

201-15865B

**Substance Group:** Group 2 - Arylpolyolefins

**Summary Prepared by:** Petroleum Additives Panel  
Health, Environmental and Regulatory Task Group

**Date of last update:** April 22, 2005

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## 1.0 Physicochemical Properties

### **Robust Summary #: 2-Physchem-1 (Boiling Point-Range)**

Test Substance*:	Other TS												
Method/Guideline:	Calculated values using MPBPWIN version 1.40, a subroutine of the computer program EPIWIN version 3.04												
Year (guideline):	1999												
Type (test type):	Not applicable												
GLP:	Not applicable												
Year (study performed):	Not applicable												
Estimation Pressure:	760 mm Hg												
Test Conditions: <ul style="list-style-type: none"> <li>Note: Concentration prep., vessel type, replication, test conditions.</li> </ul>	Boiling point calculated by MPBPWIN subroutine, which is based on the method of S. Stein and R. Brown in "Estimation of Normal Boiling Points from Group Contributions". 1994. J. Chem. Inf. Comput. Sci. 34: 581-587.												
Results: Units/Value: <ul style="list-style-type: none"> <li>Note: Deviations from protocol or guideline, analytical method.</li> </ul>	<table border="1"> <thead> <tr> <th><u>Substance Component</u></th> <th><u>Calculated BP (°C)</u></th> </tr> </thead> <tbody> <tr> <td>CAS# 115733-08-9</td> <td></td> </tr> <tr> <td>  Benzene, C<sub>14</sub> alkyl derivative</td> <td>342</td> </tr> <tr> <td>  Benzene, C<sub>24</sub> alkyl derivative</td> <td>458</td> </tr> <tr> <td>CAS# 68081-77-6</td> <td></td> </tr> <tr> <td>  Benzene, C<sub>22</sub> polypropene</td> <td>388</td> </tr> </tbody> </table> <p>Commercial substances in this category have a carbon number distribution between C<sub>20</sub> and C<sub>30</sub> or C<sub>28</sub> and C<sub>88</sub>. The three chemicals selected to represent the atmospheric oxidation potential range of this category include a C<sub>20</sub>, C<sub>30</sub>, and C<sub>28</sub> arylpolyolefin that have common structures. The modeling data for physicochemical endpoints in Sections 2.2.5 to 2.2.7 are presented as ranges for category members, where possible, and are based on the highest and lowest molecular weight derivative in each member. For example, structures representing the C<sub>14</sub>-C<sub>24</sub> alkaryl derivative (CAS # 115733-08-9) include a benzene C<sub>14</sub> alkyl derivative and a benzene C<sub>24</sub> alkyl derivative. Whereas, structures representing the polypropene derivative (CAS # 68081-77-6) include only the benzene C<sub>22</sub> polypropene lowest molecular weight derivative; the benzene C<sub>82</sub> polypropene highest molecular weight derivative has not been modeled as the molecular weight of this derivative falls outside of the applicable range of the EPIWIN modeling program.</p>	<u>Substance Component</u>	<u>Calculated BP (°C)</u>	CAS# 115733-08-9		Benzene, C <sub>14</sub> alkyl derivative	342	Benzene, C <sub>24</sub> alkyl derivative	458	CAS# 68081-77-6		Benzene, C <sub>22</sub> polypropene	388
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CAS# 68081-77-6													
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Test Substance:	<ul style="list-style-type: none"> <li>CAS# 115733-08-9; Benzene C<sub>14</sub>-C<sub>24</sub> branched and linear alkyl derivatives</li> <li>CAS# 68081-77-6; Benzene polypropene derivatives</li> </ul>												

	<p>Arylpolyolefins are manufactured by mixing anhydrous alkylate (linear or branched) with benzene in the presence of catalyst and heat. More information on the Arylpolyolefin Category can be found in the American Chemistry Council; Petroleum Additives Panel; Health, Environmental, Regulatory, Task Group, High Production Volume test plan for this category (1).</p> <p>1. Health, Environmental, Regulatory, Task Group (HERTG). 2002. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Arylpolyolefin Category. American Chemistry Council, Petroleum Additives Panel, HERTG.</p>
Conclusion:	<p>Modeling data indicate that the boiling range of category members can range from 342 to 458°C for the C<sub>14</sub>-C<sub>24</sub> alkaryl derivative (CAS # 115733-08-9) and can be &gt;388°C for the polypropene derivative (CAS # 68081-77-6).</p>
Reliability:	<p>(2) Reliable with restrictions</p> <p>The results include calculated values based on chemical structure and represent a potential boiling range for substances with the 2 CAS numbers listed under test substance.</p>
Reference:	<p>Boiling point calculated by MPBPWIN subroutine, which is contained in the computer program:</p> <p>EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.</p>
Other (source):	<p>American Chemistry Council; Petroleum Additives Panel; Health, Environmental, Regulatory, Task Group</p>

\* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "melting point". Selecting this option refers the reader to information in the "freetext" field for "test substance".

**Robust Summary #: 2-Physchem-2 (Vapor Pressure Range)**

Test Substance*:	Other TS												
Method/Guideline:	Calculated values using MPBPWIN version 1.40, a subroutine of the computer program EPIWIN version 3.04												
Year (guideline):	1999												
Type (test type):	Not applicable												
GLP:	Not applicable												
Year (study performed):	Not applicable												
Estimation Temperature:	25°C												
Test Conditions: <ul style="list-style-type: none"> <li>Note: Concentration prep., vessel type, replication, test conditions.</li> </ul>	<p>Vapor Pressure calculated by MPBPWIN subroutine, which is based on the average result of the methods of Antoine and Grain. Both methods use boiling point for the calculation.</p> <p>The Antoine method is described in: Handbook of Chemical Property Estimation. Chapter 14. W.J. Lyman, W.F. Reehl and D.H. Rosenblatt, Eds. Washington, D.C.: American Chemical Society. 1990.</p> <p>The modified Grain method is described in: Neely and Blau's <u>Environmental Exposure from Chemicals</u>, Volume 1. 1985. CRC Press. Page 31.</p>												
Results: Units/Value: <ul style="list-style-type: none"> <li>Note: Deviations from protocol or guideline, analytical method.</li> </ul>	<table border="1"> <thead> <tr> <th><u>Substance Component</u></th> <th><u>Calculated VP (Pa)</u></th> </tr> </thead> <tbody> <tr> <td>CAS# 115733-08-9</td> <td></td> </tr> <tr> <td>  Benzene, C<sub>14</sub> alkyl derivative</td> <td>1.3e<sup>-2</sup></td> </tr> <tr> <td>  Benzene, C<sub>24</sub> alkyl derivative</td> <td>1.7e<sup>-6</sup></td> </tr> <tr> <td>CAS# 68081-77-6</td> <td></td> </tr> <tr> <td>  Benzene, C<sub>22</sub> polypropene</td> <td>6.2e<sup>-4</sup></td> </tr> </tbody> </table> <p>Commercial substances in this category have a carbon number distribution between C20 and C30 or C28 and C88. The three chemicals selected to represent the atmospheric oxidation potential range of this category include a C20, C30, and C28 arylpolyolefin that have common structures. The modeling data for physicochemical endpoints in Sections 2.2.5 to 2.2.7 are presented as ranges for category members, where possible, and are based on the highest and lowest molecular weight derivative in each member. For example, structures representing the C<sub>14</sub>-C<sub>24</sub> alkaryl derivative (CAS # 115733-08-9) include a benzene C<sub>14</sub> alkyl derivative and a benzene C<sub>24</sub> alkyl derivative. Whereas, structures representing the polypropene derivative (CAS # 68081-77-6) include only the benzene C<sub>22</sub> polypropene lowest molecular weight derivative; the benzene C<sub>82</sub> polypropene highest molecular weight derivative has not been modeled as the molecular weight of this derivative falls outside of the applicable range of the</p>	<u>Substance Component</u>	<u>Calculated VP (Pa)</u>	CAS# 115733-08-9		Benzene, C <sub>14</sub> alkyl derivative	1.3e <sup>-2</sup>	Benzene, C <sub>24</sub> alkyl derivative	1.7e <sup>-6</sup>	CAS# 68081-77-6		Benzene, C <sub>22</sub> polypropene	6.2e <sup>-4</sup>
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Benzene, C <sub>22</sub> polypropene	6.2e <sup>-4</sup>												

	EPIWIN modeling program.
Test Substance:	<ul style="list-style-type: none"> <li>• CAS# 115733-08-9; Benzene C<sub>14</sub>-C<sub>24</sub> branched and linear alkyl derivatives</li> <li>• CAS# 68081-77-6; Benzene polypropene derivatives</li> </ul> <p>Arylpolyolefins are manufactured by mixing anhydrous alkylate (linear or branched) with benzene in the presence of catalyst and heat. More information on the Arylpolyolefin Category can be found in the American Chemistry Council; Petroleum Additives Panel; Health, Environmental, Regulatory, Task Group, High Production Volume test plan for this category (1).</p> <p>1. Health, Environmental, Regulatory, Task Group (HERTG). 2002. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Arylpolyolefin Category. American Chemistry Council, Petroleum Additives Panel, HERTG.</p>
Conclusion:	Modeling data indicate that the vapor pressure range of category members can range from $1.3e^{-2}$ to $1.7e^{-6}$ Pa at 25 °C for the C <sub>14</sub> -C <sub>24</sub> alkaryl derivative (CAS # 115733-08-9) and can be $<6.2e^{-4}$ Pa at 25 °C for the polypropene derivative (CAS # 68081-77-6).
Reliability:	(2) Reliable with restrictions The results include calculated values based on chemical structure and represent a potential vapor pressure range for substances with the 2 CAS numbers listed under test substance.
Reference:	Melting point calculated by MPBPWIN subroutine, which is contained in the computer program: EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source):	American Chemistry Council; Petroleum Additives Panel; Health, Environmental, Regulatory, Task Group

\* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "melting point". Selecting this option refers the reader to information in the "freetext" field for "test substance".

### Robust Summary #: 2-Physchem-3 (Water Solubility Range)

Test Substance*:	Other TS												
Method/Guideline:	Calculated values using WSKOWWIN version 1.36, a subroutine of the computer program EPIWIN version 3.04												
Year (guideline):	1999												
Type (test type):	Not applicable												
GLP:	Not applicable												
Year (study performed):	Not applicable												
Estimation Temperature:	25°C												
Test Conditions: <ul style="list-style-type: none"> <li>Note: Concentration prep., vessel type, replication, test conditions.</li> </ul>	Water Solubility calculated by WSKOWWIN subroutine, which is based on a Kow correlation method described by W. Meylan, P. Howard and R. Boethling in "Improved method for estimating water solubility from octanol/water partition coefficient". Environ. Toxicol. Chem. 15:100-106. 1995.												
Results: <p>Units/Value:</p> <ul style="list-style-type: none"> <li>Note: Deviations from protocol or guideline, analytical method.</li> </ul>	<table border="0"> <thead> <tr> <th style="text-align: left;"><u>Substance Component</u></th> <th style="text-align: right;"><u>Calculated WS (mg/L)</u></th> </tr> </thead> <tbody> <tr> <td>CAS# 115733-08-9</td> <td></td> </tr> <tr> <td>    Benzene, C<sub>14</sub> alkyl derivative</td> <td style="text-align: right;">2.0e<sup>-4</sup></td> </tr> <tr> <td>    Benzene, C<sub>24</sub> alkyl derivative</td> <td style="text-align: right;">4.4e<sup>-9</sup></td> </tr> <tr> <td>CAS# 68081-77-6</td> <td></td> </tr> <tr> <td>    Benzene, C<sub>22</sub> polypropene</td> <td style="text-align: right;">1.2<sup>-7</sup></td> </tr> </tbody> </table> <p>Commercial substances in this category have a carbon number distribution between C20 and C30 or C28 and C88. The three chemicals selected to represent the atmospheric oxidation potential range of this category include a C20, C30, and C28 arylpolyolefin that have common structures. The modeling data for physicochemical endpoints in Sections 2.2.5 to 2.2.7 are presented as ranges for category members, where possible, and are based on the highest and lowest molecular weight derivative in each member. For example, structures representing the C<sub>14</sub>-C<sub>24</sub> alkaryl derivative (CAS # 115733-08-9) include a benzene C<sub>14</sub> alkyl derivative and a benzene C<sub>24</sub> alkyl derivative. Whereas, structures representing the polypropene derivative (CAS # 68081-77-6) include only the benzene C<sub>22</sub> polypropene lowest molecular weight derivative; the benzene C<sub>82</sub> polypropene highest molecular weight derivative has not been modeled as the molecular weight of this derivative falls outside of the applicable range of the EPIWIN modeling program.</p>	<u>Substance Component</u>	<u>Calculated WS (mg/L)</u>	CAS# 115733-08-9		Benzene, C <sub>14</sub> alkyl derivative	2.0e <sup>-4</sup>	Benzene, C <sub>24</sub> alkyl derivative	4.4e <sup>-9</sup>	CAS# 68081-77-6		Benzene, C <sub>22</sub> polypropene	1.2 <sup>-7</sup>
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CAS# 68081-77-6													
Benzene, C <sub>22</sub> polypropene	1.2 <sup>-7</sup>												
Test Substance:	<ul style="list-style-type: none"> <li>CAS# 115733-08-9; Benzene C<sub>14</sub>-C<sub>24</sub> branched and linear alkyl derivatives</li> </ul>												

	<ul style="list-style-type: none"> <li>• CAS# 68081-77-6; Benzene polypropene derivatives</li> </ul> <p>Arylpolyolefins are manufactured by mixing anhydrous alkylate (linear or branched) with benzene in the presence of catalyst and heat. More information on the Arylpolyolefin Category can be found in the American Chemistry Council; Petroleum Additives Panel; Health, Environmental, Regulatory, Task Group, High Production Volume test plan for this category (1).</p> <p>1. Health, Environmental, Regulatory, Task Group (HERTG). 2002. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Arylpolyolefin Category. American Chemistry Council, Petroleum Additives Panel, HERTG.</p>
Conclusion:	Modeling data indicate that the water solubility range of category members can range from $2.0e^{-4}$ to $4.4e^{-9}$ mg/L at 25 °C for the C <sub>14</sub> -C <sub>24</sub> alkaryl derivative (CAS # 115733-08-9) and can be $<1.2e^{-7}$ mg/L at 25 °C for the polypropene derivative (CAS # 68081-77-6).
Reliability:	(2) Reliable with restrictions The results include calculated values based on chemical structure and represent a potential water solubility range for substances with the 2 CAS numbers listed under test substance.
Reference:	Water solubility values calculated by WSKOWWIN subroutine, which is contained in the computer program: EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source):	American Chemistry Council; Petroleum Additives Panel; Health, Environmental, Regulatory, Task Group

\* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "melting point". Selecting this option refers the reader to information in the "freetext" field for "test substance".

### Robust Summary #: 2-Physchem-4 (Log Kow Range)

Test Substance*:	Other TS												
Method/Guideline:	Calculated values using KOWWIN version 1.65, a subroutine of the computer program EPIWIN version 3.04												
Year (guideline):	1999												
Type (test type):	Not applicable												
GLP:	Not applicable												
Year (study performed):	Not applicable												
Estimation Temperature:	25°C												
Test Conditions: <ul style="list-style-type: none"> <li>Note: Concentration prep., vessel type, replication, test conditions.</li> </ul>	Octanol / Water Partition Coefficient estimations calculated by KOWWIN subroutine, which is based on an atom/fragment contribution method of W. Meylan and P. Howard in "Atom/fragment contribution method for estimating octanol-water partition coefficients". 1995. J. Pharm. Sci. 84:83-92.												
Results: <p>Units/Value:</p> <ul style="list-style-type: none"> <li>Note: Deviations from protocol or guideline, analytical method.</li> </ul>	<table border="0"> <thead> <tr> <th style="text-align: left;"><u>Substance Component</u></th> <th style="text-align: right;"><u>Calculated Log Kow</u></th> </tr> </thead> <tbody> <tr> <td>CAS# 115733-08-9</td> <td></td> </tr> <tr> <td>    Benzene, C<sub>14</sub> alkyl derivative</td> <td style="text-align: right;">8.9</td> </tr> <tr> <td>    Benzene, C<sub>24</sub> alkyl derivative</td> <td style="text-align: right;">13.8</td> </tr> <tr> <td>CAS# 68081-77-6</td> <td></td> </tr> <tr> <td>    Benzene, C<sub>22</sub> polypropene</td> <td style="text-align: right;">12.3</td> </tr> </tbody> </table> <p>Commercial substances in this category have a carbon number distribution between C20 and C30 or C28 and C88. The three chemicals selected to represent the atmospheric oxidation potential range of this category include a C20, C30, and C28 arylpolyolefin that have common structures. The modeling data for physicochemical endpoints in Sections 2.2.5 to 2.2.7 are presented as ranges for category members, where possible, and are based on the highest and lowest molecular weight derivative in each member. For example, structures representing the C<sub>14</sub>-C<sub>24</sub> alkaryl derivative (CAS # 115733-08-9) include a benzene C<sub>14</sub> alkyl derivative and a benzene C<sub>24</sub> alkyl derivative. Whereas, structures representing the polypropene derivative (CAS # 68081-77-6) include only the benzene C<sub>22</sub> polypropene lowest molecular weight derivative; the benzene C<sub>82</sub> polypropene highest molecular weight derivative has not been modeled as the molecular weight of this derivative falls outside of the applicable range of the EPIWIN modeling program.</p>	<u>Substance Component</u>	<u>Calculated Log Kow</u>	CAS# 115733-08-9		Benzene, C <sub>14</sub> alkyl derivative	8.9	Benzene, C <sub>24</sub> alkyl derivative	13.8	CAS# 68081-77-6		Benzene, C <sub>22</sub> polypropene	12.3
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Benzene, C <sub>22</sub> polypropene	12.3												
Test Substance:	<ul style="list-style-type: none"> <li>CAS# 115733-08-9; Benzene C<sub>14</sub>-C<sub>24</sub> branched and linear alkyl derivatives</li> <li>CAS# 68081-77-6; Benzene polypropene derivatives</li> </ul>												

	<p>Arylpolyolefins are manufactured by mixing anhydrous alkylate (linear or branched) with benzene in the presence of catalyst and heat. More information on the Arylpolyolefin Category can be found in the American Chemistry Council; Petroleum Additives Panel; Health, Environmental, Regulatory, Task Group, High Production Volume test plan for this category (1).</p> <p>1. Health, Environmental, Regulatory, Task Group (HERTG). 2002. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Arylpolyolefin Category. American Chemistry Council, Petroleum Additives Panel, HERTG.</p>
Conclusion:	<p>Modeling data indicate that the log of the octanol-water partition coefficients (log <math>K_{ow}</math>) for category members are estimated to be &gt;8.9.</p>
Reliability:	<p>(2) Reliable with restrictions</p> <p>The results include calculated values based on chemical structure and represent a potential log Kow range for substances with the 2 CAS numbers listed under test substance.</p>
Reference:	<p>Log Kow values calculated by KOWWIN subroutine, which is contained in the computer program:</p> <p>EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.</p>
Other (source):	<p>American Chemistry Council; Petroleum Additives Panel; Health, Environmental, Regulatory, Task Group</p>

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## 2.0 Environmental Fate

## Category: Arylpolyolefins

### 2.1 Biodegradation

<i>Test Substance</i>	
CAS #	115733-08-9
Chemical Name	Benzene, C <sub>14</sub> -C <sub>24</sub> -branched and linear alkyl derivatives
Remarks	<p>This substance is also referred to as C<sub>14</sub>-C<sub>24</sub> alkaryl derivative in HERTG's Test Plan for Arylpolyolefin Category.</p> <p>For more information on the chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Arylpolyolefins Category.</p>
Method	
Method/Guideline followed	OECD 301F
Test Type (aerobic/anaerobic)	Aerobic
GLP (Y/N)	Yes
Year (Study Performed)	2004
Contact time (units)	29 days.
Inoculum	Return activated sludge from domestic waste water treatment plant.
Remarks for test conditions	<p>Inoculum: The sludge was aerated and stirred for 4 hours, homogenized for 2 minutes and allowed to stand for one-half to one hour. Supernatant was removed and used to assess microbial activity.</p> <p>Concentration of test chemical: 49.5 ± 0.6 mg/L (3 replicates)</p> <p>Temp of incubation: 22 ± 1°C.</p> <p>Dosing procedure: A measured volume of the inoculated mineral medium containing approximately 50 mg/L test substance is continuously stirred in a closed system for 29 days.</p> <p>Sampling: The oxygen uptake were monitored continuously and recorded every hour throughout the test.</p> <p>Controls: Canola oil (vehicle control) and sodium benzoate (positive control).</p> <p>Analytical method: Oxygen consumption was measured using a CES aerobic respirometer.</p> <p>Method of calculating measured concentrations: Compared measured O<sub>2</sub> consumption to theoretical oxygen demand (ThOD) to determine percent biodegradation.</p> <p>Other: Test was conducted for an additional day.</p>
<b>Results</b>	
Degradation % after time	58.8% after 28 days.
Kinetic (for sample, positive and negative controls)	% biodegradation (days) Reference (sodium benzoate) – 19.2% (1d), 90.9% (7d), 89.7% (28d). Test substance – 0% (1d), 28.7% (7d), 58.8 % (28d).
Breakdown Products (Y/N) If yes describe breakdown products	Not monitored.

<u>Conclusions</u>	The test substance was not readily biodegradable (58.8 %) in 28 days. The reference substance, sodium benzoate, reached a level of 89.7% in the same test period.
<u>Data Quality</u>	Reliable without restrictions
<u>References</u>	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).
<u>Other</u>	Updated: 11/24/04

## 2.2 Hydrolysis

### **Robust Summary #: 2-EnvFate-1**

Test Substance*:	Other TS
Method/Guideline:	Other: Technical discussion
Year (guideline):	Not applicable
Type (test type):	Not applicable
GLP (Y/N):	Not applicable
Year (study performed):	Not applicable
Analytical Monitoring:	Not applicable
Test Conditions: <ul style="list-style-type: none"> <li>Note: Concentration preparation, vessel type, volume, replication, deviations from guideline or protocol</li> </ul>	Not applicable
Results: <ul style="list-style-type: none"> <li>Units/Value:</li> <li>Note: Analytical method, observations, half-lives by pH, degradation products</li> </ul>	Not applicable
Test Substance:	<p>CAS# 115733-08-9; Benzene C<sub>14</sub>-C<sub>24</sub> branched and linear alkyl derivatives</p> <p>CAS# 68081-77-6; Benzene polypropene derivatives</p> <p>Arylpolyolefins are manufactured by mixing anhydrous alkylate (linear or branched) with benzene in the presence of catalyst and heat. More information on the Arylpolyolefin category can be found in the American Chemistry Council; Petroleum Additives Panel; Health, Environmental, Regulatory, Task Group, High Production Volume test plan for this category (1).</p> <p>1. Health, Environmental, Regulatory, Task Group (HERTG). 2002. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Arylpolyolefin Category. American Chemistry Council, Petroleum Additives Panel, HERTG.</p>
Conclusion:	<p><u>Summary</u></p> <p>In the environment, hydrolysis will not contribute to the degradation of chemicals in the Arylpolyolefin Category. Two CAS numbers identify substances in this category:</p>

	<ul style="list-style-type: none"> <li>• 115733-08-9; Benzene C<sub>14</sub>-C<sub>24</sub> branched and linear alkyl derivatives</li> <li>• 68081-77-6; Benzene polypropene derivatives</li> </ul> <p>As discussed below, the chemicals in these streams are composed of carbon and hydrogen and are not amenable to hydrolysis because of their molecular structure and the chemical reaction required for this type of transformation to occur.</p> <p><u>The Arylpolyolefin Category</u></p> <p>Commercial arylpolyolefins are manufactured by reacting anhydrous alkylate (linear or branched) with benzene in the presence of catalyst and heat. Linear alkylbenzenes use linear alpha olefins with AlCl<sub>3</sub> and HF as the preferred catalyst. Branched alkylbenzenes start with a tetrapropenyl (C<sub>3</sub>) stream using HF as the preferred catalyst, but triethyl aluminum (AlEt<sub>3</sub>) has also been used as a catalyst.</p> <p>Commercial substances in this category have a carbon number distribution between C<sub>20</sub> to C<sub>30</sub> or C<sub>28</sub> to C<sub>88</sub>. The chemical constituents of these substances are composed of carbon and hydrogen and share a similar structure; they are linear or branched alkyl benzenes with alkyl groups ranging between C<sub>14</sub> and C<sub>82</sub>. Because of their chemical similarity, this group is considered a category for purposes of the High Production Volume (HPV) Chemical Program, and designated <u>Arylpolyolefin</u>.</p> <p><u>Hydrolysis of Hydrocarbons as a Function of Molecular Structure</u></p> <p>Hydrolysis of an organic molecule occurs when a molecule (R-X) reacts with water (H<sub>2</sub>O) to form a new carbon-oxygen bond after the carbon-X bond is cleaved (1,2). Mechanistically, this reaction is referred to as a nucleophilic substitution reaction, where X is the leaving group being replaced by the incoming nucleophilic oxygen from the water molecule. The leaving group, X, must be a molecule other than carbon because for hydrolysis to occur, the R-X bond cannot be a carbon-carbon bond.</p> <p>The carbon atom lacks sufficient electronegativity to be a good leaving group and carbon-carbon bonds are too stable (high bond energy) to be cleaved by nucleophilic substitution. Thus, hydrocarbons are not subject to hydrolysis (2) and this fate process will not contribute to the degradative loss of chemical components in this category from the environment.</p>
	<p>Under strongly acidic conditions a carbon-carbon double bond can react with water by an addition reaction mechanism (1). The reaction product is an alcohol. This reaction is not considered to be hydrolysis because the carbon-carbon linkage is not cleaved and because the reaction is freely reversible (2).</p> <p>Chemicals that have a potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters (3). The chemicals in this category are arylpolyolefins that contain double bonds in the aromatic</p>

	<p>ring. The remaining chemical structure contains saturated hydrocarbons (paraffins). These chemicals contain only carbon and hydrogen. As such, their molecular structure is not subject to the hydrolytic mechanism discussed above. Therefore, chemicals in the Arylpolyolefin Category have a very low potential to hydrolyze, and this degradative process will not contribute to their removal in the environment.</p> <p><u>References</u></p> <ol style="list-style-type: none"> <li>1. Gould, E.S. 1959. Mechanism and Structure in Organic Chemistry, Holt, Reinhart and Winston, New York, NY, USA.</li> <li>2. Harris, J.C. 1982. "Rate of Hydrolysis," Chapter 7 in: W.J. Lyman, W.F. Reehl, and D.H. Rosenblatt, eds., Handbook of Chemical Property Estimation Methods, McGraw-Hill Book Company, New York, NY, USA.</li> <li>3. Neely, W. B. 1985. Hydrolysis. In: W. B. Neely and G. E. Blau, eds. Environmental Exposure from Chemicals. Vol I., pp. 157-173. CRC Press, Boca Raton, FL, USA.</li> </ol>
Reliability:	Not applicable
Reference:	American Chemistry Council; Petroleum Additives Panel; Health, Environmental, Regulatory, Task Group. 2002. Hydrolysis: Arylpolyolefin Category. Rosslyn, VA, USA.
Other (source):	American Chemistry Council; Petroleum Additives Panel; Health, Environmental, Regulatory, Task Group

\* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "hydrolysis". Selecting this option refers the reader to information in the "freetext" field for "test substance".

## 2.3 Photodegradation (Direct & Indirect)

### Robust Summary #: 2-Photo-1 (Direct)

Test Substance*:	Other TS
Method/Guideline:	Other: Technical discussion
Year (guideline):	Not applicable
GLP (Y/N):	Not applicable
Year (study performed):	Not applicable
Type (air, soil, water, other):	Water
Test Substance:	<p>CAS# 115733-08-9; Benzene C<sub>14</sub>-C<sub>24</sub> branched and linear alkyl derivatives</p> <p>CAS# 68081-77-6; Benzene polypropene derivatives</p> <p>Arylpolyolefins are manufactured by mixing anhydrous alkylate (linear or branched) with benzene in the presence of catalyst and heat. More information on the Arylpolyolefin category can be found in the American Chemistry Council; Petroleum Additives Panel; Health, Environmental, Regulatory, Task Group, High Production Volume test plan for this category (1).</p> <p>1. Health, Environmental, Regulatory, Task Group (HERTG). 2002. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Arylpolyolefin Category. American Chemistry Council, Petroleum Additives Panel, HERTG.</p>
Light Source:	Not applicable
Light Spectrum: <ul style="list-style-type: none"> <li>Wave length value (upper/lower)</li> </ul>	Not applicable
Relative Intensity:	Not applicable
Test Substance Spectrum:	Not applicable
Test Conditions: <ul style="list-style-type: none"> <li>Note: Concentration, temperature, test system type, replication, deviations from guideline or protocol</li> </ul>	Not applicable
Direct Photolysis: <ul style="list-style-type: none"> <li>Results: half-life, % degrad., quantum yield</li> </ul>	Not applicable
Indirect Photolysis: <ul style="list-style-type: none"> <li>Results: type of sensitizer,</li> </ul>	Not applicable

<p>concentration of sensitizer, rate const., % degrad., half-life</p>	
<p>Degradation Products:</p> <ul style="list-style-type: none"> <li>Note: Identification, concentration</li> </ul>	<p>Not applicable</p>
<p>Conclusion:</p>	<p><u>Technical Summary</u></p> <p>In the environment, direct photolysis will not contribute to the degradation of constituent chemicals of substances in the Arylpolyolefin Category. Two CAS numbers identify substances in this category:</p> <ul style="list-style-type: none"> <li>115733-08-9; Benzene C<sub>14</sub>-C<sub>24</sub> branched and linear alkyl derivatives</li> <li>68081-77-6; Benzene polypropene derivatives</li> </ul> <p>The direct photolysis of an organic molecule occurs when it absorbs sufficient light energy to result in a structural transformation (1). The reaction process is initiated when light energy in a specific wavelength range elevates a molecule to an electronically excited state. However, the excited state is competitive with various deactivation processes that can result in the return of the molecule to a non excited state.</p> <p>The absorption of light in the ultra violet (UV)-visible range, 110-750 nm, can result in the electronic excitation of an organic molecule. Light in this range contains energy of the same order of magnitude as covalent bond dissociation energies (1). Higher wavelengths (e.g. infrared) result only in vibrational and rotational transitions, which do not tend to produce structural changes to a molecule.</p> <p>The stratospheric ozone layer prevents UV light of less than 290 nm from reaching the earth's surface. Therefore, only light at wavelengths between 290 and 750 nm can result in photochemical transformations in the environment (1). Although the absorption of UV light in the 290-750 nm range is necessary, it is not always sufficient for a chemical to undergo photochemical degradation. Energy may be re-emitted from an excited molecule by mechanisms other than chemical transformation, resulting in no change to the parent molecule.</p>
<p>Conclusion: (continued)</p>	<p>A conservative approach to estimating a potential photochemical degradation rate is to assume that degradation will occur in proportion to the amount of light wavelengths &gt;290 nm absorbed by the molecule (2). Saturated hydrocarbons do not absorb light above 200 nm. Therefore, those constituents of substances in this category will not exhibit photolytic degradation. Single ring aromatics do not absorb sufficient light energy above 290 nm to cause photolysis (1). Therefore, the arylpolyolefins in this category are also not subject to photolytic processes.</p> <p><u>References</u></p>

	<ol style="list-style-type: none"> <li>1. Harris, J. C. 1982. "Rate of Aqueous Photolysis," Chapter 8 in: W. J. Lyman, W. F. Reehl, and D. H. Rosenblatt, eds., Handbook of Chemical Property Estimation Methods, McGraw-Hill Book Company, New York, USA.</li> <li>2. Zepp, R. G. and D. M. Cline. 1977. Rates of Direct Photolysis in the Aqueous Environment, Environ. Sci. Technol., 11:359-366.</li> </ol>
Reliability:	Not applicable
Reference:	American Chemistry Council; Petroleum Additives Panel; Health, Environmental, Regulatory, Task Group. 2002. Hydrolysis: Arylpolyolefin Category. Rosslyn, VA, USA.
Other (source):	American Chemistry Council; Petroleum Additives Panel; Health, Environmental, Regulatory, Task Group

\* Other TS is an option in the Test Substance pick list within the IUCLID data entry field for Photodegradation (direct). Selecting this option refers the reader to information in the "freetext" field for "test substance".

**Robust Summary #: 2-Photo-2 (Indirect)**

Test Substance*:	Other TS															
Method/Guideline:	Calculated values using AOPWIN version 1.89, a subroutine of the computer program EPIWIN version 3.04															
Year (guideline):	1999															
GLP (Y/N):	Not applicable															
Year (study performed):	Not applicable															
Type (air, soil, water, other):	Not applicable															
Light Source:	Sunlight															
Light Spectrum: • Wave length value (upper/lower)	Natural sunlight															
Relative Intensity:	1															
Test Substance Spectrum:	Not applicable															
Test Conditions: • Note: Concentration, temperature, test system type, replication, deviations from guideline or protocol	Indirect photodegradation, or atmospheric oxidation potential, is based on the structure-activity relationship methods developed by R. Atkinson.  Temperature: 25°C Sensitizer: OH radical Concentration of Sensitizer: 1.5 E <sup>6</sup> OH radicals/cm <sup>3</sup>															
Direct Photolysis: • Results: half-life, % degradation, quantum yield	Not applicable															
Indirect Photolysis: • Results: type of sensitizer, concentration of sensitizer, rate constant, % degradation, half-life	AOPWIN estimates the rate constant for the atmospheric, gas-phase reaction between photochemically produced hydroxyl radicals and organic chemicals. The rate constants estimated by the program are then used to calculate atmospheric half-lives for organic compounds based upon average atmospheric concentrations of hydroxyl radicals.  Since the reactions only take place in the presence of sunlight, the atmospheric half-life is normalized for a 12-hour day.  <table border="0"> <thead> <tr> <th style="text-align: left;"><u>Substance Component</u></th> <th style="text-align: center;"><u>Calculated* half-life (hrs)</u></th> <th style="text-align: center;"><u>OH- Rate Constant (cm<sup>3</sup>/molecule-sec)</u></th> </tr> </thead> <tbody> <tr> <td>CAS# 115733-08-9</td> <td></td> <td></td> </tr> <tr> <td style="padding-left: 20px;">Benzene, C<sub>14</sub> alkyl derivative</td> <td style="text-align: center;">5.67</td> <td style="text-align: center;">23e-12</td> </tr> <tr> <td style="padding-left: 20px;">Benzene, C<sub>24</sub> alkyl derivative</td> <td style="text-align: center;">3.49</td> <td style="text-align: center;">37e-12</td> </tr> <tr> <td>CAS# 68081-77-6</td> <td></td> <td></td> </tr> </tbody> </table>	<u>Substance Component</u>	<u>Calculated* half-life (hrs)</u>	<u>OH- Rate Constant (cm<sup>3</sup>/molecule-sec)</u>	CAS# 115733-08-9			Benzene, C <sub>14</sub> alkyl derivative	5.67	23e-12	Benzene, C <sub>24</sub> alkyl derivative	3.49	37e-12	CAS# 68081-77-6		
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CAS# 68081-77-6																

	<p>Benzene, C<sub>22</sub> polypropene 4.10 31e-12</p> <p>* Atmospheric half-life values are based on a 12-hr day.</p> <p>Commercial substances in this category have a carbon number distribution between C20 and C30 or C28 and C88. The three chemicals selected to represent the atmospheric oxidation potential range of this category include a C20, C30, and C28 arylpolyolefin that have common structures. Calculated air oxidation potential values are presented as ranges for category members, where possible, and are based on the highest and lowest molecular weight derivative in each member. For example, structures representing the C<sub>14</sub>-C<sub>24</sub> alkaryl derivative (CAS # 115733-08-9) include a benzene C<sub>14</sub> alkyl derivative and a benzene C<sub>24</sub> alkyl derivative. Whereas, structures representing the polypropene derivative (CAS # 68081-77-6) include only the benzene C<sub>22</sub> polypropene lowest molecular weight derivative; the benzene C<sub>82</sub> polypropene highest molecular weight derivative has not been modeled as the molecular weight of this derivative falls outside of the applicable range of the EPIWIN modeling program.</p> <p>References</p> <ol style="list-style-type: none"> <li>1. Atkinson, R. 1988. Estimation of gas-phase hydroxyl radical rate constants for organic chemicals. Environ. Toxicol. Chem. 7:435-442.</li> <li>2. Atkinson, R. 1989. Kinetics and mechanisms of the gas-phase reactions of the hydroxyl radical with organic compounds. J. Phys. Chem. Ref. Data Monograph No. 1, Amer. Inst. Physics &amp; Amer. Chem. Soc., New York, NY, USA.</li> <li>3. Meylan, W.M. and P.H. Howard. 1993. Computer estimation of the atmospheric gas-phase reaction rate of organic compounds with hydroxyl radicals and ozone. Chemosphere. 12:2293-2299.</li> </ol>
<p>Degradation Products:</p> <ul style="list-style-type: none"> <li>• Note: Identification, concentration</li> </ul>	<p>Unknown</p>
<p>Test Substance:</p>	<ul style="list-style-type: none"> <li>• CAS# 115733-08-9; Benzene C<sub>14</sub>-C<sub>24</sub> branched and linear alkyl derivatives</li> <li>• CAS# 68081-77-6; Benzene polypropene derivatives</li> </ul> <p>Arylpolyolefins are manufactured by mixing anhydrous alkylate (linear or branched) with benzene in the presence of catalyst and heat. More information on the Arylpolyolefin Category can be found in the American Chemistry Council; Petroleum Additives Panel; Health, Environmental, Regulatory, Task Group, High Production Volume test plan for this category (4).</p> <ol style="list-style-type: none"> <li>4. Health, Environmental, Regulatory, Task Group (HERTG). 2002. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Arylpolyolefin Category. American</li> </ol>

	Chemistry Council, Petroleum Additives Panel, HERTG.
Conclusion:	<p>Atmospheric oxidation can contribute to the degradation of substances in this category. However, their low vapor pressures suggest that constituents of these substances will not partition to a great extent into the air phase where this reaction takes place. Therefore, this degradation process is not expected to significantly contribute to the degradative loss of these substances in the environment.</p> <p>Based on calculated values, substances in this category can have an atmospheric half-life range of 3.5 to 5.7 hours. These data suggest that the fraction of constituents that do partition to the air phase will degrade rapidly.</p> <p>These data represent a key study for characterizing the atmospheric oxidation potential of the Arylpolyolefin Category, which includes benzene C<sub>14</sub>-C<sub>24</sub> alkyl derivatives (CAS # 115733-08-9) and benzene polypropene derivatives (CAS # 68081-77-6).</p>
Reliability:	<p>(2) Reliable with restrictions</p> <p>The results include values calculated using the AOPWIN program and represent a potential atmospheric half-life range for substances with the 2 CAS numbers listed under test substance.</p>
Reference:	Meylan, M., SRC. 1994-1999. AOPWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source):	American Chemistry Council; Petroleum Additives Panel; Health, Environmental, Regulatory, Task Group

\* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "photodegradation". Selecting this option refers the reader to information in the "freetext" field for "test substance".

**2.4 Fugacity**

**Category: Arylpolyolefins**

**Robust Summary #: 2-Fugacity-1**

Test Substance*:	Other TS																							
Method/Guideline:	Calculated according to Mackay Level I, EQC Model version 1.01																							
Year (guideline):	1997																							
Type (test type):	Not applicable																							
GLP:	Not applicable																							
Year (study performed):	Not applicable																							
Estimation Temperature:	25°C																							
<p>Test Conditions:</p> <ul style="list-style-type: none"> <li>Note: Concentration prep., vessel type, replication, test conditions.</li> </ul>	<p>The EQC Level I is a steady state, equilibrium model that utilizes the input of basic chemical properties including molecular weight, vapor pressure, and water solubility to calculate distribution within a standardized regional environment.</p> <p>Physical properties used with the model were calculated by the EPIWIN Estimation v 3.04 program (1). Output data from the equilibrium model provide basic information on the potential distribution of chemicals between selected environmental compartments (i.e., air, water, soil, sediment, suspended sediment, biota).</p> <p>1. EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.</p>																							
<p>Results:</p> <p>Units/Value:</p> <ul style="list-style-type: none"> <li>Note: Deviations from protocol or guideline, analytical method.</li> </ul>	<p>The following chemicals are representative of the two CAS numbers in the Arylpolyolefin Category, each of which contains complex, multi-constituent substances. The partitioning data characterize the range of constituent chemicals in each substance as well as the overall partitioning behavior of these substances.</p> <table border="1"> <thead> <tr> <th rowspan="2"><u>Substance Component</u></th> <th colspan="2"><u>Calculated*</u> <u>Percent Distribution</u></th> </tr> <tr> <th><u>Soil</u></th> <th><u>Sediment</u></th> </tr> </thead> <tbody> <tr> <td colspan="3">CAS# 115733-08-9</td> </tr> <tr> <td>Benzene, C<sub>14</sub> alkyl derivative</td> <td>97.7</td> <td>2.17</td> </tr> <tr> <td>Benzene, C<sub>24</sub> alkyl derivative</td> <td>97.7</td> <td>2.17</td> </tr> <tr> <td colspan="3">CAS# 68081-77-6</td> </tr> <tr> <td>Benzene, C<sub>22</sub> polypropene</td> <td>97.7</td> <td>2.17</td> </tr> <tr> <td>Benzene, C<sub>82</sub> polypropene</td> <td>97.8</td> <td>2.17</td> </tr> </tbody> </table> <p>* Distribution values determined using input data calculated by the EPIWIN program.</p>	<u>Substance Component</u>	<u>Calculated*</u> <u>Percent Distribution</u>		<u>Soil</u>	<u>Sediment</u>	CAS# 115733-08-9			Benzene, C <sub>14</sub> alkyl derivative	97.7	2.17	Benzene, C <sub>24</sub> alkyl derivative	97.7	2.17	CAS# 68081-77-6			Benzene, C <sub>22</sub> polypropene	97.7	2.17	Benzene, C <sub>82</sub> polypropene	97.8	2.17
<u>Substance Component</u>	<u>Calculated*</u> <u>Percent Distribution</u>																							
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Results: (continued)																								

<p>Units/Value:</p> <p>Note: Deviations from protocol or guideline, analytical method.</p>	<p>Distribution of representative chemicals to each remaining compartment (air, water, suspended sediment, biota) was calculated as less than 0.2%. Potential for mobility throughout the environment is expected to be low due to the relatively high log Kow values and low water solubility of constituent chemicals.</p> <p>Commercial substances in this category have a carbon number distribution between either C20 and C30 or C28 and C88. The four chemicals selected to represent the transport / distribution range of this category include a C20, C30, C28, and C88 arylpolyolefin that have common structures and represent the potential range of data for the two category substances.</p>
<p>Test Substance:</p>	<ul style="list-style-type: none"> <li>• CAS# 115733-08-9; Benzene C<sub>14</sub>-C<sub>24</sub> branched and linear alkyl derivatives</li> <li>• CAS# 68081-77-6; Benzene polypropene derivatives</li> </ul> <p>Arylpolyolefins are manufactured by mixing anhydrous alkylate (linear or branched) with benzene in the presence of catalyst and heat. More information on the Arylpolyolefin Category can be found in the American Chemistry Council; Petroleum Additives Panel; Health, Environmental, Regulatory, Task Group, High Production Volume test plan for this category (2).</p> <p>2. Health, Environmental, Regulatory, Task Group (HERTG). 2002. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Arylpolyolefin Category. American Chemistry Council, Petroleum Additives Panel, HERTG.</p>
<p>Conclusion:</p>	<p>Substances in the Arylpolyolefin Category are expected to distribute primarily to soil with a small percentage partitioning to sediment.</p> <p>These data represent a key study for characterizing the fugacity of the Arylpolyolefin Category, which includes benzene C<sub>14</sub>-C<sub>24</sub> alkyl derivatives (CAS # 115733-08-9) and benzene polypropene derivatives (CAS # 68081-77-6). Comparatively, their potentials to partition in the environment are expected to be similar, based on their high log Kow and low water solubility values.</p>
<p>Reliability:</p>	<p>(2) Reliable with restrictions</p> <p>The input data used to run the EQC Level I model include estimated values calculated by the EPIWIN program based on chemical structure. The partitioning data represent a potential distribution range for substances in the two CAS numbers listed under test substance. Computer modeling is an accepted method of assessing environmental distribution of chemicals.</p>
<p>Reference:</p>	<p>Mackay, D.A. DiGuardo, S. Paterson, and C. Cowan. EQC Model Version 1.01. 1997. Available from the Environmental Modeling Centre, Trent University, Canada.</p>

Other (source):	American Chemistry Council; Petroleum Additives Panel; Health, Environmental, Regulatory, Task Group
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\* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "transport / distribution". Selecting this option refers the reader to information in the "freetext" field for "test substance".

## 3.0 AQUATIC ORGANISMS

3.1 Acute Toxicity to Fish**Robust Summary 2-FISH-1**

<b><u>Test Substance</u></b>	
CAS #	115733-08-9
Chemical Name	C14-C24 derivative
Remarks	Test material purity not provided.
<b><u>Method</u></b>	
Method/Guideline followed	1985 EPA/TSCA Part 797, Subpart B- Aquatic Guidelines, Section 797.1440 Fish Acute Toxicity Test
Test Type	Acute Toxicity to Fish (Water Soluble Fraction)
GLP (Y/N)	Y
Year (Study Performed)	1989
Species/Strain	Rainbow Trout ( <i>Oncorhynchus mykiss</i> )
Fish Number	30/concentration (10/exposure chamber, triplicate chambers/concentration; 0.34 grams of fish/liter)
Fish Size	Average length 37 mm (32 to 43mm); Average weight 0.51 g (0.31 to 0.84 g)
Analytical Monitoring	Yes (Total Organic Carbon determinations)
Nominal Test Substance Concentration Levels	0 and 1000 mg/l
Test Concentration Preparation	Test solutions were prepared separately for each replicate test concentration by adding an appropriate aliquot (by weight) of test material to 15 liters of dilution water in 15-liter glass vessels that were then covered with aluminum foil. The solutions were stirred vigorously for approximately 20 hours. Following a settling period of 30 minutes the water soluble fraction (WSF) of each replicate test concentration was separated from floating or settled test material by siphoning 14 liters WSF from a central point approximately 20 cm above the bottom of the mixing vessel into each replicate test vessel.
Exposure Period	96 hours
Exposure Conditions	Static-renewal test conditions. At 24, 48 and 72 hours of exposure the test fish were carefully transferred into aquaria containing fresh test solutions.
Vehicle	None
Statistical Analysis	None required based on the results.
Dose Rangefinding Study	Yes at 0 and 1000 mg/liter
Test Chambers	18.9-liter glass aquaria containing 14 liters of test solution
Diluent Water	Soft water reconstituted from deionized water
Diluent Water Chemistry	Hardness 34-38 mg/l as CaCO <sub>3</sub> Alkalinity 35-35 mg/l as CaCO <sub>3</sub> Conductivity 130 umhos/cm pH 7.5-7.8
Diluent Water Chemistry During 96 Hour Exposure Period.	Dissolved Oxygen: 81 to 95% saturation pH: 7.3-8.0
Photoperiod	16 hours of light, 8 hours of dark

Temperature Range	13-14 °C during 14 day holding period 10-14 °C during exposure period
Remarks field for test conditions	All organisms were observed for mortality and the number of individuals exhibiting clinical signs of toxicity or abnormal behavior at 24, 48, 72, and 96 hours after initiation of test material exposure.
<b><u>Results</u></b>	<p>Analysis of freshly prepared (72 hour) control and test solutions for total organic carbon resulted in measurements of 1.6 to 2.6 and 3.2 to 5.0 mg/L respectively. Old (96 hour) solutions contained 5.2-7.6 mg/L total organic carbon in the control and 11 mg/L in the test solutions.</p> <p>Throughout the test period a film of dissolved test material was observed on the surface of the 1000 mg/L test solutions. Fish in the negative control group were normal throughout the study. At 1000 mg/L, 10% cumulative mortality was observed at 72 hours in one of the three treated cultures at this concentration. At 96 hours 10% cumulative mortality was observed in the second of three cultures at 1000 mg/L for a total of 20% mortality in the treated fish. There were no clinical signs of toxicity observed in the test material treated fish. The 96-hour LC50 was greater than 1000 mg/L (WSF).</p>
<b><u>Conclusions</u></b>	Under the conditions of this study the 96-hour LC50 was greater than 1000 mg/L (WSF).
<b><u>Data Quality</u></b>	Reliable with restriction (Klimisch Code). Restriction due to some inconsistencies noted in the text of the final report.
<b><u>References</u></b>	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).
<b><u>Other</u></b>	Updated: 10/29/2002

### 3.2 Acute Toxicity to Aquatic Invertebrates (e.g. Daphnia)

#### Robust Summary 2-DAPH-1

<b><u>Test Substance</u></b>	
CAS #	115733-08-9
Chemical Name	C14-C24 derivative
Remarks	For more information on this chemical, see Section 2.0 “General Substance Information” in HERTG’s Test Plan for Arylpolyolefins Category.
<b><u>Method</u></b>	
Method/Guideline followed	Test protocol followed US EPA Toxic Substances Control Act Test Guideline #797.1300 (1985, 1987), OECD Guideline for Testing of Chemicals #202 <i>Daphnia</i> sp. Acute Immobilization Test and Reproduction Test (1984).
Test Type	Static acute toxicity test
GLP (Y/N)	Y
Year (Study Performed)	1990
Species/Strain	<b><u>Daphnia magna</u></b>
Analytical Monitoring	Total organic carbon (TOC) measurements of initial (0-h) test solutions and at 24 hours post initiation of exposure.
Exposure Period (unit)	48 hours
Statistical methods	The nominal concentrations tested and the dose response data were used to estimate 24 and 48-hour median effect concentrations (EC50). The NOEC, no observed effect concentration, was defined as the highest concentration tested at and below which there was no toxicant-related immobilization or physical and/or behavioral abnormalities.
Remarks field for test conditions (fill as applicable)	<p>Juvenile daphnids less than 24-hours old were produced from laboratory in-house culture.</p> <p>Individual water soluble fractions (WSFs) were prepared for each test level and renewed daily. A measured weight of test material was added to a measured volume of dilution water (3 L) in a glass vessel and stirred for 20 hours. Stirring was accomplished using a Teflon coated magnetic stir bar. Following the mixing period, the test solutions were allowed to stand for 30 minutes before the water phase was gently siphoned (2 liters) from the mixing vessel into corresponding replicate test vessels (1 liter/vessel).</p> <p>The toxicity test was conducted in 1-liter glass beakers that contained 1 liter of test solution. Twenty daphnids, less than 24 hours old were distributed into each concentration (10 daphnids/replicate) within 30 minutes of test solution preparation. At 24 hours the test solutions were replaced with newly prepared WSF and all surviving daphnids were carefully transferred into the corresponding test vessel.</p> <p>Daphnids were not fed during exposure. Control test chambers/daphnids were handled in an identical fashion.</p> <p>Light cycles were maintained at 16-hour light per day with an intensity of 70 to 120 foot-candles at the surface of the culture solutions. Test solutions were maintained at 20 ± 1 C.</p> <p>Dilution water was filtered well water adjusted to the appropriate hardness of 120-180 mg/L as CaCO<sub>3</sub>.</p>

<u>Test Concentrations</u>	130, 220, 370, 600 and 1000 mg/l WSF
<u>Range Finding Study</u>	Yes; concentration range of 10 to 1000 mg/L WAF
<u>Results</u>	48-h $EL_{50} > 1,000$ mg/L (WSF). A no effect level was not established.
<u>Remarks</u>	<p>Water chemistry: Dissolved oxygen: 6.2 – 9.2 mg/L; pH: 7.6 - 8.1; conductivity: 860 – 880 ohms/cm.</p> <p>Total Organic Carbon measurements were 1 mg/L and 0.8 mg/L in the 130 and 1000 mg/L test concentration solutions. Analysis of 24-hour test solutions resulted in measurements of 1.3-1.7 mg/L and 1.4-1.7 mg/L in the 130 and 1000 mg/L test concentration solution. TOC analysis of the control solutions at 0 and 24 hours resulted in measurements of 0.8 mg/L and 2.1-2.3 mg/L respectively.</p> <p>Throughout the exposure period a film of undissolved test material was observed on the surface of all test solutions. Following 48 hours of exposure, no immobilized organisms were observed at the highest treatment level (1000 mg/L). The percent of immobilized organisms did not exceed 15% at the remaining lower treatment levels (130-600 mg/L). Throughout the 48-hour exposure all surviving daphnids at all concentration levels tested were lethargic.</p> <p>The 48-hour <math>EC_{50}</math> was empirically estimated to be greater than 1000 mg/L, the highest concentration tested. The no observed effect concentration was established as less than 130 mg/L, the lowest concentration tested.</p>
<u>Conclusions</u>	48-h $EC_{50} > 1,000$ mg/L (WSF). A no effect level was not established.
<u>Data Quality</u>	Reliable without restriction (Klimisch Code)
<u>References</u>	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).
<u>Other</u>	Updated: 10/28/2002

## 4.0 Toxicity

Category: Arylpolyolefins

### 4.1 Acute Toxicity

#### 4.1.1 Acute Oral Toxicity

##### Robust Summary #: 2-Acute Oral-1

<b><u>Test Substance</u></b>	
CAS #	CAS# 115733-08-9
Chemical Name	Benzene C14-C24 alkyl derivatives
Remarks	For more information on this chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Arylpolyolefins Category.
<b><u>Method</u></b>	
Method/Guideline followed	FHSA 16CFR1500.3
Test Type	Acute oral toxicity
GLP (Y/N)	N
Year (Study Performed)	1978
Species/Strain	Rats/ Sprague-Dawley strain
Sex	Male/Female
No. of animals/dose	5/sex
Vehicle	Corn oil
Route of administration	Oral (intragastric)
Dose level	5 g/kg
Dose volume	10 ml/kg
Control group included	No
Remarks field for test conditions	A single dose of the test material was administered intragastrically to five fasted male and female rats at each treatment level. The animals were observed for signs of toxicity or behavioral changes during the 4 hours post dosing and daily thereafter. Individual weights were recorded on the day of dosing, on day 7 and at termination. All animals were euthanized at the conclusion of the observation period. Gross autopsies were performed on all animals after 14 days.
<b><u>Results</u></b>	LD50 > 5 g/kg (males and females)
Remarks	All animals survived the duration of the study. Two males and two females were hypoactive at 1 hour post dosing and two females exhibited urine staining of the fur at 4 hours post dosing. All animals exhibited progressive body weight gains at each weighing interval. At necropsy one male exhibited an enlarged spleen and one female exhibited hydrometra of the uterus.
<b><u>Conclusions</u></b>	The test article, when administered to male and female Sprague-Dawley rats, had an acute oral LD50 of >5 g/kg.
<b><u>Data Quality</u></b>	Reliable without restriction (Klimisch Code).
<b><u>References</u></b>	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).
<b><u>Other</u></b>	Updated: 1/21/02

**Robust Summary #: 2-Acute Oral-2**

<b><u>Test Substance</u></b>	
CAS #	CAS# 68081-77-6
Chemical Name	Benzene, polypropene derivatives
Remarks	For more information on this chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Arylpolyolefins Category.
<b><u>Method</u></b>	
Method/Guideline followed	43 CFR 37336, 163.81-1
Test Type	Acute oral toxicity
GLP (Y/N)	Y
Year (Study Performed)	1980
Species/Strain	Rats/Sprague-Dawley strain
Sex	Male/Female
No. of animals/dose	5/sex
Vehicle	None
Route of administration	Oral (intra-gastric)
Dose level	5g/kg
Dose volume	6.35 ml/kg
Control group included	No
Remarks field for test conditions	A single dose of the undiluted test material was administered intra-gastrically to ten fasted (over night) animals at a dose level of 5 g/kg. A control group was not included. The animals were observed for signs of toxicity or behavioral changes twice daily. Individual weights were recorded on the day of dosing and on days 7 and 14. All animals were euthanized at the conclusion of the observation period. Gross autopsies were performed on all animals after 14 days.
<b><u>Results</u></b>	LD50 >5g/kg (males and females)
Remarks	All of the treated animals survived the duration of the study. One male exhibited wheezing at 1 to 4 hours post dosing. Three males and all of the females exhibited urine soaked fur through day 1 on test. No other abnormal clinical signs were observed. All animals gained body weight during the study. No treatment related gross postmortem findings were evident at necropsy.
<b><u>Conclusions</u></b>	The test article, when administered as received to male and female Sprague-Dawley rats, had an acute oral LD50 >5g/kg.
<b><u>Data Quality</u></b>	Reliable without restriction (Klimisch Code)
<b><u>References</u></b>	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).
<b><u>Other</u></b>	Updated: 1/21/02

### 4.1.2 Acute Dermal Toxicity

#### Robust Summary #: 2-Acute Dermal-1

<b><u>Test Substance</u></b>	
CAS #	CAS# 115733-08-9
Chemical Name	Benzene C14-C24 alkyl derivatives
Remarks	For more information on this chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Arylpolyolefins Category.
<b><u>Method</u></b>	
Method/Guideline followed	OECD Test Guideline 402
Test Type	Acute dermal toxicity (Limit Test)
GLP (Y/N)	Y
Year (Study Performed)	1980
Species/Strain	Rabbits/New Zealand White
Sex	Male and female
No. of animals/sex/group	5
Vehicle	None
Route of administration	Dermal
Dose level	2 g/kg
Dose volume	2.3 ml/kg
Control group included	No
Remarks field for test conditions	Approximately 24 hours prior to topical application of the test material, the hair of each animal was closely clipped. The skin was not abraded. A single dose of 2 g/kg of the undiluted test material was administered dermally to five male and female animals. The test material was kept in contact with the skin for a period of 24 consecutive hours under a surgical dressing and plastic film. The application site was wiped clean of residual test material at the end of the 24-hour exposure period using saline. The animals were observed frequently for clinical signs on the day of dosing and once daily for 14 days after treatment. Individual body weights were recorded on the day of dosing and on days 7 and 14. Gross necropsies were performed on all animals on Day 14
<b><u>Results</u></b>	
Remarks	LD50 > 2.0 g/kg (males and females) No mortality was observed. The mean body weight of the males increased slightly during the study. The mean body weight of the females was unchanged during the study. Dermal irritation (erythema and edema) was observed in all rabbits and persisted at least 4 days post dosing. No treatment related gross necropsy effects were evident.
<b><u>Conclusions</u></b>	The test article, when administered dermally as received to 5 male and 5 female New Zealand white rabbits had an acute dermal LD50 of greater than 2.0 g/kg.
<b><u>Data Quality</u></b>	Reliable without restriction (Klimisch Code).
<b><u>References</u></b>	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).
<b><u>Other</u></b>	Updated: 1/21/02

**Robust Summary #: 2-Acute Dermal-2**

<b><u>Test Substance</u></b>	
CAS #	CAS# 68081-77-6
Chemical Name	Benzene, polypropene derivatives
Remarks	For more information on this chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Arylpolyolefins Category.
<b><u>Method</u></b>	
Method/Guideline followed	43 CFR 37336, 163.81-2
Test Type	Acute dermal toxicity (Limit Test)
GLP (Y/N)	Y
Year (Study Performed)	1980
Species/Strain	Rabbits/New Zealand White
Sex	Male and female
No. of animals/sex/group	5
Vehicle	None
Route of administration	Dermal
Dose level	2 g/kg
Dose volume	2.54 ml/kg
Control group included	No
Remarks field for test conditions	Approximately 24 hours prior to topical application of the test material, the hair of each animal was closely clipped. Immediately prior to dosing the skin was abraded. A single dose of 2 g/kg of the undiluted test material was administered dermally to five male and female animals. The test material was kept in contact with the skin for a period of 24 consecutive hours under an elastic bandage. The application site was wiped clean of residual test material at the end of the 24-hour exposure period. The animals were observed for abnormal clinical signs twice daily for 14 days after treatment. Skin condition was evaluated daily. Individual body weights were recorded on the day of dosing and on days 7 and 14. Gross necropsies were performed on all animals on Day 14
<b><u>Results</u></b>	LD50 > 2.0 g/kg (males and females)
Remarks	No mortality was observed. All animals gained weight during the study. No abnormal clinical signs were observed during the study. One male exhibited slight and moderate erythema and one female exhibited slight erythema during the study. These animals also exhibited desquamation. No treatment related gross necropsy effects other than skin effects were evident.
<b><u>Conclusions</u></b>	The test article, when administered dermally as received to 5 male and 5 female New Zealand white rabbits had an acute dermal LD50 of greater than 2.0 g/kg.
<b><u>Data Quality</u></b>	Reliable without restriction (Klimisch Code).
<b><u>References</u></b>	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).
<b><u>Other</u></b>	Updated: 1/21/02

## 4.2 Genetic Toxicity

### Robust Summary #: 2-GenTox-1

<u>Test Substance</u>																																									
CAS #	CAS# 115733-08-9																																								
Chemical Name	Benzene C14-C24 alk derivatives																																								
Remarks	For more information on this chemical, see Section 2.0 "General Substance Information" in HERTG's Test Plan for Arylpolyolefins Category.																																								
<u>Method</u>																																									
Method/Guideline followed	OECD Guideline 471																																								
Test Type	Bacterial Reverse Mutation Assay																																								
GLP (Y/N)	Y																																								
Year (Study Performed)	1981																																								
Test System	<b><u>Salmonella typhimurium</u></b>																																								
Strains Tested	<i>Salmonella typhimurium</i> tester strains TA98, TA100, TA1535, TA1537, TA1538																																								
Exposure Method	Plate incorporation																																								
Test Substance Doses/concentration levels	0.025, 0.075, 0.25, 0.75 and 2.5 mg/plate with and without activation																																								
Metabolic Activation	With and without (S9 fraction mix of livers of Aroclor 1254 pretreated Sprague Dawley rats)																																								
Vehicle	Ethyl acetate																																								
Tester strain, activation status, Positive Controls and concentration level	<table border="0"> <tbody> <tr> <td>TA98</td> <td>+S9</td> <td>2-aminoanthracene</td> <td>5 ug/plate</td> </tr> <tr> <td>TA98</td> <td>-S9</td> <td>2-nitrofluorene</td> <td>5 ug/plate</td> </tr> <tr> <td>TA100</td> <td>+S9</td> <td>2-aminoanthracene</td> <td>5 ug/plate</td> </tr> <tr> <td>TA100</td> <td>-S9</td> <td>sodium azide</td> <td>30 ug/plate</td> </tr> <tr> <td>TA1535</td> <td>+S9</td> <td>2-aminoanthracene</td> <td>5 ug/plate</td> </tr> <tr> <td>TA1535</td> <td>-S9</td> <td>sodium azide</td> <td>30 ug/plate</td> </tr> <tr> <td>TA1537</td> <td>+S9</td> <td>2-aminoanthracene</td> <td>5 ug/plate</td> </tr> <tr> <td>TA1537</td> <td>-S9</td> <td>9-aminoacridine</td> <td>10 ug/plate</td> </tr> <tr> <td>TA1538</td> <td>+S9</td> <td>2-aminoanthracene</td> <td>5 ug/plate</td> </tr> <tr> <td>TA1538</td> <td>-S9</td> <td>2-nitrofluorene</td> <td>5 ug/plate</td> </tr> </tbody> </table>	TA98	+S9	2-aminoanthracene	5 ug/plate	TA98	-S9	2-nitrofluorene	5 ug/plate	TA100	+S9	2-aminoanthracene	5 ug/plate	TA100	-S9	sodium azide	30 ug/plate	TA1535	+S9	2-aminoanthracene	5 ug/plate	TA1535	-S9	sodium azide	30 ug/plate	TA1537	+S9	2-aminoanthracene	5 ug/plate	TA1537	-S9	9-aminoacridine	10 ug/plate	TA1538	+S9	2-aminoanthracene	5 ug/plate	TA1538	-S9	2-nitrofluorene	5 ug/plate
TA98	+S9	2-aminoanthracene	5 ug/plate																																						
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TA100	+S9	2-aminoanthracene	5 ug/plate																																						
TA100	-S9	sodium azide	30 ug/plate																																						
TA1535	+S9	2-aminoanthracene	5 ug/plate																																						
TA1535	-S9	sodium azide	30 ug/plate																																						
TA1537	+S9	2-aminoanthracene	5 ug/plate																																						
TA1537	-S9	9-aminoacridine	10 ug/plate																																						
TA1538	+S9	2-aminoanthracene	5 ug/plate																																						
TA1538	-S9	2-nitrofluorene	5 ug/plate																																						
Vehicle Control	Ethyl acetate																																								
Statistical Analysis	Mean revertant colony count and standard deviation were determined for each dose point.																																								
Dose Rangefinding Study	No																																								
S9 Optimization Study	No																																								
Remarks field for test conditions	<p>This study was conducted prior to the development of OECD Guideline No. 471. This study deviates from the guideline in that Tester Strain TA 1538 is not called for in the guideline but it was included. In addition E. coli WP2 urvA Tester Strain called for in the guideline was not include.</p> <p>There were two treatment sets for each tester strain, with (+S9) and without (-S9) metabolic activation. Each of the tester strains was dosed with five concentrations of test substance, vehicle control, and a positive control. Three plates/dose group/strain/treatment set were evaluated. 50-100 ul of test material, positive control or vehicle control were added to each plate along with 100 ul of tester strain, S9 mix (if needed) and 2.0 ml of top agar. This was overlaid onto the surface of minimal bottom agar in a petri dish. Plates were incubated</p>																																								

	for 48 hours at 37°C. The numbers of revertant colonies were counted with an automated colony counter. The test material was considered a mutagen if a dose related increase was found in the number of revertant colonies and if the first dose level considered for the increase had an average number of revertant colonies that was three times that of the vehicle control.
<u>Results</u>	The test substance was not genotoxic in this assay with or without metabolic activation.
Remarks	All data were acceptable and no positive increases in the number of revertants/plate were observed with any of the tester strains with or without metabolic activation.  The positive control for each respective test strain exhibited an appropriate response (with or without S9) over the mean value of the vehicle control for a given strain, confirming the expected positive control response.
<u>Conclusions</u>	Under the conditions of this study, the test material was not mutagenic.
<u>Data Quality</u>	Reliable with restriction (Klimisch Code). Restriction due to the lack of any information regarding the selection of dose levels used during the study. In addition no information is presented regarding cytotoxicity or the presence of test material precipitate in the cultures.
<u>References</u>	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).
<u>Other</u>	Updated: 10/24/2002

**HIGH PRODUCTION VOLUME (HPV)  
CHEMICAL INITIATIVE**

**REFERENCES**

**For**

**ARYLPOLYOLEFINS CATEGORY**

**Prepared by  
The American Chemistry Council  
Petroleum Additives Panel  
Health Environmental and Regulatory Task Group**

**April 22, 2005**

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**Assessment Plan for Benzene, C<sub>6-12</sub> Alkyl Derivatives  
(CAS#68608-80-0, Alkylate Top) in Accordance with  
the USEPA High Production Volume Challenge  
Program**

**Prepared for**

**Huntsman LLC**

**March 12, 2003**



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## APPENDICES

Appendix      Table A-1. Summary of Data Available for the Alkylate Top

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Table 1.      Representative Structures of the Constituent Compounds of the Alkylate Top

## I. INTRODUCTION

The High Production Volume (HPV) Challenge Program is a voluntary initiative of the US chemical industry to complete hazard data profiles for approximately 2800 HPV chemicals as identified on the US Environmental Protection Agency's (USEPA) 1990 Toxic Substances Control Act (TSCA) Inventory Update Rule (IUR). In the US, HPV chemicals are those that are manufactured or imported in quantities greater than 1 million pounds per year. The hazard data to be provided in the program are those that meet the requirements of the Screening Information Data Set (SIDS) Program. SIDS, which has been internationally agreed to by member countries of the Organization for Economic Cooperation and Development (OECD), provides the basic screening data needed for an initial assessment of the physical-chemical properties, environmental fate, and adverse human and environmental effects of chemicals. The information for completing the SIDS can come from existing data or may be generated as part of the HPV Challenge Program. Once the available studies are identified or conducted, "robust summaries" are prepared. These summaries are then entered into the standard International Uniform Chemical Information Database (IUCLID) software and present the salient information from each of the reliable studies.

The USEPA, industry, and non-governmental organizations (NGOs) are unified in their commitment to minimize the numbers of animals tested in the HPV Challenge Program whenever it is scientifically justifiable. One approach toward this consideration is to evaluate closely related chemicals as a group, or category, rather than solely as individual chemicals. This approach takes advantage of structure activity relationships (SARs), which is based on the understanding that chemicals with similar structures often have similar and/or predictable characteristics and behavior in the environment and in mammalian systems. The use of categories and SARs is encouraged by USEPA in the HPV Challenge Program. Appropriate use of SARs can allow for a more efficient evaluation of the available data and significantly reduce the number of animals required for testing.

Huntsman LLC (formerly Huntsman Corporation) has agreed to assemble and review available public and private toxicological data, develop and provide an assessment plan for the sponsored material and conduct additional research, including testing when necessary, for a mixture of alkylated benzenes and *n*-paraffins (CAS #68608-80-0; hereafter referred to as an "Alkylate Top"). While Huntsman LLC is not proposing this material as part of a category approach *per se*, as a mixture it is appropriate to review the pertinent data of the principal constituents using SAR as a means to help characterize the Alkylate Top's properties and characteristics.

This assessment plan is the result of Huntsman LLC's efforts and provides a summary and analysis of the available data, and identifies any data gaps in the SIDS data profile. Section II of this assessment plan provides a characterization of the sponsored Alkylate Top production process and use patterns. Section III reviews the methods used in the collection of published and unpublished data. Section IV reviews the evaluation of data quality. Section V is an in-depth evaluation of the available data, first for the Alkylate Top itself, then for its principal constituents and for Linear Alkylbenzene (LAB). Section VI is a summary of the Alkylate Top and constituents properties. Section VII presents the conclusions regarding data availability.

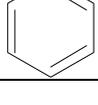
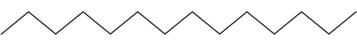
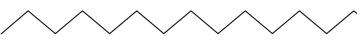
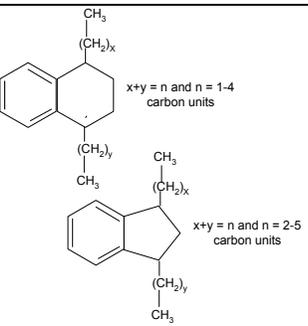
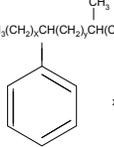
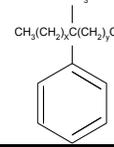
## II. IDENTIFICATION OF THE SPONSORED MIXTURE

### A. Production Process

Huntsman LLC is sponsoring Benzene, C<sub>6-12</sub> alkyl derivatives (CAS #68608-80-0; called “Alkylate Top” hereafter), in the USEPA HPV Challenge Program. This Alkylate Top is a mixture of aromatic and aliphatic hydrocarbons derived as a low boiling point co-product from the LAB manufacturing process. The LAB production process entails the partial conversion of C<sub>10-14</sub> *n*-paraffins to internal *n*-olefins by catalytic dehydrogenation. The resulting mixture of *n*-paraffins and *n*-olefins is selectively hydrogenated to reduce diolefins and fed into an alkylation reactor together with benzene (in excess) and hydrofluoric acid as a catalyst for the Friedel-Crafts reaction producing C<sub>10-14</sub> secondary linear alkylbenzenes (LAB). The Alkylate Top results from an intermediate distillation cut prior to the isolation of the final LAB product and serves to remove impurities with a lower boiling point than LAB. Following the removal of the Alkylate Top, a final distillation removes commercial detergent grade LAB as the distillate.

This production process results in an alkylated benzene mixture, the Alkylate Top, which consists predominantly of C<sub>7-10</sub> secondary linear alkylbenzenes, C<sub>14</sub> paraffin, other aromatics (mainly dialkylindanes and dialkyltetralins), and other LAB (likely mono-methyl branched [iso-LAB]). Overall, the Alkylate Top consists of approximately 48-56% C<sub>7</sub>-C<sub>10</sub> linear alkylbenzenes, 13-35% paraffins, 8% dialkylindanes/tetralins, and 6-22% iso-LAB. The current Alkylate Top product is designated L210 by Huntsman LLC. Fractions of L210 may vary slightly depending on whether the samples are collected during light (L210L) or heavy (L210H) fractionation, which differ slightly due to slight differences in the chain length distribution of the paraffin employed during LAB production. Table 1 shows representative structures of the constituents that make up greater than 99% of the current Alkylate Top mixture based on chemical analyses conducted in the fall of 2002 (Rapko 2002). The ranges for light and heavy paraffin samples are shown separately, although in practice the two are not segregated and only the combined L210 product is distributed.

**Table 1. Representative Structures of the Constituent Compounds of the Alkylate Top**

COMPOUND	Relative % - Light [Mean]	Relative % - Heavy [Mean]	REPRESENTATIVE STRUCTURE
C <sub>10</sub> -LAB	15-34 [23]	25-36 [30]	$\text{CH}_3(\text{CH}_2)_x\text{CH}(\text{CH}_2)_y\text{CH}_3$  $x+y = n \text{ and } n = 7$ carbon units
Sec-nonylbenzene	14-34 [24]	2-9 [8]	$\text{CH}_3(\text{CH}_2)_x\text{CH}(\text{CH}_2)_y\text{CH}_3$  $x+y = n \text{ and } n = 6$ carbon units
Sec-octylbenzene/ heptabenzene	7-11 [9]	8-11 [10]	$\text{CH}_3(\text{CH}_2)_x\text{CH}(\text{CH}_2)_y\text{CH}_3$  $x+y = n \text{ and } n = 4-5$ carbon units
n-Tetradecane	4-20 [13]	31-39 [35]	
n-Pentadecane	0.3-0.4 [0.3]	0.3-0.7 [0.5]	
Other Components (mainly dialkylindanes and dialkyltetralins)	5-12 [8]	8-9 [8]	 $x+y = n \text{ and } n = 1-4$ carbon units $x+y = n \text{ and } n = 2-5$ carbon units
Other LAB (likely mono-methyl branched [iso-LAB])	20-27 [22]	5-8 [6]	$\text{CH}_3(\text{CH}_2)_x\text{CH}(\text{CH}_2)_y\text{CH}(\text{CH}_2)_z\text{CH}_3$  $x+y+z = n \text{ and } n = 2-5$ carbon units $\text{CH}_3(\text{CH}_2)_x\text{C}(\text{CH}_3)(\text{CH}_2)_y\text{CH}_3$  $x+y = n \text{ and } n = 3-6$ carbon units

Note: Relative percent shows the range of 10 samples during light (L) and 11 samples during heavy (H) paraffin campaigns collected from September-October 2002 at the Chocolate Bayou, Texas, LAB production unit. Samples were analyzed by GC and GC/MS.

## **B. Relationship to Tested Materials**

The current Alkylate Top material is approximately 48-56% C<sub>7</sub>-C<sub>10</sub> linear alkylbenzenes, 13-36% paraffins, 8% other components from the dehydrogenation process (mainly dialkylindanes and dialkyltetralins), and 6-22% iso-LAB. The Alkylate Top material used in much of the biodegradation and toxicity testing consisted of approximately 44% alkylbenzenes, 29% paraffins, and 24% dialkylindanes.

Furthermore, in the earlier production of Alkylate Tops, the two fractions (L210L and L210H) were used separately and therefore underwent separate safety and toxicity testing. Due to modifications in the efficiency of the production process, the L210L and L210H fractions are no longer segregated and are considered a single mixture designated as L210. The modification in the production process also has significantly reduced the occurrence of dialkylindanes and dialkyltetralins. For example, in a biodegradation study conducted on a Monsanto Alkylate Top mixture in 1980, the test material included a substantial amount of alkylindanes (24%). Chemical analysis of the current Alkylate Top (Rapko 2002) resulted in a substantially lower amount, with 7-9% other components of the dehydrogenation process considered to be mainly dialkylindanes and dialkyltetralins. Dialkylindanes and dialkyltetralins, and other LAB (likely mono-methyl branched [iso-LAB]), are known to be formed in the LAB production process (de Almeida et al. 1994; Nielsen et al. 1997). Concentrations in LAB range from <1% to 8% dialkylindanes and dialkyltetralins and <1% to 6% iso-LAB.

The alkylbenzene constituents of the Alkylate Top are secondary linear or mono-methyl branched alkyl chain materials (e.g., C<sub>7-9</sub> linear alkylbenzenes, C<sub>10</sub>-LAB, and iso-LABs) that can be attached to the benzene ring at the 2, 3, 4, or 5 positions. However, the primary alkylbenzenes (e.g., nonyl- and decylbenzene) are chemical isomers and would be expected to have properties essentially similar to the secondary alkylbenzenes. Therefore, data for the primary alkylbenzenes are utilized where appropriate. Similarly, data for the C<sub>14</sub> and C<sub>15</sub> paraffin constituents of the Alkylate Top are included when available<sup>1</sup>. Because the Alkylate Top is derived as a co-product from the LAB manufacturing process, and because LAB has been extensively studied, LAB data are provided as a benchmark for comparison.

## **C. Use Patterns and Exposure Potential**

Currently, 100% of the sponsored Alkylate Top is sold into the marine diesel fuel market as a blend stock for viscosity control. This is the only commercial use of the material. During production, it is sufficient for workers to employ standard personal protective equipment to minimize exposure. During use, very limited human and environmental exposure to marine diesel fuel is expected, given its destruction during the combustion process. Environmental exposure may occur if the diesel fuel is spilled in transit and thus presents the same limited exposure potential as other types of fuel spills. Because the Alkylate Top is only a component of the fuel, the potential for significant exposure would be even further reduced.

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<sup>1</sup> Additional data relevant to the evaluation of the constituent paraffin materials are being compiled by the American Chemistry Council Hydrocarbon Solvents Panel.

### III. COLLECTION OF PUBLISHED AND UNPUBLISHED DATA

Huntsman LLC contributed in-house data on physical-chemical properties, environmental fate and transport, ecotoxicity, and mammalian toxicity for the sponsored Alkylate Top mixture. To supplement these data, literature searches were conducted of on-line databases (e.g., Hazardous Substances Databank [HSDB], Registry of Toxic Effects of Chemical Substances [RTECS], and Aquatic Toxicity Information Retrieval [AQUIRE]), standard scientific data compendia (e.g., *CRC Handbook of Chemistry and Physics* and *The Merck Index*), and other published sources (e.g., International Uniform Chemical Information Database [IUCLID]). The literature search encompassed the Alkylate Top itself, as well as its principal constituents and the structural similar primary linear alkylbenzenes. Chemical analysis of the Alkylate Top was conducted in the fall of 2002 to characterize its constituent makeup (Rapko 2002). All of these sources were used to compile the data presented in this document.

### IV. EVALUATION OF DATA FOR QUALITY AND ACCEPTABILITY

The collected data were reviewed for quality and acceptability following the general USEPA and OECD SIDS guidance and the systematic approach described by Klimisch et al. These methods include consideration of the reliability, relevance and adequacy of the data in evaluating their usefulness for hazard assessment purposes. The Klimisch approach specifies four categories of reliability for describing data adequacy. These are:

- 1 Reliable without Restriction:** Includes studies or data complying with Good Laboratory Practice (GLP) procedures, or with valid and/or internationally accepted testing guidelines, or in which the test parameters are documented and comparable to these guidelines.
- 2 Reliable with Restrictions:** Includes studies or data in which test parameters are documented but vary slightly from testing guidelines.
- 3 Not Reliable:** Includes studies or data in which there are interferences, or that use non-relevant organisms or exposure routes, or which were carried out using unacceptable methods, or where documentation is insufficient.
- 4 Not Assignable:** Includes studies or data in which insufficient detail is reported to assign a rating, e.g., listed in abstracts or secondary literature.

Only those studies which are deemed reliable for current HPV Challenge Program purposes are included in the data set for this assessment plan. Reliable studies include both categories rated 1 (Reliable without restriction) and 2 (Reliable with restrictions). Studies rated 3 (Not reliable) were not used. Studies rated 4 (Not assignable) were used when professional judgment deemed it appropriate as part of a weight-of-evidence approach. Finally, some older studies were not included if they had been superseded by more recent studies rated 1.

Some of the available data were from study reports conducted by either outside contract laboratories or in-house industry laboratories. These study reports followed standard procedures for testing of physical-chemical properties, environmental fate and transport, aquatic toxicity, and mammalian toxicity. The most recent studies were conducted under GLP provisions. Additional data were obtained from the published, peer-reviewed, scientific literature. Reliable data from all of these sources were incorporated into the data set as appropriate.

## **V. EVALUATION OF THE AVAILABLE DATA**

All of the available data were compiled and robust summaries were prepared according to the format recommended by the USEPA and OECD. These summaries were then entered into the standard International Uniform Chemical Information Database (IUCLID) software and present the salient information from each of the reliable studies. All of the summaries are collected into a dossier that includes the sponsored Alkylate Top mixture as well as its principal constituents and structurally related materials. In addition, because the Alkylate Top is formed during the production process for LAB and its constituents include structural similarities, data for LAB are included. The dossier containing the robust summaries for the Alkylate Top and related chemicals should be used in conjunction with this assessment plan.

Table A-1 in the Appendix to this assessment plan is a matrix of SIDS/HPV endpoints and the available data for the sponsored Alkylate Top and related materials. The table includes data for LAB as a benchmark for comparison. The materials are organized left to right in the table beginning with LAB, followed by the sponsored Alkylate Top, the principal constituents of the Alkylate Top mixture (pentadecane, tetradecane, and C<sub>10</sub>-LAB), and then the structurally similar primary C<sub>9</sub> and C<sub>10</sub> linear alkylbenzenes. Data drawn from the robust summaries are shown in the table for each endpoint when available. Endpoints for which specific data are not available are identified by "--" in the table. The data presented for LAB were obtained from a completed European dossier and risk assessment report (Revision June 1997) and an updated USEPA SIDS report provided to OECD in 2002. The extent to which each of the endpoints is adequately characterized by the available data is evaluated.

### **A. *Evaluation of the Available Data on the Alkylate Top***

Adequate data for key physical-chemical, environmental fate, acute ecotoxicity, and acute mammalian toxicity properties of the Alkylate Top are available. These data are summarized below.

#### **Physical-Chemical Properties**

Boiling point and water solubility information for the Alkylate Top material is available from Huntsman LLC Material Safety Data Sheets. While the quality of these data could not be adequately assessed, the boiling point values are consistent with the expected values compared to LAB.

## **Environmental Fate**

The ultimate biodegradability (i.e., mineralization) of the Alkylate Top and other alkylated materials was evaluated in 1980 by Monsanto using a shake flask CO<sub>2</sub> evolution test similar to the standard ASTM practice, which is similar to the current OECD protocol. Periodic removal and titration of a barium hydroxide solution was used to determine the CO<sub>2</sub> evolved. Results show a mean of 46% degradation (range 43-51%) after 35 days. This represents a moderate biodegradation rate, primarily due to the degradation of the paraffin and alkylbenzene components. It should be noted that the composition of the material tested was 29% paraffin, 44% alkylbenzenes and 24% dialkylindanes/tetralins. Due to modifications in the manufacturing process, current Alkylate Top consists of 13-36% paraffin, 48-56% linear alkylbenzenes, approximately 8% dialkylindanes/tetralins, with about 6-22% iso-LAB. Since the high percentage of the less degradable dialkylindanes/tetralins would depress the overall biodegradation rate of the mixture, it is likely that this study actually represents an under-prediction of the degradation of the current Alkylate Top. Therefore, the available data indicate that current Alkylate Top will biodegrade in the environment.

## **Aquatic Toxicity**

The aquatic toxicity of the Alkylate Top was determined by ABC Laboratories in 1981 using a standard fish toxicity test under GLP conditions. Fathead minnows were exposed to five nominal concentrations ranging from 100 to 1000 mg/L for 96 hours. Acetone was used as a solvent to assist in dissolving the test material to levels significantly over its water solubility limit (as evidenced by an oily film on the surface of all test solutions). No mortality or sublethal effects were observed and the 96-hour LC<sub>50</sub> value was determined to be greater than 1000 mg/L.

## **Mammalian Toxicity**

The acute toxicity of the Alkylate Top mixture has been evaluated in a series of studies conducted in the early and late 1970s by Younger Laboratories. Oral toxicity studies in rats were conducted in 1973 at a limit dose of 15,800 mg/kg, and were repeated in 1978 at a limit dose of 10,000 mg/kg. In both sets of studies, rats were given a single undiluted dose of L210L or L210H (both CAS#68608-80-0) by gavage and observed for 14 days. No mortality was observed in any of the studies at these doses, resulting in oral LD<sub>50</sub> values greater than 15,800 mg/kg and 10,000 mg/kg.

Acute dermal studies were conducted at the same time as the oral studies. Undiluted L210L or L210H was applied to the intact skin of New Zealand albino rabbits for 24 hours and the rabbits were observed for 14 days. Results indicate acute LD<sub>50</sub> values of greater than 5,010 mg/kg in both the earlier tests and greater than 2,000 mg/kg and 1,260 mg/kg for the L210L and L210H, respectively, in the later tests. Rabbits treated with higher doses (e.g., 7,940 mg/kg in the earlier tests, 5,010 mg/kg in the later tests) experienced mortality and gross visceral alterations during the studies.

Acute inhalation studies were also conducted by Younger Laboratories. For these tests, Sprague-Dawley albino male rats were exposed to vapor concentrations of L210L or L210H ranging up to

0.9 mg/L. Rats were held in 35 L exposure chambers with the test materials for 6 hours at 27 °C, then removed and observed for 14 days. No mortality or other toxic signs were observed in any of the tests conducted.

In summary, adequate data are available for the sponsored Alkylate Top to characterize its acute mammalian toxicity. Results show that the Alkylate Top mixture tested is not acutely toxic at environmentally relevant levels. Single dose oral and inhalation studies result in no observable acute toxicity, and the dermal exposures result in acute toxicity only at extremely high levels. It can be concluded that the Alkylate Top does not present an unreasonable acute risk to mammals.

### **Summary of the Available Data on the Alkylate Top**

Adequate data exist to characterize the biodegradation, acute toxicity to fish, and acute toxicity to mammals of the sponsored Alkylate Top. These data demonstrate that the Alkylate Top will undergo substantial degradation in the environment and does not present an acute toxicity concern for fish or mammals. The sole use of Alkylate Top as a component that is blended into marine diesel fuel, which then undergoes destruction during the combustion process, significantly limits any exposure potential.

Specific data are not available to characterize the Alkylate Top mixture's toxicity to aquatic invertebrates or to characterize the potential effects of long-term mammalian exposure. Therefore, the available environmental fate and toxicity data for the principal constituents of the mixture have been reviewed and evaluated in order to assist in the characterization of the Alkylate Top. Data for the structurally similar primary alkylbenzenes were also evaluated when data were available. Given the mixture's production in the LAB production process, comparison to the properties of LAB is also appropriate. This evaluation is summarized below.

#### **B. *Evaluation of the Available Data on LAB and the Constituent Compounds***

As discussed above, the principal constituents of the Alkylate Top mixture are secondary alkylbenzenes (primarily C<sub>10</sub>-LAB) and paraffins (specifically, tetradecane and pentadecane).

### **Physical-Chemical Properties**

As can be seen in Table A-1, the principal constituents and structurally related materials all have very similar and predictable physical-chemical properties. All have boiling points less than LAB, as is necessitated by the distillation process by which the Alkylate Top mixture and its constituents are produced. All of the constituents are of low to moderate volatility and very low water solubility. The reported log octanol/water partition coefficients are all very high and fall within a narrow range of 7.11 to 7.72. These data indicate similarity with the existing data for the Alkylate Top and LAB. While data on the physical-chemical properties of the Alkylate Top itself are limited, the data for the principal constituents show a consistency that allows for the estimation of properties for the sponsored mixture. Based on the sum of the information one can predict that the Alkylate Top will have a low to moderate volatility, low water solubility and high octanol/water partitioning.

## **Environmental Fate**

Studies conducted on the Alkylate Top indicate that it biodegrades under environmental conditions. Available data for its constituents also indicate substantial biodegradation.

## **Aquatic Toxicity**

A study conducted on the Alkylate Top demonstrates that the mixture is not acutely toxic to fish even at concentrations enhanced via solvents to levels much greater than its solubility in water. Studies conducted on decylbenzene confirm that the material is not acutely toxic to fish or *Daphnia* at the water solubility limit. Furthermore, data for LAB also demonstrate no acute toxicity to fish, *Daphnia*, or algae at saturation. Exposure to enhanced concentrations using solvents also do not result in toxicity to algae and the EC<sub>50</sub> for *Daphnia* is 1.1 mg/L – far above the solubility limit of LAB. Given the structural similarities between the Alkylate Top, LAB, and the constituent materials, one would expect that toxicity to fish, *Daphnia* and algae would be similar. Thus, no acute toxicity at the water solubility limit would be expected. Chronic aquatic toxicity data are not available, but environmental exposure is limited to spill situations and therefore chronic exposures are very unlikely. In addition, the estimated log K<sub>ow</sub> values of the constituents are generally high (7.11-9.12), falling at or above the range of values that would suggest the need for chronic testing.

## **Mammalian Toxicity**

The Alkylate Top has been adequately characterized for acute toxicity, as described above, and does not present a concern. Data for all of the other endpoints are available for LAB (Table A-1) and indicate low concern. The presence of significant levels of LAB constituents (e.g., C<sub>10</sub>-LAB, dialyklindanes/tetralins, iso-LABs) in Alkylate Top (Table 1) and the consistency of the acute toxicity data between LAB and Alkylate Top indicate that the Alkylate Top would be expected to show a similar lack of genotoxicity and chronic toxicity. While LAB does not contain the paraffin constituents found in the Alkylate top, the acute toxicity data for pentadecane and the repeated dose value for tetradecane support the low concern for the Alkylate Top. The lack of significant exposure potential also indicates a lack of toxicological concern for the Alkylate Top.

## **VI. SUMMARY OF THE AVAILABLE DATA**

The sponsored Alkylate Top is a mixture of aromatic and aliphatic hydrocarbons derived as a low boiling point co-product from the LAB manufacturing process. Available data indicate that the Alkylate Top has very low solubility in water, will biodegrade in the environment, will not be acutely toxic to aquatic organisms at its water solubility limit, and is not acutely toxic to mammals by the oral or inhalation routes of exposure. No acute effects were observed at relatively high doses following dermal exposures, although some effects were noted at extremely high dermal contact with the material. However, the exclusive use of the Alkylate Top mixture as a component blended into marine diesel fuel significantly limits environmental and consumer exposure. The Alkylate Top manufacturing process is closed and workers can use personal protective equipment to effectively minimize risk. Data for LAB and *n*-paraffins, the principal

constituents of the mixture, as well as structurally related alkylbenzenes help to fill in any gaps in the characterization of the Alkylate Top.

## **VII. CONCLUSIONS**

Given the availability of data for the key endpoints, the biodegradation potential, the lack of significant toxicity concerns, and the extremely limited exposure potential, no further testing is deemed necessary to characterize the Alkylate Top mixture.

## **VIII. REFERENCES**

De Almeida, J.L.G., Dufax, M., Ben Taarit, Y. and Naccache, C. 1994. Linear alkyl benzene. *J. Am. Chem. Soc.* 71:675ff.

European Risk Assessment Report for Benzene C<sub>10-13</sub> Alkyl Derivs, CAS #67774-74-7 (last revision June 1997).

Nielsen, A.M., Britton, L.N., Beall, C.E., McCormick, T.P., and Russell, G.L. 1997. Biodegradation of co-products of commercial linear alkylbenzene sulfonate. *Environ. Sci. Technol.* 31:3397-3404.

Rapko, J. 2002. Summary of L210 Analyses.

USEPA. 2002. Updated LAB SIDS report. (SIDS Initial Assessment Report (SIAR), Benzene, C10-16 Alkyl Derivatives, CAS Nos. 123-01-3, etc.)

**Table A-1**  
**Summary of Data Available for the LAB Alkylate Top**

Section	Description	Benzene C10-13 alkyl derivs. (LAB)	Benzene, C6-12 alkyl derivatives "Alkylate Top"	Pentadecane (C15 normal paraffin)	Tetradecane (C14 normal paraffin)	C10-LAB	Decylbenzene	Nonylbenzene
	CAS Number	6774-74-7	68608-80-0	629-62-9	629-59-4	340017-14-3	104-72-3	1081-77-2
<b>Physical-Chemical Data</b>								
2.1	Melting Point	< -70°C	--	10 C	6 C	--	-14 C	-24 C
2.2	Boiling Point	278-314°C	240-250 C	271 C	253 C	276-286 C 262-286 C **	300 C	282 C
2.4	Vapour Pressure	0.017 hPa *	--	0.0046 hPa	0.0155 hPa	--	0.0017 hPa	0.0076 hPa *
2.5	Octanol/Water Partition Coefficient (log)	7.5-9.12 *	--	7.72	7.2	7.5	7.35	7.11 *
2.6.1	Water Solubility	0.041 mg/L at 27°C 0.037 mg/L	< 1,000 mg/L	0.00008 mg/L	0.0022 mg/L	0.040 mg/L	0.0024 mg/L	0.035 mg/L. *
<b>Environmental Fate and Pathways</b>								
3.1.1	Photodegradation	< 1% after 14 days	--	t <sub>1/2</sub> = 7.1 hrs *	t <sub>1/2</sub> = 7.7 hrs *	--	t <sub>1/2</sub> = 7.5 hrs *	t <sub>1/2</sub> = 8.1 hrs *
3.1.2	Stability in Water	--	stable	--	--	--	--	--
3.5	Biodegradation	56-61% biodeg after 35 days 64-67% biodeg after 28 days	46% after 35 days	100% in seawater in 8 weeks; 75% degradation by sediment microbes in 8 days	100% in seawater in 8 weeks; Biodegrades easily	--	--	65% after 10 days; 72% degradation by sediment microbes in 8 days
<b>Ecotoxicity</b>								
4.1	Acute/Prolonged Toxicity to Fish	No effects up to soluble limits LC <sub>50</sub> > 1,000 mg/L with a solvent	LC <sub>50</sub> > 1,000 mg/L with a solvent	NOEC > 1240 ppm	NOEC > 2110 ppm	LC <sub>50</sub> > Water Solubility (0.079 mg/L)	--	--
4.2	Acute Toxicity to Daphnia	No effects at saturated concentration (up to 0.041 mg/L); EC <sub>50</sub> = 1.1 mg/L with a solvent	--	--	--	EC <sub>50</sub> > 0.10 mg/L	--	--
4.3	Toxicity to Aquatic Plants (e.g., algae)	No effects up to soluble limits EC <sub>50</sub> > 1,000 mg/L with a solvent	--	--	--	EC <sub>50</sub> > 0.10 mg/L	--	--
<b>Toxicity</b>								
5.1.1	Acute Oral Toxicity	LD <sub>50</sub> (rat) > 5,000 mg/kg	LD <sub>50</sub> (rat) >10,000; >15,800 mg/kg	--	--	--	--	--
5.1.2	Acute Inhalation Toxicity	LC <sub>50</sub> > 1.82 mg/L LC <sub>50</sub> = 71 mg/L	No toxic effects after 6 hours at concentrations of up to 0.9 mg/L	--	--	--	--	--
5.1.3	Acute Dermal Toxicity	LD <sub>50</sub> > 2,000 mg/kg	LD <sub>50</sub> (rabbit) >2000; >1,260; >5,010 mg/kg	--	--	--	--	--
5.1.4	Acute Toxicity by Other Routes	--	--	LD <sub>50</sub> (i.v., mouse) = 3493 mg/kg	--	--	--	--
5.4	Repeated Dose Toxicity	NOEL = 102 mg/m <sup>3</sup> (inhalation) LOEL = 125 mg/kg (oral)	--	--	TD <sub>10</sub> (mice) = 9600 mg/kg for 20 weeks	--	--	--
5.5	Genetic Toxicity in-vitro (Bacterial test)	Negative	--	--	--	--	--	--
5.5	Genetic Toxicity in-vitro (Non-bacterial test)	Negative	--	--	--	--	--	--
5.6	Genetic Toxicity in-vivo	Negative	--	--	--	--	--	--
5.8	Toxicity to Reproduction	NOAEL (maternal) = 50 mg/kg NOAEL (fetal) = 50 mg/kg	--	--	--	--	--	--
5.9	Developmental Toxicity/Teratogenicity	NOAEL (maternal) = 125 mg/kg Not teratogenic	--	--	--	--	--	--

\* Estimated Values

\*\* Estimated data for C9-LAB based on regression analysis

# I U C L I D

## D A T A S E T

Existing Chemical                      Benzene, C6-12 Alkyl Derivatives (CAS# 68608-80-0)

Producer

Company:                                  Huntsman LLC

Creation date:                              May 2, 2001

Prepared by

Company:                                      THE WEINBERG GROUP INC.

Printing date:                                February 24, 2003

Revision date:

Date of last update:                        February 24, 2003

Number of pages:                            48

# I U C L I D

# D a t a S e t

**Existing Chemical**            Substance ID: Atops

**Producer Related Part**

**Company:**                    The Weinberg Group Inc.  
**Creation date:**            02-MAY-2001

**Substance Related Part**

**Company:**                    The Weinberg Group Inc.  
**Creation date:**            02-MAY-2001

**Printing date:**              24-FEB-2003

**Revision date:**

**Date of last Update:**    **24-FEB-2003**

**Number of Pages:**         **48**

**Chapter (profile):**         Chapter: 1, 2, 3, 4, 5, 7

**Reliability (profile):**    Reliability: without reliability, 1, 2, 3, 4

**Flags (profile):**            Flags: without flag, confidential, non confidential, WGK  
(DE), TA-Luft (DE), Material Safety Dataset, Risk  
Assessment, Directive 67/548/EEC

### **1.0.1 OECD and Company Information**

**Name:** Huntsman LLC

29-JAN-2003

### **1.0.2 Location of Production Site**

**Remark:** The production site is located in North America.

03-OCT-2001

### **1.0.3 Identity of Recipients**

**Remark:** Not applicable

03-OCT-2001

## **1.1 General Substance Information**

**Substance type:** organic

**Physical status:** liquid

**Remark:** A mixture of alkylated benzenes and n-paraffins derived as a lower boiling point co-product from the LAB manufacturing process. Benzene, C6-12 alkyl derivs. (68608-80-0)

24-FEB-2003

### **1.1.1 Spectra**

**Remark:** Not applicable

03-OCT-2001

## **1.2 Synonyms**

**Remark:** Alkylate Top

22-OCT-2001

## **1.3 Impurities**

**CAS-No:**

**EINECS-No:**

**EINECS-Name:**

**Remark:** Not specified

03-OCT-2001

### **1.4 Additives**

**CAS-No:**

**EINECS-No:**

**EINECS-Name:**

**Remark:** Not specified

03-OCT-2001

### **1.5 Quantity**

**Quantity**

1 000 - 5 000 tonnes

08-NOV-2001

### **1.6.1 Labelling**

**Labelling:**

**Remark:** There are no specific labeling requirements for the alkylate top.

03-OCT-2001

### **1.6.2 Classification**

**Classification:**

**Class of danger:**

**R-Phrases:**

**Remark:** There are no specific classification requirements for the alkylate top.

03-OCT-2001

### **1.7 Use Pattern**

**Type:**

**Category:**

**Remark:** 100% of the sponsored alkylate top is sold into the marine diesel fuel market as a blend stock for viscosity control.

21-JAN-2003

### **1.7.1 Technology Production/Use**

**Remark:** Not applicable

03-OCT-2001

### **1.8 Occupational Exposure Limit Values**

**Type of limit:**

**Limit value:**

**Remark:** No TLV's have been established.  
03-OCT-2001

### **1.9 Source of Exposure**

**Memo:** Very limited potential for human or environmental exposure.  
03-OCT-2001

### **1.10.1 Recommendations/Precautionary Measures**

**Remark:** Use of appropriate personel protective equipment.  
03-OCT-2001

### **1.10.2 Emergency Measures**

**Remark:** Flush with water. Ventilate area. Wipe up or absorb on  
suitable material and shovel into appropriate container.  
03-OCT-2001

### **1.11 Packaging**

**Memo:** Product is available in tank cars and tank trucks.  
03-OCT-2001

### **1.12 Possib. of Rendering Subst. Harmless**

**Type of  
destruction:**

**Remark:** Flush with water  
03-OCT-2001

### **1.13 Statements Concerning Waste**

**Memo:** Dispose of waste in accordance with appropriate RCRA and local  
requirements.  
03-OCT-2001

### **1.14.1 Water Pollution**

**Classified by:**  
**Labelled by:**  
**Class of danger:**  
**Remark:** Not required  
03-OCT-2001

### **1.14.2 Major Accident Hazards**

**Legislation:**  
**Substance listed:**  
**Remark:** As with all chemicals, avoid contact with skin, eyes or clothing.  
03-OCT-2001

### **1.14.3 Air Pollution**

**Classified by:**  
**Labelled by:**  
**Number:**  
**Class of danger:**  
**Remark:** Not required  
03-OCT-2001

### **1.15 Additional Remarks**

**Memo:** None  
03-OCT-2001

### **1.16 Last Literature Search**

**Date of Search:** 16-OCT-2002  
29-JAN-2003

### **1.17 Reviews**

**Memo:** None  
03-OCT-2001

### **1.18 Listings e.g. Chemical Inventories**

**Additional Info:** Listed on TSCA Inventory, Canadian DSL, and EINECS or ELINCS  
03-OCT-2001

## 2.1 Melting Point

**Value:** < -70 degree C  
**Decomposition:** no  
**Sublimation:** no  
**Method:** other: DIN 51 583  
**GLP:** no data  
**Remark:** No data specifying done as GLP, but presumed GLP based on reported use of DIN protocol.  
**Source:** Wibarco 1993.  
**Test substance:** Benzene C10-13 alkyl derivs. (LAB) (67774-74-7)  
**Reliability:** (2) valid with restrictions  
Reported in LAB Risk Assessment document citing a DIN protocol.  
24-FEB-2003 (7)

**Value:** = 10 degree C  
**Method:** other: no data  
**GLP:** no data  
**Test substance:** Pentadecane (C15 normal paraffin) (629-62-9)  
**Reliability:** (2) valid with restrictions  
Standard reference text.  
22-OCT-2001

**Value:** = 6 degree C  
**Method:** other: no data  
**GLP:** no data  
**Source:** Rossini 1953.  
**Test substance:** Tetradecane (C14 normal paraffin) (629-59-4)  
**Reliability:** (2) valid with restrictions  
Standard reference text.  
29-JAN-2003 (36)

**Value:** = -14 degree C  
**GLP:** no data  
**Source:** Jeng 1992.  
**Test substance:** Decylbenzene (104-72-3)  
**Reliability:** (1) valid without restriction  
25-JUL-2001 (25)

**Value:** = -24 degree C  
**GLP:** no data  
**Source:** Jeng 1992.  
**Test substance:** Nonylbenzene (1081-77-2)  
**Reliability:** (1) valid without restriction  
25-JUL-2001 (25)

## 2.2 Boiling Point

**Value:** = 278 - 314 degree C at 1013 hPa  
**Decomposition:** yes  
**Method:** other: ASTM D 86  
**Year:** 1989  
**GLP:** no  
**Source:** EniChem Augusta Industriale 1993.  
**Test substance:** Benzene C10-13 alkyl derivs. (LAB) (67774-74-7)  
**Reliability:** (2) valid with restrictions  
Reported in LAB Risk Assessment.  
24-FEB-2003 (12)

**Value:** = 240 - 250 degree C  
**GLP:** no data  
**Source:** Huntsman MSDS 2000.  
**Test substance:** Alkylate L-210 (Benzene, C6-12 alkyl derivatives; 68608-80-0)  
**Reliability:** (4) not assignable  
Data from MSDS but original study report not available for review.  
25-JUL-2001 (21)

**Value:** = 271 degree C  
**Method:** other: no data  
**GLP:** no data  
**Source:** Rossini 1953.  
**Test substance:** Pentadecane (C15 normal paraffin) (629-62-9)  
**Reliability:** (2) valid with restrictions  
Standard reference text.  
29-JAN-2003 (36)

**Value:** = 253 degree C  
**Method:** other: no data  
**GLP:** no data  
**Source:** Rossini 1953.  
**Test substance:** Tetradecane (C14 normal paraffin) (629-59-4)  
**Reliability:** (2) valid with restrictions  
Standard reference text.  
29-JAN-2003 (36)

**Value:** = 276 - 286 degree C  
**Method:** other: Internal laboratory analysis  
**GLP:** no data  
**Remark:** Normal boiling points at 1 atm for 2, 3, 4, and 5-phenyldecane.  
**Source:** Huntsman 2001.  
**Test substance:** C10-LAB (340017-14-3)  
**Reliability:** (2) valid with restrictions  
29-JAN-2003 (22)

---

**Value:** = 262 - 286 degree C  
**GLP:** no  
**Method:** Estimation of C9-LAB 2, 3, 4, and 5 phenyl isomers based on a regression analysis of the C10-C14 LAB positional isomer data.  
**Source:** Rapko 2001.  
**Test substance:** C9-LAB  
**Reliability:** (2) valid with restrictions  
08-NOV-2001 (33)

**Value:** = 300 degree C  
**Method:** other: no data  
**GLP:** no data  
**Source:** Rossini 1953.  
**Test substance:** Decylbenzene (104-72-3)  
**Reliability:** (2) valid with restrictions  
Standard reference text.  
29-JAN-2003 (36)

**Value:** = 282 degree C  
**Method:** other: no data  
**GLP:** no data  
**Source:** Rossini 1953.  
**Test substance:** Nonylbenzene (1081-77-2)  
**Reliability:** (2) valid with restrictions  
Standard reference text.  
29-JAN-2003 (36)

### 2.3 Density

**Type:**  
**Value:**  
**Remark:** Not a High Production Volume Challenge Program endpoint.  
03-OCT-2001

#### 2.3.1 Granulometry

**Type of  
distribution:**

**Remark:** Not a High Production Volume Challenge Program endpoint.  
03-OCT-2001

---

## 2.4 Vapour Pressure

**Value:** = .0017 hPa at 25 degree C  
**Method:** other (calculated)  
**GLP:** no  
**Source:** EPIWIN V.3.10  
**Test substance:** Benzene C10-13 alkyl derivs. (LAB) (67774-74-7)  
**Reliability:** (2) valid with restrictions  
Standard EPA peer-reviewed database and estimation software.  
25-JUL-2001

**Value:** = .0046 hPa at 25 degree C  
**GLP:** no data  
**Source:** Daubert 1989.  
**Test substance:** Pentadecane (C15 normal paraffin) (629-62-9)  
**Reliability:** (2) valid with restrictions  
Cited in HSDB but original report not available for review.  
25-JUL-2001 (42)

**Value:** = .0155 hPa at 25 degree C  
**GLP:** no data  
**Source:** Daubert 1989.  
**Test substance:** Tetradecane (C14 normal paraffin) (629-59-4)  
**Reliability:** (2) valid with restrictions  
Cited in HSDB but original report not available for review.  
02-NOV-2001 (10)

**Value:** = .0017 hPa at 25 degree C  
**GLP:** no data  
**Source:** Daubert 1989.  
**Test substance:** Decylbenzene (104-72-3)  
**Reliability:** (2) valid with restrictions  
Cited in HSDB but original report not available for review.  
02-NOV-2001 (10)

**Value:** = .0076 hPa at 25 degree C  
**Method:** other (calculated)  
**GLP:** no data  
**Source:** EPIWIN V.3.10  
**Test substance:** Nonylbenzene (1081-77-2)  
**Reliability:** (2) valid with restrictions  
Standard EPA peer-reviewed database and estimation software.  
02-NOV-2001 (46)

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## 2.5 Partition Coefficient

**log Pow:** = 7.5 - 9.12 at 25 degree C  
**Method:** other (calculated): Fragment constants by Hansch and Leo  
**Year:** 1979  
**GLP:** no  
**Remark:** The individual calculated values using the fragment constant method are 7.5, 8.04, 8.58, and 9.12 for LABs of alkyl chain length C10, C11, C12, and C13, respectively.  
**Source:** Sherblom et al 1988; Hansch and Leo.  
**Test substance:** Benzene C10-13 alkyl derivs. (LAB) (67774-74-7)  
**Reliability:** (2) valid with restrictions  
25-JUL-2001 (16) (41)

**log Pow:** = 7.72  
**Method:** other (calculated): Extrapolated from Hutchinson et al  
**Year:**  
**GLP:** no data  
**Source:** Coates et al 1985; Hutchinson et al 1980.  
**Test substance:** Pentadecane (C15 normal paraffin) (629-62-9)  
**Reliability:** (2) valid with restrictions  
25-JUL-2001 (8) (23)

**log Pow:** = 7.2  
**Method:** other (measured): Head space chromatographic method  
**Year:**  
**GLP:** no data  
**Source:** Sangster 1989; Coates et al 1985.  
**Test substance:** Tetradecane (C14 normal paraffin) (629-59-4)  
**Reliability:** (1) valid without restriction  
25-JUL-2001 (8) (40)

**log Pow:** = 7.35  
**Method:** other (measured): Shake flask  
**Year:**  
**GLP:** no data  
**Source:** Sangster 1989; Bruggeman et al 1982.  
**Test substance:** Decylbenzene (104-72-3)  
**Reliability:** (1) valid without restriction  
01-NOV-2001 (5) (40)

**log Pow:** = 7.11  
**Method:** other (calculated): EPIWIN V.3.10  
**Year:**  
**GLP:** no data  
**Test substance:** Nonylbenzene (1081-77-2)  
**Reliability:** (2) valid with restrictions  
Standard EPA peer-reviewed database and estimation software.  
25-JUL-2001

### 2.6.1 Water Solubility

**Value:** = .041 mg/l at 27 degree C  
**Qualitative:** of very low solubility  
**Method:** other: Monsanto method  
**GLP:** yes  
**Remark:** Gas chromatographical determination: aqueous solubility was reported as the sum of linear C9-13 alkylbenzene GC peak areas.  
**Source:** Gledhill et al 1991.  
**Test substance:** Benzene C10-13 alkyl derivs. (LAB) (67774-74-7)  
**Reliability:** (1) valid without restriction  
25-JUL-2001 (15)

**Value:** = .037 mg/l  
**GLP:** yes  
**Method:** Six mL of LAB were deposited on the top of approximately 700 mL of ultra-pure water in a reaction vessel. The solution was stirred and maintained at 20-23 degrees Celcius. After 96 hours, 100 mL aliquots were sampled and the water accommodated fraction determined.  
**Remark:** The WAF were determined to be 0.037, 0.040, and 0.049 mg/L for LAB, Phenyl C-10, and Phenyl C-12, respectively. The total solubility seems to be independent of the number of components in the mixture, and therefore for a single compound, the final water concentration in saturated solutions will depend on the total number of isomers/homologues present in the mixture. Further, the relative composition of the saturated solutions differs from that observed for the mixture, these differences seem to be regulated by a more complex mechanism than lipophilicity.  
**Source:** Alonso et al 1999.  
**Test substance:** Phenyl-C10 (C10 LAB) and LAB (67774-74-7)  
**Reliability:** (1) valid without restriction  
03-OCT-2001 (2)

**Value:** < 1000 mg/l  
**GLP:** no data  
**Remark:** Data listed in MSDS as < 0.1%.  
**Source:** Huntsman 2000.  
**Test substance:** Alkylate L-210 (Benzene, C6-12 alkyl derivatives; 68608-80-0)  
**Reliability:** (4) not assignable  
Data from MSDS but original study report not available for review.  
03-OCT-2001 (21)

**Value:** = .00008 mg/l  
**Method:** other: Extrapolated from Hutchinson et al  
**GLP:** no data  
**Source:** Coates et al 1985; Hutchinson et al 1980.  
**Test substance:** Pentadecane (C15 normal paraffin) (629-62-9)  
**Reliability:** (2) valid with restrictions  
25-JUL-2001 (8) (23)

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**Value:** = .0022 mg/l at 25 degree C  
**Method:** other: Shake flask  
**Remark:** Methods meeting current standards were used. Flasks were shaken gently for 12-hours, then allowed to sit at 25 plus or minus 0.1 degrees Celcius for another 24 hours to allow dispersed droplets to rise to the surface. Aliquots of 100 mL were removed and filtered through a 0.45 micrometer Millipore filter to remove any small hydrocarbon droplets still in suspension. This filtration step is necessary to remove colloidal hydrocarbon and to determine a true water solubility.  
**Source:** Sutton and Calder 1974.  
**Test substance:** Tetradecane (C14 normal paraffin) (629-59-4)  
**Reliability:** (1) valid without restriction  
25-JUL-2001 (43)

**Value:** = .0024 mg/l  
**GLP:** no data  
**Source:** Krop et al 1997.  
**Test substance:** Decylbenzene (104-72-3)  
**Reliability:** (2) valid with restrictions  
As cited in HSDB.  
25-JUL-2001 (26)

**Value:** = .035 mg/l at 25 degree C  
**Method:** other: EPIWIN V.3.10  
**GLP:** no data  
**Test substance:** Nonylbenzene (1081-77-2)  
**Reliability:** (2) valid with restrictions  
Standard EPA peer-reviewed database and estimation software.  
25-JUL-2001

### 2.6.2 Surface Tension

**Remark:** Not a High Production Volume Challenge Program endpoint.  
03-OCT-2001

### 2.7 Flash Point

**Value:** ca. 117 degree C  
**Type:**  
**Method:**  
**Year:**  
**Source:** Huntsman Petrochemical Corporation 2000.  
**Test substance:** Alkylate L-210 (Benzene, C6-12 alkyl derivatives; 68608-80-1)  
22-OCT-2001 (21)

### **2.8 Auto Flammability**

**Value:**

**Remark:** Not a High Production Volume Challenge Program endpoint.  
03-OCT-2001

### **2.9 Flammability**

**Result:**

**Remark:** Not a High Production Volume Challenge Program endpoint.  
03-OCT-2001

### **2.10 Explosive Properties**

**Result:**

**Remark:** Not a High Production Volume Challenge Program endpoint.  
03-OCT-2001

### **2.11 Oxidizing Properties**

**Result:**

**Remark:** Not a High Production Volume Challenge Program endpoint.  
03-OCT-2001

### **2.12 Additional Remarks**

**Memo:**

None  
01-NOV-2001

**3.1.1 Photodegradation**

**Type:** other: Acetonitrite solution  
**Light source:** Sun light  
**Rel. intensity:** = 1 based on Intensity of Sunlight  
**Conc. of subst.:** 2 mg/l at 18 degree C  
**DIRECT PHOTOLYSIS**  
**Degradation:** < 1 % after 14 day  
**Method:** other (measured): EPA  
**Year:** 1979 **GLP:** no  
**Test substance:** other TS: Alkylate 215 (LAB) (67774-74-7) Average alkyl chain length = C11.1  
**Method:** Test solutions were exposed to natural sunlight for 14 days during the summer (52% possible sunlight). Controls wrapped in aluminum foil were also included. Duplicate photolysis tubes were sacrificed at 0, 2, 5, 9, and 14 days and analyzed by HPLC.  
**Remark:** Greater than 99% of the original material remained at the end of the test period. As natural water solutions were not used, sensitized photolysis tubes were sacrificed at 0, 2, 5, 9, and 14 days and analyzed by HPLC.  
**Source:** Gledhill 1991.  
**Reliability:** (1) valid without restriction  
 21-JAN-2003 (15)

**Type:**  
**DIRECT PHOTOLYSIS**  
**Halflife t1/2:** = 7.1 hour(s)  
**Method:** other (calculated): EPIWIN V.3.10  
**Year:** **GLP:** no  
**Test substance:** other TS: Pentadecane (C15 normal paraffin) (629-62-9)  
**Remark:** Hydroxyl radical reaction in air calculated from its estimated rate constant of  $1.82 \times 10^{-11}$  cm cubed/mol-sec at 25 degrees Celcius determined using the structure estimation method of Meylan and Howard.  
**Source:** USEPA and Syracuse Research Corporation 2000.  
**Reliability:** (2) valid with restrictions  
 Standard EPA peer-reviewed database and estimation software.  
 22-OCT-2001 (46)

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**Type:**  
**DIRECT PHOTOLYSIS**  
**Half-life t1/2:** = 7.7 hour(s)  
**Method:** other (calculated): EPIWIN V.3.10  
**Year:** **GLP:** no  
**Test substance:** other TS: Tetradecane (C14 normal paraffin) (629-59-4)  
**Remark:** Hydroxyl radical reaction in air calculated from its estimated rate constant of  $1.68 \times 10^{-11}$  cm cubed/mol-sec at 25 degrees Celcius determined using the structure estimation method of Meylan and Howard.  
**Source:** USEPA and Syracuse Research Corporation 2000.  
**Reliability:** (2) valid with restrictions  
Standard EPA peer-reviewed database and estimation software.  
22-OCT-2001 (46)

**Type:**  
**DIRECT PHOTOLYSIS**  
**Half-life t1/2:** = 7.5 hour(s)  
**Method:** other (calculated): EPIWIN V.3.10  
**Year:** **GLP:** no  
**Test substance:** other TS: Decylbenzene (104-72-3)  
**Remark:** Hydroxyl radical reaction in air calculated from its estimated rate constant of  $1.72 \times 10^{-11}$  cm cubed/mol-sec at 25 degrees Celcius determined using the structure estimation method of Meylan and Howard.  
**Source:** USEPA and Syracuse Research Corporation 2000.  
**Reliability:** (2) valid with restrictions  
Standard EPA peer-reviewed database and estimation software.  
22-OCT-2001 (46)

**Type:**  
**DIRECT PHOTOLYSIS**  
**Half-life t1/2:** = 8.1 hour(s)  
**Method:** other (calculated): EPIWIN V.3.10  
**Year:** **GLP:**  
**Test substance:** other TS: Nonylbenzene (1081-77-2)  
**Remark:** Hydroxyl radical reaction in air calculated from its estimated rate constant of  $1.58 \times 10^{-11}$  cm cubed/mol-sec at 25 degrees Celcius determined using the structure estimation method of Meylan and Howard.  
**Source:** USEPA and Syracuse Research Corporation 2000.  
**Reliability:** (2) valid with restrictions  
Standard EPA peer-reviewed database and estimation software.  
22-OCT-2001 (46)

### **3.1.2 Stability in Water**

**Type:**  
**Method:**  
**Year:** **GLP:**  
**Test substance:** other TS: Benzene, C6-12 alkyl derivatives (68608-80-0)  
**Remark:** Stable. Hydrolysis is not expected to occur due to the lack of hydrolyzable functional groups.  
03-OCT-2001

### **3.1.3 Stability in Soil**

**Type:** **Radiolabel:**  
**Concentration:**  
**Cation exch. capac.:**  
**Microbial biomass:**  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** Not a High Production Volume Challenge Program endpoint.  
03-OCT-2001

### **3.2 Monitoring Data (Environment)**

**Type of measurement:**  
**Medium:**  
**Remark:** Not a High Production Volume Challenge Program endpoint.  
03-OCT-2001

### **3.3.1 Transport between Environmental Compartments**

**Type:**  
**Media:**  
**Method:**  
**Year:**  
**Remark:** See section 3.3.2.  
21-JAN-2003

**3.3.2 Distribution**

**Media:** air - biota - sediment(s) - soil - water  
**Method:** Calculation according Mackay, Level III  
**Year:** 2002  
**Remark:** Air 1.0% to 1.8%  
Water 7.6% to 11.9%  
Soil 28.5% to 29%  
Sediment 57.5% to 62.9%

The ranges of values reported for each compartment are based on the EpiSuite V.3.10 fugacity modeling for the five surrogate test substances listed below. Input assumptions are those physical-chemical parameters for each substance residing in the database included with the EpiSuite model. Because the Alkylate Top is a mixture, the fugacity modeling for the major constituents provide an estimate of what might be expected for the mixture. Results indicate a similar distribution among environmental compartments across all of the constituents. Based on this consistency, confidence is high that the distribution of the Alkylate Top would fall into the reported ranges.

**Source:** EPIWIN V.3.10  
**Test substance:** Benzene C10-13 alkyl derivs. (LAB) (67774-74-7); Tetradecane (C14 normal paraffin) (629-59-4); Pentadecane (C15 normal paraffin) (629-62-9); Decylbenzene (104-72-3); Nonylbenzene (1081-77-2)  
**Reliability:** (2) valid with restrictions

22-JAN-2003

(46)

**3.4 Mode of Degradation in Actual Use**

**Memo:** Biodegradation  
03-OCT-2001

### 3.5 Biodegradation

**Type:** aerobic  
**Inoculum:** domestic sewage, adapted  
**Concentration:** 20 mg/l related to DOC (Dissolved Organic Carbon)  
**Degradation:** = 67 % after 28 day  
**Result:** readily biodegradable  
**Kinetic:**  
7 day = 0 %  
10 day = 14 %  
14 day = 30 %  
25 day = 65 %  
28 day = 67 %  
**Method:** OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO2 evolution)"  
**Year:** **GLP:** yes  
**Test substance:** other TS: Benzene C10-13 alkyl derivs. (LAB) (67774-74-7)  
**Remark:** The biodegradation was measured by CO2 evolution. An emulgator was added to disperse the poorly soluble LAB.  
**Source:** Huls 1987.  
**Reliability:** (2) valid with restrictions  
Data reported in LAB Risk Assessment Report, June 1997 revision.  
24-FEB-2003 (17)

**Type:** aerobic  
**Inoculum:** domestic sewage  
**Contact time:** 28 day  
**Degradation:** = 64 % after 28 day  
**Result:** readily biodegradable  
**Method:** OECD Guide-line 301 F "Ready Biodegradability: Manometric Respirometry Test"  
**Year:** **GLP:** yes  
**Test substance:** other TS: Benzene C10-13 alkyl derivs. (LAB) (67774-74-7)  
**Source:** Istituto Guido Donegani 1995.  
**Reliability:** (2) valid with restrictions  
Data reported in LAB Risk Assessment Report, June 1997 revision.  
24-FEB-2003 (24)

**Type:** aerobic  
**Inoculum:** other: not specified  
**Concentration:** 18 mg/l related to Test substance  
**Contact time:** 35 day  
**Degradation:** = 56 - 61 % after 35 day  
**Method:** other: Shake Flask Carbon Evolution Procedure  
**Year:** 1975 **GLP:** yes  
**Test substance:** other TS: Benzene C10-13 alkyl derivs. (LAB) (67774-74-7)  
**Remark:** The degradation was less than in other studies, possibly because the test was conducted at LAB concentrations far exceeding the solubility limit. For this reason, studies in more natural systems (Standard River Die-away Test) were carried out using lower LAB concentrations (100-500 ppb) and GC analytical determination. The results show a primary biodegradation of > 90% and a half-life of 4-15 days. Sewage treatment plants remove most of LAB released in sewage. Average percent removals from > 69% to > 98% for trickling filter and activated sludge plants, respectively, are reported.

**Source:** Gledhill et al 1991.  
**Reliability:** (1) valid without restriction  
25-JUL-2001 (15)

**Type:** aerobic  
**Inoculum:** other: Soil, raw sewage, and activated sludge mixed liquor  
**Degradation:** = 46 % after 35 day  
**Method:** other: Monsanto shake flask procedure  
**Year:** **GLP:** no data  
**Test substance:** other TS: L-210L (Benzene, C6-12 alkyl derivatives; 68608-80-0)  
**Method:** The Monsanto shake flask procedure used is similar to the ASTM Draft No. 3 proposed standard practice for the determination of the ultimate biodegradability of organic chemicals, which is similar to the current OECD301 protocol. An acclimated inoculum is prepared by the stepwise addition of test compound to a defined medium over a 14-day period. After acclimation, 100 mL of inoculum are mixed with 900 mL of minimal salts media. After aerating the mixture with 70% oxygen in nitrogen, a known quantity of test component is added to each flask. An open reservoir containing 10 mL of 0.15N barium hydroxide is suspended via a glass tube inserted in a neoprene stopper. After sealing, the flasks are agitated in the dark at ambient temperature. Periodic removal (i.e., 3, 7, 14, 21, 28 and 35 days) and titration of the barium hydroxide solution are used to determine the CO<sub>2</sub> evolved. CO<sub>2</sub> evolution values obtained with the control are subtracted from values for the test compound.

**Remark:** While only the 35 day mean CO<sub>2</sub> evolution was reported, the data clearly show that degradation occurred during the study. It should be noted that the light aromatic naphtha (L-210L) is predominantly a mixture of paraffins, alkylbenzene, and indanes. The CO<sub>2</sub> evolution of 46% of theory probably arises from degradation of the paraffin and alkylbenzene components. The L-210L tested (in 1980) consisted of 29% paraffin, 44%

alkylbenzene, 24% alkyl indanes, with an avg.C # = 13.5. Because of advances in the production process, the current composition contains a smaller percentage of the less degradable alkyl indanes. Therefore, this study likely under predicts the actual biodegradation of the current Alkylate Top product.

**Source:** Saeger 1980.  
**Reliability:** (1) valid without restriction  
24-FEB-2003 (28) (38)

**Type:** aerobic  
**Inoculum:** other: Enriched sediment medium  
**Degradation:** = 75 % after 8 day  
**Method:** other: Experimental conditions have been devised to accelerate the processes of degradation of hydrocarbons in sediments.

**Year:** **GLP:** no data  
**Test substance:** other TS: Pentadecane (C15 normal paraffin) (629-62-9)  
**Method:** Sediments previously freed from all organic matter were used. After drying, these sediments were mixed with pentadecane. The material was then incubated for 8 days in a medium containing an initial bacterial MLP inoculum of 1x10E+8 cells/g of sediment. At the end of the incubation period the sediment was harvested and extracted. The FA fraction was analyzed.

**Remark:** The experimental conditions make it possible to determine the correlations between bacterial activity and the accumulation of petroleum constituents and so lead to a better knowledge of the potentialities of auto-purification of the marine medium.

**Source:** Azoulay et al 1983.  
**Reliability:** (2) valid with restrictions  
02-NOV-2001 (3)

**Type:** aerobic  
**Inoculum:** other: crude oil  
**Degradation:** 100 % after 56 day  
**Method:**

**Year:** **GLP:** yes  
**Test substance:** other TS: Pentadecane (C15 normal paraffin) (629-62-9)  
**Method:** Heated Arabian light crude oil was added to a concentration of 1 g/L to a natural seawater medium. This solution was cultivated at 20 degrees Celcius under constant shaking (100 strokes/min) to promote the growth of indigenous oil-degrading microorganisms. Each experimental set was cultivated in duplicate with a set of negative controls. The abundance of approximately 50 constituent compounds was determined using GC-MS in SIM mode after 8 weeks.

**Remark:** Pentadecane was 100% biodegraded within 8 weeks.

**Source:** Dutta and Harayama 2000.  
**Reliability:** (2) valid with restrictions  
24-FEB-2003 (11)

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**Type:** aerobic  
**Inoculum:** other: crude oil  
**Degradation:** 100 % after 56 day  
**Method:**  
**Year:** **GLP:** yes  
**Test substance:** other TS: Tetradecane (C14 normal paraffin) (629-59-4)  
**Method:** Heated Arabian light crude oil was added to a concentration of 1 g/L to a natural seawater medium. This solution was cultivated at 20 degrees Celcius under constant shaking (100 strokes/min) to promote the growth of indigenous oil-degrading microorganisms. Each experimental set was cultivated in duplicate with a set of negative controls. The abundance of approximately 50 constituent compounds was determined using GC-MS in SIM mode after 8 weeks.  
**Remark:** Tetradecane was 100% biodegraded within 8 weeks.  
**Source:** Dutta and Harayama 2000.  
**Reliability:** (2) valid with restrictions  
24-FEB-2003 (11)

**Type:**  
**Inoculum:**  
**Result:** other: Biodegrades easily  
**Method:** other: No data  
**Year:** **GLP:** no data  
**Test substance:** other TS: Tetradecane (C14 normal paraffins) (629-59-4)  
**Remark:** Tetradecane was listed as a compound that biodegrades and was classified in level 2 (degraded without much difficulty) in a 5-tiered rating system on ease of biodegradability.  
**Source:** Abrams et al 1975.  
**Reliability:** (2) valid with restrictions  
As cited in HSDB.  
25-JUL-2001 (1)

**Type:** aerobic  
**Inoculum:** other: Enriched sediment medium  
**Degradation:** = 72 % after 8 day  
**Method:** other: Experimental conditions have been devised to accelerate the processes of degradation of hydrocarbons in sediments.  
**Year:** **GLP:** no data  
**Test substance:** other TS: Nonylbenzene (1081-77-2)  
**Method:** Sediments previously freed from all organic matter were used. After drying, these sediments were mixed with nonylbenzene. The material was then incubated for 8 days in a medium containing an initial bacterial MLP inoculum of 1x10E+8 cells/g of sediment. At the end of the incubation period the sediment was harvested and extracted. The FA fraction was analysed.  
**Remark:** The experimental conditions make it possible to determine the correlations between bacterial activity and the accumulation of petroleum constituents and so lead to a better knowledge of the potentialities of auto-purification of the marine medium.  
**Source:** Azoulay et al 1983.  
**Reliability:** (2) valid with restrictions  
03-OCT-2001 (3)

**Type:** aerobic  
**Inoculum:** other: Alcaligenes sp. PHY12 originating from a mixed bacterial community isolated from seafoam  
**Degradation:** = 65 % after 10 day  
**Method:**  
**Year:** **GLP:** no data  
**Test substance:** other TS: Nonylbenzene (1081-77-2)  
**Method:** Pyrex flasks containing 120 mL of medium composed of seawater supplemented with yeast extract, ammonium chloride, sodium phosphate and n-nonylbenzene were used. Aeration was realized with strong agitation at 30 degrees Celcius on a reciprocal shaker (96 rpm). Traces of anthraquinone were added as a photosensitivity agent.  
**Remark:** The reported degradation value is for biodegradation alone. Concurrent studies demonstrate that in the presence of light, photo-oxidation of the more refractory biodegradation products results in even greater total degradation (84% in 10 days).  
**Source:** Rotani 1987.  
**Reliability:** (1) valid without restriction  
22-OCT-2001 (37)

**3.6 BOD5, COD or BOD5/COD Ratio**

**Remark:** Not a High Production Volume Challenge Program endpoint.  
01-NOV-2001

**3.7 Bioaccumulation**

**Species:**  
**Exposure period:**  
**Concentration:**  
**BCF:**  
**Elimination:**  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** Not a High Production Volume Challenge Program endpoint.  
01-NOV-2001

**3.8 Additional Remarks**

**Memo:** None  
01-NOV-2001

**AQUATIC ORGANISMS****4.1 Acute/Prolonged Toxicity to Fish**

**Type:** other: Static daily renewal  
**Species:** Brachydanio rerio (Fish, fresh water)  
**Exposure period:** 14 day  
**Unit:** mg/l **Analytical monitoring:** yes  
**LC50:** > .01  
**Method:** other: OECD Guideline 202  
**Year:** 1984 **GLP:** yes  
**Test substance:** other TS: Benzene C10-13 alkyl derivs. (LAB) (67774-74-7)  
**Method:** The LAB tested was comprised of 93% alkylbenzenes, of which 18% was 2-phenylalkanes. The relative percentage of the C10-13 homologues is 14:34:31:21, respectively. The treatment solutions were prepared by adding 5 g of LAB to 5 L of reconstituted water. After being vigorously stirred for 24 hours and allowed to stand for 4 hours, the aqueous phase was separated and filtered. This solution was considered the solubility concentration and was used in the experiment. In addition to the undiluted concentration, two more test concentrations were obtained by 2:1 and 1:1 dilutions with reconstituted water. Test solutions were renewed daily. Ten fish were exposed to each concentration and the control.  
**Remark:** No toxic effects were observed. The measured concentration in the undiluted sample at the beginning and end of the study were 0.0074 mg/L and 0.013 mg/L, respectively (mean = 0.010 mg/L).  
**Source:** Calcinai et al 2001.  
**Reliability:** (1) valid without restriction  
21-JAN-2003 (6)

**Type:** static  
**Species:** Lepomis macrochirus (Fish, fresh water)  
**Exposure period:** 96 hour(s)  
**Unit:** mg/l **Analytical monitoring:** no  
**LC50:** > 1000  
**Method:** other: EPA-660/3-7-009: Method for acute toxicity tests with fish, macroinvertebrates and amphibians. Five nominal concentrations plus a control and solvent control were tested. Acetone (maximum 1 mL/L) was used as the solvent.  
**Year:** 1975 **GLP:** yes  
**Test substance:** other TS: Benzene C10-13 alkyl derivs. (LAB) (67774-74-7)  
**Remark:** The test shows no adverse effects after 96 hours at a nominal concentration (1000 mg/L) up to and exceeding the water solubility using a solvent carrier. Rainbow trout and fathead minnows were also tested with the same results. The materials tested were the commercial LABs Alkylate 215, Alkylate 225, and Alkylate 230 with average alkyl chain lengths of C11.1, C11.8, and C13.2, respectively. All LABs tested had the same results, no acute effects at the concentrations tested, which were at least in excess of 100 times the LAB water solubility of 0.041 mg/L.  
**Source:** Gledhill et al 1991.

**Reliability:** (1) valid without restriction  
29-JAN-2003 (15)

**Type:** static  
**Species:** Leuciscus idus (Fish, fresh water)  
**Exposure period:** 48 hour(s)  
**Unit:** mg/l **Analytical monitoring:** no data  
**LC50:** > 1000  
**Method:** other: Bestimmung der Wirkung von wasserinhaltsstoffen auf Fische, DIN 38412 Teil 15  
**Year:** 1982 **GLP:** yes  
**Test substance:** other TS: Benzene C10-13 alkyl derivs. (LAB) (67774-74-7)  
**Remark:** This test shows no adverse effects after 48 hours at nominal concentration (1000 mg/L) up to and exceeding the water solubility using an emulsifier.  
**Source:** Huls 1994.  
**Reliability:** (2) valid with restrictions  
 Reported in LAB Risk Assessment.

24-FEB-2003 (18)

**Type:** flow through  
**Species:** Brachydanio rerio (Fish, fresh water)  
**Exposure period:** 21 day  
**Unit:** mg/l **Analytical monitoring:** yes  
**LC50:** > .079  
**Method:** OECD Guide-line 203 "Fish, Acute Toxicity Test"  
**Year:** 1992 **GLP:** yes  
**Test substance:** other TS: Phenyl-C10 (C10 LAB) (340017-14-3) and LAB (67774-74-7)  
**Remark:** The exposure period was 3 weeks.  
 Twenty fish were exposed to duplicate chambers of a single concentration (limit test) in a flow through system. Acetone was used as a solvent. The mean measured concentrations were 0.058 and 0.079 mg/L for the LAB and phenyl C-10, respectively. These assayed concentrations were higher than water solubility limits. The LAB had the following alkyl chain distribution: C10 9.9%, C11 37.9%, C12 32.7%, C13 17.7%, and C14 0.8%. Test temperature was 20°C, pH ranged from 6.33 to 7.41, and total hardness was 49-61 mg CaCO3/L  
**Result:** No toxic effects were observed.  
**Source:** Fernandez et al 2000.  
**Reliability:** (1) valid without restriction  
 29-JAN-2003 (13)

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**Type:** static  
**Species:** Pimephales promelas (Fish, fresh water)  
**Exposure period:** 96 hour(s)  
**Unit:** mg/l **Analytical monitoring:** no  
**LC50:** > 1000  
**Method:** other: Methods of acute toxicity tests with fish, macroinvertebrates, and amphibians  
**Year:** 1975 **GLP:** yes  
**Test substance:** other TS: L210-L (Benzene, C6-12 alkyl derivs.; CAS # 68608-80-0)  
**Remark:** Ten fish were placed in 5-gallon glass vessels containing 15 L of soft reconstituted water for each test nominal concentration (100, 180, 320, 560, and 100 mg/L). Test temperature was maintained at 22°C, pH between 6.5-7.1, and dissolved oxygen between 5.7-9.1 mg/L. Total water hardness was 45 mg CaCO<sub>3</sub>/L. No adverse effects were observed after 96 hours at nominal concentrations up to 1000 mg/L. Acetone (10 mL/15L) was used as a solvent to enhance solubility. An oily film was observed of the surface of all test solutions.  
**Source:** Thompson and Griffen 1981.  
**Reliability:** (2) valid with restrictions  
 22-JAN-2003 (44)

**Type:** flow through  
**Species:** Salmo gairdneri (Fish, estuary, fresh water)  
**Exposure period:** 7 day  
**Unit:** mg/l **Analytical monitoring:** yes  
**NOEC:** > 1240  
**Method:**  
**Year:** 1983 **GLP:** yes  
**Test substance:** other TS: Tetradecane (C14 normal paraffin) (629-59-4)  
**Method:** Rainbow trout were fed experimental diets containing a mixture of n-paraffins. Fish were fed twice a day (at 0900 h and 1630 h) for seven days. Feces were recovered automatically and the relative absorption of different carbon chain lengths was measured. All fish were maintained at 14 degrees Celcius in a 50 liter aquaria under a constant flow of 4 L/min and a 12 hour photoperiod.  
**Remark:** No mortality was observed in the study.  
**Source:** Cravedi 1983.  
**Reliability:** (1) valid without restriction  
 03-OCT-2001 (9)

**Type:** flow through  
**Species:** Salmo gairdneri (Fish, estuary, fresh water)  
**Exposure period:** 7 day  
**Unit:** mg/l **Analytical monitoring:** yes  
**NOEC:** > 2110  
**Method:**  
**Year:** 1983 **GLP:** yes  
**Test substance:** other TS: Pentadecane (C15 normal paraffin) (629-62-9)  
**Method:** Rainbow trout were fed experimental diets containing a mixture of n-paraffins. Fish were fed twice a day (at 0900 h and 1630 h) for seven days. Feces were recovered automatically and the relative absorption of different carbon chain lengths was measured. All fish were maintained at 14 degrees Celcius in a 50 liter aquaria under a constant flow of 4 L/min and a 12 hour photoperiod.  
**Remark:** No mortality was observed in the study. The maximum digestibility of all n-paraffins tested was observed for pentadecane.  
**Source:** Cravedi 1983.  
**Reliability:** (1) valid without restriction  
 02-NOV-2001 (9)

#### 4.2 Acute Toxicity to Aquatic Invertebrates

**Species:** Daphnia magna (Crustacea)  
**Exposure period:** 48 hour(s)  
**Unit:** mg/l **Analytical monitoring:** yes  
**NOEC:** > .013  
**EC50:** > .013  
**Method:** Directive 84/449/EEC, C.2 "Acute toxicity for Daphnia"  
**Year:** **GLP:** yes  
**Test substance:** other TS: A commercial LAB produced in an HF alkylation process (67774-74-7)  
**Method:** The LAB tested was comprised of 93% alkylbenzenes, of which 18% was 2-phenylalkanes. The relative percentage of the C10-C13 homologues is 14:34:31:21, respectively. The treatment solutions were prepared by adding 5 g of LAB to 5 L of reconstituted water. After being vigorously stirred for 24 hours and allowed to stand for 4 hours, the aqueous phase was separated and filtered. This solution considered was the solubility concentration and was used in the experiment. Measured concentrations at the start of the test were 0.039 to 0.041 mg/L. Measured concentrations at the end of the 48-hour study were 0.010 to 0.013 mg/L. Twenty daphnids were exposed to the test material and the control.  
**Remark:** No effects of immobilization were observed at the solubility concentration of 0.010 to 0.013 mg/L.  
**Source:** Calcinai et al 2001.  
**Reliability:** (1) valid without restriction  
 21-JAN-2003 (6) (47)

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**Species:** Daphnia magna (Crustacea)  
**Exposure period:** 48 hour(s)  
**Unit:** mg/l **Analytical monitoring:** yes  
**Method:** OECD Guide-line 202, part 1 "Daphnia sp., Acute Immobilisation Test"  
**Year:** 1984 **GLP:** yes  
**Test substance:** other TS: A commercial LAB produced in an HF alkylation process (67774-74-7)  
**Remark:** A test was conducted with LAB dissolved in acetone. In the test, acetone-assisted concentrations of 0.05, 0.1, 0.2, 0.4, 0.8, 1.0, 1.2, and 1.4 mg/L were prepared. Results of the test show that LAB is not toxic to Daphnia at the limit of solubility.  
**Source:** Verge et al. 1999.  
**Reliability:** (1) valid without restriction  
21-JAN-2003 (47)

**Species:** Daphnia magna (Crustacea)  
**Exposure period:** 48 hour(s)  
**Unit:** mg/l **Analytical monitoring:** yes  
**EC50:** > .04  
**Method:** OECD Guide-line 202, part 1 "Daphnia sp., Acute Immobilisation Test"  
**Year:** 1984 **GLP:** yes  
**Test substance:** other TS: A commercial LAB produced in an HF alkylation process (67774-74-7)  
**Remark:** A test was conducted with LAB without solvent. In the test, a saturated LAB solution (0.040 mg/L) was tested as is and diluted to 0.030, 0.020, 0.010, and 0.005 mg/L. In the test the EC50 was 1.1 mg/L, which is much higher than the solubility concentration.  
**Source:** Verge et al. 1999.  
**Reliability:** (1) valid without restriction  
24-FEB-2003 (47)

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**Species:** Daphnia magna (Crustacea)  
**Exposure period:** 48 hour(s)  
**Unit:** mg/l **Analytical monitoring:** yes  
**EC50:** > .1  
**Method:** OECD Guide-line 202, part 1 "Daphnia sp., Acute Immobilisation Test"  
**Year:** **GLP:** yes  
**Test substance:** other TS: Phenyl-C10 (C10 LAB) (340017-14-3)  
**Remark:** Ten daphnids were exposed to each of four nominal concentrations (0.1, 0.05, 0.025, 0.0125 mg/L) using acetone (0.1%) as a vehicle. Temperature was 20+/-1°C. A distinction was made between immobilized and effected. No effects were observed up to 48 hours. The study was extended out to 144 hours and the EC50s were 0.083 at 96 hours, 0.035 at 120 hours, and 0.025 at 144 hours. The results show that the absence of toxicity can be related to the limited exposure period. If the exposure time is expanded up to 5 days, the EC50 values for waterborne exposures reach the solubility level. This hypothesis is clearly consistent with the assumption of non-polar narcosis as mode of action and toxicity related to the total body burden of LAB. Due to the low water solubility, prolonged waterborne exposures are required to reach the lethal body burden, as has been demonstrated for other poorly soluble hydrocarbons.  
**Source:** Fernandez et al 2000.  
**Reliability:** (1) valid without restriction  
29-JAN-2003 (14)

#### 4.3 Toxicity to Aquatic Plants e.g. Algae

**Species:** Selenastrum capricornutum (Algae)  
**Endpoint:** growth rate  
**Exposure period:** 96 hour(s)  
**Unit:** mg/l **Analytical monitoring:** no data  
**EC50:** > 1000  
**Method:** other: EPA 600/9-78-018 The Selenastrum capricornutum Printz algal assay. Five nominal concentrations plus a control and solvent were tested. Acetone (maximum 1 mL/L) was used as the solvent.  
**Year:** 1978 **GLP:**  
**Test substance:** other TS: Benzene C10-13 alkyl derivs. (LAB) (67774-74-7)  
**Remark:** Selenastrum capricornutum is not affected after 96 hours at nominal concentration (1000 mg/L) up to and exceeding the water solubility with a solvent carrier. The material tested was commercial LAB (Alkylate 215) with an average alkyl chain length of C11.1. Concentrations at least in excess of 100 times the LAB water solubility of 0.014 mg/L were tested without effect on algal growth or survival.  
**Source:** Gledhill et al 1991.  
**Reliability:** (1) valid without restriction  
22-JAN-2003 (15)

**Species:** Scenedesmus subspicatus (Algae)  
**Endpoint:** growth rate  
**Exposure period:** 72 hour(s)  
**Unit:** mg/l **Analytical monitoring:** no  
**EC50:** > .1  
**Method:** OECD Guide-line 201 "Algae, Growth Inhibition Test"  
**Year:** 1984 **GLP:** yes  
**Test substance:** other TS: LAB (67774-74-7) and individual homologues (phenyl C8, phenyl C10, phenyl C12, phenyl C14)  
**Remark:** LAB concentrations tested were 0.025, 0.050, and 0.100 mg/L. No inhibition of growth was observed for LAB or any of the individual homologues. Commercial LAB had the following alkyl chain length distribution: C10 8.8%, C11 41.7%, C12 31.7%, C13 16.1%, C14 0.9%, of which 17.5% is 2-phenylalkanes. Test temperature was 20°C and pH was 7.1+/-0.1.  
**Source:** Moreno et al 2000.  
**Reliability:** (1) valid without restriction  
21-JAN-2003 (32)

**4.4 Toxicity to Microorganisms e.g. Bacteria**

**Type:**  
**Species:**  
**Exposure period:**  
**Unit:** **Analytical monitoring:**  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** Not a High Production Volume Challenge Program endpoint.  
03-OCT-2001

**4.5 Chronic Toxicity to Aquatic Organisms**

**4.5.1 Chronic Toxicity to Fish**

Species:  
Endpoint:  
Exposure period:  
Unit: Analytical monitoring:  
Method: GLP:  
Year:  
Test substance:  
Remark: Not a High Production Volume Challenge Program endpoint.  
03-OCT-20  
01

**4.5.2 Chronic Toxicity to Aquatic Invertebrates**

Species:  
Endpoint:  
Exposure period:  
Unit: Analytical monitoring:  
Method: GLP:  
Year:  
Test substance:  
Remark: Not a High Production Volume Challenge Program endpoint.  
03-OCT-2001

**TERRESTRIAL ORGANISMS**

**4.6.1 Toxicity to Soil Dwelling Organisms**

Type:  
Species:  
Endpoint:  
Exposure period:  
Unit:  
Method: GLP:  
Year:  
Test substance:  
Remark: Not a High Production Volume Challenge Program endpoint.  
03-OCT-20  
01

#### **4.6.2 Toxicity to Terrestrial Plants**

**Species:**  
**Endpoint:**  
**Expos. period:**  
**Unit:**  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** Not a High Production Volume Challenge Program endpoint.  
03-OCT-2001

#### **4.6.3 Toxicity to other Non-Mamm. Terrestrial Species**

**Species:**  
**Endpoint:**  
**Expos. period:**  
**Unit:**  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** Not a High Production Volume Challenge Program endpoint.  
03-OCT-2001

#### **4.7 Biological Effects Monitoring**

**Memo:** Not a High Production Volume Challenge Program endpoint.  
03-OCT-2001

#### **4.8 Biotransformation and Kinetics**

**Type:**  
**Remark:** Not a High Production Volume Challenge Program endpoint.  
03-OCT-2001

#### **4.9 Additional Remarks**

**Memo:** Refer to the Benzene, C6-12 alkyl derivatives (Alkylate Top) assessment plan for more information.  
29-JAN-2003

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## **5.1 Acute Toxicity**

### **5.1.1 Acute Oral Toxicity**

**Type:** LD50  
**Species:** rat  
**Sex:** male/female  
**Number of Animals:**  
**Vehicle:** other: none  
**Value:** > 5000 mg/kg bw  
**Method:** other: OECD Guide-line 401: Rats were given a single oral administration by gavage.  
**Year:** **GLP:** yes  
**Test substance:** other TS: Benzene C10-13 alkyl derivs. (LAB) (67774-74-7). Average side chain length of 11.1 to 11.8.  
**Remark:** No deaths were observed. Pilo-erection was observed shortly after dosing in all treated rats.  
**Source:** Huntingdon Research Centre 1984.  
**Reliability:** (2) valid with restrictions  
Data as reported in LAB Risk Assessment, revised June 1997.  
24-FEB-2003 (20)

**Type:** LD50  
**Species:** rat  
**Sex:** male/female  
**Number of Animals:** 5  
**Vehicle:**  
**Value:** > 10000 mg/kg bw  
**Method:** other: Undiluted test material was provided to three male and two female rats in a single oral dose.  
**Year:** 1978 **GLP:** no data  
**Test substance:** other TS: L-210H and L-210L (68608-80-0)  
**Remark:** No signs of toxicity were observed with the exception of some weight loss at one to two days. Viscera were normal after 14 days. An earlier study by the same laboratory (1973) tested at a higher dose resulted in an LD50 > 15,800 mg/kg bw.  
**Source:** Younger Laboratories 1978.  
**Reliability:** (2) valid with restrictions  
21-JAN-2003 (50)

**5.1.2 Acute Inhalation Toxicity**

**Type:** LC50  
**Species:** rat  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Exposure time:**  
**Value:** > 1.82 mg/l  
**Method:** other  
**Year:** **GLP:** yes  
**Test substance:** other TS: Benzene C10-13 alkyl derivs. (LAB) (67774-74-7). Average side chain length of 11.1 to 11.8.  
**Method:** The substance was administered as an aerosol containing > 90% particles with diameter less than 10 microns.  
**Remark:** No deaths were observed.  
**Source:** Monsanto 1982.  
**Reliability:** (2) valid with restrictions  
 Data reported in LAB Risk Assessment Report, June 1997 revision. Original report not reviewed.

24-FEB-2003 (30)

**Type:** LC50  
**Species:** rat  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Exposure time:**  
**Value:** = 71 mg/l  
**Method:** other  
**Year:** **GLP:** no data  
**Test substance:** other TS: Benzene C10-13 alkyl derivs. (LAB) (67774-74-7)  
**Method:** The substance was administered as an aerosol.  
**Reliability:** (2) valid with restrictions  
 Data reported in LAB Risk Assessment Report, June 1997 revision. Original report not reviewed.

24-FEB-2003 (45)

**Type:** LC50  
**Species:** rat  
**Sex:** male  
**Number of Animals:** 6  
**Vehicle:** other: none  
**Exposure time:** 6 hour(s)  
**Value:** > .9 mg/l  
**Method:**  
**Year:** 1973 **GLP:** no data  
**Test substance:** other TS: Benzene C6-12 alkyl derivs. (68608-80-0)  
**Method:** A.T.S. Sprague-Dawley albino male rats were exposed in a 35 L inhalation chamber for 6 hrs at 27 degrees Celcius. The air flow rate was 4.0 L/min.

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**Remark:** Four studies were performed with the same results. The concentrations of test substance in the different studies were 0.9, 0.55, 0.3, and 0.34 mg/L.

**Result:** No significant toxic signs were observed in any of the studies. Viscera appeared normal after 14 days.

**Source:** Younger Laboratories 1973; Younger Laboratories 1978.

**Reliability:** (2) valid with restrictions

03-OCT-2001 (49) (50)

### 5.1.3 Acute Dermal Toxicity

**Type:** LD50

**Species:** rat

**Sex:** male/female

**Number of Animals:**

**Vehicle:** no data

**Value:** > 2000 mg/kg bw

**Method:** OECD Guide-line 402 "Acute dermal Toxicity"

**Year:** **GLP:** yes

**Test substance:** other TS: Benzene C10-13 alkyl derivs. (LAB) (67774-74-7). Average side chain length of 11.1 to 11.8.

**Result:** After a single dermal administration in rats, no deaths were observed, no signs of systemic toxicity were observed, and terminal autopsy findings were normal.

**Source:** Huntingdon Research Centre 1984.

**Reliability:** (2) valid with restrictions

Data reported in LAB Risk Assessment Report, June 1997 revision.

25-JUL-2001 (19)

**Type:** LD50

**Species:** other: New Zealand Albino Rabbits

**Sex:** male/female

**Number of Animals:** 7

**Vehicle:** no data

**Value:** > 1260 mg/kg bw

**Method:** **GLP:** no data

**Test substance:** other TS: Benzene, C6-12-alkyl derivs. (68608-80-0) (L-210H)

**Method:** One male or female was exposed dermally to six doses (794, 1000, 1260, 2000, 3160, 5010 mg/kg) of undiluted test substance for 24 hours. The animals were observed for 14 days.

**Result:** All animals exposed to doses up to 1260 mg/kg survived. Mortality occurred for animals exposed to doses of 2000 mg/kg and higher. Weight loss was observed at two through six days in survivors. Animals in the higher concentrations experienced increasing weakness, collapse, and death. Gross autopsy of the decedents included lung and liver hyperemia, enlarged gall bladder, darkened kidneys, and gastrointestinal inflammation. Viscera appeared normal in the surviving

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animals.

**Source:** Younger Laboratories 1978.  
**Reliability:** (2) valid with restrictions  
 21-JAN-2003 (50)

**Type:** LD50  
**Species:** other: New Zealand Albino Rabbits  
**Sex:** male/female  
**Number of Animals:** 4  
**Vehicle:** no data  
**Value:** > 2000 mg/kg bw  
**Method:** other: One male or one female was exposed dermally to four doses (1260, 2000, 3160, 5010 mg/kg) of undiluted test substance for 24 hours. The animals were observed for 14 days.

**Year:** **GLP:** no data  
**Test substance:** other TS: Benzene, C6-12-alkyl derivs. (68608-80-0) (L-210L)  
**Result:** Animals exposed to doses up to 2000 mg/kg survived while mortality occurred for animals exposed to the two highest doses. Weight loss was observed at two to four days in survivors. Animals in the higher concentrations experienced increasing weakness, collapse, and death by day two. Gross autopsy of the decedents included lung and liver hyperemia, enlarged gall bladder, darkened kidneys, and gastrointestinal inflammation. Viscera appeared normal in the surviving animals.

**Source:** Younger Laboratories 1978.  
**Reliability:** (2) valid with restrictions  
 21-JAN-2003 (50)

**Type:** LD50  
**Species:** other: New Zealand Albino Rabbits  
**Sex:** male/female  
**Number of Animals:** 4  
**Vehicle:** no data  
**Value:** > 5010 mg/kg bw  
**Method:** other: One male or one female rabbit was exposed to three doses (3160, 5010, 7940 mg/kg) of the undiluted test substance for 24 hours. The animals were observed for 14 days.

**Year:** **GLP:** no data  
**Test substance:** other TS: Benzene, C6-12-alkyl derivs. (68608-80-0) (L210H + L210L)  
**Result:** Animals exposed to 3160 and 5010 mg/kg survived. Female and male rabbits exposed to the 7940 mg/kg dose died on days 2 and 10, respectively. Signs of intoxication included reduced appetite and activity (days four to seven in survivors), increasing weakness, collapse, and death. Gross autopsy of the decedents revealed hemorrhagic lungs, mottled and discolored liver, enlarged gall bladder, and gastrointestinal inflammation. Viscera in the survivors appeared normal.

**Source:** Younger Laboratories 1973.  
**Reliability:** (2) valid with restrictions

21-JAN-2003

(48) (49)

### 5.1.4 Acute Toxicity, other Routes

**Type:** LD50  
**Species:** mouse  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Route of admin.:** i.v.  
**Value:** = 3493 mg/kg bw  
**Method:**  
**Year:** **GLP:** no data  
**Test substance:** other TS: Pentadecane (C15 normal paraffin) (629-62-9)  
**Source:** Louis 1996.  
**Reliability:** (4) not assignable  
25-JUL-2001 (27)

### 5.2 Corrosiveness and Irritation

#### 5.2.1 Skin Irritation

**Species:**  
**Concentration:**  
**Exposure:**  
**Exposure Time:**  
**Number of Animals:**  
**PDII:**  
**Result:**  
**EC classificat.:**  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** Not a High Production Volume Challenge Program endpoint.  
01-NOV-2001



**5.4 Repeated Dose Toxicity**

**Species:** rat **Sex:** male/female  
**Strain:** Sprague-Dawley  
**Route of admin.:** inhalation  
**Exposure period:** 70 day(s) (14 week period)  
**Frequency of treatment:** 6 hours per day/5 days per week  
**Post. obs. period:**  
**Doses:** 0, 102, 298, or 580 mg LAB per cubic meter of air in 10m3 inhalation chambers  
**Control Group:** yes, concurrent no treatment  
**NOAEL:** = 102 ppm  
**Method:** other: EPA/TSCA.  
**Year:** **GLP:** yes  
**Test substance:** other TS: Benzene C10-13 alkyl derivs. (LAB) (67774-74-7)  
**Method:** 15 male and 15 female rats were exposed per group.  
**Remark:** Skin and mucous membrane irritation and respiratory problems were evident at the mid- and high exposure concentrations. Body weight gains were also depressed at these levels. While liver weights and serum levels of hepatic enzymes were elevated in females from the high concentrations, there were no gross or histopathological changes.  
**Source:** Monsanto 1986.  
**Reliability:** (2) valid with restrictions  
 Data reported in LAB Risk Assessment Report, June 1997 revision.

25-JUL-2001 (31)

**Species:** rat **Sex:**  
**Strain:** no data  
**Route of admin.:** oral feed  
**Exposure period:** 4 weeks  
**Frequency of treatment:** daily in diet  
**Post. obs. period:**  
**Doses:** various concentrations up to 20000 ppm (2%)  
**Control Group:**  
**LOAEL:** = 125 mg/kg bw  
**Method:** other: EPA/TSCA  
**Year:** **GLP:** yes  
**Test substance:** other TS: Benzene C10-13 alkyl derivs. (LAB) (67774-74-7)  
**Remark:** Reduction in body weight and food consumption were observed at all exposure levels. No gross pathological changes were noted. Histopathology was not carried out. The lowest dose tested was 2500 ppm, which corresponds to 125 mg/kg bw.  
**Source:** Monsanto.  
**Reliability:** (2) valid with restrictions  
 Data reported in LAB Risk Assessment Report, June 1997 revision.

25-JUL-2001 (29)

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**Species:** mouse **Sex:**  
**Strain:**  
**Route of admin.:**  
**Exposure period:** 20 weeks  
**Frequency of treatment:**  
**Post. obs. period:**  
**Doses:**  
**Control Group:**  
**LOAEL:** = 9600 mg/kg  
**Method:**  
**Year:** **GLP:**  
**Test substance:** other TS: Tetradecane (629-59-4)  
**Remark:** Patty's reports this result as "the lowest toxic dose (TDLo) of tetradecane for mice is 9600 mg/kg for 20 weeks." No further information is provided and Patty's lists only an incorrect citation. Therefore, then reliability of this value cannot be determined.  
**Source:** Sandmeyer 1981.  
**Reliability:** (4) not assignable  
 08-NOV-2001 (39)

### 5.5 Genetic Toxicity 'in Vitro'

**Type:** Bacterial reverse mutation assay  
**System of testing:** Salmonella typhimurium TA 1535, TA 100, TA 1537, and TA 98  
**Concentration:** 0, 100, 1000, 4000, 8000, and 10000 ug/plate  
**Metabolic activation:** with and without  
**Result:** negative  
**Method:** Directive 84/449/EEC, B.14 "Other effects - Mutagenicity (Salmonella typhimurium - reverse mutation assay)"  
**Year:** 1984 **GLP:** no data  
**Test substance:** other TS: Benzene C10-13 alkyl derivs. (LAB) (67774-74-7)  
**Source:** Bronzetti et al 1991.  
**Reliability:** (2) valid with restrictions  
 Data reported in LAB Risk Assessment Report, June 1997 revision.  
 01-NOV-2001 (4)

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**Type:** Mammalian cell gene mutation assay  
**System of testing:** Chinese Hamster Ovary (CHO) cells  
**Concentration:** 100 to 2000 micrograms/mL  
**Metabolic activation:** with and without  
**Result:** negative  
**Method:** other: EPA/TSCA  
**Year:** **GLP:** yes  
**Test substance:** other TS: Benzene C10-13 alkyl derivs. (LAB) (67774-74-7)  
**Remark:** V79/HGPRT and Saccharomices cerevisiae genetic toxicity studies conducted on LAB by other authors also showed negative results.  
**Result:** There were no statistically significant increases in mutation frequencies for the substance compared to the negative control. Cytotoxicity was significant at and above 1250 micrograms/mL with and without metabolic activation.  
**Source:** Robinson and Nair 1992.  
**Reliability:** (2) valid with restrictions  
Data reported in LAB Risk Assessment Report, June 1997 revision.

25-JUL-2001 (34)

**Type:** Bacterial reverse mutation assay  
**System of testing:** Salmonella typhimurium TA 1535, TA 100, TA 1537, and TA 98  
**Concentration:** .03, 12, 60, 300, 1000, 3000 ug/plate  
**Metabolic activation:** with and without  
**Result:** negative  
**Method:** other: EPA/TSCA  
**Year:** **GLP:** yes  
**Test substance:** other TS: Benzene C10-13 alkyl derivs. (LAB) (67774-74-7)  
**Remark:** The highest concentration produced evidence of either toxicity or insolubility.  
**Source:** Robinson and Nair 1992.  
**Reliability:** (2) valid with restrictions  
Data reported in LAB Risk Assessment Report, June 1997 revision.

02-NOV-2001 (34)

**5.6 Genetic Toxicity 'in Vivo'**

**Type:** other: Bone marrow chromosome aberration assay  
**Species:** rat **Sex:** male/female  
**Strain:** Sprague-Dawley  
**Route of admin.:** gavage  
**Exposure period:** single treatment  
**Doses:** 1200, 4000, and 12700 mg/kg bw  
**Result:** negative  
**Method:** other: EPA/TSCA - Bone marrow chromosome aberration  
**Year:** 1992 **GLP:** yes  
**Test substance:** other TS: LAB undiluted or dissolved in corn oil (67774-74-7)  
**Result:** A significant mean body weight loss was found in the groups treated with the highest dose. No statistically significant increases in chromosomal aberration or gaps were observed in the treated groups in any of the sampling times. Both mean chromosome numbers and mean mitotic indices were similar in test and vehicle control groups.  
**Source:** Robinson and Nair 1992.  
**Reliability:** (2) valid with restrictions  
 Data reported in LAB Risk Assessment Report, June 1997 revision.

25-JUL-2001

(34)

**5.7 Carcinogenicity**

**Species:** **Sex:**  
**Strain:**  
**Route of admin.:**  
**Exposure period:**  
**Frequency of treatment:**  
**Post. obs. period:**  
**Doses:**  
**Result:**  
**Control Group:**  
**Method:** **GLP:**  
**Year:**  
**Test substance:**  
**Remark:** Not a High Production Volume Challenge Program endpoint.  
 01-NOV-2001

### 5.8 Toxicity to Reproduction

**Type:** Two generation study  
**Species:** rat **Sex:** male/female  
**Strain:** other: CD (Charles River Breeding Laboratories)  
**Route of admin.:** gavage  
**Exposure Period:** 35 weeks  
**Frequency of treatment:** single daily dose  
**Premating Exposure Period**  
**male:** 10 weeks  
**female:** 10 weeks  
**Duration of test:** 35 weeks  
**Doses:** 0, 5, 50, and 500 mg/kg/d  
**Control Group:**  
**NOAEL Parental:** = 50 mg/kg bw  
**NOAEL F1 Offspr.:** = 50 mg/kg bw  
**Method:** other  
**Year:** **GLP:** no data  
**Test substance:** other TS: linear alkylbenzene in corn oil (6774-74-7)  
**Method:** Four groups of 30 male and 30 female were given the test substance by gavage once daily for about 10 weeks before mating. Once mated (as evidence by a copulatory or sperm in the vaginal smear), females were housed separately for the remainder of gestation. Females were dosed during mating, gestation and lactation for a total of 127 days of treatment. After weaning, 30 males and 30 females of the F1 generation were dosed for an 11-week pre-mating period. Dosing of F1 females continued through mating, gestation, and lactation. All of the resulting F2 pups were euthanized on day 13 of gestation.

**Remark:** All adults and pups received a gross post-mortem examination. Histopathology studies were conducted on reproductive tissues, tissues with gross lesions, and the pituitary gland taken from each adult in the control and high dose groups.

**Result:** There was evidence of toxicity in adults and offspring at the 500 mg/kg/day dose level, with the most consistent effects being depressed weight gains in adults, smaller litters, and fewer live pups; decreased pup survival and lower pup survival at some intervals. At 50 mg/kg/day, only a reduction in F1 of pup weight gain on day 7 was observed, but this effect had returned to normal at days 14 and 21. This temporary reduction in pup weight occurred in one generation, and this was not consistent across generations. Based on the significant effects at 500 mg/kg/day and the non consistent effects at the lower dose, the NOAEL for reproductive toxicity is 50 mg/kg/day for both parental and neonatal animals.

**Source:** Robinson and Nair 1992.  
**Reliability:** (2) valid with restrictions

24-FEB-2003 (34)

**5.9 Developmental Toxicity/Teratogenicity**

**Species:** rat **Sex:** female  
**Strain:** other: CD (Charles River Breeding Laboratories)  
**Route of admin.:** gavage  
**Exposure period:** days 6-15 of gestation  
**Frequency of treatment:** single daily dose  
**Duration of test:** 20 days  
**Doses:** 125, 500, and 2000 mg/kg bw/day  
**Control Group:**  
**NOAEL Maternalt.:** = 125 mg/kg bw  
**Method:** other  
**Year:** **GLP:** yes  
**Test substance:** other TS: Alkylate 215 (68648-87-3) as a surrogate for LAB (67774-74-7) Average alkyl chain length = C11.1  
**Method:** Groups of 24 mated rats were given the test substance in corn oil on days 6-15 of gestation. Rats were observed twice daily and the body weights recorded on gestation days 0, 6, 10, 12, 15, and 20. Fetuses were delivered by caesarean section on gestation day 20 and the numbers of live, dead, and researched fetuses, total implantations, and corpora lutea were recorded. Fetuses and surviving mated females received post mortem examinations.  
**Remark:** The substance should not be considered as a developmental toxicant since an increased incidence of ossification variations and delayed ossification only at dose levels including maternal toxicity cannot be considered as specific effects on prenatal development.  
**Result:** Depressed maternal food consumption and weight gains were observed at 500 mg/kg/day and 2000 during treatment, but significantly increased in the post treatment period. No treatment-related increases in soft tissue malformations and variations were observed in either the maternal or fetal generations. Some skeletal malformations (wavy ribs) and ossification variations were observed in the highest doses.  
**Source:** Robinson and Schroeder 1992.  
**Reliability:** (1) valid without restriction  
 21-JAN-2003 (35)

**5.10 Other Relevant Information**

**Type:**  
**Remark:** None  
 03-OCT-2001

**5.11 Experience with Human Exposure**

**Memo:** None  
 03-OCT-2001

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7. Risk Assessment

date: 24-FEB-2003  
Substance ID: Atops

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### **7.1 Risk Assessment**

**Memo :** Refer to LAB Alkylate Top Assessment Plan  
01-NOV-2001

## Reproductive and Developmental Toxicity Studies of a Linear Alkylbenzene Mixture in Rats<sup>1</sup>

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Reproductive and Developmental Toxicity Studies of a Linear Alkylbenzene Mixture in Rats. ROBINSON, E. C. AND SCHROEDER, R. E. (1992). *Fundam. Appl. Toxicol.* 18, 549-556.

Alkylate 215, a mixture of linear decyl- to tridecylbenzenes, is an intermediate in the manufacture of detergent sulfonates. A two-generation reproduction study and a developmental toxicity study were conducted using single daily doses given by gastric intubation in a corn oil vehicle. In the reproduction study, groups of 30 rats/sex/group were given doses of 0, 5, 50, or 500 mg/kg/day. F<sub>0</sub> animals received a 10-week pre-mating treatment period and were then mated to produce a single litter; F<sub>1</sub> adults were selected from the F<sub>1</sub> litters. F<sub>1</sub> animals were dosed for 11 weeks before mating to produce a single litter. Adults and weaned pups received a gross post-mortem examination. Histopathology studies were conducted on reproductive tissues, tissues with gross lesions, and the pituitary gland taken from each adult in the control and high dose groups. In the developmental toxicity study, groups of 24 mated female rats were given 0, 125, 500, or 2000 mg/kg/day on Days 6 through 15 of gestation. Dams were terminated on gestation Day 20 and fetuses were examined for external, soft tissue, and skeletal defects. Results of the reproduction study were as follows. At 50 mg/kg/day, pup weights were decreased at Day 7 in the F<sub>1</sub> litter. At 500 mg/kg/day, decreases were found in the F<sub>0</sub> females in pre-mating and early lactation weight gains; in both generations in pre-mating weight gains in males and in weight gains during gestation in females; and in litter size, pup viability at birth, Day 0-4 survival, and pup weights on Days 14 and 21. The NOAEL for reproductive effects was 5 mg/kg/day. The developmental toxicity study found effects on several parameters. The only effect noted at 125 mg/kg/day was a slight decrease in maternal weight gain. Maternal weight gains were depressed to a greater extent at 500 and 2000 mg/kg/day. Ossification variations and delayed ossification were increased significantly at 2000 mg/kg/day and were above control levels at 500

mg/kg/day. The NOAEL for developmental toxicity was 125 mg/kg/day. Alkylate 215 did not have any unusual or selective reproductive or developmental toxicity. © 1992 Society of Toxicology.

Alkylate 215 (A-215) is a commercial linear alkylbenzene mixture used in the manufacture of detergent sulfonates. These detergent sulfonates have been tested extensively for health effects, including developmental and reproductive effects (Palmer *et al.*, 1975, 1975a; Nolen *et al.*, 1975). In contrast, no such studies were available on the linear alkylbenzene precursors or on related materials. These effects are of interest because of the possibility of exposure of workers during manufacturing and subsequent processing operations. In a companion paper, A-215 and two related products were shown to be negative in a battery of genotoxicity assays (Robinson and Nair, 1992). The present studies were undertaken to assess the possible effects of A-215 on reproduction and fetal development in rats.

### METHODS

**Test material.** A-215 (CAS number 68648-87-3) is a clear liquid which has a boiling point of 406°F. Commercial grade test material was supplied by Monsanto Co. with a purity of 98.5%. This material is a mixture of linear alkylbenzenes in which the phenyl group is attached at various internal carbon positions on the chain. The composition of the linear alkyl chains is as follows: C<sub>10</sub>, 21.43%; C<sub>11</sub>, 42.60%; C<sub>12</sub>, 35.23%; and C<sub>13</sub>, 0.74%. The test material was always given by gavage as a single daily dose in a corn oil vehicle at a volume of 5 ml/kg. Control groups received the same volume of corn oil only. Before the studies began, dosing solutions were analyzed for homogeneity of mixing and stability; analyses for concentration were carried out periodically throughout the studies to confirm A-215 concentration.

**Test animals and housing conditions.** CD rats (Charles River Breeding Laboratories, Portage, MI and Wilmington, MA) were housed in wire mesh cages and given free access to commercial laboratory feed (Ralston Purina Co., St. Louis, MO) and tap water. Animal rooms were on a 12-hr light/dark cycle; the temperature range was 65-79°F, and relative humidity was between 17 and 76%.

**Experimental design of reproduction study.** Four groups of 30 male and 30 female rats, designated as the F<sub>0</sub> generation, were given the test material

<sup>1</sup> This work was reported in part at the 26th Annual Meeting of the Society of Toxicology, February 24-27, 1987, Washington, DC, and at the 29th Annual Meeting of the Society of Toxicology, February 12-16, 1990, Miami Beach, FL.

at dosages of 0, 5, 50, and 500 mg/kg/day for a period of about 10 weeks before mating. For mating, one male rat was cohoused with one female within the same treatment group nightly until evidence of mating was observed or until 7 nights had elapsed. At this time, all unmated females were housed nightly with different males within their treatment group for a second 7 day interval. The same procedure was repeated for a third 7-day interval for unmated females. The presence of a copulatory plug or sperm in the vaginal smear was considered to be sufficient evidence that a female had mated. The day on which such evidence was observed was designated as Day 0 of gestation. Once mated, the females were housed individually for the remainder of gestation. Females were dosed during mating, gestation, and lactation for a total of 127 days of treatment. Dosing of males continued for 2 weeks after mating, at which time they were euthanized after a total of 105 treatment days.

The offspring of the F<sub>0</sub> generation were designated as the F<sub>1</sub> generation. After the F<sub>1</sub> pups were weaned, the F<sub>0</sub> females were euthanized. Two pups per sex per litter were chosen at random to become a pool of animals from which the F<sub>1</sub> adult generation was chosen. In the final selection of 30 males and 30 females, each litter weaned was represented by at least one pup per sex. Selected F<sub>1</sub> rats were dosed for an 11-week pre-mating period which began during study week 18. The mating procedure for the F<sub>1</sub> generation was the same as for the F<sub>0</sub> generation. Rats in the F<sub>1</sub> generation that either did not mate or did not show evidence of fertility during the normal study interval were used in a special mating study. They were cohoused with rats which had not been used in the study, one on-test male with two females and one on-test female with one male. Cohousing continued nightly until the female mated or for 10 nights. In all cases, dosing of the F<sub>1</sub> females continued through mating, gestation, and lactation. F<sub>1</sub> males which had impregnated a female were euthanized 3 weeks after mating. F<sub>1</sub> females that delivered a litter were euthanized after weaning of the F<sub>2</sub> pups. All F<sub>2</sub> pups were euthanized at weaning. The females in the special mating study were euthanized on Day 13 of gestation since only mating and fertility were measured in this segment, and the remaining F<sub>1</sub> males were euthanized 1 week later.

All adult and weanling rats were observed for mortality and clinical signs of toxicity twice daily. Detailed physical examinations were performed weekly. Male body weights were recorded weekly; female body weights were recorded weekly before mating, on Days 0, 7, 14, and 20 of gestation, on

Days 0, 4, 14, and 21 of lactation, and weekly again after lactation. Food consumption was measured weekly during the pre-mating treatment period. Litters were examined twice daily for general appearance of the pups and for dead pups. The number of pups in each litter and the pup sex distribution were recorded at birth (Day 0) and at Days 4, 7, 14, and 21 of lactation. Individual pup weights were recorded on Days 0, 4, 7, 14, and 21 of lactation.

Complete gross postmortem examinations were done on all animals in the study, both adults and pups. The pituitary glands, testes and epididymides, prostate and seminal vesicles, vagina, uterus, ovaries, and gross lesions were examined microscopically for all F<sub>0</sub> and F<sub>1</sub> adults in the control and high-dose groups. Gross lesions were also examined from the low- and mid-dose groups. All tissues taken for histological examination were fixed in 10% Formalin, dehydrated, defatted, and embedded in paraffin. A 6-μm section of each tissue was stained with hematoxylin and eosin. Histopathological changes were evaluated and scored by a pathologist on a scale of 1 to 5 for degree or amount present, where 1 is minimal (≤1% of tissue on slide affected), 2 is mild (2-10%), 3 is moderate (11-30%), 4 is moderately severe (31-60%), and 5 is severe (≥60%).

For each study group, the mating index for males was defined as the number of males that mated with a female divided by the number of males cohoused with females; for females, it was the number of females showing evidence of mating divided by the total number of females. The pregnancy rate was defined as the number of pregnant females divided by the number mated. The fertility index for males was the number of males impregnating a female divided by the number mating. Each of the indices was calculated for the matings of the F<sub>0</sub> and F<sub>1</sub> animals; male indices were calculated for the special study of the F<sub>1</sub> animals as well. Pup survival indices, the number of pups alive at a given interval divided by the number of pups at the previous interval, were also calculated for the Day 0-4 and Day 4-21 intervals during lactation.

**Experimental design & developmental toxicity study.** In a preliminary study, groups of five mated rats were given A-215 at dosages of 0, 125, 250, 500, 1000, and 2000 mg/kg/day on Days 6-15 of gestation in order to select doses for the full studies. The only effect noted was a reduction in mean maternal weight gain during the treatment period at the 2000 mg/kg/day level. Based on these results, doses of 125, 500, and 2000 mg/kg/day were selected for the full teratology study. The high-dose level was expected to cause maternal toxicity, based on preliminary results.

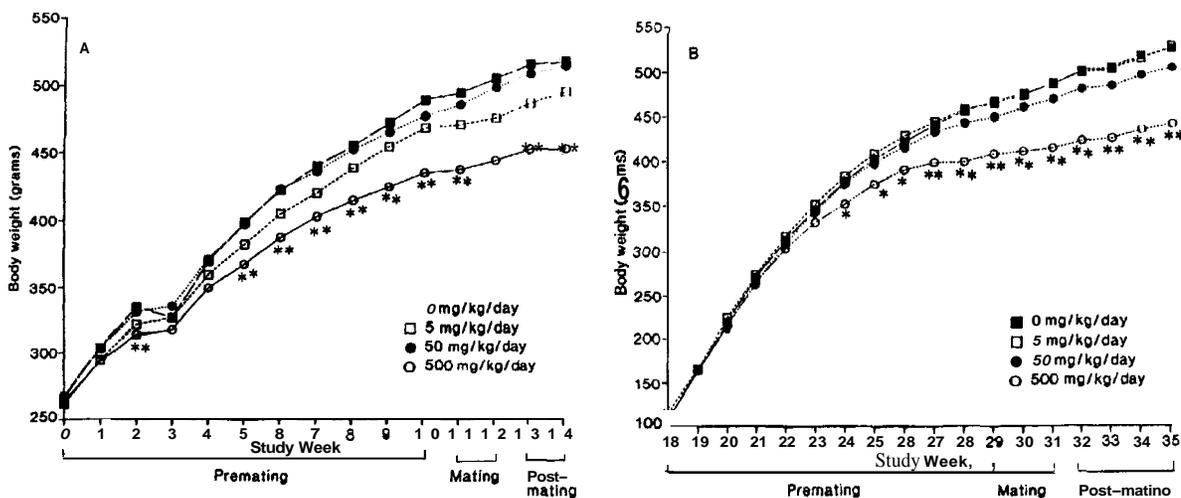


FIG. 1. Mean body weights for F<sub>0</sub>(A) and F<sub>1</sub>(B) adult male rats in the reproduction study. \*Statistically different from control,  $p \leq 0.05$ ; \*\*statistically different from control,  $p \leq 0.01$ .

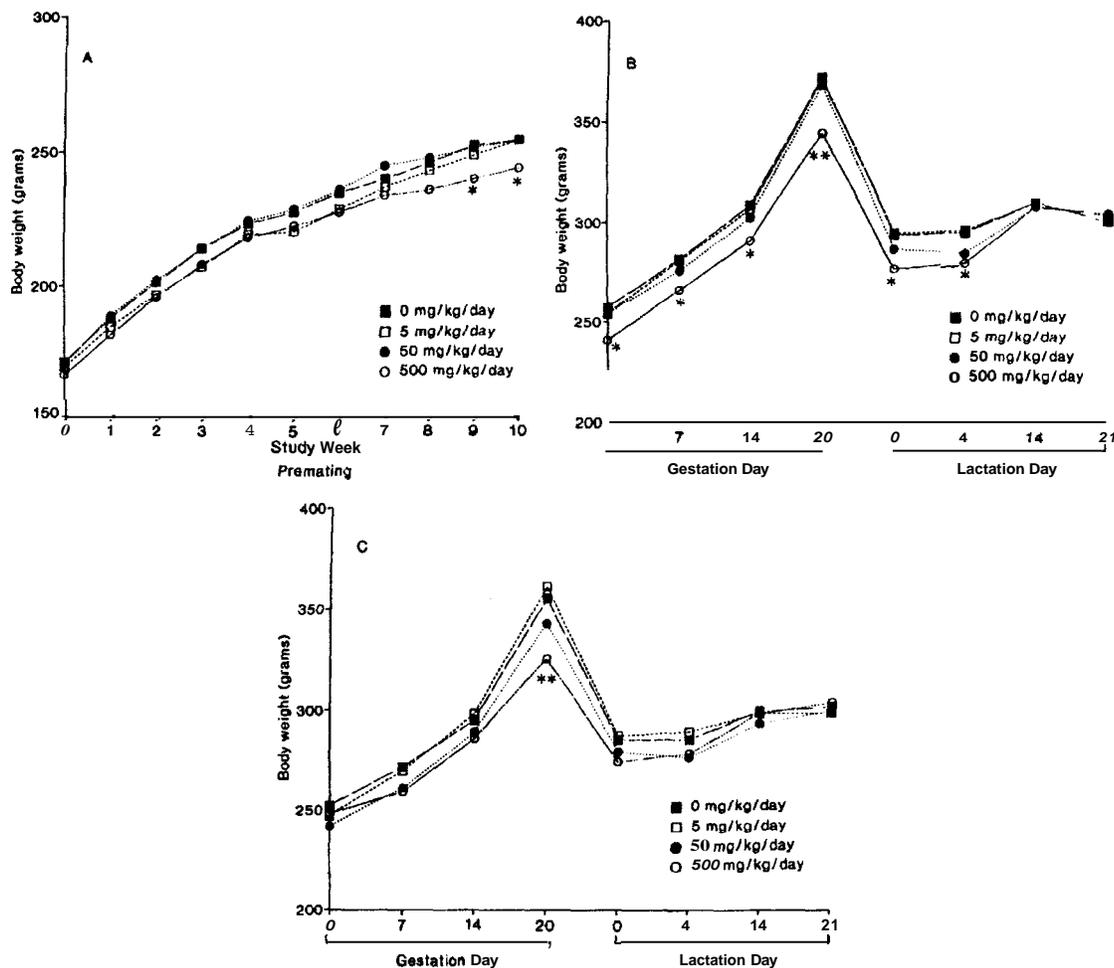


FIG. 2. Mean body weights for  $F_0$  (A, B) and  $F_1$  (C) adult female rats in the reproduction study. Body weights for  $F_1$  females during the pre-mating period were similar to controls at all intervals and are not shown. The number of female rats during gestation and lactation ranged from 18 to 29 (B, C). \*Statistically different from control,  $p \leq 0.05$ ; \*\*statistically different from control,  $p \leq 0.01$ .

For the full teratology study, groups of 24 mated rats were given A-215 on the same schedule as in the preliminary study. Rats were observed twice daily throughout the study, and the body weights were recorded on gestation Days 0, 6, 10, 12, 15, and 20. After the rats were euthanized on gestation Day 20, the fetuses were delivered by caesarean section. The numbers of live, dead, and resorbed fetuses, total implantations, and corpora lutea were recorded. All mated females surviving to Day 20 of gestation were given a complete gross postmortem examination.

All fetuses were weighed, externally sexed, and examined for external alterations, including the palate. About one-half of the fetuses were fixed in Bouin's solution and subsequently examined for soft tissue alterations using a microdissection procedure similar to that described by Staples (1974). The rest of the fetuses were processed for staining with alizarin red S by a method similar to that described by Cray (1962), and examined for skeletal alterations.

**Statistical methods.** Mean body weights, mean weight change, food consumption, corpora lutea, uterine implantation sites, numbers of live fe-

tuses, number of resorptions, preimplantation loss ratio, resorption/implant ratio, gestation lengths, and numbers of offspring were analyzed statistically using methods described previously (Nair *et al.*, 1990). Incidence data, which included mortality rates, pregnancy rates, fertility indices, mating indices, litter survival indices, the incidence of fetuses and litters with malformations and variations, and the incidence of females with resorption sites were analyzed using contingency tables (Nair & *et al.*, 1990). The level of significance for analysis of variance was  $p \leq 0.01$ ; for all other tests, it was  $p \leq 0.05$ .

These studies were conducted in compliance with the United States Environmental Protection Agency's Good Laboratory Practice Standards (U.S. EPA, 1983).

## RESULTS

Prestudy analysis of dosing solutions demonstrated that the formulations were homogeneous and stable when held

**TABLE 1**  
**Mating, Pregnancy, and Fertility Rates**

Dose/group (mg/kg/day)	Mating				Pregnancy		Fertility <sup>b</sup>	
	Females		Males		Females		Males	
	No.	%	NO.	%	No.	%	No.	%
F <sub>0</sub> mating for F <sub>1</sub> litters								
0	28/28	100.0	27/28	96.4	27/28	96.4	26/27	96.3
5	30/30	100.0	27/30	90.0	28/30	93.3	26/27	96.3
50	28/28	100.0	27/28	96.4	<b>25/28</b>	89.3	24/27	88.9
500	28/29	96.6	28/30	93.3	24/28	85.7	25/28	89.3
F <sub>1</sub> mating for F <sub>2</sub> litters								
0	30/30	100.0	25/29	86.2	26/30	86.7	23/25	92.0
5	30/30	100.0	21/30	70.0	29/30	96.1	20/21	95.2
50	26/29	89.7	23/29	79.3	26/26	100.0	23/23	100.0
500	28/30	93.3	21/28	75.0	23/28	82.1	18/21	85.7
Special mating study—F <sub>1</sub> mating for F <sub>2</sub> litters								
0			6/6	100.0			5/6	83.3
5			10/10	100.0			9/10	90.0
50			3/7	42.9			3/3	100.0
500			8/10	80.0			8/8	100.0

<sup>a</sup> Number of females showing evidence of mating—plug, sperm, or pregnancy; number of males for which mating was confirmed in at least one female.

<sup>b</sup> Number of males mated with at least one female for which parturition was evident.

**TABLE 2**  
**Litter Size and Pup Survival Indices in the Reproduction Study**

Dose group (mg/kg/day)	Litter size <sup>a</sup>	Pup viability index at birth <sup>b</sup>		Pup survival indices (days)					
		No.	%	0-4 <sup>c</sup>		0-4 <sup>c</sup>		4-21 <sup>d</sup>	
				No.	%	NO.	%	No.	%
F <sub>1</sub> litters									
0	12.7	339/342	99.1	318/339	93.8			199/108	95.7
5	12.8	350/337	98.0	327/350	93.4			201/221	91.0
50	13.1	313/328 <sup>e</sup>	95.4	289/313	92.3			160/290 <sup>f</sup>	84.2
500	10.0 <sup>g</sup>	229/240 <sup>e</sup>	95.4	187/220 <sup>d,e,f</sup>	85.0			142/150	94.7
F <sub>2</sub> litters									
0	11.3	289/293	98.6	232/289	80.2	232/248 <sup>g</sup>	93.5	154/157	98.1
5	11.6	331/337	98.2	289/331 <sup>e</sup>	87.3	389/306 <sup>g</sup>	94.4	198/204	97.1
50	13.1	256/263	97.3	229/256 <sup>e</sup>	89.5	229/248 <sup>g</sup>	92.3	155/174 <sup>e</sup>	89.1
500	7.0 <sup>h</sup>	138/155 <sup>e</sup>	89.0	116/138	84.1	116/135 <sup>e,g</sup>	85.9	108/111	97.3

<sup>a</sup> Mean No. of pups/litter.

<sup>b</sup> No. of live pups at Day 0/total No. of pups born (live plus dead).

<sup>c</sup> No. of live pups at Day 4 (pre-cull)/total No. of live pups at Day 0.

<sup>d</sup> No. of live pups at Day 21/total No. of live pups at Day 4 (post-cull).

<sup>e</sup> Statistically significant differences from control,  $p \leq 0.05$ .

<sup>f</sup> Excludes data for one female that died on Day 2. At time of death, one live pup remained in the litter.

<sup>g</sup> Excludes data for litters in which all pups died during the Day 0-3 interval.

<sup>h</sup> Statistically significant differences from control  $p \leq 0.01$ .

TABLE 3  
Mean Pup Weights (g) in the Reproduction Study

Dose group (mg/kg/day)	Day:					
	0	4		7	14	21
	F <sub>0</sub> generation (F <sub>1</sub> litters)					
0	6.0	8.4	8.4	13.2	27.0	42.7
5	5.9	8.1	8.1	12.9	27.3	42.1
50	5.8	7.5	7.6	11.4 <sup>a</sup>	25.1	39.6
500	5.8	8.1	8.1	11.4 <sup>a</sup>	23.5 <sup>a</sup>	37.7 <sup>a</sup>
	F <sub>1</sub> generation (F <sub>2</sub> litters)					
0	5.8	8.1	8.3	13.9	27.0	40.5
5	5.8	8.5	8.5	14.4	26.9	42.0
50	6.0	8.1	8.1	13.4	25.3	39.5
500	5.8	8.1	8.1	12.1	22.3 <sup>a</sup>	34.6 <sup>a</sup>

<sup>a</sup> Statistically significant differences from control,  $p \leq 0.05$ .

at room temperature for 5 hr. Analyses of dosing solutions during the studies averaged 90.2%, 90.0%, and 97.1% of nominal concentrations for the low-, mid-, and high-dose groups, respectively, in the reproduction study, and 91.5%, 92.9%, and 97.7% in the same respective groups in the teratology study.

### Reproduction Study

Mortality rates were low in all groups during the F<sub>0</sub> and F<sub>1</sub> generations; there were no significant differences between control and treated groups. Mean body weights for the adult animals are presented in Figs. 1 and 2. Mean body weights in the high-dose-group males were significantly and consistently below control weights in the pre-mating, mating, and postmating periods beginning in the 5th pre-mating week for the F<sub>0</sub> generation and in the 7th pre-mating week for the F<sub>1</sub> generation. Significant differences in the high-dose females were found in the F<sub>0</sub> generation during the last 2 weeks of the pre-mating period, all of gestation, and the 1st week of lactation. F<sub>1</sub> high-dose females had significantly decreased weight gains only on Day 20 of gestation. Male body weights appeared to be more consistently affected over the course of the study, and the weights of the F<sub>0</sub> females more so than those of the F<sub>1</sub> females. No adverse effect of treatment was evident from the gross postmortem and histopathological evaluations.

Mating, pregnancy, and fertility rates are given in Table 1. Male mating indices for the F<sub>1</sub> generation were lower than control values in each of the treated groups, although the differences were not statistically significant. To investigate this finding, the special mating study was set up. When the reproductive performance of the F<sub>1</sub> males in the initial study

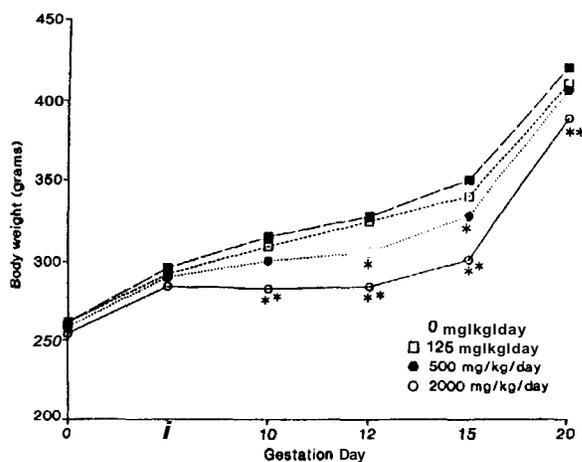


FIG. 3. Mean body weights for dams in the developmental toxicity study. \*Statistically different from control,  $p \leq 0.05$ ; \*\*statistically different from control,  $p \leq 0.01$ .

mating and the special mating were combined, there were no significant differences between the control and the treated groups. A slight decrease in male mating index was found in the mid-dose group (26/30 versus 30/30 in controls), but no dose-related trend was evident, and the high-dose group had 28 of 30 males successfully mating. Therefore, it was concluded that the male mating indices were unaffected by treatment in the F<sub>1</sub> generation.

Mean gestation length was comparable between control and treated groups in both generations with one exception. In the high-dose group, gestation length was significantly increased for the F<sub>2</sub> litter interval from 22.0 days in controls to 22.4 days. Mean pup survival indices are shown in Table 2. The mean numbers of live and total pups at birth were significantly lower than controls in the high-dose groups for

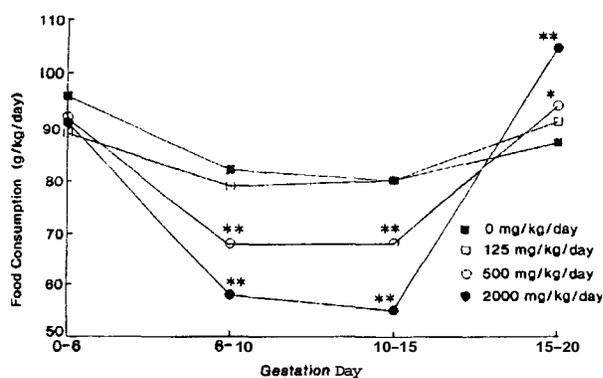


FIG. 4. Mean food consumption for dams in the developmental toxicity study. \*Statistically different from control,  $p \leq 0.05$ ; \*\*statistically different from control,  $p \leq 0.01$ .

**TABLE 4**  
**Incidence of Fetal Skeletal Alterations in the Developmental Toxicity Study**

Dose group (mg/kg/day): No. fetuses (litters) examined:	No. fetuses (litters) affected			
	0 143 (23)	125 129 (23)	500 145 (23)	2000 133 (22)
<b>Malformations</b>				
Cervical vertebrae-transverse process fused	0 (0)	0 (0)	0 (0)	1 (1)
Wavy ribs	1 (1)	0 (0)	0 (0)	3 (2)
Total fetuses (litters) with malformations	1 (1)	0 (0)	0 (0)	4 (3)
Percentage fetuses (litters) with malformations	0.7 (4.3)	0 (0)	0 (0)	2.3 (9.1)
<b>Variations</b>				
<b>Skull</b>				
Interparietal, incompletely ossified	5 (4)	2 (2)	7 (4)	17 (7)
Hyoid, not ossified	15 (8)	4 (4)	7 (6)	24 (11)
Hyoid, incompletely ossified	3 (3)	1 (1)	1 (1)	0 (0)
Hyoid split	1 (1)	0 (0)	0 (0)	0 (0)
Supraoccipital, incompletely ossified	10 (7)	0 (0)	6 (4)	22 (11)
Supraoccipital, split	0 (0)	0 (0)	0 (0)	1 (1)
Parietal, incompletely ossified	0 (0)	0 (0)	0 (0)	9 (3)
Frontal, incompletely ossified	0 (0)	0 (0)	0 (0)	6 (3)
Nasal, incompletely ossified	0 (0)	0 (0)	0 (0)	3 (2)
Maxilla, incompletely ossified	1 (1)	0 (0)	0 (0)	9 (4)
Malar, incompletely ossified	4 (3)	0 (0)	0 (0)	10 (5)
Squamosal, incompletely ossified	1 (1)	0 (0)	0 (0)	4 (2)
<b>Vertebrae</b>				
Cervical, incompletely ossified	2 (2)	1 (1)	2 (2)	3 (3)
7th cervical ossification adjacent to transverse process	0 (0)	0 (0)	0 (0)	1 (1)
Thoracic, incompletely ossified	11 (6)	15 (13)	14 (10)	31 (17)
Thoracic, split	2 (2)	3 (2)	1 (1)	2 (1)
Thoracic, not ossified	0 (0)	0 (0)	0 (0)	2 (2)
Lumbar, transverse process incompletely ossified	0 (0)	0 (0)	0 (0)	0 (0)
Lumbar, centra incompletely ossified	0 (0)	0 (0)	0 (0)	2 (2)
5th Lumbar present	64 (3)	1 (1)	8 (4)	3 (3)
Sacral, incompletely ossified	9 (6)	5 (3)	7 (4)	15 (7)
Sacral, not ossified	5 (3)	0 (0)	2 (2)	6 (3)
Caudal, transverse process incompletely ossified	10 (8)	6 (4)	7 (5)	16 (8)
Caudal, not ossified	2 (2)	1 (1)	0 (0)	1 (1)
Caudal, centra incompletely ossified	0 (0)	0 (0)	0 (0)	1 (1)
<b>Sternebrae</b>				
6th not ossified	18 (10)	5 (5)	4 (4)	14 (7)
5th not ossified	28 (11)	20 (13)	10 (7)	21 (11)
5th split	2 (1)	0 (0)	0 (0)	1 (1)
4th incompletely ossified	1 (1)	0 (0)	0 (0)	1 (1)
4th not ossified	0 (0)	0 (0)	0 (0)	1 (1)
2nd not ossified	0 (0)	0 (0)	0 (0)	1 (1)
<b>Ribs</b>				
Rudimentary	20 (14)	15 (10)	48 (18)	52 (20)
Incompletely ossified	0 (0)	0 (0)	0 (0)	2 (2)
Thickened	1 (1)	0 (0)	0 (0)	4 (3)
Short	4 (3)	0 (0)	8 (4)	4 (4)
Floating	0 (0)	1 (1)	0 (0)	0 (0)
14 pairs present	0 (0)	0 (0)	0 (0)	1 (1)
Metatarsals, not ossified	0 (0)	1 (1)	0 (0)	0 (0)
Pubis, incompletely ossified	1 (1)	0 (0)	0 (0)	5 (4)
Pubis, not ossified	1 (1)	0 (0)	0 (0)	0 (0)
ischium, incompletely ossified	0 (0)	0 (0)	0 (0)	0 (0)
Total fetuses (litters) with variations	82 (21)	54 <sup>a</sup> (22)	82 (23)	106 <sup>a</sup> (22)
Percentage fetuses (litters) with variations	57.3 (91.3)	41.9 <sup>a</sup> (95.7)	57.2 (100)	79.7 <sup>a</sup> (100)

<sup>a</sup> Significantly different from control  $p \leq 0.05$ .

both litter intervals. The mean numbers of dead pups were unaffected by treatment. The pup viability index at birth was reduced significantly in both mid- and high-dose groups for the  $F_1$  litters but only in the high-dose group of the  $F_2$  litters. For the  $F_1$  litters, survival during the Day 0–4 and 4–21 lactation period intervals was significantly reduced in the high-dose and mid-dose groups, respectively. All pups died during the Day 0–3 interval for three  $F_2$  litters in the control group, two in the mid-, and two in the high-dose groups; the cause of death in each case was undetermined. Considering all  $F_2$  litters, survival was significantly increased in the low- and mid-dose groups relative to controls because of low survival in controls. If litters with early total mortality are excluded, survival in the Day 0–4 interval was significantly reduced only in the high-dose group. In the high-dose group, significant decreases in pup weights were found at most intervals after Day 4 in both generations (Table 3). In the mid-dose group, pup weights in the  $F_1$  litters were lower than controls at all intervals, but the differences were statistically significant only at the Day 7 interval.

#### Developmental Toxicity Study

The death of a single female in the high-dose group was attributed to injury from the dosing procedure; no other animals died on test. Maternal body weights during gestation are given in Fig. 3. Mean weight gains were slightly reduced at the low dose and significantly reduced at the mid and high doses when compared to controls during the treatment period. Compensatory increases in weight gain occurred in the Day 15–20 posttreatment period in both the mid- and the high-dose groups. Food consumption (Fig. 4) was also significantly reduced during treatment and significantly increased after treatment for these two groups. Reproductive parameters did not appear to be affected by treatment.

No treatment-related increases in soft tissue malformations and variations were found. Fetal skeletal malformations and variations are described in Table 4. There were no significant differences between control and treated groups in the number of fetuses and litters with malformations. The most common skeletal malformation was wavy ribs, found in one control fetus (one litter) and three high-dose fetuses (two litters). The incidence of fetuses with at least one ossification variation was significantly decreased in the low-dose group and significantly increased in the high-dose group. The decrease in skeletal variations at the low dose was not considered treatment related. In the mid-dose group, rudimentary rib structures were notably increased. At the high-dose level, incomplete ossification of several cranial bones and vertebral elements was increased. The incidence of rudimentary rib structures was also increased in this group.

#### DISCUSSION

In the A-215 reproduction study, there was evidence of toxicity in both adults and offspring at the 500 mg/kg/day

dose level. The most consistent effects were depressed weight gains in adults, smaller litters, and fewer live pups; decreased pup survival and lower pup weights were also found at some intervals, as was increased gestation length for the  $F_2$  litters. At the 50 mg/kg/day dose level, there was no consistent effect of treatment through the two generations and the two litter intervals in parental or neonatal animals. Decreased pup survival at this level for both litters during the Day 4–21 lactation period was not considered related to treatment because of the lack of a similar effect at the high dose. The slight decrease in pup weights at this level may have been related to treatment. Maternal body weights during gestation and lactation also tended to be lower in the mid-dose group than in controls, although not significantly so. However, the finding of a significant pup weight change only in one generation and time point suggests a marginal effect occurred, if any. Under the conditions of this study, treatment at the 5 mg/kg/day dose level had no observed adverse effects.

The findings in the developmental toxicity study were consistent with those in the reproduction study. Depressed maternal weight gains were seen at 500 mg/kg/day and increasingly so at 2000 mg/kg/day. The relationship to treatment of the slight increase in fetuses with wavy ribs at 2000 mg/kg/day is unclear. Khera (1985) has shown a high correlation between fetal rib malformations, including wavy ribs, and maternal toxicity in the rat during pregnancy. It is possible that the slight increase in wavy ribs was related to the maternal toxicity seen at this dose level. At the 500 and 2000 mg/kg/day levels, the general ossification retardation found is suggestive of a fetotoxic response to treatment. Staples and Wilson (1975) have suggested that agents should be classified as teratogenic only if they produce fetal effects at doses which are not overtly toxic to the maternal animal. By this definition, A-215 is not classified as a teratogen.

Developmental effects were found in both studies at doses which were also toxic to the parental animals. It cannot be determined whether or not the effects in the offspring were secondary to those in the adults. When using these studies within the framework of an overall risk assessment, it is important to consider both the dose levels and the status of the parental animals. Johnson (1988) has concluded that when embryotoxicity is found only at maternally toxic doses, and when exposure is below the level producing adult toxicity, "relatively modest safety factors are sufficient for safe cross-species extrapolation." The use of proper handling procedures during the manufacture of this intermediate and its subsequent conversion into the sulfonate should keep exposure of workers far below levels which have been found to produce toxicity in adult rats or their offspring.

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Alkylate 215 / 53570-71-1  
 Alkylate 225 / 53570-72-2  
 Alkylate 230 / 53570-73-3

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 10-July-2002

## The Genotoxic Potential of Linear Alkylbenzene Mixtures in a Short-Term Test Battery<sup>1</sup>

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The Genotoxic Potential of Linear Alkylbenzene Mixtures in a Short-Term Test Battery. ROBINSON, E. C., AND NAIR, R. S. (1992). *Fundam. Appl. Toxicol.* 18, 540-548.

Alkylate 215 (A-215), Alkylate 225 (A-225), and Alkylate 230 (A-230) are mixtures of C<sub>10</sub>-C<sub>14</sub> linear alkylbenzenes used as intermediates for the manufacture of detergents. These products were evaluated for genotoxic activity in the Ames bacterial mutagenesis assay (strains TA98, 100, 1535, and 1537), the CHO/HGPRT mammalian cell forward gene mutation assay, and the *in vivo* rat bone marrow chromosome assay. The Ames and CHO/HGPRT assays were conducted both with and without the addition of Aroclor-induced rat liver S9. The maximum concentrations evaluated were 10 mg/plate (A-215) and 3 mg/plate (A-225 and A-230) for the Ames test, and 1.5 mg/ml (A-215 and A-225) and 2.0 mg/ml (A-230) for the CHO/HGPRT assay. In each case, the highest concentrations produced evidence of either toxicity or insolubility. The highest dose in the bone marrow cytogenetics assay was 12,700 mg/kg, a level which produced significant weight loss. The results of all tests were negative, indicating a lack of genotoxic activity as measured by the battery of tests used. © 1992 Society of Toxicology.

mation relevant to the human health effects of LABs used in detergent manufacture. Because of the use of these materials as intermediates, there is a potential for exposure to occur in the workplace. Genotoxicity testing of three LAB products designated Alkylates 215, 225, and 230 (A-215, A-225, and A-230) is the subject of the present report. These materials have been found to be practically nontoxic orally and dermally in rats and rabbits, respectively, with acute oral LD50 values of greater than 15,000 mg/kg and dermal LD50 values of greater than 10,200 mg/kg (Monsanto, unpublished data). All were slightly irritating to the rabbit eye and slightly to moderately irritating to rabbit skin. In human patch tests, A-215 was a primary irritant and a possible cumulative irritant. To investigate whether exposure could pose a genetic risk to the human population, we carried out a series of studies including both *in vitro* and *in vivo* assays: the *Salmonella/typhimurium* histidine reversion assay, the CHO/HGPRT gene mutation assay, and the *in vivo* bone marrow cytogenetics assay in rats.

### METHODS

**Test Materials.** A single lot of each test material was used in the three assays: lot CC7996 for A-215, lot CC8036 for A-225, and lot CC7655 for A-230. Commercial grade test materials were supplied by Monsanto Chemical Co. and each had a purity of approximately 98.5%. These materials are mixtures of linear alkylbenzenes in which the phenyl group is attached at various internal carbon positions on the chain. The composition of the alkyl chains for each test material is given in Table 1.

***Salmonella typhimurium* mammalian microsome assay.** The assays were conducted using *Salmonella* strains TA1535, TA100, TA1537, and TA98 in the presence and absence of Aroclor-induced rat and mouse liver microsomes (S9) by the standard plate incorporation method (Ames *et al.*, 1975; Maron *et al.*, 1981). The S9 mix used for A-225 and A-230 studies was prepared in-house and used at a 5% concentration; the mix used for A-215 studies was purchased (Litton Bionetics Inc., Kensington, MD) and used at a 10% concentration. The test materials were dissolved in DMSO and tested at concentrations of 3000, 1000, 300, 60, 12, and 3 µg/plate (A-225 and A-230) or 10, 4, 3, 1.5, 1.0, 0.25, 0.2, 0.1, 0.04, and 0.01 µl/plate (A-215). A spot test was also performed for A-215 using both rat and mouse liver Aroclor-induced microsomes at a concentration of 25 µl. The solvent control for all assays was DMSO. Statistical methods were used to make decisions on test results from plate incorporation tests. Values of revertants per plate were transformed using log (base 10) for further analysis. Bartlett's test (A-215) (Snedecor and Cochran, 1967) or Levene's test (A-225 and A-230) (Levene,

C<sub>10</sub>-C<sub>14</sub> linear alkylbenzene (LAB)<sup>2</sup> mixtures are used as intermediates in the manufacture of the sulfonated derivatives which are marketed as surfactants in detergents. The linear products replaced the branched chain isomers in detergent applications 27 years ago because of their greater biodegradability. About 600,000,000 lb is produced annually in the United States. Although they are manufactured from benzene, their toxicity profile is quite different, possibly because of both volatility and metabolic differences. While toxicity data for aquatic organisms have recently been published (Gledhill *et al.*, 1991), there is little published infor-

<sup>1</sup> This work was reported, in part, at the 29th Annual Meeting of the Society of Toxicology, February 12-16, 1990, Miami Beach, FL.

<sup>2</sup> Abbreviations used: DMSO, dimethyl sulfoxide; 4NQ, 4-nitroquinoline; EMS, ethyl methanesulfonate; B(a)P, benzo[a]pyrene; CP, cyclophosphamide; 2NF, 2-nitrofluorene; NaNO<sub>2</sub>, sodium nitrite; 9AA, 9-aminoanthracene; 2AAF, 2-acetylaminofluorene; DMN, dimethylnitrosamine; CHO/HGPRT, Chinese hamster ovary hypoxanthine-guanine phosphoribosyl transferase; LAB, linear alkylbenzene.

TABLE 1  
Composition by Percentage of Alkyl Chains  
in Linear Alkylbenzene Test Materials

	A-215	A-225	A-230
C <sub>10</sub>	21.43	10.58	0.71
C <sub>11</sub>	42.60	26.99	2.99
C <sub>12</sub>	35.23	51.09	11.62
C <sub>13</sub>	0.74	10.65	43.64
C <sub>14</sub>	0.0	0.69	41.05

1960) was performed to determine if significant differences exist among treatment variables. Treatments were compared with the controls using Dunnett's *t* test (Dunnett, 1955, 1964) and within-levels pooled variance. Dose response was evaluated for all treatments which were not significantly lower ( $p \leq 0.01$ ) than the controls. Dose response was analyzed with regression analysis for a log-log straight line. A *t* test was used to evaluate the significance of the dose response. A positive response was indicated if three or more treatments on the initial test, and retest if performed, were significantly greater than the control ( $p \leq 0.01$ ) and if there was a significant positive dose response for the initial test or retest, if performed.

**CHO/HGPRT gene mutation assay.** The assays were performed according to O'Neill *et al.* (1977a,b); methods were consistent with published guidelines (Li, 1985; Li *et al.*, 1987). The mutation frequency was transformed using the most suitable transformation factor  $(X + 1)^{0.15}$ , to reduce scatter and produce a more homogeneous variance among treatment types. The transformed mutation frequency for each test article concentration causing no greater than 90% toxicity was compared to that of the solvent control by a one-tailed Student *t* test using the pooled, intergroup variance. This analysis determined whether the treatment groups were the same as the controls or greater than the controls with a significance level of  $p \leq 0.01$ . Dose-response analyses were performed on the transformed mutation frequency by the one-way analysis of variance method outlined by Snee and Irt (1981). The significance level for the dose-response analyses was  $p \leq 0.01$ . Two independent mutagenicity experiments were performed. In the first experiment, A-215, A-225, and A-230 at concentrations of 100–1600  $\mu\text{g/ml}$  were tested in the absence of S9 or in the presence of 1, 2, 5, and 10% S9 (v/v, S9 in cofactor mixture). In the second experiment, 100–2000  $\mu\text{g/ml}$  of A-215, A-225, and A-230 were tested in the absence and presence of 1 and 5% S9, respectively. Alkylate solutions were prepared in ethyl alcohol, and the same solvent was used as with the control. A positive response was indicated if at least one of the three highest concentrations with a mean survival rate of at least 10% had a mean mutation frequency significantly greater than the control values ( $p \leq 0.01$ ), and if the change in this value with increasing concentration had a significant ( $p \leq 0.01$ ) linear component of the dose-response relationship up to a maximum toxicity level of 90%.

**Mammalian genotoxicity in vivo: Rat bone marrow cytogenetics.** A-215, A-225, and A-230 were given via gavage undiluted or dissolved in corn oil, and the solutions were given once to three groups of 18–24 male and female Sprague-Dawley CD rats at dosages of 2000, 6000, and 12,700 mg/kg (A-215) or 1200, 4000, and 12,700 mg/kg (A-225 and A-230). Vehicle control groups of 24 male and 24 female rats were given corn oil, and 6 males and 6 females were given 40 mg/kg of CP as the positive control. Six animals of each sex for each of the control and treated groups were euthanized at 6, 12, 24, and 48 hr after treatment. The positive control animals were terminated at 24 hr. Two hr before termination, colchicine (2 mg/kg) was given to all animals by intraperitoneal injection to arrest cells in metaphase. Immediately after termination, bone marrow cells were collected from both femurs of each animal and processed for slide preparation according to the modified techniques described by Evans (1976) and Killian *et al.* (1977). When possible, 60 cells per animal (360 cells per treatment per time period)

were examined for chromosome aberrations. The mean mitotic indices, mean chromosome numbers, percentage aberrant cells, and the mean number of aberrations per cell for each group were statistically compared using the Kruskal-Wallis nonparametric analysis of variance (KW-ANOVA) and nonparametric pairwise group comparisons using a significance level of  $p \leq 0.05$ .

## RESULTS

### *Microbial Mutagenicity: Salmonella/Histidine Reversion Assay*

The spot test with A-215 did not reveal any significant differences from the controls with rat S9, mouse S9, or without microsomal activation. The initial plate incorporation assay with A-215 resulted in a significant difference ( $p \leq 0.01$ ) between the solvent controls and the sample with strain TA98 plus S9 at all concentrations. Most of the treated cultures were slightly greater than twice the control value. A significant difference was also found with strain TA1535 without S9 at a single concentration. There was no significant dose response in either case. After a second and third retest of strain TA98 with S9, a significant difference from the control was found at 200 nl/plate only after the second retest and at none of the levels after the third. Again, there was no significant dose response. A retest with strain TA1535 without S9 found no significant differences or dose response. Retests of strain TA100 with and without S9 and of strain TA1535 with S9 were carried out because of initial unacceptably high solvent controls; no statistically significant differences were found. For A-225 and A-230, there were no statistically significant differences between solvent controls and samples, nor were there any significant dose-response relationships found. The positive controls yielded the expected positive responses (Table 2).

### *Mammalian Genotoxicity in vitro: CHO/HGPRT Gene Mutation*

In cytotoxicity studies, significant effects ( $\geq 50\%$  cell killing) occurred at the 100  $\mu\text{g/ml}$  level for A-215 only without added S9. A-225 had significant effects at the same level both with and without S9. Cytotoxicity did not reach the 50% level with A-230 at any level tested. Two individual experiments were performed for the evaluation of LABs in CHO cells. In the preliminary assay, LABs at concentrations from 100 to 1600  $\mu\text{g/ml}$  were tested for mutagenicity in the absence or presence of 0.74, 1, 1.48, 2, 3.7, 5, 7.4, or 10% S9. Significant cytotoxicity was observed for A-215 concentrations at and above 250  $\mu\text{g/ml}$  without S9 and 1000  $\mu\text{g/ml}$  with S9. Cytotoxicity was also significant for A-225 at levels of 500  $\mu\text{g/ml}$  and above without S9 and also with 1 and 2% S9, and at 1100  $\mu\text{g/ml}$  with 5% S9. For A-230, cytotoxicity was significant at 1600  $\mu\text{g/ml}$  both with and without S9, except for the 1% S9 assay. In the cultures without metabolic activation, a statistically significant higher mutant frequency was found at the 250  $\mu\text{g/ml}$  dose of A-215.

TABLE 2  
Mutagenicity Testing in *Salmonella typhimurium* Strains TA1535, TA100, TA1537, and TA98

Test Material and Treatment ( $\mu\text{g}$ or nl/plate)	Revertants/plate				
	S9 mix	TA1535	TA100	TA1537	TA98
<b>I. Spot test</b>					
A-215 25,000	-	24	277	11	17
Solvent control <sup>a</sup>	-	19	294	6	23
A-215 25,000	+	20	260	12	40
Solvent control	+	19	233	6	27
A-215 25,000	+ <sup>b</sup>	34	327	20	45
Solvent control	+ <sup>b</sup>	25	392	13	38
<b>II. Plate incorporation assays</b>					
First run					
A-215 10	-	28.3 $\pm$ 3.51	307 $\pm$ 51.5 <sup>c</sup>	8.0 $\pm$ 1.0	25.7 $\pm$ 5.13
40	-	23.0 $\pm$ 2.65	344 $\pm$ 33.5	9.0 $\pm$ 3.6	19.3 $\pm$ 5.51
200	-	29.0 $\pm$ 8.00	310 $\pm$ 17.6	10.7 $\pm$ 0.58	17.3 $\pm$ 3.79
1,000	-	23.3 $\pm$ 3.21	318 $\pm$ 33.3	10.0 $\pm$ 1.0	18.7 $\pm$ 1.15
3,000	-	34.7 $\pm$ 5.03**	296 $\pm$ 57.4	9.0 $\pm$ 1.7	21.7 $\pm$ 2.08
10,000	-	27.3 $\pm$ 4.62	297 $\pm$ 59.2	10.3 $\pm$ 1.5	27.3 $\pm$ 6.03
Solvent control	-	21.7 $\pm$ 0.58	395 $\pm$ 30.8 <sup>d</sup>	7.3 $\pm$ 3.5	23.7 $\pm$ 0.58
Positive controls					
NaNO <sub>2</sub> 9,000	-	691			
9AA 100	-			1620	
2NF 2	-		627		354
Second run					
A-215 10	-		321 $\pm$ 17.7		
40	-		297 $\pm$ 25.1		
200	-		292 $\pm$ 39.0		
1,000	-		307 $\pm$ 20.3		
1,500	-	16.0 $\pm$ 1.0			
3,000	-	14.3 $\pm$ 0.58	322 $\pm$ 58.2		
4,000	-	12.0 $\pm$ 4.0			
10,000	-		322 $\pm$ 33.2		
Solvent control	-	13.0 $\pm$ 3.46	258 $\pm$ 25.5		
Positive controls					
2NF 2	-		814		
NaNO <sub>2</sub> 9,000	-	564			
Third run					
A-215 10	-		245 $\pm$ 11.5		
40	-		236 $\pm$ 30.7		
200	-		166 $\pm$ 57.6		
1,000	-		203 $\pm$ 49.2		
3,000	-		230 $\pm$ 11.8		
10,000	-		179 $\pm$ 22.3		
Solvent control	-		233 $\pm$ 27.0		
Positive control					
2NF 2	-		506		
First run					
A-215 10	+	25.7 $\pm$ 5.8	309 $\pm$ 44.9	11.3 $\pm$ 1.5	72.7 $\pm$ 5.8**
40	+	21.3 $\pm$ 5.5	294 $\pm$ 31.0	10.3 $\pm$ 2.3	79.3 $\pm$ 5.5**
200	+	20.3 $\pm$ 1.2	283 $\pm$ 12.7	7.3 $\pm$ 2.5	63.7 $\pm$ 13.9**
1,000	+	24.3 $\pm$ 2.1	339 $\pm$ 38.4	6.7 $\pm$ 1.5	71.7 $\pm$ 16.0**
3,000	+	22.7 $\pm$ 3.8	303 $\pm$ 27.4	13.7 $\pm$ 2.5	71.7 $\pm$ 4.2**
10,000	+	28.7 $\pm$ 4.9	367 $\pm$ 62.4	12.3 $\pm$ 3.2	70.7 $\pm$ 0.53**
Solvent control	+	24.3 $\pm$ 1.5 <sup>d</sup>	314 $\pm$ 20.3 <sup>d</sup>	9.7 $\pm$ 2.1	29.0 $\pm$ 9.5

TABLE 2—Continued

Test Material and Treatment ( $\mu\text{g}$ or nl/plate)	Revertants/plate				
	S9 mix	TA1535	TA100	TA1537	TA98
Positive controls					
B(a)P 5	+		938		459
2AA 20	+	661		155	
			Second run		
A-215 10	+	15.7 $\pm$ 3.2	280 $\pm$ 46.6		27.3 $\pm$ 2.5
40	+	11.0 $\pm$ 3.6	299 $\pm$ 15.0		33.7 $\pm$ 4.9
200	+	15.3 $\pm$ 2.1	294 $\pm$ 24.4		39.0 $\pm$ 1.0**
1,000	+	21.3 $\pm$ 3.1	297 $\pm$ 26.8		30.0 $\pm$ 7.2
3,000	+	21.0 $\pm$ 11.5	301 $\pm$ 39.9		32.0 $\pm$ 7.2
10,000	+	13.7 $\pm$ 2.5	296 $\pm$ 6.8		36.0 $\pm$ 4.6
Solvent control	+	13.7 $\pm$ 5.7	304 $\pm$ 29.0 <sup>d</sup>		27.0 $\pm$ 1.7
Positive controls					
B(a)P 5	+		1611		896
2AA 20	+	511			
			Third run		
A-215 10	+		191 $\pm$ 43.0		
40	+		210 $\pm$ 3.06		
200	+		227 $\pm$ 15.0		39.0 $\pm$ 6.2
250	+				35.3 $\pm$ 9.3
1,000	+		229 $\pm$ 12.9		32.0 $\pm$ 5.3
3,000	+		238 $\pm$ 29.7		
10,000	+		204 $\pm$ 12.2		
Solvent control	+		219 $\pm$ 39.8		34.7 $\pm$ 3.2
Positive control					
B(a)P 5	+		1649		810
A-225 3	-	25.3 $\pm$ 2.5	109.0 $\pm$ 15.7	8.7 $\pm$ 0.6	20.0 $\pm$ 2.0
12	-	24.0 $\pm$ 1.0	106.7 $\pm$ 7.6	8.3 $\pm$ 7.1	22.3 $\pm$ 4.5
60	-	23.3 $\pm$ 1.2	97.7 $\pm$ 12.4	7.0 $\pm$ 2.0	19.3 $\pm$ 4.0
300	-	22.7 $\pm$ 4.5	83.0 $\pm$ 12.5	10.0 $\pm$ 2.8	17.7 $\pm$ 3.2
1,000	-	27.7 $\pm$ 1.5	103.0 $\pm$ 6.1	4.7 $\pm$ 3.1	19.0 $\pm$ 4.0
3,000	-	25.7 $\pm$ 1.5	103.0 $\pm$ 12.1	9.3 $\pm$ 1.5	20.3 $\pm$ 4.6
Solvent control	-	24.0 $\pm$ 6.0	101.0 $\pm$ 15.1	11.0 $\pm$ 1.0	22.0 $\pm$ 2.0
Positive controls					
4NQ 0.1	-		858		172
0.05	-		475		118
0.01	-		191		47
NaNO <sub>2</sub> 5,000	-	587			
2,500	-	387			
500	-	85			
9AA 30	-		164		
15	-		20		
3	-		10		
A-225 3	+	12.7 $\pm$ 3.2	98.0 $\pm$ 7.0	8.7 $\pm$ 4.0	34.7 $\pm$ 6.8
12	+	15.7 $\pm$ 2.1	94.0 $\pm$ 8.7	9.7 $\pm$ 2.1	46.0 $\pm$ 12.1
60	+	10.3 $\pm$ 4.2	92.0 $\pm$ 12.5	12.0 $\pm$ 3.0	39.3 $\pm$ 17.0
300	+	15.0 $\pm$ 3.5	95.0 $\pm$ 15.9	10.3 $\pm$ 3.1	29.0 $\pm$ 4.4
1,000	+	13.7 $\pm$ 2.1	100.3 $\pm$ 6.4	12.0 $\pm$ 3.0	33.3 $\pm$ 7.4
3,000	+	10.7 $\pm$ 4.5	94.7 $\pm$ 12.6	8.7 $\pm$ 4.0	32.7 $\pm$ 6.5
Solvent control	+	14.0 $\pm$ 2.6	103.3 $\pm$ 12.1	11.3 $\pm$ 2.1	33.7 $\pm$ 6.7
Positive controls					
B(a)P 2	+		342		
1	+		183		
0.2	+		128		

TABLE 2—Continued

Test Material and Treatment ( $\mu\text{g}$ or nl/plate)		Revertants/plate				
		S9 mix	TA1535	TA100	TA1537	TA98
2AA	30	+	T <sup>c</sup>		T	
	15	+	T		173	
	3	+	392		99	
2AAF	30	+				1038
	15	+				877
	3					366
A-230	3	-	20.3 $\pm$ 5.9	108.0 $\pm$ 16.0	8.7 $\pm$ 2.1	24.7 $\pm$ 1.5
	12	-	23.7 $\pm$ 2.1	100.3 $\pm$ 8.6	11.3 $\pm$ 2.9	25.3 $\pm$ 7.6
	60	-	24.7 $\pm$ 2.3	96.3 $\pm$ 10.5	7.7 $\pm$ 0.6	17.0 $\pm$ 2.6
	300	-	21.0 $\pm$ 6.6	96.3 $\pm$ 11.6	10.0 $\pm$ 4.6	24.0 $\pm$ 4.0
	1,000	-	21.3 $\pm$ 2.1	104.0 $\pm$ 13.2	8.3 $\pm$ 3.1	25.0 $\pm$ 6.2
	3,000	-	14.0 $\pm$ 5.6	98.0 $\pm$ 5.3	9.3 $\pm$ 2.3	20.3 $\pm$ 6.7
	Solvent control	-	24.0 $\pm$ 6.0	101.0 $\pm$ 15.1	11.0 $\pm$ 1.0	22.0 $\pm$ 2.0
Positive controls						
4NQ	0.10	-		858		172
	0.05	-		475		118
	0.01	-		191		47
NaNO <sub>2</sub>	5,000	-	587			
	2,500	-	387			
	500	-	85			
9AA	30	-			164	
	15	-			20	
	3	-			10	
A-230	3	+	14.0 $\pm$ 3.6	112.7 $\pm$ 38.0	8.7 $\pm$ 3.1	42.0 $\pm$ 7.9
	12	+	10.3 $\pm$ 4.2	98.3 $\pm$ 6.0	8.0 $\pm$ 1.0	33.7 $\pm$ 12.5
	60	+	7.7 $\pm$ 1.5	101.7 $\pm$ 5.7	11.7 $\pm$ 4.2	39.3 $\pm$ 17.6
	300	+	10.0 $\pm$ 1.7	98.0 $\pm$ 19.7	9.7 $\pm$ 3.2	32.0 $\pm$ 2.6
	1,000	+	9.7 $\pm$ 3.1	100.7 $\pm$ 4.0	11.7 $\pm$ 3.1	34.7 $\pm$ 6.1
	3,000	+	12.3 $\pm$ 4.7	117.3 $\pm$ 9.2	9.3 $\pm$ 3.5	36.0 $\pm$ 0.0
Solvent control		+	14.0 $\pm$ 2.6	103.3 $\pm$ 12.1	11.3 $\pm$ 2.1	33.7 $\pm$ 6.7
Positive controls						
B(a)P	2	+		342		
	1	+		183		
	0.2	+		128		
2AA	30	+	T		T	1038
	15	+	T		173	877
	3	+	392		99	366
2AAF	30	+				1038
	15	+				877
	3	+				366

<sup>a</sup> Solvent control was DMSO.

<sup>b</sup> Mouse liver S9.

<sup>c</sup> Plate incorporation assay values are the means of three values  $\pm$  standard deviations.

<sup>d</sup> A solvent control value was outside the acceptable range for this assay, leading to a retest.

<sup>e</sup> T, toxicity was observed.

\*\* Significantly different from solvent control;  $p \leq 0.05$  level.

No significant increases were found for A-225 or A-230 and no statistically significant dose-response relationships were found for any of the LABs. In the final mutagenicity assay, LABs at concentrations from 100 to 2000  $\mu\text{g}/\text{ml}$  were tested in the absence or presence of 1 and 5% S9. Cytotoxicity was

significant for A-215 without S9 at 500  $\mu\text{g}/\text{ml}$  and higher concentrations; with 1% S9, cytotoxicity was seen at 1000  $\mu\text{g}/\text{ml}$ . For A-225, significant cytotoxicity was found at and above 1250  $\mu\text{g}/\text{ml}$  both with and without S9; for A-230, similar effects were found at 2000  $\mu\text{g}/\text{ml}$ . There were no statistically significant

TABLE 3  
Cytotoxicity and Mutagenicity in CHO Cells at Various Concentrations of Aroclor 1254-Induced Rat Liver S9

	Dose (µg/ml)	A-215	A-225	A-230		Dose (µg/ml)	A-215	A-225	A-230
Cytotoxicity <sup>a</sup> (R.S.)					Solvent control				
No S9	0.333	107.4	111.1	100.8	Positive control	10	7.2	—	—
	1.0	105.0	107.3	94.2	DMN	100	103.6	—	—
	3.33	113.7	108.6	93.6	2% S9	100	—	4.5	0.6
	10	106.9	102.7	83.2		500	—	6.1	—
	33.3	109.0	126.2	79.4		1000	—	—	2.3
	100	110.4	88.2	79.4		1100	—	5.6	—
	333	27.3	66.2	58.0		1600	—	—	5.2
	1000	13.7	46.6	58.7	Solvent control	10	—	16.3	6.1
1% S9	0.333	86.6	114.9	82.4	3.7% S9	100	13.0	—	—
	1.0	89.5	105.2	75.7		1000	24.4	—	—
	3.33	110.0	119.4	85.3		1500	2.0	—	—
	10	110.0	104.2	78.4	Solvent control	10	20.9	—	—
	33.3	98.7	90.9	74.8	5% S9	100	—	2.3	2.6
	100	120.4	132.6	72.3		500	—	4.5	—
	333	110.0	53.9	70.5		1000	—	—	3.7
	1000	52.5	17.1	62.1		1100	—	8.1	—
2% S9	0.333	136.5	92.6	86.5		1600	—	—	7.6
	1.0	163.9	107.3	68.0	Solvent control	10	—	7.9	7.1
	3.33	169.1	100.5	73.8	7.4% S9	100	7.7	—	—
	10	174.5	107.6	73.1		1000	10.8	—	—
	33.3	189.7	119.1	76.3		1500	6.3	—	—
	100	149.2	116.6	68.4	Solvent control	10	6.3	—	—
	333	123.0	69.3	59.0	10% S9	100	—	7.3	0.7
	1000	70.3	6.8	56.9		500	—	8.2	—
5% S9	0.333	96.7	94.3	81.2		1000	—	—	4.0
	1.0	144.4	76.0	73.4		1100	—	6.1	—
	3.33	123.3	87.3	72.5		1600	—	—	5.1
	10	135.1	90.7	69.4	Solvent control	10	—	6.2	7.2
	33.3	111.8	120.4	64.5	Positive control				
	100	135.1	110.6	64.7	DMN	100	—	234.2	247.2
	333	143.3	53.2	61.5	Mutagenicity (mutant frequency <sup>b</sup> × 10 <sup>-6</sup> )				
	1000	59.6	23.6	57.2	No S9	100	19.0	2.2	15.4
10% S9	0.333	123.9	85.8	85.9		150	18.1	—	—
	1.0	113.5	96.6	96.3		250	24.0	—	—
	3.33	109.8	89.5	83.5		500	7.8	2.3	—
	10	107.6	107.8	91.6		750	10.2	—	—
	33.3	87.4	80.2	83.0		1000	—	3.0	10.5
	100	103.2	102.2	82.3		1100	—	13.2	—
	333	74.1	55.4	52.6		1250	—	1.1	—
	1000	62.0	45.8	68.2		1500	—	1.6	14.3
Preliminary mutagenicity (mutant frequency <sup>b</sup> × 10 <sup>-6</sup> )						1750	—	—	14.6
No S9	100	3.0	17.6	2.6		2000	—	—	14.5
	250	44.9	—	—		2000	—	—	7.9
	500	—	24.0	—	Solvent control	10	21.6	3.5	—
	1000	0.8	—	3.5	Positive control				
	1100	—	13.2	—	EMS	200	284.5	237.9	167.4
	1600	—	—	1.6	1% S9	100	13.2	—	—
Solvent control <sup>c</sup>	10	3.5	5.5	2.1		250	12.6	—	—
Positive control						500	20.0	—	—
EMS	200	81.1	195.2	322.1		750	41.6	—	—
0.74% S9	100	13.4	—	—		1000	24.8	—	—
	1000	14.4	—	—	Solvent control	10	17.6	—	—
	1500	0.8	—	—	Positive control				
Solvent control	10	4.3	—	—	B(a)P	4	415.8	—	—
1% S9	100	—	5.6	1.6	5% S9	100	—	0.4	17.6
	500	—	11.7	—		500	—	0.8	—
	1000	—	—	2.8		1000	—	8.1	18.2
	1100	—	11.1	—		1250	—	3.7	—
	1600	—	—	2.8		1500	—	0.8	9.1
Solvent control	10	—	3.2	3.5		1750	—	—	15.0
1.48% S9	100	16.3	—	—		2000	—	—	8.3
	1000	16.0	—	—	Solvent control	10	—	4.3	14.8
	1500	21.8	—	—	Positive control				
					DMN	100	—	202.8	155.2

<sup>a</sup> Percentage survival relative to solvent control (average of triplicate treatments).

<sup>b</sup> Mutants per 10<sup>6</sup> clonable cells; average of duplicate treatments in preliminary assays and triplicate treatments in final assays.

<sup>c</sup> Solvent control was ethanol.

*EXP 2*

*EXP 1*

TABLE 4  
*In Vivo* Bone Marrow Chromosome Study in Rats: Body Weight Change at Termination

	Mean body weight change <sup>a,b</sup> (g)	Mean body weight change <sup>a,b</sup> (g)
24-hr termination—males		
A-215		
Vehicle control <sup>c</sup>	-5.500 ± 6.442	
2,000 mg/kg	-8.833 ± 7.574	
6,000 mg/kg	-8.833 ± 10.870	
12,700 mg/kg	-39.000 ± 11.507**	
Cyclophosphamide 40 mg/kg	+1.167 ± 2.639	
A-225		
Vehicle control	+3.833 ± 17.105	
1,200 mg/kg	+15.333 ± 23.062	
4,000 mg/kg	-11.333 ± 11.708	
12,700 mg/kg	-22.500 ± 8.735**	
Cyclophosphamide 40 mg/kg	-1.167 ± 3.601	
A-230		
Vehicle control	-1.833 ± 5.115	
1,200 mg/kg	+1.167 ± 3.061	
4,000 mg/kg	+2.500 ± 8.983	
12,700 mg/kg	-15.000 ± 8.532**	
Cyclophosphamide 40 mg/kg	+0.333 ± 5.854	
24-hr termination—females		
A-215		
Vehicle control	-3.000 ± 5.727	
2,000 mg/kg	-1.167 ± 6.047	
6,000 mg/kg	-8.833 ± 7.627	
12,700 mg/kg	-14.500 ± 9.028**	
Cyclophosphamide 40 mg/kg	+2.833 ± 3.869	
A-225		
Vehicle control	-3.833 ± 1.329	
1,200 mg/kg	-0.167 ± 5.529	
4,000 mg/kg	-7.667 ± 7.554	
12,700 mg/kg	-19.333 ± 5.241**	
Cyclophosphamide 40 mg/kg	+1.833 ± 6.676	
A-230		
Vehicle control	-1.167 ± 6.676	
1,200 mg/kg	-1.167 ± 4.167	
4,000 mg/kg	-4.467 ± 9.368	
12,700 mg/kg	-14.500 ± 7.893	
Cyclophosphamide 40 mg/kg	-6.000 ± 9.230	
48-hr termination—males		
A-215		
Vehicle control	+2.833 ± 4.446	
2,000 mg/kg	+2.500 ± 5.577	
6,000 mg/kg	-25.167 ± 13.408**	
12,700 mg/kg	-47.167 ± 8.954**	
A-225		
Vehicle control	+4.333 ± 5.047	
4,000 mg/kg	-4.000 ± 24.133	
12,700 mg/kg	-10.833 ± 32.823**	
A-230		
Vehicle control	+1.000 ± 4.147	
1,200 mg/kg	-1.000 ± 4.000	
4,000 mg/kg	-4.500 ± 4.461	
12,700 mg/kg	-36.500 ± 13.278**	
48-hr termination—females		
A-215		
Vehicle control	-1.167 ± 20.760	
2,000 mg/kg	-5.167 ± 4.355	
6,000 mg/kg	-16.167 ± 11.303	
12,700 mg/kg	-21.333 ± 7.448**	
A-225		
Vehicle control	+1.000 ± 6.899	
4,000 mg/kg	-15.833 ± 10.381	
12,700 mg/kg	-3.833 ± 36.013**	
12,700 mg/kg	-26.50 ± 9.292** <sup>d</sup>	
A-230		
Vehicle control	+0.833 ± 6.306	
1,200 mg/kg	-6.333 ± 6.563	
4,000 mg/kg	-15.667 ± 6.861**	
12,700 mg/kg	-18.667 ± 3.266**	

<sup>a</sup> Values are the means of six values ± standard deviations.

<sup>b</sup> Statistical results were obtained from analysis of covariance of the final weight with the initial weight as the covariate; \*\**p* ≤ 0.05 level.

<sup>c</sup> Vehicle control was corn oil.

<sup>d</sup> Two of the six animals had weight gains considered improbable. These were excluded and the remaining four reanalyzed for significance.

increases in mutation frequencies for any of the LABs when compared to the negative controls. The positive controls EMS, B(a)P, and DMN yielded the expected positive results in all experiments (Table 3).

#### *Mammalian Genotoxicity in vivo: Rat Bone Marrow Cytogenetics*

Body weights were measured before treatment and before colchicine administration for the 24- and 48-hr terminations. A significant mean body weight loss was found in all LAB-

treated groups dosed with 12,700 mg/kg at both time intervals, with the single exception of females dosed with A-230 at the 24-hr interval. In this group, a large weight loss also occurred in several animals, but it was not statistically significant because other animals gained weight. Significant weight losses also occurred at 48 hr in the males terminated after treatment with 6000 mg/kg of A-215 and in females terminated after 4000 mg/kg of A-230 (Table 4).

The most commonly found aberrations were chromatid gaps and breaks, which occurred in both the solvent control

TABLE 5  
Chromosomal Aberration Frequencies Observed in Bone Marrow Cells from Rats Treated with Alkylates

	No. of cells	Normal	Chromatid gaps	Chromosome gaps	Chromatid breaks	Chromosome breaks	Exchanges	Percentage aberrant cells
6-hr sampling time								
A-215								
Vehicle control <sup>a</sup>	633	633	0	0	0	0	0	0
2,000 mg/kg	547	547	0	0	0	0	0	0
6,000 mg/kg	540	540	0	0	0	0	0	0
12,700 mg/kg	512	512	0	0	0	0	0	0
A-225								
Vehicle control	600	600	0	0	0	0	0	0
1,200 mg/kg	635	634	1	0	1	0	0	0.16
4,000 mg/kg	600	599	0	0	1	0	0	0.17
12,700 mg/kg	641	641	0	0	0	0	0	0
A-230								
Vehicle control	600	600	0	0	0	0	0	0
1,200 mg/kg	630	630	0	0	0	0	0	0
4,000 mg/kg	600	599	0	0	0	0	1	0.17
12,700 mg/kg	599	597	1	0	2	0	0	0.36
12-hr sampling time								
A-215								
Vehicle control	600	599	2	1	0	0	0	0.17
2,000 mg/kg	568	566	2	0	2	0	0	0.35
6,000 mg/kg	540	540	0	0	0	0	0	0
12,700 mg/kg	401	397	2	0	5	0	0	1.00
A-225								
Vehicle control	608	607	1	0	1	0	0	0.16
1,200 mg/kg	626	625	1	1	1	0	0	0.16
4,000 mg/kg	631	630	4	0	1	1	0	0.16
12,700 mg/kg	644	643	2	0	1	0	0	0.16
A-230								
Vehicle control	600	598	0	0	2	0	0	0.33
1,200 mg/kg	600	598	2	0	2	0	0	0.33
4,000 mg/kg	636	636	3	0	0	0	0	0
12,700 mg/kg	607	606	1	0	1	0	0	0.16
24-hr sampling time								
A-215								
Vehicle control	564	564	1	0	0	0	0	0
2,000 mg/kg	641	640	0	0	1	0	0	0.16
6,000 mg/kg	559	558	2	0	1	0	0	0.18
12,700 mg/kg	610	607	0	0	2	0	1	0.49
Positive control								
CP-40 mg/kg	331	282	6	1	68	3	9	14.80
A-225								
Vehicle control	575	574	2	0	1	0	0	0.17
1,200 mg/kg	623	622	4	0	1	0	0	0.16
4,000 mg/kg	559	556	3	0	4	0	1	0.54
12,700 mg/kg	620	618	1	0	2	0	0	0.32
Positive control								
CP 40 mg/kg	517	433	8	0	93	4	31	16.25
A-230								
Vehicle control	667	667	3	0	0	0	0	0
1,200 mg/kg	616	614	2	0	2	0	0	0.32
4,000 mg/kg	570	568	3	0	2	0	0	0.35
12,700 mg/kg	538	536	2	0	2	0	0	0.37
Positive control								
CP 40 mg/kg	414	301	6	0	126	2	49	27.29

<sup>a</sup> Vehicle control was corn oil.

and the treated groups at low frequencies. No statistically significant increases in chromosomal aberrations or gaps were observed in the treated groups at any of the sampling times. Both mean chromosome numbers and mean mitotic indices were similar in test and vehicle control groups. The doses used were sufficiently high, as demonstrated by the occurrence of toxicity at the higher dose levels. The expected high frequencies of chromosomal aberrations were observed for the positive control groups. Since no evidence of mitotic delay was seen after analysis of mitotic indices 24 hr after treatment, slides from the 48-hr termination were not analyzed for chromosomal aberrations (Table 5).

### DISCUSSION

Three LAB mixtures were evaluated in a battery of genotoxicity assays. The endpoints used included microbial gene mutation, *in vitro* mammalian gene mutation, and *in vivo* bone marrow cytogenetics. Negative results were obtained for all of these assays.

Several genotoxicity test results have been published for a related compound. Dodecylbenzene was not mutagenic in the *S. typhimurium* and *E. coli* WP2 reversion assays (Shimizu *et al.*, 1985), and in V79 Chinese hamster cells at the ouabain resistance locus (Lankas *et al.*, 1978). The presence or absence of branching in the dodecyl chain of these test materials was unspecified; Lankas *et al.* (1978) noted that their material was phenyl substituted in the C-1 position. These results are all consistent with the conclusion that C<sub>10</sub>-C<sub>14</sub> alkylbenzenes generally are not mutagenic.

Other short term tests on alkylbenzenes have been directed at detecting either *in vitro* promotion (Lankas *et al.*, 1978; Bohrman, *et al.*, 1988; Aarsaether *et al.*, 1987) or cell transformation (Aarsaether *et al.*, 1987). These studies yielded a mixture of positive and negative results, the interpretation of which is made difficult by the lack of extensive validation of each of these assay systems (Langenbach *et al.*, 1988). Both the present results and the published data support the conclusion that alkylbenzenes in the C<sub>10</sub>-C<sub>14</sub> alkyl range are unlikely to fall into the category of genotoxic agents.

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