noes/default.html>. 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. 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. The NOES is the most recent and comprehensive source of this information. Because some time has passed since the NOES was completed, EPA acknowledges that there may be instances where changes in various industrial sectors (e.g., due to market demand, advances in technology, and other mitigating factors) have led to a decrease (or increase) 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 to be relevant to the Agency's determination to require testing of a particular chemical substance under TSCA section 4. Although Dyno Nobel claimed that only eight employees were potentially exposed to PETN at its manufacturing plant, Dyno Nobel did not describe the processes during which employees might be exposed to PETN or how certain work areas are secured to keep that number of employees to a minimum. EPA also reviewed 2002 IUR data (EPA 2004d) which indicated that there is another manufacturer of PETN and two importers. No information was submitted by these companies estimating the number of employees exposed to PETN at their facilities or the facilities of their customers, which may be users or processors of PETN. Therefore, in the absence of more comprehensive recent data which estimate worker exposure to PETN in all facilities where it is manufactured,

processed, and used, EPA will continue to rely on the NOES estimate that 2,650 employees (NIOSH 1983a) are potentially exposed to this chemical. Because this number exceeds 1,000, which EPA generally relies on as a numerical threshold to identify “substantial” worker exposure (EPA 1993), and because the commenter has provided no reason why EPA should use a different threshold in the final test rule, EPA continues to make the finding for substantial human exposure to PETN during manufacturing, processing, and use under TSCA section 4(a)(1)(B)(i)(II) and is requiring the testing of PETN.

Comment. SII commented that the primary exposure group for PETN is not workers involved in its manufacture, but instead individuals taking PETN therapeutically for control of angina pectoris, and possibly also workers involved in the manufacture of the therapeutic form of PETN. SII argues that the therapeutic form of PETN should be the test substance and that its manufacturers should be responsible for testing.

Response. EPA is aware that PETN is used in pharmaceuticals as a vasodilating drug. The pharmaceutical use of PETN, however, falls under the jurisdiction of the Food and Drug Administration (FDA), and EPA does not have the authority under TSCA section 4 to require manufacturers or processors of PETN solely for that use to conduct testing.

Comment. SII, Dyno Nobel, and IME stated that PETN is used primarily in detonators, detonating cord, boosters, sheet and plastic explosives, priming compositions, and military uses. Dyno Nobel commented that, because heat, friction, or shock can cause PETN to detonate, PETN is too sensitive to test. Dyno Nobel also commented that the 99% purity level specified for testing PETN in the proposed test rule is extremely dangerous and would jeopardize the safety of all personnel that would handle the PETN during the testing process. Dyno Nobel added that the Department of Transportation (DOT) has forbidden the shipment of 99% PETN across public highways and SII noted that PETN is only shipped in lower concentrations in combination with other diluting and/or desensitizing substances. SII commented that when testing PETN, it should be combined with a lactose stabilizer to render it nonexplosive, which is how PETN is altered so that it can be used therapeutically to control angina pectoris.

Response: EPA agrees that PETN cannot be tested at 99% purity because of its explosive properties and must be diluted in water or tested with a stabilizer as discussed in Unit V.D. of the final test rule (EPA 2005b) and required in § 799.5085 (a) of its regulatory text. Many toxicity studies have been conducted with PETN combined with a lactose stabilizer (i.e., PETN,NF) (EPA 2004f), some of which were cited and discussed in the comments submitted by SII. PETN, NF is the form of PETN which was tested by NTP in several toxicity studies described in a report entitled *Toxicology and carcinogenesis studies of pentaerythritol tetranitrate (CAS No. 78-11-5) with 80% D-lactose monohydrate (PETN, NF) in F344/N rats and B6C3F1 mice (feed studies)* (NTP 1989).

Comment. SII also commented that the lactose stabilizer has been found to be a teratogen, and recommends that tests for reproductive/developmental effects, in particular, should use the

lactose-stabilized PETN as the test substance, with the testing of pure lactose as a control to see what if any effect can be attributed to PETN.

Response. SII has not provided sufficient information to EPA to support its contention that lactose may be an experimental teratogen. However, EPA agrees with SII that the final test rule should include a control for the stabilizing compound, D-lactose monohydrate, to identify the effect, if any, on PETN when PETN is tested with the lactose stabilizer (EPA 2004f), and has included a provision to that effect.

Comment. SII commented that because of its extremely low solubility, PETN is “unlikely to enter [into solution with] surface water at concentrations harmful to algae.” SII stated that three different sources reported PETN’s aqueous solubility to be 1.5 milligrams/Liter (mg/L), 2.1 mg/L, and 43 mg/L. SII also commented that because the algal toxicities of related nitrate esters, ethylene glycol dinitrate (EGDN) and diethyleneglycol dinitrate (DEGDN), either exceeded or were close to the solubility of PETN, even modest dilution of PETN would reduce its concentration to well below the Effective Concentration for 50% of the algae (EC_{50} for algae). For these reasons, SII believes that it is unlikely that accurate algae tests with five different concentrations, as required in ASTM 1218, could be carried out and that the EC_{50} test for algae should not be required for PETN.

Response. EPA does not agree. EPA does not believe that PETN’s solubility properties should preclude conducting the test for toxicity to algae (EPA 2004e). SII’s concern that this is so is based on the assumption that PETN’s EC_{50} for algae is similar to that of DEGDN, which has an EC_{50} for algae of 39 mg/L, and that of EGDN, which SII states has an EC_{50} for algae close to PETN’s water solubility, i.e., 1.5 mg/L to 43 mg/L. Based on an SAR analysis, EPA believes that PETN’s EC_{50} for algae will be closer to that of nitroglycerine at 0.4 mg/L (EPA 2004e). EPA believes that testing PETN in accordance with ASTM E 1218 at concentrations below and slightly above the concentration of 0.4 mg/L should not pose solubility problems for PETN given that its solubility has been reported by SII to be 1.5, 2.1, and 43 mg/L. Because toxicity to algae is an important part of a chemical’s toxicity profile, EPA is requiring the determination of PETN’s EC_{50} for algae as described in Table 2 in § 799.5085(j) of the regulatory text of the final test rule (EPA 2005b).

Comment. SII commented that information is available in the literature regarding the biodegradation of PETN and that the proposed environmental fate test with activated sludge will only confirm the information that is already available. For this reason, SII believes that the environmental fate test using activated sludge should not be required for PETN.

Response. EPA disagrees with SII that sufficient information exists in the literature regarding biodegradation. The purpose of the proposed inherent biodegradability test is to assess the ultimate biodegradation of the test substance under specified conditions, which include mixed inoculum from natural sources such as soil or sewage and relatively high biomass concentration. In general, the objective is to determine environmental biodegradability, but under conditions

assumed to be favorable to biodegradation. It is normally not the function of such testing to determine metabolites or track primary loss of substrate. In contrast, the studies available in the literature are pure culture studies or studies of microbial consortia in which pathways of biodegradation are clarified. While such studies are helpful in determining fate because they suggest mechanisms by which a substance might be degraded, they do not yield the information sought by inherent biodegradation testing. Therefore, the studies cited by SII using pure cultures or microbial consortia are not sufficient because one cannot estimate environmental biodegradability using enrichment cultures (EPA 2003). In addition, the studies cited by SII were for analogs of PETN, not PETN itself. In general, extrapolation of such data is difficult and a substance would need to be a very close analog in order to justify this. EPA does not consider the analog identified by SII, glycerol trinitrate, to be close enough to PETN to extrapolate its results for ultimate biodegradation, as derived from a ready or inherent biodegradation test, to PETN. In part, this is due to the fact that PETN has a quaternary carbon, generally considered to impart resistance to ultimate biodegradation (but not necessarily primary degradation such as denitration), and glycerol trinitrate does not (EPA 2003). Therefore, EPA is requiring the development of test data on biodegradation of PETN as described in Table 2 in § 799.5085(j) of the regulatory text of the final test rule (EPA 2005b).

Comment. SII commented that, with the exception of the *n*-octanol/water partition coefficient, four of the five physical/chemical properties proposed for determination have already been measured for PETN. SII included a table in its comments listing values, and their sources, for melting point, boiling point, vapor pressure, and water solubility. SII argued that the final test rule should be clear that the *n*-octanol/water partition coefficient is the only physical/chemical property of PETN that needs to be determined by testing under the final test rule .

Response. EPA agrees in part. EPA believes that, in addition to a test to determine the *n*-octanol/water partition coefficient, a test to determine solubility in water is also needed. SII cited three sources which reported the water solubility of PETN to be either 1.5, 2.1, or 43 mg/L. Because these sources are somewhat dated and the current test method may be superior (EPA 2004g), EPA is requiring that the test for water solubility be conducted. This testing should resolve the disparity between the currently available values. The regulatory text of the final test rule (EPA 2005b) has been modified in Table 2 of § 799.5085(j) to indicate that the only physical/chemical properties of PETN that need to be determined by testing are water solubility and the *n*-octanol/water partition coefficient.

3. 2,4-Hexadienoic acid, (2E,4E)-.

Comment. The Ashland Distribution Company (ADC) stated that it imports and distributes 2,4-hexadienoic acid, (2E,4E)- (CAS No. 110- 44-1), also known as sorbic acid, solely for FDA-regulated uses. ADC commented that sufficient data exist to address EPA's reproduction/developmental screening level test requirement for sorbic acid and provided a list of such studies with their comments. ADC acknowledged that the procedures followed in conducting the studies are not equivalent to current test guidelines, but that consideration should

be given to the results of these studies, which indicate a low level of risk to reproduction from sorbic acid exposure, before conducting another test merely to achieve consistency with current guidelines.

Response. EPA appreciates that ADC informed EPA of existing studies pertaining to reproduction/developmental toxicity screening testing for sorbic acid. EPA reviewed four of the studies (Walker; Demaree; Food and Drug Research Labs; Anon) identified by ADC to determine if they could satisfy the data need for a reproductive and developmental toxicity screening test of sorbic acid. EPA's review of the studies found that, although the studies were dated, there was no evidence in the multi-generation reproduction studies (Demaree; Anon) to suggest that the chemical is a reproductive toxicant at the concentrations tested, and also that there is no evidence in the teratological study (Food and Drug Research Labs) to suggest that sorbic acid is a developmental toxicant at the concentrations tested (EPA 2004i).

Therefore, EPA is not finalizing the reproduction/developmental toxicity screening test proposed for sorbic acid. However, the other tests proposed for sorbic acid to develop data on physical chemical properties and aquatic toxicity are being required in the final test rule and are listed in Table 2 and described in Table 3 in § 799.5085(j) of the regulatory text of the final test rule (EPA 2005b).

4. *Dodecane, 1-chloro-*.

Comment. EPA received a comment from Lonza regarding worker exposure to 1-chlorododecane (CAS No. 112-52-7). Lonza commented that EPA's estimate that more than 1,000 workers are exposed to 1-chlorododecane based on NOES data is inaccurate. Lonza reported that its production of 1-chlorododecane exceeds 1 million lbs. per year, and that more than 95% of this amount is used as a site-limited intermediate, 4.5% is exported to facilities of Lonza International, and the remaining 0.5% (approximately 5,000 lbs./yr) is sold to four domestic customers. Lonza stated that Degussa Huls is the only other company to report the manufacture or import of 1-chlorododecane according to 1998 IUR data reported to EPA. Lonza estimated the potential number of workers exposed at its facilities, those of its customers, the facilities of Degussa Huls, and the customers of Degussa Huls to be less than 100.

Response. EPA disagrees. EPA has reviewed the information provided by Lonza, and has also reviewed IUR data from 1990 to 2002. Although the 2002 IUR data indicate that Lonza was the only manufacturer of 10,000 lbs. or more of 1-chlorododecane in the United States and that there were no importers, the three previous reporting years for IUR, i.e., 1990, 1994, and 1998, indicated that there were three other companies that manufactured or imported 1-chlorododecane (EPA 2004h). Because these companies and others may still be manufacturing (including importing) 1-chlorododecane in amounts less than the IUR reporting threshold of 10,000 lbs. per year, EPA believes that Lonza may not be the only manufacturer of 1-chlorododecane in the United States and Lonza may not have counted every worker potentially exposed to 1-chlorododecane in the United States. Even if Lonza were the only manufacturer, worker exposure could occur to 1-chlorododecane manufactured in previous years, but for whatever reason, not

processed or used until later. In addition, more than half of the number of workers estimated in NOES to be potentially exposed to 1-chlorododecane are molding and casting machine operators in the rubber and plastics industries (NIOSH 1983c), which is a worker population that Lonza did not discuss in its comment nor include in its estimate of exposed workers. Therefore, EPA cannot agree with Lonza that the number of workers exposed to 1-chlorododecane is unlikely to exceed 1,000. In the absence of more complete current data, EPA will continue to rely on the NOES data that 8,071 workers in the United States are potentially exposed to 1-chlorododecane. Because the NOES estimate of 8,071 exceeds the threshold of 1,000 workers, which is one of the thresholds EPA generally relies upon to make the finding for “substantial” human exposure (EPA 1993) under TSCA section 4(a)(1)(B)(i)(II), and because the commenter has provided no reason why EPA should use a different threshold in the final test rule, testing of 1-chlorododecane is required in the final test rule .

Comment. PETA and PCRM commented that 1-chlorododecane should be grouped with other halogenated solvents and tested as a category.

Response. EPA has advocated the use of categories in the voluntary HPV Challenge Program and has provided support for their use by developing documents that provide step-by-step guidance to assist industry participants and others in constructing scientifically defensible categories (EPA 1999b). Although nine other chemicals in the proposed test rule that were identified by PETA and PCRM as possible candidates for inclusion in categories have subsequently been sponsored either directly in the voluntary HPV Challenge Program or indirectly through the ICCA HPV Initiative, unfortunately no one has volunteered to sponsor 1-chlorododecane. A technical rationale to construct a scientifically defensible category approach for this chemical has not been developed. See also Unit E. of this document for general responses to comments related to the use of SAR and category approaches in the context of TSCA section 4 HPV SIDS test rules.

5. Heptenone, methyl-

Comment. EPA received a comment from ExxonMobil Chemical Company regarding worker exposure to methylheptenone (CAS No. 409-02-9). ExxonMobil claims that methyl- heptenone “is a component of a site-limited intermediate mixture that is either subsequently consumed internally or disposed of as a waste” and “there is essentially no exposure to the chemical, as the production and subsequent consumption are conducted in closed systems.”

Response. EPA does not agree. While EPA appreciates the comments submitted by ExxonMobil describing the production and use of methylheptenone in its company, which it used to support its claim that there is essentially no worker exposure to methylheptenone, there are other uses of methylheptenone that ExxonMobil did not mention in its comments. In addition to its use in organic synthesis, the opinion of the Scientific Committee on Cosmetic Products and Non-Food Products (SCCNFP) on *The 1st Update of the Inventory of Ingredients Employed in Cosmetic Products* indicates that methyl heptenone is used as a fragrance in consumer products. Also, methylheptenone is used as a synthetic flavoring agent in foods and pharmaceuticals (Hawley’s

Dictionary). Although IUR data indicate that ExxonMobil is the sole manufacturer of methylheptenone reporting in 2002 (EPA 2004c), IUR data do not capture the production or imports that occur at less than 10,000 lbs. per year per company, which may supply the methylheptenone required for the production of consumer products in which it is used as a fragrance. Because ExxonMobil's estimate did not account for employee exposure in the production of such products, EPA will continue to rely on the NOES estimate of 1,557 workers potentially exposed to methylheptenone. Because this figure exceeds the threshold of 1,000 workers, which is one of the thresholds that EPA generally relies upon to make a finding for "substantial" human exposure (EPA 1993) under TSCA section 4(a)(1)(B)(i)(II), and because the commenter has provided no reason why EPA should use a different threshold in the final test rule, EPA is requiring the testing of methylheptenone in the final test rule .

Comment. PCRМ commented that methyl heptenone is a constituent of lemongrass and a naturally occurring component of certain essential oils. PCRМ notes that this substance and its derivatives are used in perfumes and as flavoring agents in various food items. PCRМ states that conducting the mammalian acute toxicity test would not further the understanding of the hazards posed by this chemical. PCRМ believes that because methylheptenone is a component of many household products, including food items, a human observational study could easily show if it is acutely toxic at typical consumer or occupational exposures.

Response. EPA disagrees with PCRМ's comment that the mammalian acute toxicity test would not further the understanding of the hazards posed by this chemical and that a human observational study would provide a suitable substitute for the data which would be developed by testing in accordance with a mammalian acute toxicity test standard under the final test rule . The fact that a substance is present in perfumes and foods is not in and of itself adequate evidence to demonstrate the safety of the substance under all conditions of its use. The testing required in the final test rule , including the mammalian acute toxicity test, is essentially identical in scope and applicability to that which has been internationally agreed upon by the OECD as providing the consistent minimum set of information that can be used to make informed preliminary judgements about the relative hazards and risks of HPV chemicals and to judge if additional testing is necessary. Developing toxicity data in accordance with established testing guidelines, in which dosages of the test substance and other variables are known and controlled (which is difficult to achieve in a human observational study), can provide useful information, in particular a dose-response relationship, for evaluating the potential hazard of a chemical. By developing testing data that are consistent with the OECD HPV SIDS Program via the final test rule , EPA is ensuring that the data and information generated can be contributed to the international effort for use by governments and others worldwide and, thereby, avoid unnecessary or duplicative testing. The data obtained via the final test rule will be used by EPA, other Federal agencies, the public, industry, and others to determine if additional testing, including more in-depth or advanced testing, is needed to adequately assess the risks posed by exposure to a given chemical.

Comment. In its comments on the proposal to the final test rule , ExxonMobil claimed that methyl heptenone is a closed system intermediate. ExxonMobil claimed that methyl heptenone is

a component of a site-limited intermediate mixture whose production and subsequent consumption are conducted in closed systems. ExxonMobil also stated that some of the mixture is disposed of as a waste.

Response. In the proposal (EPA 2000c) to the final test rule, EPA stated that certain of the chemicals for which Mammalian Toxicity--Repeated Dose/Reproduction/ Developmental Toxicity testing is required may be used solely as "closed system intermediates," and, if that were the case, such chemicals may be eligible for a reduced testing battery which substitutes a developmental toxicity study for the SIDS requirement to address repeated dose, reproduction, and developmental toxicity. EPA requested persons who believe their chemical is used solely as a closed system intermediate to submit appropriate information along with their comments which substantiate this belief. In the proposed test rule, EPA stated that if EPA agreed that the chemical is used solely as a closed system intermediate, then the Agency would address any developmental toxicity testing need in a subsequent rulemaking (EPA 2000c, p. 81671).

ExxonMobil stated in its comments that some of the mixture is disposed of as a waste, which EPA understood to mean not in a closed system. Because of this and also because EPA believes that other companies are manufacturing (including importing) methyl heptenone for uses not addressed by ExxonMobil, as discussed in this Unit K.5. of this document, EPA does not consider methyl heptenone to be used solely as a closed system intermediate, and, therefore, does not consider it appropriate for reduced testing which would require only a developmental toxicity test instead of the Combined Repeated Dose/Reproduction/ Developmental Toxicity Screening Test.

6. *Benzenesulfonic acid, [[4-[[4-(phenylamino)phenyl][4-(phenylimino)-2,5-cyclohexadien-1-ylidene]methyl][phenyl]amino]-*

Comment. CPMA commented that the testing endpoints for [[4-[[4-(phenylamino)phenyl][4-(phenylimino)-2,5-cyclohexadien-1-ylidene]methyl][phenyl]amino]benzenesulfonic acid (CAS No. 1324-76-1), also known as alkali blue pigment, do not appear appropriate, given that alkali blue pigment is an organic pigment, and organic pigments, with only a few exceptions, are extremely insoluble, very low in bioavailability, and non-toxic. CPMA stated that there are acute toxicity data on other pigments, and that the vast majority of the LD₅₀ values are above 5,000 mg/kg and no LD₅₀ values are known to be below 2,000 mg/kg. As a result, CPMA believes that organic pigments should not be assigned a high regulatory priority based on toxicity.

Response. CPMA's claims that alkali blue pigment is insoluble and non-toxic were not substantiated by CPMA with any data specific to alkali blue, but rather were based on alkali blue pigment being a member of the large chemical category of organic pigments. Nor did CPMA present SAR reasons to argue that the toxicity and solubility of alkali blue pigment should closely approximate that of another pigment for which data were available.

Comment. PCRMR commented that there is no value in conducting acute toxicity tests on rodents with alkali blue pigment when the substance is currently so widely used and handled by humans in

the workplace. PCR/M believes that, given the fact that workers are likely to frequently contact this substance, occupational studies of these workers could demonstrate if alkali blue pigment is acutely toxic.

Response. EPA disagrees. EPA believes that frequent contact with alkali blue pigment by a substantial number of workers is a compelling reason to require testing for this chemical. The testing required in the final test rule, including the mammalian acute toxicity test, is essentially identical in scope and applicability to that which has been internationally agreed upon by the OECD as providing the consistent minimum set of information that can be used to make informed preliminary judgements about the relative hazards and risks of HPV chemicals and to judge if additional testing is necessary. Developing toxicity data in accordance with established testing guidelines, in which dosages of the test substance and other variables are known and controlled (which is difficult to achieve in an occupational study), can provide useful information, in particular a dose-response relationship, for evaluating the potential hazard of a chemical. By developing testing data via the final test rule that are consistent with the OECD HPV SIDS Program, EPA is ensuring that the data and information generated can be contributed to the international effort for use by governments and others worldwide and, thereby, avoid unnecessary or duplicative testing. The data obtained via the final test rule will be used by EPA, other Federal agencies, the public, industry, and others to determine if additional testing, including more in-depth or advanced testing, is needed to adequately assess the risks posed by exposure to a given chemical.

7. Light oil (coal), coke-oven.

Comment. The American Coke and Coal Chemicals Institute (ACCCI) commented that the NOES data used to substantiate EPA's assertion that more than 1,000 workers may be exposed to coke oven light oil (light oil) (CAS No. 65996-78-3) is out-dated and no longer valid. ACCCI noted that the 1983 NOES data estimated that 3,047 workers are exposed to light oil at 46 sites, but that as of 2001, the number of sites producing light oil has fallen to 18.

The ACCCI provided data collected by an independent consulting firm, Ron Outen Associates (ROA), commissioned by ACCCI to evaluate worker exposure to light oil. ROA reportedly contacted all 18 facilities producing light oil, which are also members of ACCCI, and determined that no full-time workers and only 25 part-time workers are exposed to light oil during its manufacture. Of the 25 part-time workers with potential exposure, all of them are engaged in transfer operations of light oil as opposed to production operations. ACCCI claims that this low number of potentially exposed workers is justified by reports that most, if not all, production and handling systems at these facilities are fully enclosed. The ROA survey also reported that only 2 sites process light oil in its sole use, which is as a feedstock from which constituent chemicals (primarily benzene, toluene, and xylenes) are recovered by hydrogenation, distillation, and fractionation. Light oil is consumed in this recovery process, making processors the end-use customers. A total of 78 additional workers (45 workers in transportation and 33 in processing) have a potential for exposure to light oil. Therefore, according to ROA, the total number of workers with potential exposure to light oil during its manufacture, transport, processing, and use

is 103, and not the 3,047 workers estimated by the NOES.

Response. EPA does not agree. ACCCI apparently assumed that the NOES estimate of 3,047 pertained only to potential worker exposure at light oil production and processing facilities. As a result, ROA's evaluation did not look beyond light oil production and processing facilities to identify other potentially exposed employees. The breakdown of the NOES estimate of 3,047 workers exposed to light oil attributes the exposure of 2,559 of those workers to their occupation as roofers (NIOSH 1983b). EPA has no evidence that suggests that roofers are not exposed to light oil and cannot agree with ACCCI that it is unlikely that 1,000 or more workers are potentially exposed to light oil. Therefore, EPA is relying on the NOES estimate of 3,047 as being a more comprehensive estimate of worker exposure. Because 3,047 workers exceeds the threshold of 1,000 workers, which is one of the thresholds that EPA generally relies on to make a finding for "substantial" human exposure (EPA 1993) under TSCA section 4(a)(1)(B)(i)(II), EPA is requiring testing of light oil in the final test rule (EPA 2005b).

Comment. ACCCI commented that light oil (CAS No. 65996-78-3) is a mixture whose non-trace (more than 1%) constituents either have a full SIDS data set and are being addressed by the voluntary HPV Challenge Program, or can be characterized adequately using data from structurally similar chemicals. ACCCI asked EPA to agree that testing of light oil is not necessary.

Response. EPA notes that light oil is a Class 2 chemical under TSCA and not a mixture as stated by ACCCI. Class 2 chemicals differ from mixtures in that a Class 2 chemical cannot be manufactured by combining chemical substances because a Class 2 chemical is comprised of unknown, variable, or complex combinations of chemicals. In contrast, a mixture may be manufactured by combining other chemical substances. Although EPA has the authority to require testing of both Class 2 chemicals and components of Class 2 chemicals (as well as mixtures and components of mixtures), EPA needs and is requiring test data on light oil and not its components so that any possible synergism, antagonism, or addition of effects due to the interaction of the components will be reflected in the results. Also, limiting the screening-level evaluation of light oil to the non-trace constituents listed in ACCCI's comments fails to account for potential components of light oil which may be unknown or variable, but nonetheless toxic.

Comment. PETA and PCRМ commented that coke oven light oil (from coal) shares many properties with other heavy oil mixtures found in the petroleum industry and could potentially be incorporated into one of the categories being developed by API in the voluntary HPV Challenge Program.

Response. EPA has advocated the use of categories in the voluntary HPV Challenge Program and has provided support for their use by developing documents that provide step-by-step guidance to assist industry participants and others in constructing scientifically defensible categories (EPA 1999b). Although nine other chemicals in the proposed test rule that were identified by PETA and PCRМ as possible candidates for inclusion in categories have subsequently been sponsored

either directly in the voluntary HPV Challenge Program or indirectly through the ICCA HPV Initiative, unfortunately no one has volunteered to sponsor coke oven light oil . A technical rationale to construct a scientifically defensible category approach for this chemical has not been developed. See also Unit E. of this document for general responses to comments related to the use of SAR and category approaches in the context of TSCA section 4 HPV SIDS test rules.

L. TSCA Section 4 Findings

1. Policy basis for making TSCA section 4(a)(1)(B) finding.

Comment. ACC (ACC 2001) and ETAD commented that the criteria EPA used to require testing under TSCA section 4(a)(1)(B) rely on EPA's "B" policy (EPA 1993), which sets general numerical thresholds for the substantial production, release, and exposure findings, but that EPA has not shown that these thresholds are consistent with TSCA.

Response. EPA disagrees. The Agency's findings in the final test rule for substantial production and substantial human exposure are based on production volume data reported to EPA under its IUR and NOES employee exposure data, respectively. EPA believes the thresholds it generally relies upon are consistent with TSCA. The threshold of one million lbs. used to make the finding for substantial production is based on the Agency's belief that it is reasonable to interpret the word "substantial" to mean a large number. The rationale for this threshold is presented in EPA's "B" policy (EPA 1993, p. 28746). EPA believes that, as in the case of the final test rule, where production volume is one million lbs. or more for a chemical for which the rule would require testing, it will generally be reasonable to require the testing of that chemical (assuming the other statutory criteria are met). The threshold of 1,000 workers used to make the finding for substantial human exposure is based on the Agency's belief that it is reasonable to interpret the word "substantial" to mean exposure to large numbers of people. The rationale for this threshold is presented in EPA's "B" policy (EPA 1993, pp. 28742 and 28746). EPA believes that, as in the case of the final test rule, where 1,000 or more workers are potentially exposed to a chemical for which the rule would require testing, it will generally be reasonable to require the testing of that chemical (again, assuming the other criteria are met) (EPA 1993). 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)).

Comment. ETAD contended that EPA's "B" policy has no binding effect because it is not a regulation nor has it been evaluated by the courts.

Response. EPA agrees that the policy has no binding effect, and does not treat it as binding. EPA generally looks to the thresholds as guidance to interpret what the TSCA term "substantial"

means. These thresholds have come to be known as the “B” Policy (EPA 1993). Since 1993, when EPA issued the B policy, EPA has seen general acceptance of and agreement with the numerical thresholds from the regulated community. The numerical thresholds provide useful guidance to both EPA and the regulated community. Nonetheless, the thresholds are no more than guidance. As stated in the “B” Policy, “However, EPA does not intend to limit itself to the use of these criteria in making ‘B’ findings and reserves the ability to consider other factors on a case-by-case basis” (EPA 1993, p. 28737). EPA continues to believe those thresholds are generally appropriate and has not identified any reason why they are not appropriate for the final test rule ; nor did commenters suggest alternative numbers or alternative approaches to determining what is “substantial.”

2. *Substantial production, TSCA section 4(a)(1)(B)(i).*

Comment. ETAD commented that neither the proposed test rule nor the references cited in the proposed test rule provide evidence that the C.I. Direct Black 22 is or will be produced or imported at volumes exceeding the threshold of one million lbs. per year. In similar comments, the Coke Oven Environmental Task Force of ACCCI and SII stated that EPA did not make the underlying data available on specific production volumes for light oil and pentaerythritol tetranitrate (PETN), respectively, thereby denying the public the ability to evaluate EPA’s justification for the exposure-based finding.

Response. The finding for substantial production made in the final test rule (EPA 2005b) is based on production volume data reported to EPA under its IUR. The numerical basis for each chemical’s substantial production finding was not included in the preamble to the proposed test rule because most of the IUR production volumes that have been reported to EPA have been claimed as confidential business information (CBI). Pursuant to Agency confidentiality regulations at 40 CFR part 2, subpart B, EPA cannot make information claimed as confidential available to the public until and unless the Agency has followed those regulatory procedures necessary to declassify the information (which may include a determination that the information is not entitled to confidential treatment under law). EPA has not issued confidentiality determinations for the chemical substances subject to the final test rule . Because there were only a few manufacturers per chemical for most IUR chemicals, the aggregated production volumes were treated as CBI to prevent back calculation to individual production volumes. EPA does, however, make the aggregated production volumes of individual chemicals in the TSCA Inventory available to the public in ranges of one-million to ten-million lbs., greater than ten-million to one-hundred million lbs., and greater than one-hundred million to one-billion lbs. By using production volume ranges, EPA does not jeopardize the confidentiality claims of the IUR data. The public can access this public version of IUR information at <http://www.epa.gov/opptintr/iur/index.html>. The production volume ranges for the chemicals in the final test rule are also provided in the Economic Analysis prepared for the final test rule (EPA 2005a). Companies had the opportunity to comment on the proposed test rule and submit current information to refute EPA’s finding that production for any of the test rule chemicals is substantial. If EPA agreed with information submitted by the companies which demonstrated that

less than one million lbs. of a subject chemical is manufactured (including imported), that chemical would not be included in the final test rule . For example, the Sodium Formaldehyde Bisulfite Manufacturers Association (SFBMA), which represents the major manufacturers and importers of methanesulfonic acid, hydroxy-, monosodium salt (CAS No. 870-72-4) in the United States, informed EPA that the production volume of this chemical is much less than one million lbs. The 2002 IUR data for this chemical confirmed that this was the case and EPA did not include methanesulfonic acid, hydroxy-, monosodium salt in the final test rule (See Unit VII.B. of the final test rule (EPA 2005b)).

Comment. PETA and PCRM commented that EPA did not adequately demonstrate that high production volume equates to high exposure to humans and/or high release to the environment, and that EPA must justify basing the proposed testing on production volume. ARDF commented that production volume may have no correlation with a chemical's safety or risk potential.

Response. The "substantial production" finding is one of several findings EPA must make before a chemical may be subject to testing under TSCA section 4(a)(1)(B). EPA did not base its finding that there is substantial release or substantial or significant human exposure under TSCA section 4(a)(1)(B)(i)(I) and (II) upon production volume data, but upon the NOES exposure estimates discussed in Unit K.2. of this document. EPA does not believe that high production volume equates to high exposure to humans and/or high release to the environment, although it is generally accepted that chemicals having a high level of production have an increased potential for exposure in comparison to low production volume chemicals.

3. *Substantial human exposure finding, TSCA section 4(a)(1)(B)(i)(II).*

Comment. ETAD commented that there is no evidence to show that potential human exposure to any of the test rule chemicals exceeds the "B" policy threshold of 1,000 workers. In similar comments, SOCMA and PCRM commented that EPA has not adequately supported its finding of substantial human exposure in the proposed test rule because, according to SOCMA, EPA did not provide information in the docket on the specific NOES estimates of the number of employees potentially exposed to each chemical in the proposal to the final test rule . The Coke Oven Environmental Task Force of ACCCI and SII stated that by not making the underlying data available on the actual number of workers exposed, EPA denied the public the ability to evaluate EPA's justification for the exposure-based finding.

Response. EPA disagrees. The finding for substantial human exposure made in the proposal to the final test rule and again in the final test rule is based on NOES worker exposure data. The specific number of potentially exposed workers was not stated in the proposed test rule because the selection process used to identify candidates for the proposed test rule only considered HPV chemicals with potential worker exposure "in excess of 1,000 workers according to NOES data." (EPA 1998d). One thousand workers is one of the numerical thresholds that EPA generally looks to in determining whether the TSCA requirement of "substantial" is met when making findings for substantial human exposure (EPA 1993). The NOES reports for the chemical substances

subject to the final test rule can be accessed electronically at: <http://www.cdc.gov/noes/default.html>. The public had the opportunity to comment on the proposed test rule and submit current worker information to refute EPA's finding that a substantial number of employees is or may be exposed. The public also had the opportunity to assert that 1,000 workers is not an appropriate threshold and to offer alternative approaches to making the substantial exposure finding. If EPA agreed with information submitted by commenters which demonstrated that fewer than 1,000 employees were exposed to a chemical, that chemical would not be included in the final test rule.

Comment. ACC (ACC 2001) and SOCMA commented that EPA's assertion that there is substantial human exposure to workers should be accompanied by up-to-date supporting evidence and not simply by the data collected in the NOES, which ended in 1983. ACC and SOCMA stated their concern that NOES data pertain only to the number of workers at plant sites and that the survey did not attempt to identify the manner in which employees were exposed to the chemicals, the duration and concentration levels of exposure, or whether protective measures (such as the use of personal protective equipment) reduced exposure levels. Because of these limitations, ACC and SOCMA believe the NOES estimates have little validity and fail to provide reasonable support for EPA's TSCA section 4(a)(1)(B) findings of "substantial human exposure." ACC notes that many of these concerns are presented in detail in a critique of the NOES data previously provided to EPA (Buell, et al.). In addition, SOCMA claimed that the NOES indicates that for the overall chemicals and allied products industry, approximately 90% [of the companies surveyed] require or recommend the use of personal protective equipment for plant workers. ACC (ACC 2001) also commented that EPA should make an effort to determine if uses and potential exposures have changed over time, as typically is the case, or should ask for that information in the proposed test rule. ACC stated that EPA should not rely on NOES data absent some other more recent indication of reliability for a particular chemical/use scenario. PETA and PCRM commented that, because some of the HPV chemicals proposed for testing have been detected in the ambient and occupational environment at levels that are orders of magnitude below the recommended exposure limits, it is incumbent on EPA to demonstrate that there is significant exposure to these substances before requiring testing under TSCA.

Response. The Agency believes that it is reasonable to interpret "substantial human exposure" to mean exposure of large numbers of people. EPA does not rely on levels of exposure in determining substantial human exposure, as ACC, SOCMA, PCRM, and ARDF recommend, because the risk presented by a particular level of exposure cannot be determined unless the toxicity of the chemical is known. EPA believes that, in the case of the final test rule, where 1,000 or more workers may be exposed to each chemical for which the rule would require testing, it is reasonable to require test data on each chemical. 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)).

This interpretation of TSCA section 4(a)(1)(B) is also supported by the structure of TSCA section 4. Findings under TSCA section 4(a)(1)(A) include a determination that a chemical may present an unreasonable risk to health or the environment, and thus involve some consideration of both hazard and exposure. In contrast, TSCA section 4(a)(1)(B) authorizes EPA, in part, to require the testing of chemicals that are produced in substantial quantities and to which there is or may be substantial human exposure (where EPA also finds that existing data are insufficient and testing of the chemical is necessary). Congress intentionally omitted hazard and risk considerations as a factor in making findings under TSCA section 4(a)(1)(B) (EPA 1993, p. 28736-37). In EPA's view, a finding of "significant human exposure" under TSCA section 4(a)(1)(B)(i)(II) involves a judgment regarding the nature of the exposure (i.e. how direct or prolonged the exposure may be), whereas a finding of "substantial human exposure" under the same section is determined solely with reference to whether large numbers of people are or may be exposed. (EPA 1993, pp. 28741-28744).

Concerning ACC's comment that EPA should consider not only the number of workers exposed to a chemical, but also the frequency, duration, and level of that exposure, EPA's policy is that such information, although almost always essential for a risk analysis, is not required for a finding under TSCA section 4(a)(1)(B), which requires no risk analysis (EPA 1993, p. 28742). The utility of the frequency, duration, and levels of exposure is limited when EPA is acting in the absence of information about the hazard of the chemical substance in question (EPA 1993, p. 28742). Given the statutory framework, the legislative history, and the case law interpreting the section 4 testing provisions, EPA believes that it is not 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 (EPA 1993, p. 28742).

Although EPA is not required to consider the factors mentioned by ACC in making its "substantial" human exposure finding, information of the sort described by ACC, as well as information on the physical and biological properties and toxicity of the test substance, is nevertheless relevant to other decisions leading to a determination as to whether to require testing under TSCA section 4. In making findings under TSCA sections 4(a)(1)(B)(ii) and 4(a)(1)(B)(iii), i.e. findings as to 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 the substance is necessary to develop such data, all available and relevant information concerning the substance are taken into consideration (EPA 1993, p. 28743).

In those instances where interested parties provided such relevant information on chemical substances prior to the publication of the final test rule (EPA 2005b), EPA carefully reviewed that information before making its final testing decisions. For example, as discussed in Unit K.2. of this document and Unit VII.C.1. of the final test rule (EPA 2005b), EPA reviewed data submitted by SII on the physical/chemical properties of PETN (CAS No. 78-11-5). EPA believes the submitted data are sufficient for melting point, boiling point and vapor pressure, and, therefore, EPA is not finalizing the proposed testing to determine the melting point, boiling point and vapor pressure of PETN in the final test rule. Also, as discussed in Unit K.3. of this document and Unit VII.C.2. of the final test rule (EPA 2005b), EPA reviewed four studies on sorbic acid (2,4-hexadienoic acid, (2E,4E)-) (CAS No. 110-44-1) which ADC thought might satisfy the testing

proposed to obtain screening level data on the reproductive and developmental toxicity of sorbic acid. EPA determined that the studies provided sufficient information on this endpoint(s) at this time for sorbic acid, and, therefore, EPA is not requiring the reproduction/developmental toxicity screening test of sorbic acid in the final test rule .

While the NOES 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. EPA believes that the data in the NOES database concerning numbers of workers potentially exposed to a specific chemical substance can provide a reasonable basis to support the finding that there is or may be substantial human exposure to such substance. The NOES is the most recent and comprehensive source of this information. EPA's proposed test rule asked interested parties to provide any information they believed to be relevant to the Agency's determination to require testing of a particular chemical substance under TSCA section 4. However, EPA acknowledges that because some time has passed since the NOES was completed, there are likely to be instances where changes have occurred in various industrial sectors (i.e., markets, advances in technology, and other mitigating factors), which may have led to a decrease or an increase in the number of workers potentially exposed to certain chemical substances. For this reason, EPA's proposed test rule asked interested parties to provide any information they believed to be relevant to the Agency's determination to require testing of a particular chemical substance under TSCA section 4. EPA carefully and fully considers comments that provide information on the number of workers potentially exposed to chemicals contained in a proposed test rule containing preliminary worker-based substantial human exposure findings. Such information could result in an Agency decision not to finalize testing requirements that had been proposed for a chemical.

As noted by SOCMA, the NOES also contains estimates of the percent of facilities that require or recommend personal protective equipment (PPE) and, in particular, the NOES estimates that, for the overall chemicals and allied products industry, approximately 90% of the companies surveyed require or recommend use of PPE. The estimates of PPE usage contained in NOES provide useful information about the extent of PPE usage. However, the NOES estimates include, without distinction, both those facilities that require use of PPE as a condition of employment and those where use of PPE is recommended (i.e., encouraged but not required). In addition, NOES does not provide information about the effectiveness of the PPE used for individual chemicals and exposure situations. As a result, EPA would have no basis upon which to modify the NOES worker exposure estimates based on PPE usage. Also, it should be noted that not all workers potentially exposed to the 17 chemicals addressed by the final test rule are employed in the chemicals and allied products industry. The NOES estimates of the percent of facilities requiring or recommending use of PPE is significantly less than 90% in other industry sectors; the overall percentage for all industries surveyed is approximately 77%. The nature of the PPE used in these facilities and the effectiveness of that PPE for reducing worker exposure to a given chemical cannot be ascertained from the information collected in NOES (NIOSH 1988).

Comment. ARDF commented that if human exposure is very limited, the extent of necessary toxicity assessment should be correspondingly low.

Response. EPA disagrees that the levels of human exposure need to be determined to dictate the appropriate level of testing under TSCA section 4. As explained above in Unit L.3. of this document, EPA has made a TSCA section 4(a)(1)(B)(i)(II) finding for substantial human exposure (in addition to the other required findings as discussed herein) for the 17 chemicals in the final test rule. Also, the testing required by the final test rule is not extensive, but only the minimum set of screening level data that EPA believes is necessary to begin to understand a chemical's potential toxicity.

4. Data are insufficient, TSCA section 4(a)(1)(B)(ii).

Comment. ACCCI and PCRM stated that EPA failed to show that there is a lack of data to reasonably determine or predict the effects on health or the environment of the chemicals proposed for testing. PCRM commented that it is incumbent on EPA to demonstrate that it conducted a thorough review of all available data and found insufficient data to perform a hazard assessment.

Response. The six endpoints to be addressed by the proposed SIDS screening level tests are internationally recognized as essential for a preliminary understanding of a chemical's environmental fate and effects on health and the environment (See Unit II.D. of the final test rule (EPA 2005b)). Evaluations of the available published data on HPV chemicals have been conducted by EPA (EPA 1998a), ACC (ACC 1998), and ED (ED 1997) to determine if the available data addressed the six OECD SIDS endpoints. Each of these evaluations identified a lack of publicly available basic screening level data on HPV chemicals, including the 37 chemicals for which EPA proposed testing in December, 2000 (EPA 2000c), and the 17 chemicals for which testing is required in the final test rule. EPA's search strategy used a total of 11 publicly accessible databases in its analysis; details of the search strategy can be found in the Agency's report (EPA 1998a). ACC's evaluation of public data availability for HPV chemicals was conducted with 11 main data sources, including data sources other than those searched by EPA for its evaluation. The ACC report reached conclusions similar to EPA, that is, that only limited toxicity and environmental fate data appear to exist in the public domain for many U.S. HPV chemicals, including the 37 chemicals for which EPA proposed testing in December, 2000 (EPA 2000c), and the 17 chemicals for which testing is required in the final test rule. Details of the search strategy ACC used can be found in its report (ACC 1998). Likewise, ED's evaluation of public data availability for HPV chemicals found that baseline data on health effects were not publicly available for the HPV chemicals ED selected for its evaluation (ED 1997). In the proposal to the final test rule, EPA did not propose testing under TSCA section 4 for endpoints which had available data based on these evaluations. The fact that no data are publicly available for the SIDS endpoints for which testing was proposed under TSCA section 4 supports the finding that existing, publicly available data are insufficient to reasonably predict the risk of adverse effects from exposure to the chemicals.

Comment. PETA commented that EPA must present robust summaries of the data upon which it based its proposed testing requirements for the chemicals in the proposal to the final test rule.

Absent this information, PETA asserts, the public is unable to comment on existing data that have been overlooked, exposure data, or any other relevant information that could reduce the number of animal tests conducted on the chemicals in the final test rule .

Response. No data were identified pertaining to the endpoints for which EPA proposed testing. A robust summary to support testing requirements for chemicals in the final test rule cannot be created when the data necessary to develop such a robust summary do not exist. Nor does EPA consider a robust summary the only way to present analysis of data to support a data insufficiency finding under TSCA section 4(a)(1)(B)(ii).

5. *TSCA Section 4 (a)(1)(B)(iii), testing is necessary.*

Comment. ACC (ACC 2001) commented that EPA does not consider all available and relevant exposure information, including level, frequency, and duration of exposure, before making a TSCA section 4(a)(1)(B)(ii) and (iii) finding that available data are insufficient and testing is necessary. In ACC's view, EPA should consider such information.

Response. EPA considers all relevant exposure information that is available to the Agency before making findings under TSCA section 4(a)(1)(B)(ii) and (iii) that available data are insufficient and testing is necessary. Often, however, additional relevant exposure information exists but is not available to the Agency prior to publishing a proposed test rule. When available to the Agency, information of this nature may result in the Agency's deciding not to propose testing. When exposure information is provided to EPA during the comment period in response to a proposed test rule, EPA does consider that information before deciding to finalize the proposed testing requirements. However, it may not result in the Agency's dropping a chemical from the final rule because such information is often incomplete, e.g. it represents an industry segment rather than the entire industry. EPA does invite the submission of all relevant information, including information concerning frequency, level, and duration of exposure, at any time during the course of a TSCA section 4 rulemaking.

6. *TSCA section 4(a)(1)(A) finding.*

Comment. ACC (ACC 2001) provided a general critique of how EPA makes hazard-based findings under TSCA section 4(a)(1)(A)(i).

Response. This comment is not relevant to the final test rule, which is taken under the authority of TSCA section 4(a)(1)(B). EPA will address comments related to its development of findings under TSCA section 4(a)(1)(A) in its final rules relying on these findings.

M. Animal Welfare Considerations

1. *Opposition to animal testing.*

Comment. A number of groups and individuals commented on the use of animals to develop data on chemical toxicity. The commenters were opposed to the use of animals in general and specifically in tests to develop data on the health and environmental effects of the chemicals in the final test rule. PETA and DDAL commented that EPA is violating the implementation guidelines of the 1993 National Institute of Health Revitalization Act (Public Law 103-43). They indicated that this statute requires regulatory agencies to promote and encourage the use of alternatives to animal test methods, maintain flexibility concerning new and revised methodologies that may apply to their programs, and help drive the development of novel and innovative test methods that will provide for improved risk assessment.

Response. As stated in the proposed test rule (EPA 2000c, p. 81666), EPA recognizes the concerns that have been expressed about the use of test procedures that require the use of animals. EPA is making every effort to ensure that as this TSCA section 4 HPV SIDS test rule is promulgated and the voluntary HPV Challenge Program is implemented, unnecessary or duplicative testing is avoided and the use of animals is minimized. As a general matter, EPA does not require that tests on animals be conducted if an alternative scientifically validated method is found acceptable and available for use. Where animal testing must be conducted to develop adequate data, the Agency is committed to reducing the number of animals used for testing, replacing test methods requiring animals with alternative test methods when acceptable alternative methods are available, and refining existing test methods to optimize animal use when there is no substitute for animal testing. EPA believes that these reduction, replacement, and refinement objectives are all important elements in the overall consideration of alternative testing methods. The Agency's ongoing emphasis on these objectives is in full accord with the 1993 NIH Revitalization Act (Public Law 103-43) and the ICCVAM Authorization Act of 2000 (Public Law 106-545) which established ICCVAM as a permanent committee.

2. Delay in vivo tests until in vitro tests are available to replace them.

Comment. PETA, PCRM, DDAL, and HSUS noted that mammalian acute toxicity testing had been proposed for 14 of the 37 chemicals included in the proposal to the final test rule. These commenters along with ARDF commented that EPA must delay any mammalian acute toxicity testing until the non-animal NRU assay can be used as a replacement for the LD₅₀ test on animals. NEAVS urged EPA to cease all animal testing under the final test rule and the voluntary HPV Challenge Program until the test methods can be replaced with non-animal tests.

Response. As part of the voluntary HPV Challenge Program, EPA asked participants in that program to observe certain principles laid out in a letter (EPA 1999d) in which EPA also indicated its intention that related TSCA section 4 HPV SIDS rulemaking, such as the final test rule, proceed in a manner consistent with the principles. EPA requested that all animal testing on individual chemicals under the voluntary HPV Challenge Program and associated TSCA section 4 HPV SIDS rule(s) not be initiated earlier than November 2001, and that testing of chemicals solely manufactured as closed system intermediates not begin earlier than 2003. The purpose for the requested delay was to allow time for the evaluation and validation of *in vitro* tests under

development. Despite the lapse of 5 years since EPA encouraged the voluntary HPV Challenge Program participants, at the behest of animal welfare groups, to not initiate certain tests until November 2001 and other tests until 2003, the awaited *in vitro* tests are not yet available to replace any of the proposed tests. Based on the publication date of the final test rule, the earliest the mammalian acute toxicity tests required for 8 of the 17 chemicals in the final test rule could be initiated is late 2005/early 2006. EPA cannot continue to postpone testing while waiting for replacement *in vitro* tests; to do so would place EPA in the position of ignoring its mission under TSCA to protect public health and the environment by developing needed information on the toxicity of chemical substances. However, to the extent that such tests are validated and meet the regulatory and statutory needs of the Agency, they might be useable as substitutes for animal methods in TSCA section 4 HPV SIDS rules.

3. *Require, not encourage, in vitro over in vivo testing, and combined over separate tests.*

Comment. PETA, PCRM, DDAL, HSUS, and ARDF commented that animal welfare considerations should be mandatory rather than discretionary. For example, some of these commenters suggest that the rule should require *in vitro* over *in vivo* testing and combined tests over separate tests whenever *in vitro* and combined tests have been accepted as scientifically valid. PETA, PCRM and HSUS stated that EPA should require the use of the bacterial reverse mutation test (40 CFR 799.9510) and the *in vitro* mammalian chromosome aberration test (40 CFR 799.9537) for the mammalian genotoxicity endpoint, unless the physical properties of a chemical preclude the use of these methods. They also commented that EPA should require the use of the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (40 CFR 799.9365) for the mammalian dose/reproduction/developmental toxicity endpoint in place of the separate performance of these protocols (40 CFR 799.9365 and 799.9305).

Response. PETA, PCRM and HSUS are incorrect in thinking that EPA did not propose to require the use of the bacterial reverse mutation test (40 CFR 799.9510). This test is the only test proposed to be used to test for gene mutations (EPA 2000c, pp. 81670 and 81684); EPA did not propose any *in vivo* tests as alternatives for testing this endpoint. EPA disagrees with commenters that it should require the use of an *in vitro* mammalian chromosome aberration test (40 CFR 799.9537) or the use of the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (40 CFR 799.9365). EPA does not believe that either test will provide more accurate data than any of the other test methods which test sponsors may select from Table 3 in § 799.5085(j) of the regulatory text of the final test rule (EPA 2005b) in developing data relevant to the mammalian genotoxicity and repeated dose/reproduction/developmental toxicity endpoints. However, in the final test rule, EPA is encouraging persons required to conduct testing for chromosomal damage to use the *in vitro* Mammalian Chromosome Aberration Test (40 CFR 799.9537) to generate the needed data unless known chemical properties (e.g., physical/chemical properties, chemical class characteristics) preclude its use. A subject person who uses one of the *in vivo* methods instead of the *in vitro* method to address a chromosomal damage test requirement must submit to EPA a rationale for

conducting that alternate test in the final study report. EPA is also recommending use of the Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (40 CFR 799.9365). However, in acknowledgment that there may be valid reasons to test a particular chemical using both 40 CFR 799.9355 and 40 CFR 799.9305 to fill the Mammalian Toxicity - Repeated Dose/Reproduction/Developmental data needs, EPA is requiring in the final test rule that a subject person who uses the combination of 40 CFR 799.9355 and 40 CFR 799.9305 in place of 40 CFR 799.9365 to submit to EPA a rationale for conducting these alternate tests in the final study reports.

Based on past Agency experience, EPA anticipates that test sponsors will generally choose to conduct the less costly and less resource intensive *in vitro* and combined tests unless there are sound scientific reasons not to do so. For this reason, and since it is difficult to identify the circumstances under which *in vivo* methods may be scientifically preferable, EPA is not choosing to require the test methods specified by the commenter whenever they are valid, but is following its general practice of leaving a degree of discretion to those conducting the testing. However, if a test sponsor does choose to conduct alternative testing, it is appropriate for the Agency to require submission of their rationale for this choice as part of their final report given that the final test rule solely seeks screening-level hazard data. EPA continues, however, to encourage the use of *in vitro* and combined studies, where scientifically appropriate, insofar as they reduce the number of animals required for testing.

Comment. When a test sponsor wishes to use *in vivo* rather than *in vitro* genotoxicity testing, or conduct separate instead of combined repeated dose/reproductive/developmental toxicity studies, PETA, PCRM, DDAL, and ARDF urge EPA to require notice and approval of this choice prior to the initiation of testing, rather than submission of a justification after testing. Similarly, HSUS commented that a rationale for conducting *in vivo* or separate tests should be included in the test plan, and that the test plan should be published to give the public an opportunity to comment. SOCMA commented that requiring the submission of rationale for choosing one standard over another is an unnecessary burden, but that it understood that in some cases EPA may want an explanation for the test sponsor's choice of using one method over another.

Response. EPA solicited comment as to whether, in lieu of requiring test sponsors to submit a rationale for conducting genotoxicity testing via an *in vivo* (rather than *in vitro*) method or for conducting repeated dose/reproductive/developmental toxicity testing via separate (rather than combined) tests in their final study reports, the Agency should require that persons wishing to use an alternate testing scheme submit to EPA a notice that includes the rationale for conducting the alternative tests prior to initiation of these studies (EPA 2000c, pp. 81670-71). In particular, the Agency requested suggestions as to efficient procedures that could be used for any such prior notification process.

The Agency has decided not to implement a prior notification process in the final test rule. Test sponsors are already required to indicate the test methods they will be using in their study plans, which will be submitted to the Agency and made available in the docket prior to the initiation of testing (40 CFR 790.50). Although the study plans will not necessarily contain the rationale for any planned use of alternative tests, the study plans will notify EPA and the public

when such alternative tests will be conducted. Thus, a separate prior notification process regarding the use of alternative methods is unnecessary. In addition, none of the comments supporting implementation of a prior notification process including submission of a rationale for use of alternative testing made specific suggestions as to how the Agency could go about doing this efficiently, so as not to unnecessarily delay the generation of data under the rule. Publication of study plans in order to provide an opportunity for public comment on the inclusion of any alternative tests, as suggested by HSUS, could cause a significant delay in the initiation of testing. Although EPA is committed to carrying out its responsibilities under TSCA in a way that avoids unnecessary animal testing, the Agency does not believe that the delay that would result from the commenter's proposed approach is warranted in view of the opportunity for public input already provided, and in view of the overall objective of TSCA to ensure that adequate data be developed regarding the effect of chemical substances on health and the environment.

Based on past Agency experience, EPA anticipates that test sponsors will generally choose to conduct the less costly and less resource intensive *in vitro* and combined tests unless there are sound scientific reasons not to do so. However, if a test sponsor does choose to conduct alternative testing, it is appropriate for the Agency to require submission of their rationale for this choice as part of their final report given that the final test rule solely seeks screening-level hazard data. EPA continues, however, to encourage the use of *in vitro* and combined studies, where scientifically appropriate, insofar as they reduce the number of animals required for testing.

4. *Use of existing data.*

Comment. DDAL, HSUS, and AAVS urged EPA to ensure that companies subject to the rule conduct a qualitative analysis in assessing the adequacy of existing data, rather than using a “checklist” approach and embarking upon a series of animal tests, some of which may be unnecessary.

Response. As stated in Unit B. of this document, all relevant existing data should be submitted to EPA for review to potentially avoid unnecessary testing. If at any time, including after the test rule is finalized, but prior to initiation of testing under the final test rule, the Agency receives adequate existing data that fulfill a specific data need, EPA will ensure that unnecessary testing is not required (EPA 2000c, p. 81666). If past experience under the voluntary HPV Challenge Program is considered, EPA believes that industry will not overlook existing data that might satisfy a test requirement in order to avoid the burden of new testing.

5. *Coordinate testing programs to avoid duplicative testing.*

Comment. HSUS believes that there is a critical need for coordination among all programs focused on HPV chemicals, including international programs, to avoid duplicative testing. As mentioned in the proposed test rule, other programs focused on HPV chemicals, aside from the U.S. voluntary HPV Challenge Program and the final test rule, include the OECD HPV SIDS Program and the program organized by the ICCA. HSUS believes appropriate harmonization of these programs as well as other emerging national and international programs is absolutely

essential to avoid unnecessary, duplicative testing.

Response. During the past decade, EPA has worked with OECD to harmonize its test guidelines with those in use by OECD and its member countries. As a result, testing conducted according to EPA's TSCA or FIFRA guidelines meets all guideline aspects of testing conducted according to OECD guidelines. Furthermore, a primary focus of the U.S. HPV activities, including the voluntary HPV Challenge Program and associated TSCA section 4 HPV SIDS rulemaking, is to implement these efforts as contributors to a larger international activity with global involvement and in a manner consistent with meeting the needs of the OECD HPV SIDS program and to further the goals under Programme Area (C) of Agenda 21, Chapter 19 of the *Report of the United Nations Conference on Environment and Development* (UNCED) concerning information exchange on toxic chemicals and chemical risks. Any U.S. HPV chemicals that are handled under the OECD HPV SIDS Program or the ICCA HPV Initiative are considered by EPA to be "sponsored" under the voluntary HPV Challenge Program and are not intended to be addressed in the voluntary HPV Challenge Program or considered for any TSCA section 4 HPV SIDS rulemaking unless the international commitments are not met. Also, ICCA testing/assessment work is tied directly to that under the OECD HPV SIDS Program and to the U.S. HPV activities, which further minimizes the possibility of duplicative testing occurring.

N. Viable Commitments

Comment. ACC (ACC 2001) noted that the proposed test rule indicates that companies that did not previously make timely voluntary HPV Challenge Program commitments for chemicals included in proposed TSCA section 4 HPV SIDS rulemaking may make "viable" commitments to sponsor chemicals under that Program before the close of the test rule comment period (EPA 2000c, p. 81663). ACC requested clarification on whether and how EPA will make information about these "viable" commitments public. ACC also urged the Agency to clarify how the Agency will handle voluntary HPV Challenge Program sponsorship commitments received for chemicals not in the proposed test rule as well as how sponsorship of chemicals under the ICCA HPV Initiative and OECD HPV SIDS program will be treated.

Response. Sponsors can participate in the HPV Challenge Program either directly through the Program or indirectly through the ICCA HPV Initiative and/or the OECD HPV SIDS Program. Thus, chemicals sponsored through the ICCA HPV Initiative and/or the OECD HPV SIDS Program are considered as commitments to the HPV Challenge Program.

Because of the voluntary nature of the HPV Challenge Program, EPA has continued to accept sponsorship commitments beyond the deadlines set forth in the early implementation of the Program. Such late commitments for direct sponsorship under the HPV Challenge Program are known as "viable" commitments. Persons who wish to sponsor a chemical through a "viable" commitment should include in their submission copies of full studies in addition to a robust summary as described in the proposal to the final test rule (EPA 2000c, p. 81663). Commitments for direct sponsorship under the voluntary HPV Challenge Program for chemicals not included in the final rule will also be considered "viable" commitments. Late commitments made through the

ICCA HPV Initiative are not considered nor are they treated as “viable” commitments. EPA has received commitments to sponsor 13 chemicals in response to the proposal to the final test rule , 11 for chemicals sponsored directly through the HPV Challenge Program (i.e., “viable” commitments) and 2 are sponsored indirectly through the ICCA HPV Initiative. See Unit VII.A. of the final test rule (EPA 2005b) for a list of the 13 chemicals.

All commitments to the voluntary HPV Challenge Program are listed on Program website (<http://www.epa.gov/chemrtk/hpvchmlt.html>). Information received under a viable commitment is made public through the voluntary HPV Challenge Program’s Robust Summaries and Test Plans website (www.epa.gov/chemrtk/viewsrch.html) in the same manner as information received under all other commitments. EPA has provided guidance for companies interested in making commitments to sponsor their chemicals on the website for the voluntary HPV Challenge Program (<http://www.epa.gov/chemrtk/volchall.htm>).

O. Commitments to Other Testing Programs

Comment. ACC (ACC 2001) asked how a chemical listed in the proposed test rule will be treated if it were sponsored under the ICCA Initiative. Both ACC and CPMA asked how a chemical proposed for testing under a TSCA section 4 HPV SIDS rulemaking would be treated if the chemical is selected for review in the OECD SIDS Program, or if a SIDS dossier has already been prepared for the OECD SIDS Program (OECD 2003).

Response. Any U.S. HPV chemical that is handled under the OECD HPV SIDS Program or the ICCA HPV Initiative is considered by EPA to be “sponsored” and is not at this time intended to be addressed in either the voluntary HPV Challenge Program or in any TSCA section 4 HPV SIDS rulemaking unless the international commitments are not met. Data needs which remain unmet in the voluntary HPV Challenge Program or through international efforts may be addressed through TSCA section 4 HPV SIDS rulemaking, where EPA is able to make the necessary findings (EPA 2000c, p. 81664).

P. EPA Should Adopt an Integrated Approach to Data Generation

Comment. ACC (ACC 2001) commented that EPA has proposed numerous new test rules, testing initiatives and reporting requirements in addition to the voluntary HPV Challenge Program. ACC urged EPA to undertake a program to “integrate” its data and information requests in such a way that each request considers and, if appropriate, incorporates the work of one initiative into the work of another in a timely manner.

Response. EPA does not initiate any rule, program, or reporting requirement without first verifying that the needed information has not been obtained or requested by a separate effort within EPA. The review process within EPA informs other Offices in EPA what information or action is being sought by a particular Office and invites comment that will prevent duplication of effort. If more than one Office is evaluating the same chemical, albeit with a different, Office-related focus, those Offices will work together to share and integrate the information each Office

obtains. Thus, EPA believes it already has in place a system to achieve the integration of data and information requests which ACC advocates.

Q. Export Notification

Comment. API and SOCMA commented on the burden of complying with TSCA section 12(b) export notification requirements. 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 EPA of such export or intent to export. EPA in turn will notify the government of the importing country of EPA's regulatory action with respect to the substance. API commented that EPA should consider the export notification burden imposed as a result of this and other final TSCA section 4 test rules, and stated that EPA makes only minimal acknowledgment of the export notification burden that is associated with promulgating these final rules. API urged EPA to change its export notification regulations, which API believes are unnecessarily burdensome to its members and EPA and do not produce discernible benefits. SOCMA commented that EPA has not identified any benefit to applying TSCA section 12(b) export notification requirements to chemicals that are the subject of TSCA section 4 test rules when they are impurities in a chemical for export, and that the cost of compliance outweighs any benefit. SOCMA urged EPA to reconsider the 12(b) notification requirements as they apply to impurities and establish a threshold concentration of at least 1% or more before the requirements would apply to chemical impurities present in a shipment.

Response. As a general matter, comments on EPA's regulations under TSCA section 12(b) are beyond the scope of the final test rule, which EPA is undertaking pursuant to the authority of TSCA section 4 and not TSCA section 12(b).

Concerning the comment that export notification is burdensome, EPA estimates the cost of the TSCA section 12(b)(1) export notification, which, as a result of the final rule, would be required one time only per exporter per country of export for each chemical subject to the rule, would have a negligible impact on exporters of the chemicals in the final rule, regardless of the size of the exporter (EPA 2005a). EPA estimates the cost of the TSCA section 12(b) export notification requirement for each final testing action triggering the requirement.

Relatedly, the public was provided with an opportunity to comment on the burden of compliance with TSCA section 12(b) requirements. Prior to submission to OMB, EPA announced in the **Federal Register** of August 19, 2002 the availability of the EPA Information Collection Request (ICR) No. 795 for public comment (EPA 2002b). The public had 60 days to provide comments on EPA's request for approval of its information collection activities related to export notification under TSCA section 12(b)(1). The information collection activities described in that ICR were approved under OMB control number 2070-0030. The final test rule does not contain any new collection activities requiring additional OMB review and approval.

R. Submittal and Posting of Information Exceeding Requirements

Comment. SOCMA commented that although the required tests are outlined in the proposed test

rule, some sponsors will choose to volunteer, as in the voluntary HPV Challenge Program, to provide data beyond those required. SOCMA opines that these sponsors may want to submit use and exposure information on a purely voluntary basis because they think that making only hazard information publicly available may lead to misinterpretation of the potential risks of their chemicals. SOCMA believes that if a sponsor submits use and exposure information that EPA should treat it in a similar fashion to information submitted under the voluntary HPV Challenge Program, i.e., it should be posted on the EPA website, unedited, and available for public comment. Similarly, ACC (ACC 2001) commented that if sponsors provide use and exposure information in the context of the voluntary HPV Challenge Program, it should be posted, along with hazard information, to make it equally accessible.

Response. EPA's policy is to post on its website information received under the voluntary HPV Challenge Program, even where the information goes beyond the scope of the voluntary HPV Challenge Program (e.g., exposure or risk characterizations), but with the disclaimer that the information will not be evaluated by EPA within the scope of that program (EPA 2004b). Exposure-related information submitted by a sponsor may be accurate and comprehensive from the perspective of the submitting company; however, such information typically does not account for all possible uses of the chemical and all possible exposures to the chemical in the United States, and EPA does not want the public to assume that this might be the case. Because the final test rule is intended to complement the voluntary HPV Challenge Program by obtaining data on certain of the HPV chemicals not sponsored in the voluntary HPV Challenge Program, additional data submitted beyond the scope of the final test rule will be posted in accordance with the policies established by the voluntary HPV Challenge Program. Therefore, for example, it is EPA's policy that any robust summaries of test results submitted by a test sponsor for studies required under the final test rule, and voluntarily submitted exposure-related information should be posted in accordance with the policies established by the voluntary HPV Challenge Program. Unlike the voluntary HPV Challenge Program, if EPA believes that a robust summary of test results submitted by a test sponsor for a study required under the final test rule is not supported by or does not accurately represent the results of that study, EPA would not want to provide the public with information that is misleading and would, therefore, issue its own robust summary, based in part on the company's submission, that accurately reflects the results of the submitted study. Additionally, unlike the voluntary HPV Challenge Program, EPA will not invite comment on the robust summaries of studies conducted pursuant to the final test rule, because these summaries would already have been either verified to be accurate by EPA or, when necessary, developed by EPA. EPA will, however, accept comment on other information submitted voluntarily on chemicals in the final test rule, such as information on use and exposure. EPA may respond to these comments, as appropriate, within the context of the voluntary HPV Challenge Program.

S. Management of Data Submitted under the Voluntary HPV Challenge Program

Comment. ACC (ACC 2001) urged EPA to use the International Uniform Chemical Information Database (IUCLID) to manage data submitted under the voluntary HPV Challenge Program.

Response. ACC's comment on the management of data submitted under the voluntary HPV Challenge Program is not relevant to the final test rule. All data developed under the final test rule will be publicly available in the public docket established for the final test rule (docket ID number OPPT-2005-0033) and summaries of these data will be included, at a minimum, on OPPT's Chemical Information Collection and Data Development (Testing) website (<http://www.epa.gov/oppt/chemtest/index.html>). EPA also intends to include robust summaries developed for chemicals covered by this test rule in the High Production Volume Information System (HPVIS), which, when implemented, can be accessed on EPA's HPV website at <http://www.epa.gov/chemrtk/volchall.htm>.

Comment. ACC is concerned that EPA and others will confuse hazard data on HPV chemicals with risk information, and, based on hazard information alone, might immediately seek to initiate inappropriate or unnecessary risk management or chemical controls without providing an opportunity to put identified hazards in a risk context. ACC asked EPA to describe what steps it will take to prevent this from happening.

Response. When EPA makes information on HPV chemicals available to the public on the voluntary HPV Challenge Program website, EPA clearly refers to it as basic screening level hazard data, and indicates that the primary use of basic screening level hazard data is to screen chemicals for potential hazards and then prioritize the chemicals for further evaluation. EPA also clearly indicates on the voluntary HPV Challenge Program website that such screening level hazard data on a given chemical, when used in combination with information about the chemical's uses and exposures, will enable EPA and others to better characterize the potential for adverse human health or environmental effects and decide if further testing or other action is necessary. EPA does not suggest nor has it suggested that screening level hazard data collected in the voluntary HPV Challenge Program are generally indicative of risk in the absence of exposure information. The Agency will continue to stress this point in its communications with the public.

T. Information Collection Request No. 1139.06

Comment. In response to EPA's request for public comment on the proposal to the final test rule, CRE submitted comments to EPA and to OMB on EPA's renewal of Information Collection Request No. 1139.06 (TSCA Existing Chemical Test Rules, Consent Orders, Test Rule Exemptions, and Voluntary Test Data Submissions). Specifically, CRE requested OMB to disapprove the pending ICR renewal request and to require the EPA to issue a new Notice of Proposed Rulemaking (NPRM) and 60-day comment period

Response. After consideration of public comments on the proposed ICR renewal and revisions to the ICR renewal supporting statement, as needed to adequately address public and OMB comments, the ICR applicable to this TSCA section 4 rule (ICR 1139.06) was approved by OMB on October 15, 2001. A notice of this approval by OMB was subsequently issued by EPA and published in the **Federal Register** of June 10, 2002 (EPA 2002a). See additional discussion on

the ICR under Paperwork Reduction Act (PRA) in Unit XI.B. of the final test rule (EPA 2005b).

U. Economic Impact Analysis

1. *EPA's analysis does not capture the full magnitude of the potential testing cost.*

Comment. ACC (ACC 2001) states that EPA should have considered all HPV chemical candidates (roughly 400-450 unsponsored chemicals) as potentially subject to the testing requirements in the proposed test rule as a single group and should have developed an aggregate economic analysis for all TSCA section 4 HPV SIDS test rules, rather than developing an economic analysis for each separate TSCA section 4 HPV SIDS test rule.

Response. EPA uses economic analysis as a tool to help evaluate options for specific regulatory actions. These analyses are developed as part of the process of determining the appropriate regulatory requirements of the rule. When considering economic impacts of a particular rule, EPA does not consider the impacts that could possibly occur as a result of future potential regulations. Such an analysis would merely be speculative, distort the expected impacts, and would not be useful in assisting EPA in choosing its regulatory approach for the particular rule.

2. *Use of annual gross revenue.*

Comment. SOCMA is concerned about EPA's use of annual gross revenue to determine potential economic impact and to define small business entities. SOCMA claims that basing the impact of a regulation on gross sales of a chemical, or the size of a company defined by its annual gross revenue, as EPA is proposing, is misleading because the costs of doing business are not included. A company with higher sales revenue does not necessarily make more money than a company selling the same number of units at a lower price, especially if the latter company is operating at a lower profit margin than the first company. SOCMA urges EPA to use company profits, which are readily available to the public, and not gross sales revenue when performing economic analyses.

Response. EPA has a long history of using the relationship between cost of compliance with a regulation and total revenue of the firm (price times quantity of goods sold) to determine whether a regulation has a significant economic impact. Although profit may at first seem like a reasonable measure of impacts, there is often a substantial difference between economists' conception of profits and what is measured through accounting techniques as profits. Economists might use profits as a measure of ability to meet regulatory costs, and when used this way profits are a short-run measure equal to revenues minus only variable costs, which are the minimum costs required to continue production. This ideal economic measure of profit, however, is not what accountants calculate and report. Accounting profits correspond to definitions developed for accounting and tax purposes, and thus should not be used to assess the economic impact of compliance costs for the following reasons:

- Accounting profits generally are lower than the actual sums firms have available

for such expenses as complying with environmental regulations. This is due to the subtraction of depreciation from accounting profits even though the funds set aside over the long run to replace machinery, etc. are available in the short run to meet the day-to-day expenses of a firm, including costs of complying with regulations.

- The use of accelerated depreciation lowers accounting profits and taxes even more when in fact the firm has a higher cash-flow and, hence, greater ability to pay for regulatory costs. Accelerated depreciation allows qualifying firms to depreciate capital equipment more rapidly in those areas where the Federal government wants to encourage investment.
- Short-run profits are what remain after variable costs, i.e., business expenses, have been deducted. The more expenses a company identifies as a business expense, the less profit that company will show. If a company were to pay the company president the residual profits instead of a fixed salary, that company would never show a profit. The possibility that this could occur may be greater with small businesses, which are the entities generally covered by the Regulatory Flexibility Act (RFA). Entities which are not publicly traded are not required to subject themselves to an annual audit and reporting according to strict accounting standards. Under these circumstances, owners of the firm have wide discretion in determining what constitutes a “business expense.”
- Unlike revenue data, profit data are not widely collected. There are some proprietary databases which assemble profit data, but these data are based on very small sample sizes. Small sample sizes mean that data on profits are not very robust (i.e., the ranges of uncertainty which result from use of these data are large). This is all the more true because the definition of ‘profit’ is not consistent among databases (for example, some collect pre-tax profit while others tabulate post-tax), and so the samples cannot be combined to yield a larger sample and consequently more robust estimates.
- Unless demand for the product is perfectly elastic (i.e., there are numerous, perfect substitutes for the product), firms in the industry will have the ability to pass at least some of these costs along to their consumers. To the extent that compliance costs are borne not by the regulated firms, but by their customers, the predictive power of a comparison of past short-run profits with incremental regulatory costs is essentially nil.

The primary advantage of using revenue to measure impacts is that it is a stable, easily accessible, and easily understood measure which provides a basis for comparing the final test rule to other rules. Unlike profits information, the definition is consistent and not subject to the widely varying definitions and interpretations of terms that affect ‘profit’ measures. Another advantage is that revenue data, unlike profits information, are widely available. The proprietary databases which assemble profits data not only also have revenue data, but the proportion of firms for which revenue data are available generally greatly exceeds the proportion of firms for which profit data are available. In addition, there are a number of databases, including the Census, which collect and publish revenue data but not profit data.

The third important advantage of using revenue as opposed to profit data for impact

analyses is that revenue data are easily understood. For example, if the impact of compliance costs on a firm is 1% of revenue, in order to cover the costs of the regulation a firm would need to raise its prices 1%. This is a clear, easy to understand measure, that can help decision-makers determine whether additional measures to reduce the impact of a regulation are warranted.

In summary, EPA believes that the revenue test used in the analysis of the final test rule is preferable because it is simple to apply and based on readily available data, which allows consistent application of the methodology from rule to rule. Therefore, EPA does not agree that it needs to use a different measure to determine economic impacts.

3. Small business definition. In the proposal to the final test rule, EPA solicited comment on whether the Agency should consider an alternative definition to an employee-based definition of “small business,” and 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 (EPA 2000c, p. 81677).

Comment. SOCMA commented that fluctuations in markets and business cycles make it especially difficult to use any kind of sales figure as a basis for defining small business entities. SOCMA urged EPA to use the employee-based U.S. Small Business Administration (SBA) definitions for small business entities.

Response. EPA has used the SBA employee-based definition, which SOCMA stated it prefers, to assess the size of businesses. As an additional measure, EPA also included a definition based upon sales for purposes of comparison. EPA found that the determination of the number of small businesses was different for the two measures; however, the number of firms impacted at greater than 1 % and greater than 3 % of sales did not differ. EPA considered the number of small businesses identified under the SBA employment definition in developing the rule and sees no reason to alter its assessment.

4. Inadequate information is a market failure. Executive Order 12866 states that agencies shall identify the problem that a regulation addresses. In its economic analysis for the final test rule, EPA has included a discussion identifying the problem that the final test rule intends to address as a problem of market failure due to inadequate information.

Comment. SOCMA urges EPA to avoid using general economic theory to support its claim of potential market failure due to the lack of adequate information on the chemicals in the final test rule. SOCMA states that the Agency should identify and support its conclusion that the proposed requirements would provide an appropriate level of information.

Response. EPA believes that SOCMA’s suggestion has already been addressed by the existing economic analysis. Market failure is a theoretical construct based in economic theory that is a rationale for considering a corrective policy intervention. EPA’s analysis of the rule identifies the existence of a market failure in the area of imperfect information, i.e., there are insufficient data upon which the effects of the chemicals in the final test rule on health and the environment can

reasonably be determined or predicted. This type of failure is necessarily described using general economic theory to provide readers an understanding of what the market has not provided and why there is a need for the rule. However, EPA also analyzes the effects of the rule in terms of the costs it imposes and the benefits expected to accrue. The benefits discussion describes the types of information that will be provided and the expected uses of that information. These benefits are described qualitatively, not quantitatively; however, this approach is customary when data or models do not support a reasonable quantitative evaluation. Therefore, EPA believes that it has established that the rule will provide an appropriate level of information.

5. *Market characterization.*

Comment. SOCMA commends EPA on the thoroughness of its market characterization. SOCMA advises caution when attempting to use prices for similar compounds. The process for “attaching” functional groups to compounds is not always straight-forward, and can require multiple steps. Generally, performing more steps increases the cost of producing a material, which can translate into a different price per pound than otherwise assumed.

Response. To assess the potential for the test rule to result in an adverse economic impact for a chemical manufacturer, EPA compares annualized compliance costs to an estimate of annual revenues generated from the chemical. Annual revenues are estimated by multiplying the price of the chemical by the annual production of the chemical. When prices were not available for a chemical, EPA used estimates, often derived from similar compounds. EPA was unable to determine prices for several chemicals and therefore, provided estimates. The commenter has not provided any information that would improve those estimates, nor have they identified those that they believe are inaccurate. The commenter seems to suggest that EPA’s price estimates may be too low. However, if EPA were to increase the value of its price estimates, it would also increase the value of estimated annual revenues and, in the process, reduce any estimated potential for an adverse economic impact. Therefore, EPA has not changed its approach to developing estimates of chemical prices based upon the comment.

6. *Costs that may not have been addressed.*

Comment. SOCMA states that the Agency has done a good job in addressing many of the costs associated with testing and SOCMA commends EPA on the conservative approach used. However, SOCMA has identified costs that do not seem to be included. For completeness and transparency, SOCMA recommends that EPA include the following costs, or explain how they are addressed in the analysis:

- Analytical method development and analytical method validation for physical/chemical properties testing.
- Analytical method development and analytical method validation for aquatic toxicity testing.
- Consulting services for test plans and robust summary preparation.
- Consortium member travel costs.

- Opportunity costs associated when companies leave specific chemical markets.
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Response. Many of the costs identified by the commenter have already been included in EPA's estimate of administrative costs of the rule. For example, administrative costs include test plan development and robust summary preparation. EPA does agree that toxicity testing may require the development and validation of analytical methodologies for measuring the amount of chemical in a dosing matrix. Therefore, EPA has revised its cost estimates to include the costs for analytical method development and analytical method validation for aquatic toxicity testing as well as other relevant toxicity tests. However, EPA does not believe it is reasonable to include costs for analytical method development and analytical method validation for testing physical/chemical properties, because there is no need to measure the amount of chemical in such studies. Therefore, EPA has not included any additional costs for these types of tests.

EPA has seen no evidence that companies would actually exit markets as a result of the required testing. EPA's analysis has considered the potential for an adverse impact on the sales of particular chemicals, and does not believe that the impacts are sufficient to cause companies to exit from the chemical markets.

7. Annualizing total social costs over 3 years.

Comment. SOCMA notes that the economic analysis mentions that "costs are not expected to occur in a single year." However, the language in the proposed test rule suggested a 13-month time period in which to complete testing and present the results. Therefore, SOCMA states that it does not make sense to annualize something over three years that is expected to be completed in just one.

Response. The commenter has accurately noted that EPA has annualized the social costs of the rule over three years. Social costs include compliance costs for the industry as well as government costs. While certain activities, e.g., conduct of testing and submission of final test reports, may occur over the period of 13 months, other cost incurring activities will occur over a longer time horizon. In particular, the costs associated with EPA's review and evaluation of the data developed from the HPV rule are expected to occur over several years. These are considered part of the social costs of the rule. Therefore, EPA annualized the social costs of the rule over the 3-year time period when the costs occur.

8. Annualizing industry's compliance costs over 15 years.

Comment. SOCMA notes that the economic impact analysis annualizes industry's cost of complying with the proposed test rule over 15 years, and is based on EPA's presumed "useful life" for the chemical. The reimbursement period for the rule is five years. SOCMA claims that carrying costs beyond the reimbursement period will place a sponsor at a competitive disadvantage in the market. SOCMA states that, whenever possible, regulations should not place those who comply at a competitive disadvantage. Therefore, SOCMA recommends that the model should annualize the costs to no more than the reimbursement period.

Response. EPA's assessment of the final test rule's economic impact on industry is a simplified approach for looking at how industry's profitability might be affected by complying with the final rule. Profitability is evaluated by looking at the net present value of cash flows associated with the chemical, in this case, the costs of complying with the rule and the revenues from the chemical, and annualizing them over time. A measure of the chemical's profitability is made by looking at the total earnings stream of the chemical as year to year profitability can fluctuate dramatically. Losses experienced in a year(s) can be offset by gains in other years. Therefore, it is not appropriate to assess impacts on earnings in only the year(s) in which testing is performed, paid for, or over the reimbursement period, but over the productive life of the chemical.

9. *Small entity impact analysis.*

Comment. SOCMA notes that the small entity impact analysis section in the Economic Impact Analysis for the proposed test rule (EPA 2000a) uses "ultimate" parent companies for sales and employment data, assuming that they would be willing to absorb the impact of the affected subsidiary. SOCMA states that this assumption is not reflective of the business world. Companies that are subsidiaries or joint-ventures of larger parent companies operate independently more often than not.

Response. EPA disagrees with the approach proposed by the commenter. In accordance with § 601 of the RFA, EPA used SBA's definition of a small business to evaluate small entity impacts. This Section of RFA states that the term "small business" has the same meaning as "small business concern" as found in §3 of the Small Business Act. The definition of small business concerns are further described in SBA's Small Business Size Regulations found at 13 CFR Part 121. Specifically, SBA defines a small business concern under 13 CFR Part 121.105 to include joint ventures. Additionally, under 13 CFR Part 121, SBA determines affiliation of entities when one "controls or has the power to control the other" "whether control is exercised," which describes the relationship between a parent company and subsidiary. The specific size standards developed by SBA are applied to business concerns, including affiliates to, determine eligibility for SBA programs.

EPA has developed its analysis to be consistent with SBA's definition of small business and has evaluated business size based upon the resources of ultimate corporate entities. The definitions developed by SBA presume that certain affiliations or other business relationships, such as parent-subsidiary, allow for some sharing of resources that could exclude a business from being considered small. EPA believes this to be a reasonable understanding of business relationships and has not received any information from the commenter that would demonstrate otherwise.

10. *Unintended market effects.*

Comment. SOCMA claims that, unless a single chemical represents a significant interest to a company, a company will likely choose to leave or not enter a market when faced with additional costs such as testing. SOCMA states that this is seen routinely in the new chemicals registration

process and that SOCMA members affected by the proposed test rule have already begun the decision-making process for staying in or leaving specific markets. SOCMA states that leaving a specific chemical market results in market consolidation, which, in turn, can lead to a monopolistic situation. SOCMA does not believe that this proposed test rule intends to consolidate the market for specific chemicals; however, market consolidation can be considered an unintended consequence, and, therefore, an unforeseen cost of a regulation. The economic impact on small companies is much more significant than the screening-level analysis conducted by EPA indicates. SOCMA urges EPA to include foregone revenues and unintended market effects as part of the opportunity costs in the economic impact analysis.

Response. The commenter has described potential changes in markets that could occur if some producers were to cease production of a chemical as a result of the costs of the regulation, leaving only a few manufacturers or a sole manufacturer of the chemical. However, the progression of market changes described in the comment is speculative and no support is provided to suggest that any of the steps will occur. If market consolidation were to occur, the commenter notes that these would be unforeseen. Furthermore, the statement that companies “will likely choose to leave or not enter a market when faced with additional costs” seems a significant oversimplification of the considerations that a company would make in determining whether or not to continue the production of a chemical. A decision to exit a market is not merely based upon an increase in costs of production. A number of factors are typically considered, including firm financial status, prospective revenues, price trends, profits, product demand, market share, and long-term market and firm expectations.

EPA’s economic analysis has considered the economic impact of the costs of the regulation on businesses and does not find an indication that the markets for the chemicals evaluated would become monopolies as a result of the regulation. Unforeseen costs cannot be estimated, particularly when there is no indication that they might occur. Given the results of its analysis and the speculative nature of the comment, the Agency sees no need to arbitrarily add costs associated with lost revenues or market changes related to the final test rule .

11. *Quantifying benefits.*

Comment. SOCMA agreed with EPA that there are benefits associated with obtaining information on the hazards of chemicals and believes that quantitation of benefits should be included in economic analyses for proposed TSCA testing rules. SOCMA urged EPA to begin work on quantifying the benefits associated with the generation of hazard information, which can be applied to all future TSCA test rule analyses. If it is not reasonable or practical to place a monetary value on a benefit, SOCMA believes that an attempt should at least be made to use some other quantitative description.

Response. Quantification of all benefits is rarely possible in any economic analysis and it is standard practice to qualitatively describe benefits where it is either impractical or otherwise not possible to develop quantitative estimates. EPA does not believe that there currently exist adequate data or methodologies to support a reasonable and sound quantification of the benefits of

the final test rule and therefore, EPA will continue to provide only a qualitative description in its economic analysis.

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