Safety Assessment of Octyldodecyl Stearoyl Stearate as Used in Cosmetics

Status:	Re-Review for Panel Consideration
Release Date:	September 1, 2022
Panel Meeting Date:	September 26-27, 2022

The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; David E. Cohen, M.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; Allan E. Rettie, Ph.D.; David Ross, Ph.D.; Thomas J. Slaga, Ph.D.; Paul W. Snyder, D.V.M., Ph.D.; and Susan C. Tilton, Ph.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D. This report was prepared by Regina Tucker, M.S., Scientific Analyst/Writer, CIR.

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Memorandum

To: CIR Expert Panel Members and Liaisons
From: Regina Tucker, MS
Scientific Analyst/Writer, CIR
Date: September 1, 2022
Subject: Re-Review of the Safety Assessment of Octyldodecyl Stearoyl Stearate

The Expert Panel for Cosmetic Ingredient Safety (Panel) previously issued an insufficient data conclusion on Octyldodecyl Stearoyl Stearate, and a final report with this conclusion was published in 2001(identified as *originalreport1_OctyldodecylStearoylStearate_092022* in the pdf). Subsequently, the Panel's data needs were met, and a final amended report with the following conclusion was published in 2005: Octyldodecyl Stearoyl Stearate is safe as a cosmetic ingredient in the practices of use and concentration described in this safety assessment. The published final amended report is included for your use (identified as *originalreport2_OctyldodecylStearoylStearate_092022*).

Because it has been at least 15 years since the final amended report was published, in accordance with CIR Procedures, the Panel should consider whether the safety assessment of Octyldodecyl Stearoyl Stearate should be reopened. An exhaustive search of the world's literature was performed for studies dated 2000 forward. It should be noted that this search for safety test data on Octyldodecyl Stearoyl Stearate that have entered the scientific literature since that time did not reveal any new information *(newdata_OctyldodecylStearoylStearate_092022).*

Also included for your review are current and historical use data on Octyldodecyl Stearoyl Stearate (*usetable_OctyldodecylStearoylStearate_092022)*. The reported use frequency of this ingredient increased from 105 formulations (in the 2005 final amended report) to 605 formulations in 2022. Some trends of note are an increase in incidental ingestion and mucous membrane contact from 1 to 48 uses, as well as eye area use from 35 in 2005 to 322 in 2022. The highest use concentration currently reported is in lipstick (28%).

If, upon review of the updated frequency and concentration of use data, the Panel determines that a re-review is warranted, a full draft amended report will be presented at an upcoming meeting.

Re-Review – Octyldodecyl Stearoyl Stearate - History and New Data

(Regina Tucker – September 2022 meeting)

Ingredient (1)	Citation	Conclusion	Use - New Data	Use -Historical Data	Notes
Octyldodecyl Stearoyl Stearate	IJT 20(suppl. 3): 51-59, 2001 IJT 24 (suppl. 3):65-74, 2005	insufficient safe as used	Octyldodecyl Stearoyl Stearate frequency of use (2022): 605 uses conc of use (2022): 0.50-28%	Octyldodecyl Stearoyl Stearate frequency of use (2005): 106 uses conc of use (2001): 2-15%	frequency of use increased; concentration of use increased; two new use categories Hair-(Coloring) and (Non-Coloring)

NOTABLE NEW DATA			
Publication	**Study Type**	**Results – Brief Overview**	**Different from Existing Data?**
no new published data			

Search (from 2000 on)

PubMed

(((“Octyldodecyl Stearoyl Stearate”) OR (90052-75-8[EC/RN Number])) AND (("2000"[Date - Publication]: "3000"[Date - Publication])) – 2 hits; none useful

Current and historical frequency and concentration of use according to duration and exposure for Octyldodecyl Stearoyl Stearate

	# of Uses		*Max Conc of Use (%)*	
	2022[1]	**2005[2]**	**2020[3]**	**2005[2]**
Totals*	**605**	**106**	**0.50-28**	**2-15**
Duration of Use				
Leave-On	*601*	*102*	*0.5-28*	*2-15*
Rinse-Off	*4*	*4*	*3.3-3.5*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*
Eye Area	322	35	0.5-18.5	4-10
Incidental Ingestion	48	1	*3.4-28*	5-10
Incidental Inhalation-Spray	7[a];5[c]	1;5[a];2[c]	NR	8[a]; 4-15[c]
Incidental Inhalation-Powder	105; 5[c]	34; 2[c]	1.9-7.5; 1[b]	2-7; 4-15[c]
Dermal Contact	556	103	0.5-25.4	2-15
Deodorant (underarm)	NR	NR	NR	NR
Hair - Non-Coloring	1	NR	NR	NR
Hair-Coloring	NR	NR	3.3-3.5	NR
Nail	NR	2	NR	NR
Mucous Membrane	48	1	3.4-28	5-10
Baby Products	NR	NR	NR	NR

*Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.

[a] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.

[b] It is possible these products are powders, but it is not specified whether the reported uses are powders.

[c] Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories

NR – no reported use

REFERENCES

1. U.S. Food and Drug Administration Center for Food Safety & Applied Nutrition (CFSAN). 2020. Voluntary Cosmetic Registration Program - Frequency of use of Cosmetic Ingredients. College Park, MD. Obtained under the Freedom of Information Act from CFSAN; requested as "Frequency of Use Data" January 4, 2022; received January 11, 2022

2. Andersen FA. Final amended report on the safety assessment of Octyldodecyl Stearoyl Stearate. *Int J Toxicol.* 2005;24 Suppl 3:65-74.

3. Personal Care Products Council Concentration of use by FDA Product Category: 2020 Octyldodecyl Stearoyl Stearate. Unpublished data submitted by the Personal Care Products Council on October 13, 2020

Final Report on the Safety Assessment of Octyldodecyl Stearoyl Stearate[1]

Octyldodecyl Stearoyl Stearate functions as an occlusive skin-conditioning agent and as a nonaqueous viscosity-increasing agent in many cosmetic formulations. Current concentrations of use are between 0.7% and 23%, although historically higher concentrations were used. The chemical is formed by a high-temperature, acid-catalyzed esterification reaction of long-chain alcohols (primarily C-20) and a mixture of primarily C-18 fatty acids. Levels of stearic acid, octyldodecanol, and octylydocecyl hydroxystearate in the final product are 5% or less—no other residual compounds are reported. Only limited safety test data were available on Octyldodecyl Stearoyl Stearate, but previous safety assessments of long-chain alcohols and fatty acids found these precursors to be safe for use in cosmetic formulations. Octyldodecyl Stearoyl Stearate produced no adverse effects in acute exposures in rats. The chemical was mostly nonirritating to animal skin at concentrations ranging from 7.5% to 10%; one study did find moderate irritation in rabbit skin at a concentration of 7.5%. Clinical tests at a concentration of 10.4% confirmed the absence of significant irritation in humans. An ocular toxicity study in rabbits found no toxicity. No evidence of genotoxicity was found in either a mammalian test system or in the Ames test system, with or without metabolic activation. The available data on Octyldodecyl Stearoyl Stearate and the previously considered data on long-chain alcohols and fatty acids, however, did not provide a sufficient basis to make a determination of safety. Additional data needs include (1) chemical properties, including the octanol/water partition coefficient; and (2) if there is significant dermal absorption or if significant quantities of the ingredient may contact mucous membranes or be ingested, then reproductive and developmental toxicity data may be needed. Until such time as these data are received, the available data do not support the safety of Octyldodecyl Stearoyl Stearate as used in cosmetic formulations.

INTRODUCTION

Octyldodecyl Stearoyl Stearate is an ester that functions as a skin-conditioning agent—occlusive and a viscosity-increasing agent—nonaqueous in cosmetic product formulations. Only limited data on Octyldodecyl Stearoyl Stearate were found. The safety of the following related ingredients has been reviewed, with the conclusions listed below:

Stearyl Alcohol, Oleyl Alcohol, and Octyl Dodecanol are safe as currently used in cosmetics (Elder 1985a).

Oleic Acid, Lauric Acid, Palmitic Acid, Myristic Acid, and Stearic Acid are safe in the present practices of use and concentration in cosmetics (Elder 1987).

Butyl, Cetyl, Isobutyl, Isocetyl, Isopropyl, Myristyl and Octyl, Stearate are safe as cosmetic ingredients in the present practices of use (Elder 1985b).

Pertinent data from these reports have been added to this review (*italicized text*) as a further basis for the assessment of safety of Octyldodecyl Stearoyl Stearate.

CHEMISTRY

Definition and Structure

Octyldodecyl Stearoyl Stearate (CAS No. 90052-75-8) is an ester that conforms generally to the formula presented in Figure 1. Synonyms for Octyldodecyl Stearoyl Stearate include Octadecanoic Acid, 12-[(1-Oxooctadecyl)Oxy]-, 2-Octyldodecyl Ester; Octadecanoic Acid, 12-[(1-Oxooctadecyl)Oxy]-2-Octyldodecyl Ester; and 12-[(1-Oxooctadecyl)Oxy]Octadecanoic Acid, 2-Octyldodecyl Ester (Wenninger, Canterbery, and McEwen 2000).

Related Ingredients

Octyl Dodecanol is the long-chain saturated fatty alcohol that conforms to the structure presented in Figure 2 (Elder 1985a).

Stearic Acid is found primarily as a glyceride in animal fats and oils; lard and tallow contain approximately 10% and 20% Stearic Acid, respectively. Most vegetable oils contain 1% to 5% Stearic Acid; cocoa butter contains approximately 35%. Cosmetic grade Stearic Acid occurs as a mixture of fatty acids, depending on the method of manufacture and source. Commercial Stearic Acid is primarily a mixture of varying amounts of Stearic and Palmitic Acids. Components of Stearic Acid are octadecanoic acid (39% to 95%), hexadecanoic acid (5% to 50%), tetradecanoic acid (0% to 3%), 9-octadecenoic acid (0% to 5%), heptadecanoic acid (0% to 2.5%), eicosanoic acid (0% to 2%), and pentadecanoic acid (0% to 1%). Butylated hydroxytoluene can be added to preparations containing fatty acids as an antioxidant at concentrations of 0.01% to 0.1% for unsaturated materials (Elder 1987).

Received 15 May 2001; accepted 12 July 2001.

[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.

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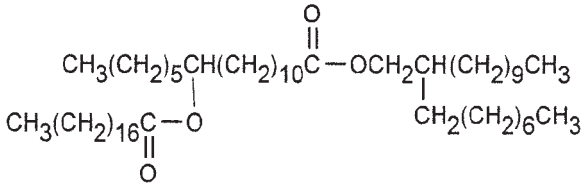

FIGURE 1
Octyldodecyl Stearoyl Stearate.

The Stearates are esters of stearic acid; Octyl Stearate conforms generally to the formula in Figure 3 (Elder 1985b).

Chemical and Physical Properties

The physical form of Octydodecyl Stearoyl Stearate, as the trade compound, occurs as an amber, yellow liquid with a mild, characteristic odor. Its specifications include saponification number of 115.0 to 135.0; specific gravity (25°C) range 0.86 to 0.88; and a refractive index (25°C) of 1.45 to 1.47 (ISP Van Dyke, Inc. 1997).

Octydodecyl Stearoyl Stearate is soluble in silicones; esters; mineral oil; vegetable oils; alcohols; aliphatic, aromatic, and chlorinated hydrocarbons; and is insoluble in water. It has a theoretical molecular weight of 846 Da, a freezing point of −15°C, and a flash point of over 180°C (Alzo, Inc. 1998). Octyldodecyl Stearoyl Stearate is partly soluble in 95% ethanol, propylene glycol, glycerine, 70% sorbitol, and PEG 400 (Trivent Chemical Company, Inc. 1998).

Related Ingredients

Stearic Acid occurs as a hard, white or faintly yellow, glossy crystals or leaflets or as an amorphous white or yellow-white powder. It has a slight odor and tallow-like flavor. Stearic Acid is water insoluble, slightly soluble in alcohol and benzene, soluble in chloroform, and very soluble in ether. The molecular weight is ~284.5 Da (Elder 1987).

Octyl Stearate and the other Stearates are either oily liquids or waxy solids that typically are soluble in organic solvents such as chloroform and acetone. The molecular weight of Octyl Stearate is 396 Da, the ester value is 144 to 154, the acid value and iodine value each have a maximum of 1.0. The Stearates can undergo conversion into stearic acid and the corresponding alcohol by chemical or enzymatic hydrolysis, conversion into amides by ammonolysis, and conversion into different esters by alcoholysis or transesterification. Purer grades of the saturated Stearates are not expected to autoxidize readily (Elder 1985b).

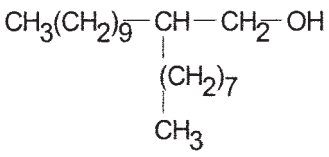

FIGURE 2
Octyl Dodecanol.

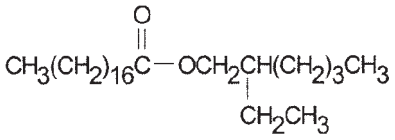

FIGURE 3
Octyl Stearate.

Method of Manufacture

Octyldodecyl Stearoyl Stearate is manufactured by an inorganic acid catalyzed, high temperature (150°C to 160°C) esterification reaction of guerbet alcohol. Guerbet alcohol is comprised of a mixture of guerbet alcohols (primarily C-20) and no other impurity and a mixture of fatty acids (primarily C-18) and no other impurities. The product is neutralized to a water-soluble soap, washed to purity, dried, and filtered (Alzo, Inc. 1998).

Related Ingredients

Octyl Dodecanol is produced by the condensation of two molecules of decyl alcohol, and occurs naturally in small quantities as components of wax esters in plants (Elder 1985a).

Methods of processing Stearic Acid include hydrolysis of tallow or hydrogenation of unsaturated fatty acids in cottonseed and other vegetable oils, followed by fractional distillation or crystallization. Concentrations of Stearic Acid as great as 95% to 99% have been reported from the hydrogenation of unsaturated fatty acids (Elder 1987).

The Stearates are prepared by esterification of stearic acid with the appropriate alcohol in the presence of an acid catalyst. The reaction products are refined either by catalyst neutralization, vacuum distillation, or various decolorization-deodorization techniques to remove residual traces of alcohol (Elder 1985b).

Impurities

Octyldodecyl Stearoyl Stearate is composed of Stearic Acid (2.5% maximum), Octyldodecanol (5.0% maximum), Octyldodecyl Hydroxystearate (5.0% maximum), and Octyldodecyl Stearoyl Stearate (88.0% maximum) (Alzo, Inc. 1998).

Related Ingredients

Stearic Acid contains varying amounts of unsaponifiable matter (0.3% maximum), and can contain glyceryl monostearate (0.07% maximum). Typical impurities are glyceryl monomyristate (0.07% maximum), 9-hexadecanoic acid, 9,12-octadecadienoic acid (Elder 1987).

USE

Cosmetic

Octyldodecyl Stearoyl Stearate functions as a skin-conditioning agent—occlusive and viscosity increasing agent—nonaqueous in cosmetic product formulations (Wenninger, Canterbery, and McEwen 2000).

In 1998, industry reported to the Food and Drug Administration (FDA) that Octyldodecyl Stearoyl Stearate was used in 86 cosmetic formulations (FDA 1998). Table 1 gives the number of formulations in each cosmetic product category containing Octyldodecyl Stearoyl Stearate, along with the total number of formulations in each category. Concentration of use data provided by industry, ranging from a low of 0.7% in makeup preparations to 20% in lipstick, are also included in Table 1. Table 2 gives the historical (FDA 1984) concentration and frequency of use of Octyldodecyl Stearoyl Stearate. For comparison purposes, historical concentration and frequency of use data for Stearic Acid and Octyl Stearate, as reported to FDA in 1984, are included in Table 2.

International

Octyldodecyl Stearoyl Stearate is listed in the *Japanese Comprehensive Licensing Standards of Cosmetics by Category (CLS)* (Santucci 1999). Octyldodecyl Stearoyl Stearate has precedent for use without restriction in all *CLS* categories. According to Notification 990 of the Pharmaceutical and Medical Safety Bureau of the Japan Ministry of Health and Welfare, issued September 29, 2000, Octyldodecyl Stearoyl Stearate is not prohibited or restricted in its use beyond a basic obligation of manufacturers to use all ingredients in a manner which guarantees safety (Japan Ministry of Health and Welfare 2000).

GENERAL BIOLOGY

No data on absorption, distribution, metabolism, or excretion of Octyldodecyl Stearoyl Stearate were available.

Related Ingredients

Stearic Acid and other fatty acids are digested from the diet, absorbed in micellar aggregates, and transported after

TABLE 1
Product formulation data

Product category (total formulations in category) (FDA 1998)	Total no. of formulations containing Octyldodecyl Stearoyl Stearate (FDA 1998)	Current concentration of use (CTFA 1998a, 1998c, 1999) %
Bubble baths (200)	1	—
Eyebrow pencil (91)	2	0.8
Eyeliner (514)	1	4–12
Eye shadow (506)	20	11.7
Other eye makeup preparations (120)	2	5
Powders (fragrance) (247)	2	3–3.4
Other fragrance preparations (148)	1	4–4.3
Hair tints	—	0.8
Blushers (all types) (238)	5	2–7.4
Face powders (250)	29	7
Foundations (287)	5	5–6.3
Lipstick (790)	1	4–20
Makeup bases (132)	4	—
Rouges (12)	1	—
Other makeup preparations	—	0.7–15
Cuticle softeners (19)	1	21
Nail creams and lotions (17)	1	—
Shaving cream	—	3
Cleansing preparations (653)	2	—
Face and neck (excluding shaving) (263)	1	—
Moisturizing preparations (769)	3	—
Night preparations (188)	1	—
Paste masks (mud packs) (255)	1	—
Other skin care preparations (692)	2	—
1998 total for Octyldodecyl Stearoyl Stearate	**86**	

TABLE 2
Historical concentrations and frequencies of use (FDA 1984)

	Concentration of use (%)							
Ingredient	≤0.1	>0.1–1	>1–5	>5–10	>10–25	>25–50	>50	1984 Total
Octyldodecyl Stearoyl Stearate	2	2	7		9			20
Octyl Dodecanol	4	23	60	195	70	18	1	371
Stearic Acid	6	231	1826	231	148	22	1	2465
Octyl Stearate		7	2		1			10

esterification to glycerol in chylomicrons and very-low-density lipoproteins. Stearic Acid is primarily transported via the lymph system. Fatty acids originating from adipose tissue stores are either bound to serum albumin or remain unesterified in the blood. Stearic Acid was the most poorly absorbed of the common fatty acids; the digestibility of fatty acids decreased with increased fatty acid chain length. Radioactivity has been traced to the heart, liver, lungs, spleen, kidneys, muscles, intestines, adrenal glands, blood, and lymph, and to adipose, mucosal, and dental tissues after administration of radioactive Stearic Acid to rats, dogs, sheep, chicks, frogs, and humans. Uptake and transport of fatty acids into the brain has been observed, and free fatty acids readily cross the placental barrier in rabbits, guinea pigs, rats, and humans. Fatty acids that are taken up by tissues are either stored in the form of triglycerides or oxidized for energy (Elder 1987).

ANIMAL TOXICOLOGY

Octydodecyl Stearoyl Stearate, tested as a trade compound at an oral dose of 5.0 mg/kg in 10 rats (5 of each sex) for 14 days, produced no deaths (Wells Laboratories, Inc. 1993). Octydodecyl Stearoyl Stearate, tested as a trade compound, had an oral LD50 of >20 g/kg in albino rats (Food and Drug Research Labs, Inc. 1983). No additional animal toxicology data were available. No data on the carcinogenicity and reproductive and developmental toxicity of Octyldodecyl Stearoyl Stearate were available.

Related Ingredients

No deaths were observed during acute oral toxicity studies when 5 to 10 rats were treated with 5 g/kg of undiluted Octyl Dodecanol or with a lipstick (25 g/kg, diluted to 50%) containing 10.2% Octyl Dodecanol (1.28 g/kg total dose). In an acute dermal toxicity study, intact and abraded skin sites of six guinea pigs were treated with 3.0 g/kg of the undiluted alcohol under occlusive patches. No deaths occurred as a result of treatment, and no gross lesions were observed at necropsy (Elder 1985a).

Little acute toxicity was observed when Stearic Acid or cosmetic formulations containing Stearic Acid at concentrations up to 13% were given orally to rats at doses of 15 to 19 g/kg. In subchronic oral studies, Stearic Acid (5% to 50%) caused thrombosis, aortic atherosclerosis, anorexia, and mortality in rats. Chicks fed 5% Stearic Acid had no signs of toxicity. Topical applications of 5 g/kg Stearic Acid to rabbits did not cause adverse effects. Intradermal administration of 10 to 100 mM Stearic Acid caused mild erythema and slight induration in guinea pigs and rabbits (Elder 1987).

Octyl Stearate generally had "very low" acute oral toxicity in rats and mice. Undiluted Octyl Stearate at a dose of 8 ml/kg did not cause deaths in five rats per sex. Body weight gain averaged 25.7% during the 2-week observation period (Elder 1985b).

Ocular Irritation

An EYETEX in vitro irritation assay was performed on a nail cuticle pencil containing 20.6% Octyldodecyl Stearoyl Stearate. The test material produced scores consistent with minimal to mild irritation (CTFA 1998b).

An undiluted eyeliner containing 7.5% Octyldodecyl Stearoyl Stearate was applied three times to the unrinsed eyes of six rabbits. One rabbit had conjunctival scores of 6, 2, and 2 on days 1, 3, and 4, respectively, and a corneal score of 5 on day 1. Another had a conjunctival score of 4 on day 1. None of the rabbits had signs of ocular toxicity on days 2 or 7. The total Draize scores were 4/110 on day 1 and 1/110 on days 3 and 4. The investigators concluded that the eyeshadow was moderately irritating under the conditions of this study.

A concealer containing 12.7% Octyldodecyl Stearoyl Stearate was applied once to the unrinsed eyes of six rabbits. One rabbit each had conjunctival scores of 2 on days 1 and 2. None of the rabbits had signs of irritancy on days 3, and 4, or 7. The total Draize scores were 1/110 on days 1 and 2 and the formulation was classified as mildly irritating.

In a third study, none of the six rabbits had signs of ocular irritation after treatment with a lipstick containing 7.8% Octyldodecyl Stearoyl Stearate. The lipstick was classified as nonirritating (CTFA 1998b).

Octydodecyl Stearoyl Stearate, tested as a trade compound, was instilled (0.1 ml) into the right conjunctival sac of six rabbits. The contralateral eye served as the control. Eyes were not rinsed. Reactions were scored on days 1 to 4, and 7 according to the Draize scale. No reactions were observed (Consumer Product Testing 1978).

A single application of 0.1 ml of Octydodecyl Stearoyl Stearate, at a 10% *w/w* dilution in corn oil, was instilled into one eye each of six rabbits. The contralateral eye served as the control and the eyes were not rinsed. Reactions were scored on days 1 to 3, and 4 and 7 if irritation persisted. No reactions were observed (Wells Laboratories, Inc. 1993).

Related Ingredients

Six rabbits were treated with 100% Octyl Dodecanol. The average ocular irritation scores were 4/110 at day 1 and 0/110 by day 4. In a second study using the same procedure, the scores were 1/110 at day 1 and 0/110 by day 4. Cosmetic formulations containing 3% to 10.2% Octyl Dodecanol caused either no ocular irritation or minimal, transient irritation in the eyes of rabbits (Elder 1985a).

Undiluted Octyl Stearate caused slight, transient ocular irritation in rabbits (Elder 1985b).

Skin Irritation and Sensitization

An undiluted eyeshadow containing 7.5% Octyldodecyl Stearoyl Stearate was moderately irritating to the skin in a single insult occlusive patch test using nine rabbits. Erythema and edema were observed at 2 and 24 hours after application of the test material. The primary irritation index (PII) for the group was 3.89/8.00.

In a similar study, a concealer containing 7.8% Octyldodecyl Stearoyl Stearate was tested using nine rabbits. The skin sites were evaluated 2 and 24 hours after application of the test material. No signs of irritancy were observed at 24 hours, but erythema was observed at 2 hours. The PII for the group was 0.67/8.00, and the formulation was classified as minimally irritating.

A lipstick containing 7.8% Octyldodecyl Stearoyl Stearate was tested similarly using nine rabbits. None of the animals had erythema or edema 2 or 24 hours after application of the test material, and the PII was 0.00/8.00. In a 4-day cumulative study, the lipstick was "essentially non-irritating" (CTFA 1998b).

Octydodecyl Stearoyl Stearate, tested as a trade compound, was applied (0.5 ml) under a 24-hour occlusive patch to abraded and intact sites on the backs of six rabbits. Sites were examined for erythema and edema at 24 and 72 hours. The maximum possible score was 8. The PII for Octydodecyl Stearoyl Stearate was 0.38. It was considered to have a "potential for slight irritation—rarely irritating to people" (Consumer Product Testing 1978).

A single dermal application of 0.5 ml of Octyldodecyl Stearoyl Stearate, at a 10% *w/w* dilution in corn oil, was applied to one abraded and one intact site on six New Zealand white rabbits. Each test site was observed for erythema and edema 24 and 72 hours after application. The PII for this product was 0.0 (Wells Laboratories, Inc. 1993).

In a rabbit dermal irritation test Octyldodecyl Stearoyl Stearate had a PII of 0.38. No additional details were available (International Specialty Products 1998).

Related Ingredients

Octyl Dodecanol was applied for 24 hours under occlusive patches to the skin of six rabbits during three studies. The irritation scores for a concentration of 100% were 1.13/4, 0.5/4, and 0/4. At a concentration of 30%, it produced scores of 0/4 for all three studies.

Techical grade Octyl Dodecanol (0.1 to 0.5 g) caused severe irritation (+++) to the skin of six albino rabbits and moderate irritation (++) to the skin of six Hartley guinea pigs and six Wistar rats. The compound was nonirritating (−) when applied to the skin of six Pitman-Moore miniature swine. For the study using rabbits, 0.1 g Octyl Dodecanol was applied for 24 hours, the skin sites were graded, and the compound was reapplied for another 24 hours. The treated skin sites were graded after Evans blue solution was injected intravenously. The rabbits were killed 1 hour later, and skin samples were prepared. For the guinea pig study, two dorsal areas were clipped free of hair. One site was treated with 0.1 g for 24 hours and the other was left untreated. The remainder of the study was identical to the one using rabbits. For the swine, the dorsal area was clipped free of hair, and 0.5 g Octyl Dodecanol was applied under occlusive patches for 48 hours. Skin of the rabbits, guinea pigs, and rats had acanthosis, hyperkeratinization, swelling of cells, and proliferation of basal cells. Vasodilatation, edema, alteration of collagenous fibers, and mononuclear and polymorphonuclear leukocytes infiltration of the dermis were also observed.

A formulation containing 4% Octyl Dodecanol was nonirritating to mildly irritating (0/4 to 1.08/4) during primary skin irritation studies. Minimal to mild irritation was observed when a formulation containing 10.2% of the alcohol was applied to the skin of rabbits for 3 to 4 consecutive days. In these studies, the degree of irritation observed did not increase with the concentration tested (Elder 1985a).

No irritation was observed when Stearic Acid was applied (18 mmol %) to the skin of the external ear canals of albino rabbits over a period of 6 weeks. Slight local edema was observed when New Zealand white rabbits were treated with 2% Stearic Acid in formulation for 4 weeks. During a 13-week study, cosmetic formulations containing up to 5% Stearic Acid caused moderate skin irritation in rats (4.0 mg/kg, 227 mg/kg). In single-insult patch tests, 35% to 65% Stearic Acid caused no to moderate erythema and slight, if any, edema to the skin of rabbits. In maximization studies, 1% Stearic Acid caused weak reactions at challenge, and was considered a grade 1 sensitizer. Stearic Acid at a concentration of 2.8% did not cause photosensitization in guinea pigs (Elder 1987).

Undiluted Octyl Stearate produced at most minimal or moderate skin irritation in rabbits. Application of the stearate to the skin of rabbits caused irritation after 60 days of treatment; vesicles and slight epidermal exfoliation were observed, and Octyl Stearate was considered "poorly tolerated." Microscopic changes in the treated skin included epidermal acanthosis and "congestive" dermatitis. Application of 10% aqueous Octyl Stearate daily for 60 days caused irritation (vesicles) in the skin

of rabbits, but was "relatively well tolerated." No significant lesions were observed at microscopic examination of the treated skin (Elder 1985b).

GENOTOXICITY

A micronucleated polychromatic erythrocyte (MPCE) assay was used to determine the genotoxicity of Octyldodecyl Stearoyl Stearate tested under a trade name. CD-1 mice (5/sex/group) were gavaged with a single dose of 2.0, 5.0, or 10.0 ml/kg Octyldodecyl Stearoyl Stearate. One negative-control group was designated for each of the three runs of each treatment group. One group was designated as the positive control. Five male and five female mice were killed from each dose and vehicle control at 24, 48, and 72 hours after the initiation of treatment. Five mice from each sex were killed from the positive-control group 24 hours after treatment. The positive control depressed the polychromatic erythrocyte/normochromatic erythrocyte (PCE/NCE) ratio and showed a statistically significant increase in MPCEs. The mean numbers of MPCEs in 1000 PCEs were 58.8 and 65.2 for the male and female mice, respectively, which fulfilled the criteria for a valid assay. No significant increases occurred in the proportion of MPCEs in the test groups compared to the concurrent negative-control groups (Sitek Research Laboratories 1994a).

A *Salmonella typhimurium* gene mutation assay was used to evaluate Octyldodecyl Stearoyl Stearate for its ability to induce mutations in strains TA98, TA100, TA1535, TA1537, and TA1538. Octyldodecyl Stearoyl Stearate was dosed at concentrations of 1.0, 5.0, 10.0, 50.0, and 100.0 μl/plate. The positive controls and Octyldodecyl Stearoyl Stearate were tested with and without S-9 activation. All test concentrations, including the positive and negative controls, were tested in triplicate and a confirmation assay was performed. Octyldodecyl Stearoyl Stearate and control treatments were performed under ultraviolet (UV)-filtered lights to avoid photoinactivation. Positive controls were considered acceptable because the treated strains had reversion frequencies three times or greater than the mean reversion frequency of the solvent control plates in all positive-control cultures with and without S-9 activation. Octyldodecyl Stearoyl Stearate did not induce any positive increase in the number of revertant colonies for any of the tester strains with or without S-9 activation (Sitek Research Laboratories 1994b).

Related Ingredients

Stearic Acid did not induce an increase of mitotic crossovers during in vitro mutagenicity assays. It was inactive during aneuploidy induction tests, and was nonmutagenic in the Ames test (Elder 1987).

CARCINOGENICITY

No data on the carcinogenicity of Octyldodecyl Stearoyl Stearate were available.

Related Ingredients

Mice that received single or repeated subcutaneous (SC) injections of Stearic Acid (up to 82 mg) had low incidences of carcinomas, sarcomas, and lymphomas. Mice fed up to 50 g/kg/day Stearic Acid did not develop neoplasms (Elder 1987).

CLINICAL ASSESSMENT OF SAFETY

The human irritancy potential of an eyeshadow pencil having 10.4% Octyldodecyl Stearoyl Stearate was evaluated in a single-insult patch test using 19 subjects. The PII was 0/8, and no differences in irritancy were observed between subjects of the test and control groups.

A concealer containing 5.0% Octyldodecyl Stearoyl Stearate was tested for primary irritation using 20 subjects. The PII was 0.08, and no significant differences in irritancy were observed between test subjects and controls. A lipstick having 15.0% Octyldodecyl Stearoyl Stearate was similarly tested using 18 subjects. The PII was 0.00/8.00, and no differences in irritancy were observed between groups (CTFA 1998b).

Thirteen volunteers, 10 of whom completed the study, were used in a cumulative irritation study of an eyeshadow having 10.4% Octyldodecyl Stearoyl Stearate. The test material was applied to the skin of the back 21 times for 23-hour intervals. Scoring for cumulative irritation and reapplication of the eyeshadow occurred every 24 hours. The test sites were covered with closed Parke-Davis patches with Webril. The total score was 1/630, and the eyeshadow was classified as a mild irritant (Hill Top Research 1983a).

The same eyeshadow (10.4%) was evaluated in a repeat-insult patch test using 107 subjects. Applications were made three times weekly during the 22-day induction period. The test material was applied for 24 hours to the skin of the back under a closed patch, and the skin sites were scored 48 or 72 hours after application. Challenge applications were made using 24-hour occlusive patches. No evidence of contact sensitization was observed in any of the test subjects (Hill Top Research 1983b).

A lipstick containing 7.8% Octyldodecyl Stearoyl Stearate was tested in a repeat-insult patch test using 87 panelists, 85 of whom completed the study. Occlusive patches containing the test materials were applied to the skin of the upper back for 24 hours, three times weekly, for 3 weeks. Challenge applications were made 3 weeks after the last induction treatment, and the skin sites were scored 24 and 48 hours after patch removal. None of the subjects had erythematous responses during induction or challenge, and the investigators concluded that the lipstick did not have allergic sensitization potential (CTFA 1998b).

The contact sensitization potential of a concealer containing 5.0% Octyldodecyl Stearoyl Stearate was determined using a maximization test. Patches were applied to the outer arm throughout three phases: pretesting, induction, and challenge. In the pretesting phase, approximately 0.1 g of the material was applied to a skin site under a 15-mm Webril patch, which was fixed to the skin with occlusive tape (Blenderm) and covered with Scanpor tape. The patch was removed after 48 hours and the skin site was examined for signs of irritation. During the induction phase, ~0.1 ml of aqueous sodium lauryl sulfate (SLS,

1%) was applied to a different site and similarly covered for 24 hours. After removal of the SLS patch, 0.1 g of the test material was applied to the same site and covered with an occlusive patch. This patch was removed after 48 or 72 hours, when the site was examined for irritation. This procedure was repeated for a total of five induction exposures. If irritation developed during induction, the 24-hour SLS patch was eliminated and only the test material was administered, after a 24-hour period, during which no patch was applied. After a 10-day nontreatment period, a new skin site on the opposite arm was treated with 0.1 ml of 10.0% SLS under an occlusive patch. The site was then challenged with a single application of the test material, and this patch was removed after 48 hours. The treatment site was examined for irritation 1 and 24 hours after patch removal. None of the 27 subjects had adverse reactions, and no contact sensitization was observed (Ivy Laboratories 1991).

A clinical use study was performed using the same lipstick and 62 female subjects. The women applied the lipstick at least twice daily for 3 weeks. No clinical changes were observed after use of the lipstick (CTFA 1998b).

Related Ingredients

Octyl Dodecanol at a concentration of 100% caused mild irritation in 1 of 40 subjects during a 24-hour single-insult patch test; in a similar test, a moisturizing cream (4.0%) was nonirritating or minimally irritating. Occlusive patches containing 0.05 g (undiluted) Octyl Dodecanol were affixed to the backs of 50 adult males. The patches were removed at 48 hours and the treated sites were evaluated 30 minutes later and at 72 to 120 hours. No signs of irritation were observed. When 3% Octyl Dodecanol was patch tested daily for 21 consecutive days, the alcohol was "essentially nonirritating" or "slightly irritating."

No signs of sensitization were observed when 3% to 10.2% Octyl Dodecanol was tested in a Draize-Shelanski repeat-insult patch test. In other studies, no signs of phototoxicity or photosensitization were observed when a lipstick containing 10.2% Octyl Dodecanol was tested using 23 subjects (Elder 1985a).

Stearic Acid was nonirritating in clinical primary or cumulative irritation studies at concentrations of 100% or 40% to 50% in mineral oil. Cosmetic formulations containing up to 93% Stearic Acid and other fatty acids caused mild to intense erythema, but the reactions were not considered related to the fatty acid content of the products. Stearic Acid at concentrations up to 13% was not a sensitizer, and formulations containing 1% to 13% Stearic Acid were not photosensitizing (Elder 1987).

A suntan lotion and protective facial cream containing 7.6% Octyl Stearate were applied to the skin of 56 subjects daily under 24-hour closed patches for a total of 10 induction applications; after a 10- to 14-day nontreatment period, a 24-hour challenge patch was applied. No signs of irritation or sensitization were observed. In a phototoxicity study using the same formulations (10 subjects), no significant reactions were noted. In a photosensitization study on the same formulations (27 subjects), slight reactions were observed in 4 subjects during induction. One had erythema at challenge, and three subjects only reacted during induction. The investigator concluded that the formulations did not produce photosensitization (Elder 1985b).

SUMMARY

Octyldodecyl Stearoyl Stearate is an ester that functions as a skin-conditioning agent and viscosity-increasing agent in cosmetic products. In 1998, it was reported used in 86 cosmetic formulations. Data submitted by industry indicated that Octyldodecyl Stearoyl Stearate historically was used at concentrations in the 10% to 25% range, but in current data the maximum concentration is in the 5% to 23% range.

Little acute toxicity was reported in animal tests of Octyldodecyl Stearoyl Stearate, Stearic Acid, and Octyl Stearate.

A formulation having 20.6% Octyldodecyl Stearoyl Stearate was classified as minimally to mildly irritating in an in vitro ocular irritation assay. Rabbits treated three times with a formulation having 7.5% of the ingredient had moderate irritation. Formulations having 7.8%, 10.0%, and 12.7% Octyldodecyl Stearoyl Stearate were nonirritating to mildly irritating in the Draize ocular irritation test.

An eyeshadow having 7.5% Octyldodecyl Stearoyl Stearate was moderately irritating to the skin of rabbits, with a PII of 3.89/8. In two primary irritation studies and a 4-day cumulative irritation study, however, formulations having 7.8% Octyldodecyl Stearoyl Stearate were nonirritating to minimally irritating, with PIIs of 0 to 0.67/8, and a single application of the ingredient at 10% produced no irritation.

In clinical single-insult patch tests using up to 20 subjects, formulations having 5.0% to 15.0% Octyldodecyl Stearoyl Stearate were nonirritating to mild (PIIs 0 to 0.08/8). In a cumulative irritation study, a formulation having 10.4% Octyldodecyl Stearoyl Stearate caused mild irritation when tested using 10 subjects. Formulations having 5.0% to 10.4% Octyldodecyl Stearoyl Stearate were nonsensitizing in two repeat-insult patch tests using 27 to 85 panelists and a maximization test using 107 subjects. No adverse effects were observed in 62 women who took part in a 3-week in-use study of a formulation having 7.8% Octyldodecyl Stearoyl Stearate.

As a further basis for the assessment of safety of Octyldodecyl Stearoyl Stearate, data on related ingredients (Octyl Dodecanol, Stearic Acid, and Octyl Stearate) were included in this review.

Related Ingredients

Fatty acids are digested from the diet and esterified to glycerol. Stearic Acid is the most poorly absorbed of the common fatty acids. Free fatty acids readily cross the placental barrier and are stored in the tissues or oxidized for energy.

Undiluted Octyl Dodecanol was nontoxic during acute oral and dermal studies using rats and guinea pigs. Stearic Acid was nontoxic during acute oral studies using rats, but caused toxicity during subchronic studies. Rabbits treated topically with the acid were not affected adversely, and mild erythema and slight

induration were observed when Stearic Acid was administered intradermally to guinea pigs and rabbits. Octyl Stearate had very low acute oral toxicity in rats and mice.

Octyl Dodecanol caused no to minimal ocular irritation in rabbits when administered at concentrations up to 100%. Octyl Dodecanol (100%) caused primary skin irritation scores of 0/4 to 1.13/4 in studies using rabbits, and a concentration of 30% was nonirritating. Technical grade Octyl Dodecanol, however, caused moderate to severe irritation in the skin of rabbits, guinea pigs, and rats, but was nonirritating in the skin of miniature swine. A formulation containing 4% Octyl Dodecanol was not to mildly irritating in the skin of rabbits. Stearic Acid was not to moderately irritating in studies using rabbits and rats, and did not cause photosensitization in guinea pigs. In studies using rabbits, undiluted Octyl Stearate caused slight, transient ocular irritation and, at most, minimal to moderate skin irritation.

Stearic Acid did not induce mitotic crossovers and aneuploidy, and was nonmutagenic in the Ames test. In an MPCE genotoxicity assay Octyldodecyl Stearoyl Stearate produced no significant increases in the proportion of MPCE in the test groups compared to the concurrent negative-control groups. In a Salmonella typhimurium *gene mutation assay Octyldodecyl Stearoyl Stearate did not induce any positive increase in the number of revertant colonies for any of the tester strains with or without S-9 activation. In a feeding study using mice, Stearic Acid was noncarcinogenic at doses up to 50 g/kg/day. Mice given SC injections of the acid had low incidences of carcinomas, sarcomas, and lymphomas.*

In clinical studies, concentrations of up to 100% Octyl Dodecanol were not to mildly irritating, nonsensitizing, nonphototoxic, and nonphotosensitizing. Stearic Acid was nonirritating at concentrations up to 100%, and at concentrations up to 13% it was nonsensitizing and nonphotosensitizing. Octyl Stearate (7.6%) in formulation was nonirritating, nonsensitizing, and nonphotosensitizing.

DISCUSSION

Section 1, paragraph (p) of the Cosmetic Ingredient Review (CIR) Procedures states that "a lack of information about an ingredient shall not be sufficient to justify a determination of safety." In accordance with Section 30(j)(2)(A) of the Procedures, the Expert Panel informed the public of its decision that the data on Octyldodecyl Stearoyl Stearate were not sufficient for determining whether the ingredients, under relevant conditions of use, were either safe or unsafe.

In response to specific requests for data, current concentration of use, dermal irritation and sensitization, and ocular toxicity data were received. In addition, genotoxicity, skin irritation/sensitization, ocular irritation, animal toxicity, cosmetic use, and chemical and physical properties data were provided. These data support the absence of any significant acute or chronic toxicity associated with this ingredient, and demonstrate that skin irritation or sensitization is unlikely. The CIR Expert Panel reviewed the two genotoxicity studies, one micronucleated polychromatic erythrocyte assay and one Ames assay, and concluded that these data support the absence of a carcinogenesis risk. The Panel, however, did not find data that described or even predicted the skin penetration of Octyldodecyl Stearoyl Stearate. Absent such data, the Panel concluded that the following additional data are needed:

1. Chemical properties, including the octanol/water partition coefficient
2. If there is significant dermal absorbtion or if significant quantities of the ingredient may contact mucous membranes or be ingested, reproductive and developmental toxicity data may be needed.

In accordance with Section 45 of the CIR Procedures, the Expert Panel has issued a Final Safety Evaluation Report—Insufficient Data. When the requested new data are available, the Panel will reconsider the Final Report in accordance with Section 46 of the CIR Procedures, Amendment of a Final Report.

CONCLUSION

The CIR Expert Panel concludes that the available data are insufficient to support the safety of Octyldodecyl Stearoyl Stearate for use in cosmetic products.

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Final Amended Report on the Safety Assessment of Octyldodecyl Stearoyl Stearate[1]

Octyldodecyl Stearoyl Stearate is an ester that functions as a skin-conditioning agent and viscosity-increasing agent. It is reported to be used in 105 cosmetic products at concentrations from 2% to 15%. In an isolated human skin permeation and penetration study, 0.005% of the applied dose permeated the skin, around 3% was found in the epidermis, around 1.5% was in tape stripped skin layers, and around 95% stayed in the material applied to the skin. A formulation having 20.6% Octyldodecyl Stearoyl Stearate was classified as minimally to mildly irritating in an in vitro ocular irritation assay. Several tests of products containing from 7.5% to 12.7% Octyldodecyl Stearoyl Stearate using rabbits produced minimal to mild ocular irritation. One test of 100% Octyldodecyl Stearoyl Stearate (a trade compound) and another of 10% Octyldodecyl Stearoyl Stearate in corn oil using rabbits produced no ocular irritation. Tests using rabbits demonstrated that Octyldodecyl Stearoyl Stearate at use concentrations was non- to mildly irritating to skin; only one study reported moderate irritation. Octyldodecyl Stearoyl Stearate was not mutagenic, with or without S-9 activation, in an Ames test and did not produce a significant increase in micronucleated cells in a mouse in vivo study. In clinical single-insult patch tests at use concentrations, Octyldodecyl Stearoyl Stearate was nonirritating to mildly irritating; in a cumulative irritation study, it caused mild irritation. Octyldodecyl Stearoyl Stearate was nonsensitizing in clinical tests. Because few toxicity data were available on Octyldodecyl Stearoyl Stearate, summaries of data from existing safety assessments of related ingredients (Octyl Dodecanol, Stearic Acid, and Octyl Stearate) were included. Undiluted Octyl Dodecanol was nontoxic during acute oral and dermal studies using rats and guinea pigs. Stearic Acid was nontoxic to rats during acute oral studies, but caused toxicity during subchronic studies. Rabbits treated topically with the acid were not affected adversely, and mild erythema and slight induration were observed when Stearic Acid was administered intradermally to guinea pigs and rabbits. Octyl Stearate had very low acute oral toxicity in rats and mice. Octyl Dodecanol produced only transient mild ocular irritation in rabbits when administered at concentrations up to 100%. Octyl Dodecanol (30% and 100%) was nonirritating to skin in one study using rabbits. In another study using multiple species, 100% Octyl Dodecanol (described as technical grade) caused severe skin irritation in rabbits, moderate irritation in guinea pigs and rats, and no irritation in swine. Stearic Acid was non- to moderately irritating in animal studies, and did not cause photosensitization. In studies using rabbits, undiluted Octyl Stearate caused slight, transient ocular irritation, and minimal skin irritation. Stearic Acid did not induce mitotic crossovers and aneuploidy in *Saccharomyces cerevisiae*, and was nonmutagenic in the Ames test. In a feeding study using mice, Stearic Acid was noncarcinogenic at doses up to 50 g/kg/day. Mice given subcutaneous injections of the acid had low incidences of carcinomas, sarcomas, and lymphomas. In clinical studies, concentrations of up to 100% Octyl Dodecanol were non- to mildly irritating, nonsensitizing, nonphototoxic, and nonphotosensitizing. Stearic Acid was nonirritating at concentrations up to 100%, and at concentrations up to 13% it was nonsensitizing and nonphotosensitizing. Octyl Stearate (7.6%) in formulation was nonirritating, nonsensitizing, and nonphotosensitizing. Based on skin permeation and penetration data, the Panel does not expect any significant amount of Octyldodecyl Stearoyl Stearate to be systemically available. There is no evidence of systemic toxicity associated with any of the related chemicals reviewed in previous safety assessments. None of the available toxicology or clinical data suggest a concern about adverse skin reactions to Octyldodecyl Stearoyl Stearate, or to any of the related chemicals. There is no evidence of ocular toxicity, except for a mild, transient ocular irritation associated with Octyldodecyl Stearoyl Stearate and the related chemicals. Overall, Octyldodecyl Stearoyl Stearate was considered safe as used in cosmetics.

INTRODUCTION

This amended safety assessment updates and supersedes an earlier Cosmetic Ingredient Review (CIR) safety assessment of Octyldodecyl Stearoyl Stearate (CIR 1999). New data from human skin penetration and permeation studies have been incorporated in this report.

It remains true that there are only limited data on Octyldodecyl Stearoyl Stearate. Summaries of pertinent data from related ingredients have been added to this review as a further basis for the assessment of safety of Octyldodecyl Stearoyl Stearate. The CIR Expert Panel found that Stearyl Alcohol, Oleyl Alcohol, and Octyl Dodecanol are safe as currently used in cosmetics (Elder 1985a); Oleic Acid, Lauric Acid, Palmitic Acid, Myristic Acid, and Stearic Acid are safe in the present practices of use and concentration in cosmetics (Elder 1987); and that Butyl, Cetyl, Isobutyl, Isocetyl, Isopropyl, Myristyl, and Octyl Stearate are safe as cosmetic ingredients in the present practices of use (Elder 1985b).

On the basis of the available data, including these additional data, the CIR Expert Panel is issuing this amended safety assessment.

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[1]Reviewed by the Cosmetic Ingredient Review Expert Panel.

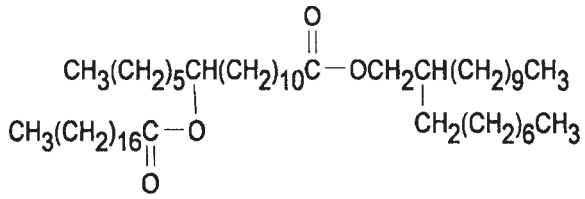

FIGURE 1
Octyldodecyl Stearoyl Stearate.

CHEMISTRY

Definition and Structure

Octyldodecyl Stearoyl Stearate

Octyldodecyl Stearoyl Stearate (CAS no. 90052-75-8) is an ester that conforms generally to the structure presented in Figure 1. Synonyms for Octyldodecyl Stearoyl Stearate include

- Octadecanoic Acid, 12-[(1-Oxooctadecyl)Oxy]-, 2-Octyldodecyl Ester;
- Octadecanoic Acid, 12-((1-Oxooctadecyl)Oxy)-2-Octyldodecyl Ester; and
- 12-[(1-Oxooxradecyl) Oxy]Octadecanoic Acid, 2-Octyldodecyl Ester (Pepe et al. 2002).

The formula for Octyldodecyl Stearoyl Stearate is given as $C_{56}H_{110}O_4$. Another synonym is 2-Octyldodecyl-12-Stearoyl Stearate (International Specialty Products 1998).

Summaries of Related Ingredients

Octyl Dodecanol. Octyl Dodecanol is the long-chain saturated fatty alcohol that conforms to the structure presented in Figure 2 (Elder 1985a).

Stearic Acid. Stearic Acid is found primarily as a glyceride in animal fats and oils. Lard and tallow, for example, contain approximately 10% and 20% Stearic Acid, respectively. Most vegetable oils contain 1% to 5% Stearic Acid. Cocoa butter contains approximately 35% Stearic Acid. Cosmetic grade Stearic Acid occurs as a mixture of varying amounts of Stearic and Palmitic Acids (Elder 1987).

Octyl Stearate. The stearates are esters of stearic acid; Octyl Stearate conforms generally to the formula in Figure 3 (Elder 1985b).

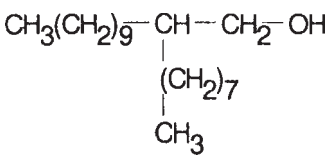

FIGURE 2
Octyl Dodecanol.

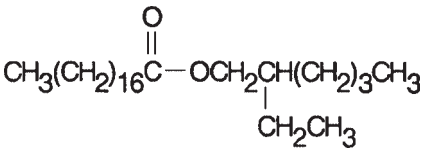

FIGURE 3
Octyl Stearate.

Chemical and Physical Properties

Octyldodecyl Stearoyl Stearate

The physical form of Octyldodecyl Stearoyl Stearate occurs as an amber, yellow liquid with a mild, characteristic odor. Its specifications include; saponification number of 115.0 to 135.0, specific gravity (25°C) range 0.86 to 0.88 and a refractive index (25°C) of 1.45 to 1.47 (ISP Van Dyke, Inc. 1997). In their material safety data sheet (MSDS), International Specialty Products (1998) describes Ceraphyl 847 (trade name for Octyldodecyl Stearoyl Stearate) as a straw white to yellow colored liquid with a fatty odor, a specific gravity of 0.872, and a molecular weight of 846.87. The MSDS also notes that carbon dioxide and monoxide may be formed when this material is heated to decomposition.

Octyldodecyl Stearoyl Stearate is soluble in silicones, esters, mineral oil, vegetable oils, alcohols, aliphatic, aromatic and chlorinated hydrocarbons and is insoluble in water. It has a theoretical molecular weight of 846, a freezing point of −15°C, and a flash point of over 180°C (Alzo, Inc. 1998). Octyldodecyl Stearoyl Stearate is partly soluble in 95% ethanol, propylene glycol, glycerine, 70% sorbitol and PEG 400 (Trivent Chemical Company, Inc. 1998).

Summaries of Related Ingredients

Stearic Acid. Stearic Acid occurs as hard, white or faintly yellow, glossy crystals or leaflets or as an amorphous white or yellow-white powder. It has a slight odor and tallow-like flavor. Stearic Acid is water-insoluble, slightly soluble in alcohol and benzene, soluble in chloroform, and very soluble in ether. The molecular weight is ~284.5 (Elder 1987).

Octyl Stearate. Octyl Stearate and the other Stearates are either oily liquids or waxy solids that typically are soluble in organic solvents such as chloroform and acetone. The molecular weight of Octyl Stearate is 396, the ester value is 144 to 154, the acid value and iodine value each have a maximum of 1.0. The Stearates can undergo conversion into stearic acid and the corresponding alcohol by chemical or enzymatic hydrolysis, conversion into amides by ammonolysis, and conversion into different esters by alcoholysis or transesterification. Purer grades of the saturated Stearates are not expected to autoxidize readily (Elder 1985b).

Method of Manufacture

Octyldodecyl Stearoyl Stearate

Octyldodecyl Stearoyl Stearate is manufactured by an inorganic acid catalyzed, high temperature (150°C to 160°C)

esterification reaction of guerbet alcohol. Guerbet alcohol is comprised of a mixture of alcohols (primarily C-20) and a mixture of fatty acids (primarily C-18) with no impurities. The product is neutralized to a water-soluble soap, washed to purity, dried, and filtered (Alzo, Inc. 1998).

Summaries of Related Ingredients

Octyl Dodecanol. Octyl Dodecanol is produced by the condensation of two molecules of decyl alcohol, and occurs naturally in small quantities as components of wax esters in plants (Elder 1985a).

Stearic Acid. Methods of processing Stearic Acid include hydrolysis of tallow or hydrogenation of unsaturated fatty acids in cottonseed and other vegetable oils, followed by fractional distillation or crystallization. Concentrations of Stearic Acid as great as 95 to 99% have been reported from the hydrogenation of unsaturated fatty acids (Elder 1987).

Octyl Stearate. The Stearates are prepared by esterification of stearic acid with the appropriate alcohol in the presence of an acid catalyst. The reaction products are refined either by catalyst neutralization, vacuum distillation, or various decolorization-deodorization techniques to remove residual traces of alcohol (Elder 1985b).

Impurities

Octyldodecyl Stearoyl Stearate

Octyldodecyl Stearoyl Stearate is composed of Stearic Acid (2.5% max.), Octyldodecanol (5.0% max.), Octyldodecyl Hydroxystearate (5.0% max.), and Octyldodecyl Stearoyl Stearate (88.0% max.) (Alzo, Inc. 1998).

Summaries of Related Ingredients

Stearic Acid. Stearic Acid contains varying amounts of unsaponifiable matter (0.3% max.), and can contain glyceryl monostearate (0.07% max.). Typical impurities are glyceryl monomyristate (0.07% max.), 9-hexadecanoic acid, 9,12-octadecadienoic acid (Elder 1987).

USE

Cosmetic

Octyldodecyl Stearoyl Stearate

Octyldodecyl Stearoyl Stearate functions as a skin conditioning agent—occlusive and viscosity increasing agent—nonaqueous in cosmetic product formulations (Pepe et al. 2002). In 2001, Octyldodecyl Stearoyl Stearate was reported to the Food and Drug Administration (FDA) by industry to be used in 105 cosmetic formulations, representing a range of product types, as shown in Table 1 (FDA 2001). Table 1 also shows product types in which Octyldodecyl Stearoyl Stearate is reported to be used at the given concentrations (CTFA 2001). This ingredient is reportedly used in some product categories, but the concentrations of use are not available. In other cases, information regarding use concentration for a specific product categories is provided, but the number of such products is not known.

The European Commission (EC) has not restricted the use of Octyldodecyl Stearoyl Stearate in cosmetic products (EC 2002).

Octyldodecyl Stearoyl Stearate had been included in the list of ingredients for which there is precedence for use in all cosmetics in Japan (Elder 1999). Japan no longer maintains a list of ingredients for which there is precedence for use. In the current Ministry of Health, Labor and Welfare (MHLW) regulations, Octyldodecyl Stearoyl Stearate is not included on a negative list (MHLW 2000a), on a list of ingredients for which there are restrictions to use in cosmetics (MHLW 2000b), or on a list of quasi-drugs for which listing is required (MHLW 2000c).

ABSORPTION, DISTRIBUTION, METABOLISM, AND EXCRETION

Octyldodecyl Stearoyl Stearate

An-eX Analytical Services, Ltd. (An-eX 2001) conducted an in vitro study of skin penetration and permeation of Octyldodecyl Stearoyl Stearate. [^{14}C]Octyldodecyl Stearoyl Stearate at a concentration of 10% in a safflower oil vehicle with a target activity level of 200 μCi/g was used in the study. Skin samples were obtained from cosmetic reduction surgery (site not identified) from four human female donors. Subcutaneous fat was removed by dissection and the skin was heated (60°C for 45 s) to and separate the dermis from the epidermis. The epidermis was dried, frozen, and thawed immediately prior to mounting in a Franz-type diffusion cell. The temperature of the skin layer was maintained at 32.0°C $\pm$ 1°C by placing the apparatus in a water bath. Samples (200 μl) were taken at 4, 8, 12, 24, and 48 h and the presence of ^{14}C determined by liquid scintillation counting. The skin was removed from the diffusion cell, and tape stripped. The total recovery of the radioactivity was 98.7% $\pm$ 1.1% of the applied dose. The distribution of the ^{14}C radiolabel at 48 h is shown in Table 2. Permeation at 48 h was 0.023 $\pm$ 0.005 μg/cm^2, representing 0.005% $\pm$ 0.001% of the applied dose. Permeation at 24 h was higher, but the authors cautioned that the actual scintillation counts measured in the receptor fluid were very close to background levels. A total of 4% to 5% of the label was found in the tape strips and remaining epidermis combined.

Summaries of Related Ingredients

Octyl Dodecanol. No data on absorption, distribution, metabolism, or excretion of Octyl Dodecanol were available (Elder 1985a).

Stearic Acid. Stearic Acid and other fatty acids are digested from the diet, absorbed in micellar aggregates, and transported after esterification to glycerol in chylomicrons and very low density lipoproteins. Stearic Acid is primarily transported via the lymph system. Fatty acids originating from adipose tissue stores are either bound to serum albumin or remain unesterified in the blood. Stearic Acid was the most poorly absorbed of the common fatty acids; the digestibility of fatty acids decreased

TABLE 1
Use of Octyldodecyl Stearoyl Stearate in Cosmetic Products

Product category (total no. formulations in category) (FDA 2001)	Total no. of formulations containing ingredient (FDA 2001)	Current concentration of use (CTFA 2001) (%)
Eyebrow pencil (99)	2	—
Eyeliner (533)	1	4
Eye shadow (551)	30	4–10
Other eye makeup preparations (151)	2	—
Powders (dusting and talcum)—excluding face (272)	2	4
Other fragrance preparations (173)	1	—
Blushers—all types (243)	8	2–7
Face powders (301)	32	2–7
Foundations (319)	5	4–9
Lipstick (942)	1	5–10
Makeup bases (136)	5	10
Rouges (16)	1	—
Other makeup preparations (186)	1	5
Cuticle softeners (19)	1	—
Nail creams and lotions (15)	1	—
Cleansing preparations (733)	3	—
Face and neck creams, lotions, etc.—excluding shaving (304)	1	4
Body and hand creams, lotions, etc.—excluding shaving (827)	1	15
Moisturizing preparations (881)	4	—
Night preparations (200)	1	—
Paste masks/mud packs (269)	1	—
Other skin care preparations (715)	2	—
Suntan gels, creams, and liquids	—	8
2001 total uses/ranges for Octyldodecyl Stearoyl Stearate	105	2–15

with increased fatty acid chain length. Stearic Acid metabolites are detected in the heart, liver, lungs, spleen, kidneys, muscles, intestines, adrenal glands, blood, and lymph, and in adipose, mucosal, and dental tissues after administration of radioactive Stearic Acid to rats, dogs, sheep, chicks, frogs, and humans. Uptake and transport of fatty acids into the brain has been observed, and free fatty acids readily cross the placental barrier in rabbits, guinea pigs, rats, and humans. Fatty acids that are taken up by tissues are either stored in the form of triglycerides or oxidized for energy (Elder 1987).

TABLE 2
Forty-eight-hour distribution of ^{14}C radiolabel in penetration/permeation study (An-eX 2001)

Site	% applied dose	Octyldodecyl Stearoyl Stearate ($\mu g/cm^2$)
48-Hour rinse	94.18 ± 1.39	477.4 ± 16.1
Tape strips 1–4	1.051 ± 0.162	5.33 ± 0.82
Tape strips 5–12	0.433 ± 0.101	2.18 ± 0.50
Remaining epidermis	3.021 ± 0.406	15.12 ± 1.90
Permeated	0.005 ± 0.001	0.023 ± 0.005
Total recovery	98.69 ± 1.12	

Octyl Stearate. No data on absorption or distribution of Octyl Stearate were available. These esters are generally metabolized to the corresponding alcohol and fatty acid, oxidized to carbon dioxide and water, and excreted (Elder 1985b).

ANIMAL TOXICOLOGY

Octyldodecyl Stearoyl Stearate

Octyldodecyl Stearoyl Stearate, tested as a trade compound at an oral dose of 5.0 g/kg in 10 rats (5 of each sex) for 14 days, produced no deaths (Wells Laboratories, Inc. 1993). Octyldodecyl Stearoyl Stearate, tested as a trade compound, had an oral LD_{50} of >20 g/kg in albino rats (Food and Drug Research Labs, Inc. 1983).

Summaries of Related Ingredients

Octyl Dodecanol. No deaths were observed during acute oral toxicity studies when 5 to 10 rats were treated with 5 g/kg of undiluted Octyl Dodecanol or with a lipstick (25 g/kg, diluted to 50%) containing 10.2% Octyl Dodecanol (1.28 g/kg total dose of Octyl Dodecanol). In an acute dermal toxicity study, intact and abraded skin sites of six guinea pigs were treated with 3.0 g/kg of the undiluted alcohol under occlusive patches. No deaths occurred as a result of treatment, and no gross lesions were observed at necropsy (Elder 1985a).

Stearic Acid. No signs of acute toxicity were observed when Stearic Acid or cosmetic formulations containing Stearic Acid at concentrations up to 13% were given orally to rats at doses of 15 to 19 g/kg. In subchronic oral studies, Stearic Acid (5% to 50%) caused thrombosis, aortic atherosclerosis, anorexia, and mortality in rats. Chicks fed 5% Stearic Acid had no signs of toxicity. Topical applications of 5 g/kg Stearic Acid to rabbits did not cause adverse effects. Intradermal administration of 10 to 100 mM Stearic Acid caused mild erythema and slight induration in guinea pigs and rabbits (Elder 1987).

Octyl Stearate. Octyl Stearate generally had "very low" acute oral toxicity in rats and mice. Undiluted Octyl Stearate at a dose of 8 ml/kg did not cause deaths in five rats per sex (Elder 1985b).

Ocular Irritation

Octyldodecyl Stearoyl Stearate

An EYETEX in vitro irritation assay was performed on a nail cuticle pencil containing 20.6% Octyldodecyl Stearoyl Stearate. The test material produced scores consistent with minimal to mild irritation (CTFA 1998).

An undiluted eyeliner containing 7.5% Octyldodecyl Stearoyl Stearate was applied three times to the unrinsed eyes of six rabbits. One rabbit had conjunctival scores of 6, 2, and 2 on days 1, 3, and 4, respectively, and a corneal score of 5 on day 1. Another had a conjunctival score of 4 on day 1. None of the rabbits had signs of ocular toxicity on day 2 or 7. The total Draize scores were 4/110 on day 1 and 1/110 on days 3 and 4. The investigators concluded that the eye shadow was moderately irritating under the conditions of this study.

A concealer containing 12.7% Octyldodecyl Stearoyl Stearate was applied once to the unrinsed eyes of six rabbits. One rabbit each had conjunctival scores of 2 on days 1 and 2. None of the rabbits had signs of irritancy on days 3, 4, or 7. The total Draize scores were 1/110 on days 1 and 2 and the formulation was classified as mildly irritating.

In a third study, none of the six rabbits had signs of ocular irritation after treatment with a lipstick containing 7.8% Octyldodecyl Stearoyl Stearate. The lipstick was classified as nonirritating (CTFA 1998).

Octyldodecyl Stearoyl Stearate, tested as a trade compound, was instilled (0.1 ml) into the right conjunctival sac of six rabbits. The contralateral eye served as control. Eyes were not rinsed. Reactions were scored on days 1 to 4 and 7 according to the Draize scale. No reactions were observed (Consumer Product Testing 1978).

A single application of 0.1 ml of Octyldodecyl Stearoyl Stearate, at a 10% *w/w* dilution in corn oil, was instilled into one eye each of six rabbits. The contralateral eye served as the control and the eyes were not rinsed. Reactions were scored on days 1 to 3, and 4 and 7 if irritation persisted. No reactions were observed (Wells Laboratories, Inc. 1993).

Summaries of Related Ingredients

Octyl Dodecanol. Six rabbits were treated with 100% Octyl Dodecanol. The average ocular irritation scores were 4/110 at day 1 and 0/110 by day 4. In a second study using the same procedure, the scores were 1/110 at day 1 and 0/110 by day 4. Cosmetic formulations containing 3% to 10.2% Octyl Dodecanol caused either no ocular irritation or minimal, transient irritation in the eyes of rabbits (Elder 1985a).

Stearic Acid. In Draize tests, reactions ranged from "none" to mild, transient irritation, but there was no apparent relationship with the concentration of the Stearic Acid tested (Elder 1987).

Octyl Stearate. Undiluted Octyl Stearate caused slight, transient ocular irritation in rabbits (Elder 1985b).

Skin Irritation and Sensitization

Octyldodecyl Stearoyl Stearate

An undiluted eyeshadow containing 7.5% Octyldodecyl Stearoyl Stearate was moderately irritating to the skin in a single insult occlusive patch test using nine rabbits. Erythema and edema were observed at 2 and 24 h after application of the test material. The primary irritation index (PII) for the group was 3.89/8.00.

In a similar study, a concealer containing 7.8% Octyldodecyl Stearoyl Stearate was tested using nine rabbits. The skin sites were evaluated 2 and 24 h after application of the test material. No signs of irritancy were observed at 24 h, but erythema was observed at 2 h. The PII for the group was 0.67/8.00, and the formulation was classified as minimally irritating.

A lipstick containing 7.8% Octyldodecyl Stearoyl Stearate was tested similarly using nine rabbits. None of the animals had erythema or edema 2 or 24 h after application of the test material, and the PII was 0.00/8.00. In a 4-day cumulative study, the lipstick was "essentially non-irritating" (CTFA 1998).

Octyldodecyl Stearoyl Stearate, tested as a trade compound, was applied (0.5 ml) under a 24-h occlusive patch to abraded and intact sites on the back of six rabbits. Sites were examined for erythema and edema at 24 and 72 h. The maximum possible score was 8. The PII for OSS was 0.38. It was considered to have a "potential for slight irritation—rarely irritating to people" (Consumer Product Testing 1978).

A single dermal application of 0.5 ml of Octyldodecyl Stearoyl Stearate, at a 10% *w/w* dilution in corn oil, was applied to one abraded and one intact site on six New Zealand white rabbits. Each test site was observed for erythema and edema

24 and 72 h after application. The PII for this product was 0.0 (Wells Laboratories, Inc. 1993).

Summaries of Related Ingredients

Octyl Dodecanol. Octyl Dodecanol was applied for 24 h under occlusive patches to the skin of six rabbits during three studies. The irritation scores for a concentration of 100% were 1.13/4, 0.5/4, and 0/4. At a concentration of 30%, it produced scores of 0/4 for all three animals (Elder 1985a).

Technical grade Octyl Dodecanol (0.1 to 0.5 g) caused severe irritation (+++) to the skin of six albino rabbits and moderate irritation (++) to the skin of six Hartley guinea pigs and six Wistar rats. The compound was nonirritating (−) when applied to the skin of six Pitman-Moore miniature swine. For the study using rabbits, 0.1 g Octyl Dodecanol was applied for 24 h, the skin sites were graded, and the compound was reapplied for another 24 h. The treated skin sites were graded after Evans blue solution was injected intravenously. The rabbits were killed 1 h later, and skin samples were prepared. For the guinea pig study, two dorsal areas were clipped free of hair. One site was treated with 0.1 g for 24 h and the other was left untreated. The remainder of the study was identical to the one using rabbits. For the swine, the dorsal area was clipped free of hair, and 0.5 g Octyl Dodecanol was applied under occlusive patches for 48 h. Skin of the rabbits, guinea pigs, and rats had acanthosis, hyperkeratinization, swelling of cells, and proliferation of basal cells. Vasodilatation, edema, alteration of collagenous fibers, and mononuclear and polymorphonuclear leukocyte infiltration of the dermis were also observed (Elder 1985a).

A formulation containing 4% Octyl Dodecanol was nonirritating to mildly irritating (0/4 to 1.08/4) during primary skin irritation studies. Minimal to mild irritation was observed when a formulation containing 10.2% of the alcohol was applied to the skin of rabbits for 3 to 4 consecutive days. In these studies, the degree of irritation observed did not increase with the concentration tested (Elder 1985a).

Stearic Acid. No irritation was observed when Stearic Acid was applied (18 mmol %) to the skin of the external ear canals of albino rabbits over a period of 6 weeks. Slight local edema was observed when New Zealand white rabbits were treated with 2% Stearic Acid in formulation for 4 weeks. During a 13-week study, cosmetic formulations containing up to 5% Stearic Acid caused moderate skin irritation in rats (4.0 mg/kg, 227 mg/kg). In single-insult patch tests, 35% to 65% Stearic Acid caused no to moderate erythema and slight, if any, edema to the skin of rabbits. In maximization studies, 1% Stearic Acid caused weak reactions at challenge, and was considered a grade 1 sensitizer. Stearic Acid at a concentration of 2.8% did not cause photosensitization in guinea pigs (Elder 1987).

Octyl Stearate. Undiluted Octyl Stearate produced at most minimal or moderate skin irritation in rabbits. Application of the stearate to the skin of rabbits caused irritation after 60 days of treatment; vesicles and slight epidermal exfoliation were observed, and Octyl Stearate was considered "poorly tolerated." Microscopic changes in the treated skin included epidermal acanthosis and "congestive" dermatitis. Application of 10% aqueous Octyl Stearate daily for 60 days caused irritation (vesicles) in the skin of rabbits, but was "relatively well tolerated." No significant lesions were observed at microscopic examination of the treated skin (Elder 1985b).

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

No data on the reproductive and developmental toxicity of Octyldodecyl Stearoyl Stearate, Octyl Dodecanol, Stearic Acid, or Octyl Stearate were available. Female rats fed diets with 6.25% Butyl Stearate for 10 weeks were mated—no adverse effects on fertility, litter size, or survival of offspring were noted, although reduced fetal growth during both the preweaning and postweaning periods (up to 21 days) was found (Elder 1985b).

GENOTOXICITY

Octyldodecyl Stearoyl Stearate

A micronucleus assay was used to determine the genotoxicity of Octyldodecyl Stearoyl Stearate. A single dose of 2.0, 5.0 or 10.0 ml/kg Octyldodecyl Stearoyl Stearate was given to CD-1 mice (5/sex/group) by gavage. One negative-control group was designated for each of the three runs of each treatment group. A positive-control group received triethylenemelamine via intraperitoneal injection at a dose of 1 mg/kg. Five male and five female mice were killed from each dose and vehicle control at 24, 48, and 72 h after the initiation of treatment. Five mice from each sex were killed from the positive control group 24 h after treatment. The positive-control depressed the polychromatic erythrocyte to normochromatic erythrocyte (PCE/NCE) ratio and showed a statistically significant increase in micronucleated polychromatic erythrocytes (MPCEs). The mean numbers of MPCEs in 1000 PCEs were 58.8 and 65.2 for the male and female mice, respectively, which fulfilled the criteria for a valid assay. No significant increases occurred in the proportion of MPCEs in the test groups compared to the concurrent negative-control groups (Sitek Research Laboratories 1994a).

A *Salmonella typhimurium* gene mutation assay was used to evaluate Octyldodecyl Stearoyl Stearate using strains TA98, TA100, TA1535, TA1537, and TA1538. Octyldodecyl Stearoyl Stearate was used at concentrations of 1.0, 5.0, 10.0, 50.0, and 100.0 μl/plate. The positive controls and Octyldodecyl Stearoyl Stearate were tested with and without S-9 activation. All test concentrations, including the positive and negative controls, were tested in triplicate and a confirmation assay was performed. Octyldodecyl Stearoyl Stearate and control treatments were performed under ultraviolet (UV)-filtered lights to avoid photoinactivation. Positive controls were considered acceptable because the treated strains had reversion frequencies three times or greater than the mean reversion frequency of the solvent control plates in all positive control cultures with and without S-9 activation. Octyldodecyl Stearoyl Stearate did not induce any positive increase in the number of revertant colonies for any of

the tester strains with or without S-9 activation (Sitek Research Laboratories 1994b).

Summaries of Related Ingredients

Octyl Dodecanol. No genotoxicity tests were available on Octyl Dodecanol, but Stearyl Alcohol was nonmutagenic in the Ames test (Elder 1985a).

Stearic Acid. Stearic Acid did not increase mitotic aneuploidy and chromosome crossovers during in the D_6 strain of *Saccharomyces cerevisiae* in an vitro mutagenicity assay. It was nonmutagenic in the Ames test (Elder 1987).

Octyl Stearate. No genotoxicity tests were available on Octyl Stearate (Elder 1985b).

CARCINOGENICITY

Carcinogenicity data were not available for Octyldodecyl Stearoyl Stearate, or for Octyl Dodecanol or Octyl Stearate. Mice that received single or repeated subcutaneous (s.c.) injections of 0.05 to 1.0 mg Stearic Acid two times per week for up to 57 weeks had subcutaneous sarcomas at the injection site in only the low-dose group—no neoplasms were found in high-dose animals. Mice fed up to 0.3% Stearic Acid, in one study, or 50 g/kg/day Stearic Acid in another, did not develop neoplasms (Elder 1987).

CLINICAL ASSESSMENT OF SAFETY

Octyldodecyl Stearoyl Stearate

Thirteen volunteers, 10 of whom completed the study, were used in a cumulative irritation study of an eyeshadow having 10.4% Octyldodecyl Stearoyl Stearate. The test material was applied to the skin of the back 21 times for 23-h intervals. Scoring for cumulative irritation and reapplication of the eyeshadow occurred every 24 h. The test sites were patched. The total score was 1/630, and the eyeshadow was classified as a mild irritant (Hill Top Research 1983a).

The same eyeshadow (10.4%) was evaluated in a repeat insult patch test using 107 subjects. Applications were made three times weekly during the 22-day induction period. The test material was applied for 24 h to the skin of the back under a closed patch, and the skin sites were scored 48 or 72 h after application. Challenge applications were made using 24-h occlusive patches. No evidence of contact sensitization was observed in any of the test subjects (Hill Top Research 1983b).

The contact sensitization potential of a concealer containing 5.0% Octyldodecyl Stearoyl Stearate was determined using a maximization test. Patches were applied to the outer arm throughout three phases: pretesting, induction, and challenge. In the pretesting phase, approximately 0.1 g of the material was applied to a skin site under a 15-mm Webril patch, which was fixed to the skin with occlusive tape (Blenderm) and covered with Scanpor tape. The patch was removed after 48 h and the skin site was examined for signs of irritation. During the induction phase, ~0.1 ml of aqueous sodium lauryl sulfate (SLS, 1%) was applied to a different site and similarly covered for 24 h. After removal of the SLS patch, 0.1 g of the test material was applied to the same site and covered with an occlusive patch. This patch was removed after 48 or 72 h, when the site was examined for irritation. This procedure was repeated for a total of five induction exposures. If irritation developed during induction, the 24-h SLS patch was eliminated and only the test material was administered, after a 24-h period during which no patch was applied. After a 10-day nontreatment period, a new skin site on the opposite arm was treated with 0.1 ml of 10.0% SLS under an occlusive patch. The site was then challenged with a single application of the test material, and this patch was removed after 48 h. The treatment site was examined for irritation 1 h and 24 h after patch removal. None of the 27 subjects had adverse reactions, and no contact sensitization was observed (Ivy Laboratories 1991).

The human irritancy potential of an eyeshadow pencil having 10.4% Octyldodecyl Stearoyl Stearate was evaluated in a single-insult patch test using 19 subjects. The PII was 0/8, and no differences in irritancy were observed between subjects of the test and control groups (CTFA 1998).

A concealer containing 5.0% Octyldodecyl Stearoyl Stearate was tested for primary irritation using 20 subjects. The PII was 0.08, and no significant differences in irritancy were observed between test subjects and controls. A lipstick having 15.0% Octyldodecyl Stearoyl Stearate was similarly tested using 18 subjects. The PII was 0.00/8.00, and no differences in irritancy were observed between test subjects and control groups (CTFA 1998).

A lipstick containing 7.8% Octyldodecyl Stearoyl Stearate was tested in a repeat insult patch test using 87 panelists, 85 of whom completed the study. Occlusive patches containing the test materials were applied to the skin of the upper back for 24 h, three times weekly, for 3 weeks. Challenge applications were made 3 weeks after the last induction treatment, and the skin sites were scored 24 and 48 h after patch removal. None of the subjects had erythematous responses during induction or challenge, and the investigators concluded that the lipstick did not have allergic sensitization potential (CTFA 1998).

A clinical use study was performed using the same lipstick and 62 female subjects. The women applied the lipstick at least twice daily for 3 weeks. No clinical changes were observed after use of the lipstick (CTFA 1998).

Summaries of Related Ingredients

Octyl Dodecanol. Octyl Dodecanol at a concentration of 100% caused mild irritation in one of 40 subjects during a 24-h single-insult patch test. In a similar test, a moisturizing cream (4.0%) was nonirritating or minimally irritating. Occlusive patches containing 0.05 g (undiluted) Octyl Dodecanol were affixed to the backs of 50 adult males. The patches were removed at 48 h and the treated sites were evaluated 30 min later and at 72 to 120 h. No signs of irritation were observed. When 3% Octyl Dodecanol was patch-tested daily for 21 consecutive days, the

alcohol was "essentially nonirritating" or "slightly irritating" (Elder 1985a).

No signs of sensitization were observed when 3% to 10.2% Octyl Dodecanol was tested in a Draize-Shelanski repeat-insult patch test. In other studies, no signs of phototoxicity or photosensitization were observed when a lipstick containing 10.2% Octyl Dodecanol was tested using 23 subjects (Elder 1985a).

Stearic Acid. Stearic Acid was nonirritating in clinical primary or cumulative irritation studies at concentrations of 100% or 40% to 50% in mineral oil. Cosmetic formulations containing up to 93% of Stearic Acid and other fatty acids caused mild to intense erythema, but the reactions were not considered related to the fatty acid content of the products. Stearic Acid at concentrations up to 13% was not a sensitizer, and formulations containing 1% to 13% Stearic Acid were not photosensitizing (Elder 1987).

Octyl Stearate. A suntan lotion and protective facial cream containing 7.6% Octyl Stearate were applied to the skin of 56 subjects daily under 24-h closed patches for a total of 10 induction applications. After a 10 to 14-day nontreatment period, a 24-h challenge patch was applied. No signs of irritation or sensitization were observed. In a phototoxicity study using the same formulations (10 subjects), no significant reactions were noted. In a photosensitization study on the same formulations (27 subjects), slight reactions were observed in 4 subjects during induction. One had erythema at challenge, and three subjects only reacted during induction. The investigator concluded that the formulations did not produce photosensitization (Elder 1985b).

SUMMARY

Octyldodecyl Stearoyl Stearate is an ester of fatty alcohols and fatty acids that functions as a skin-conditioning agent and viscosity-increasing agent reported to be used in 105 cosmetic products. Data submitted by industry indicated that Octyldodecyl Stearoyl Stearate is used at concentrations from 2% to 15%.

In an isolated human skin permeation and penetration study, 0.005% of the applied Octyldodecyl Stearoyl Stearate permeated the skin, around 3% was found in the epidermis, around 1.5% was in tape stripped skin layers, and around 95% stayed in the material applied to the skin.

A formulation having 20.6% Octyldodecyl Stearoyl Stearate was classified as minimally to mildly irritating in an in vitro ocular irritation assay. Rabbits treated three times with a formulation having 7.5% of the ingredient had moderate irritation. Formulations having 7.8% and 12.7% Octyldodecyl Stearoyl Stearate were nonirritating to mildly irritating in the Draize ocular irritation test using rabbits. Octyldodecyl Stearoyl Stearate neat (a trade name product) and at 10% in corn oil produced no ocular irritation in rabbits.

An eyeshadow having 7.5% Octyldodecyl Stearoyl Stearate was moderately irritating to the skin of rabbits with a PII of 3.89/8. In two primary irritation studies and a 4-day cumulative irritation study, all using rabbits, formulations having 7.8% Octyldodecyl Stearoyl Stearate were nonirritating to minimally irritating, with PIIs of 0/8 to 0.67/8. A single application of Octyldodecyl Stearoyl Stearate at 10% produced no irritation in rabbits.

In clinical single insult patch tests using up to 20 subjects, formulations having 5.0% to 15.0% Octyldodecyl Stearoyl Stearate produced reactions that ranged from nonirritating to mild irritation (PIIs 0/8 to 0.08/8). In a cumulative irritation study, a formulation having 10.4% Octyldodecyl Stearoyl Stearate caused mild irritation when tested using 10 subjects. Formulations having 5.0%–10.4% Octyldodecyl Stearoyl Stearate were nonsensitizing in two repeat-insult patch tests using 27 to 85 panelists and a maximization test using 107 subjects. No adverse effects were observed in 62 women who took part in a 3-week in-use study of a formulation having 7.8% Octyldodecyl Stearoyl Stearate.

Because few toxicity data were available on Octyldodecyl Stearoyl Stearate, summary data from earlier safety assessments of Octyl Dodecanol, Stearic Acid, and Octyl Stearate were included in this review as a further basis for the assessment of safety.

Undiluted Octyl Dodecanol was nontoxic during acute oral and dermal studies using rats and guinea pigs. Stearic Acid was nontoxic during acute oral studies using rats, but caused toxicity during subchronic studies. Rabbits treated topically with the acid were not affected adversely, and mild erythema and slight induration were observed when Stearic Acid was administered intradermally to guinea pigs and rabbits. Octyl Stearate had very low acute oral toxicity in rats and mice.

Octyl Dodecanol caused no to minimal ocular irritation in rabbits when administered at concentrations up to 100%. Octyl Dodecanol (100%) caused primary skin irritation scores of 0/4 to 1.13/4 in studies using rabbits, and a concentration of 30% was nonirritating. Technical grade Octyl Dodecanol, however, caused moderate to severe irritation in the skin of rabbits, guinea pigs, and rats, but was nonirritating in the skin of miniature swine. A formulation containing 4% Octyl Dodecanol ranged from not irritating to mildly irritating in the skin of rabbits. Stearic Acid was nonirritating to moderately irritating in studies using rabbits and rats, and did not cause photosensitization in guinea pigs. In studies using rabbits, undiluted Octyl Stearate caused slight, transient ocular irritation, and, at most, minimal to moderate skin irritation.

Stearic Acid did not induce mitotic crossovers and aneuploidy, and was nonmutagenic in the Ames test. In an micronucleus assay, Octyldodecyl Stearoyl Stearate produced no significant increases in micronucleated erythrocytes in the test groups compared to the concurrent negative-control groups. In a *Salmonella typhimurium* gene mutation assay, Octyldodecyl Stearoyl Stearate did not induce any positive increase in the number of revertant colonies for any of the tester strains with or without S-9 activation. In a feeding study using mice, Stearic Acid was noncarcinogenic at doses up to 50 g/kg/day. Mice given s.c. injections of the acid had low incidences of carcinomas, sarcomas, and lymphomas.

In clinical studies, Octyl Dodecanol at concentrations of up to 100% produced reactions that ranged from nonirritating to mildly irritating, and were nonsensitizing, nonphototoxic, and nonphotosensitizing. Stearic Acid was nonirritating at concentrations up to 100%, and at concentrations up to 13% it was nonsensitizing and nonphotosensitizing. Octyl Stearate (7.6%) in formulation was nonirritating, nonsensitizing, and nonphotosensitizing.

DISCUSSION

The CIR Expert Panel had previously considered the available data on Octyldodecyl Stearoyl Stearate to be insufficient; the data needed were chemical properties, including the octanol/water partition coefficient, the extent of dermal absorption, and whether significant quantities of the ingredient may contact mucous membranes or be ingested. If a significant penetration or ingestion would occur, the Panel considered the possibility that reproductive and developmental toxicity data may be needed. Dermal absorption data were provided.

Skin permeation and penetration data using isolated human skin indicated that only a small portion of the applied dose permeates the skin (0.005%), only 4% to 5% actually enters the skin, and that almost 95% remained in the material applied to the skin. Based on these data, the Panel does not expect any significant amount of Octyldodecyl Stearoyl Stearate to be available to create a systemic exposure. Although few data are available on the systemic toxicity of Octyldodecyl Stearoyl Stearate, there is no systemic toxicity associated with any of the structurally related chemicals reviewed in previous safety assessments.

None of the available toxicology or clinical data suggest a concern about adverse skin reactions to Octyldodecyl Stearoyl Stearate. Only a mild, transient ocular irritation was associated with Octyldodecyl Stearoyl Stearate.

This ingredient is reportedly used in some product categories, but the concentrations of use are not available. In other cases, information regarding use concentration for a specific product categories is provided, but the number of such products is not known. Although there are gaps in knowledge about product use, the overall information available on the types of products in which this ingredient is used and at what concentration indicate a pattern of use. Within this overall pattern of use, the Panel considers this ingredient to be safe.

CONCLUSION

The CIR Expert Panel concludes that Octyldodecyl Stearoyl Stearate is safe for use in cosmetic products in the practices of use and concentration described in this safety assessment.

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