Amended Safety Assessment of Dodecylbenzenesulfonate, Decylbenzenesulfonate, and Tridecylbenzenesulfonate Salts as Used In Cosmetics

March 24, 2009
Abstract: Sodium Dodecylbenzenesulfonate is one of a group of salts of alkylbenzene sulfonates used in cosmetics as surfactant-cleansing agents. Sodium Dodecylbenzenesulfonate is soluble in water and partially soluble in alcohol, with dermal absorption dependent on pH. Dodecylbenzenesulfonate salts are not toxic in single-dose oral and dermal animal tests, and no systemic toxicities were observed in repeat-dose dermal animal studies. For example, in dermal animal studies, no evidence of reproductive or developmental toxicity was reported. At high concentrations, Dodecylbenzenesulfonate salts were severely irritating to the skin of animals and humans, but they were not skin sensitizers in animal or clinical tests. The CIR Expert Panel concluded that the irritant properties of these ingredients are similar to those of other detergents, with severity dependent on concentration and pH. Products containing these ingredients should be formulated to ensure that the irritancy potential is minimized.

INTRODUCTION

The Cosmetic Ingredient Review (CIR) Expert Panel reviewed the safety of Sodium Dodecylbenzenesulfonate, TEA-Dodecylbenzenesulfonate, Sodium Decylbenzenesulfonate as used in cosmetics in an earlier report, with the conclusion that these ingredients were safe as cosmetic ingredients in the [then] present practices of use (Elder 1993).

In a routine re-review of this earlier safety assessment, the CIR Expert Panel determined that the available data were sufficient to support the safety of the entire group of salts of sulfonated alkylbenzenes used in cosmetics. Accordingly, this safety assessment has been expanded to include:

- Ammonium Dodecylbenzenesulfonate,
- Calcium Dodecylbenzenesulfonate,
- DEA-Dodecylbenzenesulfonate,
- Isopropylamine Dodecylbenzenesulfonate,
- Magnesium Isododecylbenzenesulfonate,
- MIPA-Dodecylbenzenesulfonate,
- Potassium Dodecylbenzenesulfonate,
- Sodium Decylbenzenesulfonate,
- Sodium Dodecylbenzenesulfonate,
- Sodium Tridecylbenzenesulfonate,
- TEA-Dodecylbenzenesulfonate (TEA-DDBS), and
- TEA-Tridecylbenzenesulfonate.

Sodium Dodecylbenzenesulfonate is a linear alkylbenzene sulfonate. As described in the original safety assessment (Elder 1993), linear alkylbenzene sulfonate (LAS) is not a specific chemical name but the name has been used to describe the material studied in several publications. LAS can be considered to have an average molecular weight close to that of Sodium Dodecylbenzenesulfonate, but could contain some of alkyl groups of similar size. Also, the point of attachment of the benzene ring to the alkyl chain would be distributed along the chain, with attachment at the number 2 carbon being prominent; several isomers would be present. Data from 3 manufacturers reported in the original safety assessment, for example, demonstrated that a 12-carbon chain length moiety comprises 18.1% to 35% and a 10-carbon chain length moiety comprises 0.5% to 20.6% of commercial LAS products.

The CIR Expert Panel also has reviewed the safety of several ingredients that form a portion of the ingredient structures addressed in this safety assessment. These include DEA (diethanolamine), TEA (triethanolamine), and MIPA (monoisopropanolamine). Table 1 list these and related ingredients and the conclusion regarding safety reached by CIR.

CHEMISTRY

Definition and Structure

The definitions and technical/other names of the cosmetic ingredients included in this assessment as given in the International Cosmetic Ingredient Dictionary and Handbook (Gottschalk and Bailey 2008) are listed in Table 2. All of these ingredients are in the chemical class alky aryl (benzene) sulfonates and function as surfactant - cleansing agents.

Figure 1 shows the structures of the cosmetic ingredients addressed in this safety assessment.

Sodium Decylbenzenesulfonate is also known as Decyl Benzene Sodium Sulfonate and Sodium Decylbenzenesulfonamide (Sweet 1987).

Sodium Dodecylbenzenesulfonate is also known as Dodecyl Benzene Sodium Sulfonate; Dodecylbenzenesulphonate, Sodium Salt; Sodium Laurylbensulphonate (Sweet 1987); and Dodecylbenzene Sodium Sulfonate (Windholz et al. 1983).

TEA-Dodecylbenzenesulfonate is also known as Linear Alkylbenzene Sulfonate and Triethanolamine Salt (Hunting 1983).

Photodegradation

Murakami et al. (1992) reported that Sodium Dodecylbenzenesulfonate exposed to a combination of ultraviolet radiation (UVR) and ozone for 4 h breaks down into formaldehyde and glyoxal. When exposed to UVR and ozone for up to 10 h, linear dodecylsulfonates decreased in a linear manner up to 5 h while the concentrations of formaldehyde and glyoxal increased until ~5 h then decreased. When exposed to ozone alone, linear dodecylsulfonates decreased in a linear manner for up to 15 h and formaldehyde and glyoxal increased and leveled off at ~7 h. The concentrations for formaldehyde and glyoxal were lower when just exposed to ozone and not UVR.
<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Conclusion</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DEA and TEA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TEA and DEA</td>
<td>Safe in rinse off products; safe at less than 5% in leave on products; should not be used where N-nitroso compounds could be formed</td>
<td>Elder 1983b</td>
</tr>
<tr>
<td><strong>DEA containing ingredients</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cocamide DEA</td>
<td>Safe in rinse off products; safe at less than 10% in leave on products; should not be used where N-nitroso compounds could be formed</td>
<td>Elder 1986</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Andersen 1996</td>
</tr>
<tr>
<td>Isostearamide DEA</td>
<td>Safe in rinse off products; safe at less than 40% in leave on products (which would limit ethanolamines to 5%); should not be used where N-nitroso compounds could be formed</td>
<td>CIR 1995</td>
</tr>
<tr>
<td>Lauramide DEA</td>
<td>Safe in rinse off products; safe at less than 10% in leave on products; should not be used where N-nitroso compounds could be formed</td>
<td>Andersen 1996</td>
</tr>
<tr>
<td>Linoleamide DEA</td>
<td>Safe in rinse off products; safe at less than 10% in leave on products; should not be used where N-nitroso compounds could be formed</td>
<td>Andersen 1996</td>
</tr>
<tr>
<td>Myristamide DEA</td>
<td>Safe in rinse off products; safe at less than 40% in leave on products (which would limit ethanolamines to 5%); should not be used where N-nitroso compounds could be formed</td>
<td>CIR 1995</td>
</tr>
<tr>
<td>Stearamide DEA</td>
<td>Safe in rinse off products; safe at less than 40% in leave on products (which would limit ethanolamines to 5%); should not be used where N-nitroso compounds could be formed</td>
<td>CIR 1995</td>
</tr>
<tr>
<td><strong>TEA containing ingredients</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TEA-Cocoyl Hydrolyzed Collagen</td>
<td>Safe as a cosmetic ingredient</td>
<td>Elder 1983a</td>
</tr>
<tr>
<td></td>
<td>Confirmed</td>
<td>Andersen 2005</td>
</tr>
<tr>
<td>TEA-EDTA</td>
<td>Safe as a cosmetic ingredient</td>
<td>Andersen 2002</td>
</tr>
<tr>
<td>TEA-Lauryl Sulfate</td>
<td>Safe up to 10.5%, formulate to not cause irritation</td>
<td>Elder 1982</td>
</tr>
<tr>
<td><strong>MIPA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MIPA*, Monisopropanolamine,</td>
<td>Safe as cosmetic ingredients</td>
<td>Elder 1987</td>
</tr>
<tr>
<td></td>
<td>Confirmed</td>
<td>Andersen 1996</td>
</tr>
</tbody>
</table>

* Included Diisopropanolamine, Triisopanolamine, and Mixed Isopropanolamines
Table 2. The definition of and technical/other names listed in the *International Cosmetic Ingredient Dictionary and Handbook* for the ingredients that are included in this safety assessment (Gottschalck and Bailey 2008).

<table>
<thead>
<tr>
<th>Ingredient (CAS No.)</th>
<th>Definition</th>
<th>Technical/other names</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ammonium Dodecylbenzenesulfonate (CAS No. 1331-61-9)</td>
<td>substituted aromatic compound with structure shown in Figure 1</td>
<td>• Ammonium Lauryl Benzene Sulfonate and • Benzenesulfonic Acid, Dodecyl-, Ammonium Salt</td>
</tr>
<tr>
<td>Calcium Dodecylbenzenesulfonate (CAS No. 26264-06-2)</td>
<td>substituted aromatic compound with structure shown in Figure 1</td>
<td>• Benzenesulfonic Acid, Dodecyl-, Calcium Salt and • Dodecylbenzenesulfonic Acid, Calcium Salt</td>
</tr>
<tr>
<td>DEA-Dodecylbenzenesulfonate (CAS No. 26545-53-9)</td>
<td>diethanolamine salt of dodecylbenzene sulfonic acid (q.v.) with the structure shown in Figure 1</td>
<td>• Benzenesulfonic Acid, Dodecyl-, Compd. with 2,2'-Iminobis<a href="">Ethanol</a> and • Diethanolamine Dodecylbenzene Sulfonate</td>
</tr>
<tr>
<td>Isopropylamine Dodecylbenzenesulfonate (CAS No 26264-05-1)</td>
<td>salt of isopropylamine and dodecylbenzene sulfonic acid (q.v.) with the structure shown in Figure 1</td>
<td>• Benzenesulfonic Acid, Dodecyl-, Compd. with 2-Propanamine (1:1); • Dodecylbenzenesulfonic Acid, Comp. with 2-Propanamine (1:1); and • Isopropylammonium Dodecylbenzenesulfonate</td>
</tr>
<tr>
<td>Magnesium Isododecylbenzenesulfonate (CAS No. 27479-45-4)</td>
<td>organic compound with structure shown in Figure 1</td>
<td>• None listed</td>
</tr>
<tr>
<td>MIPA-Dodecylbenzenesulfonate (CAS No. 42504-46-1, 54590-52-2)</td>
<td>monoisopropanolamine salt of a substituted aromatic compound with structure shown in Figure 1</td>
<td>• Benzenesulfonic Acid, Dodecyl-, Compd with 1-Amino-2-Propanol (1:1) and • Monoisopropanolamine Dodecylbenzenesulfonate</td>
</tr>
<tr>
<td>Potassium Dodecylbenzenesulfonate (CAS No. 27177-77-1)</td>
<td>substituted aromatic compound with structure shown in Figure 1</td>
<td>• Benzenesulfonic Acid, Dodecyl-, Potassium Salt and • Dodecylbenzenesulfonic Acid, Potassium Salt</td>
</tr>
<tr>
<td>Sodium Decylbenzenesulfonate (CAS No. 1322-98-1)</td>
<td>substituted aromatic compound with structure shown in Figure 1</td>
<td>• Benzenesulfonic Acid, Decyl-, Sodium Salt and • Decylbenzenesulfonic Acid, Sodium Salt</td>
</tr>
<tr>
<td>Sodium Dodecylbenzenesulfonate (CAS No 25155-30-0)</td>
<td>substituted aromatic compound with structure shown in Figure 1</td>
<td>• Sodium Lauryl Benzene Sulfonate; • Benzenesulfonic Acid, Dodecyl-, Sodium Sulfate; • Dodecylbenzenesulfonic Acid, Sodium Sulfate; and • Sodium Lauryl Phenyl Sulfonate</td>
</tr>
<tr>
<td>Sodium Tridecylbenzenesulfonate (CAS No. 26248-24-8)</td>
<td>substituted aromatic compound with structure shown in Figure 1</td>
<td>• Benzenesulfonic Acid, Tridecyl-, Sodium Salt and • Tridecylbenzenesulfonic Acid, Sodium Salt</td>
</tr>
<tr>
<td>TEA-Dodecylbenzenesulfonate (CAS No. 27323-41-7)</td>
<td>substituted aromatic compound with structure shown in Figure 1</td>
<td>• Benzenesulfonic Acid; Dodecyl-, Compd with 2,2',2&quot;-Nitrilotris [ethanol] (1 :1); • Dodecylbenzenesulfonic Acid, Compd with 2,2',2&quot;-Nitrilotris[Ethanol] (1 :1); and • Triethanolamine Dodecylbenzenesulfonate</td>
</tr>
<tr>
<td>TEA-Tridecylbenzenesulfonate (CAS No. 59599-58-5, 61886-59-7)</td>
<td>substituted aromatic compound with structure shown in Figure 1</td>
<td>• Benzenesulfonic Acid, Tridecyl-, Compd. with 2,2',2&quot;-Nitrilotris<a href="">Ethanol</a>; • Tridecylbenzenesulfonic Acid, Compd. with 2,2',2&quot;-Nitrolotris <a href="">Ethanol</a>; and • Triethanolamine Tridecylbenzenesulfonate</td>
</tr>
</tbody>
</table>
Figure 1. Chemical structures for salts of alkylbenzene sulfonates: (a) Ammonium Dodecylbenzenesulfonate, (b) Calcium Dodecylbenzenesulfonate, (c) DEA-Dodecylbenzenesulfonate, (d) Isopropylamine Dodecylbenzenesulfonate, (e) Magnesium Isododecylbenzenesulfonate, (f) MIPA-Dodecylbenzenesulfonate, (g) Potassium Dodecylbenzenesulfonate, (h) Sodium Decylbenzenesulfonate, (i) Sodium Dodecylbenzenesulfonate, (j) Sodium Tridecylbenzenesulfonate, (k) TEA-Dodecylbenzenesulfonate, (l) TEA-Tridecylbenzenesulfonate.
Chemical and Physical Properties
Sodium Dodecylbenzenesulfonate is commercially available as a yellow colored slurry or off-white dry product (CTFA 1991a). The slurry is usually 30% to 50% active (percentage activity defined as solids minus salts (Nikitakis 1990). Slurries with activity >50% contain a hydrotrope, usually sodium xylene sulfonate, for easier handling (CTFA 1991a). The dry product, which can be in the form of a powder, flake, or bead, is usually 40% to 90% active. The chemical and physical properties of SDDBS are summarized in Table 3.

TEA-Dodecylbenzenesulfonate is a clear yellow liquid that is commercially available as 40% to 60% aqueous solutions (CTFA 1991b). Properties of TEA-DDBS are also summarized in Table 3.

Sodium Decylbenzenesulfonate has a molecular weight of 320.46 (Sweet 1987). Chemical and physical properties were not available for the other ingredients in this safety assessment.

Manufacture and Production
Sodium Dodecylbenzenesulfonate is made by reacting dodecylbenzene with sulfuric acid (Oleum process) or air/SO$_2$ to produce dodecylbenzene sulfonic acid (CTFA 1991a). The dodecylbenzenesulfonic acid is then neutralized with sodium hydroxide. SDDBS is then sold as a slurry. It can be dried by a drum drier to form flakes and powders or dried by a spray drier to form beads.

TEA-Dodecylbenzenesulfonate is made by reacting dodecylbenzenesulfonate with sulfuric acid (Oleum process) or air/SO$_2$ to produce dodecylbenzene sulfonic acid (CTFA 1991 b). The dodecylbenzene sulfonic acid is then neutralized with triethanolamine.

Linear Alkylbenzene Sulfonate is made by the sulfonation of straight-chain alkylbenzenes prepared from petroleum distillates (Buehler et al. 1971).

In 1987, approximately 2.15 billion pounds of linear alkylbenzene sulfonate were used in North America, Western Europe, and Japan, with Dodecylbenzene Sulfonate being the most widely used (Greek and Layman 1989).

Analytical Methods
Sodium Dodecylbenzenesulfonate was analyzed by high-pressure liquid chromatography (HPLC) and Karl Fisher titration (Coy et al. 1990). Two-phase titration can be used for the determination of total cationic or anionic surfactants in mixtures (Mohammed and Cantwell 1980; Tsubouchi and Mallory 1983).

Linear Alkylbenzene Sulfonate was determined by HPLC (Yoshikawa et al. 1984); by spectroscopic methods, particularly HPLC with UV detection; by chromatographic techniques; by spectrophotometric methods, especially the assay for methylene blue active substances (MBAS); by volumetric methods; by potentiometric methods; and by physicochemical methods (Arthur D. Little, Inc. 1991). MBAS and spectrophotometric methods are considered to be inadequate for trace surfactant measurements requiring identification of specific surfactants and isomers.

Impurities
Sodium Dodecylbenzenesulfonate contains impurities that include neutral oil (unsulfonated materials), arsenic (As), iron (Fe), and lead (Pb) (Estrin et al. 1982).

TEA-Dodecylbenzenesulfonate contains sulfates (as TEA hydro-sulfate) at a maximum of 4.0% (Elder 1983b).

Linear Alkylbenzenesulfonates are produced by the alkylation of benzene, which results in a number of side reactions (Arthur D. Little, Inc. 1991). Some of the dialkylbenzenes that result from the side reactions could not be separated from the primary product with ease and, following sulfonation, remained in commercial Linear Alkylbenzenesulfonates. Other dialkylbenzenes and the diphenylalkanes that form as products of the side reactions boil at temperatures sufficiently above the linear monoalkylbenzene, facilitating their removal.

Six samples of commercial Linear Alkylbenzenesulfonates were analyzed for dialkyltetralins and dialkylnaphthalenes (Vista Chemical Co. 1992a). These compounds were detected as impurities in concentrations ranging from 0% to 15% and 0% to 0.25%, respectively. Gas chromatography and mass spectral analysis also revealed the presence of dialkyllindanes in these Linear Alkylbenzenesulfonates samples; however, the concentration of these impurities amounted to only about 1/10 of that of alkyltetralins.

Ultraviolet Absorption
Three commercial samples of Linear Alkylbenzene Sulfonate, dissolved in water at concentrations up to 1.0 g/l, did not absorb in the UVB region of the spectrum. All absorption maxima were in the UVC region; $\lambda_{max}$ 218-224, $\lambda_{max}$ 254-255, and $\lambda_{shoulder}$ 260-261 (Vista Chemical Company 1992b).

USE
Cosmetic
According to information supplied to the Food and Drug Administration (FDA) by industry as part of the Voluntary Cosmetic Ingredient Reporting Program (VCRP) in the original report, Sodium Dodecylbenzenesulfonate was used in a total of 45 cosmetic products in 1992. Use concentrations were not reported (Elder 1993).
Table 3. Physical and chemical properties of Sodium Dodecylbenzenesulfonate, Sodium Decylbenzenesulfonate, TEA-Dodecylbenzenesulfonate, and Linear Alkylbenzene Sulfonates.

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sodium Dodecylbenzenesulfonate</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical appearance</td>
<td>Yellow colored slurry or off-white dry product (powder, flakes, or beads)</td>
<td>CTFA 1991a</td>
</tr>
<tr>
<td></td>
<td>Pale yellow paste or slurry, spray-dried powder, or as a flake</td>
<td>Hunting 1983</td>
</tr>
<tr>
<td>Odor</td>
<td>Bland</td>
<td>Estrin et al. 1982</td>
</tr>
<tr>
<td>% Active Slurry</td>
<td>30 - 50%</td>
<td>CTFA 1991a</td>
</tr>
<tr>
<td></td>
<td>Usually 30% - 60%</td>
<td>Hunting 1983</td>
</tr>
<tr>
<td>Dried product</td>
<td>40% - 90%</td>
<td>CTFA 1991a</td>
</tr>
<tr>
<td></td>
<td>~90%</td>
<td>Hunting 1983</td>
</tr>
<tr>
<td>Molecular weight</td>
<td>349</td>
<td>CTFA 1991a</td>
</tr>
<tr>
<td></td>
<td>348.52</td>
<td>Sweet 1987</td>
</tr>
<tr>
<td></td>
<td>348.49</td>
<td>Windholz et al. 1983</td>
</tr>
<tr>
<td>Solubility</td>
<td>Water dispersible, soluble at low concentrations</td>
<td>Hunting 1983</td>
</tr>
<tr>
<td></td>
<td>Soluble in water; partially soluble in alcohol</td>
<td>Estrin et al. 1982</td>
</tr>
<tr>
<td>Stability</td>
<td>Stable in the presence of a strong acid and base; generally non-reactive and does not polymerize</td>
<td>CTFA 199a</td>
</tr>
<tr>
<td>Specific gravity (at 25°C)</td>
<td>Slurry: 1.02 - 1.05; dry product: 0.45 - 0.65</td>
<td>CTFA 1991a</td>
</tr>
<tr>
<td>pH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10%</td>
<td>Slurry: 7 - 8; dry product: 7 - 9</td>
<td>CTFA 1991a</td>
</tr>
<tr>
<td></td>
<td>7.0 - 9.0</td>
<td>Estrin et al. 1982</td>
</tr>
<tr>
<td>Impurities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutral oil</td>
<td>1% maximum</td>
<td></td>
</tr>
<tr>
<td>Arsenic (as As)</td>
<td>3 ppm maximum</td>
<td></td>
</tr>
<tr>
<td>Iron (as Fe)</td>
<td>10 ppm maximum</td>
<td></td>
</tr>
<tr>
<td>Lead (as Pb)</td>
<td>20 ppm maximum</td>
<td></td>
</tr>
<tr>
<td>Moisture</td>
<td>3.5% maximum</td>
<td>Estrin et al. 1982</td>
</tr>
<tr>
<td>Ionic type</td>
<td>Anionic</td>
<td>Hunting 1983</td>
</tr>
<tr>
<td><strong>Sodium Decylbenzenesulfonate</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Molecular weight</td>
<td>320.46.</td>
<td>Sweet 1987</td>
</tr>
</tbody>
</table>
Table 3. Physical and chemical properties of Sodium Dodecylbenzenesulfonate, Sodium Decylbenzenesulfonate, TEA-Dodecylbenzenesulfonate, and Linear Alkylbenzene Sulfonates.

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TEA-Dodecylbenzenesulfonate</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical appearance</td>
<td>Clear yellow liquid</td>
<td>CTFA 1991b</td>
</tr>
<tr>
<td></td>
<td>Clear yellow or amber liquid</td>
<td>Hunting 1983</td>
</tr>
<tr>
<td></td>
<td>Clear, pale yellow viscous liquid</td>
<td>Estrin et al. 1982</td>
</tr>
<tr>
<td>Odor</td>
<td>Mild, slightly oily</td>
<td></td>
</tr>
<tr>
<td>% Activity</td>
<td>40% - 60%</td>
<td>CTFA 1991a</td>
</tr>
<tr>
<td></td>
<td>50% - 60%</td>
<td>Hunting 1983</td>
</tr>
<tr>
<td>Aqueous solution</td>
<td>60%</td>
<td>Estrin et al. 1982</td>
</tr>
<tr>
<td>Molecular weight</td>
<td>475</td>
<td>CTFA 1991b</td>
</tr>
<tr>
<td></td>
<td>476.77</td>
<td>Sweet 1987</td>
</tr>
<tr>
<td>Solubility</td>
<td>Soluble in water</td>
<td>Hunting 1983</td>
</tr>
<tr>
<td></td>
<td>Soluble in water and alcohol</td>
<td>Estrin et al. 1982</td>
</tr>
<tr>
<td>Stability</td>
<td>Stable under normal cosmetic use conditions</td>
<td>CTFA 1991b</td>
</tr>
<tr>
<td>Specific gravity (at 25°C/25°C)</td>
<td>1.08</td>
<td>Estrin et al. 1982</td>
</tr>
<tr>
<td>pH</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10%</td>
<td>CTFA 1991b</td>
</tr>
<tr>
<td></td>
<td>5.5 - 7.5</td>
<td>Estrin et al. 1982</td>
</tr>
<tr>
<td></td>
<td>At 25°C</td>
<td>6.8 - 7.5</td>
</tr>
<tr>
<td>Viscosity (at 25°C)</td>
<td>6.8 - 7.5</td>
<td>Estrin et al. 1982</td>
</tr>
<tr>
<td>Assay (average molecular weight 462)</td>
<td>54% - 60%</td>
<td>Estrin et al. 1982</td>
</tr>
<tr>
<td>Impurities</td>
<td>Sulfates (as TEA hydrosulfate) 4.0% maximum</td>
<td>Estrin et al. 1982</td>
</tr>
<tr>
<td></td>
<td>Water 3% - 42%</td>
<td>Estrin et al. 1982</td>
</tr>
<tr>
<td><strong>Linear Alkylbenzene Sulfonates</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Impurities</td>
<td>Dialkyltetralin, dialkynaphthalene, and to a lesser extent dialkylindane may be present in the final product</td>
<td>Vista Chemical Co. 1992a</td>
</tr>
</tbody>
</table>

Currently, VCRP data indicated that Sodium Dodecylbenzenesulfonate is used in 12 cosmetic products (FDA 2007). A survey of current use concentrations conducted by the Personal Care Products Council (Council) reported a range from 2% to 3% (Council 2008).

Based on VCRP data, TEA-Dodecylbenzenesulfonate was used in a total of 54 cosmetic products at the time of the first safety assessment (Elder 1993). Currently, VCRP indicated that it is used in 39 products (FDA 2007) at concentrations ranging from 0.002% to 3% (Council 2008).

Sodium Decylbenzenesulfonate is reported to be used at a concentration of 0.02% (Council 2008).

Available use and use concentration data are listed in Table 4. There were no reported uses or use concentrations for Ammonium Dodecylbenzenesulfonate, Calcium Dodecylbenzenesulfonate, DEA-Dodecylbenzenesulfonate, Isopropylamine Dodecylbenzenesulfonate, Magnesium Isodecylbenzenesulfonate, MIPA-Dodecylbenzenesulfonate, Potassium Dodecylbenzenesulfonate, Sodium, and TEA-Tridecylbenzenesulfonate. Straight-chain sodium alkylbenzenesulfonate is on the list of quasi-drugs in Japan (Ministry of Health, Labor, and Welfare [MHLW] 2001).

Non-Cosmetic
Sodium Dodecylbenzenesulfonate is used as a detergent in hospitals (Tsubouchi and Mallory 1983) and as an industrial neutral cleansing agent (Itokawa et al. 1973). Large quantities of Dodecylbenzene Sulfonates are used in household detergent and dishwashing products (Hunting 1983). Almost 80% of the total U.S. production of LAS is used in household products (Arthur D. Little 1991).
Table 4. Historical and current cosmetic product uses and concentrations\textsuperscript{a} for Ingredient Sodium Dodecylbenzenesulfonate, TEA-Dodecylbenzenesulfonate, and Sodium Decylbenzenesulfonate.

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>Sodium Dodecylbenzenesulfonate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baby products</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>-</td>
<td>-</td>
<td>3</td>
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<tr>
<td>Bath products</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oils, tablets, and salts</td>
<td>-</td>
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<td>-</td>
</tr>
<tr>
<td>Soaps and detergents</td>
<td>6</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>Bubble baths</td>
<td>33</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Other personal cleanliness products</td>
<td>3</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Eye makeup</td>
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<td></td>
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</tr>
<tr>
<td>Eyeliners</td>
<td>3</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Other</td>
<td>-</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td><strong>Total uses/ranges for Sodium Dodecylbenzenesulfonate</strong></td>
<td><strong>45</strong></td>
<td><strong>12</strong></td>
<td><strong>2-3</strong></td>
</tr>
<tr>
<td>TEA-Dodecylbenzenesulfonate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baby products</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shampoo(s)</td>
<td>-</td>
<td>-</td>
<td>0.02</td>
</tr>
<tr>
<td>Noncoloring hair care products</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conditioners</td>
<td>-</td>
<td>-</td>
<td>0.01-0.02</td>
</tr>
<tr>
<td>Shampoo(s)</td>
<td>18</td>
<td>6</td>
<td>0.002-5</td>
</tr>
<tr>
<td>Tonics, dressings, etc.</td>
<td>-</td>
<td>-</td>
<td>0.003</td>
</tr>
<tr>
<td>Hair coloring products</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyes and colors</td>
<td>36</td>
<td>31</td>
<td>-</td>
</tr>
<tr>
<td>Skin care products</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin cleansing creams, lotions, liquids, and pads</td>
<td>-</td>
<td>1</td>
<td>0.9</td>
</tr>
<tr>
<td>Moisturizers</td>
<td>-</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td><strong>Total uses/ranges for TEA-Dodecylbenzenesulfonate</strong></td>
<td><strong>54</strong></td>
<td><strong>39</strong></td>
<td><strong>0.002-5</strong></td>
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<tr>
<td>Sodium Decylbenzenesulfonate</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Skin care products</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moisturizers</td>
<td>n/a</td>
<td>-</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Total uses/ranges for Sodium Decylbenzenesulfonate</strong></td>
<td>n/a</td>
<td>-</td>
<td><strong>0.02</strong></td>
</tr>
</tbody>
</table>

\textsuperscript{a} Concentration of use was not recorded at the time of the first assessment.

Sodium Dodecylbenzenesulfonate was used in a microemulsion system with butanol and decane to partition cytochrome \( c \) between an aqueous phase in equilibrium (Jolivalt et al. 1993).

Tsukatani et al. (2006) suggested that Dodecylbenzenesulfonate anions have a possible use as a chelate extraction solvent.

Sodium \( n \)-Dodecylbenzenesulfonate is used in the removal of heavy metals (Tokuyama and Iwama 2007).

As given in the Code of Federal Regulations (CFR), FDA has approved Sodium Dodecylbenzenesulfonate and Linear Alkylbenzene Sulfonate as chemicals used in washing or to assist in the peeling of fruits and vegetables at levels not to exceed 0.2 percent in wash water. May be used in washing or to assist in the lye peeling of fruits and vegetables (21CFR Sec. 173.315).

**GENERAL BIOLOGY**

**Absorption, Distribution, Metabolism and Excretion**

*Sodium Dodecylbenzenesulfonate*

Six female Colworth-Wistar rats were dosed with either 0.1 or 0.5 ml \( ^{14} \text{C} \)-Sodium Dodecylbenzenesulfonate; 3 animals were dosed by i.p. injection and 3 animals by s.c. injection (Howes 1975).
The animals were killed 24 h after being dosed. Both the i.p. and s.c. administrations had the same rate and route of excretion. After 24 h, 78 ± 4% of the dose was recovered in the urine, 1.5 ± 0.6% was recovered in the feces, and <0.1% was recovered in expired CO2. In the carcass, 22 ± 5% was recovered after 24 h. 

14C-Sodium Dodecylbenzenesulfonate was used to determine the distribution and elimination of Sodium Dodecylbenzenesulfonate in rats; the location of the 14C in the molecule was not stated (Lay et al. 1983). Twelve male Wistar rats were fed 14C-Sodium Dodecylbenzenesulfonate in the diet, ad libitum, at a concentration of 1.4 mg/kg for 35 days. Every 24 h, feed consumption was measured and urine and feces were collected. On day 35, 6 of the rats were killed and a determination of radioactive residues was made. The remaining 6 rats were kept for 1 wk to determine clearance.

During the test period, the rats consumed approximately 34.66 µg 14C-Sodium Dodecylbenzenesulfonate daily; the 14C was excreted rapidly. A total of 81.8% of the 14C was excreted; 52.4% in the feces and 29.4% in the urine. During the clearance period, 6.55% of the remaining 14C was excreted in the feces and 1.27% was excreted in the urine, for a total of 7.82%. The fecal and urinary 14C-Sodium Dodecylbenzenesulfonate-derived activity consisted of highly polar metabolites. Approximately 90% of the 14C in the feces and 65% in the urine was recovered, and unchanged Sodium Dodecylbenzenesulfonate was not detected.

All the tissues examined after 35 days of treatment had small but significant amounts of 14C residue. The relatively high concentrations in the colon and small intestine suggested the excretion of 14C in the bile.

In another experiment, 8 male Wistar rats received a single intraperitoneal (i.p.) injection of 384.7 µg 14C-Sodium Dodecylbenzenesulfonate in a 0.6% NaCl solution. Feces and urine were monitored for 10 days for 14C excretion. On day 1, 84.7% of the dose was excreted, 35.0 ± 4.6% in the feces and 49.7 ± 5.7% in the urine. During days 2 through 10, 14C was primarily excreted in the feces. By day 10, 94.5% of the dose was excreted. The fecal and urinary 14C-Sodium Dodecylbenzenesulfonate-derived activity consisted of highly polar metabolites (Lay et al. 1983).

Linear Alkylbenzenesulfonate

Michael (1968) orally administered 35S-labeled LAS (0.6, 1.2, 8.0, or 40.0 mg; 1.0 ml) to male albino Charles River rats (n = 3 or 5) after fasting. The animals were housed individually and urine and feces were collected daily for 3 days. The rats were then killed, radioassayed and necropsied. After 3 days, radioactivity from the test substance was detected in the urine at 40.2%, 57.7%, 40.2%, and 41.7% for 0.6, 1.2, 8.0, or 40.0 mg, respectively and in the feces at 56.1%, 38.9%, 41.1% and 43.5%, respectively. After 3 days, no 35S residue (< 0.1% of the dose) could be detected in the carcasses that received the 40 mg dose.

The route of absorption was investigated by the oral administration of 35S-Linear Alkylbenzene Sulfonate (40 mg) to thoracic duct-cannulated rats (n = 3). Lymph was collected in a single 42-h fraction. 35S was detected in the lymph collected (1.6% of total). The author concluded that absorption was from the gastrointestinal tract and transported by some route other than the lymphatic system.

The ability of the rats to absorb Linear Alkylbenzene Sulfonate (1.2 mg) administered orally was determined in bile-duct ligated rats. The urine and feces were collected for 90 h. The test substance (83% recovered) was excreted mostly in the urine (89% of 35S recovered) and not the feces (11%). The author stated that this indicates absorption from the gastrointestinal tract.

In bile duct-cannulated rats (n = 2) fed 35S-Linear Alkylbenzene Sulfonate (1.2 mg), 46% of the recovered test substance was detected in the urine, 29% in the feces, and 25% in the bile. Recovery was 90%.

In another experiment, the proximal end of the bile duct was cannulated on rat 1 which then fed into the distal end of the bile duct of rat 2. Rat 1 was then administered Linear Alkylbenzene Sulfonate (1.2 mg) by stomach tube. Bile was collected from an additional cannula in rat 2. Urine and feces were collected from both rats for 90 h. The 35S-containing compounds that were excreted in the bile of rat 1 and transferred to rat 2 were completely absorbed from the gastrointestinal tract of rat 2; nearly 2/3 of this activity was excreted in the bile of rat 2. The author concluded that 89 to 90% of an oral dose of Linear Alkylbenzene Sulfonate was readily absorbed from the gastrointestinal tract (Michael 1968).

Four adult rhesus monkeys, 2 males and 2 females, were administered 30 mg/kg 14C-Linear Alkylbenzene Sulfonate in aqueous solution, approximately 25 µCi, by oral intubation to study the excretion of 14C-Linear Alkylbenzene Sulfonate (Cresswell et al. 1978). Urine was collected 0-8 and 8-24 h after dosing, and then at 24 h intervals for 4 days; feces were collected at 24 h intervals for 5 days. Blood samples were taken 30, 48, 72, and 96 h after dosing. To determine plasma radioactivity concentrations, blood samples were drawn prior to dosing, at various times within the initial 24 h period following dosing, and then at 24 h intervals until radioactivity concentrations were below the limit of detection.

The majority of the radiolabel was excreted within 24 h of administration. In the first 24 h, male monkeys eliminated 66.5% and female monkeys eliminated 72.1% of the radioactivity in urine. Over 5 days, the total amount excreted in the urine by male and female monkeys was 68.3% and 74.0%, respectively. The male monkeys excreted 14.9% and the female monkeys 12.7% of the 14C-Linear Alkylbenzene Sulfonate in the feces in the first 24 h; over the 5 day period, these values were 25.9% and 20.3%, respectively.

Approximately 5% of the dose was recovered in cage washing and debris. The mean overall recovery of radioactivity was 100.3%. After 30 h, the mean plasma radioactivity concentration was 1.5 µg/ml; this value decreased to 0.2 µg/ml after 96 h.

The same animals were used to study plasma concentrations (Cresswell et al. 1978). The animals were administered single oral doses of 150 mg/kg or 300 mg/kg 14C-Linear Alkylbenzene Sulfonate, both ~ 26 µCi, at intervals of 2 to 3 weeks. Approximately 2 to 3 weeks after the last single dose, each animal received 7 consecutive daily oral doses of 14C-Linear
Alkylbenzene Sulfonate at a dose of 30 mg/kg, approximately 28 µCi/day, in water.

To determine plasma concentrations, blood samples were taken prior to the first of these doses and at various intervals for the first 7.5 h afterwards. Blood samples were also taken immediately before administration of the remaining doses. After the last dose, samples were taken at various times until the animals were killed. The animals were killed 2, 4, 24, or 48 h after the last dose.

After a single oral dose of 150 mg/kg 14C-Linear Alkylbenzene Sulfonate, plasma radioactivity concentrations reached a maximum mean plasma concentration of 0.0056% dose/ml (41.2 µg/ml) at 4 h. The concentrations decreased during the 6 to 24 h period and were below the limit of detection, <0.0001% dose/ml or <1.0 µg/ml, at 48 h. The mean half-life was ~6.5 h.

After the single 300 mg/kg dose, mean plasma concentrations of radioactivity reached a maximum of 0.0024% dose/ml, 36.3 µg/ml, at 4 h. Plasma concentrations decreased during 6 to 24 h and the mean concentrations were below the limits of detection at 48 h. The mean half-life was approximately 5.5 h.

After the first daily 30 mg/kg dose, a maximum mean plasma concentration of 33.6 µg/ml was reached at 4 h; this value decreased to 1.8 µg/ml at 24 h. The mean elimination half-life was ~5 h. The predose concentration on the following 5 days did not increase. The mean concentration 24 h after the sixth dose was 2.2 µg/ml. After the seventh dose, the maximum mean plasma concentration was 43.5 µg/ml at 4 h; this value decreased until 24 h. The mean half-life was ~6 h.

Plasma concentrations in the male and female monkeys killed 24 and 48 h after the last dose were 2.4 and 1.0 µg/ml, respectively. In the monkey killed 2 h after the last of the 7 consecutive doses, there were high concentrations of radioactivity in the stomach, liver, kidneys, lungs, pancreas, adrenal glands, and pituitary gland. After 4 h, the concentrations were decreased in all of these tissues except for the pituitary gland, in which the concentration had increased; the concentrations also were increased in the heart, brain, gonads, eyes, spleen, thyroid gland, and subcutaneous (s.c.) fat. After 24 h, the concentration of 14C was less than 2 µg/g in all tissues except for the intestinal tract, 255.4 µg/g, and the liver, 10.5 µg/g. After 48 h, concentrations in all tissues were generally less. The concentration of 14C was lower in most tissues than in the plasma, indicating no specific accumulation or localization of either Linear Alkylbenzene Sulfonate or its metabolites in the tissues.

Four adult rhesus monkeys, 2 males and 2 females, were used to study the excretion of a single s.c. dose of 14C-Linear Alkylbenzene Sulfonate (Cresswell et al. 1978). An injection of 1 mg/kg 14C-Linear Alkylbenzene Sulfonate, 16 to 40 µCi, in water was administered into the s.c. tissue of the scapular region. Urine, blood, and feces were collected as described earlier. The washings from the cages and cage debris were collected every 24 h.

The majority of the dose was excreted in the first 48 h. In the first 24 h, male monkeys eliminated 55.1% and female monkeys eliminated 50.3% of the dose in urine; over 5 days, the total amount of the dose excreted in the urine by male and female monkeys was 63.8% and 64.3%, respectively. The male monkeys excreted 4.9% and the female monkeys excreted 1.6% of the 14C-label in the feces in the first 24 h; over the 5 day period, these values were 12.5% and 9.2%, respectively. The mean overall recovery of radioactivity was 94.6%. The plasma concentrations of radioactivity determined from the blood samples were less than 0.5 µg/ml for all samples; mean concentrations declined from 0.3 µg/ml at 30 h to 0.1 µg/ml at 96 h.

The same animals were used to study plasma concentrations after receiving s.c. injections of 0.5 mg/kg (8 to 22 µCi) and 0.1 mg/kg (2 to 5 µCi) 14C-Linear Alkylbenzene Sulfonate at intervals of 2 to 3 weeks. Approximately 2 to 3 weeks after the last single dose, each animal received daily s.c. injections of 1 mg/kg 14C-Linear Alkylbenzene Sulfonate, approximately 24 pCi/day, in water for 7 days. Blood samples were taken as described previously. The animals were killed 2, 4, 24, or 48 h after the last dose.

After a single s.c. dose of 0.1 mg/kg 14C-Linear Alkylbenzene Sulfonate, mean plasma radioactivity concentrations reached a maximum of 0.16 µg/ml after 2h. This concentration decreased rapidly during the 7.5 to 24 h period; the mean concentration was 0.03 µg/ml at 24 h and 0.01 µg/ml at 72 h. The mean half-life was approximately 8 h.

After the single 0.50 mg/kg dose, mean plasma radioactivity concentrations reached a maximum of 0.72 µg/ml at 4 h. This concentration decreased rapidly during the 7.5 to 24 h period; the mean concentration was 0.15 µg/ml at 24 h and 0.03 µg/ml at 120 h. The mean half-life was approximately 8.5 h.

After the first daily 1 mg/kg dose, a mean maximum concentration of 1.13 µg/ml was reached at 2 h. The mean half-life was approximately 10 h. The mean predose concentration on the following 6 days increased gradually to 0.71 µg/ml prior to the seventh dose. After the seventh dose, the maximum mean plasma concentration was 1.1 µg/ml at 4 h; this value decreased until 24 h. The mean half-life was ~13 h.

Plasma radioactivity concentrations in male and female monkeys killed 24 and 48 h after the last dose were 0.49 and 0.47 µg/ml, respectively. In the monkey killed 2 h after the seventh daily dose, the greatest concentrations of radioactivity were in the intestine, kidneys, lungs, spleen, thyroid gland, and pituitary gland. After 4 h, the concentrations were decreased in all of these tissues except the liver and kidneys. The relatively high concentrations of radioactivity in the gastrointestinal tract indicated the probable presence of material eliminated in the bile. After 24 h, the concentrations had decreased in most tissues. After 24 and 48 h, the concentrations were greatest in the tissues of the liver, kidneys, lungs, and adrenal glands. However, the tissue concentrations were less than the plasma concentration after 24 h. With the exception of the gastrointestinal tract, the concentration of 14C was similar to or less than that in the plasma in most tissues after 48 h; this indicated that there was no specific accumulation or localization of Linear Alkylbenzene Sulfonate or its metabolites in the tissue (Cresswell et al. 1978).
Dermal Absorption

Campeau (1960) tested the dermal absorption of Dodecylbenzenesulfonate in the form of triethanolamine salt of alkyl (kerosene) benzenesulfonic acid (alkyl benzenesulfonate [52%], triethanolamine sulfate [8%], and water [40%]) in rabbits and guinea pigs (not provided). The test substance was used as a scrub for 2 min. The substance was extracted from the skin using acid methanol in a test tube with a known area of the mouth by inverting the test tube over the skin 30 times. The absorption was determined by the amount of recovered Dodecylbenzenesulfonate. On the flanks of depilated or shaved albino rabbits, the amount of Dodecylbenzenesulfonate recovered was 78 and 0 µg/cm² skin. On the shaved flanks of shaved albino guinea pigs, 20 µg/cm² skin was recovered.

Two-tenths ml of a 3 mM aqueous suspension of Sodium p-1-[1-14C] Dodecylbenzenesulfonate (8.5 µCi/mg) was applied to the dorsal skin of 6 lightly anesthetized female Colworth-Wistar rats (Howes 1975). The test solution was applied to a 7.5 cm² area of skin on the back that was clipped free of hair. The solution was lathered over the test area for 1 min. After 15 min, the skin was rinsed thoroughly and dried. Restraining collars were used to prevent grooming. After 24 h the animals were killed and the treated skin was removed.

No 14C was detected in expired CO₂ urine, feces, and carcasses. The treated skin was examined by autoradiography for 14C; heavy deposition of SDBBS was found on the skin surface and in the upper regions of the hair follicles. Penetration, based on the amount of 14C excreted in the urine, feces, and expired CO₂ during the 24 h after application plus the amount in the carcass at 24 h, was determined to be <0.1 µg/cm² (Howes 1975).

In Vitro Dermal Penetration

Human abdominal skin samples were obtained from females at autopsy and prepared epidermal samples were mounted in penetration cells (Howes 1975). One-tenth ml of a 6 mM Sodium p-1-[1-14C] Dodecylbenzenesulfonate (8.5 µCi/mg) solution was placed on the corneum and 8.0 ml of saline was kept in the sampling compartment. At various times, 1.0 ml samples were removed and replaced with an equal volume of fresh saline to monitor 14C. After 48 h, the corneum was washed with distilled water and monitored for 14C by solubilizing.

No measurable penetration of SDBBS was observed until 24 h after application; the rate of penetration then increased rapidly. After 48 h, 87.2 ± 24.1 µg/cm² had penetrated. After rinsing, 30% to 50% of the applied 14C remained in the epidermis.

In another experiment, the dorsal skin of female Colworth-Wistar rats was clipped 24 h prior to killing the animals, after which the skin was excised and mounted in penetration cells. A 6 mM Sodium p-1-[1-14C] Dodecylbenzenesulfonate (8.5 µCi/mg; 0.25 ml) solution was placed on the epidermal surface of the skin and 10.0 ml of saline added to the sampling compartment against the dermis. Hourly, 1.0 ml of saline was removed and replaced with an equal volume of fresh saline to monitor 14C. After 24 h, the epidermal surface was washed with distilled water and monitored for 14C by solubilizing.

No measurable penetration was found up to 24 h after application. The 14C-SDBBS was not easily removed from the skin; after washing with distilled water, 30% of the 14C was recovered in the rinse water and 70% remained in contact with the skin (Howes 1975).

Miscellaneous Studies

Organ Effects

An increase in the release of alkaline phosphatase was observed when the jejunum was perfused with Ringer's bicarbonate solution that contained 0.5% Sodium Dodecylbenzenesulfonate (Kimura et al. 1982; Kimura and Yoshida 1982).

Gupta et al. (1986) orally administered Linear Alkylbenzenesulfonate (50, 100, 250 mg/kg) to developing male albino rats for 10 weeks. At the end of treatment, the rats were killed, the liver and kidneys removed and enzyme activity measured. For the livers, adenosine triphosphatase activity was decreased in all treatment groups (p < .01 and .001). Acid phosphatase activity was increased (p < .001) and glutamic pyruvic transaminase activity was reduced (p < .01) in the high-dose group. Alkaline phosphatase and glutamic oxaloacetic transaminase activity were unaffected.

In the kidneys, adenosine triphosphatase activity was decreased in the high-dose group (p < .01). Alkaline phosphatase activity was decreased in the mid- (p < .01) and high-dose (p < .001) groups. Acid phosphatase, glutamic oxaloacetic transaminase activity, and glutamic pyruvic transaminase were unaffected. The authors concluded that ingestion of Linear Alkylbenzenesulfonate can affect enzymatic activity in the liver and kidneys, possibly due to cellular injury (Gupta et al. 1986).

Antimicrobial Effects

Sodium Dodecylbenzenesulfonate may act bacteriostatically on micro-organisms (Yamada 1979). In some strains of Escherichia coli, a longer lag phase due to the presence of SDBBS has been observed (Pollack and Anderson 1970).

Bautista-Toledo et al. (2008) exposed the bioluminescent marine bacteria Vibrio fisheri NRRL-B-11177 to Sodium Dodecylbenzenesulfonate for 15 min and used the luminescence as a measure of inhibition. There was no inhibition below 5 mg/l. Inhibition started at 10 mg/l and increased to ~45% at 50 mg/l. Versteeg et al. (1997) reported the effective concentration to inhibit growth by 20% (EC₂₀) of Sodium Alkylbenzenesulfonate on Brachionus calyciflorus, a rotifer, to be 1.4 (confidence interval 0.882 to 2.27) mg/l and the EC₅₀ to be 2.0 (1.70 to 2.33) mg/l.

Enzyme Effects

Freeman et al. (1945) reported that a mixture of Sodium Alkylbenzenesulfonates inhibited activity of amylase, lipase, trypsin, pepsin, and phosphatase enzymes collected from a dog and a human.

A decrease in sucrase and alkaline phosphatase activities was observed when Wistar rats were fed diet containing 2.5% Sodium Dodecylbenzenesulfonate, with and without the addition of fiber (Kimura and Yoshida 1982; Kimura et al. 1980).

In an in vitro study using an enzyme preparation from the small intestine, 0.1% Sodium Dodecylbenzenesulfonate inhibited
sucrase, maltase, and leucine aminopeptidase activity; alkaline phosphatase activity was not affected. Albino rats were fed 0.25 g/kg body wt Sodium Dodecylbenzenesulfonate in feed for 3 months and then administered a single dose of either Sodium Dodecylbenzenesulfonate or water; the blood glucose concentration of rats given a single dose of 0.094 g/ml/100 g body wt of Sodium Dodecylbenzenesulfonate was increased compared to rats given a single dose of distilled water (Antal 1972).

Immunosuppressive Potential

Coy et al. (1990) used a human mixed lymphocyte reaction to evaluate the immunosuppressive potential of Sodium Dodecylbenzenesulfonate. The ingredient was nontoxic and non inhibitory, suggesting no immunosuppressive potential.

ANIMAL TOXICOLOGY

Acute Oral Toxicity

**Sodium Dodecylbenzenesulfonate**

The oral median lethal dose (LD₅₀) of Sodium Dodecylbenzenesulfonate was 2.0 g/kg for mice and 1.26 g/kg for rats (Sweet 1987).

The oral LD₅₀ of a detergent solution containing 15% Sodium Dodecylbenzenesulfonate was 7.5 ml/kg for rats and 12.6 ml/kg for mice (Arthur D. Little 1991). A lethal dosage for dogs was 400 ml/kg; 100 ml/kg had no effect.

**TEA-Dodecylbenzenesulfonate**

Five groups of Sprague-Dawley rats (5 males and 5 females per group) were dosed orally by gavage with 0.464, 1.00, 2.15, 4.64, or 10.00 ml/kg of a 1:128 aqueous dilution (195.3 mg/kg body wt) of TEA-Dodecylbenzenesulfonate (Hilltop Research 1977). The animals were observed for 14 days, after which they were killed and necropsied. No deaths occurred. Diarrhea was the only clinical sign. No significant observations were made at necropsy. The oral LD₅₀ of a 1:128 aqueous dilution in rats was >10 ml/kg.

**Linear Alkylbenzene Sulfonate**

The oral LD₅₀ of 10% and 40% solutions of Linear Alkylbenzene Sulfonate in distilled water administered intragastrically to male and female FDLR strain (Wistar derived) rats was determined (Oser and Morgareidge 1965). Linear Alkylbenzene Sulfonate had a nominal chain length of 12 carbon atoms (range, C9-C12), an average molecular weight of 346, and was 39.5% active. For male and female rats, the LD₅₀ (expressed on an active ingredient basis) was 0.65 ± 0.063 g/kg, with a slope factor of 0.173. The oral LD₅₀ of LAS for mice was 2.30 g/kg (Tiba 1972).

**Alkyl Aryl Sulfonate**

Hine et al. (1953) orally administered a product containing Alkyl Aryl Sulfonate (alkyl aryl sulfonate ≥40%, moisture ~2%, unsulfonated oil ~1%; 1.4, 1.8, 2.1, 2.4, or 2.5 g/kg) to Fisher albino mice (n = 10) and observed them for 6 days. There exhibited gelatinous diarrhea containing traces of blood in 90% of the mice. There was a decrease in motor activity immediately after administration. Necropsy revealed bloody feces, and slight hemorrhage in the pyloric mucosa. Mortality was 0, 2, 6, 8, and 10 for 1.4, 1.8, 2.1, 2.4, and 2.5 g/kg, respectively. All but 1 death in the high-dose group occurred within 12 h.

The above experiment was repeated with Golden Syrian hamsters. The hamsters had diarrhea and decreased motor activity. Mortality was 0 of 10, 1 of 10, 8 of 11, and 8 of 8 for 0.7, 1.0, 1.2, and 1.5 g/kg. The average time to death was 14 h.

The same experiment on young Long Evans rats resulted in severe diarrhea and sluggishness. Mortality was 0 of 12, 5 of 14, and 15 of 20 for 2.0, 2.6, and 3.5 g/kg, respectively. Deaths occurred between 16 h and day 1 except for 1 on day 6.

The same experiment on adult albino Fisher rabbits resulted in diarrhea and sluggishness. Mortality was 0 of 4, 2 of 4, and 3 of 4 for 0.5, 1.5, and 2.2 g/kg, respectively. Deaths occurred between days 1 and 3 (Hine et al. 1953).

Acute Dermal Toxicity

**TEA-Dodecylbenzenesulfonate**

A dose of 21.5 ml/kg of a 1:128 aqueous dilution of TEA-Dodecylbenzenesulfonate was applied under an occlusive patch for 24 h to clipped skin on the backs of New Zealand white rabbits (4 males, 4 females); the skin of 4 of the rabbits was abraded (Hilltop Research, 1977). Following patch removal, residual test material was removed and the animals were observed for 14 days, after which they were killed and necropsied. No deaths occurred. Diarrhea and emaciation in 2 rabbits and erythema were the only physical observations. No significant observations were made at necropsy. The dermal LD₅₀ of a 1:128 aqueous dilution of TEA-Dodecylbenzenesulfonate in rabbits was >21.5 ml/kg.

**Linear Alkylbenzene Sulfonate**

Two mg/kg of 5%, 10%, and 25% w/v aqueous Linear Alkylbenzene Sulfonate solution was applied to the skin (site unspecified) of rabbits (number, species, and sex unspecified) under occlusive patches for 24 h (Arthur D. Little, Inc. 1991). No evidence of systemic toxicity or mortality was observed.

The minimum lethal dosage of a 20% solution the test formulations applied to intact skin of rabbits was in the range of 200 to 1,260 mg/kg (Arthur D. Little, Inc. 1991). The dermal LD₅₀ for Linear Alkylbenzene Sulfonate solution for rabbits was determined to be >500 mg/kg (Arthur D. Little, Inc. 1991).

Acute Intravenous Toxicity

**Sodium Dodecylbenzenesulfonate**

The intravenous (i.v.) LD₅₀ of SDDBS for mice was 105 mg/kg (Sweet 1987).

Short-term Oral Toxicity

**Sodium Dodecylbenzenesulfonate**

Hazleton Laboratories (1956) incorporated Sodium Dodecylbenzenesulfonate (200, 2000, 10,000, or 20,000 ppm; 0.02%, 0.2%, 1.0% 2.0%, respectively) in the feed of male albino rats (strain not specified; n = 5) for 33 days. No controls were used. At the end of the treatment period, the rats were killed and necropsied.

There were no deaths during the treatment period. There were incidences of wheezing, nasal discharge, rough fur, a blood-like
discharge around the eyes or nose, excitability, and unthriftness. These observations were greater in the 10,000 and 20,000 ppm groups. At necropsy, all doses had occasional pale and/or granular livers or kidneys. At 20,000 ppm, the urinary bladder of 1 rat was slightly distended with urine and another rat had marked reduction in body fat stores (Hazleton Laboratories 1956).

Reagent-grade Sodium Dodecylbenzenesulfonate was dissolved in tap water and administered to 8 groups of 8 male Wistar rats with either normal or polychlorinated biphenyl (PCB)-supplemented feed (Itoh et al. 1975). The control group received normal diet and tap water, groups 2 to 4 were fed PCB-supplemented diet at concentrations ranging from 10 to 500 ppm and tap water, group 5 was fed normal diet and water containing 1000 ppm Sodium Dodecylbenzenesulfonate, group 6 was fed PCB-supplemented diet at 10 ppm and water containing 1000 ppm Sodium Dodecylbenzenesulfonate, group 7 received PCB-supplemented diet at 100 ppm and water containing 1000 ppm Sodium Dodecylbenzenesulfonate, and group 8 was fed PCB-supplemented diet at 500 ppm and water containing 1000 ppm Sodium Dodecylbenzenesulfonate. Both feed and water were provided ad libitum; consumption of both was measured every 2 days. The rats were killed after 1 month.

No significant differences in feed or water consumption were observed between treated and control groups. In group 5, Sodium Dodecylbenzenesulfonate only, the relative liver weight and serum urea and iron levels were similar to controls as were serum, total, and free cholesterol in the liver. Aniline hydroxylase, sodium-potassium-magnesium-dependent ATPase, and magnesium-dependent ATPase activities in the liver were similar to controls.

In the 2 groups that were given 500 ppm PCB, body weight gains were decreased. Liver weights increased with increased PCB concentrations; a synergistic effect of Sodium Dodecylbenzenesulfonate upon PCB was observed in the groups given 500 ppm PCB. Also, serum urea concentrations increased in the groups given 500 ppm PCB. Iron concentrations increased in groups 7 and 8; which the authors suggested was probably due to the hemolytic action of Sodium Dodecylbenzen-sulfonate. In group 8, serum cholesterol and liver free cholesterol concentrations were increased. In the groups given 100 and 500 ppm PCB, total liver cholesterol concentrations increased. Cholesterol concentrations were more marked in the groups in which PCB and Sodium Dodecylbenzenesulfonate were combined. Aniline hydroxylase activity increased and Na-K-Mg-dependent ATPase decreased, both changing in proportion with the PCB concentration. In the 500 ppm PCB-treated groups, Mg-dependent ATPase was slightly decreased. No changes in serum and liver triglyceride and nonesterified fatty acid concentrations were observed in any group (Itoh et al 1975).

**Alkylbenzenesulfonate**

Hine et al. (1953) incorporated a product containing Alkylbenzenesulfonate (alkyl aryl sulfonate ≥ 40%, moisture ~2%, unsulfonated oil ~1%; 10, 25, or 50%) into the feed of young Long-Evans rats (n = 10) for 45 days. The rats were then killed and necropsed. All rats survived the treatment period. Feed consumption and weight gains were similar between groups. Pathological examinations were unremarkable. The authors concluded that Alkylbenzenesulfonate was not classified as a toxic compound. The authors applied the product (5% aqueous) to the backs of rats and rabbits 6 days/week for 30 days. There were no clinical signs. One rabbit showed a +1 erythema at day 11 which was clear by day 12 (Hine et al. 1953).

**Sodium Alkylbenzenesulfonate Mixture**

Freeman et al. (1945) orally administered a Sodium Alkylbenzenesulfonate (2.0, 3.0, or 4.0 g/d) mixture to dogs (25 to 30 lbs; breed not specified; n = 2) in capsules just before feeding for 1 month. The dogs were then killed and necropsed. The dogs in the high-dose group had decreased feed consumption after 1 week. One dog in the high-dose group died at 3 weeks. The other dog in the high-dose group and one in the mid-dose group were killed due to poor condition. One dog in the low-dose group developed anorexia that worsened over time. One dog in the mid-dose group vomited the first few days then developed anorexia and stopped eating in week 3. Both dogs in the high-dose group stopped eating by week 3. Necropsy revealed an excess of mucous and bile in the small intestine and liquid stools in the colons of 5 dogs. There was some accentuation of the lobular markings of the liver in the dogs that died at 3 weeks. Histological examination revealed only a few discrete foci of leucocyte infiltration in the cortex of the kidneys of 1 mid-dose dog.

In another experiment, the Sodium Alkylbenzenesulfonate mixture (0.5g/100 g feed) was incorporated into the feed of rats (strain not specified; 21 days old; n = 21) for 65 days. Control rats received the basal diet. The rats were then killed and necropsied. The treated rats had slight weight loss for the first 3 days of treatment then weights were similar to controls. Hemoglobin determinations at 35 and 65 days were similar. Macroscopic and microscopic examinations revealed no abnormalities (Freeman et al. 1945).

**Short-term Oral and Subcutaneous Toxicity**

**Linear Alkylbenzenesulfonate**

Heywood et al. (1978) simultaneously administered Linear Alkylbenzenesulfonate to Rhesus monkeys (Macaca mulatta; n = 6; 3 males, 3 females) orally (0, 30, 150, 300 mg/kg/d in distilled water) and subcutaneously (0.1, 0.5, 1.0 mg/kg/d in saline) for 28 days. All the monkeys in the high-dose group vomited frequently, usually within 3 h of dosing. There was also salivation and/or retching. In the mid- and high-dose group, there was an increase in frequency of passage of loose or liquid stool. Body weights and feed and water consumption were similar among groups. There was an increase in the occurrence of chronic inflammatory cell infiltration (mainly fibroblasts) at the s.c. injection sites in a dose-dependent manner. There were injection-associated pseudocysts, hemorrhage, and necrosis. There were no treatment related findings with regards to ophthalmological, laboratory, and other pathological tests.

**Short-term Dermal Toxicity**

**Linear Alkylbenzenesulfonate**

Rabbits (number, gender, and strain unspecified) were dosed with
30% Linear Alkylbenzenesulfonate for several weeks (Sadai and Mizuno 1972). No systemic toxicity was observed at concentrations of ≤20%. Weight loss was observed after 15 days of dosing with 30% LAS.

### Subchronic Oral Toxicity

**Sodium Dodecylbenzenesulfonate**

Industrial Bio-Test Laboratories, Inc. (1961a) incorporated Sodium Dodecylbenzenesulfonate (0.020%, 0.10%, or 0.50%) into the feed of weanling Sprague-Dawley rats (n = 20; 10 males, 10 females) for 90 days. After the test period, the rats were killed and necropsied. Two sets of controls (n = 20; 10 males, 10 females) were fed either the basal diet or the basal diet incorporated with sodium sulfate (0.125%). All rats were fed ad libitum. After the test period, the rats were killed and necropsied. There were no mortalities or clinical signs observed during the test period. Body weights and weight gains were similar between groups; the high-dose male group had decreased growth but did not reach significance. The authors concluded that the decreased weight was due to palatability issues. There were no differences in the hematological studies and urinalysis among groups. There were no gross pathological findings attributable to Sodium Dodecylbenzenesulfonate ingestion. Gross and microscopic histopathological studies were unremarkable (Industrial Bio-Test Laboratories, Inc. 1961a).

Industrial Bio-Test Laboratories, Inc. (1961b) incorporated Sodium Dodecylbenzenesulfonate (0, 0.020%, 0.10%, or 0.50%) into the feed of Beagle dogs (n = 6; 3 males, 3 females) for 90 days. After the test period, the dogs were killed and necropsied. There were no mortalities during the test period. There were no differences between the controls and treatment groups with regards to weight, hematologic studies, urinalysis, or gross and microscopic pathology. There was no evidence of organ dysfunction. Feed consumption of the treatment groups was below that of the control group for the first few weeks of the experiment. It then increased but remained below that of the controls. The authors suggested that it was due to palatability and differences in the initial body weights between groups.

Industrial Bio-Test Laboratories, Inc. (1961c) incorporated Sodium Dodecylbenzenesulfonate (0.020%, 0.10%, or 0.50%) into the feed of weanling Sprague-Dawley rats (n = 20; 10 males, 10 females) for 90 days. After the test period, the rats were killed and necropsied. Two sets of controls (n = 20; 10 males, 10 females) were fed either the basal diet or the basal diet incorporated with sodium sulfate (0.125%). All rats were fed ad libitum. After the test period, the rats were killed and necropsied. There were no mortalities or clinical signs observed during the test period. Body weights and weight gains were similar between the controls and low- and mid-dose groups; the high-dose group had decreased body weights and weight gains, especially in the males. The dogs in the high-dose group had decreased feed consumption; the males in the mid-dose group had a slightly decreased feed consumption. There were lower values for hemoglobin, hematocrit, and erythrocyte counts in the high-dose group. There was microscopic evidence of hepatotoxic effects in the high-dose group; the livers of 4 dogs had mild degenerative changes in the form of slight hepato-cellular edema without evidence of hepatic cell loss. A fifth dog, that was killed early due to poor condition, had extensive hepato-cellular degeneration associated with mononuclear infiltrates. Absolute organ weights were similar to controls. Organ/body ratios were increased among dogs in the high-dose group. The authors suggested that this was due to weight loss of this group (Industrial Bio-Test Laboratories, Inc. 1962a).

Rats (number, gender, and strain unspecified) received a
formulation containing 15% SDDBS and 13% ammonium fatty alcohol polyglycolether sulfate in drinking water (Arthur D. Little 1991). A slight decrease in growth rate was observed for male rats given 2.5 ml/kg/d for 9 weeks followed by 3.75 ml/kg/d for an additional 9 weeks. Rapid weight loss was observed when the dosage was increased to 5.0 ml/kg/d at 18 weeks. The animals were given untreated water after 22 weeks; an increase in body weight gain was observed and control values were attained by week 26. Mild necrosis of intestinal mucosa with hemosiderosis of the spleen, liver, and kidneys were observed at microscopic examination. These lesions were not observed for animals in the group given 0.5 ml/kg/d.

In a second experiment, dogs (number, gender, and strain unspecified) were fed 10, 100, or 1,000 mg/kg/d of a formulation containing 15% SDDBS in the diet for 6 months. The only observation was a slight decrease in body weight gain for females of the 1,000 mg/kg/d group compared to controls. There was no difference between treated and control groups in hematologic or urine chemistry values. At microscopic examination, hemorrhagic necrosis of the intestine and infiltration of chronic inflammatory cells were observed in dogs given 10 mg/kg and hemosiderosis of the liver and spleen was observed in dogs administered 100 and 1,000 mg/kg (Arthur D. Little, Inc. 1991).

**Sodium Alkylbenzenesulfonate**

Freeman et al. (1945) reported a no observed effects level (NOEL) of 1 g/d for 6 months for dogs orally administered Sodium Alkylbenzenesulfonate.

Woodard and Calvery (1945) reported a NOEL of 0.2% Sodium Alkylbenzenesulfonate administered in drinking water for 6 months for guinea pigs.

Fitzugh and Nelson (1948) reported a NOEL of 1.0% Sodium Alkylbenzenesulfonate administered in feed for 16 weeks for rats. Rats fed 4% Sodium Alkylbenzenesulfonate grew very little and died within the first week of the experiment. This dose group had severe bloating and diarrhea.

**Linear Alkylbenzene Sulfonates**

Three groups of Sprague-Dawley rats (10 males, 10 females per group) were fed diet containing 0.02%, 0.1%, or 0.5% Linear Alkylbenzene Sulfonates for 90 days (Kay et al. 1965). A control group of 20 rats was fed untreated diet for the same time period. Body weights and feed consumption were measured weekly. Hematologic studies and urinalysis were performed on samples taken from 5 males and 5 females from each group prior to dose initiation and after 30, 60, and 90 days of testing. At study termination, all animals were killed and necropsied. The tissues of some animals were examined microscopically. There was no difference in behavior between animals of the test and control groups. No differences were observed in either body weight, feed consumption, survival, hematological values, or urinalysis. Liver-to-body weight ratios were increased for male and female rats of the 0.25 g/kg/d group compared to rats of the control group. No microscopic lesions were observed that were attributed to test article administration (Oser and Morgareidge 1965).

Rats (number, gender, and strain unspecified) were dosed orally with ≤0.6% Linear Alkylbenzene Sulfonates for 6 months (Arthur D. Little, Inc. 1977). Slight renal damage was observed at a dose of 0.2%; this damage was increased at 0.6%.

**Alkylbenzenesulfonate**

Hine et al. (1953) incorporated a product containing Alkylbenzenesulfonate (alkyl aryl sulfonate ≥40%, moisture ≤2%, unsulfonated oil ≤1%; 1, 10, or 2 ppm) into the feed of Long-Evans rats for 6 months. At the end of the treatment period, the rats were killed and necropsied. There were no clinical signs during the treatment period. One rat in the low-dose group died in week 3 due to non-treatment causes. Feed consumption and body weights were similar among groups. Hematological tests and urinalysis were unremarkable. Females in the high-dose group had increased kidney weights compared to controls; there was no evidence of kidney damage. There were no morphologic lesions caused by Alkylbenzenesulfonate.

**Sodium Alkylbenzenesulfonate Mixture**

Freeman et al. (1945) orally administered a Sodium Alkylbenzenesulfonate mixture (1.0 g/d) to dogs (25 to 30 lbs; breed not specified; n = 5) in capsules just before feeding for 6 months. The dogs were then killed and necropsied. Four of the dogs gained weight (2.5 to 8.5 lbs) and 1 lost weight (1.0 lb). A
liver function test at ~6 weeks showed no adverse effects. Gross and microscopic examination revealed 1 dog with bilateral cortical retention cysts or abscesses, one on the cortex of each kidney. Another dog had some pitting of the outer surface of the kidneys. There were few foci of leukocytic infiltration into the cortex in 3 dogs with occasional hyaline casts. The authors concluded that the kidney abnormalities were not related to treatment.

Subchronic Dermal Toxicity

**TEA-Dodecylbenzenesulfonate**

Burnett et al. (1976) applied a semipermanent hair dye formulation containing 0.5% TEA-Dodecylbenzenesulfonate dermally, twice weekly for 13 weeks, to a group of New Zealand white rabbits (6 males and 6 females). The test material was applied to shaved areas on the dorsolateral aspects of the thoracic-lumbar area, one on each side of the midline at a dose of 1 ml/kg; application sites were alternated to minimize irritation. Test sites of 3 males and 3 females were abraded on the first treatment day of each week. The test sites were rinsed 1 h after dosing. Three negative control groups of 12 rabbits per group were treated in the same manner as the test group, but no dye was applied.

All rabbits were weighed weekly; clinical chemistry and hematologic and renal function parameters were examined at the beginning of the study and at 3, 7, and 13 weeks. At the end of 13 weeks, all animals were killed and necropsied. Organ-to-body weight ratios were determined and selected tissues were examined microscopically.

No clinical signs of toxicity due to test substance administration were observed. Body weight gains of the test animals were at least equal to those of the controls. Relative organ-to-body weights may have been statistically different than the combined value of the three control groups, but no difference was observed when test group weights were compared with values from individual control groups; the differences were not accompanied by histologic evidence of toxicity.

The blood urea nitrogen values for all test rabbits and the leukocyte count for male rabbits were increased and the methemoglobin value for female rabbits was decreased compared to the control values. These differences were not considered toxicologically significant. Neither gross nor microscopic lesions due to test substance administration were observed. A semipermanent hair dye formulation containing 0.5% TEA-DDBS did not produce systemic toxicity (Burnett et al. 1976).

**Linear Alkylbenzenesulfonate**

Rabbits (number, gender, and strain unspecified) were given 2 ml applications of ≤10% Linear Alkylbenzenesulfonate (2 mg/kg) to abraded skin daily for 28 days and to intact skin for 91 days. No systemic toxicity was observed (Arthur D. Little, Inc. 1991).

**Chronic Oral Toxicity**

**Sodium Dodecylbenzenesulfonate**

Hazleton Laboratories (1956) incorporated Sodium Dodecylbenzenesulfonate (0 [n = 20 males, 20 females], 200 [n = 20 males], 1000 [n = 20 males, 20 females], or 2,000 ppm [n = 20 males]; 0, 0.02%, 0.1%, or 0.2%, respectively) in the feed of male and female albino rats (Carworth Farms strain) for 104 weeks. At the end of the treatment period, the rats were killed and necropsied. All rats that died during treatment were necropsied.

There were no behavioral or clinical signs in any of the treatment groups. Several rats in all treatment groups had unthrifty appearance, rough coats, alopecia, bloody noses and eyes, dyspnea, and sores on the head or body. Hematologic test at baseline, 13, 52, 78, and 104 weeks showed no differences between control and treatment groups. Treated males in all groups had lower growth rates. The body weights and feed consumption for both treated males and females were not different from controls. Mortality was comparable between the control, 1000, and 2000 ppm groups. Mortality was higher in the 200 ppm group; this was probably not related to treatment. Pneumonitis was the cause of death for most of the rats that died before the end of treatment. Gross necropsy results were comparable between controls and treatment groups. There were no characteristic findings through histopathology. Organ/body weight ratios were comparable between controls and treatment groups (Hazleton Laboratories 1956).

Industrial Bio-Test Laboratories, Inc. (1962b) incorporated Sodium Dodecylbenzenesulfonate (0.02%, 0.10%, or 0.50%) into the feed of Beagle dogs (n = 6; 3 males, 3 females) for 104 weeks. Due to poor palatability, the high dose was adjusted to 0.10% in the feed and the remaining dose was administered by capsule. The control group was fed the basal diet containing 0.050% sodium sulfate. At the end of the test period, the dogs were killed and necropsied.

The high-dose group was observed to have comparative weakness and lack of activity. There were no differences in body weights in the low- and mid-dose groups; there was reduced weight gain in the high-dose group. Feed consumption was decreased in the high-dose group throughout the test period. The male dogs in the mid-dose group also had decreased feed consumption, but to a lesser extent. Hematologic studies revealed lower values for hemoglobin, hematocrit, and erythrocyte counts in the high-dose group. The high-dose group was anemic. The urinalysis revealed no differences among groups. There were no differences noted in gross pathologic examination.

Microscopic examination revealed that the livers of 4 of the dogs in the high-dose group had mild degenerative changes in the form of slight hepatocellular edema without evidence of hepatocyte loss. A fifth dog had extensive hepatocellular degeneration associated with a mononuclear infiltrate (this dog was killed shortly before the conclusion of the test period due to poor condition). Some organ/body ratios were increased in the high-dose group. The authors suggested that this was due to decreased body weights since there were no differences in absolute organ weights (Industrial Bio-Test Laboratories, Inc. 1962b).

Itokawa et al. (1975), studied 4 groups of 12 male Wistar rats. The first group served as the control group and received normal diet and tap water, the second group received normal diet and tap water that contained 1000 ppm Sodium Dodecyl-
benzenesulfonate, the third group received diet that was PCB-supplemented at 500 ppm and tap water, and the fourth group received PCB-supplemented diet at 500 ppm and tap water containing 1000 ppm Sodium Dodecylbenzenesulfonate. Both diet and water were available ad libitum. Feed and water consumption were measured every 2 days. After 1, 3, or 7 months, 4 rats from each group were weighed and killed.

There were no differences in feed or water consumption between any of the treated groups and the control group. There was no differences between controls and the Sodium Dodecylbenzenesulfonate only group.

In the groups receiving PCB alone or PCB plus Sodium Dodecylbenzenesulfonate, body weights were significantly decreased and liver weights significantly increased when compared to the controls. Swelling of individual hepatic cells, pyknotic nuclei, cytoplasmic vacuolation, and other degenerative changes were prominent in scattered areas of the liver. Also, the hepatic DNA concentration was decreased, but no significant change occurred in the total DNA content. Total RNA and protein content per liver increased proportionally with increased liver weight; no significant change was observed in RNA or protein concentration compared to controls.

After 7 months, the testicular weights had decreased in male rats that received both PCB and Sodium Dodecylbenzenesulfonate; the testicle-to-body weight ratio was 0.26 ± 0.03% for these rats compared to 0.44 ± 0.02% for male control rats. Upon microscopic examination, degeneration was considerable in the testes of these rats. Necrosis of the seminiferous tubules, lost of spermatogenic cells, hypertrophy of the interstitium between the tubules, and, in some cases, the appearance of bizarre spermatogenic cells were observed. No other significant microscopic changes were observed in any other tissues.

After 1, 3, and 7 months, serum cholesterol concentrations increased in rats that received PCB only or PCB plus Sodium Dodecylbenzenesulfonate. Total cholesterol concentrations increased markedly in the liver of rats in the PCB only group and particularly in the rats that received both PCB and Sodium Dodecylbenzenesulfonate after 3 and 7 months. After 7 months, serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) activities were increased. Total hepatic cholesterol concentrations increased with test article administration.

In rats of the PCB only group, hepatic aniline hydroxylase activity was significantly increased; this increase in enzymatic activity was even greater when PCB and Sodium Dodecylbenzenesulfonate were combined. No changes were observed in either serum alkaline phosphatase or choline esterase activities.

In rats that received PCB only or PCB plus Sodium Dodecylbenzenesulfonate, hepatic Na-K-Mg-dependent ATPase activity decreased; this decrease was greater in rats that received both substances. No significant difference in Mg-dependent ATPase activity was observed (Itokawa et al. 1975).  

**Sodium Alkylbenzenesulfonate**  
Tusing et al. (1960) incorporated Sodium Alkylbenzenesulfonate (0, 0.5%, or 0.1%) into the feed of albino rats (Carworth Farms; n = 80; 40 female, 40 male) for 104 weeks. Ten of the rats of each sex of each group were killed and necropsied at 26 and 52 weeks. Any rats that died during treatment were necropsied. At the end of the treatment period the remaining rats were killed and necropsied.

The authors conducted a parallel study to compare consumption from drinking water. The rats (n = 40, 20 females, 20 males) were fed the basal diet above. Their drinking water contained 0.1% Sodium Alkylbenzenesulfonate. However, the daily intake was not comparable to the 0.1% feed group. The amount in the drinking water was adjusted to 0.04% to 0.06% after 4 weeks. In the feed study, there were no differences between control and treatment groups with regard to mortality, body weights, feed consumption, hematological tests, or biochemical tests. There were no lesions observed in the test groups. There were no pathological differences between control and test groups. There were no differences in organ weights that could be attributed to the test substance except for cecums in males at 104 weeks which were heavier.

The results in the drinking water study were similar to the feed study. There was an increase in consumption in the test groups with no other signs of stress. The liver/body weight ratio in males and the empty cecum/body weight ratio in females were increased compared to controls. However, there was no evidence in the blood chemistry of stress to the organs. The authors concluded that there was no evidence of toxicity by Sodium Alkylbenzenesulfonate at these levels (Tusing et al. 1960).

**Linear Alkylbenzenesulfonates**

Four groups of Charles River rats, 50 males and 50 females per group, were fed diets containing 0.02%, 0.1%, or 0.5% LAS for 2 years; one group of rats, 50 males and 50 females, was fed a normal diet and used as a control group (Buehler et al. 1971). Feed and water were available ad libitum. Body weights and feed consumption were measured weekly for 12 weeks, after which they were measured monthly. Five males and 5 females from each group were killed after 8 and 15 months. An interim necropsy was performed and various hematologic parameters were evaluated. After 2 years, all surviving animals were killed for necropsy and hematologic parameters were evaluated.

During months 4, 11, 15, and 21, blood was obtained from the tails of 5 males and 5 females from each group for analysis. The same animals were used throughout the study; if any of these animals died during the study, they were replaced. At the interim sacrifice, no difference was observed in the body weights of animals in the test groups and controls. Organ to body weight ratios for rats of the high-dosage group were not different at these times compared to the controls. After 8 months, the rats of the 0.02% and 0.1% LAS groups had decreased liver-to-body weight ratios compared to controls. At study termination, no differences in body weights or organ-to-body weight ratios were observed for any of the test groups compared to the controls. Hematologic values that were different from the controls were not considered test substance-related. No test compound-related gross or microscopic lesions were observed. Test compound-related effects were not observed during microscopic examination of the testicle-to-body weight ratio was 0.26 ± 0.03% for these rats compared to 0.44 ± 0.02% for male control rats. Upon microscopic examination, degeneration was considerable in the testes of these rats. Necrosis of the seminiferous tubules, lost of spermatogenic cells, hypertrophy of the interstitium between the tubules, and, in some cases, the appearance of bizarre spermatogenic cells were observed. No other significant microscopic changes were observed in any other tissues.

Tusing et al. (1960) incorporated Sodium Alkylbenzenesulfonate (0, 0.5%, or 0.1%) into the feed of albino rats (Carworth Farms; n = 80; 40 female, 40 male) for 104 weeks. Ten of the rats of each sex of each group were killed and necropsied at 26 and 52 weeks. Any rats that died during treatment were necropsied. At the end of the treatment period the remaining rats were killed and necropsied.

The authors conducted a parallel study to compare consumption from drinking water. The rats (n = 40, 20 females, 20 males) were fed the basal diet above. Their drinking water contained 0.1% Sodium Alkylbenzenesulfonate. However, the daily intake was not comparable to the 0.1% feed group. The amount in the drinking water was adjusted to 0.04% to 0.06% after 4 weeks. In the feed study, there were no differences between control and treatment groups with regard to mortality, body weights, feed consumption, hematological tests, or biochemical tests. There were no lesions observed in the test groups. There were no pathological differences between control and test groups. There were no differences in organ weights that could be attributed to the test substance except for cecums in males at 104 weeks which were heavier.

The results in the drinking water study were similar to the feed study. There was an increase in consumption in the test groups with no other signs of stress. The liver/body weight ratio in males and the empty cecum/body weight ratio in females were increased compared to controls. However, there was no evidence in the blood chemistry of stress to the organs. The authors concluded that there was no evidence of toxicity by Sodium Alkylbenzenesulfonate at these levels (Tusing et al. 1960).
tissues from animals that died on study (Buehler et al. 1971).

**Ocular Irritation**

**TEA-Dodecylbenzenesulfonate**

A volume of 0.1 ml of a 1:128 aqueous solution of TEA-Dodecylbenzenesulfonate was instilled in the conjunctival sac of the right eye of 9 New Zealand White rabbits (Hilltop Research 1977). The eyes of 3 rabbits were rinsed after 30 sec; the eyes of the other 6 rabbits were not rinsed. After 24 h, the eyes were scored for irritation; observations were made through day 7. No irritation was observed.

**Sodium Decylbenzenesulfonate**

Three drops of a 1% Sodium Decylbenzenesulfonate solution were instilled into the conjunctival sac of the eye of a rabbit (Feldman et al. 1948). Observations were made every 30 min for 3 h and then on the following day. On day 2, the rabbit was dosed twice; the second dose was administered 3 h after the first. Sodium Decylbenzenesulfonate produced severe irritation.

**Sodium Alkylbenzenesulfonate**

Maurer and Parker (1996) conducted a modified Draize test where the test substance is applied directly to the cornea. Sodium Alkylbenzenesulfonate (35.07% active; 10 µl) was instilled in the right eye of adult New Zealand albino rabbits (n = 6) and adult male Sprague-Dawley rats (n = 6). The eyelids were not held shut and the eyes were not washed. The eyes were observed after 3 h. Half of each group was then killed and the eyes and eyelids removed and examined. The remaining animals were observed on days 1, 2, 3, 4, 7, 14, 21, 28, and 35 then killed and the eyes removed and examined.

At 3 h, the overall mean score was 26.0 out of 110 for rabbits and 24.2/110 for rats. There was mild damage to the cornea (10.0/80 and 15.0/80 for rabbits and rats, respectively), conjunctiva (11.0/20 and 5.0/20, respectively), and the iris (5.0/10 and 4.2/10, respectively). The days to recovery for the rabbits was 4 to 7 days, and 3 to 7 days for the rats. Microscopic examination of the rabbit and rat corneas after 3 h showed erosion and denudation of the epithelium and neutrophils in the substantia propria. Examination of the conjunctiva showed erosion and denudation of the epithelium as well as edema and neutrophils in the substantia propria. At 35 days, microscopic examination of the rabbit conjunctiva showed a decreased prominence of goblet cells in the rabbits. The authors concluded that Sodium Alkylbenzenesulfonate was a mild irritant (Maurer and Parker 1996).

Maurer et al. (1998) performed the test describe above test on rats (n = 40). Sodium Alkylbenzenesulfonate (35.07% active, 10 µl) was instilled directly on the cornea. The eyelids were not held shut and the eyes were not washed. The eyes were examined at 3 h, and 1, 2, 3, 4, 7, 14, and 35 days. At each examination time, 5 rats were killed, the eyes removed, and examined.

At 3 h, the irritant score was 34.3 out of 110. The score for the cornea was 21.6 out of 80, 9.1 out of 20 for the conjunctiva, and 3.6 out of 10 for the iris. The conjunctiva had erosion/attenuation and denudation which was no longer evident on days 3 or 7. Regeneration was observed beginning on day 1 and no longer evident on day 14. Edema of the substantia propria occurred at 3 h and was no longer evident on days 4 or 7. Inflammation, principally neutrophilic associated with substantia propria, was noted at 3 h and no longer evident on day 14. The cornea had epithelial cell loss at 3 h with erosion/attenuation and denudation.

Regeneration in the form of conjunctivalization was observed beginning day 1. In the stroma, keratinocyte loss was evident at 3 h but not on day 7. Edema and inflammation, principally neutrophils, were present beginning at 3 h. Edema was no longer evident on days 4 or 7; inflammation was no longer evident on day 4. Neovascularization associated with the anterior stroma was observed beginning on day 2. Inflammation associated with the iris/ciliary body occurred in one rat at day 1. At day 35, 2 rats still had not fully recovered (Maurer et al. 1998).

**Linear Alkylbenzenesulfonate**

Concentrations of ≥1% Linear Alkylbenzenesulfonate produced irritation in the eyes of rabbits (Arthur D. Little, Inc. 1977).

Instillation of ≥5% LAS into the conjunctival sac of rabbits produced irritation. Congestion and edema have been observed at concentrations of 0.5 to 1.0%. Concentrations of ≥0.1% Linear Alkylbenzenesulfonate produced mild to no irritation (Arthur D. Little, Inc. 1991).

**Dermal Irritation**

**Sodium Dodecylbenzenesulfonate**

Fujise and Aoyama (1984) evaluated the irritation potential of SDBS by applying an olive oil dissolvent containing 10% SDBS to a shaved dorsal area on the head and neck of male Wistar rats for 4 days. Three rats treated in the same manner, with the exception that olive oil or water only was applied, served as the negative control group. On day 5, the rats were killed and skin samples from the application site were prepared by two methods to determine proline hydroxylase activity. Erythema was visible on day 3; on day 5 erythema was evident on 3 rats. Erythema was not observed in the control group. Proline hydroxylase activity was increased three-fold for both methods of preparation compared to control values.

Schoenberg (1985) used 3 male albino rabbits to determine the irritation potential of Sodium Dodecylbenzenesulfonate. The test material was adjusted to a total of 15.0% active material at a pH of 7.0. The abdomens of the rabbits were shaved. Two application sites were abraded and 2 were left intact. The solution, 0.5 ml, was applied to the skin under gauze that was held in place for 24 h. After 24 h, the patches were removed and the skin was examined for irritation. The sites were re-examined after 72 h. SDBS was severely irritating to the skin of rabbits, with a primary irritation score of 5.3/8.0.

In a study by Naruse et al. (1991), male ddY mice, 3 per group, were given a 0.1 ml i.v. injection of 1% Evan’s blue in...
physiological saline immediately followed by a s.c. injection of 0.2 ml of 0.02, 0.10, 0.20, 0.30, 0.40, or 0.50 mg/ml Sodium Dodecylbenzenesulfonate in physiological saline into the dorsal area. Mice of the control group were given an s.c. injection of physiological saline. The mice were killed 3 h after dosing and the s.c. reaction was evaluated. The strength of the reaction in terms of skin irritation was determined by multiplying the relative concentration of extravasated dye by the dye diameter. A score of 1 corresponded to a weak reaction, 2 to an intermediate reaction, and 3 to a strong reaction.

The mice dosed with physiological saline or 0.02 mg/ml Sodium Dodecylbenzenesulfonate had an average activity score of 0. The other test groups had the following average scores: 0.10 mg/ml was 0.1; 0.20 mg/ml was 0.8; 0.30 mg/ml was 1.6; 0.40 mg/ml was 2.0; and 0.50 mg/ml was 2.9 (Naruse et al. 1991).

**TEA-Dodecylbenzenesulfonate**

Six New Zealand white rabbits (gender not specified) were dosed with 0.5 ml of a 1:128 aqueous dilution of TEA-DDBS (Hilltop Research 1977). The solution was applied to a shaved intact and abraded area on the back of each rabbit under an occlusive patch for 24 h. After patch removal, any residual test material was removed. After 24 and 72 h, the primary irritation values were both 0 out of 8. Readings were not taken on 2 intact and 2 abraded sites.

**Linear Alkylbenzenesulfonate**

In the short-term dermal toxicity study reported by Arthur D. Little, Inc. (1991) described earlier, in which 2 mg/kg of 5%, 10%, or 25% w/v aqueous Linear Alkylbenzenesulfonate solution was applied to the skin (site unspecified) of rabbits (number, strain, and sex unspecified) under occlusive patches for 24 h, moderate skin irritation was observed at the 2 greatest concentrations.

In another short-term dermal toxicity study, described earlier, in which rabbits (number, sex, and strain unspecified) were administered 2 ml applications of 10% Linear Alkylbenzenesulfonate (2 mg/kg) on abraded skin daily for 28 days and on intact skin for 91 days, severe dermal irritation was observed at the application site. This report also indicated that rabbits were either treated for 28 days using an abraded test site or for 91 days using an intact test site with a 10% solution of a formulation containing 19% Linear Alkylbenzene-sulfonate and 19% tallow alkyl ethoxylate sulfate. Moderate dermal irritation was observed.

Three 6-h applications of a 1% (w/v) aqueous solution of Linear Alkylbenzenesulfonate produced primary skin irritation using rabbits (number, strain, and gender not given) (Arthur D. Little, Inc. 1991). No effect was observed after the first application. Moderate to severe erythema and moderate edema, which were still evident after 7 days, were observed by the third application. Upon microscopic examination after 7 days, a moderate degree of hyperkeratosis and epidermal acanthosis with crusting focally was observed.

Rats (number, gender, and strain unspecified) were treated with an aqueous solution of 30% Linear Alkylbenzenesulfonate for 15 days; the application site was clipped (Sadai and Mizuno 1972). No severe dermal damage was observed with a dose of 20%, while 30% Linear Alkylbenzenesulfonate produced what the authors described as fairly pronounced dermal damage.

A 10% Linear Alkylbenzenesulfonate solution was an acute dermal irritant in rabbits; a 1% solution did not produce any dermal irritation (Arthur D. Little, Inc. 1977).

Imokawa examined dermal irritation as a function of different Linear Alkylbenzenesulfonate structures. The dermal irritation of a 2 g/100 ml aqueous solution of C_{12} Linear Alkylbenzenesulfonate (97.88% purity) was evaluated using albino guinea pigs (gender not specified). A 1.5 cm² occlusive patch was used to apply 0.1 ml of the test material to the shaved backs of at least 6 guinea pigs for 24 h. The test sites were scored 2 and 24 h after patch removal by rating erythema and edema on a scale of 0 to 2 and then combining the scores for a maximum total score of 4. Moderate to severe dermal irritation resulted, with an irritation score of 3.0/4.0 at both readings. Using the same test procedure, a mixed Linear Alkylbenzenesulfonate solution (99.8% purity) containing 33.7% C_{12} and 7.0% C_{10} produced a dermal irritation score of 2.75/4.0 at both readings.

In a cumulative open patch test, a 2.0 g/100 ml aqueous solution of C_{12} Linear Alkylbenzenesulfonate (97.88% purity) in 10 mm diameter tubes was applied to the same site on the shaved backs of guinea pigs (number and gender unspecified) twice daily for a total of 9 treatments. The test sites were scored prior to each patch application as stated above. The dermal irritation score for the cumulative open patch test was 1.42/4.0. Following the same test procedure, a mixed Linear Alkylbenzenesulfonate solution (99.8% purity) containing 33.7% C_{12} and 7.0% C_{10} resulted in a dermal irritation score of 0.58/4 (Imokawa 1979).

**Alkylbenzenesulfonate**

Hine et al. (1953) performed a Draize test on intact and abraded skin using shaved rabbits. A product containing Alkylbenzenesulfonate (alkyl aryl sulfonate ≥40%, moisture ~2%, unsulfonated oil ~1%; 1, 10, or 20 ppm) was applied to occluded skin for 24 h. The skin was washed and evaluated immediately and at 48 and 96 h. There were no deaths and no evidence of absorption of the product. There was moderate edema, erythema, and scabbing of the abraded skin that returned to normal. There were no effects to the intact skin.

The authors applied the product (0.5 g) to 4 shaved areas (intact and abraded) on the backs of albino rabbits and the areas were occluded for 24 h. The covering was removed and the areas read immediately and at 72 h. There were no readings taken for the intact skin (no explanation given). Abraded skin had slight persistent edema and erythema (Hine et al. 1953).

**Dermal Sensitization**

**Linear Alkylbenzenesulfonate**

Guinea pigs (number unspecified) were injected intradermally with a 1% w/v aqueous solution of Linear Alkylbenzenesulfonate and challenged topically (Arthur D. Little, Inc. 1991). A sensitization reaction was not observed.

Robinson et al. (1989) observed positive sensitization results in up to 76% of the guinea pigs treated in a maximization test, with an induction injection of 0.6% to 5%, induction patch application
of 0.1% to 1%, and challenge patch application of 1%. No dose-response pattern was evident. A repeat insult patch test (RIPT) conducted concurrently using 1.2% to 2.5% Linear Alkylbenzenesulfonate at induction and 0.5 to 1% at challenge produced only weakly positive responses.

This same author reported another RIPT, in which Linear Alkylbenzenesulfonate (with >90% of the alkyl chain lengths for the mixture in the range of C10 to C14) was tested at induction concentrations of 2% to 100% followed by challenge applications of 1% or 2% produced weak to moderate sensitization reactions using guinea pigs.

**Alkylbenzenesulfonate**

Hine et al. (1953) injected a product containing Alkylbenzenesulfonate (alkyl aryl sulfonate ≥40%, moisture ≤2%, unsulfonated oil ≤1%; 0.1% in 0.9% saline) intradermally into the backs of albino guinea pigs (n = 3) on alternate days for 10 injections. The first injection was 0.05 ml, all others were 0.01 ml. Readings were taken 24 h after each injection. Two weeks after the last injection a test injection (0.05 ml) was made into the flank. There was no erythema or wheal formation 24 h after the challenge injection. The authors concluded that Alkylbenzenesulfonate is non-irritating.

**REPRODUCTIVE and DEVELOPMENTAL TOXICITY**

**Oral**

**Sodium Alkylbenzenesulfonate**

Tusing et al. (1960) used 10 males and 10 females from each group in the Sodium Alkylbenzenesulfonate feeding study described earlier for a reproductive and developmental toxicity study. After 14 weeks on the treated feed (0, 0.05%, or 0.1% Sodium Alkylbenzenesulfonate), the rats were paired and mated while continuing on the test diet. After 3 days, the males were returned to their original cages; the females were allowed to deliver and nurse for 21 days. They were then returned to their original cages and the pups were fed the parental diet. At ~130 day, the F1 pups were paired and mated. The F2 pups were continued on the parental diet for 8 weeks. Sodium Alkylbenzenesulfonate had no observed effects on fertility, litter size, lactation, or survival of offspring. There were no remarkable findings in the hematologic studies, urinalysis, or blood urea nitrogen tests. Gross and microscopic examinations of the offspring were also unremarkable.

**Alkylbenzenesulfonate**

Omori et al. (1968) incorporated Alkylbenzenesulfonate (0, 0.25%, 0.1%, 0.5%, 1.0%, or 2.0%) into the diets of pregnant rats (n = 15 [0, 0.25%, and 0.5%], 16 [0.1%], 14 [1.0%], 5 [2.0%]; strain not specified). Dams in the 1.0% and 2.0% groups had diarrhea. No clinical signs were noted in the other groups. Feed intake was decreased in the high-dose group. At necropsy, placenta weights were decreased compared to controls in the high-dose group (0.26 ± 0.01 vs. 0.36 ± 0.01). The number of pups per litter was reduced in the high-dose group (3.6 ± 2.4 vs 10.4 ± 0.7). The number of dead litters and dead pups were increased and the number of resorptions were reduced in the high-dose group. In the high-dose group, body weight, body length, and tail length of the pups were reduced. There were no differences in organ weights of the pups.

Mice (n = 22 to 24; strain not specified) were orally administered Alkylbenzenesulfonate (0, 24, or 240 mg/kg) on days 7 and 13 of pregnancy. There was a slight decrease in maternal weight gain (80.6, 62.9, 56.3 g, respectively). There were no effects observed on the fetuses from dams in the low-dose group. The number of dead pups increased in the high-dose group. There were no congenital malformations observed in either treatment group (Omori et al. 1968).

**Linear Alkylbenzenesulfonate**

Charles River rats that were being used in a chronic toxicity study were concurrently used in a 3-generation reproductive study (Buehler et al. 1971). Twenty male and 20 female rats from each group were fed a diet containing 0, 0.5%, 0.1%, or 0.02% LAS then were mated after being on study for 84 days. There were no effects observed associated with Linear Alkylbenzenesulfonate administration.

Palmer et al. (1975a) tested for teratogenic effects of LAS in CD rats (n = 20), CD-1 mice (n = 20), and New Zealand white rabbits (n = 13). Linear Alkylbenzenesulfonate (0, 0.2, 2.0, 300, or 600 mg/kg/d in water) was orally administered from day 6 to day 15 in rats and mice and to day 18 in rabbits. The rats, mice, and rabbits were killed and necropsied on days 20, 17, and 29, respectively.

For the mice, 7 dams died in the 300 mg/kg/d group and 18 died in the 600 mg/kg/d group; all others survived. For the rats, only 1 died in the 600 mg/kg/d group. For the rabbits, 1, 11, and 13 died in the 2, 300, and 600 mg/kg/d groups, respectively. The mice in the 300 mg/kg/d group had retarded weight gains and weight loss was observed in the 600 mg/kg/d group. There was retarded weight gains for the rats in the 600 mg/kg/d group. There was weight loss for rabbits in the 300 and 600 mg/kg/d groups. In all species toxic effects of the gastrointestinal tract were observed, especially in the rabbits (diarrhea, anorexia, weight loss, and cachexia prior to death. Total litter loss (abortion and/or total resorption) tended to occur as a secondary consequence. The authors concluded that 300 and 600 mg/kg/d caused marked maternal toxicity or undue interference with maternal economy. At maternally toxic dosages there was increased fetal loss and reduced litter size in rabbits and mice, mostly due to total litter loss. At nontoxic and slight to moderately toxic dosages, values for litter size and fetal loss were unaffected (mice and rabbits, 0.2 and 2.0 mg/kg/d; rat, all dosages).

Examination of the fetuses revealed no increase in abnormalities (Palmer et al. 1975a).

Pregnant ICR-SLC mice were dosed with 10, 100, or 300 mg/kg Linear Alkylbenzenesulfonate by stomach tube on days 6-15 of gestation (Shiobara and Imahori, 1976). The mice were killed on day 17 and their fetuses examined. Marked maternal and embryonic toxic effects, including maternal death, premature delivery, total litter loss, and high fetal death rate, were observed for mice of the 300 mg/kg dosage group. Maternal body weight gains and fetal body weights were significantly decreased in each of the dose groups. External malformations, such as cleft palate and exencephaly, were observed sporadically for fetuses of the control and dose groups.
**Sodium Alkylbenzenesulfonate Mixture**

As described earlier, Freeman et al. (1945) conducted a subchronic toxicity study in which the fertility of the treated rats also was determined. A Sodium Alkylbenzenesulfonate mixture (0.5g/100 g feed) was incorporated into the feed of rats (strain not specified; 21 days old; n = 21) for 65 days. Control rats received the basal diet. According to these authors, the Sodium Alkylbenzenesulfonate mixture had no effect on fertility in rats.

**Dermal**

**TEA-Dodecylbenzenesulfonate**

A semipermanent hair dye formulation containing 0.5% TEA-Dodecylbenzenesulfonate was applied dermally to a shaved dorsoscapular area of 20 pregnant Charles River CD rats (Burnett et al. 1976). A dose of 2 ml/kg was applied on days 1, 4, 7, 10, 13, 16, and 19 of gestation. Three negative control groups were shaved but not treated. The rats were killed on day 20 of gestation and the fetuses were examined. No signs of toxicity and no dermal irritation were observed in the treatment groups, other than discoloration of the skin and hair at the test site. There were no differences in body weight gains or feed consumption between the treated and negative control groups. The authors concluded that the test material did not produce embryotoxic or teratogenic effects.

Burnett et al. (1981) reported a study in which 25 male Sprague-Dawley CD rats were dosed dermally with 0.5 ml of a semipermanent hair dye formulation that contained 0.2% to 0.3% TEA-Dodecylbenzenesulfonate twice weekly for 10 weeks. The formulation was applied to a shaved 1 in² area on the back of each rat. A second group of 25 male Sprague-Dawley CD rats was untreated and served as a control group. After 10 weeks of dosing, each of the 25 treated male rats was mated with 3 10-week-old female Sprague-Dawley CD rats (1/week for 3 weeks) for a total of 75 mated females per group. The gravid females were allowed to deliver and the number and gender of live and dead pups were recorded. After 4 days, each litter was culled to a maximum of 6 males.

Two healthy 21-day-old males were selected from each litter as the F₁ males and kept until maturity. After 12 weeks, 100 F₁ males per group were mated with 3 sexually mature females (1/week for 3 weeks). The females were killed on days 14 to 16 of gestation and their uteri and fetuses were examined. There were no differences in body weight gains between the treated and control groups. The level of fertility was high for the initial test males as well as the controls, and the results of the matings of the F₁ males were similar for both groups.

There were no differences in the number of total and average live pups between the treated and control group. The authors concluded that the test material did not produce any adverse effects on reproduction in male Sprague-Dawley CD rats.

**Linear Alkylbenzenesulfonate**

Pregnant ICR-JCL mice were administered dermal applications of 0.5 ml of 0.85%, 1.7%, 2.55%, or 3.4% Linear Alkylbenzenesulfonate solutions on days 1 to 13 of gestation (Masuda et al. 1974). Controls were dosed with distilled water. The number of gravid dams was 20, 21, 16, 17, and 10 for the control, 0.88%, 1.7%, 2.55%, and 3.4% groups, respectively. The final mean body weight of the 10 dams of the 3.4% Linear Alkylbenzenesulfonate group was increased compared to the final mean body weight of 10 dams of the control group. The absolute liver, kidney, and spleen weights were also increased for this group. There was no difference in body weight gain between test and control dams and no visceral defects were observed. Pregnancy rate was decreased in the 3.4% dose group, with a rate of 33.3% as compared to 69.0% for the controls; considerable dermal irritation was observed at the application site. Live fetus growth was decreased in all test groups except for the 1.7% group when compared to the controls. There was no difference in external or internal fetal anomalies. However, the frequency of retarded ossification of sternebrae was 25% and 27% for the 2.55% and 3.4% dose groups, respectively, as compared to 11% for the control group. The authors concluded that there was no conclusive evidence of teratogenic effects.

Pregnant ddY mice were administered dermal applications of 0.017%, 0.17%, or 1.7% Linear Alkylbenzenesulfonate solutions on days 2 to 14 of gestation. Two control groups were dosed with distilled water or were untreated. The number of gravid dams was 10, 7, 4, 10, and 5 for the untreated control, 0, 0.017%, 0.17%, and 1.7% groups, respectively. No adverse effects were observed for the test fetuses as compared to the controls. The authors concluded that there was no conclusive evidence of teratogenic effects (Masuda et al. 1974).

Palmer et al. (1975b) applied Linear Alkylbenzenesulfonate (0, 0.03%, 0.3%, or 3.0% in distilled water; 0.5 or 10 ml) to the shaved backs of CD-1 mice (n = 20), CD rats (n = 20), and New Zealand white rabbits (n = 13) to test for teratogenic effects. The mice were treated days 2 to 13 of pregnancy, rats were treated days 2 to 15, and rabbits were treated days 1 to 16. The applications were not occluded or washed. One mouse died in the low-dose group, no rats died during treatment, and 1 rabbit in the mid-dose group died. The mouse and rabbit dams had dermal reactions consisting of erythema and edema with peak response at day 6 to 7. The mice also had dead skin and accumulated test material formed a scabrous layer; the rabbits had cracking and bleeding of the skin. There were minor dermal reactions in the rats. Recovery was evident in rats and rabbits after the peak response was attained. All animals had increasing irritability, with peak hypersensitivity at the same time as the local reactions. There was weight loss or marked weight retardation for mice and rabbits in the high-dose group. There was a decrease in number of litters containing viable young in the high-dose groups. The authors concluded that for the dams, marked toxicity was evident in the high-dose groups of mice and rabbits. Mild toxicity was observed in the mid-dose groups for mice and rabbits and the high-dose group for rats. Litter and mean pup weights were not affected by any dose in any of these species. There were no abnormalities associated with treatment at the low- and mid-dose levels. The high-dose level did not have enough litters for assessment.

Daly et al. (1980) tested the reproductive and developmental effects of dermally applied Linear Alkylbenzenesulfonate to clipped pregnant Wistar rats (n = 20 or 21). The test material was applied to the shaved backs of CD-1 mice (n = 20), CD rats (n = 20), and New Zealand white rabbits (n = 13) to test for teratogenic effects. The mice were treated days 2 to 13 of pregnancy, rats were treated days 2 to 15, and rabbits were treated days 1 to 16. The applications were not occluded or washed. One mouse died in the low-dose group, no rats died during treatment, and 1 rabbit in the mid-dose group died. The mouse and rabbit dams had dermal reactions consisting of erythema and edema with peak response at day 6 to 7. The mice also had dead skin and accumulated test material formed a scabrous layer; the rabbits had cracking and bleeding of the skin. There were minor dermal reactions in the rats. Recovery was evident in rats and rabbits after the peak response was attained. All animals had increasing irritability, with peak hypersensitivity at the same time as the local reactions. There was weight loss or marked weight retardation for mice and rabbits in the high-dose group. There was a decrease in number of litters containing viable young in the high-dose groups. The authors concluded that for the dams, marked toxicity was evident in the high-dose groups of mice and rabbits. Mild toxicity was observed in the mid-dose groups for mice and rabbits and the high-dose group for rats. Litter and mean pup weights were not affected by any dose in any of these species. There were no abnormalities associated with treatment at the low- and mid-dose levels. The high-dose level did not have enough litters for assessment.
Linear Alkylbenzenesulfonate (20.5%), alkylbenzene (0.2%), ash (0.6%), and water (77.7%). The 3 control groups were untreated and unclipped, clipped, or clipped and treated with water. The test groups were treated with the test material (1%, 5%, or 20% in water; 20, 100, or 400 mg/kg/d, respectively) by applying the test material, rubbing it in for 3 min, leaving it on for 30 min, and then rinsing off with water. The other test groups were treated with test material (0.05%, 0.1%, or 0.5%; 1, 2, or 10 mg/kg/d) which was not removed after application. The dams were treated daily from day 0 to 20 of gestation then killed and necropsied. The fetuses were examined for deformities. There were no mortalities during the test period. The mean body weights of the high-dose wash-off group were decreased compared to controls for gestation day 12 to 21. Feed consumption was comparable in all groups. There were no cutaneous manifestations in the 0.05%, 0.1%, or 0.5% leave-on groups. There was a light brown skin discoloration in 3 dams on days 3 to 6 of the 1.0% wash-off group, and 14 of 20 dams in the 5.0% wash-off group had slight erythema and dry skin on days 3 to 6 and slight skin thickening in 7 of 20 animals. After day 6, erythema and fissuring were no longer observed. Brown discoloration continued in 1 or 2 animals throughout treatment. The high-dose wash-off group had slight erythema on most dams on days 2 to 4. After day 6, this reaction was no longer observed. There was slight skin thickening at the application site on 2 dams on day 2 and on all dams by day 5. Moderate skin thickening was noted in 6 dams the first half of gestation. Slight fissuring was noted in 18 dams from day 4. Clear exudate and brown skin discoloration were occasionally noted.

There were no differences between groups with regards to number of corpora lutea, implantations, viable fetuses, or resorptions. No abnormalities were observed at necropsy. There were no differences among groups of offspring for viability or deformities. The authors concluded that Linear Alkylbenzenesulfonate applied to the skin of pregnant rats (either left on or washed off) elicits skin reactions and decreases maternal body weight but does not have any teratogenic or embryopathic effects (Daly et al. 1980).

A 20% Linear Alkylbenzenesulfonate solution (Nomura et al. 1980; Nomura et al. 1987) or a detergent containing a mixture of Linear Alkylbenzenesulfonate (27%) and alcohol sulfate was applied twice daily to the dorsal skin of pregnant JCL:ICR mice during the preimplantation period (days 0-2 of gestation). There was an increase in the number of embryos collected on day 3 that were severely deformed or remained at the morula stage. Most of the abnormal embryos were fragmented or remained at the 1- to 8-cell stages and were either dead or dying. The number of embryos in the oviducts was greater for the mice dosed with Linear Alkylbenzenesulfonate as compared to the control mice used in that study (which were dosed with water). No pathological changes were detected in the major organs of the dams.

### GENOTOXICITY

**Sodium Dodecylbenzenesulfonate**

Kawachi et al. (1980) performed a variety of mutagenicity assays using Sodium Dodecylbenzenesulfonate. An Ames test using *Salmonella typhimurium* strains TA98 and TA100, a rec assay using *Bacillus subtilis* without metabolic activation, and a chromosomal aberration test using hamster lung fibroblast cells without metabolic activation all had negative results.

In another test, these authors used Sodium Dodecylbenzenesulfonate in a mutation test involving silk worms. The results were negative (Kawachi et al. 1980).

**Linear Alkylbenzenesulphonate**

In an in vitro transformation assay of Linear Alkylbenzenesulfonate, cryopreserved hamster embryo cells (n = 9) were used as the source of target and feeder cells. No transformations were produced at concentrations up to 50 μg/ml, but Linear Alkylbenzenesulfonate was cytotoxic at this concentration (Inoue et al. 1980).

**Linear Dodecylbenzenesulfonates/Ozone/UV**

Murakami et al (1992) exposed Linear Dodecylbenzenesulfonates to ozone and UV for 4 and 8.5 h or ozone alone for 16 h (with an anti-foaming agent). A mutation frequency assay was performed using the resulting degradation products (0 to 100 μl/plate) and *S. typhimurium* (TA98, TA100, and TA104) with and without metabolic activation. The LDS decomposition products were lethal at 10^4 M. The degradation products from the 4-h treatment were mutagenic in a concentration dependent manner for all 3 strains, with and without metabolic activation. The products of the 8.5 h and ozone alone treatments were mildly mutagenic. The experiment was repeated with formaldehyde and glyoxal at the same concentrations as that resulting from the 4-h ozone/UV experiment and various concentrations of Linear Dodecylbenzenesulfonates and anti-foaming agent. There were no interactions or effects observed. The same assay was repeated with just formaldehyde or glyoxal. Formaldehyde was mutagenic for TA104 with and without activation and TA100 with activation. Glyoxal was mutagenic for TA104 and TA100 with and without activation. The authors suggest that the mutagenic activity of decomposed Linear Dodecylbenzenesulfonates was in part due to formaldehyde and glyoxal, but not entirely.

Murakami et al. (1996) exposed Sodium Linear Dodecylbenzenesulfonates to UV and ozone for 4 h. The resulting degradation products (0.1 ml) or Linear Dodecylbenzenesulfonates (0.1 ml) were used in a mutation assay using *S. typhimurium* (TA100 and TA104) with and without metabolic activation. Sodium LDS was not mutagenic.

The decomposition products were mutagenic for both strains with and without activation. Linear Dodecylbenzenesulfonates with activation was not lethal to TA104 up to ~10^{-2} mol/l or without activation up to ~10^{-4} mol/l, but was above these concentrations. Linear Dodecylbenzenesulfonates with activation was not lethal to TA100 up to ~10^{-1} mol/l or without activation up to ~10^{-4} mol/l, but was above these concentrations. The authors calculated the total amount of formaldehyde and glyoxal in the decomposed Linear Dodecylbenzenesulfonates solution accounted for 44.9% of the total mutagenicity of the decomposed Linear Dodecylbenzenesulfonates solution without metabolic activation and 68.4% with activation for TA104. Formaldehyde and glyoxal accounted for 31.75% and 88.0% of the total.
mutagenicity for TA100, respectively. However, when Linear Dodecylbenzenesulfonates, formaldehyde, and glyoxal were assayed in different combinations, the authors concluded that the mixture does not increase the mutagenicity by interaction between formaldehyde and glyoxal.

**CARCINOGENICITY**

**Oral**

*Sodium Dodecylbenzenesulfonate*

Rats (number, gender, and strain unspecified) were given 100 ppm (0.01%) Sodium Dodecylbenzenesulfonate in drinking water for 100 weeks (Bornmann et al. 1961). Lesion occurrence, including incidences of neoplasms, was not changed. Body weight gain was not affected.

**Linear Alkylbenzenesulfonate**

Rats (gender and strain unspecified), 23 per group, were administered 0.01%, 0.05%, or 0.1% LAS in drinking water for 2 years (Tiba 1972). A control group of 21 rats was administered untreated water. No increase in neoplasm incidence was observed. Body weight was not affected.

**Dermal**

*TEA-Dodecylbenzenesulfonate*

A skin painting study was performed to determine the carcinogenic potential of a semipermanent hair dye formulation containing 0.5% TEA-Dodecylbenzenesulfonate (Burnett et al. 1980). The hair dye formulation, 0.05 ml, was applied to a shaved 1 cm² area of the intrascapular region of 100 Swiss Webster mice (50 males and 50 females) once a week for 23 months. Three negative control groups were shaved but not dosed for 23 (1 group) or 21 months (2 groups). Animals were observed daily for mortality, changes in behavior, and physical appearance, evidence of lesions was recorded weekly, and body weights were recorded monthly. After 9 months of dosing, 10 males and 10 females from each group were killed for necropsy; liver and kidney weights were recorded and organ to body weight ratios were determined. Gross and microscopic examinations were performed. There were no differences observed in mean or absolute liver or kidney weights or in organ to body weight ratios among the mice killed after 9 months. There was no difference in survival rate between the test and control groups. The incidence of neoplasms in test and control groups was also similar. The authors concluded that the test material did not produce carcinogenic effects.

**Linear Alkylbenzenesulfonate**

Percutaneous application of a formulation containing 15.6% Linear Alkylbenzenesulfonate to Swiss ICR mice (number, gender, and strain unspecified) at concentrations of 0.1%, 1.0%, or 10.0% 3 times per week for 18 months produced neither a dermal nor a systemic carcinogenic response (Arthur D. Little, Inc. 1991). In the 10% test group (50 animals), acanthosis and/or hyperkeratosis of the treated skin and one squamous papilloma were observed.

**Physicochemical Screening Test**

*Sodium Dodecylbenzenesulfonate*

A physicochemical screening test, the k, test, was used to screen for the carcinogenic potential (Bakale and McCreary 1987); Sodium Dodecylbenzenesulfonate was determined not to be potentially carcinogenic.

**CLINICAL ASSESSMENT of SAFETY**

**Oral Absorption**

**Linear Alkylbenzenesulfonate**

In a human oral absorption study (144 h after dermal administration of 35S-Linear Alkylbenzenesulfonate in another study) 90% of the radioactivity was excreted in the urine and feces. Approximately 50% of the dose was absorbed and excreted in the urine within 24 h (Arthur D. Little, Inc. 1991).

**Dermal Absorption**

*Dodecylbenzenesulfonate*

Campeau (1960) tested the dermal absorption of Dodecylbenzenesulfonate in the form of triethanolamine salt of alkyl (kerosene) benzenesulfonic acid (alkyl benzenesulfonate [52%], triethanolamine sulfate [8%], and water [40%]). The test substance was used as a scrub for 2 min. The substance was extracted from the skin using acid methanol in a test tube with a known area of the mouth by inverting the test tube over the skin 30 times. The absorption was used to determine the amount of recovered Dodecylbenzenesulfonate (n not provided). On the human palm, 570 µg/cm² was recovered. On the fingertips and the forearm, 360 and 94 µg/cm² Dodecylbenzenesulfonate was recovered, respectively. When pH was adjusted, the amount of Dodecylbenzenesulfonate recovered increased as pH decreased. At a low pH of 3, adsorption continues even after prolonged scrub periods, but at pH 7, the rate of adsorption does not increase after 8 min. Dodecylbenzenesulfonate is completely removed from the skin with soap. The authors concluded that Dodecylbenzenesulfonate adsorbs readily to the skin.

**Linear Alkylbenzenesulfonate**

A human dermal absorption study determined that 144 h after dermal application of 35S-Linear Alkylbenzenesulfonate, 99% of the radioactivity was recovered in the urine and feces. Approximately 0.01% of the radioactivity was removed from the application site and < 0.01% of the radioactivity was recovered, respectively. When pH was adjusted, the amount of Dodecylbenzenesulfonate recovered increased as pH decreased. At a low pH of 3, adsorption continues even after prolonged scrub periods, but at pH 7, the rate of adsorption does not increase after 8 min. Dodecylbenzenesulfonate is completely removed from the skin with soap. The authors concluded that Dodecylbenzenesulfonate adsorbs readily to the skin.

**Oral Toxicity**

*Sodium Alkylbenzenesulfonate*

Freeman et al. (1945) orally administered a Sodium Alkylbenzenesulfonate mixture (100 mg/d) in capsule form to male adults (n = 6) with meals (33.3 mg/meal) for 4 months. Red and white blood cell counts and hemoglobin content were not affected. There was no change in kidney function. There was transient flatulence and loss of appetite in 2 subjects. One subject...
In another experiment, feces were collected from male subjects (n = 6) in 2 5-day periods, one with a consistent diet and the other with the consistent diet plus 33.3 mg Sodium Alkylbenzenesulfonate mixture in capsules at each of 3 meals/d. In 5 of the subjects, there were no effects on the fat and nitrogen content of the feces. The sixth subject had an increase in fecal fat and nitrogen. The authors concluded that the Sodium Alkylbenzenesulfonate mixture has a low order of toxicity when ingested with food or when taken just before a meal (Freeman et al. 1945).

Dermal Irritation

**Sodium Dodecylbenzenesulfonate**

An aqueous solution of 12.5 mmol Sodium Dodecylbenzenesulfonate (pH 6.4)/l (with a correction being made for percentage of active mass) was applied to an area on the forearm of 18 subjects, 8 males and 10 females (Tupker et al. 1989). Irritation was determined by measuring transepidermal water loss (TEWL) and by visual observation. The subjects were treated with 0.3 ml of the solution and treated twice daily each working day for 3 weeks (for a total of 28 applications). The solution was applied to a disc of absorbent Whatman paper that was taped to the volar side of the forearm, near the elbow, for 45 min. The mean interval between applications was 3 h and the test site was rinsed and dried after removal of the paper.

Sodium Dodecylbenzenesulfonate application resulted in an increase in TEWL over the 3 weeks, with a mean TEWL of 10.1 g/m²h on day 19; the mean baseline TEWL was 4.9 g/m²h. Using mean TEWL values as the standard for comparison, Sodium Dodecylbenzenesulfonate was less irritating than sodium lauryl sulfate. After 3 weeks of dosing, the TEWL value increased to ≅5 g/m²h and the visual score was 1 + for almost 70% of the subjects (Tupker et al. 1989).

**Linear Alkylbenzenesulfonates**

The soap chamber test was used to evaluate the irritation potential of 1.0% and 0.1% solutions of Linear Alkylbenzenesulfonates (Frobe et al. 1990). Occlusive patches were used to apply 0.2 ml of the aqueous solutions to the volar forearm of 8 female subjects for 24 h. After patch removal, the application site was rinsed and scored for erythema. On the following 4 days, patches were applied for 6 h to the same site. Erythema was scored at the test site prior to patch application and 72 h after removal of the final patch.

A 1% Linear Alkylbenzenesulfonates solution produced moderate/intense erythema in all subjects within 48 h; therefore, testing at this concentration was discontinued. The 0.1% Linear Alkylbenzenesulfonates solution produced negligible or mild erythema. The mean erythema score 72 h after removal of the final patch was 1.2/3 and 0/3 for the 2 groups tested with 0.1% Linear Alkylbenzenesulfonates solutions.

Cumulative irritation patch testing using 0.05% and 0.2% aqueous Linear Alkylbenzenesulfonates on 71 and 81 subjects, respectively, produced mild to moderate irritation (Arthur D. Little, Inc. 1991).

In Vitro

A study was performed correlating in vitro epidermis curling and in vivo dermal irritation (Tavss et al. 1985). Application of a 2.4% solution of LAS (pH 5.3) to epidermal strips caused the strips to twist and curl, resulting in a curling ratio of 0.25 ± 0.011. Application of a 10% solution of LAS (neutral pH) for 5 days to the forearms of 2 to 3 subjects using Duhring chambers produced severe irritation within the first day.

The relative intensity of skin roughness produced by LAS formulations of varying alkyl chain length was evaluated (Imokawa et al. 1975). LAS formulations with alkyl chain length of 12 carbons produced more skin roughening than LAS formulations with alkyl chain lengths of 8, 14, or 16 carbons.

Dermal Sensitization

**Linear Alkylbenzenesulfonate**

The sensitization potential of 0.05 and 0.2% aqueous concentrations of Linear Alkylbenzenesulfonate was evaluated using 71 and 81 subjects, respectively (Arthur D. Little, Inc. 1991). Sensitization reactions were not observed at either concentration.

The sensitizing potentials of a 0.1% aqueous Linear Alkylbenzenesulfonate solution and a 0.1% LAS solution in 50% ethanol/water were evaluated on 86 subjects (Arthur D. Little, Inc. 1991). The 0.1% aqueous solution of LAS did not produce a sensitization reaction in any subject. The 0.1% solution in 50% ethanol/water produced a sensitization response in 6 subjects. Subsequent testing of the 50% ethanol/water solution alone determined that the positive response was due to ethanol.

Human repeated insult patch testing of 0.01% to 0.113% Linear Alkylbenzenesulfonate alone using 2,294 subjects and 0.001% to 0.09% Linear Alkylbenzenesulfonate in formulation using 17,887 subjects did not produce a sensitization reaction in any of the subjects (Robinson et al. 1989). Extended product use testing reported no evidence of sensitization or any other skin reactions due to Linear Alkylbenzenesulfonate; patch testing of 79 consumers with skin problems due to products containing Linear Alkylbenzenesulfonate did not result in positive reactions to Linear Alkylbenzenesulfonate.

SUMMARY

An earlier safety assessment of Sodium Dodecylbenzenesulfonate, TEA-Dodecylbenzenesulfonate, and Sodium Decylbenzenesulfonate was expanded to include Ammonium Dodecylbenzenesulfonate, Calcium Dodecylbenzenesulfonate, DEA-Dodecylbenzenesulfonate, Isopropylamine Dodecylbenzenesulfonate, Magnesium Isodecylbenzenesulfonate, MIPA-Dodecylbenzenesulfonate, Potassium Dodecylbenzenesulfonate, Sodium Tridecylbenzenesulfonate, and TEA-Tridecylbenzenesulfonate.

Sodium Dodecylbenzenesulfonate is a linear alkylbenzene sulfonate. The breakdown products of Sodium Dodecylbenzenesulfonate exposed to a combination of ultraviolet irradiation and ozone includes formaldehyde and glyoxal. Sodium Dodecylbenzenesulfonate is soluble in water; partially soluble in alcohol. Impurities can include organic fillers, sodium...
solution containing 15% Sodium Dodecylbenzenesulfonate was

The oral LD₅₀ of Sodium Dodecylbenzenesulfonate was 2.0 g/kg

inhibitory up to 5.7 x 10⁻⁶ M for the human mixed lymphocyte

Sodium Dodecylbenzenesulfonate was nontoxic and non

sucrase, maltase, and leucine aminopeptidase activity; alkaline

in sucrase and alkaline phosphatase activities was observed when the

various enzymes collected from a dog and a human. An increase

A mixture of Sodium Alkylbenzenesulfonates had inhibitory
effects on amylase, lipase, trypsin, pepsin, phosphatase and

Dermal absorption was pH dependent. Derrmally applied Sodium
Dodecylbenzenesulfonate was found on the skin surface and in the
upper regions of the hair follicles. There was no measurable
penetration of Sodium Dodecylbenzenesulfonate in human
abdominal skin observed until 24 h after application; the rate of
penetration then increased rapidly. There was no measurable
penetration found up to 24 h after application of ¹⁴C-Sodium
Dodecylbenzenesulfonate.

Orally administered Linear Alkylbenzenesulfonates to
developing rats for 10 weeks affected enzymatic activity in the
liver and kidneys.

A mixture of Sodium Alkylbenzenesulfonates had inhibitory
effects on amylase, lipase, trypsin, pepsin, phosphatase and
various enzymes collected from a dog and a human. An increase
in the release of alkaline phosphatase was observed when the
jejunum was perfused with Ringer's bicarbonate solution
containing 0.5% Sodium Dodecylbenzenesulfonate. A decrease
in sucrase and alkaline phosphatase activities was observed when
rats were fed a diet containing 2.5% Sodium Dodecyl-
benzenesulfonate. In an enzyme preparation from the small
intestine, 0.1% Sodium Dodecylbenzenesulfonate inhibited
sucrase, maltase, and leucine aminopeptidase activity; alkaline
phosphatase activity was not affected.

Sodium Dodecylbenzenesulfonate was nontoxic and non
inhibitory up to 5.7 x 10⁻⁶ M for the human mixed lymphocyte
reaction.

The oral LD₅₀ of Sodium Dodecylbenzenesulfonate was 2.0 g/kg
for mice and 1.26 g/kg for rats. The oral LD₅₀ of a detergent
solution containing 15% Sodium Dodecylbenzenesulfonate was

7.5 ml/kg for rats and 12.6 ml/kg for mice. A lethal dosage for
dogs was 400 ml/kg; 100 ml/kg had no effect. The oral LD₅₀ of
a 1:128 aqueous dilution of (195.3 mg/kg body wt) TEA-
Dodecylbenzenesulfonate in rats was >10 ml/kg. For male and
female rats, the LD₅₀ of Linear Alkylbenzene Sulfonate was 0.65
± 0.063 g/kg. The oral LD₅₀ of Linear Alkylbenzene Sulfonate
for mice was 2.30 g/kg. Alkylbenzene Sulfonate administered
orally to mice caused death in all 8 mice administered 1.5 g/kg.
At 3.5 g/kg, 15 of 20 rats died. At 2.2 g/kg, 3 of 4 rabbits died.

The dermal LD₅₀ of a 1:128 aqueous dilution of TEA-
Dodecylbenzenesulfonate in rabbits was >21.5 ml/kg. The
dermal LD₅₀ for Linear Alkylbenzene Sulfonate for rabbits was
>500 mg/kg. The i.v. LD₅₀ of Sodium Dodecylbenzenesulfonate
for mice was 105 mg/kg.

In a short term study, there were incidences of wheezing, nasal
discharge, rough fur, a blood-like discharge around the eyes or
nose, excitability, and unthriftiness in rats fed Sodium Dodecyl-
benzenesulfonate up to 20,000 ppm. There were no effects
observed in rats and dogs fed Sodium Dodecylbenzenesulfonate
up to 0.50% for 90 days in several studies. In one other study,
dogs administered 0.50% had generalized, comparative weakness
and lack of activity, decreased body weights and weight gains,
decreased feed consumption, lower values for hemoglobin,
hematocrit, and erythrocyte counts. Microscopic examination
showed mild degenerative changes of the liver. Sodium Dodecyl-
benzenesulfonate had synergistic hepatic effects when combined
with polychlorinated biphenyl.

No significant changes were observed in rats fed Linear
Alkylbenzene Sulfonate at ~ 5000 ppm or up to 0.25 g/kg/d for
12 weeks. Alkylbenzenesulfonate was not classified as a toxic
compound in rats at concentrations up to 50% for 45 days. Dogs
orally administered a Sodium Alkylbenzenesulfonate up to 4.0
g/d showed anorexia.

There was increased chronic inflammatory cell infiltration at the
subcutaneous injection sites and injection-associated pseudocysts,
hemorrhage, and necrosis in rhesus monkeys injected s.c. with
Linear Alkylbenzene Sulfonate after oral administration of Linear
Alkylbenzene Sulfonate. There were no treatment related
findings with regards to ophthalmological, laboratory, and other
pathological tests.

No systemic toxicity was observed at concentrations of up to
10% Linear Alkylbenzene Sulfonate applied to intact and
abraded skin of rabbits except for weight loss at the highest dose.
A semipermanent hair dye formulation containing 0.5% TEA-
DDBS was applied dermally, twice weekly for 13 weeks, to
rabbits did not produce systemic toxicity.

In a subchronic study, Sodium Dodecylbenzenesulfonate at 2.5
ml/kg/d in drinking water growth rates were decreased in rats
which became rapid weight loss at 5.0 ml/kg/d. Weight
increased with discontinuation of treatment. Mild necrosis of
intestinal mucosa with hemosiderosis of the spleen, liver, and
kidneys were observed at necropsy.

Sodium Alkylbenzenesulfonate had an oral NOEL of 1 g/d over
6 months for dogs, 0.2% in the drinking water of guinea pigs for
6 months, and 1.0% for 16 weeks for rats. No effects were
observed in rats fed a diet containing up to 0.5% Linear Alkylbenzene Sulfonate for 84 days. Renal damage was observed in rats administered Linear Alkylbenzene Sulfonate at 0.2 or 0.6%.

No effects were observed for rats administered feed with ≥40% alkylbenzene sulfonate at 2 ppm except that females had increased kidney weights compared to controls; there was no evidence of kidney damage.

A Sodium Alkylbenzenesulfonate mixture (1.0 g/d) administered to dogs in capsules for 6 months had no adverse effects. Rats fed 0.5 g/100 g feed also had no adverse effects after 65 days.

Sodium Dodecylbenzenesulfonate in the feed of rats at 2,000 ppm over 104 weeks caused no behavioral or clinical signs. Several rats had unthrifty appearance, rough coats, alopecia, bloody noses and eyes, dyspnea, and sores on the head or body and had lower growth rates. Beagles fed Sodium Dodecylbenzenesulfonate at 0.5% for 104 weeks had weakness, lack of activity, decreased feed consumption, and anemia. Livers had slight degenerative changes. At microscopic examination, dogs given 100 and 1,000 mg/kg. Sodium Dodecylbenzenesulfonate in the diet had hemorrhagic necrosis of the intestine and infiltration of chronic inflammatory cells.

There was no evidence of toxicity by Sodium Alkylbenzenesulfonate at 0.1% in feed or drinking water to rats for 104 weeks. There were no adverse effect to rats administered feed with 0.5% Linear Alkylbenzene Sulfonate for 2 years. A decrease in body weight gain, tissue damage in the cecum and liver, and increased severity of renal lesions, specifically glomerular atrophy and necrosis of urinary tubules were observed in rats fed high doses (not specified) of Linear Alkylbenzene Sulfonate.

Sodium Alkylbenzenesulfonate at 1% was a mild ocular irritant in rabbits. Sodium Alkylbenzenesulfonate at 35% caused erosion/attenuation and denudation of the conjunctiva, edema of the substantia propria, and inflammation, principally neutrophilic associated with substantia propria. The cornea had epithelial cell loss at 3 h with erosion/attenuation and denudation. At day 35, 2/40 rats still had not fully recovered. Concentrations of ≥0.1% Linear Alkylbenzene Sulfonate produced mild to no irritation in rabbits. TEA-Dodecylbenzenesulfonate at a 1:128 dilution was not an ocular irritant in rabbits. Sodium Decylbenzenesulfonate produced severe ocular irritation in rabbits. There was a moderate response that disappeared by 96 h in the eyes of rabbits treated with Alkylbenzenesulfonate at 40%.

Sodium Dodecylbenzenesulfonate at 15.0% was severely irritating to the skin of rabbits, with a primary irritation score of 5.3/8.0. Erythema was evident on 3 rats dermally treated with Sodium Dodecylbenzenesulfonate at 10% after 5 days. A 0.5 ml of a 1:128 aqueous dilution of TEA-Dodecylbenzenesulfonate was not irritating to rabbit skin.

Moderate skin irritation was observed when a 10% and 25% w/v aqueous Linear Alkylbenzene Sulfonate solution was applied to rabbits. When rabbits were administered 2 ml applications of ≤10% Linear Alkylbenzene Sulfonate on abraded skin daily for 28 days and on intact skin for 91 days, severe dermal irritation was observed at the application site. Rabbits administered 3 6-h applications of 5% to 25% Linear Alkylbenzene Sulfonate resulted in moderate to severe erythema and moderate edema. Administration of 30% Linear Alkylbenzene Sulfonate produced dermal damage in rats. A 1% Linear Alkylbenzene Sulfonate solution did not produce any dermal irritation in rabbits. In guinea pigs, a 2g/100ml aqueous solution of C12 Linear Alkylbenzene Sulfonate (97.88% purity) produced moderate to severe dermal irritation, with irritation scores of 3.0/4.0 and 1.42/4.0 and a mixed Linear Alkylbenzene Sulfonate solution (99.8% purity) containing 33.7% C12, and 7.0% C10, produced dermal irritation scores of 2.75/4.0 and 0.58/4.

Alkylbenzenesulfonate applied to the abraded skin of shaved rabbits caused slight persistent edema and erythema. None to moderate sensitization to Linear Alkylbenzene Sulfonate was observed in guinea pigs. Alkylbenzenesulfonate was nonsensitizing.

There were no teratotoxic effects of 0.5% TEA-DDBS in rats. Application of a hair dye formulation containing 0.3% TEA-DDBS did not produce any adverse effects on reproduction in male rats. Dermal application of Linear Alkylbenzene Sulfonate at 3.0% produced marked toxicity that was evident in mice and rabbit dams whereas there were no effects to the pups. Linear Alkylbenzene Sulfonate, up to 10 mg/kg/d, applied to the skin of pregnant rats elicited skin reactions and decreased maternal body weight but did not have any teratogenic or embryopathic effects. Orally administered Sodium Alkylbenzenesulfonate at 1% had no observed effects on fertility, litter size, lactation, or survival of offspring in rats. Orally administered Alkylbenzenesulfonate at 1% and 2% caused diarrhea in pregnant rats. The weight of the placenta was reduced, the number of pups per litter was reduced, the number of dead litters and dead pups were increased, and the number of resorptions were reduced in the high-dose group. In the high-dose group, body weight, body length, and tail length of the pups were reduced. Pregnant mice orally administered Alkylbenzenesulfonate had decreased maternal weight gain. There were no effects observed on the fetuses from dams at 24 mg/kg/d. The number of dead pups increased at 240 mg/kg/d. There were no congenital malformations observed in either treatment group.

There were no developmental effects observed associated with Linear Alkylbenzene Sulfonate, up to 0.02%, in the feed of pregnant rats. Linear Alkylbenzene Sulfonate was toxic to pregnant mice at 300 mg/kg/d, rabbits at 300 mg/kg/d, and rats at 600 mg/kg/d; at nontoxic and slight to moderately toxic dosages, values for litter size and fetal loss were unaffected. Maternal body weight gains and fetal body weights of mice were decreased at 10 mg/kg/d. A 20% Linear Alkylbenzene Sulfonate solution or a detergent containing a mixture of Linear Alkylbenzene Sulfonate (27%) dermally applied to pregnant mice resulted in an increase in the number of embryos that were severely deformed or remained at the morula stage on day 3.

Sodium Dodecylbenzenesulfonate was not mutagenic in an Ames test and a silkworm test. Linear Alkylbenzene Sulfonate was not mutagenic but was cytotoxic at 50 µg/ml. Linear Alkylbenzene
Sodium Dodecylbenzenesulfonate, treated with ozone and UV, was mutagenic to *S. typhimurium.* Sodium Dodecylbenzenesulfonate at 0.01%, and Linear Alkylbenzene Sulfonate, at 0.1%, were not carcinogenic to rats when administered in drinking water for up to 2 years.

The dermal application of a hair dye formulation containing 0.5% TEA-Dodecylbenzenesulfonate did not produce carcinogenic effects in mice. At 10%, Linear Alkylbenzene Sulfonate caused acanthosis and/or hyperkeratosis of the treated skin of mice with one squamous cell papilloma observed. Sodium Dodecylbenzenesulfonate was predicted to be not carcinogenic using the electron attachment rate constant ($k_e$) test.

A Sodium Alkylbenzenesulfonate mixture has a low order of toxicity when humans ingested it with food or when taken just before a meal. In a human oral absorption study conducted 144 h after dermal administration of $^{35}$S-Lineal Alkylbenzene Sulfonate, 90% of the radioactivity was excreted in the urine and feces. Dodecylbenzenesulfonate adsorbs readily to human skin. After dermal application of Linear Alkylbenzene Sulfonate to human skin for 2 min, 99% was removed from the application site and < 0.01% was recovered in the urine and feces.

An aqueous solution of 12.5 mmol Sodium Dodecylbenzenesulfonate applied to human skin resulted in a minimal redness for almost 70% of the subjects. A 1% Linear Alkylbenzene Sulfonate solution produced moderate/intense erythema in all subjects within 48 h; 0.1% Linear Alkylbenzene Sulfonate solutions produced negligible or mild erythema. Repeated patch testing using 0.05% and 0.2% aqueous Linear Alkylbenzene Sulfonate produced mild to moderate irritation. Application of a 10% solution of Linear Alkylbenzene Sulfonate (neutral pH) for 5 days to subjects produced severe irritation within the first day.

Sensitization reactions were not observed at 0.05 and 0.2% Linear Alkylbenzene Sulfonate. Extended product use testing of 0.01% to 0.113% Linear Alkylbenzene Sulfonate and 0.001% to 0.09% Linear Alkylbenzene Sulfonate in formulation resulted in no evidence of sensitization or any other skin reactions. Patch testing of consumers with skin problems due to products containing Linear Alkylbenzene Sulfonate did not result in positive reactions to Linear Alkylbenzene Sulfonate.

**DISCUSSION**

The irritant properties of Sodium Dodecylbenzenesulfonate are similar to those of other detergents, with the severity of irritation dependent on the concentration and pH of the ingredient. While ocular irritation by Sodium Dodecylbenzenesulfonate may be dependent on the test setting, the CIR Expert Panel recognized that Sodium Dodecylbenzene-sulfonate, at pH 9, may be an ocular irritant. In preparations containing Sodium Dodecylbenzenesulfonate designed to remain in contact with the skin, the product should be formulated to ensure that the irritancy potential is minimized.

The Expert Panel further noted that DEA, TEA, and MIPA had been evaluated previously and were found to be safe as used. Dialkynaphthalenes and dialkyltetralin are impurities in alkylbenzylsulfonates. While the the concentrations are low, they may absorb through the skin. No evidence of carcinogenic activity was reported in oral studies of Sodium Dodecylbenzenesulfonate or Linear Alkylbenzene Sulfonate, or in dermal studies of TEA-Dodecylbenzenesulfonate or Linear Alkylbenzene Sulfonate, suggesting that the low level of such impurities were not carcinogenic. Because of concern about the carcinogenicity of N-nitroso compounds, however, these salts of alkylbenzene sulfonates should not be used in products where N-nitroso compounds may be formed.

The CIR Expert Panel recognized that there are data gaps regarding use and concentration of this ingredient. However, the overall information available on the types of products in which this ingredient is used and at what concentration indicated a pattern of use, which was considered by the Expert Panel in assessing safety.

Although there were minimal toxicity data available on the other ingredients in this report, the Expert Panel determined that the chemical structures of Sodium Dodecylbenzenesulfonate, Ammonium Dodecylbenzenesulfonate, Calcium Dodecylbenzenesulfonate, DEA-Dodecylbenzenesulfonate, Isopropylamine Dodecylbenzenesulfonate, Magnesium Isodecylbenzenesulfonate, MIPA-Dodecylbenzenesulfonate, Potassium Dodecylbenzenesulfonate, Sodium Decylbenzenesulfonate, Sodium Dodecylbenzenesulfonate, Sodium Tridecylbenzenesulfonate, TEA-Dodecylbenzenesulfonate, and TEA-Tridecylbenzenesulfonate were all sufficiently similar, such that the safety test data available in this report could be extended to support the safety of all of the salts of alkylbenzene sulfonates.

**AMENDED CONCLUSION**

Salts of alkylbenzene sulfonates, including Ammonium Dodecylbenzenesulfonate, Calcium Dodecylbenzenesulfonate, DEA-Dodecylbenzenesulfonate, Isopropylamine Dodecylbenzenesulfonate, Magnesium Isodecylbenzenesulfonate, MIPA-Dodecylbenzenesulfonate, Potassium Dodecylbenzenesulfonate, Sodium Decylbenzenesulfonate, Sodium Dodecylbenzenesulfonate, Sodium Tridecylbenzenesulfonate, TEA-Dodecylbenzenesulfonate, and TEA-Tridecylbenzenesulfonate, are safe as cosmetic ingredients in the practices of use given in this safety assessment when formulated to be non-irritating.  

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1 Were ingredients in this group not in current use to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in the group, and also would be formulated to be non-irritating.
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2Available for review from the Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington DC, 20036, U.S.A.


