Status Report on the High Production Volume (Hpv) Challenge Program–October 12, 2001

SUMMARY

The Chemical Right-to-Know Initiative was launched in April, 1998, with the goal of obtaining screening level data for the approximately 2,800 chemicals manufactured or imported into the United States in quantities exceeding one million pounds per year. Manufacturers and importers were invited to participate in a voluntary "challenge" program to provide basic toxicity data on the high production volume chemicals they produce. A framework for the High Production Volume (HPV) Challenge Program was announced on October 9, 1998, by EPA, Environmental Defense, the American Chemistry Council and the American Petroleum Institute. The HPV Challenge Program is based on the Organization for Economic Cooperation and Development's Screening Information Data Set (OECD/SIDS), an internationally agreed upon set of tests for screening high production volume chemicals for human and environmental hazards. Companies were asked to indicate their commitment to supply the SIDS-level data on their chemicals by December, 1999. To date, 469 companies and 187 consortia have agreed to sponsor 2,155 chemicals. The balance is being addressed in the OECD HPV SIDS Program or as candidates for a rule under Section 4 of the Toxic Substances Control Act (TSCA). As part of the HPV Challenge Program commitment, sponsors submit to EPA a Test Plan and supporting robust summaries of existing data. The submitted information undergoes a 120-day public comment period to allow others to review and comment on the plan and to submit additional data that may be used to obviate the need for any proposed testing. 55 Test Plans covering 383 chemicals have been submitted by sponsors. An examination of a majority of the submitted Test Plans reveals that, sponsors are doing a good job following the various guidance documents EPA has prepared for the HPV Challenge Program; a significant amount of unpublished data is being provided to support the Test Plans; and the amount of new testing being proposed to address the SIDS endpoints is less than initially envisioned.

THE HPV CHALLENGE PROGRAM

A 1997 study by the Environmental Defense Fund (now Environmental Defense) showed that, for a sample of 100 HPV chemicals, there were relatively few US HPV chemicals which met minimum data requirements for health hazard screening. EPA undertook a similar study of approximately 2,800 chemicals manufactured or imported in the U.S. in quantities exceeding one million pounds per year. EPA's report found a similar dearth of publicly available data. These findings were subsequently supported by a study conducted by the Chemical Manufacturers Association (now the American Chemistry Council). As a result of these findings, EPA launched the HPV Challenge Program as part of the Chemical Right-to-Know Initiative on the eve of Earth Day, April 21, 1998. The goal was to encourage the manufacturers and importers of HPV chemicals to make publicly available existing data, or conduct testing if necessary, to address the

screening level endpoints established by the OECD HPV SIDS Program. These include physicochemical properties, environmental fate data, acute ecological effects (chronic or terrestrial studies if appropriate), and a number of human health endpoints. A framework was established for the overall program through the collaboration of EPA, Environmental Defense, the American Chemistry Council and the American Petroleum Institute. The framework was announced on October 9, 1998.

Companies were asked to participate in the HPV Challenge Program by committing to supply the SIDS-level data by no later than 2005. As part of the commitment, companies were asked to specify a start year (1999 through 2003) in which they would supply a Test Plan and supporting robust summaries of existing data for public comment. Test Plans for categories of chemicals were requested to be submitted in one of the first two start years (not including 1999) so that in the event that the category hypotheses proposed in the Test Plan were not borne out, there would be sufficient time to conduct additional testing by the end of 2004, in order that a complete data set could be generated and all data made publicly available in robust summary form by 2005.

Concurrently with the US HPV Challenge Program, the International Council of Chemical Associations (ICCA) HPV Chemicals Initiative was created with the goal of handling HPV chemicals of international interest within the OECD HPV SIDS Program. Nearly 700 chemicals have been committed to through the ICCA HPV initiative. EPA has agreed to act as the sponsor country for over 200 ICCA chemicals to be evaluated in the OECD HPV SIDS Program. Confirmed ICCA commitments are recognized in the HPV Challenge Program, since the same set of screening data is made publicly available through the two programs.

To date, 2155 chemicals have been sponsored by 469 companies and 187 consortia. Non-sponsored chemicals will be considered for rulemaking under Section 4 of TSCA. Currently, a proposed Section 4 rule covers 37 chemicals. The 120-day comment period for the proposed rule closed on April 25, 2001, and a final rule is expected by spring 2002.

IMPLEMENTING THE PROGRAM

In order to assist sponsors in meeting their commitments to the HPV Challenge Program, the Agency prepared a number of guidance documents that were designed to maximize the use of existing information and various estimation techniques so that the level of any new testing proposed under the program would be minimized. This would reduce costs substantially and address animal welfare concerns by reducing the number of animals used in the HPV Challenge Program. The principal guidance documents are: Searching for Chemical Information and Data; The Use of Structure-Activity Relationships (SAR); Development of Chemical Categories; Developing Robust Summaries; Assessing Adequacy of Existing Data; and Fact Sheet on Animal Welfare. Other guidance documents include What to Test and Testing Closed System Intermediates. All guidance documents can be found at http://www.epa.gov/chemrtk/guidocs.htm. In addition, in a letter to program participants dated

October 14, 1999, the Agency outlined 10 principles that sponsors were asked to observe as they meet their commitments. These 10 principles identified animal welfare considerations in the HPV Challenge Program and established a 120-day public comment period between posting and implementation of Test Plans. Follow-up letters were sent to participants in October, 2000, reiterating EPA's commitment to the principles outlined in the October, 14, 1999, letter.

Public review of submitted Test Plans is largely done electronically through the use of the HPV Challenge Program Website. Sponsors were advised to send Test Plan submissions to the Post Office Box established for the HPV Challenge Program or electronically via the Challenge Website. Submissions can also be sent directly by e-mail to chem.rtk@epa.gov or oppt.ncic@epa.gov. After receipt by EPA, submissions are assigned an Administrative Record Number and placed in the TSCA Administrative Record, File Number AR201, established for the HPV Challenge Program. The submissions are then prepared for Website posting by converting all submissions to a uniform posting format. The first review step by EPA is to determine if a complete package is available for review. This step entails checking the Test Plan to determine whether and how each endpoint has been addressed. If the sponsor indicates that adequate data are available to address a particular endpoint, then a robust summary of those data must be provided. Any omissions are noted and the sponsor is directed to revise the submission. Once submissions are determined to be complete, they are prepared for posting on the HPV Challenge Website. Posting of the submission starts the 120-day public comment period. Concurrently, EPA technical staff review the submissions to develop EPA's comments. EPA and all other public comments are sent to the sponsors electronically for their consideration. All comments on Test Plans are also posted on the Challenge Website.

STATUS OF THE PROGRAM

To date, EPA has received 55 Test Plans covering 383 chemicals. The Test Plans cover 28 categories of chemicals and 27 single chemicals. Over 90 percent of the chemicals are addressed in category Test Plans. Fifty-one Test Plans have been posted on the HPV Challenge Program Website for public comment (http://www.epa.gov/chemrtk/viewsrch.htm). The balance is undergoing initial EPA review or on hold pending sponsor revisions. The 120-day public comment period has closed for 29 Test Plans. Public and EPA comments can be viewed under each Test Plan entry on the Website.

To gauge how well the HPV Challenge Program is being implemented and to determine the degree to which sponsors are using the HPV Challenge Program guidance, a number of analyses were conducted looking at data/study sources (that is, whether published or unpublished data were being submitted to support the data needs identified in the program), how the SIDS endpoints were being addressed, and whether sponsors were following the principles outlined in the October 14, 1999, letter to program participants.

Data/Study Sources

As discussed earlier, the prime impetus for the HPV Challenge Program was the consistent finding in the series of reports that publicly available hazard information was lacking on a majority of the 2,800 US HPV chemicals. Following EPA's guidance, sponsors are to identify existing data on HPV chemicals and submit these data in the form of robust summaries. To determine the source of the existing data (that is, published or unpublished data), each Test Plan posted on the Website as of October 4, 2001, was examined (46 Test Plans). The Table below presents the results for the ecological and human health endpoints, and selected physicochemical and environmental fate endpoints (some endpoints are routinely determined with estimation techniques). The number of published and unpublished studies documented in the robust summaries prepared for each SIDS endpoint is listed in the columns below.

ENDPOINT AREA	SPECIFIC ENDPOINT	PUBLISHED	UNPUBLISHED	TOTAL
Health Effects	Acute–Oral	64	109	173
	Acute-Inhalation	38	47	85
	Acute-Dermal	13	68	81
	Repeat Dose	73	124	197
	Gene Tox-In-Vitro	128	154	282
	Gene Tox-In-Vivo	52	73	125
	Repro/Dev	79	74	153
Environmental Effects	Acute–Fish	37	73	110
	Acute-Daphnid	23	55	78
	Acute-Algae	24	41	65
Environmental Fate	Biodegradation	39	42	81
Physicochemical Properties	Water Solubility	39	40	79
	Vapor Pressure	48	67	115
	Partition Coefficient	27	40	67
	Boiling Point	79	60	139
Grand Totals		763	1067	1830

As can be seen from the numbers of studies listed in the Table, a significant amount of

unpublished data have been made public by the sponsors. This indicates that the sponsors, either individually or through the many consortia participating in the program, have made a concerted effort to bring forth existing data. This has had a significant effect on the amount of new testing that sponsors have proposed (see below). This is also in keeping with the Agency's experience implementing the testing provision of Section 4 of TSCA where industry has made every effort to bring forth existing data in response to proposed testing actions.

Directly related to the above discussion is an analysis of how sponsors have proposed to address the SIDS endpoints. The following analysis looked at the first 46 Test Plans posted on the HPV Challenge Website to determine how the health and environmental effects endpoints were addressed in the Test Plan. Three methods to meet the minimum data requirements for each SIDS endpoint were proposed. Data needs were met by (1) the use of existing scientifically adequate data, (2) the use of an estimation technique (SAR, "read-across" in categories) or by providing a rationale for no testing, or (3) proposing new testing. For human health effects, five endpoints (acute, repeat dose, reproductive, developmental, and genetic toxicity) were considered. The analysis was done with and without the API Petroleum Gases Test Plan. It was decided to also generate results with and without this Test Plan, because it covers a very large category of 161 chemicals, nearly all of which had no data submitted, it was critical that these data did not skew the results of the analysis. For environmental effects, three acute toxicity endpoints were examined (acute toxicity to fish, daphnia, and algae). Again, the analysis was done with and without the API Test Plan. The 46 Test Plans (including the API Test Plan) address 325 chemicals in 23 categories and 23 single chemicals. Each calculation below is based on the total number of endpoints that could be addressed for each chemical multiplied by the total number of chemicals. This formula was employed since it was impossible to identify all scientifically adequate existing studies prior to the start of the HPV Challenge Program.

<u>Human Health</u>

1. All Chemicals considering 5 endpoints
325 X 5 = 1625 Total Endpoints

DATA SOURCE	NUMBER	PERCENT
Adequate study(ies)	400	24.6
Estimation/No testing	1124	69.2
Proposed testing	101	6.2

2. All chemicals considering 5 endpoints minus the API Test Plan (161 chemicals)
164 X 5 = 820 Total Endpoints

DATA SOURCE	NUMBER	PERCENT
Adequate study(ies)	397	48.4
Estimation/No testing	348	42.4
Proposed testing	75	9.2

Environmental Effects

1. All chemicals considering 3 endpoints
325 X 3 = 975 Total Endpoints

DATA SOURCE	NUMBER	PERCENT
Adequate study(ies)	163	16.7
Estimation/No testing	759	77.8
Proposed testing	53	5.4

2. All chemicals considering 3 endpoints minus the API Test Plan (161 chemicals)
164 X 3 = 492

DATA SOURCE	NUMBER	PERCENT
Adequate study(ies)	163	33.1
Estimation/No testing	276	56.1
Proposed testing	53	10.8

As can be seen by the above analysis, sponsors have made maximum use of the guidance concerning the use of SAR and category proposals, and in combination with the significant amount of unpublished data made available through the robust summaries, only a minimal amount of testing has been proposed. Overall, for health and environmental effects, approximately six percent of the endpoints are proposed to be addressed with new testing. Even after removing the API Test Plan from the calculations, the overall amount of proposed testing is less than 10 percent. The exact mix and number of new tests may change as sponsors consider EPA and public comments (comment periods on 17 Test Plans have not closed); however, there is no reason to believe that the overall conclusions highlighted through analyses of these 46 Test Plans will change significantly. Comments could lead to some additional tests being performed, but could also result in fewer tests. For instance, the American Petroleum Institute originally proposed to conduct five acute inhalation tests in the Petroleum Gases Test Plan. However, the revised Test Plan, taking into consideration EPA and public comments, removed those five tests from the category Test Plan.

Conformance with October 14, 1999 Letter to Program Participants

On October 14, 1999, EPA provided additional guidance to manufacturers and importers participating in the HPV Challenge Program. The letter outlined 10 principles that sponsors were asked to observe in Test Plans submitted under the HPV Challenge Program. In some cases, sponsors may choose to deviate from these principles because of testing needs not associated with the HPV Challenge Program if a rationale is provided. In essence, the principles address the development of a well-considered Test Plan for HPV chemicals that accounts for all scientifically sound information, and uses categories of chemicals and SAR where appropriate. By developing the Test Plans in this way, unnecessary testing can be avoided while the need for the development of scientifically defensible health and environmental effects information on HPV chemicals will be fulfilled.

To see how well sponsors were following the 10 principles, the first 40 Test Plans posted on the HPV Challenge Program Website were examined (see Appendix). It should be noted that some of the principles include subjective judgements. For instance, the first principle requests that sponsors conduct a "thoughtful, qualitative analysis rather than use a rote checklist approach." Since sponsors are not required to justify testing under the HPV Challenge Program (the OECD HPV SIDS Program also does not support such a requirement, since it has already been established that the SIDS test battery represents the minimal set of data needs for screening HPV chemicals) the absence of text discussing the testing decisions from a number of the single chemical Test Plans does not necessarily indicate that the sponsors did not do a "thoughtful analysis." Also, it is difficult, considering only the Test Plan rationales, to judge the thought, time, and effort that went into developing the Test Plans for single chemicals.

In examining the 40 Test Plans it was determined that, overall, sponsors were following the guidance and were making extensive use of categories and SAR/estimation techniques which reduced the need for additional testing. While EPA may not have agreed with all aspects of some of the category proposals, it was clear that sponsors have devoted considerable time and thought in constructing the category Test Plans. Some of the single chemical Test Plans had considerable discussion of the proposals, while others merely provided a matrix of available data and proposed testing. Again, the HPV Challenge Program does not require justification for proposed testing.

However, a number of instances were noted where it appeared that sponsors did not follow the guidance. One sponsor proposed terrestrial toxicity testing (earthworm and plants) because land application was a known use of the material. This is entirely consistent with OECD SIDS guidance in this area. Dermal toxicity testing was proposed in five test plans. In three test plans the sponsor was proposing testing because of non-U.S. testing requirements, one sponsor decided not to do the dermal test in response to comments, and the other is under review (the proposed dermal irritation study is outside the scope of the HPV Challenge Program). Similarly, in-vivo genetic toxicity testing was proposed in a few Test Plans. It was subsequently determined that in three Test Plans, the testing was proposed to meet non-U.S. testing needs, and in another the sponsor - citing positive in-vitro genetic toxicity tests and the need for responsible product stewardship - has decided to conduct the study. Testing of single chemicals in advance of the request to delay such testing until November, 2001, was noted in a few Test Plans. For three

Test Plans (the same three discussed above), this was being done for non-U.S. testing requirements (the sponsor subsequently agreed to delay the testing) and in two Test Plans it was reported in public comments that testing had already been conducted.

Summary

It appears that when all the HPV Challenge guidance is taken into consideration, sponsors are making good faith efforts to follow that guidance. The conclusion is that following the guidance has resulted in the need to conduct fewer tests than originally envisioned. Sponsors have provided a considerable amount of unpublished data to support their Test Plans, which in combination with the extensive use of categories, this has resulted in about six percent of the health and ecological effects endpoints being addressed with new testing. There have been some deviations from the principles articulated in the October 14, 1999 letter to program participants; however, in many instances this was because the sponsor needed to address testing needs beyond the scope of the HPV Challenge Program.

LESSONS LEARNED/NEXT STEPS

To date, the overall experience in implementing the HPV Challenge Program is positive. A few recommendations to improve the processing and review of Test Plans are noted below. Occasionally, Test Plans are sent directly to EPA officials involved in the HPV Challenge Program. To speed the processing for Website posting and entry into the Administrative Record, all submissions should be sent to the e-mail addresses cited above or by following the directions on the HPV Challenge Website for electronic submissions. If submitting paper copies to the HPV Challenge Post Office Box, a disk with electronic files should be included with the submission. This will permit the preparation of more accurate electronic files for posting. Paper copies alone are scanned, which is time consuming and increases the potential for error.

In the Test Plans themselves, it would be helpful for submitters to explain the rationale for any testing that is proposed beyond the SIDS endpoints. A number of times sponsors have included in their Test Plans, tests they need to perform to meet non-U.S. data requirements. Oftentimes, the goal is to avoid duplicative testing; however, the lack of an explanation leads to needless speculation about why the tests were proposed and the generation of comments requesting explanations for the proposed tests. In category Test Plans, greater attention should be placed on how the category hypothesis addresses the main endpoints (human health, environmental effects, environmental fate, and physicochemical properties). A number of times it appeared that the category was based mainly on human health endpoints and the other endpoint areas were not as thoroughly discussed or supported. EPA recommends that basic physicochemical properties for discrete substances be measured instead of estimated, since these values are used in other estimation models (e.g., transport and distribution). Using estimated values multiplies uncertainty in the results from the subsequent modeling. Finally, it is recommended that sponsors include the results of literature searches conducted in addition to the

robust summaries, i.e., lists of those studies reviewed but not considered key studies (see the end of Section 5 in the Assessing Adequacy of Existing Data guidance document).

EPA is receiving Test Plans and robust summaries in a number of formats. An MS Access Data Input Tool and database were created to assist sponsors in submitting their robust summaries to EPA. Over 250 CD-ROMs have been distributed to sponsors. However, only a few sets of robust summaries have been submitted so far in this format. In any event, all robust summaries received, regardless of the format in which the data are being submitted, are input to the Access database so that a searchable database will be available. Although all the Test Plans and robust summaries submitted to date (and which have successfully completed the initial review) are now available on the HPV Challenge Website, there is no search capability. The MS Access database will serve as an interim tool until an Oracle-based system is available in late 2002.

CONCLUSIONS

Although this report represents only a "snapshot" in time, it appears that the HPV Challenge Program is being implemented in a cost-efficient, judicious manner. Sponsors are providing a large amount of unpublished data and are following the various guidance documents to a significant degree. However, more attention should be devoted in the category Test Plans to documenting how all the major endpoints (health, ecological, fate, and physicochemical properties) are addressed by the category rationale. Sponsors are using category approaches, SAR, and other estimation techniques to reduce costs and the need for new testing. The net result is that new testing is being proposed for about six percent of the health and ecological endpoints, due in large part to the amount of test data, particularly unpublished data, brought forward. The analysis of the degree to which sponsors were following the principles listed in the October 14, 1999, letter to program participants did not reveal any significant trends, except that sponsors were not adequately explaining why they were proposing tests that were beyond the base set of screening tests and/or were not consistent with EPA's guidance.

Introduction

On October 14, 1999, EPA Deputy Assistant Administrator Susan H. Wayland provided a test plan development framework for manufacturers and importers participating in the HPV Challenge Program (http://www.epa.gov/chemrtk/ceoltr2.htm). This framework outlined 10 animal welfare principles that sponsors were asked to observe in all Test Plans submitted under the HPV Challenge Program; although sponsors may determine the need to deviate from the principles based on testing needs not associated with the HPV Challenge Program, but a rationale should be provided. In essence, the principles address the development of a well-considered plan for testing HPV chemicals that accounts for all available scientifically sound information, and uses categories of chemicals and Structure Activity Relationships (SAR) where appropriate. By developing the plans in this way, unnecessary animal testing will be eliminated while the need for the development of scientifically defensible health and environmental effects information on high production volume chemicals will be fulfilled.

Methodology

This report consists of individual tables for the first 40 Test Plans for HPV Challenge Program chemicals/ categories. Their order of presentation in this report is the same as the order of appearance on the EPA HPV Challenge Program website (http://www.epa.gov/chemrtk/viewsrch.htm). The individual tables are structured in the following way. The first column presents a short summary of the principles under review (Table 1 contains the complete text of the principles from the October 14, 1999 letter and the summary text used in the individual tables). The middle column contains an assessment of the Test Plan for each principle, and the right column contains an evaluation of compliance. A table is presented at the end which provides a summary of the individual reviews. It should be noted that this assessment was limited to the October 14, 1999 letter. EPA is providing comments on these issues as well as on the technical/scientific aspects of the Test Plans directly to the sponsors.

The assessment column contains explanatory information about each Test Plan and should be used in conjunction with the compliance information. For example, the second principle requires submitters to analyze available, scientifically valid data so that further testing will be minimized. Although a Test Plan may appear to have adequately reported available data, commentors may identify additional studies not presented in the Test Plan. In this case, the individual table would indicate that the Test Plan appeared to present all available studies, but commentors have noted otherwise. The four levels of compliance used are: (1) compliance, (2) noncompliance, (3) equivocal or unclear compliance, and (4) not applicable. "Equivocal or unclear" compliance is used, for example, when a submitter notes that some of the chemicals under consideration are GRAS, but does not use this information in any of the justification for testing. "Not applicable" compliance is used, for example, where compliance with principle 3 ("[w]ere categories of related chemicals and structure activity relationships used to minimize further testing?") is evaluated for a single chemical. It should be noted that for some of the principles, compliance is achieved with either a "Yes" or "No" answer. For example, if a chemical under consideration is GRAS, then compliance with principle 8 is "Yes," while compliance is achieved with a "No" answer for non-GRAS chemicals.

As noted above, the October 14, 1999 letter contained 10 principles. For this review, however, principle 1, which requires the submission of a "thoughtful" Test Plan, was reviewed for categories only. Assessing "thoughtfulness" for single chemical submissions, many of which provide only tabular Test Plans, was difficult (the amount of thought that was devoted to a tabular Test Plan could not be determined). Principle 1 for single chemicals, therefore, is assigned an "unclear or equivocal" designation in the tables as a place holder. Finally, this report considers those HPV Challenge Program submissions posted on EPA's Challenge program website as

of March 22, 2001 (40 Test Plans). It therefore represents only a “snapshot” in time.

Conclusion

The overall conclusion of the assessment, as depicted in the Summary Table, is that HPV Challenge Program sponsors are following the guidance in the October 14, 1999 letter to a significant degree.

Table 1. Summary Text Used in the Individual Tables

Text from the 14 October 1999 Letter	Summary Text
1. In analyzing the adequacy of existing data, participants shall conduct a thoughtful, qualitative analysis rather than use a rote checklist approach. Participants may conclude that there is sufficient data, given the totality of what is known about a chemical, including human experience, that certain endpoints need not be tested.	Was the analysis thoughtful and qualitative?
2. Participants shall maximize the use of existing and scientifically adequate data to minimize further testing. To reinforce this approach, EPA will consider information contained in the databases identified in the enclosure, or in databases maintained by the organizations identified in the enclosure, to have been known to the Agency within the meaning of Section 8(e) of the Toxic Substances Control Act (TSCA), 42 U.S.C. 2607(e). This policy is limited to information reported by participants under the HPV Challenge program and generated for or contained in these databases as of the date of this letter. In addition, any other potential liability under TSCA Section 8(e) for existing data on HPV Challenge program chemicals will be limited according to the terms of the "Registration Agreement for TSCA Section 8(e) Compliance Audit Program (56 Fed. Reg. 4128, Feb. 1, 1991)." This policy does not affect prior 8(e) enforcement actions.	Were available data used to minimize further testing?
3. Participants shall maximize the use of scientifically appropriate categories of related chemicals and structure activity relationships.	Were categories of related chemicals and structure activity relationships used to minimize further testing?
4. Consistent with the Screening Information Data Set (SIDS) program of the Organization for Economic Cooperation and Development (OECD), participants shall not conduct any terrestrial toxicity testing.	Was any terrestrial toxicity testing proposed (*e.g.*, OECD Testing guidelines 206, 207, 208, 213, and 214)?
5. Participants are encouraged to use in vitro genetic toxicity testing to generate any needed genetic toxicity screening data, unless known chemical properties preclude its use.	Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?
6. Consistent with the OECD/SIDS program, participants generally should not develop any new dermal toxicity data.	Was any dermal toxicity testing proposed?
7. Participants shall not develop sub-chronic or reproductive toxicity data for the HPV chemicals that are solely closed system intermediates, as defined by the OECD/SIDS guidelines.	For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?
8. In analyzing the adequacy of screening data for chemicals that are substances Generally Recognized as Safe (GRAS) for a particular use by the Food and Drug Administration (FDA), participants should consider all relevant and available information supporting the FDA's conclusions. Participants reviewing the adequacy of existing data for these chemicals should specifically consider whether the information available makes it unnecessary to proceed with further testing involving animals. As with all chemicals, before generating new information, participants should further consider whether any additional information obtained would be useful or relevant.	Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?

Text from the 14 October 1999 Letter	Summary Text
9. Because validated non-animal tests for some SIDS endpoints may be available soon, participants shall make the following revisions to the sequence of testing: (a) Testing of closed system intermediates, which present less risk of exposure, shall be deferred until 2003; (b) Individual chemicals (i.e., those HPV chemicals not proposed for testing in a category) that require further testing on animals shall be deferred until November 2001. These revisions should not be construed to suggest that delay or deferral is appropriate with respect to testing of scientifically appropriate categories of related chemicals.	Was testing delayed for closed-system intermediates and single chemicals?
10. Companies shall allow 120 days between the posting of test plans and the implementation of any testing plans.	Was a 120 day waiting period implemented?

Dicarboxylic Acids Category

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Yes	**U**
2. Were available data used to minimize further testing?	Yes, based on a preliminary review.	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Yes, Dicarboxylic Acids is a category	**U**
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	Yes. However, it is unclear if information supporting FDA's conclusions were incorporated into the Test Plan. The GRAS status of this chemical was not directly used in the justification for limiting the testing needs of the category, even though no health effects testing was proposed.	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	Not Applicable	NA
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan, but the submitters indicated that they would wait until the comment period was over and had received any submitted remarks before beginning any action.	†

U Compliant with 14 October 1999 letter to manufacturers and importers
Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

Dinitrile Category

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Yes	**U**
2. Were available data used to minimize further testing?	Yes, based on a preliminary review.	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Yes, dinitriles is a category. The use of structure activity relationships were referenced, however, no specific information was presented.	**U**
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	Yes, dermal and eye irritation studies are planned.	**Y**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	Not applicable	NA
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

U Compliant with 14 October 1999 letter to manufacturers and importers
Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

1,1-Difluoroethane

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Yes	**U**
2. Were available data used to minimize further testing?	Yes, based on a preliminary review.	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Not applicable; 1,1-difluoroethane is a single chemical.	NA
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	Yes	**U**
10. Was a 120 day waiting period implemented?	Yes	**U**

U Compliant with 14 October 1999 letter to manufacturers and importers
Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

Glycolic Acid

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Yes	**U**
2. Were available data used to minimize further testing?	Yes, based on a preliminary review.	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Not Applicable; glycolic acid is a single chemical.	NA
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	Yes	**U**
10. Was a 120 day waiting period implemented?	Yes	**U**

U Compliant with 14 October 1999 letter to manufacturers and importers
Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

Acetoacet-o-Anisidide

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Yes	**U**
2. Were available data used to minimize further testing?	Yes, based on a preliminary review.	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Not Applicable; acetoacet-o-anisidide is a single chemical	NA
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No new testing is proposed. The submitted suggests that acetoacet-o-anisidide is a closed-system intermidiate; however, little supporting information is presented.	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	No testing was proposed for this chemical.	NA
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

U Compliant with 14 October 1999 letter to manufacturers and importers
Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

Methanol

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Yes	**U**
2. Were available data used to minimize further testing?	Yes	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Not applicable; methanol is a single chemical.	NA
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	Not Applicable	NA
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	No testing was proposed for this chemical.	NA
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

U Compliant with 14 October 1999 letter to manufacturers and importers
Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

Tall Oil and Related Substances Category

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Yes	**U**
2. Were available data used to minimize further testing?	Yes	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Yes, tall oil and related substances is a category	**U**
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	Not applicable.	NA
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

U Compliant with 14 October 1999 letter to manufacturers and importers
Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

Dipropylene Glycol Dibenzoate

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Unclear or equivocal.	†
2. Were available data used to minimize further testing?	Yes	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Not Applicable, dipropylene glycol dibenzoateis a single chemical.	NA
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	No testing was proposed for this chemical.	NA
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

U Compliant with 14 October 1999 letter to manufacturers and importers
Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

p-Methylstyrene

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Unclear or equivocal.	†
2. Were available data used to minimize further testing?	Yes	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Not Applicable, p-methylstyrene is a single chemical	NA
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	No health effects testing was proposed for this chemical.	NA
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

U Compliant with 14 October 1999 letter to manufacturers and importers
Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

Cyclohexyl isocyanate

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Unclear or equivocal.	†
2. Were available data used to minimize further testing?	Yes	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Not Applicable, cyclohexylisocyanate is a single chemical	NA
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	No information was presented in the submission.	†
10. Was a 120 day waiting period implemented?	Yes	**U**

U Compliant with 14 October 1999 letter to manufacturers and importers
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NA Not applicable

C6-C10 Aliphatic Aldehydes and Carboxylic Acids Category

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Yes	**U**
2. Were available data used to minimize further testing?	Yes	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Yes, C6-C10 Aliphatic Aldehydes and Carboxylic Acids is a cateogry	**U**
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	Yes	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	Not Applicable	NA
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

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NA Not applicable

Tall Oil Fatty Acids and Related Substances Category

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Yes	**U**
2. Were available data used to minimize further testing?	Yes	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Yes, Tall Oil Fatty Acids and Related Substances is a category	**U**
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	Not Applicable	NA
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

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Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

Alkylphenols Category

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Yes	**U**
2. Were available data used to minimize further testing?	Yes	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Yes, alkylphenols is a category	**U**
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	Not Applicable	NA
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

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† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

Ethanol

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Unclear or equivocal.	†
2. Were available data used to minimize further testing?	Yes	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Not Applicable, ethanol is a single chemical	NA
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	No testing was proposed for this chemical.	NA
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

U Compliant with 14 October 1999 letter to manufacturers and importers
Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

Cyclic Anhydrides

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Yes	**U**
2. Were available data used to minimize further testing?	Yes	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Yes, cyclic anhydrides is a category	**U**
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	Not applicable	NA
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

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NA Not applicable

FYROL FR-2 [Tris(1,3-dichloro-2-propyl) phosphate]

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Unclear or equivocal.	†
2. Were available data used to minimize further testing?	Yes	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Not Applicable, FYROL FR-2 is a single chemical	NA
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	No health effects testing was proposed for this chemical.	NA
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

U Compliant with 14 October 1999 letter to manufacturers and importers
Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

Terpenoid Primary Alcohols and Related Esters Category

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Yes	**U**
2. Were available data used to minimize further testing?	Yes, although the discussion is not always presented in a straightforward manner.	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Yes, Terpenoid Primary Alcohols and Related Esters is a category.	**U**
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	Yes, 3 of the 4 members of the proposed category are considered GRAS by FDA. Nonetheless, the GRAS status of these chemicals was not directly used in the justification for limiting the testing needs of the category, even though no health effects testing was proposed. It is unclear if information supporting FDA's conclusions were incorporated into the Test Plan.	†
9. Was testing delayed for closed-system intermediates and single chemicals?	Not applicable	NA
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

U Compliant with 14 October 1999 letter to manufacturers and importers
Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

Spent Pulping Liquor and Cooking Liquors Category

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Yes, based on a preliminary review.	**U**
2. Were available data used to minimize further testing?	Yes, according to the submission, however, very little data are available; available data appear to have been used appropriately.	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Not applicable, categories are not appropriate for this substance.	NA
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	Not applicable	NA
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

U Compliant with 14 October 1999 letter to manufacturers and importers
Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

Terpenoid Tertiary Alcohols and Related Esters Category

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Yes. The Test Plan, however, was difficult to follow and failed to support some of the conclusions made.	**U**
2. Were available data used to minimize further testing?	Yes, although the discussion is not always presented in a straightforward manner.	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Yes, Terpenoid Tertiary Alcohols and Related Esters is a category; however, the category justification was difficult to follow.	**U**
4. Was any terrestrial toxicity testing proposed?	No	**U**
5.Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	Yes, 10 of 13 chemicals in the proposed category are considered GRAS by FDA. Nonetheless, the GRAS status of these chemicals was not directly used in the justification for limiting the testing needs of the category, even though no health effects testing was proposed. It is unclear if information supporting FDA's conclusions were incorporated into the Test Plan.	†
9. Was testing delayed for closed-system intermediates and single chemicals?	Not applicable	NA
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

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NA Not applicable

2,3-Dihydro-2,2-dimethyl-7-benzofuranol

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Unclear or equivocal	†
2. Were available data used to minimize further testing?	Yes, based on a preliminary review.	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Not applicable. Test data were presented for this chemical only by the sponsor; no SAR comparisons were necessary.	NA
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	Yes (chromosomal aberrations), no rationale was provided in the Test Plan.	**Y**
6. Was any dermal toxicity testing proposed?	Yes (acute dermal), no rationale was provided in the Test Plan.	**Y**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	No information was presented in the submission.	†
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

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† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

Methallyl Chloride

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Unclear or equivocal.	†
2. Were available data used to minimize further testing?	Yes, based on a preliminary review.	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Not applicable. Test data were presented for this chemical only by the sponsor; no SAR comparisons were necessary.	NA
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	No information was presented in the submission.	†
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

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Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

Alkyl Acetate C6 - C13 Category

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Yes, although the Test Plan includes the C11-C14 branched alkyl acetate esters in the category; these esters do not appear to have the same pattern of toxicity as the other members of the group	**U**
2. Were available data used to minimize further testing?	Yes, based on a preliminary review.	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Yes, Alkyl Acetate C6 - C13 is a category.	**U**
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	Not applicable	NA
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

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Y Non-compliant with 14 October 1999 letter to manufacturers and importers
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NA Not applicable

Cinnamyl Derivatives Category

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Yes, although some additional explanation of the justification for the ecotoxicity testing was needed.	**U**
2. Were available data used to minimize further testing?	Yes	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Yes, Cinnamyl Derivatives is a category.	**U**
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	Yes, 3 of 4 chemicals in the proposed category are listed as GRAS chemicals by FDA. The GRAS designation was only mentioned in Section 2.2 "Background Information" of the Test Plan and does not appear to be part of the reasoning used to eliminate health effects tests. It is unclear if information supporting FDA's conclusions were incorporated into the Test Plan.	†
9. Was testing delayed for closed-system intermediates and single chemicals?	Not applicable	NA
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

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Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

1,3,5-Trioxane

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Unclear or equivocal	†
2. Were available data used to minimize further testing?	Yes	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Not applicable. Test data were presented for this chemical only by the sponsor; no SAR comparisons were necessary.	NA
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	No testing was proposed for this chemical.	NA
10. Was a 120 day waiting period implemented?	No testing was proposed for this chemical.	NA

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Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

1,3-Dioxolane

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Unclear or equivocal	†
2. Were available data used to minimize further testing?	Yes	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Not applicable. Test data were presented for this chemical only by the sponsor; no SAR comparisons were necessary.	NA
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	No testing was proposed for this chemical.	NA
10. Was a 120 day waiting period implemented?	No testing was proposed for this chemical.	NA

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Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

C5 Noncyclics Category

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Yes, although there were errors in the Test Plan.	**U**
2. Were available data used to minimize further testing?	Yes; however, commentors suggest that the test plan does not fully use existing data, particularly in the area of toxicokinetics.	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Yes, C5 Non-cyclics is a category.	**U**
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	Yes, a mouse chromosomal aberration test has been proposed in the Test Plan. The inhalation route of exposure was chosen because inhalation is the most relevant exposure route for the C5 Non-Cyclics streams. The mouse micronucleus test was chosen for chromosomal effects testing because isoprene is negative in *in vitro* tests of genotoxicity but positive in the mouse micronucleus test. 2-Methyl-2-butene is also positive in the mouse micronucleus test. These data indicate that *in vivo* tests would be more likely to identify genotoxic effects from this group of chemicals.	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No (all test streams are commercial products or isolated intermediates)	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	Not applicable	NA
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

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Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

Dimethyl Ether

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Unclear or equivocal	†
2. Were available data used to minimize further testing?	Yes, based on a preliminary review.	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Not applicable. Test data were presented for this chemical only by the sponsor; no SAR comparisons were necessary.	NA
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	No testing was proposed for this chemical.	NA
10. Was a 120 day waiting period implemented?	No testing was proposed for this chemical.	NA

U Compliant with 14 October 1999 letter to manufacturers and importers
Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

Petroleum Gas Category

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Yes, but the Test Plan did not adequately support the proposed category.	**U**
2. Were available data used to minimize further testing?	Yes, a commentor, however, states that the American Petroleum Institute failed to review the current toxicologic literature for available test information. No specific additional toxicologic studies were cited in the comment that support this conclusion.	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Yes; however, according to comments, additional data exist for related chemicals. It is unclear if these are scientifically appropriate.	**U**
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	Yes. A limited rationale (i.e., the inability of the existing *in vitro* tests to detect genetic activity and the lack of any *in vivo* data) was used to support the proposed *in vivo* testing in the mouse micronucleus test (OECD 474).	†
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No. While most of the "petroleum gases are intermediate process streams that do not leave the refinery", the components proposed for testing are present in finished commercial products.	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	Not applicable	NA
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

U Compliant with 14 October 1999 letter to manufacturers and importers
Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

AMPS® Category

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Yes	**U**
2. Were available data used to minimize further testing?	Yes, data are available for at least one member of the category for every end point.	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Yes, AMPS® is a category.	**U**
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	Not applicable	NA
10. Was a 120 day waiting period implemented?	No testing was proposed for this category.	NA

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NA Not applicable

Silane, [3-(2,3-epoxypropoxy)propyl]trimethoxy

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Unclear or equivocal	†
2. Were available data used to minimize further testing?	Yes, physical and chemical properties that precluded certain testing were discussed.	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	No, although structure activity relationships were considered in the Silicones Environmental, Health and Safety Council response to EPA comments.	**U**
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	Solubility in water was the only study proposed for this chemical.	NA
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

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† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

Tris(2,4-di-(tert)-butylphenyl)phosphite

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Unclear or equivocal.	†
2. Were available data used to minimize further testing?	Yes, a commentor, however, states that this chemical is listed as an FDA food contact substance and suggests that this indicates that a toxicologic profile exists. No indication of what specific data may be available from FDA was provided.	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Not applicable. Test data were presented for this chemical only by the sponsor; no SAR comparisons were necessary.	NA
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	Stability in water was the only study proposed for this chemical.	NA
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

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NA Not applicable

Octadecyl 3,5-di(tert)-butyl-4-hydroxyhydrocinnamate

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Unclear or equivocal	†
2. Were available data used to minimize further testing?	Yes, a commentor, however, states that this chemical is listed as an FDA food contact substance and suggests that this indicates that a toxicologic profile exists. No indication of what specific data may be available from FDA was provided. Additional studies on mutagenicty and induction of microsomal enzymes were cited.	†
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Not applicable. Test data were presented for this chemical only by the sponsor; no SAR comparisons were necessary.	NA
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	No testing was proposed for this chemical.	NA
10. Was a 120 day waiting period implemented?	No testing was proposed for this chemical.	NA

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NA Not applicable

Tetrakis-(methylene-(3,5-ditertbutyl-4-hydrocinnamate)methane

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Unclear or equivocal	†
2. Were available data used to minimize further testing?	Yes, a commentor, however, states that this chemical is listed as an FDA food contact substance and suggests that this indicates that a toxicologic profile exists. No indication of what specific data may be available from FDA was provided. Additional studies on acute toxicity and genotoxicity were cited (unpublished government reports) along with a study on the "inhibition of metabolic cooperation" from the open literature.	†
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Not applicable. Test data were presented for this chemical only by the sponsor; no SAR comparisons were necessary.	NA
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	No testing was proposed for this chemical.	NA
10. Was a 120 day waiting period implemented?	No testing was proposed for this chemical.	NA

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Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

Tris (Nonylphenol) Phosphite

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Unclear or equivocal	†
2. Were available data used to minimize further testing?	Yes, a commentor, however, states that this chemical is listed as an FDA food contact substance and suggests that this indicates that a toxicologic profile exists. No indication of what specific data may be available from FDA was provided.	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	No; according to commentors, however, some SAR comparison opportunities exist, although no carefully constructed scientific assessment was included in the comments.	NA
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	*In vivo* genetic toxicity testing was proposed in the Test Plan, but no rationale supporting the testing was provided.	**Y**
6. Was any dermal toxicity testing proposed?	Dermal toxicity testing was proposed in the Test Plan, but no rationale supporting the testing was provided.	**Y**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	No	**Y**
10. Was a 120 day waiting period implemented?	Yes	**U**

U Compliant with 14 October 1999 letter to manufacturers and importers
Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

p-Cumylphenol

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Unclear or equivocal	†
2. Were available data used to minimize further testing?	Yes, a commentor, however, states that this chemical is listed as an FDA food contact substance and suggests that this indicates that a toxicologic profile exists. No indication of what specific data may be available from FDA was provided.	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Not applicable. Test data were presented for this chemical only by the sponsor; no SAR comparisons were necessary.	NA
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	*In vivo* genetic toxicity testing was proposed in the Test Plan, but no rationale supporting the testing was provided.	**Y**
6. Was any dermal toxicity testing proposed?	Dermal toxicity testing was proposed in the Test Plan, but no rationale supporting the testing was provided.	**Y**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	No	**Y**
10. Was a 120 day waiting period implemented?	Yes	**U**

U Compliant with 14 October 1999 letter to manufacturers and importers
Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

Phosphorous Acid, Cyclic NeoPentanetetrayl Diphenyl Ester

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Unclear or equivocal	†
2. Were available data used to minimize further testing?	Yes	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	No, according to commentors, however, some SAR comparison opportunities exist, although no carefully constructed scientific assessment was included in the comments.	NA
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	*In vivo* genetic toxicity testing was proposed in the Test Plan, but no rationale supporting the testing was provided.	**Y**
6. Was any dermal toxicity testing proposed?	Dermal toxicity testing was proposed in the Test Plan, but no rationale supporting the testing was provided.	**Y**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	No	**Y**
10. Was a 120 day waiting period implemented?	Yes	**U**

U Compliant with 14 October 1999 letter to manufacturers and importers
Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

Alkyl Sulfide Category

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Yes, although some supporting data were missing from the Test Plan.	**U**
2. Were available data used to minimize further testing?	Yes, based on a preliminary review.	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Yes, although EPA comments suggest that the justification for the category based on health effects is weak.	**U**
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	Not applicable	NA
10. Was a 120 day waiting period implemented?	Yes	**U**

U Compliant with 14 October 1999 letter to manufacturers and importers
Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

High Butadiene C4 Category

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Yes, although there were some inconsistencies in the Test Plan.	**U**
2. Were available data used to minimize further testing?	Yes	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Yes, High Butadiene C4 is a category.	**U**
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	Yes, a mouse chromosomal aberration test (apparently to be administered by inhalation) has been proposed in the Test Plan. The mouse micronucleus test (OECD 474) was chosen for chromosomal effects testing because there are no *in vivo* genetic toxicity data available for the low (~10%) 1,3 butadiene stream. These data indicate that *in vivo* tests would be more likely to identify genotoxic effects from this group of chemicals.	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	Unclear. The low butadiene stream was chosen for a combined repeat dose/ reproductive effects/neurotoxicity screen. It is unclear from the Test Plan if this stream is a closed-system intermediate. Nonetheless, this test is proposed in order to support the sponsors' premise that butadiene is the dominant toxicant in this category.	†
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	Not applicable	NA
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

U Compliant with 14 October 1999 letter to manufacturers and importers
Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

Aminosilanes Category

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Yes	**U**
2. Were available data used to minimize further testing?	Yes, based on a preliminary review.	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Yes, a commentor, however, states that there are existing data on hydrolysis products of related chemicals, but specific data were not provided.	**U**
4. Was any terrestrial toxicity testing proposed?	No	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	Not applicable	NA
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

U Compliant with 14 October 1999 letter to manufacturers and importers
Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

Petroleum Coke Category

Question	Assessment	Compliance
1. Was the analysis thoughtful and qualitative?	Yes	**U**
2. Were available data used to minimize further testing?	Yes, based on a preliminary review.	**U**
3. Were categories of related chemicals and structure activity relationships used to minimize further testing?	Yes, Petroleum Coke is a category.	**U**
4. Was any terrestrial toxicity testing proposed?	Yes, earthworms and plants will be tested to better understand the impact of petroleum coke in soil. This is consistent with OECD guidance.	**U**
5. Was *in vivo* genetic toxicity testing proposed to generate genetic toxicity screening data?	No	**U**
6. Was any dermal toxicity testing proposed?	No	**U**
7. For chemicals that are solely closed-system intermediates, was subchronic or reproductive toxicity testing proposed?	No	**U**
8. Are any GRAS chemicals proposed for testing? If so, was this information (or other available information supporting the FDA's conclusions) used to obviate the need for SIDS-level testing?	No	**U**
9. Was testing delayed for closed-system intermediates and single chemicals?	Not applicable	NA
10. Was a 120 day waiting period implemented?	No information on this element was presented in the cover letter or test plan.	†

U Compliant with 14 October 1999 letter to manufacturers and importers
Y Non-compliant with 14 October 1999 letter to manufacturers and importers
† Compliance with 14 October 1999 letter to manufacturers and importers is unclear or equivocal
NA Not applicable

Summary

Test Submission Name	Principles Discussed in October 14, 1999 Letter from Deputy Assistant Administrator Susan H. Wayland to Manufacturers/Importers									
	1	2	3	4	5	6	7	8	9	10
Dicarboxylic Acids Category	U	U	U	U	U	U	U	U	NA	†
Dinitrile Category	U	U	U	U	U	Y	U	U	NA	†
1,1-Difluoroethane	U	U	NA	U	U	U	U	U	U	U
Glycolic Acid	U	U	NA	U	U	U	U	U	U	U
Acetoacet-o-anisidide	U	U	NA	U	U	U	U	U	NA	†
Methanol	U	U	NA	U	U	U	NA	U	NA	†
Tall Oil and Related Substances Category	U	U	U	U	U	U	U	U	NA	†
Dipropylene Glycol Dibenzoate	†	U	NA	U	U	U	U	U	NA	†
p-Methylstyrene	†	U	NA	U	U	U	U	U	NA	†
Cyclohexyl Isocyanate	†	U	NA	U	U	U	U	U	†	U
C6-C10 Aliphatic Aldehydes & Carboxylic Acids Category	U	U	U	U	U	U	U	U	NA	†
Tall Oil Fatty Acids and Related Substances Category	U	U	U	U	U	U	U	U	NA	†
Alkylphenols Category	U	U	U	U	U	U	U	U	NA	†
Ethanol	†	U	NA	U	U	U	U	U	NA	†
Cyclic Anhydrides	U	U	U	U	U	U	U	U	NA	†
Fyrol FR-2	†	U	NA	U	U	U	U	U	NA	†
Terpenoid Primary Alcohols and Related Esters Category	U	U	U	U	U	U	U	†	NA	†
Spent Pulping Liquor and Cooking Liquors Category	U	U	NA	U	U	U	U	U	NA	†
Terpenoid Tertiary Alcohols and Related Esters Category	U	U	U	U	U	U	U	†	NA	†
2,3-Dihydro-2,2-dimethyl-7-benzofuranol	†	U	NA	U	Y	Y	U	U	†	†
Methallyl Chloride	†	U	NA	U	U	U	U	U	†	†
Alkyl Acetate C6 - C13 Category	U	U	U	U	U	U	U	U	NA	†
Cinnamyl Derivatives Category	U	U	U	U	U	U	U	†	NA	†
1,3,5-Trioxane	†	U	NA	U	U	U	U	U	NA	NA
1,3-Dioxolane	†	U	NA	U	U	U	U	U	NA	NA
C5 Noncyclics Category	U	U	U	U	U	U	U	U	NA	†
Dimethyl Ether	†	U	NA	U	U	U	U	U	NA	NA
Petroleum Gas Category	U	U	U	U	†	U	U	U	NA	†
AMPS® Category	U	U	U	U	U	U	U	U	NA	NA
Silane,[3-(2,3-epoxypropoxy)propyl]trimethoxy	†	U	U	U	U	U	U	U	NA	†

Tris(2,4-di-(tert)-butylphenyl)phosphite	†	**U**	NA	**U**	**U**	**U**	**U**	**U**	NA	†
Octadecyl 3,5-di(tert)-butyl-4-hydroxyhydrocinnamate	†	†	NA	**U**	**U**	**U**	**U**	**U**	NA	NA
Tetrakis-(methylene-(3,5-ditertbutyl-4-hydrocinnamate)methane	†	†	NA	**U**	**U**	**U**	**U**	**U**	NA	NA
Tris (Nonylphenol) Phosphite	†	**U**	NA	**U**	**Y**	**Y**	**U**	**U**	**Y**	**U**
p-Cumylphenol	†	**U**	NA	**U**	**Y**	**Y**	**U**	**U**	**Y**	**U**
Phosphorous Acid, Cyclic NeoPentanetetrayl Diphenyl Ester	†	**U**	NA	**U**	**Y**	**Y**	**U**	**U**	**Y**	**U**
Alkyl Sulfide Category	**U**	**U**	**U**	**U**	**U**	**U**	**U**	**U**	NA	**U**
High Butadiene C4 Category	**U**	**U**	**U**	**U**	**U**	**U**	†	**U**	NA	†
Aminosilanes Category	**U**	**U**	**U**	**U**	**U**	**U**	**U**	**U**	NA	†
Petroleum Coke Category	**U**	**U**	**U**	**U**	**U**	**U**	**U**	**U**	NA	†

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NA Not applicable