JOURNAL OF THE AMERICAN COLLEGE OF TOXICOLOGY
Volume 12, Number 3, 1993
Mary Ann Liebert, Inc., Publishers

Final Report on the Safety Assessment of Sodium Dodecylbenzenesulfonate/ TEA-Dodecylbenzenesulfonate/ Sodium Decylbenzenesulfonate

ABSTRACT

The oral LD_{50} for Sodium Dodecylbenzenesulfonate (SDDBS) in rats was 1.26 g/kg. No significant toxic effects were observed when rats were given oral doses of 1000 ppm SDDBS in water. No systemic toxicity was observed in rabbits given dermal applications of ≤10% SDDBS to abraded skin for 28 days; severe dermal irritation was observed at the application site. Mild necrosis of intestinal mucosa with hemosiderosis of the spleen, liver, and kidneys was observed in rats given a varying dosage of 2.5–5.0 ml/kg/day of a formulation containing 15% SDDBS for a total of 22 weeks; lesions were not observed for rats given 0.5 ml/kg/day. Renal damage was observed in rats dosed orally with ≤0.6% SDDBS for 6 months. For dogs fed ≤1000 mg/kg/day of a formulation containing 15% SDDBS in the diet for 6 months, hemorrhagic necrosis of the intestine and infiltration of inflammatory cells were observed at 10 mg/kg and hemosiderosis of the liver and spleen was observed at 100 and 1000 mg/kg. SDDBS, adjusted to 15% active and a pH of 7.0, applied to intact and abraded sites was severely irritating. A solution containing 1.9% SDDBS and 1.9% tallow alkyl ethoxylate sulfate was moderately irritating to the skin of rabbits. This compound was not a sensitizer when tested at low concentrations. Concentrations of ≥5% Linear Alkylbenzene Sulfonate (LAS) were irritants to the eyes of rabbits; ≤0.1% LAS produced mild to no irritation. (LAS is a commercial preparation that has the average molecular weight of SDDBS.) No reproductive effects were produced by dermal application of LAS or TEA-DDBS or by oral administration of LAS. The results of mutagenic assays using SDDBS were negative. Dermal carcinogenicity studies using LAS and TEA-DDBS and oral carcinogenicity studies using SDDBS and LAS were negative. On the basis of the animal and clinical data presented in this report, it is concluded that Sodium Dodecylbenzenesulfonate, TEA-Dodecylbenzenesulfonate, and Sodium Decylbenzenesulfonate are safe as cosmetic ingredients in the present practices of use. The full report includes a discussion on how the various types of safety test data were interpreted, both individually and collectively.

INTRODUCTION

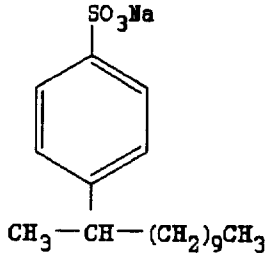
SODIUM DODECYLBENZENESULFONATE, TEA-DODECYLBENZENESULFONATE, and Sodium Decylbenzenesulfonate are substituted aromatic compounds that function as surfactants—cleansing agents (Nikitakis, 1988). Sodium Decylbenzenesulfonate also functions as a surfactant–hydrotrope.

Sodium Dodecylbenezenesulfonate is a linear alkylbenzene sulfonate. If the term Linear Alkylbenzene Sulfonate (LAS) and not a specific chemical name is used, it is referring to a commercial preparation of linear alkylbenzene sulfonates that would have an average molecular weight close to that of Sodium Dodecylbenzenesulfonate, but it would contain some of the neighboring homologues (Booman, 1991). 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 that a 12-carbon chain length moiety comprises 18.1–35% and a 10-carbon chain length moiety comprises 0.5–20.6% of commercial LAS products (Arthur D. Little, Inc., 1991). Therefore, if a paper used the term LAS instead of Sodium Dodecylbenzenesulfonate, the term LAS was used in this report.

CHEMISTRY

Definition and Structure

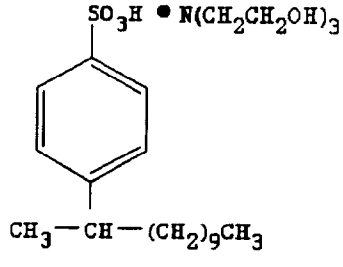
Sodium Dodecylbenzenesulfonate (CAS No. 25155-30-0) is the substituted aromatic compound (Nikitakis et al., 1991) that generally conforms to the formula:



The dodecyl radical of Sodium Dodecylbenzenesulfonate may have many isomers and the benzene may be attached to it at many positions (Hawley, 1971).

Sodium Dodecylbenzenesulfonate (SDDBS) is also known as Sodium Lauryl Benzene Sulfonate (Nikitakis et al., 1991); Benzenesulfonic Acid, Dodecyl-, Sodium Salt (Nikitakis et al., 1991; Sweet, 1987); Dodecylbenzenesulfonic Acid, Sodium Salt (Nikitakis et al., 1991; Sweet, 1987; Windholz et al., 1983); Dodecyl Benzene Sodium Sulfonate; Dodecylbenzenesulphonate, Sodium Salt; Sodium Laurylbenzenesulfonate (Sweet, 1987); Dodecylbenzene Sodium Sulfonate (Windholz et al., 1983); and by various trade names.

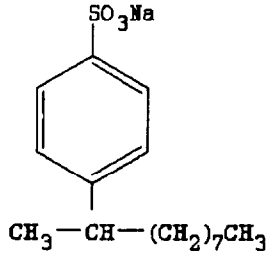
TEA-Dodecylbenzenesulfonate (CAS No. 27323-41-7) is the substituted aromatic compound (Nikitakis et al., 1991) that generally conforms to the formula:



TEA-Dodecylbenzenesulfonate (TEA-DDBS) is also known as Triethanolamine

Dodecylbenzenesulfonate; Dodecylbenzenesulfonic Acid, Compound with 2,2',2"-Nitrilotris[Ethanol] (1:1) (Nikitakis et al., 1991); Benzenesulfonic Acid; Dodecyl-, Compound with 2,2'2"-Nitrilotriethanol (1:1) (Nikitakis et al., 1991; Sweet, 1987); Linear Alkylbenzene Sulfonate, Triethanolamine Salt (Hunting, 1983); and by various trade names.

Sodium Decylbenzenesulfonate (CAS No. 1322-98-1) is the substituted aromatic compound (Nikitakis et al., 1991) that generally conforms to the formula:



Sodium Decylbenzenesulfonate (SDBS) is also known as Benzenesulfonic Acid, Decyl-, Sodium Salt (Nikitakis et al., 1991; Sweet, 1987); Decylbenzenesulfonic Acid, Sodium Salt (Nikitakis et al., 1992); Decyl Benzene Sodium Sulfonate; and Sodium Decylbenzenesulfonamide (Sweet, 1987).

Properties

SDDBS is commercially available as a yellow colored slurry or off-white dry product (CTFA, 1991a). The slurry is usually 30–50% 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 40–90% active. Properties of SDDBS are summarized in Table 1.

TEA-DDBS is a clear yellow liquid that is commercially available as 40–60% aqueous solutions (CTFA, 1991b). Properties of TEA-DDBS are summarized in Table 2.

SDBS has a molecular weight of 320.46 (Sweet, 1987). The molecular formula for SDBS is $C_{16}H_{25}O_3S \cdot Na$.

Manufacture and Production

SDDBS 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. Sodium Dodecylbenzenesulfonate 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-DDBS is made by reacting dodecylbenzenesulfonate with sulfuric acid (Oleum process) and air/SO_3 to produce dodecylbenzene sulfonic acid (CTFA, 1991b). The dodecylbenzene sulfonic acid is then neutralized with triethanolamine.

LAS 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 LAS were used in North America, Western Europe, and Japan, with Dodecylbenzene Sulfonate being the LAS most widely used (Greek and Layman, 1989). The use of LAS as a surfactant was second only to soap.

TABLE 1. PROPERTIES OF SODIUM DODECYLBENZENESULFONATE

		References
Physical appearance	Yellow colored slurry or off-white dry product (powder, flakes, or beads)	CTFA, 1991a
	Pale yellow paste or slurry, spray-dried powder, or as a flake	Hunting, 1983
Odor	bland	Estrin et al., 1982
% Activity		
Slurry	30–50%	CTFA, 1991a
	usually 30–60%	Hunting, 1983
Dried product	40–90%	CTFA, 1991a
	approx. 90%	Hunting, 1983
Molecular formula	$C_{18}H_{29}O_3S \cdot Na$	Sweet, 1987
	$C_{18}H_{29}NaO_3S$	Windholz et al., 1983
	$CH_3(CH_2)_{10}CH_2C_6H_4SO_3^-Na^+$	Hunting, 1983
Molecular weight	349	CTFA, 1991a
	348.52	Sweet, 1987
	348.49	Windholz et al., 1983
Empirical formula	$C_{18}H_{30}O_3S \cdot Na$	Nikitakis et al., 1991
Solubility	Water dispersible, soluble at low concentrations	Hunting, 1983
	Soluble in water; partially soluble in alcohol	Estrin et al., 1982
Stability	Stable in the presence of a strong acid and base; generally non-reactive and does not polymerize	CTFA, 1991a
Specific gravity (at 25°C)	Slurry: 1.02–1.05; dry product: 0.45–0.65	CTFA, 1991a
pH		
10%	Slurry: 7–8; dry product: 7–9	CTFA, 1991a
1% aqueous solution	7.0–9.0	Estrin et al., 1982
Sodium		
Sodium sulfonate	40–50%	
Sodium chloride	10–20%	Estrin et al., 1982
Impurities		
Neutral oil	1% maximum	
Arsenic (as As)	3 ppm maximum	
Iron (as Fe)	10 ppm maximum	
Lead (as Pb)	20 ppm maximum	
Moisture	3.5% maximum	Estrin et al., 1982
LAS impurities	Dialkyltetralin, dialkylnaphthalene, and to a lesser extent dialkylindane may be present in the final product	Vista Chemical Co., 1992a
Ionic type	Anionic	Hunting, 1983

Analytical Methods

SDDBS was analyzed by high-pressure liquid chromatography 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).

TABLE 2. PROPERTIES OF TEA-DODECYLBENZENESULFONATE

		References
Physical appearance	Clear yellow liquid	CTFA, 1991b
	Clear yellow or amber liquid	Hunting, 1983
	Clear, pale yellow viscous liquid	Estrin et al., 1982
Odor	Mild, slightly oily	Estrin et al., 1982
% Activity	40–60%	CTFA, 1991a
	50–60%	Hunting, 1983
Aqueous solution	60%	Estrin et al., 1982
Empirical formula	$C_{18}H_{30}O_3S \cdot C_6G_{15}NO_3$	Nikitakis et al., 1991
Molecular weight	475	CTFA, 1991b
	476.77	Sweet, 1987
Solubility	Soluble in water	Hunting, 1983
	Soluble in water and alcohol	Estrin et al., 1982
Stability	Stable under normal cosmetic use conditions	CTFA, 1991b
Specific gravity (at 25°/25°C)	1.08	Estrin et al., 1982
pH		
10%	5.5–7.5	CTFA, 1991b
at 25°C	6.8–7.5	Estrin et al., 1982
Viscosity (at 25°C)	1000–3000 cps	Estrin et al., 1982
Assay (avg. mol. wt. 462)	54–60%	Estrin et al., 1982
Sulfates (as TEA hydrosulfate)	4.0% maximum	Estrin et al., 1982
Water	36–42%	Estrin et al., 1982

TEA-DDBS was identified either by adding methylene blue TS and chloroform to a TEA-DDBS solution and shaking or by adding sodium hydroxide TS and cupric sulfate TS to the solution; a blue color in the chloroform layer or a blue–purple color develops, respectively (Yakuji Nippo Ltd., 1987).

LAS was determined by high-performance liquid chromatography (HPLC) (Yoshikawa et al., 1984); by spectroscopic methods, particularly HPLC with ultraviolet (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). It should be noted that significant problems exist with the use of MBAS and spectrophotometric methods in general for LAS identification; primarily, the techniques are considered to be inadequate for trace surfactant measurements requiring identification of specific surfactants and isomers. Problems with the other methods may also exist.

Impurities

Some industrial grades of SDDBS contain organic fillers (Hunting, 1983). SDDBS contains sodium sulfonate and sodium chloride. Some impurities of SDDBS are neutral oil (unsulfonated materials), arsenic (As), iron (Fe), and lead (Pb) (Estrin et al., 1982).

TEA-DDBS contains sulfates (as TEA Hydrosulfate) at a maximum of 4.0%. Neither data as to the amount of free di- and triethanolamines nor information as to the possible presence of N-nitrosodiethanolamine was available (Elder, 1983).

The alkylation of benzene results in a number of side reactions (Arthur D. Little, Inc., 1991). Some of the dialkylbenzenes that result from the side reactions cannot be separated from the primary product with ease and, following sulfonation, remain in commercial LAS. Six samples of commercial LAS 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 dialkylindanes in these LAS samples; however, the concentration of these impurities amounted to only about 1/10 of that of alkyltetralins. Other dialkylbenzenes and the diphenylalkanes that form as products of the side reactions boil at temperatures sufficiently above the linear monoalkylbenzene, facilitating their removal (Little, 1991).

Ultraviolet Absorption

Three commercial samples of LAS, dissolved in water at concentrations up to 1.0 g/l, did not absorb in the UVB band (λ_{max} 218–224; λ_{max} 254–255; $\lambda_{shoulder}$ 260–261) (Vista Chemical Company, 1992b).

USE

Cosmetic

The product formulation data submitted to the Food and Drug Administration (FDA) in 1992 stated that SDDBS was contained in a total of 45 cosmetic product formulations. SDDBS was used in the preparation of bubble baths, eyeliners, bath soaps and detergents, and other personal cleanliness products. The greatest reported use of SDDBS was in the preparation of bubble baths (33 formulations).

The product formulation data submitted to the FDA in 1992 stated that TEA-DDBS was contained in a total of 54 cosmetic product formulations. TEA-DDBS was used in the preparation of noncoloring hair shampoos and hair dyes and colors. The greatest reported use of TEA-DDBS was in the preparation of hair dyes and colors (36 formulations).

In 1992, SDBS was not reported to the FDA as being used in cosmetic product formulations.

Concentration of use values are no longer reported to the FDA by the cosmetic industry (Federal Register, 1992). However, product formulation data submitted to the FDA in 1984 stated that SDDBS was used at a concentration of $\leq$50% in bubble baths, 1–5% in bath soaps and detergents, and $\leq$1% in eye makeup formulations (FDA, 1984). The product formulation data submitted for TEA-DDBS stated that it was used at a concentration of $\leq$50% in noncoloring shampoos and $<$1% in hair dye and color formulations.

Product formulation data for SDDBS and TEA-DDBS are summarized in Table 3.

International

Both SDDBS and TEA-DDBS are accepted for use by the Japanese Ministry of Health and Welfare (CTFA, 1983). SDDBS is listed in the Comprehensive Licensing Standards of Cosmetics by Category (CLS), Volume VI, and the Japanese Standards of

TABLE 3. PRODUCT FORMULATION DATA*

Product category	Total no. of formulations in category	Total no. containing ingredient
Sodium dodecylbenzenesulfonate		
Bubble baths	233	33
Eyeliner	253	3
Bath soaps and detergents	324	6
Other personal cleanliness products	323	3
1992 Totals		**45**
Tea-Dodecylbenzenesulfonate		
Hair shampoos (noncoloring)	953	18
Hair dyes and colors (all types requiring caution statement and patch test)	1112	36
1992 Totals		**54**

*CIR requests that the cosmetic industry provide current formulation data on each product category.

Source: FDA, 1992.

Quasi-drug Ingredients (Nikko Chemicals Co., Ltd., 1992). It must be noted on the product label if a product contains SDDBS. TEA-DDBS is listed in the CLS, Volume II.

Noncosmetic

SDDBS 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 (Dean, 1985).

SDBS is approved as an indirect food additive (Federal Register, 1965).

GENERAL BIOLOGY

Absorption, Distribution, Metabolism, Excretion

A human dermal absorption study determined that 144 h after dermal application of ^{35}S-LAS, 99% of the radioactivity was removed from the application site and <0.01% of the radioactivity was recovered in the urine and feces (Procter and Gamble, no date).

Although penetration of LAS into human skin did not occur readily, adsorption was pH-dependent (Iimori, 1971). With a pH range of 7.0–11.0, adsorption of LAS decreased as the alkalinity of a postdose rinse increased.

In a human oral absorption study 144 h after dermal administration of ^{35}S-LAS, 90% of the radioactivity was excreted in the urine and feces (Procter and Gamble, no date). Approximately 50% of the dose was absorbed and excreted in the urine within 24 h.

^{14}C-SDDBS was used to determine the distribution and elimination of SDDBS in rats; the location of the ^{14}C in the molecule was not stated (Lay et al., 1983). Twelve male Wistar rats were fed ^{14}C-SDDBS in the diet, *ad libitum*, at a concentration of 1.4 mg/kg diet 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 the determination of radioactive residues was made. The remaining 6 rats were kept for 1 wk to determine SDDBS clearance.

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

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

Eight male Wistar rats received a single intraperitoneal (i.p.) injection of 384.7 μg ^{14}C-SDDBS in a 0.6% NaCl solution (Lay et al., 1983). Feces and urine were monitored for 10 days for ^{14}C 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 2–10, ^{14}C was primarily excreted in the feces. By day 10, 94.5% of the dose was excreted. The fecal and urinary ^{14}C-SDDBS-derived activity consisted of highly polar metabolites.

Four adult rhesus monkeys, two males and two females, received 30 mg/kg ^{14}C-LAS in aqueous solution, approximately 25 μCi, by oral intubation to study the excretion of ^{14}C-LAS (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 dose 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 ^{14}C-LAS 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 radioactivity concentrations (Cresswell et al., 1978). The animals were given single oral doses of 150 mg/kg and 300 mg/kg ^{14}C-LAS, both approximately 26 μCi, at intervals of 2–3 weeks. Approximately 2–3 weeks after the last single dose, each animal received 7 consecutive daily oral doses of ^{14}C-LAS at a concentration of 30 mg/kg, approximately 28 μCi/day, in water.

To determine plasma radioactivity 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 ^{14}C-LAS, 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 6–24 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 approximately 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 6–24 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 approximately 5 h. The predose concentration on the following 5 days did not increase significantly. 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 approximately 6 h.

Plasma radioactivity 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 ^{14}C-LAS 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 LAS 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 ^{14}C was lower in most tissues than in the plasma, indicating no specific accumulation or localization of either LAS or its metabolites in the tissues.

Four adult rhesus monkeys, two males and two females, were used to study the excretion of a single s.c. dose of ^{14}C-LAS (Cresswell et al., 1978). An injection of 1 mg/kg ^{14}C-LAS, 16–40 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 ^{14}C-DBS 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 (8–22 μCi) and 0.1 mg/kg (2–5 μCi) ^{14}C-LAS at intervals of 2–3 weeks (Cresswell et al., 1978). Approximately 2–3 weeks after the last single dose, each animal received daily s.c. injections of 1 mg/kg ^{14}C-LAS, approximately 24 μCi/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 ^{14}C-LAS, mean plasma radioactivity concentrations reached a maximum of 0.16 μg/ml after 2h. This concentration decreased rapidly during the 7.5–24 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 7.5–24 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 approximately 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 ^{14}C-LAS 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 tissue concentrations were greatest in 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 ^{14}C was similar to or less than that in the plasma in most tissues after 48 h; this indicated there there was no specific accumulation or localization of LAS or its metabolites in the tissue.

Six female Colworth-Wistar rats were dosed with either 0.1 or 0.5 ml ^{14}C-SDDBS; three animals were dosed by i.p. injection and three 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 CO_2. In the carcass, 22 ± 5% was recovered after 24 h.

Percutaneous Absorption

Two-tenths ml of a 3 mM aqueous suspension of Sodium *p*-1-[1-^{14}C] 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 cm^2 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 ^{14}C was detected in expired CO_2, urine, feces, and carcasses. The treated skin was examined by autoradiography for ^{14}C; heavy deposition of SDDBS was found on the skin surface and in the upper regions of the hair follicles. Penetration, based on the

amount of ^{14}C excreted in the urine, feces, and expired CO_2 during the 24 h after application plus the amount in the carcass at 24 h, was determined to be <0.1 μg/cm^2.

In Vitro Skin 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-^{14}C] 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 ^{14}C. After 48 h, the corneum was washed with distilled water and monitored for ^{14}C by solubilizing.

No measurable penetration of SDDBS was observed until 24 h after application; the rate of penetration then increased rapidly. After 48 h, 87.2 ± 24.1 μg/cm^2 had penetrated. After rinsing, 30–50% of the applied ^{14}C remained in the epidermis.

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 (Howes, 1975). A 6 mM Sodium *p*-1-[1-^{14}C] Dodecylbenzenesulfonate (8.5 μCi/mg) solution, 0.25 ml, 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 ^{14}C. After 24 h, the epidermal surface was washed with distilled water and monitored for ^{14}C by solubilizing.

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

Antimicrobial Activity

The antimicrobial activity of SDDBS was studied using numerous bacterial strains (Yamada, 1979; Pollack and Anderson, 1970; Anderson and Koransky, 1968; Arkin and Anderson, 1968). SDDBS may act bacteriostatically on micro-organisms (Yamada, 1979). In some strains of *Escherichia coli*, a longer lag phase due to the presence of SDDBS has been observed (Pollack and Anderson, 1970; Arkin and Anderson, 1968).

Antiproliferative Effects

The immunosuppressive potential of SDDBS was evaluated by examining its ability to inhibit the human mixed lymphocyte reaction (Coy et al., 1990). A 5.7×10^{-6} M solution of SDDBS (the greatest concentration tested) was noninhibitory and nontoxic.

Enzymatic Alterations

The enzymatic alterations produced by various concentrations of SDDBS have been investigated (Kimura et al., 1980, 1982; Kimura and Yoshida, 1982; Antal, 1972). An increase in the release of alkaline phosphatase was observed when the jejunum was perfused with Ringer's bicarbonate solution that contained 0.5% SDDBS (Kimura et al., 1982; Kimura and Yoshida, 1982). A decrease in sucrase and alkaline phosphatase activities was observed when Wistar rats were fed diet containing 2.5% SDDBS, 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% SDDBS inhibited sucrase, maltase, and leucine aminopeptidase activity; alkaline phosphatase activity was not affected. Albino rats were fed 0.25 g/kg body wt SDDBS in feed for 3 months and then given a single dose of either SDDBS or water; the blood glucose concentration of rats given a single dose of 0.094 g/ml/100 g body wt of SDDBS was increased compared to rats given a single dose of distilled water (Antal, 1972).

ANIMAL TOXICOLOGY

Acute Toxicity

Oral

Sodium dodecylbenzenesulfonate

The oral LD_{50} of SDDBS was 2.0 g/kg for mice and 1.26 g/kg for rats (Sweet, 1987). The oral LD_{50} of LAS for mice was 2.30 g/kg (Tiba, 1972). The oral LD_{50} of a detergent solution containing 15% SDDBS was 7.5 ml/kg for rats and 12.6 ml/kg for mice (Leuschner et al., 1969). A lethal dosage for dogs was 400 ml/kg; 100 ml/kg had no effect.

The oral LD_{50} of 10 and 40% solutions of LAS in distilled water administered intragastrically to male and female FDRL strain (Wistar derived) rats was determined according to the method of Miller and Tainter (1944) (Oser and Morgareidge, 1965). LAS had a nominal chain length of 12 carbon atoms (range, C_9–C_{12}), an average molecular weight of 346, and was 39.5% active. For male and female FDRL rats, the LD_{50} (expressed on an active ingredient basis) was 0.65 ± 0.063 g/kg, with a slope factor of 0.173.

TEA-dodecylbenzenesulfonate

Five groups of 10 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-DDBS (Hilltop Research, 1977). The animals were observed for 14 days, after which they were killed for necropsy. No deaths occurred. Diarrhea was the only physical observation. No significant observations were made at necropsy. The oral LD_{50} of a 1:128 aqueous dilution of (195.3 mg/kg body wt) TEA-DDBS in rats was >10 ml/kg.

Dermal

Sodium dodecylbenzenesulfonate

The minimum lethal dosage of a 20% solution of LAS formulations applied to intact skin of rabbits was in the range of 200–1,260 mg/kg (Monsanto Company, no date).

The dermal LD_{50} for LAS for rabbits was >500 mg/kg (Procter and Gamble, no date).

TEA-dodecylbenzenesulfonate

A dose of 21.5 ml/kg of a 1:128 aqueous dilution (195.3 mg/kg body wt) of TEA-DDBS was applied under an occlusive patch for 24 h to clipped skin on the backs of eight New Zealand White rabbits, four males and four females; the skin of four 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 for necropsy. No deaths occurred. Diarrhea and emaciation in two rabbits and erythema were the only physical observations. No significant observations were made at necropsy. The dermal LD_{50} of a 1:128 aqueous dilution of TEA-DDBS in rabbits was >21.5 ml/kg.

Intravenous

The intravenous (i.v.) LD_{50} of SDDBS for mice was 105 mg/kg (Sweet, 1987).

Short-Term Toxicity

Oral

Reagent-grade SDDBS was dissolved in tap water and administered to eight groups of eight male Wistar rats with either normal or polychlorinated biphenyl (PCB)-supplemented feed (Itokawa et al., 1975). The control group received normal diet and tap water, groups 2–4 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 SDDBS, group 6 was fed PCB-supplemented diet at 10 ppm and water containing 1000 ppm SDDBS, group 7 received PCB-supplemented diet at 100 ppm and water containing 1000 ppm SDDBS, and group 8 was fed PCB-supplemented diet at 500 ppm and water containing 1000 ppm SDDBS. 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 the 2 groups that were given 500 ppm PCB, body weight gains were reduced.

Liver weights increased with increased concentrations of PCB; a synergistic effect of SDDBS 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; this effect was probably due to hemolytic action of SDDBS. 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 SDDBS 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 significant changes in serum and liver triglyceride and nonesterified fatty acid concentrations were observed in any group.

Two groups of 30 FDRL rats, 15 males and 15 females per group, were fed diet containing 0.05 or 0.25 g/kg/day LAS (expressed as active ingredient) for 12 weeks (Oser and Morgareidge, 1965). The LAS had a nominal chain length of 12 carbon atoms (range, C_9–C_{12}), an average molecular weight of 346, and was 39.5% active. A control group was fed untreated diet. The rats were observed daily for signs of toxicity. Body weights and feed consumption of approximately 50% of the rats (males and females) were measured weekly. Hematology tests and urinalysis were performed on samples obtained from the remaining rats during weeks 6 and 12. At study termination, all animals were killed for necropsy. 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 statistically increased for male and female rats of the 0.25 g/kg/day group compared to rats of the control group. No microscopic lesions were observed due to test article administration.

Rats (number, gender, and strain unspecified) were fed ≤5000 ppm (0.5%) LAS for up to 12 weeks (Oser and Morgareidge, 1965). No significant changes were observed.

Dermal

Two mg/kg of 5, 10, and 25% w/v aqueous LAS solution was applied to the skin (site unspecified) of rabbits (number, species, and sex unspecified) under occlusive patches for 24 h (Procter and Gamble, no date). No evidence of systemic toxicity or mortality was observed.

Rabbits (number, gender, and strain unspecified) were given 2 ml applications of ≤10% LAS (2 mg/kg) to abraded skin daily for 28 days and to intact skin for 91 days (Procter and Gamble, no date). No systemic toxicity was observed.

Rabbits (number, gender, and strain unspecified) were dosed with ≤30% LAS 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 Toxicity

Oral

Rats (number, gender, and strain unspecified) were given a formulation containing 15% SDDBS and 13% ammonium fatty alcohol polyglycolether sulfate in drinking water (Leuschner et al., 1969). A slight decrease in growth rate was observed for male rats given 2.5 ml/kg/day for 9 weeks followed by 3.75 ml/kg/day for an additional 9 weeks. Rapid weight loss was observed when the dosage was increased to 5.0 ml/kg/day 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/day.

Three groups of 20 Sprague-Dawley rats, 10 males and 10 females per group, were fed diet containing 0.02, 0.1, or 0.5% LAS 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 for necropsy. The tissues of some animals were examined microscopically. No differences were observed in body weight, feed consumption, survival, hematologic values, urinalysis, organ weights, or organ-to-body weight ratios between animals of the treated and control groups, and there were no gross or microscopic lesions in examined tissues.

Rats (number, gender, and strain unspecified) were dosed orally with ≤0.6% LAS 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%.

Dermal

A semipermanent hair dye formulation containing 0.5% TEA-DDBS was applied dermally, twice weekly for 13 weeks, to a group of 12 New Zealand White rabbits, 6 males and 6 females (Burnett et al., 1976). A dose of 1 ml/kg was applied to shaved areas on the dorsolateral aspects of the thoracic–lumbar area, one of each side of the midline; application sites were altered to minimize irritation. Test sites of three males and three 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 for necropsy. 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 significant 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 significantly increased and the methemoglobin value for female rabbits was significantly 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.

Chronic Toxicity

Oral

As in the short-term study by Itokawa et al. (1975), reagent-grade SDDBS was either mixed with normal feed, PCB-supplemented feed, or placed in tap water and administered to 4 groups of 12 male Wistar rats (Itokawa et al., 1975; see also Itokawa et al., 1973). 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 SDDBS, 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 SDDBS. Both diet and water were available *ad libitum*. Feed and water consumption were measured every 2 days. After 1, 3, or 7 months, four rats from each group were weighed and killed.

There were no significant differences in feed or water consumption between any of the treated groups and the control group. In groups 3 and 4, body weights were significantly decreased and liver weights significantly increased when compared to the controls.

In rats of groups 3 and 4, 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 weight had decreased in male rats of group 4; 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, disappearance 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 of groups 3 and 4. Total cholesterol concentrations increased markedly in the liver of rats in group 3 and particularly in the rats of group 4 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 group 3, hepatic aniline hydroxylase activity was significantly increased; this increase in enzymatic activity was even greater when PCB and SDDBS were combined, as in group 4. No significant changes were observed in either serum alkaline phosphatase or choline esterase activities. In rats of groups 3 and 4, hepatic Na-K-Mg-dependent ATPase activity decreased; this decrease was greater in rats of group 4. No significant difference in Mg-dependent ATPase activity was observed.

Four groups of Charles River rats, 50 males and 50 females per group, were fed diet containing 0.02, 0.1, or 0.5% LAS for 2 years; one group of rats, 50 males and 50 females, was fed 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 five 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 five males and five 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 significant 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 significantly 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 terminal sacrifice, no significant differences in body weight or organ-to-body weight ratios were observed for any of the test groups compared to the controls. Hematologic values that were significantly 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 tissues from animals that died on study.

Dogs (number, gender, and strain unspecified) were fed 10, 100, or 1,000 mg/kg/day of a formulation containing 15% SDDBS in the diet for 6 months (Leuschner et al., 1969). The only observtion was a slight decrease in body weight gain for females of the 1,000 mg/kg/day 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 given 100 and 1,000 mg/kg.

Wistar rats (number, gender, and strain unspecified) were fed LAS in the diet for 6 months (Yoneyama et al., 1973). A concentration of 0.07% LAS in the diet (approx. 40 mg/kg/day) did not produce adverse effects. Minor histologic changes were observed in the kidneys of rats given a concentration of 0.2% LAS; the severity of the lesions increased at concentrations of 0.6 and 1.8% LAS. At the highest dosage (concentration not specified), 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.

Sensitization

In a Magnusson-Kligman maximization test used to assay for the sensitization potential of LAS, with an induction injection of 0.6–5%, induction patch application of 0.1–1%, and challenge patch application of 1%, positive sensitization results were observed in up to 76% of the guinea pigs (Robinson et al., 1989). No dose–response pattern was evident. A Buehler test conducted concurrently with this test using 1.2–2.5% LAS at induction and 0.5–1% at challenge produced only weakly positive responses.

In a Buehler test for sensitization, numerous samples of LAS (with >90% of the alkyl chain lengths for the mixture in the range of C_{10}–C_{14}) tested at induction concentrations of 2–100% followed by challenge applications of 1 or 2% produced weak to moderate sensitization reactions using guinea pigs (Robinson et al., 1989). No to moderate sensitization was observed for formulations containing LAS; the formulations were tested at concentrations that resulted in LAS concentrations of 0.3–10% at induction and 0.1–1% at challenge. The authors noted that "even though not all guinea pig tests of LAS were positive, the fact that different lots of LAS from different suppliers cross-reacted with one another and that analytical results revealed no significant variations among lots suggested that the sensitization reactions observed for LAS could not be attributed to a contaminant material."

Guinea pigs (number unspecified) were injected intradermally with a 1% w/v aqueous solution of LAS and challenged topically (Shell Research Limited, no date). A sensitization reaction was not observed.

Dermal Irritation

Sodium Dodecylbenzenesulfonate

Three male albino rabbits were used to determine the irritation potential of SDDBS according to the methods of Draize (Schoenberg, 1985). SDDBS was adjusted to a total of 15.0% active materials and pH 7.0. The abdomens of the rabbits were shaved and four areas approximately 10 cm apart were selected as application sites. The application sites were 1 sq. in.; 2 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. SDDBS was severely irritating to the skin of rabbits, with a primary irritation score of 5.3/8.0 on a scale of 0–8.

The irritation potential of SDDBS was evaluated by applying an olive oil dissolvent containing 10% SDDBS to a shaved dorsal area on the head and neck of male Wistar rats for 4 days (Fujise and Aoyama, 1984). Three rats that were 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 threefold for both methods of preparation compared to control values.

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 subcutaneous (s.c.) injection of 0.2 ml of 0.02, 0.10, 0.20, 0.30, 0.40, or 0.50 mg/ml SDDBS in physiological saline into the dorsal area according to the method of Sato et al. (1967) (Naruse et al., 1991). 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 SDDBS had an average reactivity score of 0. The other test groups had the following scores: 0.10 mg/ml SDDBS produced an average score of 0.1; 0.20 mg/ml SDDBS produced an average score of 0.8; 0.30 mg/ml SDDBS produced an average score of 1.6; 0.40 mg/ml SDDBS produced an average score of 2.0; and 0.50 mg/ml SDDBS resulted in an average reactivity score of 2.9.

The dermal irritation of a 2 g/100 ml aqueous solution of C_{12} LAS (97.88% purity) was evaluated using albino guinea pigs (gender not specified) (Imokawa, 1979). A 1.5 cm^2 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 0–2 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 LAS 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} LAS (97.88% purity) in 10 mm diameter tubes was applied for 2 sec to the same site on the shaved backs of guinea pigs (number and gender unspecified) twice daily for a total of nine treatments (Imokawa, 1979). 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 LAS solution (99.8% purity) containing 33.7% C_{12} and 7.0% C_{10} resulted in a dermal irritation score of 0.58/4.

Three 6 h applications of a 1% (w/v) aqueous solution of LAS produced primary skin irritation using rabbits (number, strain, and gender not given) (Shell Research Limited, no date). No effect was observed after the first application. Moderate to severe erythema and moderate edema, which were 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.

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

Rats (number, gender, and species unspecified) were dosed with an aqueous solution of ≤30% LAS 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% LAS produced fairly pronounced dermal damage.

In the short-term dermal toxicity study by Procter and Gamble (no date), described earlier, in which 2 mg/kg of 5, 10, or 25% w/v aqueous LAS 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 two greatest concentrations.

In the other short-term dermal toxicity study by Procter and Gamble (no date) described earlier in which rabbits (number, sex, and strain unspecified) were given 2 ml applications of ≤10% LAS (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. Rabbits were either dosed 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% LAS and 19% tallow alkyl ethoxylate sulfate (Procter and Gamble, no date). Moderate dermal irritation was observed.

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 two intact and two abraded sites.

Ocular Irritation

Sodium Dodecylbenzenesulfonate

Instillation of ≥5% LAS into the conjunctival sac of rabbits produced irritation. Congestion and edema have been observed at concentrations of 0.5–1.0%. Concentrations of ≤0.1% LAS produced mild to no irritation (Arthur D. Little, Inc., 1991). Concentrations of ≥1% LAS produced irritation in the eyes of rabbits (Arthur D. Little, Inc., 1977).

TEA-Dodecylbenzenesulfonate

A volume of 0.1 ml of a 1:128 aqueous solution of TEA-DDBS was placed in the conjunctival sac of the right eye of nine New Zealand White rabbits (Hilltop Research, 1977). The eyes of three rabbits were rinsed after 30 sec; the eyes of the other six 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% SDBS 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. SDBS produced severe irritation.

Teratogenic/Reproductive Effects

Dermal

Sodium Dodecylbenzenesulfonate

Pregnant ICR-JCL mice were given dermal applications of 0.5 ml of 0.85, 1.7, 2.55, or 3.4% LAS solutions on days 1–13 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% LAS group was significantly increased compared to the final mean body weight of 10 dams of the control group. The absolute liver, kidney, and spleen weights were also significantly increased for this group. There was no significant difference in body weight gain between test and control dams and no visceral defects were observed. Pregnancy rate was reduced 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 significantly reduced in all test groups except for the 1.7% group when compared to the controls. There was no significant 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 given dermal applications of 0.017, 0.17, or 1.7% LAS solutions on days 2–14 of gestation (Masuda et al., 1974). 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.

TEA-dodecylbenzenesulfonate

A semipermanent hair dye formulation containing 0.5% TEA-DDBS 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. (A pilot study reported that more frequent application was not feasible due to potential dermal irritation.) Three negative control groups were shaved but not treated and a positive control group received 250 mg/kg acetylsalicylic acid by gavage on days 6–16 of gestation. The rats were killed on day 20 of gestation and the fetuses were examined.

No signs of toxicity and no dermal irritation were observed during the study. The only observation reported was discoloration of the skin and hair at the test site. There were no significant differences in body weight gains or feed consumption between the treated and negative control groups. A semipermanent hair dye formulation containing 0.5% TEA-DDBS did not produce embryotoxic or teratogenic effects.

Twenty-five male Sprague-Dawley CD rats were dosed dermally with 0.5 ml of a semipermanent hair dye formulation that contained 0.2–0.3% TEA-DDBS twice weekly for 10 weeks (Burnett et al., 1981). The formulation was applied to a shaved 1 sq. in. area on the back of each rat. To avoid excessive dermal irritation, the application sites were switched between adjacent areas on alternate days. 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 three 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 six males.

Two healthy 21-day-old males were selected from each litter as the F_1 males and kept until maturity. After 12 weeks, 100 F_1 males per group were mated with 3 sexually mature females (1/week for 3 weeks). The females were killed on days 14–16 of gestation and their uteri and fetuses were examined.

There were no significant differences in body weight gain 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 F_1 males were similar for both groups. There were no significant differences in the number of total and average live pups between the treated and control group. Application of a hair dye formulation containing 0.2–0.3% TEA-DDBS did not produce any adverse effects on reproduction in male Sprague-Dawley CD rats.

Oral

Sodium dodecylbenzenesulfonate

Pregnant ICR-SLC mice were dosed with 10, 100, or 300 mg/kg LAS 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. Nonstatistically significant incidences of external malformations, such as cleft palate and exencephaly, were observed sporadically for fetuses of the control and dose groups.

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

A 20% LAS solution (Nomura et al., 1980; Nomura et al., 1987) or a detergent containing a mixture of LAS and alcohol sulfate (at a concentration of 27%) (Nomura et al., 1987) was applied twice daily to the dorsal skin of pregnant JCL:ICR mice during the preimplantation period (days 0–2 of gestation). A significant number of embryos collected on day 3 were severely deformed or remained at the morula stage. Most of the abnormal embryos were fragmented or remained at the one- to eight-cell stages and were either dead or dying. Nomura et al. (1980) reported that the number of embryos in the oviducts was significantly greater for the mice dosed with LAS 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.

MUTAGENICITY

Kawachi et al. (1980) performed a variety of mutagenicity assays using SDDBS. 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.

Kawachi et al. (1980) used SDDBS in a mutation test involving silk worms. The results were negative.

CARCINOGENICITY

Oral

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

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

Dermal

Sodium Dodecylbenzenesulfonate

Percutaneous application of a formulation containing 15.6% LAS 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 (Procter and Gamble, no date). In the 10% test group (which consisted of 50 animals), acanthosis and/or hyperkeratosis of the treated skin and one squamous cell papilloma were observed.

TEA-Dodecylbenzenesulfonate

A skin painting study was performed to determine the carcinogenic potential of a semipermanent hair dye formulation containing 0.5% TEA-DDBS (Burnett et al., 1980). The hair dye formulation, 0.05 ml, was applied to a shaved 1 cm^2 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, 20 randomly selected mice (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 on all mice found dead, those killed due to moribund condition, or those killed at study termination.

There were no significant 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. A hair dye formulation containing 0.5% TEA-DDBS did not produce carcinogenic effects.

Physicochemical Screening Test

A physicochemical screening test, the k_e test, was used to screen for the carcinogenic potential of SDDBS (Bakale and McCreary, 1987). The electron attachment rate constant, k_e, was used to predict the carcinogenic potential of SDDBS and then compared to the Ames test results obtained by Kawachi et al. (1980). SDDBS was determined not to be potentially carcinogenic by either Bakale and McCreary (1987) or Kawachi et al. (1980).

CLINICAL ASSESSMENT OF SAFETY

Irritation

In a study to evaluate the dermal irritation of a variety of detergents on volunteers, SDDBS and sodium lauryl sulfate were the most irritating compounds tested (Morganti and Randazzo, 1984).

An aqueous solution of 12.5 mmol SDDBS (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 produced by SDDBS 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. In addition to SDDBS, four other chemicals, the positive control sodium lauryl sulfate, and the negative control distilled water were tested on the same subjects; there was also an untreated control site. The same procedures were followed for all test sites. TEWL was measured using the ServoMed Evaporimeter (ServoMed AB, Vallingby/Stockholm, Sweden). Clinical observations were graded according to the methods of Frosch and Kligman (1979).

SDDBS application resulted in an increase in TEWL over the 3 weeks, with a mean TEWL of 10.1 g/m^2h on day 19; the mean baseline TEWL was 4.9 g/m^2h. Using mean TEWL values as the standard for comparison, SDDBS was significantly less irritating than sodium lauryl sulfate. After 3 weeks of dosing, the TEWL value increased to ≥ 5 g/m^2h and the visual score was 1+ for almost 70% of the subjects.

The soap chamber test (Frosch and Kligman, 1979) was used to evaluate the irritation potential of a 1.0% and two 0.1% solutions of LAS (Froebe 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% LAS solution produced moderate/intense erythema in all subjects within 48 h; therefore, testing at this concentration was discontinued. The 0.1% LAS solutions 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% LAS solutions.

Repeated patch testing using 0.05% and 0.2% aqueous LAS on 71 and 81 subjects, respectively, produced mild to moderate irritation (Procter and Gamble, no date).

Patch testing with a 1% LAS solution produced low-level irritation in 8 of 50 subjects (Arthur D. Little, Inc., 1991). No irritation was observed for the other subjects.

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.

Sensitization

Human repeated insult patch testing of 0.01–0.113% LAS alone using 2,294 subjects and 0.001–0.09% LAS 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 LAS; patch testing of 79 consumers with skin problems due to products containing LAS did not result in positive reactions to LAS.

The sensitization potential of 0.05 and 0.2% aqueous concentrations of active LAS was evaluated using 71 and 81 subjects, respectively (Procter and Gamble, no date). Sensitization reactions were not observed at either concentration.

The sensitizing potentials of a 0.1% aqueous LAS solution and a 0.1% LAS solution in 50% ethanol/water were evaluated on 86 subjects (Procter and Gamble, no date). 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.

SUMMARY

SDDBS, TEA-DDBS, and SDBS are surfactant–cleansing agents; SDBS is also a surfactant–hydrotrope. SDDBS is commercially available as a yellow slurry or off-white dry product and is usually 30–50% active; TEA-DDBS is a clear yellow liquid that is commercially available as 40–60% aqueous solutions.

SDDBS has been assayed by two-phase titration. Dialkyltetralins, dialkylnaphthalenes, and, to a lesser extent, diakylindanes are present as impurities in SDDBS. TEA-DDBS contains sulfates at a maximum of 4.0. SDDBS does not absorb in the ultraviolet B range.

In 1992, it was reported to the FDA that SDDBS was used in 45 cosmetic product formulations, TEA-DDBS was used in 54 cosmetic formulations, and SDBS was not in use. SDDBS was used in the formulation of bubble baths, eyeliners, bath soaps and detergents, and other personal cleanliness products. TEA-DDBS was used in noncoloring shampoos and in hair dyes and colors. In 1984, SDDBS and TEA-DDBS were reported to be used at maximum concentrations of ≤50% in bubble baths and noncoloring shampoos, respectively.

Noncosmetic uses of SDDBS include its use as a detergent in hospitals and an industrial neutral cleansing agent. SDBS is approved as an indirect food additive.

SDDBS may act bacteriostatically on micro-organisms. SDDBS does not have substantial immunosuppressive potential. SDDBS affects the activation of different enzymes.

In studies in which rats were given i.p., s.c., or oral (in the diet) doses of ^{14}C-SDDBS and monkeys were given oral and s.c. doses of ^{14}C-LAS, high percentages of radioactivity were excreted in the urine and feces. In rats, some radioactivity was thought to be excreted in the bile.

Using rats, dermal application of SDDBS resulted in minimal penetration. In an *in vitro* study using skin from rats, no measurable penetration of SDDBS was observed within 24 h. When human skin was used in these *in vitro* studies, no penetration was observed within 24 h; after 24 h, the rate of penetration increased.

The oral LD_{50} for SDDBS in rats was 1.26 g/kg and the oral LD_{50} for TEA-DDBS in rats of a 1:128 aqueous dilution (a dosage of 195.3 mg/kg body wt) was >10 ml/kg. The oral LD_{50} for SDDBS in mice was 2.0 g/kg and for SDDBS in rodents it ranged from 0.5 to 2.0 g/kg. The dermal LD_{50} for LAS in rabbits was >500 mg/kg and the dermal LD_{50} for TEA-DDBS in rabbits for a 1:128 aqueous dilution (a dosage of 195.3 mg/kg body wt) was >21.5 ml/kg. The i.v. LD_{50} for SDDBS in mice was 105 mg/kg.

Rats were given oral doses of 1000 ppm SDDBS in water with normal diet or with 100–500 ppm PCB-supplemented diet for 1 month. No significant results were observed in the group given SDDBS in water without PCB-supplemented feed. Iron, serum cholesterol, and liver free cholesterol concentrations increased in some groups given SDDBS and PCB-supplemented feed. In studies in which rats were either fed ≤5000 ppm and SDDBS for 12 weeks or 0.5% LAS for 90 days or ≤12 weeks, no significant changes were observed.

No systemic toxicity was observed in rabbits given dermal applications of ≤10% SDDBS to abraded skin for 28 days; severe dermal irritation was observed at the application site. No systemic toxicity was observed in rabbits given dermal applications of ≤25% LAS for 24 h under occlusive patches. In rabbits dosed with ≤30% SDDBS for several weeks, no systemic toxicity resulted at concentrations ≤20% and weight loss was observed with application of 30% SDDBS.

Mild necrosis of intestinal mucosa with hemosiderosis of the spleen, liver, and kidneys were observed in rats given a varying dose of 2.5–5.0 ml/kg/day of a formulation containing 15% SDDBS for a total of 22 weeks; lesions were not observed for rats given 0.5 ml/kg/day. Renal damage was observed in rats dosed orally with ≤0.6% SDDBS for 6 months. Dermal application of a semipermanent hair dye formulation containing 0.5% TEA-DDBS to New Zealand White rabbits twice daily for 13 weeks did not produce systemic toxicity.

Dogs fed ≤1,000 mg/kg/day of a formulation containing 15% SDDBS in the diet for 6 months had lesions of hemorrhagic necrosis of the intestine and infiltration of inflammatory cells at a dose of 10 mg/kg, and hemosiderosis of the liver and spleen were observed in dogs given 100 and 1,000 mg/kg. No significant results were observed when rats were given ≤0.5% LAS in the diet for 2 years. A decrease in body weight gain, lesions of the cecum and liver, and increased severity of renal lesions were observed when Wistar rats were fed LAS in the diet; renal lesions were observed at 0.2–1.8% LAS. A concentration of 0.07% LAS did not produce adverse effects. Rats were given oral doses of 1,000 ppm SDDBS in water with normal diet or with 500 ppm PCB-supplemented diet for 1, 3, or 7 months. No significant results were observed for the group given SDDBS in water and normal feed. For some rats in the other groups, body weights were reduced, testicle weight was decreased after 7 months, and other chemical parameters were changed.

SDDBS, adjusted to 15% active and a pH of 7.0, applied to intact and abraded sites was severely irritating and a 10% solution of 19% SDDBS and 19% tallow alkyl ethoxylate sulfate was moderately irritating to the skin of rabbits. A 10% solution of SDDBS was an acute skin irritant and a 1% solution was not irritating to the skin of rabbits. Three 6 h applications of a 1% (w/v) aqueous solution of LAS resulted in primary skin irritation of rabbit skin. For rats, 20% SDDBS did not produce cutaneous lesions while a 30% solution produced fairly pronounced skin lesions. Moderate to severe dermal irritation (3.0/4.0) resulted when C_{12} LAS was applied to the backs of guinea pigs under occlusive patches; the irritation was slightly less (2.75/4.0) when a mixed C_x LAS solution was used. In a cumulative open patch test, C_{12} LAS produced a dermal irritation score of 1.42/4.0 while a mixed LAS solution resulted in a score of 0.58/4.0 for guinea pigs. A 1:128 aqueous dilution of TEA-DDBS (a dosage of 195.3 mg/kg body wt) was not an irritant to either intact or abraded rabbit skin.

Concentrations of $\geq$5% LAS were irritants to the eyes of rabbits; $\leq$0.1% LAS produced mild to no irritation. A 1:128 aqueous solution of TEA-DDBS (a dosage of 195.3 mg/kg body wt) did not produce irritation in rabbit eyes. Three drops of a 1% SDBS solution placed in the eye of a rabbit produced severe irritation.

No reproductive effects were produced by either dermal application of LAS or TEA-DDBS or by oral administration of LAS.

Negative results were obtained in various mutagenicity assays using SDDBS.

Dermal carcinogenicity studies using LAS and TEA-DDBS and oral carcinogenicity studies using SDDBS and LAS were negative. Using the k_e test, SDDBS was determined not to be potentially carcinogenic.

In a study evaluating the dermal irritation of a variety of detergents on volunteers, SDDBS was one of the most irritating compounds tested. In the soap chamber test, 1% LAS produced moderate/intense erythema in all subjects; 0.1% LAS produced negligible or mild erythema. Repeated patch testing using $\leq$0.2% LAS produced mild to moderate irritation, while patch testing with a 1% LAS solution resulted in low level irritation. SDDBS was found to increase TEWL. LAS was not determined to be a sensitizer.

DISCUSSION

Section 1, paragraph (p) of the CIR Procedure states that "A lack of information about an ingredient shall not be sufficient to justify a determination of safety." In accordance with Section 30 (j)(2)(A) of the CIR Procedures, the Expert Panel informed the public of its decision that the data on Sodium Dodecylbenzenesulfonate, TEA-Dodecylbenzenesulfonate, and Sodium Decylbenzenesulfonate were insufficient to determine whether these ingredients, under each relevant condition of use, were either safe or unsafe. The Expert Panel released a Notice of Insufficient Data Announcement on February 8, 1991, outlining the data needed to assess the safety of Sodium Dodecylbenzenesulfonate, TEA-Dodecylbenzenesulfonate, and Sodium Decylbenzenesulfonate. The types of data required include: (1) human irritation data; (2) human sensitization data; (3) ultraviolet (UV) absorption data; and if absorption occurs, human photosensitization data are required.

No offer to supply the human irritation, human sensitization, or UV absorption data was received. However, human irritation and sensitization data on LAS were determined to be satisfactory for use in determination of the safety of Sodium Dodecylbenzenesulfonate, TEA-Dodecylbenzenesulfonate, and Sodium Decylbenzenesulfonate.

In review of the data on LAS, it was determined that additional data were still necessary to make an assessment of safety. The Panel therefore issued a second Insufficient Data Announcement on May 14, 1992. In the second announcement, the following data were requested: (1) concentration of use in cosmetic formulations; (2) UV absorption data, if absorption occurs, human phototoxicity data are needed; (3) quantitative impurities data, specifically, the amount of dialkylnaphthalene, dialkyltetralin, and dialkylindane in LAS.

Impurities and UV data received in response to this announcement were sufficient to use in making an assessment of the safety.

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. 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 Panel also recognizes that Sodium Dodecylbenzenesulfonate, at pH 9, may be a potential ocular irritant; induction of ocular irritation by Sodium Dodecylbenzenesulfonate may be dependent on the test setting.

In accordance with the information above, the Expert Panel recognizes that the concentration of Sodium Dodecylbenzenesulfonate used in actual bubble bath formulations would result in severe dermal and ocular irritation; however, actual exposure differs greatly from the amount contained in formulation. Information from the Washington Suburban Sanitary Commission (no date) indicate that the average full tub volume is 36 gal. Therefore, the addition of 2 oz bubble bath to a full tub of water would result in a 1:2,300 dilution factor, greatly reducing the irritation potential.

In evaluating the data used in this report, the Panel recognized that the lowest percentage activity of an ingredient can contain the greatest amount of impurities. The lowest percentage activities published for Sodium Dodecylbenzenesulfonate and TEA-Dodecylbenzenesulfonate have been 30 and 40%, respectively. The Expert Panel therefore assumed that a solution of Sodium or TEA-Dodecylbenzenesulfonate that did not give the percentage activity of the ingredient had the lowest previously reported activity of the ingredient (i.e., a 10% solution of Sodium Dodecylbenzenesulfonate (percentage activity not given) is 3% Sodium Dodecylbenzenesulfonate [10% solution of 30% active ingredient]).

Since the Expert Panel accepted data on LAS, a commercial preparation, in its determination of safety, the preceding is also applicable to LAS. Data from 3 manufacturers reported that a 12-carbon chain length moiety comprises 18.1–35% of LAS products. The amount of Sodium Dodecylbenzenesulfonate in the LAS product would be, therefore, the lowest percentage of a 12-carbon chain moiety that comprises LAS with the lowest percentage activity known for Sodium Dodecylbenzenesulfonate. Therefore, a 10% solution of LAS would contain 0.5% active Sodium Dodecylbenzenesulfonate. This derivation was employed only in evaluating the data contained in the report in which the percentage activity or 12 carbon chain length moiety composition of LAS was not stated.

Although there were minimal data available on Sodium Decylbenzenesulfonate, the Expert Panel determined that due to the chemical similarity of Sodium Dodecylbenzenesulfonate and Sodium Decylbenzenesulfonate, the data concerning Sodium Dodecylbenzenesulfonate that were presented in this report were applicable in assessing the safety of Sodium Decylbenzenesulfonate.

CONCLUSION

On the basis of the animal and clinical data presented in this report, the CIR Expert Panel concludes that Sodium Dodecylbenzenesulfonate, TEA-Dodecylbenzenesulfonate, and Sodium Decylbenzenesulfonate are safe as cosmetic ingredients in the present practices of use.

ACKNOWLEDGMENT

Monice M. Zondlo, Scientific Analyst and Writer, prepared this report.

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