Final Report on the Safety Assessment of Cocoyl Sarcosine, Lauroyl Sarcosine, Myristoyl Sarcosine, Oleoyl Sarcosine, Stearoyl Sarcosine, Sodium Cocoyl Sarcosinate, Sodium Lauroyl Sarcosinate, Sodium Myristoyl Sarcosinate, Ammonium Cocoyl Sarcosinate, and Ammonium Lauroyl Sarcosinate[1]

This safety assessment addresses cosmetic ingredients that are *N*-acyl derivatives of sarcosine and are generally referred to as acyl sarcosines, and those that are salts, known generally as acyl sarcosinates. Previous assessments have addressed the safety of each of the fatty acids that appear in these acyl sarcosines and sarcosinates (Coconut Acid, Oleic Acid, Lauric Acid, and Myristic Acid). In each case the fatty acid was either safe for use or safe as used in cosmetic formulations. Acyl sarcosines are considered modified fatty acids with greater solubility and increased acidity of the carboxylic acid group compared to the parent fatty acid. They are used in a large number of cosmetic formulations as hair-conditioning agents and surfactant-cleansing agents. In soaps, concentrations are reported to be as high as 12.9%. These ingredients have low oral toxicity in rats. Although cytotoxic to Chinese hamster cells in culture, acyl sarcosines and sarcosinates are not mutagenic in those cells, nor in bacterial cells in culture. Carcinogenicity data were not available. These ingredients are nonirritating and nonsensitizing to animal and human skin, although they can enhance the penetration of other ingredients through the skin. For that reason, caution should be exhibited in formulating cosmetic products that contain these ingredients in combination with other ingredients whose safety is based on their lack of absorption or where dermal absorption is a concern (e.g., HC Yellow No. 4, Disperse Yellow 3). Because sarcosine can be nitrosated to form *N*-nitrososarcosine, a known animal carcinogen, these ingredients should not be used in cosmetic products in which *N*-nitroso compounds may be formed. With the above caveat, and based on the available data, it was concluded that these acyl sarcosines and sarcosinates are safe as used in rinse-off products. They may be safely used in leave-on products at concentrations up to 5%, the highest concentration tested in clinical irritation and sensitization studies. Oleoyl Sarcosine is used as a corrosion inhibitor in some aerosol products, at extremely low concentrations. In this circumstance, the ingredient is not being used as a cosmetic ingredient and this report is not intended to limit that use. Because of the absence of data on inhalation toxicity, however, it was concluded that the available data were not sufficient to support the safety of acyl sarcosines and sarcosinates as cosmetic ingredients in products where they are likely to be inhaled.

INTRODUCTION

Cocoyl Sarcosine, Lauroyl Sarcosine, Myristoyl Sarcosine, Oleoyl Sarcosine, Stearoyl Sarcosine, Sodium Cocoyl Sarcosinate, Sodium Lauroyl Sarcosinate, Sodium Myristoyl Sarcosinate, Ammonium Cocoyl Sarcosinate, and Ammonium Lauroyl Sarcosinate, are *N*-acyl derivatives of sarcosine that function as hair-conditioning agents and surfactant-cleansing agents in cosmetic formulations. Cocoyl, Lauroyl, Myristoyl, Oleoyl, and Stearoyl Sarcosine are known generally as *N*-acyl sarcosines, or acyl sarcosines, as they are referred to in this report. Their salts are known generally as *N*-acyl sarcosinates, fatty acid sarcosinates, or sarcosinates. This report reviews the published literature on the acyl sarcosines and their simple sodium and ammonium salts.

Previous safety assessments by the Cosmetic Ingredient Review (CIR) Expert Panel are relevant to this safety assessment because they deal with components of the acyl sarcosines and fatty acid sarcosinates. These are:

> Coconut Oil, Coconut Acid, Hydrogenated Coconut Oil, and Hydrogenated Coconut Acid are safe for use as cosmetic ingredients (Elder 1986).
>
> Oleic, Lauric, Palmitic, Myristic, and Stearic Acids are safe in present practices of use and concentration in cosmetics (Elder 1987).

CHEMISTRY

Definition and Structure

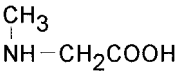
Sarcosine, also known as *N*-methylglycine or *N*-methylaminoacetic acid, is derived from the decomposition of creatine or caffeine. Sarcosine conforms generally to the formula (Sax 1979; Aldrich Chemical Co. 1992; Lewis 1997):

Received 15 June 2000; accepted 2 November 2000.

[1]Reviewed by the Cosmetic Ingredient Review Expert Panel. Rebecca S. Lanigan, former Scientific Analyst and Writer, prepared this report. Address correspondence to Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 310, Washington, DC 20036, USA.

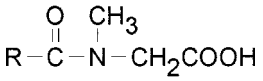
International Journal of Toxicology, 20(Suppl. 1):1–14, 2001

1071-7544/01 $12.00 + .00



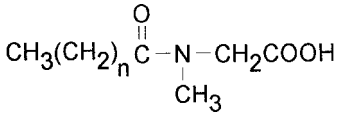
Sarcosine is also a naturally occurring amino acid found in marine animals, and is a component of actinomycin antibiotics (Technology Sciences Group, Inc. 1994a).

Cocoyl Sarcosine is the *N*-acyl derivative of sarcosine that conforms generally to the formula



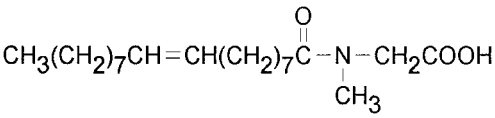
where RCO– represents the fatty acids derived from coconut oil (Wenninger, Canterbery, and McEwen 2000). The fatty acids in Cocoyl Sarcosine have the following composition: 2% to 4% C10, 55% C12, 19% to 22% C14, 0% to 7% C16, 4% to 21% C18, 0% to 8% oleic acid, and 0% to 3% unsaturated fatty acids (Geigy Industrial Chemicals 1958; 1962). Other names for Cocoyl Sarcosine include: *N*-Cocoyl-*N*-Methyl Glycine; *N*-Cocoyl Sarcosine; Glycine, *N*-Methyl, *N*-Coco Acyl Derivatives; Glycine, *N*-Methyl-*N*-(1-Oxococonut Alkyl)-; *N*-Methylglycine, *N*-Coco Acyl Derivatives; *N*-Methyl-*N*-(1-Oxococonut Alkyl) Glycine (Wenninger, Canterbery, and McEwen 2000); *N*-(Coconut Oil Acyl) Sarcosine (Occupational Health Services, Inc. 1996); and Cocobetaine (Chemline 1996). The latter synonym is also the name of an structurally similar zwitterion (CAS No. 68424-94-2) that is an *N*-dimethylglycine, *N*-coco acyl derivative (Wenninger, Canterbery, and McEwen 2000).

Lauroyl, Myristoyl, and Stearoyl Sarcosine are the condensation products of natural fatty acids with sarcosine and have the general formula



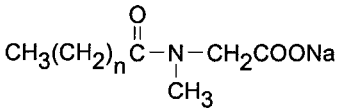
where *n* equals the fatty acid chain lengths of 10, 12, and 16, respectively. Synonyms for Lauroyl Sarcosine are Glycine, *N*-methyl-*N*-(1-oxododecyl)- and *N*-Methyl-*N*-(1-oxododecyl) glycine. Myristoyl Sarcosine is also known as Glycine, *N*-methyl-*N*-(1-oxotetradecyl)-; *N*-Methyl-*N*-(1-oxotetradecyl) glycine; and Myristoyl *N*-methylglycine. Other names for Stearoyl Sarcosine are Glycine, *N*-methyl-*N*-(1-oxooctadecyl)-; *N*-Methyl-*N*-(1-oxooctadecyl) glycine;Stearoyl *N*-methylaminoacetic acid; and Stearoyl *N*-methylglycine (Wenninger, Canterbery, and McEwen 2000). The fatty acid composition of Lauroyl Sarcosine is typically 0% to 2% C10, 95% C12, 3% C14, 0% to 1% C16, and 0% to 1% oleic acid. The fatty acid composition of Stearoyl Sarcosine is generally 0% to 2% C14, 50% C16, 47% to 49% C18, and 1% oleic acid (Geigy Industrial Chemicals 1958; 1962).

Oleoyl Sarcosine is the condensation product of oleic acid with sarcosine with the following formula:



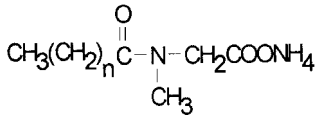
Synonyms for Oleoyl Sarcosine are Glycine, *N*-methyl-*N*-(1-oxo-9-octadecenyl)-; *N*-Methyl-*N*-(1-oxo-9-octadecenyl) glycine; Oleoyl *N*-methylaminoacetic acid; Oleyl methylaminoethanoic acid; Oleyl *N*-methylglycine; and Oleyl sarcosine (Wenninger, Canterbery, and McEwen et al. 2000). The fatty acid composition of Oleoyl Sarcosine is typically 4% to 5% C14, 3% to 4% C16, 80% to 81% oleic acid, and 11% to 12% unsaturated fatty acids (Geigy Industrial Chemicals 1958; 1962).

Sodium Cocoyl Sarcosinate, Sodium Lauroyl Sarcosinate, and Sodium Myristoyl Sarcosinate are sodium salts of the acyl sarcosines that conform generally to the structure



where *n* equals the fatty acid chain length (Wenninger, Canterbery, and McEwen 2000). Sodium Cocoyl Sarcosinate is also known as Amides, coconut oil, with sarcosine, sodium salts; and Sodium *N*-cocoyl sarcosinate. Synonyms for Sodium Lauroyl Sarcosinate are Glycine, *N*-methyl-*N*-(1-oxododecyl)-, sodium salt and *N*-Methyl-*N*-(1-oxododecyl) glycine, sodium salt. Sodium Myristoyl Sarcosinate is also known as Glycine, *N*-methyl-*N*-(1-oxotetradecyl)-, sodium salt and *N*-Methyl-*N*-(1-oxotetradecyl) glycine, sodium salt (Wenninger, Canterbery, and McEwen 2000). The fatty acid composition of Sodium Lauroyl Sarcosinate is typically 95% C12, 3% C14, 0% to 1% C16, and 0% to 1% oleic acid (Geigy Industrial Chemicals 1958; 1962).

Ammonium Cocoyl Sarcosinate and Ammonium Lauroyl Sarcosinate are the ammonium salts of their respective acyl sarcosines. They conform generally to the formula



where *n* equals the fatty acid chain length. Ammonium Cocoyl Sarcosinate is also known as Amides, coconut oil, with sarcosine, ammonium salts; Ammonium *N*-cocoyl sarcosinate; and Glycine, *N*-methyl-, *N*-coco amido deriv., ammonium salt. Synonyms for Ammonium Lauroyl Sarcosinate are Ammonium *N*-lauroyl sarcosinate; Glycine, *N*-methyl-*N*-(1-oxododecyl)-, ammonium salt; and *N*-Methyl-*N*-(1-oxododecyl)glycine, ammonium salt (Wenninger, Canterbery, and McEwen 2000).

Chemical and Physical Properties

Cocoyl, Lauroyl, Myristoyl, Oleoyl, and Stearoyl Sarcosines are considered modified fatty acids in which the hydrocarbon chains are interrupted by an amidomethyl (–$CONCH_3$–) group in the alpha position. This modification imparts greater solubility and crystallinity to the molecule, increases the acidity of the carboxylic acid group, and enhances adsorption characteristics. Acyl sarcosines have good stability at high temperatures, and can be heated at 180°C for several minutes without decomposition.

The acid forms (e.g., Cocoyl Sarcosine) can be distilled at reduced pressure with some breakdown. The sodium salts of Cocoyl Sarcosine or Oleoyl Sarcosine are not "salted out" by relatively high concentrations of alkali or neutral electrolytes (Geigy Industrial Chemicals 1958; 1962).

Acyl sarcosines are somewhat stronger acids than the parent fatty acids, and form salts in the neutral and mildly acidic pH range. The salts are similar physically and chemically to fatty acid soaps. Sarcosinates are, however, more soluble in water and less affected by water hardness than are common soaps. They are moderately strong organic acids, with pK values between those of simple fatty acids and alkyl sulfuric acids or alkyl aryl sulfonic acids (Hart 1979).

Cocoyl Sarcosine is a yellow, viscous, oily liquid. It is solube in most organic solvents, including glycols, glycerin, silicones, phosphate esters, and aliphatic hydrocarbons. Cocoyl Sarcosine is water-insoluble. The specific gravity of Cocoyl Sarcosine is 0.965 to 0.975 at 25°/25°C (Nikitakis and McEwen 1997). Cocoyl Sarcosine melts at 22° to 28°C and is combustible (Lewis 1997). The molecular weight is 280 to 290 Da and the setting point is 19°C (Geigy Industrial Chemicals 1958; 1962).

Lauroyl Sarcosine is a white to off-white waxy solid to semisolid. It has a mild, fatty acid odor (Nikitakis and McEwen 1990). Lauroyl Sarcosine is insoluble in water, and is soluble in most organic solvents, including glycols, glycerine, silicone, phosphate esters, and aliphatic hydrocarbons (Geigy Industrial Chemicals 1958; 1962). The melting range of Lauroyl Sarcosine is 28° to 36°C. When assayed (as Lauroyl Sarcosine) via NaOH titration to a phenolphthalein end point, the minimum value was 94% (Nikitakis and McEwen 1990). Lauroyl Sarcosine has a molecular weight in the range of 280 to 290 Da, a setting point of 31°C, and a specific gravity of 0.969 (Geigy Industrial Chemicals 1958; 1962).

The molecular weight range of Oleoyl Sarcosine is 340 to 350 Da, its setting point is 0°C, and its specific gravity is 0.948. Stearoyl Sarcosine has a molecular weight range of 340 to 350 Da, a setting point of 50°C, and a specific gravity of 0.924. Like Cocoyl Sarcosine and Lauroyl Sarcosine, both Oleoyl Sarcosine and Stearoyl Sarcosine are water-insoluble and are soluble in most organic solvents (Geigy Industrial Chemicals 1958; 1962).

Sodium Lauroyl Sarcosinate is available commercially as a colorless to slightly yellow, 30% aqueous solution, as solid flakes, or as a substantially anhydrous white powder with 97% active content. It is soluble in water and the pH of a 1% aqueous solution is 7.5 to 8.5. The specific gravity at 25°/25°C is 0.99 to 1.03. The melting point of the powder form is 140°C (Geigy Industrial Chemicals 1958; 1962; Nikitakis and McEwen 1990). When assayed (as Sodium Lauroyl Sarcosinate), the typical range was 28.0% to 32.0% (Nikitakis and McEwen 1990).

Reactivity

Acyl sarcosines formed salts when treated with inorganic or organic bases. Water-insoluble salts could be readily formed by exchange reactions. Methyl esters could be prepared with anhydrous hydrogen chloride catalyst, and ethylene oxide could be added to acyl sarcosines in the presence of catalytic amounts of sodium methylate. The amide linkage was resistant to alkaline hydrolysis, but was broken by boiling the compound in strong mineral acid. Acyl sarcosines were stable indefinitely on storage at ambient temperatures as long as moisture was excluded (Geigy Industrial Chemicals 1958; 1962).

Acyl sarcosines formed salts in the neutral and mildly acidic pH range. They were strongly adsorbed on various protein and protein-like substrates, such as hair, skin, wool, casein, and gelatin (Nelson and Stewart 1956; Hart 1979; Hampshire Chemical Corporation 1997a). Adsorption increased when small amounts of the free fatty sarcosinic acid existed in solution (Hart 1979). Adsorption was enhanced at lower pH and at greater concentrations; more of the acyl sarcosinates adsorbed onto damaged hair than adhered to undamaged hair (Nelson and Stewart 1956; Hampshire Chemical Corporation 1997a). Similar effects were noted in humans when skin was washed with soaps based on Lauroyl Sarcosine. The precipitated surfactant adhered readily to the skin, especially at pH 5.2, and was removed by rinsing with water (Hampshire Chemical Corporation 1997a).

The acyl sarcosines and their salts were also adsorbed onto metallic surfaces. Infrared analysis of ferrous metal coated with Oleoyl Sarcosine established that surface chelation occurred through the amino acid portion of the molecule. The carboxylate moiety oriented itself vertically, and the metallic surface was chelated, forming a five-membered ring (Hampshire Chemical Corporation 1997a).

Sarcosinates were stable in dilute hydrogen peroxide and sodium hypochlorite bleach solutions, and could thicken aqueous hypochlorite solutions. Viscosity and active chlorine content remained stable for several months, suggesting that these salts are stable in the presence of other oxidizing agents (Hart 1979).

Acyl sarcosines are resistant to decomposition and hydrolysis in both alkaline and moderately acidic media at ambient temperatures (Hampshire Chemical Corporation 1997a). The amide linkage could be broken in strong mineral acids at ambient temperatures. The acyl sarcosines were resistant to oxidation by chemicals such as hypochlorite, hydrogen peroxide, and benzoyl peroxide.

Sarcosine can react with oxidizing materials (Sax 1979) and can be nitrosated to form *N*-nitrososarcosine. *N*-nitrososarcosine has been formed by the reaction of sarcosine with sodium nitrite in an acid solution and by passing nitrous acid fumes through a sarcosine solution. *N*-nitrososarcosine can also be produced by nitrosating *N*-methylsarcosine hydrochloride or by treating creatine in an acid medium with an aqueous solution of sodium nitrite. Primary routes of potential human exposure to *N*-nitrososarcosine are inhalation, ingestion, and dermal contact (International Agency for Research on Cancer [IARC] 1978). *N*-nitrososarcosine has been detected in foodstuffs, particularly meat, at concentrations of 2 to 56 μg/kg of sample. It can be produced by various reactions in air, water, soil, food, and animal systems (National Toxicology Program [NTP] 1994).

When 50 mg of Sodium Lauroyl Sarcosinate was incubated with 100 mg of sodium nitrite in 10% hydrochloric acid, investigators detected sarcosine, Lauroyl Sarcosine, and *N*-nitrososarcosine using thin-layer chromatography (TLC). The yield of *N*-nitrososarcosine was 6.0% (Rao and Bejnarowicz 1976).

Method of Manufacture

The acyl sarcosines are the condensation products of sarcosine with natural fatty acids. The fatty acids in Cocoyl Sarcosine are derived from coconut oil. The fatty acids in Lauroyl, Myristoyl, and Stearoyl Sarcosines are primarily lauric, myristic, and stearic acids, respectively (Nikitakis and McEwen 1990; Wenninger, Canterbery, and McEwen 2000).

Acyl sarcosines are produced commercially by the Schotten-Baumann reaction of sodium sarcosine and the parent fatty acid chlorides shown in Figure 1. After completion of the reaction, the crude sodium salt is acidified to liberate the free fatty sarcosinic acid (e.g., Cocoyl Sarcosine), which is separated from the aqueous byproducts. The fatty sarcosinic acid can be used as the free fatty acid or neutralized to form the sodium or ammonium salts (Hart 1979).

Sodium Lauroyl Sarcosinate is prepared from lauroyl chloride and sarcosine in the presence of sodium hydroxide (Rosenthal, Marson, and Abriss 1954; Patil, Mhatre, and Koshti 1989). Sodium Lauroyl Sarcosinate is purified by recrystallization from alcohol, or by acidification with mineral acid, separation of the free acid, and neutralization of the free acid (Rosenthal, Marson, and Abriss 1954). The acyl sarcosinates are often supplied as 30% or 95% aqueous solutions. According to a large manufacturer, only internally prepared sodium sarcosinate is used as a starting material (Hampshire Chemical Corporation 1997a). The sodium sarcosinate is then reacted directly with the acyl chloride, which has been prepared from the free fatty acid by treatment with phosphorus trichloride (Technology Sciences Group, Inc. 1994b).

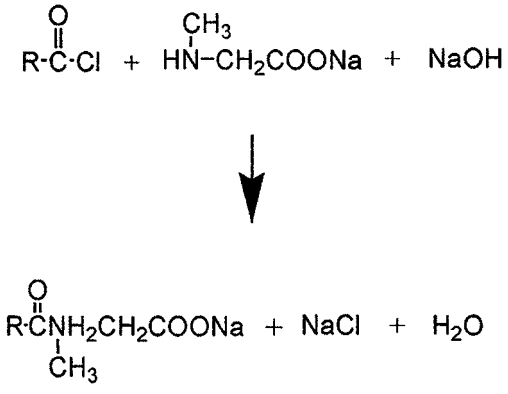


FIGURE 1
Schotten-Baumann reaction to produce Acyl Sarcosines (Hart 1979).

Impurities

Free fatty acids (6.0% maximum) are present in Cocoyl Sarcosine. The amount of moisture is 1.0% (Nikitakis and McEwen 1990). Cocoyl Sarcosine is generally 95% to 97% pure (Geigy Industrial Chemicals 1958; 1962). The minimum purity of Lauroyl Sarcosine is generally 97%, and it contains no more than 2% free fatty acids (Geigy Industrial Chemicals 1958; 1962). Acyl sarcosines contain 94% (minimum) of the active ingredient and 6% (maximum) of the free fatty acid (Hampshire Chemical Corporation 1997a).

Samples of Lauroyl Sarcosine contained 1.7% to 9.78% free lauric acid as determined by high-performance liquid chromatography (HPLC) (Patil, Mhatre, and Koshti 1989). Rao and Bejnarowicz (1976) detected sarcosine and Lauroyl Sarcosine in samples of Sodium Lauroyl Sarcosinate using TLC. Sodium Lauroyl Sarcosinate contains up to 2.0% sodium laurate and up to 0.2% inorganic salts (Geigy Industrial Chemicals 1958; 1962; Nikitakis and McEwen 1990). In the pH range of 4 to 7, the *N*-acyl sarcosinates exist in equilibrium with the free *N*-acyl sarcosinic acid (Hart 1979).

Alkaline hydrolysis occurs during the preparation of Sodium Lauroyl Sarcosinate, resulting in soap formation. This soap, the primary impurity of Sodium Lauroyl Sarcosinate, also results from the free fatty acid present in the fatty acid chloride during the manufacturing process (Patil, Mhatre, and Koshti 1989).

Thirty percent aqueous solutions of Lauroyl Sarcosine and Sodium Lauroyl Sarcosinate were analyzed for nitrosamines (test method unavailable). The detection limits were 65 ppb for *N*-nitrososarcosine in Lauroyl Sarcosine and 15 ppb in Sodium Lauroyl Sarcosinate, respectively; no nitrosamines were detected (Hampshire Chemical Corporation 1997a). The synthesis reaction is kept in a closed system for up to several days prior to the succeeding reaction to prevent contamination with nitrite precursors. The reaction conditions are not conducive to the formation of nitrosamines as contaminants, and neither nitrates nor nitrites are used in the manufacturing process (Technology Sciences Group, Inc. 1994b).

Precursors necessary for the "hypothetical formation" for polynuclear aromatic hydrocarbons are also absent from the synthesis reactions and none of the starting materials are prepared or provided in a hydrocarbon solvent. Similarly, the presence of dioxins was considered "exceedingly improbable," as no phenolic compounds were present in any of the synthesis reactions (Technology Sciences Group, Inc. 1994b).

Analytical Methods

Acyl sarcosines (at dilutions of 1:2000) have been determined in solution in the absence of interfering anionic detergents by conventional cationic/anionic titration methods (Geigy Chemical Corp. no date; Geigy Industrial Chemicals 1958; 1962). These ingredients and their sodium salts have been determined by infrared spectrometry (Geigy Chemical Corp. no date; Nikitakis and McEwen 1990), gas chromatography (Molever 1993), and TLC (Rao and Bejnarowicz 1976).

Ultraviolet (UV) Absorption

Lauroyl Sarcosine and Sodium Lauroyl Sarcosinate have no "useful absorption in UV or visible region." To determine Lauroyl Sarcosine and its free fatty acid content by reversed-phase HPLC, Sodium Lauroyl Sarcosinate was first acidified to give Lauroyl Sarcosine and then converted to the UV-absorbing phenacyl ester by introduction of an aromatic nucleus (Patil, Mhatre, and Koshti 1989).

USE

Cosmetic

The acyl sarcosines and sarcosinates function as hair-conditioning agents and surfactant-cleansing agents in cosmetic formulations (Wenninger, Canterbery, McEwen 2000). In 1998 (Table 1), Cocoyl Sarcosine, Lauroyl Sarcosine, Myristoyl Sarcosine, Oleoyl Sarcosine, and Stearoyl Sarcosine are reportedly used in 33, 6, 4, 5, and 4 cosmetic formulations, respectively. Sodium Cocoyl Sarcosinate, Sodium Lauroyl Sarcosinate, and Sodium Myristoyl Sarcosinate are used in 20, 118, and 2 formulations, respectively. The ammonium salts were not reported used (Food and Drug Administration [FDA] 1998).

Molever (1993) reported that Sodium Lauroyl Sarcosinate was used at concentrations of 2.78% to 6.86% in two liquid soaps and 12.5% to 12.9% in a bar soap, based on gas chromatographic analysis of the products (Molever 1993). Information on the concentration of use of acyl sarcosines or other of their salts was not available.

According to industry, the most widely used commercial form of acyl sarcosine is a 30% aqueous solution of Sodium Lauroyl Sarcosinate; it is widely used in shampoos, body washes, and facial washes. The acid forms of Myristoyl Sarcosine and Stearoyl Sarcosine are neutralized with triethanolamine in the manufacture of shaving gels. Sodium Myristoyl Sarcosine is used in the manufacture of facial washes. Sodium Cocoyl Sarcosine is occasionally used in the manufacture of medicated shampoo. Oleoyl Sarcosine is added to aerosolized products at concentrations of 10 to 100 ppm to inhibit corrosion of the metal cans (Hampshire Chemical Corporation 1997b).

Noncosmetic

Acyl sarcosines and their sodium salts are used in the metal finishing and processing industries for their crystal modifying, anti-rust, and anti-corrosion properties. Acyl sarcosine surfactants also have been used to improve wetting and penetration of topical pharmaceutical products (Geigy Industrial Chemicals 1958; 1962).

Sodium Lauroyl Sarcosinate serves as a detergent to permeabilize cells and extract proteins from cellular membranes during isolation and purification techniques such as sodium dodecyl sulfate–polyacrylamide gel electrophoresis (SDS-PAGE) and the indirect enzyme-linked immunosorbent assay (ELISA) (Newton et al. 1990; Anderson et al. 1995; Kippert 1995; Koontongkaew and Jitpukdeebodintra 1995). Lauroyl Sarcosine is used as a weak cation-exchange reagent in chromatographic procedures (Mefford 1987).

The Environmental Protection Agency (EPA) previously approved the use of several acyl sarcosines and closely related compounds as inert ingredients (surfactants) in formulated pesticides, and exempted closely related compounds from requirement of a tolerance for use as inert ingredients in pesticides applied to growing crops or post-harvest to raw agricultural products (Technology Sciences Group, Inc. 1994a). Additional data indicated that the maximum concentration of acyl sarcosines or sarcosinates that can be present in a formulation is approximately 10% by weight. An emulsifiable concentrate that is typical of liquid pesticide formulations contains 50% to 85% active ingredient; the maximum ratio of acyl sarcosine to active ingredient is therefore between 0.20 and 0.12 (Technology Sciences Group, Inc. 1994b).

The sarcosines and their salts are approved by FDA for use in processing, packaging, and transporting food for human consumption; such uses are codified as 21 CFR 175.105, 177.1200, 178.3130, and 178.3570. Specifically, Lauroyl and Stearoyl Sarcosines (up to 0.3%) are approved for use as release agents in food packaging cellophane. Cocoyl, Lauroyl, and Oleoyl Sarcosines are approved for use as antistatic/antifogging agents in polyolefin film used for fresh food packaging, at concentrations up to 0.15% by weight. Sodium Lauroyl Sarcosinate can be used at a concentration of up to 0.35% in vinylidine chloride copolymer packaging. Oleoyl Sarcosinate can be used as a corrosion inhibitor at concentrations up to 0.5% in lubricants for food processing machinery. Sodium Lauroyl Sarcosinate is approved for use in adhesives used in food storage or transportation.

GENERAL BIOLOGY

Absorption, Distribution, Metabolism, and Excretion

Sodium Lauroyl Sarcosinate was not hydrolyzed by either gastric or intestinal enzymes in vitro (Geigy Chemical Corp. no date; Geigy Industrial Chemicals 1958; 1962).

When [^{14}C]Sodium Lauroyl Sarcosinate was administered to rats (route of administration not available) during a metabolism study, 82% to 89% of the 50 mg/kg dose was excreted in the urine and feces within 24 hours. For the next 24 hours, 1% to 2% was excreted. Nearly all of the excreted material was found in the urine (Geigy Chemical Corp. no date).

In an oral dosing study, [^{14}C]Sodium Lauroyl Sarcosinate (labeled at the carboxyl C in the sarcosinate functional group) was dissolved in water to yield a solution with $\sim 3.4 \times 10^6$ counts/min/ml of solution (Technology Sciences Group Inc. 1994c). A dose of $\sim 2.6 \times 10^3$ μg was applied to the teeth, oral mucosa, and tongue of 15 rats. Five rats each were examined at the time of application, 4, and 24 hours. Tissue samples were analyzed for radioactivity, as well as samples of the urine and

TABLE 1
Product formulation data (FDA 1998)

Product category	Total no. of formulations in category	Total no. containing ingredient
Cocoyl Sarcosine		
Mascara	167	2
Hair conditioners	636	5
Shampoos (noncoloring)	860	4
Foundations	287	8
Makeup bases	132	9
Other makeup preparations	135	2
Moisturizing preparations	769	2
Other skin care preparations	692	1
1998 Cocoyl Sarcosine total		33
Lauroyl Sarcosine		
Shampoos (noncoloring)	860	5
Bath soaps and detergents	385	1
1998 Lauroyl Sarcosine total		6
Myristoyl Sarcosine		
Other shaving preparation products	60	4
1998 Myristoyl Sarcosine total		4
Oleoyl Sarcosine		
Hair conditioners	636	1
Hair color sprays (aerosol)	4	1
Lipstick	790	1
Body and hand (excluding shaving) preparations	796	2
1998 Oleoyl Sarcosine total		5
Stearoyl Sarcosine		
Other shaving preparation products	60	4
1998 Stearoyl Sarcosine total		4
Sodium Cocoyl Sarcosinate		
Baby shampoos	21	1
Other bath preparations	159	4
Shampoos (noncoloring)	860	5
Other personal cleanliness products	291	2
Cleansing preparations	653	6
Body and hand (excluding shaving preparations)	796	1
Other skin care preparations	692	1
1998 Sodium Cocoyl Sarcosinate total		20
Sodium Lauroyl Sarcosinate		
Other bath preparations	159	16
Shampoos (non-coloring)	860	37
Hair rinses (coloring)	33	1
Hair shampoos (coloring)	24	1
Other hair-coloring preparations	59	1
Foundations	287	4
Other manicuring preparations	61	1
Dentifrices	38	1
Bath soaps and detergents	385	25
Other personal cleanliness products	291	4

(Continued on next page)

TABLE 1
Product formulation data (FDA 1998) *(continued)*

Product category	Total no. of formulations in category	Total no. containing ingredient
Shaving cream	139	22
Other shaving preparation products	60	22
Cleansing preparations	653	142
Face and neck (excluding shaving) preparations	263	22
Body and hand (excluding shaving) preparations	796	22
Paste masks (mud packs)	255	12
Skin fresheners	184	22
Other skin care preparations	692	2
1998 Sodium Lauroyl Sarcosinate total		118
Sodium Myristoyl Sarcosinate		
Cleansing preparations	653	2
1998 Sodium Myristoyl Sarcosinate total		2

feces. Immediately after administration, the mean distribution of [^{14}C] was 1.12% in the teeth, 2.22% in the oral mucosa, and 2.95% in the tongue. At 4 hours, the mean distribution was 0.92% in the teeth, 0.95% in the oral mucosa, 0.57% in the tongue, 5.44% in the liver, 2.78% in the kidneys, 0.87% in the feces, and 33.5% in the urine. At 24 hours, the mean distribution was 0.79% in the teeth, 0.92% in the oral mucosa, 0.57% in the tongue, 1.6% in the liver, 0.8% in the kidneys, 1.8% in the feces, and 42.2% in the urine. Approximately 1% of the compound adhered to both the teeth and the oral mucosa, and 0.57% adhered to the tongue; this adherence was such that no radioactivity could be washed from those tissues by a physiological saline solution. The data indicated that Sodium Lauroyl Sarcosinate was not absorbed by the tissues of the mouth, but was swallowed and absorbed into the blood. Distribution of radioactivity in tissues at the time of treatment was 0.09 mg/g in the teeth, 0.1 mg/g in the oral mucosa, and 0.1 in the tongue. At 4 hours, the distribution was 0.07 mg/g in the teeth, 0.05 mg/g in the oral mucosa, 0.02 mg/g in the tongue, 0.003 mg/g in the blood, 0.015 mg/g in the liver, 0.026 mg/g in the kidneys, 0.006 mg/g in the bones, and 0.009 mg/g in the muscles. At 24 hours, the distribution was 0.09 mg/g in the teeth, 0.05 mg/g in the oral mucosa, 0.02 mg/g in the tongue, 0.003 mg/g in the blood, 0.005 mg/g in the liver, 0.008 mg/g in the kidneys, 0.01 mg/g in the bones, and 0.006 mg/g in the muscles. Approximately 34% of the radioactivity was excreted in the urine over a period of 4 hours, and 42% was excreted within 24 hours. Very little, if any, of the test compound was oxidized to form CO_2, which was confirmed when the rats were treated in a glass metabolism cage.

In other studies by the same investigators (Technology Sciences Group Inc. 1994c), the teeth of rats were brushed with dentifrice containing 2×10^3 μg [^{14}C]Sodium Lauroyl Sarcosinate. Sodium Lauroyl Sarcosinate was taken up from the dentifrice by the teeth, oral mucosa, and tongue such that a certain amount could not be rinsed away with saline. Frequent application did not cause an accumulation of radioactivity in bone or muscle above that found after the above study.

The octanol-water partition coefficient of Lauroyl Sarcosine at pH 5.0 was 851/11 or ~77 (log P of 0.954). At pH 9.0, the value of a 6% solution of Lauroyl Sarcosine was 2.8/5.2 or ~0.54 (log P of −0.267) (Technology Sciences Group, Inc. 1994b).

Penetration Enhancement

Aioi et al. (1993) placed shaved dorsal skin of a Wistar male rat in a Franz diffusion cell with application area of 3.14 cm^2 and receptor chamber of volume 15 ml. The receptor chamber was filled with phosphate-buffered saline (PBS), and ointment containing 0.5 g of Lauroyl Sarcosine and/or vitamin E or squalene was applied to the skin. At 6 and 24 hours, the receptor chamber PBS was analyzed by HPLC to determine the concentration of Lauroyl Sarcosine. The concentration of Lauroyl Sarcosine was determined by UV absorbance at 210 nm. The amount of transdermal penetration from 1% Lauroyl Sarcosine ointment was ~1660 μg over 24 hours. The addition of 30% vitamin E or 10% squalene enhanced Lauroyl Sarcosine penetration. The flux values (μg/cm^2) were 22.0 ± 1.9 in 1% Lauroyl Sarcosine, 35.4 ± 2.9 in 1% Lauroyl Sarcosine + 30% vitamin E, and 52.0 ± 3.9 in 1% Lauroyl Sarcosine + 10% squalene, respectively. Overall, vitamin E and squalene did not suppress the penetration of Lauroyl Sarcosine through isolated rat skin, but the compounds inhibited Lauroyl Sarcosine–induced cytotoxicity. The results suggested that Lauroyl Sarcosine–induced erythema was caused by mediators generated from keratinocytes, and that squalene or vitamin E could have inhibited the generation or release of those mediators.

In another study by these authors, plasma of a rat treated with ointment (for 24 hours) containing 6% isosorbide dinitrate

TABLE 2
Effects of vitamin E and squalene on isosorbide dinitrate (ISDN) penetration enhancement induced by Lauryl Sarcosine (LS) (Aioi et al. 1993)

	6% ISDN	6% ISDN, 1% LS	6% ISDN, 1% LS, 30% vitamin E	6% ISDN, 1% LS, 10% squalene
Erythema score	0.5	1.9	0.8	1.0
ISDN blood level (μg/ml)	0.6	1.5	1.3	2.3

(contains 60% lactose) was prepared using heparin as an anticoagulant. A 0.2-ml volume of the plasma was mixed with 0.8 ml of 3% bovine serum albumin in PBS. The mixture was shaken for 12 minutes and centrifuged for 5 minutes. The upper layer was removed, and the lower layer was separated from residual dichloromethane by freezing and then dried. The dried preparation was dissolved in 10 μl of ethyl acetate. Isosorbide dinitrate content was determined by gas chromatography and detected using an electron capture detector. The amount of isosorbide dinitrate that penetrated the skin was increased approximately threefold by the addition of 1% Lauroyl Sarcosine to the ointment, which also produced moderate to severe erythema at the application site of the treated rat. The combined addition of 1% Lauroyl Sarcosine and 30% vitamin E or 10% squalene maintained or enhanced the effect of Lauroyl Sarcosine on the penetration of isosorbide dinitrate while alleviating the erythema (Table 2) (Aioi et al. 1993).

Bettley (1965) evaluated the effect of detergents and surfactants, including 30% Sodium Lauroyl Sarcosinate (pH = 8.1), on epidermal permeability. The investigator used two opposed chambers of approximately 1.5-ml capacity separated by a 0.5-cm^2 section of human epidermis. One chamber contained 200 mEq/l sodium chloride or 10 mEq/l potassium chloride with 0.04 M of the surfactant to be tested. This solution was placed in contact with the corneal surface of the epidermis. The opposite chamber, which was in contact with the Malpighian surface, contained distilled water. After 1 week, the distilled water was removed and the sodium or potassium content was determined using a flame photometer. Both chambers were then refilled and a similar measurement made after another 1 week period. For Sodium Lauroyl Sarcosinate, potassium chloride was used. The percent penetration was >10% for the sarcosinate and controls (sodium and potassium chlorides; pH = 7) and the surface tension was 59. In contrast, the surface tensions for the controls were both 100. Bettley concluded that neither pH nor surface tension were in direct relationship to permeability.

Miscellaneous Effects

Sodium Lauroyl Sarcosinate inhibited the activity of hexokinase at concentrations as low as 0.03%, but was less effective against aldolase. It had no effect on the activities of rennin, pepsin, or pancreatic trypsin. Salivary and pancreatic lipase activities were inhibited (Bauer and La Sala 1956; Geigy Industrial Chemicals 1958; 1962).

The sarcosinates had pH-dependent antimicrobial activities. Above pH 7, they had no antibacterial or antifungal activity. At pH 5.8, they were effective against *Staphylococcus aureus*, *Streptococcus faecalis*, *Lactobacillus acidophilus*, *Tricophyton mentagrophytes*, and *Pityrosporum ovale*. At pH 4, the sarcosinates had strong activity against *Escherichia coli*, *Pseudomonas aeroginosa*, *Bacillus mesentericus*, and many fungi (Hart 1979).

Sodium Lauroyl Sarcosinate inhibited bacterial growth in human saliva at concentrations as low as 0.25%. The addition of 0.5% Sodium Lauroyl Sarcosinate to human saliva reduced the bacterial count by 90% in 5 minutes and by 99% in 4 hours. After 24 hours, the bacterial count recovered as much as 10% (Geigy Industrial Chemicals 1958; 1962).

L. acidophilus has enzymes that catalyze reactions that result in the formation of oral, caries-producing acids. "Anti-enzymes," enzymes that inhibit bacterial enzymes, have been used in dental formulations to prevent tooth decay. Sodium Lauroyl Sarcosinate inhibited nonresistant (control) strains of *L. acidophilus* at concentrations of 0.062 to 1.25 mg/ml and inhibited "resistant" strains at concentrations of 0.18 to 0.37 mg/ml. In general, little development of resistance occurred in the *L. acidophilus* strains treated with Sodium Lauroyl Sarcosinate compared to controls and other "anti-enzymes" (French, Stock, and Morrison 1958).

Sodium Lauroyl Sarcosinate inhibited carbohydrate-induced decreases in human dental plaque pH both in vivo and in vitro (Hassell and Mühlemann 1971). Sodium Lauroyl Sarcosinate reduced dental decay in humans, and had anticariegenic activity associated with its inhibition of bacterial hexokinase (Geigy Industrial Chemicals 1958; 1962).

Sodium Lauroyl Sarcosinate (0.85 mM) inhibited glycolytic acid formation in human saliva (incubated with glucose) and was adsorbed by dental plaque. Sodium Lauroyl Sarcosinate also inhibited the activity of bacterial hexokinase when the magnesium ion concentration was $\leq$0.2 mM. Sodium Lauroyl Sarcosinate did not inhibit enolase, even at concentrations up to 5.0 mM. The investigators concluded that the enzyme-inhibiting activity of Sodium Lauroyl Sarcosinate was not due to the removal of essential metallic ions (Carbon et al. 1954).

TOXICOLOGY

Acute Toxicity

The intravenous LD_{50} in rats of Sodium Lauroyl Sarcosinate was 175 mg/kg. The oral LD_{50} of Sodium Lauroyl Sarcosinate

was 4.2 to 5 g/kg in rats (Geigy Chemical Corp. no date; Geigy Industrial Chemicals 1958; 1962). The acute oral LD_{50} of Cocoyl Sarcosine in rats was 5.4 g/kg. The oral LD_{50} values of Sodium Lauroyl Sarcosinate were 2.1 g/kg (mice) and 5.0 g/kg (rats). The oral LD_{50} values of Sodium Cocoyl Sarcosinate and Sodium Oleoyl Sarcosinate in rats were 4.2 g/kg and 6.0 g/kg, respectively (Hampshire Chemical Corporation 1997a).

Male Yale Sherman Wistar rats (10 per group; 120–150 g) were treated by gavage with a single dose of 2.5% aqueous Sodium Lauroyl Sarcosinate (Technology Sciences Group Inc. 1994c). The rats were observed for 14 days for signs of toxicity. No deaths occurred when rats were given up to 1000 mg/kg Sodium Lauroyl Sarcosinate. One rat each died in the groups given 1250 and 1500 mg/kg Sodium Lauroyl Sarcosinate. Two rats died after treatment with 1750 mg/kg, 4 died after administration of 2000 mg/kg (LD_{50}), 7 died after dosing with 2250 mg/kg, and all 10 were killed by treatment with 2500 mg/kg. The investigators concluded that Sodium Lauroyl Sarcosinate was relatively nontoxic by the oral route.

In the same study, 10 rats per group were treated with a dentifrice containing 2% of the sarcosinate (100 g diluted with distilled water; total volume = 100 ml). No deaths occurred in rats given up to 25 g/kg of the dentifrice. The numbers of rats that died after treatment with 30, 40, 50 (LD_{50}), 60, 75, and 100 g/kg were 2, 4, 5, 7, 10, and 10, respectively. The investigators concluded that the dentifrice was relatively nontoxic by the oral route.

Subchronic Toxicity

Weanling rats were given diet containing 2% Sodium Lauroyl Sarcosinate for 6 months. No effect on weight gain, feeding efficiency, general health, or behavior was observed, and no abnormalities of the internal organs were observed. Rats fed 0.5% Sodium Lauroyl Sarcosinate for 100 days had no signs of toxicity (Geigy Chemical Corp. no date; Geigy Industrial Chemicals 1958; 1962).

Chronic Toxicity

Two hundred albino Sherman Wistar rats (25 rats/sex/group; 100–150 g) were fed Sodium Lauroyl Sarcosinate during a 2-year chronic oral toxicity study (Technology Sciences Group Inc. 1994c). Group 1 was fed 0.05% Sodium Lauroyl Sarcosinate in the daily diet for the first 6 months of the study and 2.0% of diet for the remaining 18 months. For the entire study period, group 2 was fed 0.2% of diet, group 3 was fed 1.0% of diet, and group 4 was fed the basal diet alone. Rats were killed at 1, 3, 6, and 24 months for necropsy and tissues collected for microscopic examination; organs examined included the liver, spleen, heart, lungs, stomach, large intestine, small intestine, adrenal glands, gonads, pancreas, and brain. Blood samples were drawn and analyzed at 30 days, 90 days, 6 months, and 24 months for red and white blood cell counts, hemoglobin content, and differential count. Males and females were housed together so that fertility could be assessed. At 1, 3, and 6 months, no significant differences were observed in lesions, fertility, mortality, hematology, or body weight gain between rats of the control and treated groups. At 24 months, the only consistent difference that could be attributed to the test article was minor hyperplasia of the stratified squamous epithelium with excess keratin formation of the cardiac mucosa of the stomach in rats receiving the highest exposure to the test article—group 1 (2% in the diet after 6 months) and group 3 (1% in the diet).

Dermal Irritation and Sensitization

Company product information from Geico Chemical Corp. (no date) stated that prolonged contact with acyl sarcosines at high concentrations could cause skin irritation, but the salts were nonirritating. No other details were available.

When a 30% aqueous solution of Sodium Lauroyl Sarcosinate was tested for primary skin irritancy (Hampshire Chemical Corporation 1997a), the primary irritation index score was 0.83/8.0 after 4 hours of exposure (nonirritating). This study used the procedure specified by the Federal Hazardous Substances Act, codified in 16 CFR 1500.41, in which intact and abraded skin sites of six albino rabbits were treated with the test substance.

Five rabbits per group were treated topically with Sodium Lauroyl Sarcosinate for 14 days (Technology Sciences Group Inc. 1994c). The abdominal region was clipped twice a week to expose skin sites that comprised at least 10% of the total body area. One group was treated with Sodium Lauroyl Sarcosinate powder, one group was treated with a 20% (*w*/*v*) solution, and one group was treated with a dentifrice formulation containing 2% Sodium Lauroyl Sarcosinate. After each application, the treated area was covered with glassine paper and a muslin binder, held in place with adhesive tape. The treated area was washed and any reactions were graded each day prior to application. No signs of irritation or dermal toxicity were observed in rabbits of any group.

In a primary irritation study (Food and Drug Research Laboratories 1989; Technology Sciences Group Inc. 1994c), a formulation containing 30% aqueous Sodium Myristoyl Sarcosinate was not a primary irritant to the skin of six New Zealand white rabbits. The back of each rabbit was clipped on the day prior to dose administration. On the day of treatment, the right dorsal side was abraded with a hypodermic needle such that the stratum corneum was penetrated, but the dermis was not disturbed and bleeding did not occur. A 0.5-ml volume of the test formulation was topically applied to one abraded site and one intact site of each rabbit. The sites were covered with gauze patches and the trunk of each rabbit was covered with plastic wrap and a stockinette sleeve. The patches were removed 4 hours after treatment and the sites were wiped clean with gauze. Dermal irritation was evaluated at 4.5, 24, and 72 hours and the sites were scored using the Draize method. The formulation containing Sodium Myristoyl Sarcosinate caused very slight to well-defined erythema and very slight to slight edema. Based on the 24- and 72-hours evaluations, the mean primary dermal irritation score was 1.7.

Aioi et al. (1993) evaluated alleviators of skin irritation induced by Lauroyl Sarcosine in several studies, the first of which was an in vitro cytotoxicity assay. Primary cultured fibroblasts were prepared from samples of shaved skin of male Wistar rats; after removal, the skin was minced with scissors and washed with physiological buffered saline (PBS, pH 7.2). The cells were digested by 0.25% trypsin in PBS for 20 minutes at 37°C. The digestion was centrifuged for 5 minutes at 670 *g*, and the cells were suspended in Eagle's minimum essential medium containing 10% fetal calf serum (FCS) and cultured in wells for 16 hours. A volume of 2.5 μl squalene or vitamin E was added to the well at a concentration of 10 μg/ml. Two hours later, 2.5 μl Lauroyl Sarcosine was added (50 μg/ml). The cells were cultured for 48 hours, dispersed in 1% citric acid in PBS, counted, and examined for evidence of cytotoxicity. Lauroyl Sarcosine produced dose-dependent cell damage. Proliferation of cells treated with Lauroyl Sarcosine was ~25%, compared to control cells (100%). Cell proliferation of cells treated with Lauroyl Sarcosine and vitamin E was ~70%, and that of cells treated with Lauroyl Sarcosine and squalene was ~110%.

In a second study (Aioi et al. 1993), transdermal patches of a hydrocarbon gel-based ointment containing 0.1 g "extra pure" Lauroyl Sarcosine (at 0.4, 0.2, 1.0, and 5.0%), vitamin E, or squalene were applied to the shaved dorsal skin of six Wistar male rats (6-week-old, 130–160 g) and fixed with gauze and bandages. After removal of the ointment (1, 3, 6, or 24 hours), the skin sites were graded for erythema using the Draize method (1, mild erythema; 2, moderate erythema; 3, severe erythema). After clinical study, the rats were killed and their dorsal skins removed, fixed and stained, and examined microscopically. Lauroyl Sarcosine–induced irritation was dose-dependent; overt erythema was observed after treatment with 0.04% to 5.0% Lauroyl Sarcosine. At 24 hours, 0.2% Lauroyl Sarcosine caused mild erythema, 1.0% caused moderate erythema, and 5.0% caused severe erythema. One to 3 hours after application of the ointment containing 1% Lauroyl Sarcosine, keratinocyte damage was observed. This damage became more marked with time and co-occurred with vasodilation. At 6 and 24 hours, infiltration with polymorphonuclear leukocytes (PMN) was observed in the dermis under the keratinocyte damage. Erythema score followed the severity of vasodilation (Table 3). Table 4 presents the results of the portion of the study which evaluated the ability of vitamin E and squalene to alleviate the irritant effect of Lauroyl Sarcosine (Aioi et al. 1993).

Ten white guinea pigs weighing 350 to 450 g were used to assess the skin sensitization potential of Sodium Lauroyl Sarcosinate (Technology Sciences Group Inc. 1994c). The skin sites were closely clipped. Each guinea pig was given an intradermal injection of 0.01% (aqueous) Sodium Lauroyl Sarcosinate every other day for a total of 10 injections; the injection sites were 3 to 4 cm^2 in diameter, immediately below the midline of the back. The first induction injection volume was 0.05 ml, and the subsequent injection volumes were 0.1 ml. A challenge injection (0.1 ml) was performed 3 weeks after the last induction injection. No signs of dermal toxicity or sensitization were observed in any of the guinea pigs tested.

TABLE 3
Macroscopic and microscopic manifestations of dermal irritation induced by 1% Lauroyl Sarcosine (Aioi et al. 1993)

Time (h)	Keratinocyte damage	Vasodilation	Infiltration with PMN	Score of erythema
1	+	−	−	0.2 ± 0.2
3	++	+	−	1.2 ± 0.2
6	+++	+	+	1.3 ± 0.2
24	+++	++	++	1.7 ± 0.2

+, slight; ++, moderate; +++, severe; −, nondetectable.

Ocular Irritation

Ten percent solutions of Sodium Cocoyl Sarcosinate at neutral or slightly acid pHs rated "equal with 10% sodium lauryl sulfate in the Draize-Woodard rabbit eye irritation test" (Geigy Industrial Chemicals 1958; 1962). Slight temporary irritation with no permanent corneal damage was observed (Geigy Chemical Corp. no date).

Ten albino rabbits weighing 2 to 3 kg were used in an ocular irritation study of Sodium Lauroyl Sarcosinate (Technology Sciences Group Inc. 1994c). A 0.1-ml volume of a 5% (*w/v*) aqueous solution was instilled on the superior limbus of the right eye of each rabbit. The lower lid of the eye was raised over the upper lid and the lids were massaged to spread the material evenly over the surface of the cornea. The left eye of each rabbit served as a control. The eyes of each rabbit were examined at 2, 4, and 24 hours after instillation and any reactions of the conjunctiva, iris, and cornea were graded using the method of Draize and Woodard. Some minimal conjunctival irritation was observed 2 hours after instillation of the test solution. This irritation persisted for 24 hours and cleared within a few days without evidence of residual injury. No apparent damage to the cornea was observed.

TABLE 4
Effect of skin irritation alleviators on Lauroyl Sarcosine–induced irritation (Aioi et al. 1993)

Test compound	Erythema score
Ointment base	0.4
1% Lauroyl Sarcosine	2.4
1% Lauroyl Sarcosine + 10% vitamin E	0.6
1% Lauroyl Sarcosine + 30% vitamin E	0
1% Lauroyl Sarcosine + 2% squalene	0.8
1% Lauroyl Sarcosine + 10% squalene	1.2

Mucosal Irritation

Male and female albino rabbits (2.5–4.0 kg; five per group) were used in an evaluation of the oral mucosal effects of Sodium Lauroyl Sarcosinate and a dentifrice containing the sarcosinate (Technology Sciences Group Inc. 1994c). Rabbits of group 1 were treated with Sodium Lauroyl Sarcosinate powder, rabbits of group 2 were treated with a 20% aqueous solution of the sarcosinate, and rabbits of group 3 were treated with a dentifrice containing 2% Sodium Lauroyl Sarcosinate. The test material was applied daily to the gums and oral mucosa of each rabbit over a 14-day period. Prior to each application, the gums and mucosa were examined and any irritation was graded and recorded. None of the test materials were irritating to the gums and oral mucosa of rabbits under the conditions of this study.

MUTAGENICITY

Blevins and Taylor (1982) evaluated the mutagenic activity of 25 cosmetic ingredients in distilled water, including Sodium Lauroyl Sarcosinate, using *Salmonella*/microsome tests. The strains of *Salmonella typhimurium* used in these assays were TA98, TA100, TA1535, TA1537, and TA1538. Negative controls were water, ethanol, dimethyl sulfoxide (DMSO), and no treatment. Positive controls were 2-aminoanthracene, 4-nitro-*o*-phenylenediamine in DMSO, sodium azide in water, and 9-aminoacridine in ethanol. In screening spot tests, test plates were prepared using 0.1 ml of a solution containing 50 μg of each cosmetic ingredient, with or without S9 activation. Cultures of TA1538 treated with Sodium Lauroyl Sarcosinate (with S9) had increases of the spontaneous plate counts; these increases, however, were not large enough to be considered mutagenic. Due to the questionable results of the spot tests, Sodium Lauroyl Sarcosinate (10 μg to 5 mg) was then tested using a plate incorporation assay.

During the plate incorporation assay, treatment with Sodium Lauroyl Sarcosinate caused a two-to threefold increase over the double distilled water plate counts using strain TA1537 with S9 mix; however, a dose-related increase was not demonstrated. Sodium Lauroyl Sarcosinate falsely appeared to be mutagenic at the highest dose (5 mg/plate). Plate counts were severalfold greater than those of the solvent controls, but there was no background lawn of unreverted bacteria. When several of the "revertant" colonies were transferred to minimal glucose agar, they failed to grow, demonstrating that they were not revertants. The investigators attributed this to the toxicity of the concentrations used: most of the bacteria were killed, and as a result, more histidine was available for utilization by the surviving unreverted mutants. On the basis of the spot and plate incorportation assays, Sodium Lauroyl Sarcosinate was not considered mutagenic in the five bacterial strains tested (Blevins and Taylor 1982).

Hartmann and Speit (1997) reported that Sodium Lauroyl Sarcosinate did not induce DNA double-strand breaks in the comet assay using V79 Chinese Hamster cells and human white blood cells, although the compound was cytotoxic.

CARCINOGENICITY

Data on the carcinogenicity of Cocoyl Sarcosine, Lauroyl Sarcosine, Myristoyl Sarcosine, Oleoyl Sarcosine, Stearoyl Sarcosine, and their sodium and ammonium salts were not available. Data on *N*-nitrososarcosine, the nitrosated form of the starting material, sarcosine, were found.

N-nitrososarcosine is regulated as a hazardous substance by a number of state, federal, and international agencies (Suspect Chemicals Sourcebook 1995). The EPA regards *N*-nitrososarcosine a potential carcinogen and the Occupational Safety and Health Administration regulates it as a chemical hazard in laboratories (NTP 1994).

N-nitrososarcosine is a known animal carcinogen (IARC 1978; 1987; NTP 1994). When administered in the diet at a concentration of 0.25% to male and female Swiss (ICR) mice for 13 months, *N*-nitrososarcosine induced squamous cell carcinomas of the nasal region. At necropsy, five lung tumors, two tumors of the small intestine, two vaginal tumors, and one each of the testis, kidneys, skin, thymus, urinary bladder, and pancreas were observed in mice of the treatment group. When given to BD rats in drinking water for 286 days, concentrations of 100 and 200 mg/kg/day *N*-nitrososarcosine induced esophageal papillomas and squamous cell carcinomas by 357 to 631 days (low dose) and 414 to 548 days (high dose) after the start of treatment. Hepatocellular carcinomas and hyperplasia were found in $(C57BL/6J \times C3HeB/FeJ)F_1$ mice of both sexes after intraperitoneal injections of 75 mg/kg/day *N*-nitrososarcosine on days 1, 4, and 7 after birth. The observed lesions developed by 50 to 85 weeks after dosing (IARC 1978). The IARC Working Group concluded that, "although there were insufficient data to evaluate the carcinogenicity of *N*-nitrososarcosine in humans, *N*-nitrososarcosine should be regarded as if it were, based on the available animal data" (IARC 1978; 1987).

In its petition to EPA to exempt the acyl sarcosines and sarcosinates from tolerance, the Technology Sciences Group Inc. (1994c) stated that:

> *N*-acyl sarcosines do not belong to any class of compounds that contains a significant number of mutagens or oncogens. Neither the compounds themselves nor any likely metabolite, i.e., the amino acid and fatty acids, are similar in structure to known oncogens or mutagens. In the absence of any structural implication for genotoxic effects and in consideration of wide and prolonged use of these compounds in personal care products without evidence of genotoxic effects, additional data are not needed to evaluate potential genotoxic hazards from use of *N*-acyl sarcosines as inert ingredients in pesticides.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

The feeding of up to 1000 mg/kg/day Sodium Lauroyl Sarcosinate did not adversely affect fertility of albino Sherman

Wistar rats during a 2-year oral toxicity study described in the Chronic Toxicity section (Technology Sciences Group Inc. 1994c).

CLINICAL ASSESSMENT OF SAFETY

In a study by van der Valk et al. (1984), skin vapor loss (SVL) measurements were performed using 27 human volunteers (8 women and 19 men; ages 21–32 years) to assess the dermal irritancy of various surfactants, including Cocobetaine (pH = 5.2). It was unclear whether the Cocobetaine tested was Cocoyl Sarcosine or the related, cocoyl *N*-dimethyl glycine derivative (see "Chemistry—Definition and Structure" in this report). The test chemicals (100 μl of 2 g/100 ml) were applied via a Finn chamber fixed to the volar forearm of each subject. The skin sites were exposed for 24 hours, and were examined 1 hours after chamber removal. The sites were graded for erythema, scaling, and fissuring by the method of Frosch and Kligman (1979). Evaporative water loss was measured at both exposed and unexposed adjacent skin sites using a Servo Med Evaporimeter. The controls were distilled water (pH = 5.6) and 0.9% NaCl (pH = 6.7). Cocobetaine markedly influenced the loss of water through the skin, and both of the controls led to an increase of SVL compared to unexposed skin. The mean SVL for Cocobetaine was 12.6 g/m^{2}h (*SD* = 2.3). The SVLs for the distilled water and NaCl controls were, respectively, 9.2 (*SD* = 2.1) and 7.7 (*SD* = 1.9) g/m^{2}h. The SVL for untreated skin was 6.2 g/m^{2}h (*SD* = 1.3). The mean scores of morphological changes are presented in Table 5.

Cocoyl Sarcosine and Sodium Lauroyl Sarcosinate reduced moisture loss from the skin through the formation of a hydrophobic protective layer on the surface of the epidermis (Hampshire Chemical Corporation 1997a). Aqueous solutions of the acyl sarcosinates were applied to the skin of highly dermatitic subjects for an epicutaneous patch test and were allowed to dry on the skin. "Practically no reaction" was observed. Other details were unavailable (Hampshire Chemical Corporation 1997a).

The primary irritancy and sensitization potential of 5% aqueous Sodium Lauroyl Sarcosinate was evaluated using the Schwatz patch test procedure (Technology Sciences Group Inc. 1994c). Lintine discs that had been saturated with the test material were applied to the backs of 200 subjects, covered with glassine paper, and secured with adhesive tape. After 48 hours, the patches were removed and the treatment sites were examined for signs of dermal irritation. None of the subjects had signs of primary irritation to the test material. Three weeks after patch removal, the subjects were treated with lintine discs saturated with the 5% solution. The challenge patches were removed after 24 hours. No signs of sensitization were observed.

The same investigators performed a repeated insult patch test using 50 subjects. Patches were prepared as above and were applied to the back for 24 hours every other day for a total of 15 induction applications. The skin sites were examined when the patches were removed. Three weeks after the last induction application, the subjects were challenged with another 24-hours patch. During induction, only a few sporadic 1+ reactions were recorded, and none of the subjects reacted to the test material at challenge.

In another study, 750 subjects were used to evaluate the potential of a dentifrice containing 2% Sodium Lauroyl Sarcosinate to cause irritation to the gums, oral mucosa, and tongue. The subjects brushed their teeth with the dentifrice twice daily for 30 days. No signs of irritation were noted during the daily examinations of the subjects' mouths.

TABLE 5
Dermal irritancy of Cocobetaine (van der Valk et al. 1984)

Test chemical	Erythema	Scaling	Fissuring	Overall score
Cocobetaine	0.574	0.037	0.204	1.093
Distilled water (control)	0.296	0.0	0.019	0.333
0.9% NaCl (control)	0.148	0.0	0.0	0.148

SUMMARY

The sarcosines are *N*-acyl derivatives and the sarcosinates are the simple salts of sarcosine. These ingredients function as hair conditioning agents and surfactant—cleansing agents in cosmetics. In 1998, they were used in 192 cosmetic formulations. Sodium Lauroyl Sarcosinate was used at concentrations of 2.78% to 12.9% in soaps, and Oleoyl Sarcosine was used at concentrations of 10 to 100 ppm in aerosolized products to prevent corrosion of the can; concentrations of use of the other ingredients were not available.

The acyl sarcosines are the condensation products of sarcosine with natural fatty acids and are produced commercially by the reaction of sodium sarcosine and the parent fatty acid chlorides. The acyl sarcosines can then be neutralized to form the sodium or ammonium salts.

Sodium Lauroyl Sarcosinate was not hydrolyzed by either gastric or intestinal enzymes in vitro. Nearly all of the excreted material was found in the urine. Traces were found in the tissues of the mouth, liver, and kidneys, and in the feces.

The amount of transdermal penetration from 1% Lauroyl Sarcosine (0.5 g) in an ointment was ~1660 μg over 24 hours for the Wistar rat, as determined using HPLC. In another study, Lauroyl Sarcosine increased the penetration of isosorbide dinitrate through the skin of the rat. In a study of the effects of surfactants on epidermal permeability, 30% Sodium Lauroyl Sarcosine did not increase permeability.

The sarcosines and sarcosinates have low oral toxicity. In rats, the intravenous LD_{50} of Sodium Lauroyl Sarcosinate was 175 mg/kg. The oral LD_{50} values of Sodium Lauroyl Sarcosinate, Cocoyl Sarcosine, and Sodium Cocoyl Sarcosinate were 4.2 to 6.0 g/kg in rats. The oral LD_{50} of Cocoyl Sarcosine in mice was

2.1 g/kg. Ten male Yale Sherman Wistar rats per group were given a single dose (gavage) of 2.5% aqueous Sodium Lauroyl Sarcosine: no deaths occurred in groups given up to 1000 mg/kg, 1 rat each died in the 1200- and 1500-mg/kg groups, 2 died in the 1750-mg/kg group, 4 died after treatment with 2000 mg/kg, 7 died in the 2250 mg/kg group, and all 10 rats died in the group given 2500 g/kg. Weanling rats fed 0.5% to 2% Sodium Lauroyl Sarcosinate for up to 6 months had no signs of toxicity. During a 2-year feeding study using Wistar rats, the no-observed-effect level of Sodium Lauroyl Sarcosinate was 1000 mg/kg/day.

During an in vitro cytotoxicity study using cultured fibroblasts from Wistar rats, 2.5 μl Lauroyl Sarcosine (50 μg/ml) caused dose-dependent cell damage. Mild, moderate, and severe erythema were observed at 24 hours during a related study (using Wistar rats) after treatment with 0.2%, 1.0%, and 5.0% Lauroyl Sarcosine. Keratinocyte damage and vasodilation was observed 1 to 3 hours after treatment with 1.0% Lauroyl Sarcosine. Sodium Lauroyl Sarcosinate was nonirritating to rabbits when administered as a 20% to 30% solution, at a concentration of 2% in formulation, or as the pure powder. A formulation containing 30% Sodium Myristoyl Sarcosinate was not a primary skin irritant in rabbits, and 0.01% aqueous Sodium Lauroyl Sarcosinate was nonsensitizing to the skin of guinea pigs. Sodium Lauroyl Sarcosinate (20% aqueous solution, 2% in formulation, powder) was nonirritating to the gums and oral mucosa of rabbits.

Sodium Cocoyl Sarcosinate (10%) at neutral or slightly acid pH caused slight, temporary ocular irritation, but no corneal damage in rabbits according to the procedures of the Draize-Woodard test. In another ocular toxicity study using rabbits, a 5% aqueous solution of Sodium Lauroyl Sarcosinate caused minimal conjunctival irritation and no apparent damage to the cornea.

Sodium Lauroyl Sarcosinate was not considered mutagenic in five strains of *S. typhimurium* during plate incorporation assays and spot tests. In addition, Sodium Lauroyl Sarcosinate did not induce double-strand DNA breaks in the comet assay using human white blood cells and V79 Chinese Hamster cells, but the compound was cytotoxic. Carcinogenicity data of the acyl sarcosines and sarcosinates were not available; however, the ingredients were not considered likely carcinogens as they and their metabolites "do not belong to any class of compounds that contains a significant number of mutagens or oncogens."

During a clinical study using 27 subjects, cocobetaine (a synonym for both Cocoyl Sarcosine and a related compound) markedly influenced skin vapor loss and caused erythema, scaling, and fissuring of the skin of the volar forearm. In another study, Cocoyl Sarcosine and Sodium Lauroyl Sarcosinate retarded moisture loss from the skin via the formation of a hydrophobic protective layer on the epidermal surface. In an epicutaneous patch test using highly eczematic subjects, "practically no reaction" was observed. In other clinical studies, Sodium Lauroyl Sarcosinate (2%–5%) was nonirritating and nonsensitizing.

DISCUSSION

The Expert Panel recognized that these ingredients, particularly Lauroyl Sarcosine, can enhance the penetration of other ingredients through the skin (e.g., HC Yellow No. 4, Disperse Yellow 3). The Panel cautioned that care should be taken in formulating cosmetic products that may contain these ingredients in combination with any ingredients whose safety was based on their lack of dermal absorption data, or when dermal absorption was a concern.

Sarcosine, a starting material in the manufacture of the Sarcosines and Sarcosinates, can react with oxidizing materials and can be nitrosated to form *N*-nitrososarcosine. *N*-nitrososarcosine is regulated as a hazardous substance, and is a known animal carcinogen. As a result, the Expert Panel concluded that the Sarcosines and Sarcosinates should not be used in cosmetic products in which *N*-nitroso compounds can be formed.

The Panel concluded that the Sarcosines and Sarcosinates are safe as used in rinse-off products. These ingredients are safe at concentrations of $\leq$5% in leave-on products, based upon the highest concentration tested in human repeat-insult patch tests. The data were insufficient to determine safety of the Sarcosines and Sarcosinates in products where the ingredients are likely to be inhaled. Correspondence received by the Expert Panel stated that Oleoyl Sarcosine was used at concentrations of 10 to 100 ppm to prevent corrosion of aerosol cans. The Panel concluded that this was a noncosmetic use for which inhalation exposure was not of concern. The data are still insufficient to determine safety of cosmetic products containing Sarcosines and Sarcosinates (as active ingredients), where these ingredients are likely to be inhaled. The Panel stated that an acute inhalation study investigating the effects on the lungs would be required to assess safety in aerosolized products.

CONCLUSION

Based on the data presented in this safety assessment, the Cosmetic Ingredient Review (CIR) Expert Panel concludes that Cocoyl Sarcosine, Lauroyl Sarcosine, Myristoyl Sarcosine, Oleoyl Sarcosine, Stearoyl Sarcosine, Sodium Cocoyl Sarcosinate, Sodium Lauroyl Sarcosinate, Sodium Myristoyl Sarcosinate, Ammonium Cocoyl Sarcosinate, and Ammonium Lauroyl Sarcosinate are safe as used in rinse-off products, safe for use in leave-on products at concentrations of $\leq$5%, and the data are insufficient to determine the safety for use in products where the sarcosines and sarcosinates are likely to be inhaled. These ingredients should not be used in cosmetic products in which *N*-nitroso compounds may be formed.

REFERENCES

Aioi, A., K. Kuriyama, T. Shimizu, M. Yoshioka, and S. Uenoyama. 1993. Effects of vitamin E and squalene on skin irritation of a transdermal absorption enhancer, lauroylsarcosine. *Int. J. Pharm.* 93:1–6.

Aldrich Chemical Co. 1992. *Catalog handbook of fine chemicals*, 1099. Milwaukee, WI: Aldrich Chemical Co.

Anderson, I. E., A. J. Herring, G. E. Jones, and J. C. Low. 1995. Development and evaluation of an indirect ELISA to detect antibodies to abortion strains of *Chlamydia psittaci* in sheep sera. *Vet. Microbiol.* 43:1–12.

Bauer, C. W., and E. F. La Sala. 1956. The effect of sodium N-lauroyl sarcosinate and of sodium dehydroacetate on the enzymes of the gastrointestinal tract. *J. Am. Pharm. Assoc.* 45:675–678.

Bettley, F. R. 1965. The influence of detergents and surfactants on epidermal permeability. *Br. J. Dermatol.* 77:98–100.

Blevins, R. D., and D. E. Taylor. 1982. Mutagenicity screening of twenty-five cosmetic ingredients with the *Salmonella*/microsome test. *J. Environ. Sci. Health* A17:217–239.

Carbon, J. A., R. Q. Blackwell, J. C. Calandra, and L. S. Fosdick. 1954. The inhibition of anaerobic glycolysis by sodium N-lauroyl sarcosinate. *Arch. Biochem.* 55:356–364.

Chemline. 1996. *Chemline database*. Bethesda, MD: National Library of Medicine.

Consumer Product Safety Commission. 1986. Federal Hazardous Substances Act Regulations. *Code of Federal Regulations*. Title 16, Subchapter IIC. Part 1500.41. Washington, DC: Office of the Federal Register.

Elder, R. L., ed. 1986. Final Report on the Safety Assessment of Coconut Oil, Coconut Acid, Hydrogenated Coconut Acid, and Hydrogenated Coconut Oil. J. Am. Coll. Toxicol. 5:103–121.

Elder, R. L., ed. 1987. Final Report on the Safety Assessment of Oleic Acid, Lauric Acid Palmitic Acid, Myristic Acid, and Stearic Acid. J. Am. Coll. Toxic. 6:321–401.

FDA. 1998. Frequency of use of cosmetic ingredients. *FDA database*. Washington, DC: FDA.

Food and Drug Research Laboratories. 1989. Hamposyl M-30-Primary Skin Irritation of Hamposyl M-30 in New Zealand White Rabbits. Unpublished data submitted by Hampshire Chemical Corporation, 5-27-97. (26 pages.)[2]

French, I. W., J. J. Stock, and F. A. Morrison. 1958. The development of "anti-enzyme" resistance by *Lactobacillus acidophilus*. *Can. Pharm. J. Sci.* 91:540–544.

Frosch, P. J., and A. M. Kligman. 1979. The soap chamber test. *J. Am. Acad. Dermatol.* 1:35–41.

Geigy Chemical Corp. No date. Properties of Sarkosyl NL-30. Submitted by FDA in response to an FOI request on PEGs Dilaurate dated 10-25-96. (14 pages.)

Geigy Industrial Chemicals. 1958. Technical bulletin on N-acyl sarcosine surfactants. Submitted by FDA in response to an FOI request dated 5-14-96. (16 pages.)

Geigy Industrial Chemicals. 1962. Technical bulletin on N-acyl sarcosine surfactants. Submitted by FDA in response to an FOI request dated 5-14-96. (16 pages.)

Grant, J., ed. 1972. *Hackh's chemical dictionary*, 4th ed., 598. New York: McGraw-Hill.

Hampshire Chemical Corporation. 1997a. Petition to Environmental Protection Agency (EPA) to exempt N-acyl sarcosines and their salts from need of tolerance and *Hampshire hamposyl surfactants*, 5th ed. (brochure). With cover letter, dated 5-27-97. (50 pages.)[2]

Hampshire Chemical Corporation. 1997b. Cosmetic use of acyl sarcosines and sarcosinates. Correspondence dated 10-1-97. (1 page.)[2]

Hart. J. R. 1979. N-acyl sarcosine surfactants. *Cosmet. Toiletries* 94:74–76.

Hartmann, A., and G. Speit. 1997. The contribution of cytotoxicity to DNA-effects in the single cell gel test (comet assay). *Toxicol. Lett.* 90:183–188.

Hassell, T. M., and H. R. Mühlemann. 1971. Effects of sodium N-lauroyl sarcosinate on plaque pH in vivo. *Helv. Odont. Acta* 15:52–53.

International Agency for Research on Cancer (IARC). 1978. *IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans. Some N-Nitroso compounds, vol. 17*, 327–336. Lyon: IARC.

IARC. 1987. *IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans*, suppl. 7. *Overall evaluations of carcinogenicity: An updating of IARC monographs vol. 1–42*, 68. Lyon: IARC.

Kippert, F. 1995. A rapid permeabilization procedure for accurate quantitative determination of beta-galactosidase activity in yeast cells. *FEMS Microbiol. Lett.* 128:201–206.

Koontongkaew, S., and S. Jitpukdeebodintra. 1995. Interaction of chlorhexidine with cytoplasmic membranes of *Streptococcus mutans* GS-5. *Caries Res.* 29:413–417.

Lewis, R. J., Sr., ed. 1997. *Hawley's condensed chemical dictionary*, 13th ed., 286, 984. New York: Van Nostrand Reinhold.

Mefford, I. N. 1987. Lauroyl sarcosine: A weak cation-exchange reagent for on-column modification of reversed-phase material. *J. Chromatogr.* 393:441–446.

Molever, K. 1993. Quantitative determination of sodium lauroyl sarcosinate by gas chromatography. *J. Am. Oil Chem. Soc.* 70:101–103.

National Toxicology Program (NTP). 1994. *Seventh Annual Report on Carcinogens (Summary)*, 306–308. Reseach Triangle Park, NC: NTP.

Nelson, M. F., and D. Stewart, Jr. 1956. The absorption of N-acyl sarcosines on various protein materials. J. Soc. Cosm. Chem. 7:22–31.

Newton, J. C., W. T. Blevins, G. R. Wilt, and L. G. Wolfe. 1990. Outer membrane protein profiles of *Edwardsiella ictaluri from fish*. *Am. J. Vet. Res.* 51:211–215.

Nikitakis, J. M., and G. N. McEwen, Jr., ed. 1990. *CTFA compendium of cosmetic ingredient composition—Descriptions I*. Washington, DC: The Cosmetic, Toiletry, and Fragrance Association (CTFA).

Occupational Health Services, Inc. 1996. *Material Safety Data Sheets database (MSDS-OHS)*. Nashville: STN International.

Patil, M. A., D. M. Mhatre, and N. M. Koshti. 1989. Determination of sodium N-lauroyl sarcosinate by HPLC. *Ind. J. Pharm. Sci.* 51:63–65.

Rao, G. S., and E. A. Bejnarowicz. 1976. Thin-layer chromatography of sarcosine and its N-lauroyl and N-nitroso derivatives. *J. Chromatogr.* 123:486–489.

Rosenthal, M. W., L. M. Marson, and A. Abriss. 1954. Some laboratory observations on the chemical, bacterial and enzymatic properties of sodium N-lauroyl sarcosinate. *J. Dent. Child.* 21L:194–201.

Sax, N. I., ed. 1979. *Dangerous properties of industrial materials*, 5th ed., 822. New York: Van Nostrand Reinhold.

Suspect Chemicals Sourcebook. 1995. *A Guide to Industrial Chemicals Covered Under Major Regulatory and Advisory Programs*, vol. 1: *Indexes*. Bethesda, MD: Roytech Publications.

Technology Sciences Group Inc. 1994a. N-Acyl Sarcosines and Sodium N-Acyl Sarcosinates Administrative Volume and Overview of Petition. Unpublished data submitted by Hampshire Chemical Corp., 5-27-97. (11 pages.)[2]

Technology Sciences Group Inc. 1994b. N-Acyl Sarcosines and Sodium N-Acyl Sarcosinates Product Chemistry and Residue Chemistry. Unpublished data submitted by Hampshire Chemical Corp., 5-27-97. (142 pages.)[2]

Technology Sciences Group Inc. 1994c. N-Acyl Sarcosines and Sodium N-Acyl Sarcosinates Toxicology. Unpublished data submitted by Hampshire Chemical Corporation, 5-27-97. (94 pages.)[2]

van der Valk, P. G. M., J. P. Nater, and E. Bleumink. 1984. Skin irritancy of surfactants as assessed by water vapor loss measurements. J. Invest. Dermatol. 82:291–293.

Wenninger, J. A., R. C. Canterbery, and G. N. McEwen, Jr., eds. 2000. *International cosmetic ingredient dictionary and handbook*, 8th ed., vol. 1–2. Washington, DC: CTFA.

[2]Available for review: Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 310, Washington, DC 20036, USA.