JOURNAL OF THE AMERICAN COLLEGE OF TOXICOLOGY
Volume 12, Number 5, 1993
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Final Report on the Safety Assessment of Sodium Cocoyl Isethionate

ABSTRACT

Sodium Cocoyl Isethionate is used as a surfactant–cleansing agent in cosmetic formulations. Sodium Cocoyl Isethionate is slightly to practically nontoxic, with an oral LD_{50} of ≥4.33 g/kg for rats. Dermal application of 1.0–36.0% w/w aqueous Sodium Cocoyl Isethionate to rats for 28 days did not produce any significant toxic effects.

The ocular irritation produced by Sodium Cocoyl Isethionate was concentration dependent, ranging from a mild reaction at a test concentration of 2.5% to a primary ocular irritant at test concentrations of 49%. Sodium Cocoyl Isethionate is neither a sensitizer nor phototoxic compound.

Sodium Cocoyl Isethionate was nonmutagenic in an *in vitro* chromosomal aberration assay and did not produce a positive response in an *S. typhimurium* reverse mutation assay.

Based on the concentration of test cited in this report, it is concluded that Sodium Cocoyl Isethionate is safe for use in cosmetic formulations at 50% in rinse-off products and at 17% in leave-on products.

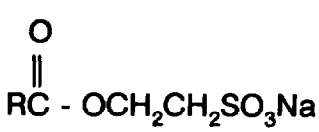
INTRODUCTION

SODIUM COCOYL ISETHIONATE IS THE SODIUM salt of the coconut fatty acid ester of isethionic acid which functions as a surfactant–cleansing agent (Nikitakis, 1988).

CHEMISTRY

Definition and Structure

Sodium Cocoyl Isethionate (CAS No. 61789-32-0) generally conforms to the formula (Estrin et al., 1982a):



where RCO- represents the coconut acid moiety.

Sodium Cocoyl Isethionate is also known as Coconut Fatty Acid, 2-Sulfoethyl Ester, Sodium Salt (Hunting, 1983); Fatty Acids, Coconut Oil, Sulfoethyl Esters, Sodium Salts; Igepon AC-78 (Estrin et al., 1982a); and Jordapon CI (CTFA, 1990a).

Physical and Chemical Properties

Sodium Cocoyl Isethionate is in the form of a fine white powder that consists of active ingredient plus minor impurities and has a mild odor (Estrin et al., 1982b). Sodium Cocoyl Isethionate is stable at a pH of 6–8 and hydrolyzes outside of this pH range (Hunting, 1983). Physical and chemical properties are summarized in Table 1.

Manufacture and Production

Sodium Cocoyl Isethionate is prepared via the following reaction: sodium isethionate is reacted with either the fatty acid mixture from coconut oil (Hoffmann, 1990) or the corresponding chlorides to form Sodium Cocoyl Isethionate (Hunting, 1983). The sodium isethionate was first prepared by adding 1 mole of ethylene oxide to sodium bisulfite.

TABLE 1. CHEMICAL AND PHYSICAL PROPERTIES OF SODIUM COCOYL ISETHIONATE

		References
Physical appearance	Fine white powder	Estrin et al., 1982b
Odor	Mild	Estrin et al., 1982b
UV absorbance—molar extinction coefficient ϵ		CTFA, 1991
210 nm	0.277–99	
290 nm	0.009–2	
320 nm	0.005–0.7	
400 nm	0.004–0.3	
500 nm	0.003–baseline	
Solubility	Soluble in warm water	Hunting, 1983
	Soluble in water	Estrin et al., 1982b
	In water:	CTFA, 1990a
	at 25°C-0.01 g/100 ml	
	at 70°C->50 g/100 ml	
Stability	Stable in pH range of 6–8; hydrolyzes outside this pH range	Hunting, 1983
Assay	83% minimum	Hunting, 1983
	82% minimum	Estrin et al., 1982b
Surface tension	At 25°C:	CTFA, 1990a
	0.01% solution-33 dynes/cm	
	0.1% solution-27 dynes/cm	
Impurities		Estrin et al., 1982b
Arsenic (As)	3 ppm maximum	
Iron (Fe)	25 ppm maximum	
Lead (Pb)	20 ppm maximum	
Sodium chloride	0.8% maximum	
Free fatty matter	10.0% maximum	
Sodium Isethionate	5%	CTFA, 1991
Free fatty acid	18%	
Sodium soap	3%	

Analytical Methods

Sodium Cocoyl Isethionate was identified via infrared spectroscopy; there was no indication of foreign materials (Estrin et al., 1982b).

Ultraviolet Absorbance

Sodium Cocoyl Isethionate was dissolved in high-performance liquid chromatography (HPLC) grade methanol at 1002 mg/L and the ultraviolet (UV) absorbance of the solution was determined using a Perkin Elmer Lambda 4B UV/VIS spectrophotometer (CTFA, 1991). The UV spectrum was scanned from 210 to 500 nm. Sodium Cocoyl Isethionate did not absorb in the UVA or UVB range.

Impurities

The impurities that may be found in Sodium Cocoyl Isethionate are listed in Table 1 (Estrin et al., 1982b; Hunting, 1983). Other impurities and by-products include soap, fatty acid, and unreacted sodium isethionate.

USE

Cosmetic

The product formulation data submitted to the Food and Drug Administration (FDA) in 1992 stated that Sodium Cocoyl Isethionate was contained in a total of 52 cosmetic product formulations (Table 2). Sodium Cocoyl Isethionate was used in the preparation of bath soaps and detergents, noncoloring shampoos, tonics, dressings, and other hair grooming aids, and skin cleansing preparations. The greatest reported use of Sodium Cocoyl Isethionate was in the preparation of bath soaps and detergents, 30 formulations.

Concentration of use values are no longer reported to the FDA by the cosmetic industry (Federal Register, 1992). However, the product formulation data submitted to the FDA in 1984 stated that Sodium Cocoyl Isethionate was used at a concentration of ≤50% in bath soaps and detergents and at 10–25% in noncoloring shampoo formulations (FDA, 1984). In 1984, Sodium Cocoyl Isethionate was not reported to be used in tonics, dressings, and other hair grooming aids or skin cleansing preparations.

Table 2. Product Formulation Data for Sodium Cocoyl Isethionate (FDA, 1992)[a]

Product category	*Total no. of formulations in category*	*Total no. containing ingredient*
Bath soaps/detergents	148	30
Hair shampoos (noncoloring)	909	7
Tonics, dressings, and other hair grooming aids	290	7
Skin cleansing preparations (cold creams, lotions, liquids, and pads)	680	8
1992 Totals		52

[a] CIR requests that the cosmetic industry provide current formulation data on each product category.

Sodium Cocoyl Isethionate is used as a mild foaming and cleansing agent (Hunting, 1983). It is manufactured primarily for use in synthetic detergent (syndet) bars.

Noncosmetic

As stated in the section on cosmetic use, Sodium Cocoyl Isethionate is used as an ingredient in syndet bars (Hunting, 1983). It is not stated whether this use is only cosmetic or if it has noncosmetic applications.

ANIMAL TOXICOLOGY

Acute Toxicity

Oral

An acute oral toxicity test of a syndet bar containing 47.5% Sodium Cocoyl Isethionate was performed on five male and five female albino Sprague-Dawley rats (Hazleton Laboratories America, Inc., 1986a). A uniform suspension of test material in distilled water, at a concentration of 0.25 g/ml, was used. A single dose of 5 g/kg at a volume of 20 ml/kg was given orally by gavage. Animals were fasted for a period of approximately 16–22 h prior to dosing; individual doses were calculated using the fasted weight. Animals were observed for clinical signs and mortality 1, 2.5, and 4 h after dosing, and for 14 days thereafter. Feed and water were available *ad libitum* following dosing. The animals were weighed before fasting, prior to dosing, and at the termination of the study.

Clinical observations for the males included: red-stained faces, diarrhea, and possible respiratory congestion. Three of the males were normal following dosing and through day 14; the other two males were normal by day 1. Observations made for the females included excessive salivation, red-stained faces, diarrhea, hypoactivity, and yellow-staining of the genital area. Two of the females appeared normal by day 1 and the remaining three appeared normal by day 2. An average weight gain was observed for both males and females over the 14 day period. All animals were killed at study termination; necropsy was not performed. The estimated oral LD_{50} was >5.0 g/kg for both male and female Sprague-Dawley rats.

An acute oral toxicity test of a gel cleanser containing 15% Sodium Cocoyl Isethionate was performed using five male and five female Sprague-Dawley CD^R rats (Bio/dynamics, Inc., 1985a). A single dose of 5 g/kg at a volume of 5 ml/kg was administered by oral intubation. Animals were fasted for approximately 18 h prior to dosing; individual doses were calculated using the fasted weight. Animals were observed for clinical signs 1, 2, and 4 h after dosing, and for 14 days thereafter; a viability check was made twice daily. Feed and water were available *ad libitum* following dosing. The animals were weighed before fasting, prior to dosing, and at study termination.

All animals were normal following dosing and for the remainder of the study except for one female with diarrhea on day 3. A weight gain was observed for all animals over the 14-day period. All animals were killed at study termination; necropsy was not performed. The estimated oral LD_{50} was >5.0 g/kg for both male and female Sprague-Dawley rats.

In a paper submitted to CTFA (1990a), the rat oral LD_{50} of pure Sodium Cocoyl Isethionate was 4.33 g/kg.

Short-Term Toxicity

Dermal

A 10-day dose-range-finding study was conducted using Charles River COBS CD^R rats (Unilever Research U.S., Inc., 1991). A daily application of 10.0, 20.0, 40.0, or 60.0% w/w aqueous Sodium Cocoyl Isethionate was applied to the shaved dorsal surface of rats (number of males and females per group not specified) and the test sites were covered by an occlusive patch for 6 h. (These concentrations resulted in dermal dosages of approximately 0.75, 1.52, 2.22, and 4.35 g/kg/day, respectively.)

Dermal irritation was observed at the test site by day 6 for all rats in the 40 and 60% Sodium Cocoyl Isethionate groups. The occurrence and severity of irritation decreased during the remainder of the study. Signs of systemic toxicity were not observed.

A 28-day dermal study was conducted using Charles River COBS CD^R rats to determine the potential systemic effects and target organ toxicity of Sodium Cocoyl Isethionate (Unilever Research U.S., Inc., 1991). Three groups of rats, 10 males and 10 females per group, were dosed with 1.0, 14.0, or 36.0% w/w aqueous suspensions of Sodium Cocoyl Isethionate. (The suspensions for the low- and mid-dose groups were dosed at a volume of 10.0 ml/kg, whereas the suspension for the high-dose group was dosed at a volume of 11.5 ml/kg due to the physical nature of the suspension.) The control group, which was also comprised of 10 males and 10 females, received dermal applications of vehicle.

The hair on the dorsal surface of the rat was shaved the day prior to study initiation. The test article was applied to a surface area of 32 cm^2 for rats <350 g, 36 cm^2 for rats 350–400 g, and 40 cm^2 for rats >400 g. The hair on an area of the hind quarters was also clipped to provide normal skin for comparison. Each animal was dosed once daily for 28 days. An occlusive covering was applied for 6 h after dosing and upon removal of the covering the test site was rinsed.

Prior to dosing, the test site was examined for irritation according to the methods of Draize (Draize, 1959). Toxicologic observations were made twice daily. Body weight and feed consumption were recorded weekly.

Very slight erythema was observed at the application sites of two male rats of the high-dose group during wks 3 and 4 of the study. However, a significant difference in dermal irritation was not observed between the males of the control and high-dose groups. Dermal irritation was not observed for males of the low- and mid-dose groups.

Very slight erythema was observed at the application sites of four of 10 female rats of both the low- and mid-dose groups during wk 1 of the study only. Very slight and well-defined erythema, which was significantly different from controls, was observed at application sites of female rats of the high-dose group on days 4, 5, 6, and 7 of the study only. Very slight edema, which was not significantly different from the controls, was also observed at application sites of females of the high dose group at times throughout the study.

During wks 2 and 3, significant differences in weight gain were observed for males as compared to the controls. A significant effect was not observed for male rats during wk 4 or over the duration of the study. A significant difference in weight gain was not observed for female rats in the test groups as compared to controls. A significant increase in feed consumption was observed for male rats of the mid-dose group during wks 1 and 4 of the study; a significant increase was also observed in cumulative feed consumption data. No other significant differences in feed consumption were observed for male or female rats in the test groups as compared to the controls.

No differences attributable to Sodium Cocoyl Isethionate administration were found in hematologic and clinical chemistry parameters.

A significant increase was observed in the relative organ to body weight ratio for the relative heart weight of males of the high-dose group and for the relative adrenal gland weight for females of the high-dose group. A significant difference in absolute weight was not observed for any of the examined organs in any of the test groups.

One male in the mid-dose group was found dead on day 19. Death was attributed to mechanical trauma and not the application of Sodium Cocoyl Isethionate. Gross and microscopic examination of all animals at study termination did not produce any observations related to dosing with Sodium Cocoyl Isethionate. Dermal application of Sodium Cocoyl Isethionate to rats for 28 days did not result in significant toxic effects.

Ocular Irritation

Ocular irritation studies for Sodium Cocoyl Isethionate are summarized in Table 3.

Three New Zealand White (NZW) rabbits, gender not specified, were used to determine the ocular irritation potential of a cosmetic formulation containing 49% Sodium Cocoyl Isethionate (Lever Research, 1988). The test article was prepared as a 50% aqueous solution and 0.1 ml was applied into the conjunctival sac of each rabbit for 5 min. After 24 h, corneal opacity was observed for all animals and positive conjunctival effects for two of three animals. These effects were not seen after 48 h. The average weighted Draize scores were 14.3/110 after 24 h, 8.0/110 after 48 h, 4.7/110 after 72 h, 2.3/110 after 7 days, and 0.0/110 after 14 days.

An ocular irritation study of a syndet bar containing 47.5% Sodium Cocoyl Isethionate was performed using three male and three female albino NZW rabbits (Hazleton Laboratories America, Inc., 1986b). The eyes of each animal were examined the day before dosing using fluorescein dye and prior to test article application without dye. Test animals were chosen on the basis of an absence of ocular injury or irritation and a body weight >1.5 kg. A dose of 100 mg of test material was placed in the conjunctival sac of one eye of each animal. The eye was held shut for 1 sec following application to prevent loss of material and it was not rinsed following test article application. The other eye of each animal was untreated and served as a control. Body weights were determined prior to test material administration and at weekly intervals throughout the study. Clinical observations were made daily. Eyes were checked for irritation on days 1, 2, 3, 4, and 7. Sodium fluorescein was used to check for corneal injury and the eyes were scored for irritation according to the methods of Draize (Draize, 1975).

The primary ocular irritation score is the total ocular irritation score for all the animals divided by the number of animals observed. The maximum average score (MAS), which is the highest primary eye irritation score, occurred on day 1 and was 34.2. Blanching of the conjunctivae and corneal epithelial peeling were observed in all six animals. On day 7, the primary eye irritation score was 20.3. At this time, the blanching of the conjunctivae and corneal epithelial peeling were still observed in four animals, pannus and corneal neovascularization were seen in three animals, and necrotic areas of the conjunctivae were observed in two animals. No clinical signs were observed throughout the study. The test article was a "primary eye irritant."

An ocular irritation study of a gel cleanser containing 15% Sodium Cocoyl Isethionate was performed using two male and four female albino NZW rabbits (Bio/dynamics, Inc., 1985b). The eyes of each animal were examined the day before

Table 3. Ocular Irritation Studies for Sodium Cocoyl Isethionate

Number, sex, strain	*Dose*	*Methods*	*Results*	*References*
3 NZW rabbits (sex not specified)	49% in formulation	The test article was prepared as a 50% aqueous solution and 0.1 ml was placed in the conjunctival sac of the eye of each animal for 5 min.	At 24 but not 48 h, corneal opacity was observed for all animals and positive conjunctival effects for 2 animals. The average weighted Draize scores were: 14.3/110-24 h; 8.0/110-48 h; 4.7/110-72 h; 2.3/110-7 days; 0.0/110-14 days	Lever Research 1988
6 albino NZW rabbits (3/sex)	47.5% in formulation	A dose of 100 mg was placed in the conjunctival sac of one eye; the eye was not rinsed. The other eye served as a control. Sodium fluorescein was used to evaluate corneal injury.	On day 1, the MAS was 34.2; all animals had blanching of the conjunctivae and corneal epithelial peeling. On day 7, the primary eye irritation score was 20.3; 4 animals had blanching of the conjunctivae and corneal epithelial peeling; 3 animals had pannus and corneal neovascularization; 2 animals had necrotic areas of the conjunctivae. The test article was a "primary eye irritant."	Hazleton Labs. Inc., 1986b
6 albino NZW rabbits (2 males and 4 females)	15% in formulation	A volume of 0.1 ml was placed in the conjunctival sac of the right eye; it was not stated whether the eye was rinsed. The left eye served as a control. Sodium fluorescein was used to evaluate corneal injury.	On day 1, the MAS was 23.3; on day 7, the average score was 1.7. Moderate conjunctival irritation, iridial changes and corneal opacities, ulceration, and stippling was observed for most animals. By day 7, 5 animals had slight conjunctival irritation, while 1 animal had no ocular irritation; none of the animals had corneal irritation. The test article produced "mild and transient ocular irritation" and was an ocular irritant.	Bio/dynamics, Inc., 1985b

Table 3. Ocular Irritation Studies for Sodium Cocoyl Isethionate (*Continued*)

Number, sex, strain	*Dose*	*Methods*	*Results*	*References*
6 albino NZW rabbits (2 males and 4 females)	15% in formulation	A volume of 10 µl was placed on the cornea of one eye; it was not stated whether the eye was rinsed.	On day 1, the MAS was 3.0; on day 3, the average score was 0.0. Slight conjunctival irritation was observed on days 1 and 2 for 5 animals. The test article was "very mildly irritating to the eye" and was not considered an ocular irritant.	Bio/dynamics, Inc., 1985c
9 New Zealand albino rabbits (sex not specified)	5% solution	A volume of 0.1 ml was placed in the conjunctival sac of the eye. The eyes of 3 rabbits were rinsed after 30 sec and the eyes of 6 rabbits were not rinsed. The other eye served as a control.	Rinsed eyes: the solution was minimally irritating, with a maximum mean total score of 8.33/110. Unrinsed eyes: the solution was mildly irritating, with a maximum mean total score of 15.33/110.	Product Safety Labs, 1984a
3 NZW rabbits (sex not specified)	as supplied	A dose of 55 mg was applied to the eye for 5 min.	Corneal opacity and transient iritis was observed in 1 animal 72 h after dosing; opacity was present on day 7 and the eye was completely healed by day 14. Slight iridial and conjunctival irritation was observed in the other 2 animals; these irritations were not observed on day 7. The average weighted Draize scores were: 12.3/110-24 h; 9.0/110-48 h; 9.1/110-72 h; 1.7/110-7 days; 0.0/110-14 days Sodium Cocoyl Isethionate "has the potential to cause sufficient ocular injury as to be considered an eye irritant."	CTFA, 1983
6 NZW rabbits (sex not specified)	2.5% gravimetric aqueous solution	A volume of 0.1 ml was placed in the conjunctival sac of the eye; the eyes were rinsed after 24 h. The other eye served as a control.	The average (Draize) irritation scores were: 3.0-24 h; 1.0-72 h; 0.0-4 days The test article was a "mild ocular irritant."	Consumer Product Testing Co., Inc., 1982

dosing using fluorescein dye and prior to test article application without using dye. A volume of 0.1 ml of test article was placed in the conjunctival sac of the right eye of each animal; the eye was held shut for 1 sec following application to prevent loss of material. (It is not stated whether or not the eye was rinsed.) The left eye of each animal served as a control.

Eyes were checked for irritation on days 1, 2, 3, and 7. On day 1, sodium fluorescein was used to determine corneal ulceration; if stain retention was observed, observation using fluorescein dye was continued until either no dye retention was seen in two observations or the study was terminated (day 7). The eyes were evaluated for irritation according to the methods of Draize (Draize, 1959). A viability check was made twice daily.

The MAS occurred on day 1 and was 23.3. On day 7, the average score was 1.7. Moderate conjunctival irritation characterized by redness, chemosis, and discharge, iridial changes and corneal opacities, ulceration, and stippling was observed for most test animals. By day 7, five animals had slight conjunctival irritation while no ocular irritation was observed for one animal; none of the animals had corneal irritation. The test article produced "moderate and transient ocular irritation" and was an ocular irritant as defined in Title 16 part 1500.3(c) of the Code of Federal Regulations (1985).

An ocular irritation study of a gel cleanser containing 15% Sodium Cocoyl Isethionate was performed using two male and four female albino NZW rabbits (Bio/dynamics, Inc., 1985c). The eyes of each animal were examined as is stated in the previous study. A volume of 10 μl of test article was placed directly on the cornea of one eye of each animal; the eyelid was released immediately after application. (It is not stated whether or not the eye was rinsed.)

Eyes were checked for irritation on days 1, 2, and 3 or until no signs of irritation were present. Irritation was determined as is stated in the previous study. A viability check was made twice daily.

The MAS occurred on day 1 and was 3.0. On day 3, the average score was 0.0. Slight conjunctival irritation characterized by redness and chemosis, was observed in five of the six animals on days 1 and 2. The test article was "very mildly irritating to the eye" and was not considered to be an eye irritant as defined in Title 16 part 1500.3(c) of the Code of Federal Regulations (1985).

Nine New Zealand albino rabbits, sex not specified, were used in a Draize (Draize et al., 1944) primary ocular irritation study of a 5% Sodium Cocoyl Isethionate solution (Product Safety Labs, 1984a). A volume of 0.1 ml of test solution was placed in the conjunctival sac of the eye of each rabbit; the other eye was untreated and served as a control. The treated eyes of three rabbits were rinsed 30 sec after test article administration; the eyes of the remaining six rabbits were not rinsed. The eyes were evaluated for irritation 24, 48, and 72 h following test article application. A 5% Sodium Cocoyl Isethionate solution was minimally irritating to rinsed eyes (classified according to Kay and Callandra, 1962), with a maximum mean total score of 8.33/110, and mildly irritating to unrinsed eyes, with a maximum mean total score of 15.33/110.

Three NZW rabbits were used to determine the ocular irritation potential of Sodium Cocoyl Isethionate (CTFA, 1983). The test article, 55 mg, was applied as supplied to the eye of each rabbit for 5 min. Corneal opacity and transient iritis were observed in one animal for 72 h after dosing. Opacity was present on day 7; the eye was completely healed by day 14. Slight iridal and conjunctival irritation was observed in the other two animals; these irritations were not observed on day 7. The average weighted Draize score was 12.3/110 after 24 h, 9.0/110 after 48 h, 9.1/110 after 72 h, 1.7/110 after 7

days, and 0.0/110 after 14 days. Sodium Cocoyl Isethionate "has the potential to cause sufficient ocular injury as to be considered an eye irritant."

Study of the primary ocular irritation of a 2.5% gravimetric aqueous solution of Sodium Cocoyl Isethionate was performed using six NZW rabbits, sex not specified (Consumer Product Testing Company, Inc., 1982). A volume of 0.1 ml was placed in the conjunctival sac of one eye, which was free from visible ocular defects, of each rabbit. The eye was held shut for 1 sec following test article application. After 24 h, the eye was rinsed. The other eye was untreated and served as a control. The eyes were scored for irritation 24, 48, and 72 h following test article application according to the methods of Draize (1975). If irritation persisted, additional observations were made on days 4 and 7. If two or more animals had a positive reaction the test article was considered an ocular irritant (unless the test was repeated with another six animals without positive reactions).

After 24 h, the average irritation score was 3.0. After 72 h, the average score was 1.0, and on day 4 it was 0.0. The test article, a 2.5% aqueous suspension of Sodium Cocoyl Isethionate, was a "mild ocular irritant."

Dermal Irritation

Three male albino rabbits were used to determine the degree of dermal irritation produced by Sodium Cocoyl Isethionate according to the methods of Draize (Schoenberg, 1985). Sodium Cocoyl Isethionate was adjusted to a total of 15.0% active and pH 7.0. The rabbits' abdomens were shaved and four areas, approximately 10 cm apart, were selected as application sites. The application sites were 1 sq. in.; two sites were abraded and two were left intact.

A volume of 0.5 ml of solution 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 evaluated for irritation. The sites were re-examined after 72 h. The primary irritation score was determined by adding the average values of erythema for intact and abraded skin at 24 and 72 h (four values) and the average values for edema at 24 and 72 h (four values), and dividing the total of the eight values by four. Sodium Cocoyl Isethionate was moderately irritating to the skin of rabbits, with a primary irritation score of 4.2/8.0.

A modified Draize test (Draize, 1975) to determine the irritation potential of a 5% Sodium Cocoyl Isethionate solution was performed using six NZW rabbits, sex unspecified (Consumer Product Testing Company, Inc., 1984). The skin of the mid-dorsal area of the trunk, between the scapulae and the pelvis, was clipped 24 h prior to dose application. Two 2.5 cm^2 areas on opposite sides of the vertebral column were chosen as test sites; the right side was abraded while the left side remained intact. A volume of 0.5 ml of test article was applied once to each site under occlusive wrap for 24 h. After wrap removal, residual test article was removed and the sites were scored for irritation using the Draize scale. The sites were scored again 72 h following dosing. The mean scores from the 24 and 72 h readings were averaged to determine the primary irritation index (PII).

The PII for the 5% Sodium Cocoyl Isethionate solution was 1.38/8.0. This score was interpreted as having potential for mild irritation and the test article may possibly be irritating to some people under occlusive wrap conditions. A 5% Sodium Cocoyl Isethionate solution was not a primary dermal irritant to rabbit skin.

Six New Zealand albino rabbits, sex not specified, were used in a primary dermal irritation study of a 5% Sodium Cocoyl Isethionate solution (Product Safety Labs, 1984b). The trunk of each animal was clipped free of hair. Two 2.5 cm^2 gauze patches

were placed over intact and abraded skin on each animal. A volume of 0.5 ml of test article was applied to intact and abraded skin under two gauze patches; the entire trunk of the animal was wrapped. The patches were removed after 24 h and remaining test article was wiped off. The test sites were evaluated for irritation 24 and 72 h after test article administration. A 5% Sodium Cocoyl Isethionate solution was a moderate primary dermal irritant to rabbits, with a primary irritation score of 2.24/5.1+.

Phototoxicity

A primary dermal irritation and phototoxicity study of a syndet bar containing 47.5% Sodium Cocoyl Isethionate was performed using three male and three female NZW rabbits (Bio/dynamics, Inc., 1987). The day before dosing, the hair on the back of each rabbit was clipped and two test sites, one on each side of the spinal column, were chosen. A Hill Top Chamber was placed on each test site and 0.4 ml of test article, 2% w/v Sodium Cocoyl Isethionate in distilled water, was applied beneath the chamber. The sites were covered by occlusive patches and collars were placed on the animals to prevent disruption of the wrapping and ingestion of test article.

Approximately 2 h after dosing, the occlusive wraps and the patch covering the test site of the right were removed. The patch covering the test site on the left was covered with aluminum foil. The right test site of each animal was subjected to light emitted from a bank of four General Electric F-40BLB UV lights positioned approximately 6 in above the site for 30 min. (The minimal erythemal dose [MED] was not given.) Following exposure, the patches were replaced on the right side of each animal and the aluminum foil was removed from the left side. The test sites were again covered by occlusive patches until 24 h after dosing. Upon patch removal, the test sites were wiped with damp gauze.

One female NZW rabbit served as the positive control and was dosed with 1% Oxsoralen, a known phototoxic agent. The positive control was then treated in the same manner as the test animals.

All sites were scored 1 h after patch removal (the 24 h reading), and 48 and 72 h following dosing according to the Draize scale (Draize, 1975). A modified primary irritation value was calculated for both irradiated and nonirradiated sites by adding the average erythema and edema scores from each reading (six values) and dividing by three.

All six test animals had very slight erythema without edema, both with and without irradiation, after 24 h. After 48 and/or 72 h, only two animals had very slight erythema. The responses of the irradiated and nonirradiated sites were comparable. The positive control had a minimal response at the nonirradiated site, but mild to moderate erythema and edema were observed at the irradiated site. The modified primary irritation values for the test article were 0.4/8 and 0.5/8 for the non-irradiated and irradiated sites, respectively. For the positive control, the primary irritation values were 0.3/8 and 5.3/8 for the non-irradiated and irradiated sites, respectively. The test article was mildly irritating to skin of rabbits, but it did not appear to be phototoxic.

The preceding results are consistent with more recent data indicating that Sodium Cocoyl Isethionate does not absorb in the UVB or UVA range.

Sensitization

The sensitization potential of a syndet bar containing 47.5% Sodium Cocoyl Isethionate was evaluated by performing a modified Buehler test using guinea pigs

(Buehler, 1965; Ritz and Buehler, 1980; Hill Top Research, Inc., 1986). The test was performed using a total of 34 Hartley albino guinea pigs (17 males and 17 females) in three phases.

The appropriate concentration for use in the primary challenge was determined during the primary irritation screen. Four guinea pigs, two males and two females, were used during this phase. The day prior to dosing, the backs of the animals were clipped to provide enough space to test four concentrations. On the day of dosing, occlusive patches incorporating a 25 mm Hill Top Chamber were moistened with 0.3 ml of 0.5%, 1.0%, 1.5%, or 2.0% w/v test article in distilled water. The patches remained in place for 6 h. The next day, a depilatory was applied to the test sites for 8 min and the sites were scored at 24 and 48 h. A concentration of 2.0% w/v in distilled water was chosen for use at induction and at primary challenge.

On the day before induction, the backs of 20 guinea pigs (10 male and 10 females) were clipped free of hair. On the day of dosing, chambers moistened with 0.3 ml of 2.0% w/v test material in distilled water were applied under occlusive patches for 6 h; the sites were scored 24 h after induction. The chambers were reapplied to the same sites, following the same method, during the next 2 wks for a total of three applications.

A primary challenge was performed approximately 2 wks after the last induction. The lower left quadrant of the back of the 20 test animals and of 10 untreated control animals (five males and five females) was clipped. On the following day, a challenge patch moistened with 0.3 ml of 2.0% w/v test article in distilled water was applied to the test and control animals for 6 h. The day after application, a depilatory was applied for 8–11 min. Two and one-half h later, the 24 h observation was made. A 48 h reading was taken the next day.

A plus/minus response, indicating slight patchy erythema, was observed for nine of 20 test animals and seven of 10 untreated controls during the challenge. The incidence and severity of the responses were comparable among the test and control groups. This indicated that sensitization was not induced.

A modified Buehler test using Hartley albino guinea pigs was performed to evaluate the sensitization potential of a gel cleanser containing 15% Sodium Cocoyl Isethionate (Springborn Institute for Bioresearch, Inc., 1985). During the irritation screen, four guinea pigs, two males and two females, were used and concentrations of 10%, 30%, 50%, and 70% test article in distilled water, 0.3 ml/site, were tested. A 70% solution of test article in distilled water was chosen for the induction and 50% test article in distilled water was chosen for the challenge; the volume of test article used in dosing was 0.3 ml for both phases.

During the induction phase, the animals, 10 males and 10 females, were inadvertently dosed with 100% test article as the first application; the following two doses were correct at 70% in distilled water. During the primary challenge, five male and five female guinea pigs were used as the untreated control group.

No responders, scores ≥ 1, were observed in either group following the challenge. Two animals had plus/minus reactions in the test group and six animals had plus/minus reactions in the control group following the primary challenge.

MUTAGENICITY

An *in vitro* chromosomal aberration assay was performed to evaluate the potential of Sodium Cocoyl Isethionate to induce chromosomal aberrations in Chinese hamster

ovary (CHO) cells (Microbiological Associates, Inc., 1991a). The test was performed with and without metabolic activation. Distilled, deionized water (vehicle) was used as the negative control. The positive controls were triethylenemelamine and cyclophosphamide with and without metabolic activation, respectively.

A toxicity test was performed using 0.5–5100 μg/ml Sodium Cocoyl Isethionate. Based on the results of the toxicity test, concentrations of 19, 38, 75, 150, and 300 μg/ml Sodium Cocoyl Isethionate (adjusted for purity of the test article, 72.45%) were used in the study. Metaphase cells were collected for microscopic evaluation 10 h after treatment initiation. At the 150 and 300 μg/ml concentrations, metaphase cells were collected 16 h and 19 h after treatment initiation with and without metabolic activation, respectively, due to a delay in cell cycle kinetics at these concentrations.

Due to excessive toxicity at a concentration of 300 μg/ml, no metaphase cells were obtained at either harvest with or without metabolic activation. Toxicity, as measured by a reduction in mitotic index, was approximately 57 and 71% at the 10 and 16 h harvest, respectively, for 150 μg/ml Sodium Cocoyl Isethionate without metabolic activation. With metabolic activation, toxicity was 94 and 74% at the 10 and 19 h harvest, respectively, for 150 μg/ml. A significant increase in chromosomal aberrations was not observed. Sodium Cocoyl Isethionate was negative in the CHO cytogenetics assay both with and without metabolic activation.

A *Salmonella typhimurium* preincubation reverse mutation assay was performed according to the methods of Ames et al. (1975) and Maron and Ames (1983) to evaluate the mutagenic potential of Sodium Cocoyl Isethionate (Microbiological Associates, Inc., 1991b). *S. typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538 were used and the study was performed with and without microsomal activation. Sterile, deionized, distilled water (vehicle) was used as the negative control. With metabolic activation, 2-aminoanthracene was used as the positive control. Without metabolic activation, the positive controls were 2-nitrofluorene for TA98 and TA1538, sodium azide for TA100 and TA1535, and ICR-191 for TA1537.

Based on the results of a dose-range-finding study using 10-10,000 μg/ml Sodium Cocoyl Isethionate, concentrations of 10-1000 μg/ml and 1.0-100 μg/ml Sodium Cocoyl Isethionate (adjusted for purity of the test article, 72.45%) were tested with and without metabolic activation, respectively. An initial and a confirmatory assay was performed. In each run, all concentrations of Sodium Cocoyl Isethionate and the positive and negative controls were plated in triplicate.

In the initial assay, a positive response was not observed with or without metabolic activation. Because observed toxicity at 100 μg/ml was marginal, the maximum dose concentration with and without metabolic activation used in the confirmatory assay was increased to 333 μg/ml.

In the confirmatory assay, a 2.0-fold non-dose responsive increase was observed using TA1537 without metabolic activation. However, this was not considered a positive response. Therefore, as in the initial assay, no positive responses were observed with or without metabolic activation.

CLINICAL ASSESSMENT OF SAFETY

Irritation

Five modified soap chamber tests (Frosch and Kligman, 1979) were performed using 8% solutions of Sodium Cocoyl Isethionate (CTFA, 1985a, 1986a, 1986b, 1988a,

1988b). The Webril discs were moistened with approximately 0.2 ml of the test solution in three studies (CTFA, 1985a, 1986a, 1986b) and with 0.1 ml of test article in two studies (CTFA, 1988a, 1988b). The initial patches were applied for 24 h in all the studies, while the patches applied on the remaining 4 days were applied for 6 h periods in all studies except one; in CTFA (1988b), the patches were applied for 5 h periods. Two studies (CTFA, 1985a, 1986a) scored erythema using a scale of 0–5. Three studies (CTFA, 1986b, 1988a, 1988b) scored erythema on a scale of 0–4 and edema and vesicles on a scale of 0–3, with the total irritation score being the sum of these three scores. It was required that all subjects used did not have any skin disorders.

Fifteen subjects completed the first study (CTFA, 1985a). The mean erythema score was 1.9733/5, with individual minimum and maximum mean scores of 0.0 and 4.4, respectively. (A score of 2 was described as moderate, uniform redness.)

The Sodium Cocoyl Isethionate used in the second study, which 14 subjects completed, was 81% active with 15% coco fatty acid (CTFA, 1986a). The test solution was applied to three sites on the right forearm and one site on the left forearm of each subject. The mean erythema scores for the sites on the right forearm were 0.529, 0.486, and 0.686 and the mean erythema score for the site on the left forearm was 1.014, with individual minimum and maximum mean scores for any site of 0.0 and 4.0, respectively. The total average mean erythema score for all four sites was 0.679/5. (A score of 1 was described as slight redness, spotty–follicular or diffuse).

The Sodium Cocoyl Isethionate used in the third study, which 15 subjects completed, was also 81% active with 15% coco fatty acid (CTFA, 1986b). The mean erythema score was 1.36/4, the mean edema score was 0.147/3, and the mean vesicle score was 0.12/3. The total mean irritation score was 1.627. The individual minimum and maximum mean scores were 0.2 and 2.6 for erythema, 0.0 and 0.6 for edema, 0.0 and 0.8 for vesicles, and 0.2 and 3.6 for total irritation score, respectively. (An erythema score of 1 was described as spotty, skin discoloration but not redness–follicular or diffuse, an edema score of 1 corresponded to slight edema, and a vesicle score of 1 corresponded to slight vesicles—one or two.)

In addition to clinical observations for irritation, transepidermal water loss (TEWL) was measured using a Servomed Evaporimeter in the fourth modified soap chamber test, which 19 subjects completed (CTFA, 1988a). TEWL values were measured on day 1 prior to the first application and 30 min after patch removal on days 2 and 5. The TEWL mean readings were 9.6 and 8.9 on days 2 and 5, respectively. The mean erythema score was 1.667/4, the mean edema score was 0.344/3, and the mean vesicle score was 0.258/3. The total mean irritation score was 2.269 (an erythema score of 2 was described as slight redness).

In the fifth study, for which there were 21 subjects at study initiation, it was necessary to discontinue testing on many subjects due to high irritation scores (CTFA, 1988b). (It was noted that irritation scores may have been aggravated by cold, dry weather conditions.) Only the data from the first two days of the study were analyzed. Using these data, an 8% aqueous solution of Sodium Cocoyl Isethionate had a mean irritation score of 2.5 ± 1.5. Sodium Cocoyl Isethionate was numerically much more irritating than the synthetic detergent tauranol, which had a mean score of 2.0.

A modified soap chamber test (Frosch and Kligman, 1979) was performed using an 8% aqueous solution of Sodium Cocoyl Isethionate (CTFA, 1990b). The Webril discs were moistened with 0.1 ml of the test solution and applied to the forearm of subjects for 28 h. Erythema was scored on a scale of 0–4 and edema and vesicles on a scale of 0–3, with the total irritation score being the sum of these three scores. Seventeen subjects,

which were free of any skin disorders, completed the study. According to the protocol, TEWL was to be measured; however, no values for TEWL were reported. The mean erythema, edema, and vesicle scores were 1.235/4, 0.294/3, and 0.0/3, respectively. The total mean irritation score was 1.529.

The primary irritation potential of a gel cleanser containing 15% Sodium Cocoyl Isethionate was evaluated using 12 subjects, seven males and five females (CTFA, 1989). Approximately 20 μl of test material, a 4% aqueous solution, was applied with an occlusive patch to the subscapular region of the back for 48 h. At the end of this 48 h period, the patch was removed and the site was scored 6, 24, and 48 h after removal. In this study, three gel cleansers were tested and it was not made clear if they all contained Sodium Cocoyl Isethionate; however, all three were non-irritating.

A 21-day cumulative irritation patch test was conducted using 0.10% w/v aqueous Sodium Cocoyl Isethionate (Hill Top Research, Inc., 1985). A commercial baby oil was used as a low-irritation control and a concentrate from a purchased deodorant was used as a high-irritation control. Of the initial test group of 40, 35 subjects, 26 females and 9 males, completed the study. A modification of the human skin test of cumulative irritation procedure by Phillips et al. (1972) was used. (The Phillips et al. procedure was a modification of a procedure described by Lanman [1968].)

A volume of 0.3 ml of 0.10% Sodium Cocoyl Isethionate in distilled water, and the same amount of each control, was pipetted onto Webril pads that were applied to the right and left paraspinal regions of the back of each subject. The assignment of test areas for each sample varied among the subjects, but each individual received the same compound on the same site for the duration of the study. Any site scored at the maximum allowable limits was not repatched for the remainder of the study. Each patch was applied for 23 h, after which it was removed and discarded by the subject. The subjects were instructed to bathe after patch removal and report to the laboratory for a 24 h scoring and new patch application. This procedure was carried out for 21 consecutive days.

The group mean score of the 35 subjects who completed 21 days of testing was 0.093/4. The highest individual mean score was 1.143. One subject developed a skin eruption adjacent to the tape area on the lowest site; the lesion was a 2 cm inflamed sebaceous cyst related to the patching procedure and not the material under test. Based on these results, Sodium Cocoyl Isethionate was considered a "very mild" irritant.

A repeat application patch test was conducted using Sodium Cocoyl Isethionate (CTFA, 1984a). Ten of 12 subjects completed the study. Sodium Cocoyl Isethionate was tested as 0.2%, 0.4%, and 1.0% w/v aqueous solutions. A test material on which historical data were known was used as a control. A volume of 0.3 ml of test and control solutions was applied to occlusive clinical patches; the patches were applied to each subject's arm in a vertical row. The assignment of test area for each sample varied among the subjects, but each individual received the same compound on the same site for the duration of the study. A site that was scored a grade of 2+/4 was not repatched for the remainder of the study.

A dot of Gentian Violet dye was applied to the skin at the center of both vertical sides of each patch so that the patch site was identifiable after patch removal. The subjects removed the patches and rinsed the site 24 h after the initial patch application. At 72 h, the subjects reported to the laboratory for scoring of the test areas and to have new patches applied. The patches were removed 24 h after the second application and the area was rinsed. At 120 h, the test areas were scored and patches were applied a third time. After 24 h, the final patches were removed and the area was rinsed. The test areas were scored 24 h following patch removal.

At study termination, the average skin grades for the 0.2%, 0.4%, and 1.0% w/v aqueous solutions of Sodium Cocoyl Isethionate were 0.30/4, 0.20/4, and 0.26/4, respectively. Sodium Cocoyl Isethionate was "very mild" at the three concentrations tested.

A 14-day irritation study of a gel cleanser containing 15% Sodium Cocoyl Isethionate was conducted using 19 subjects (CTFA, 1984b). The subjects were initially treated with 1.3 ml of a 4.0% solution. However, this volume was too large for the patches and spreading reactions resulted. On the second day of treatment, 0.1 ml of a 6.0% solution was used. After 5 days of testing, it was determined that this concentration was too irritating. A 4% solution, 0.1 ml, was used throughout the remainder of the study. The test article produced moderate to severe irritation.

Irritation/Sensitization

Four human repeated insult patch tests (HRIPTs), which consisted of nine induction patches and a challenge were performed using washing bars that contained 49.87% Sodium Cocoyl Isethionate (CTFA, 1990c). In each study, four bars were used simultaneously in a closed patch test on the back of each subject, giving a total dose of four times the patch test concentration to areas served by the same draining lymph node. In three of the four studies, the solutions were openly applied to the arms of the subjects each time patches were applied to the back. For 199 and 197 subjects, a 0.1% solution was used in the closed patch test and an 8.0% solution was used in the open test. For 191 subjects, the solutions were 0.1% and 4.0% for the closed patch and open tests, respectively. In the study using only a closed patch test, a solution of 0.5% was used on 192 subjects. The test materials did not produce a sensitization reaction.

A 9 RIPT was performed to determine the irritation and/or sensitization potential of a skin cleanser containing 17% Sodium Cocoyl Isethionate (Essex Testing Clinic, Inc., 1989). Ninety-six of the initial 106 subjects, 17 males and 89 females, completed the study. (One subject, gender unspecified, discontinued because of an intolerance to the test procedure; an autoeczematous eruption, not considered to be induced by the test article, developed.) Approximately 0.2 g of test article was applied to the back of each subject, between the scapulae and the waist and adjacent to the spinal midline, using a semi-occlusive patch that was removed 24 h after application. A 24 h nontreatment period followed the first two applications of each week and a 48 h nontreatment period followed the third application of each week; testing continued until nine applications were made. If a subject developed a reaction score of 2 (pink–red erythema, uniform in the entire contact site) or greater, the test site was moved to a previously unpatched site. If a ≥ 2 score was observed at the new site, no further applications were made but the challenge was performed.

After the ninth application, there was a non-treatment period of 10–21 days. At the end of this period, a challenge patch, dose not given, was applied to a previously unpatched site. This site was scored 24 and 48 h after test article application.

During the induction and/or challenge phases, 12 of 96 subjects had scattered, transient, barely perceptible to mild nonspecific patch test responses; none of these responses were considered to be irritant or allergenic. Two of the 96 subjects had delayed mild to moderate erythematous reactions during the challenge. The skin cleanser containing 17% Sodium Cocoyl Isethionate "did not induce clinically meaningful irritation potential in human subjects." Follow-up testing of the two panelists who had responses during the challenge was performed.

The two subjects who had a response during the challenge of the previous study were retested to determine the nature of the responses (Essex Testing Clinic, Inc., 1989). Test article, 0.2 ml, was applied under a semi-occlusive patch to previously unpatched sites on the back cleansed with 70% isopropyl alcohol. The patch remained in contact with the skin for 24 h. Concurrently, under open patch test conditions, test article was applied to the left ventral forearm near the antecubital region. The open applications were made three times daily for 3 days, for a total of nine open applications. Both patch-type sites were scored at 24, 48, and 72 h after application of the semiocclusive patch.

One subject had no reaction to either the semi-occlusive or open patch applications. The other subject developed a transient, barely perceptible to mild erythematous reaction to the semiocclusive patch application; this response was of less severity than the response to the original challenge. Very tiny papules, with no erythema, developed after nine open applications.

After five additional days of open applications, for a total of 21 open applications, slight drying with no erythema was observed. Although the subject appeared to be " 'sensitive' in an irritant manner," the response to the open testing was not considered significant. The 9 RIPT and rechallenge of the skin cleanser containing 17% Sodium Cocoyl Isethionate "did not induce allergic contact dermatitis or clinically relevant irritation in human subjects."

An RIPT was performed to determine the irritation and/or sensitization potential of a syndet soap containing 47.5% Sodium Cocoyl Isethionate using modified methods of Marzulli and Maibach (1974) (Concordia Research Laboratories, Inc., 1987). The material was tested as a 2% w/v solution. Of the initial 206 subjects, 203 completed the study. Occlusive patches were applied to the upper back, which was cleansed with 70% isopropyl alcohol, in a paraspinal position for 48 h. Upon patch removal, the site was scored for reaction to the test article. The test material was reapplied to the same site for a total of nine applications. However, if a test grade of 3 (erythema and induration) was observed, the patch was moved to an adjacent site for the remaining applications.

A 14-day nontreatment period followed the ninth application, after which a challenge patch with 2% w/v test solution was applied to an adjacent area of the back for 48 h. The site was scored upon patch removal and 72 h after the challenge was applied. The irritation and sensitization potential of the test article was "very low if existent at all."

The irritation and sensitization potential of a gel cleanser containing 15% Sodium Cocoyl Isethionate was evaluated using the Jordan-King modification (Jordan and King, 1977; Jordan, 1980) of the Draize-Shelanski procedure (CTFA, 1985b). Of the initial 158 subjects, 148 completed the study, 19 male and 129 female. The test material was applied to the scapular region of the back under occlusive patches. (It is not stated whether the test material was diluted prior to application.) The patches were applied three times a week and remained in contact with the skin for 48 h during the week and for 72 h on the weekend. Nine applications, resulting in 10 readings, were made to the same site.

There was a nontreatment period of 14 days following the ninth application, after which two consecutive challenge patches with 48 h readings were applied to a different site than previously used on the scapular region of the back. If a score of ≥ 2 (moderately intense erythema, with or without infiltration and involving at least 25% of the test area) was observed, the patch was moved to another site until it was possible to return it to the original site. The gel cleanser containing 15% Sodium Cocoyl Isethionate produced "no allergic responses."

SUMMARY

Sodium Cocoyl Isethionate is used as a surfactant–cleansing agent in cosmetic formulations. It is in the form of a fine white powder, is soluble in water, and does not absorb in the UVA or UVB range. In 1984, it was reported to the FDA that Sodium Cocoyl Isethionate was used in 35 cosmetic formulations at 0.1–50%. In 1992, Sodium Cocoyl Isethionate was reported to be used in 52 cosmetic formulations.

According to the terminology of Hodge and Sterner (1949), Sodium Cocoyl Isethionate is slightly to practically nontoxic, with an oral LD_{50} of ≥4.33 g/kg for rats. Dermal application of 1.0–36.0% w/w aqueous Sodium Cocoyl Isethionate to Charles River COBS^{R} rats for 28 days did not result in significant toxic effects. Erythema was observed at times during the study.

In ocular irritation studies using rabbits, 2.5–49% Sodium Cocoyl Isethionate was a mild to a primary ocular irritant; Sodium Cocoyl Isethionate was defined as an ocular irritant at concentrations ≥15%.

In a dermal study, Sodium Cocoyl Isethionate, 15.0% active and pH 7.0, was moderately irritating to the intact and abraded skin of rabbits. In two dermal irritation studies of 5% Sodium Cocoyl Isethionate solutions using rabbits, the test article was not a primary dermal irritant in one study (but it did have potential for mild irritation) and it was a moderate primary dermal irritant in the other study. A 2% solution of a formulation containing 47.5% Sodium Cocoyl Isethionate was not phototoxic, but it was mildly irritating to the skin of rabbits. In two studies in which a modified Buehler test was performed using guinea pigs, Sodium Cocoyl Isethionate did not produce a sensitization reaction.

Sodium Cocoyl Isethionate was negative in an *in vitro* chromosomal aberration assay at a concentration of 19–300 μg/ml in the presence and absence of metabolic activation. Sodium Cocoyl Isethionate did not produce a positive response in an *S. typhimurium* preincubation reverse mutation assay at concentrations of 10–1000 μg/ml and 1.0–100 μg/ml with and without metabolic activation, respectively.

In human irritation studies, an 8% aqueous solution of Sodium Cocoyl Isethionate produced minimal irritation in five modified soap chamber tests while testing was discontinued in a sixth study due to the resulting irritation. A 4% aqueous solution of a formulation containing 15% Sodium Cocoyl Isethionate was non-irritating. Solutions containing 0.10–1.0% Sodium Cocoyl Isethionate were mildly irritating, where as a 4–6% solution of a formulation containing 15% Sodium Cocoyl Isethionate was a moderate to severe irritant. An RIPT was performed using a formulation containing 49.87% Sodium Cocoyl Isethionate at 0.1–0.5% under a closed patch and at 4.0–8.0% under open conditions. The test article did not produce a sensitization reaction. In two RIPTs, one using a formulation containing 17% Sodium Cocoyl Isethionate and the other using a 2% solution of a formulation containing 47.5% Sodium Cocoyl Isethionate, the test article was not clinically irritating and did not induce allergic contact dermatitis. In a human study using the Jordan-King modification of the Draize-Shelanski procedure, a formulation containing 15% Sodium Cocoyl Isethionate did not produce an allergic reaction.

DISCUSSION

The CIR Expert Panel recognizes that concentration of use data are no longer submitted to the FDA by the cosmetics industry. Due to this fact, it will be difficult for

the Expert Panel to make the conclusion "Safe as used," as was previously done. The Panel must now consider making a conclusion based on the product and test concentrations used in the report.

The greatest concentration of Sodium Cocoyl Isethionate tested as a rinse-off product was 49.87%. The greatest concentration of Sodium Cocoyl Isethionate tested as a leave-on product was 17%. Therefore, the CIR Expert Panel used these concentrations in making a conclusion of safety.

The Expert Panel realizes that Sodium Cocoyl Isethionate may produce ocular irritation. The irritant effects produced by Sodium Cocoyl Isethionate are similar to those produced by other surfactants, with the severity of irritation increasing with increasing concentration.

CONCLUSION

Based on the products and concentrations tested in studies documented in this report, the CIR Expert Panel concludes that Sodium Cocoyl Isethionate is safe for use in cosmetic formulations at 50% in rinse-off products and at 17% in leave-on products.

ACKNOWLEDGMENT

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

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