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Final Report on the Safety Assessment of Stearyl Alcohol, Oleyl Alcohol, and Octyl Dodecanol

Stearyl Alcohol, Oleyl Alcohol, and Octyl Dodecanol are long-chain saturated or unsaturated (Oleyl) fatty alcohols. They are used in numerous cosmetic product categories at concentrations of less than 0.1 percent to greater than 50 percent.

The metabolism of Stearyl Alcohol and Oleyl Alcohol in rats is described. The results of acute oral toxicity studies indicate a very low order of toxicity. In rabbit irritation tests, these alcohols produced minimal ocular irritation and minimal to mild cutaneous irritation. Stearyl Alcohol produced no evidence of contact sensitization or comedogenicity.

Clinical patch testing indicates a very low order of skin irritation potential and sensitization. Photoreactivity studies on products containing these ingredients were negative for phototoxicity or photosensitization.

Based on the available data, it is concluded that Stearyl Alcohol, Oleyl Alcohol, and Octyl Dodecanol are safe as currently used in cosmetics.

INTRODUCTION

Stearyl Alcohol, Oleyl Alcohol, and Octyl Dodecanol are long-chain fatty alcohols used in a variety of cosmetic products. The materials of commerce are mixtures of fatty alcohols, and the terms Stearyl Alcohol, Oleyl Alcohol, and Octyl Dodecanol refer to these mixtures for the purposes of this report. If data pertain to the pure compound rather than the cosmetic ingredient, the distinction is noted.

CHEMICAL AND PHYSICAL PROPERTIES

Composition

Stearyl Alcohol

Stearyl Alcohol is a mixture of solid fatty alcohols that consists predominantly of n-octadecanol (90 percent minimum assay) with varying amounts of n-hexa-

decanol, n-tetradecanol, n-eriosanol, and n-dodecanol along with unspecified uneven and branched-chain alcohols. The predominant component conforms to the formula:[1-3]

$$CH_3(CH_2)_{16}CH_2OH$$

CAS Number: 112-92-5

Synonyms include Octadecanol, n-Octadecanol, Octa Decyl Alcohol, n-Octadecyl Alcohol, Stearol, USP XIII Stearyl Alcohol, and n-1-Octadecanol.

Oleyl Alcohol

Oleyl Alcohol is a mixture of fatty alcohols that consists predominantly of the straight-chain unsaturated 9-n-octadecenol (55 percent minimum assay) with varying amounts of 8-n-hexadecenol, 6-n-dodecenol, n-hexadecanol, n-octadecanol, n-tetradecanol, and 7-n-tetradecenol. The predominant component conforms to the formula:[2,4,5]

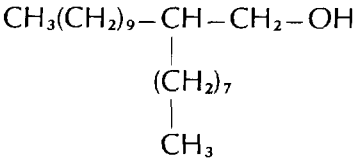
$$CH_3(CH_2)_7CH{=}CH(CH_2)_7CH_2OH$$

CAS Number: 143-28-2

Synonyms include cis-9-Octadecen-1-OL and Oleol.

Octyl Dodecanol

Octyl Dodecanol is an aliphatic alcohol with the structural formula:



Additional information concerning the composition of the material of commerce is unavailable.[2,6]

CAS Number: 5333-42-6

Synonyms include 2-Octyl Dodecanol.

Production and Occurrence

Stearyl Alcohol may be produced via Ziegler aluminum alkyl hydrolysis or the catalytic, high-pressure hydrogenation of stearic acid, followed by filtration and distillation. It may also be derived from natural fats and oils.[1,5,7-10]

Oleyl Alcohol is produced by catalytic, high-pressure hydrogenation of oleic acid followed by filtration and distillation.[4,5,7] It may also be prepared from butyl oleate by Bouveault-Blanc reduction with sodium and butyl alcohol or from triolein by hydrogenation in the presence of zinc chromite. Purification in these processes is obtained through fractional crystallization at $-40°C$ from acetone followed by distillation.[10]

Octyl Dodecanol is produced by the condensation of 2 molecules of decyl alcohol.[11] Further detail concerning the method of manufacture is unavailable.

Fatty alcohols occur in small quantities as components of wax esters in plants and animals. For example, Oleyl Alcohol has been found in the epidermis of many plants, and Stearyl Alcohol has been isolated from plants and insects. In both cases, the alcohols probably serve as components of the organisms' protective layers against water loss. Stearyl Alcohol has also been isolated from human sebaceous lipids and has been found in mammalian glands and organs. Oleyl Alcohol is found in fish oils.[10,12-23]

Properties

Stearyl Alcohol is a white, waxy, practically inert solid with a faint odor.[1,5,10,11,15] Oleyl Alcohol is a clear, odorless, viscous liquid.[4,5,11] Octyl Dodecanol is a clear, odorless, free-flowing liquid.[6,11] Other physical and chemical properties are listed in Table 1.

TABLE 1. Properties of Stearyl Alcohol, Oleyl Alcohol, and Octyl Dodecanol

Properties	*Stearyl Alcohol*[1,3,5,7,11]	*Oleyl Alcohol*[4,5,10,11,28]	*Octyl Dodecanol*[6-11]
Molecular weight (pure compound)	270.5	268.5	298.56
State	Flakes, granules	Viscous liquid	Liquid
Color	White	Clear colorless to light yellow	Colorless to pale yellow
Odor	Faint fatty	Faint	Odorless
Specific gravity	0.8124 (59°/4°C) 0.811 (35°/25°C)	0.850–0.966 (20°/20°C)	0.830–0.850 (20°/20°C)
Melting point	51–60°C 55–60°C	−7.5°C	–
Boiling point	210.5°C (15 mm)	333°C	–
Refractive index	1.4388 60°C	1.458–1.460	1.453–1.547 n_D^{20}
Acid value	1.0 max 2.0 max	1.0 max	1.0 max
Saponification value	2.0 max 3.0 max	2.0 max	10 max
Iodine value	2.0 max 5.0 max	45–98 85–95	10 max
Hydroxyl value	195–220 200–220	195–220 205–215	165–180 175–190
Soluble in	Alcohol Acetone Ether Benzene Chloroform	Alcohol Ether Acetone Light mineral oil	–
Insoluble in	Water	Water	–

Analytical Methods

Analytical methods used to detect and identify fatty alcohols include gas-liquid chromatography, thin-layer chromatography, differential scanning calorimetry, and gas chromatography.[24-27]

Impurities

Stearyl Alcohol consists of not less than 90 percent stearyl alcohol. The remainder consists chiefly of cetyl alcohol,[3] oleyl alcohol, palmityl alcohol, and other alcohols.[9] The known major constituents and minor impurities are:[1]

n-Octadecanol	90 percent minimum
n-Hexadecanol	Variable
n-Tetradecanol	Variable
n-Eriosanol	Variable
n-Dodecanol	Variable
Stearyl stearate	2 percent maximum
Octadecane	1 percent maximum
Stearic acid	0.5 percent maximum
Total hydrocarbons	1.8 percent (approx.)

Oleyl Alcohol consists of 9-n-octadecenol, but may contain some such unsaturated and saturated high molecular weight fatty alcohols as linoleyl, myristyl, and cetyl alcohols.[5,28] The known major components and minor impurities are:[4]

9-n-Octadecenol	55 percent minimum
8-n-Hexadecenol	Variable
6-n-Dodecenol	Variable
n-Hexadecanol	Variable
n-Octadecanol	Variable
n-Tetradecanol	Variable
7-n-Tetradecenol	Variable
Oleyl oleate	1.9 percent maximum
Oleic acid	0.5 percent maximum

Information on the impurities of Octyl Dodecanol is unavailable.

USES

Noncosmetic Uses

Stearyl Alcohol is used in surface-active agents, lubricants, emulsions, resins, and USP ointments and as a substitute for cetyl alcohol and antifoaming agents.[5,10,29]

Stearyl Alcohol (synthetic) has been approved as a direct food additive (DFA) ingredient, to be used under the same manufacturing practices as the natrual alcohol product. It also has indirect food additive (IFA) status for use in food con-

tainers and coatings (21 CFR 172.864; 175.300; 176.200; 176.210; 177.1200; 178.3910).[30]

Stearyl Alcohol is also used as an ingredient in over-the-counter (OTC) drugs of the miscellaneous external drug product category. It is considered to be safe at a concentration of 8 percent or less.[31]

Oleyl Alcohol is used in chemical and polymer synthesis, as a petroleum additive, and as a surfactant, plasticizer, and antifoaming agent. It is also used as an ingredient in pharmaceuticals, as a metal-machining lubricant, as a component of carbon paper, stencil paper, and ink, as an emulsifying agent, and as an emollient.[5,10,28]

Oleyl Alcohol has been approved as an IFA ingredient for use in paperboard components, as a defoaming agent, and as a lubricant (21 CFR 176.170; 176.210; 177.1210; 178.3910).[30]

Uses for Octyl Dodecanol, other than cosmetic, were not found in the review of the available literature.

Cosmetic Uses

Purpose in Cosmetic Products

The fatty alcohols, in general, are used primarily as emulsifiers, emollients, antifoaming agents, and surfactants.[5,7,32,33]

Stearyl Alcohol is used in cosmetics as an emollient, stabilizer, antifoaming agent, emulsifier, and carrier. It is used as a water in oil (w/o) emulsifier to produce firm cosmetic products at ordinary temperatures.[1,5,7,33] A personal communication from the Society of Cosmetic Chemists to the Cosmetic, Toiletry and Fragrance Association[34] states:

> Stearyl Alcohol is used in creams and lotions as an emollient, auxiliary emulsifier, bodying and pearlizing agent, thickener, and emulsion stabilizer. Stearyl Alcohol is hydrophobic in nature and will, therefore, produce a semiocclusive film on the skin that aids in inducing hydration. When used in sufficient concentrations, in the absence of liquid fats, Stearyl Alcohol emulsions leave a matte finish on the skin. In addition, Stearyl Alcohol has a sufficiently high melting point to deposit nongreasy films on the skin. When used in powders, Stearyl Alcohol improves adhesion and imparts a soft feel to the skin. Stearyl Alcohol is stable in high pH formulations, such as hair straighteners, depilatories, and cuticle removers. It is also used in shampoos and bubble baths as an opacifier.

Oleyl Alcohol is used as an emollient, emulsion stabilizer, surfactant, lubricant, and antifoaming agent.[4,7] A personal communication from the Society of Cosmetic Chemists to the Cosmetic, Toiletry and Fragrance Association[34] states:

> Oleyl Alcohol is used in a variety of cosmetic preparations as an emollient, superfatting agent, emulsion stabilizer, and pigment suspending agent. Oleyl Alcohol is miscible with fats, oils, and wax mixtures and will blend well with the oil phase of a cosmetic emulsion. Oleyl Alcohol is easily emulsified and aids in the hydration of other ingredients in a cosmetic formulation. In lipsticks, Oleyl Alcohol has excellent solvent properties, improves glide and slip, and leaves a thin film on the lips. Oleyl Alcohol has an appreciable hydroalcohol solubility and is easily incorporated into a wide variety of such lotions.

In regard to Octyl Dodecanol, the same communication[34] states:

> Octyl Dodecanol is a saturated liquid fatty alcohol with a total carbon length of 20. It is odorless, colorless, and has an indefinite shelf life. Octyl Dodecanol spreads easily when applied to the skin and leaves no visible trace of greasiness. It can be used as a carrier for oil soluble active ingredients, as an emollient, as a dispersant for pigments, and as a coupling agent for waxes and other fatty materials. Octyl Dodecanol is also used as a superfatting agent in shampoos, hair conditioners, and soaps.

Extent of Use in Cosmetic Products

The Food and Drug Administration (FDA), in voluntary cooperation with cosmetic ingredient manufacturers and formulators, compiles a list of cosmetic ingredients and the types of products and concentrations in which they are used. Filing of product formulation data with the FDA conforms to the prescribed format of preset concentration ranges and product categories as described in Title 21 part 720.4 of the Code of Federal Regulations.[30] Since certain cosmetic ingredients are supplied by the manufacturer at less than 100 percent concentration, the concentration reported by the cosmetic formulator may not necessarily reflect the true concentration found in the finished product; the actual concentration in such a case would be a fraction of that reported to the FDA. Since data are only submitted within the framework of preset concentration ranges, the opportunity exists for a 2- to 10-fold overestimation of the actual concentration of an ingredient in a particular product.

In 1981, Stearyl Alcohol was reported to be used in 425 cosmetic formulations at concentrations ranging from less than 0.1 percent to 50 percent. Oleyl Alcohol was present in 1018 different formulations at concentrations of less than 0.1 percent to greater than 50 percent. Octyl Dodecanol was listed in 371 products at concentrations of less than 0.1 percent to greater than 50 percent. Very few products contain these ingredients in the highest concentration ranges[35] (Table 2).

These compounds are found in a wide variety of cosmetic products and may, therefore, contact and enter the body through numerous routes. Some products may be applied several times daily and may remain in contact for extended periods (Table 2).

BIOLOGICAL PROPERTIES

Absorption, Metabolism, and Excretion

Stearyl Alcohol is found naturally in various mammalian tissues. This fatty alcohol is readily converted to stearic acid, another common constituent of mammalian tissues. Results from several studies indicate that Stearyl Alcohol is poorly absorbed from the gastrointestinal tract. For a review of the literature written from the years 1933 to 1978 on the absorption, metabolism, and excretion of Stearyl Alcohol, see the Evaluation of the Health Aspects of Stearyl Alcohol as a Food Ingredient, prepared for the Food and Drug Administration by The Federation of American Societies for Experimental Biology.[36]

Sieber et al.[37] studied the entry of octadecanol-1-^{14}C (Stearyl Alcohol) into

the thoracic duct lympho of the rat. The thoracic duct, abdominal aorta, and the duodenum below the pyloric valve were cannulated in male Sprague-Dawley rats. The common bile duct of some animals was also cannulated. Lymph flows were monitored, and 24 hours after surgery the radiolabeled compound (25 mCi/mmol) was administered via either the duodenal or aortic cannula. Blood and lymph were monitored for radioactivity after dosing at 0.25, 0.5, 0.75, 1, 2, 4, 6, and 24-hour intervals. Intestinal radioactivity was determined by quantifying the ^{14}C or ^{3}H of the homogenate of the intestines, which showed the percent absorbed radioactivity in the lymph was 56.6 ± 14.0. Of this, more than half was found in the triglycerides of the lymph, 6 to 13 percent in the phospholipids, 2 to 8 percent as the cholesterol esters, and 4 to 10 percent unchanged octadecanol. Ninety percent of octadecanol was carried in the chylomicron fraction. The absorption of the compound appeared to be a function of its lipid solubility.

The metabolism of Oleyl Alcohol was studied in 1 adult sheep. The rumen was cannulated and the animal received 66.0 g per day of Oleyl Alcohol in the diet for 12 days. Continuous measurement showed increased excretion of lipids (9 g/day fatty acids and 30 g/day unsaponifiables) and increased excretion of stearic and oleic acid. Oleyl Alcohol had no effect on either methane or heat production.[38]

Cis-9-octadecanol (Oleyl Alcohol) was reported to be a prominent constituent of long-chain alcohols in rat tissue. Ethanol (0.1 ml) containing 1.85 mEq cis-9-octadecanol-1-^{14}C was injected into the tail veins of rats, and the animals were sacrificed at 1, 24, 48, or 76 hours after injection. After 1 hour, the highest amount of radioactivity was found in the lungs, less in the liver, and the lowest amount in the brain. At 24, 48, and 96 hours, the rate of decline of radioactivity was greatest in the lungs and liver and least in the heart and brain. The radioactivity was incorporated mainly in glycerophosphocholines, glycerophosphoethanolamines, and neutral lipids. It was rapidly used for biosynthesis of lipids in the rat.[39]

The permeability of the blood–brain barrier to long-chain alcohols in plasma was studied using Oleyl Alcohol. Four groups of 4 male Wistar rats were fed either a standard diet (control) or the standard diet plus 160 mg of Oleyl Alcohol (available ad lib) for 7 or 14 days. The entire supplement was consumed every day by the individually caged rats. At the end of the specified times, the animals were fasted for 24 hours and killed, and the organs were analyzed. No differences in growth rates were found between experimental and control groups. The addition of Oleyl Alcohol to the diet for 7 days increased the free and esterified long-chain alcohols in the liver. After 14 days, there was a 3-fold increase in free and esterified alcohols when compared to control animals. The hepatic alk-1-enyl acyl and alkyl acyl phosphoglycerides increased 2- to 8-fold over control values during the 14-day feedings. No quantifiable changes were noted in brain lipids after 7 or 14 days.[40]

The fate of dietary Oleyl Alcohol was studied using 8 weanling male rats. For the first 5 days after weaning, the animals were fed a standard diet; then 4 rats received a mixture of 85:15 lab diet:oleyl palmitate, and the other 4 received 96:4 lab diet:Oleyl Alcohol. Two weeks after commencement of feeding of the experimental diet, tha animals were killed, and the liver and intestines were removed. Growth on the Oleyl Alcohol diet was poor when compared to the oleyl palmitate diet. The fecal distribution of ingested Oleyl Alcohol was 46 percent wax es-

TABLE 2. Product Formulation Data[35]

Product Category*	Total Formulations in Category	Total No. Containing Ingredient	No. Product Formulations Within Each Concentration Range (%)*							
			Unreported Concentration	>50	>25-50	>10-25	>5-10	>1-5	>0.1-1	≤0.1
Stearyl Alcohol										
Baby lotions, oils, powders, and creams	56	2	–	–	–	–	–	–	2	–
Eyebrow pencil	145	1	–	–	–	–	–	1	–	–
Eye shadow	2582	24	–	–	–	–	–	–	23	1
Mascara	3097	2	–	–	–	–	–	–	2	–
Other eye makeup preparations	230	2	–	–	–	–	–	–	1	1
Sachets	119	26	–	–	–	4	4	4	14	–
Hair conditioners	478	46	–	–	–	–	1	14	22	9
Hair straighteners	64	2	–	–	–	–	1	–	1	–
Permanent waves	474	5	–	–	–	–	–	–	2	3
Hair rinses (noncoloring)	158	21	–	–	–	–	–	5	10	6
Hair shampoos (noncoloring)	909	1	–	–	–	–	–	–	1	–
Hair dyes and color (all types requiring caution statement and patch test)	811	1	–	–	–	–	–	–	1	–
Hair bleaches	111	5	–	–	–	–	–	2	3	–
Other hair coloring preparations	49	2	–	–	–	–	–	2	–	–
Blushers (all types)	819	15	–	–	–	–	–	–	14	1
Makeup foundations	740	8	–	–	–	–	–	–	8	–
Leg and body paints	4	3	–	–	–	–	–	–	3	–
Lipstick	3319	3	–	–	–	–	–	–	1	2
Makeup bases	831	63	–	–	–	–	–	2	38	23
Rouges	211	1	–	–	–	–	–	–	–	1
Makeup fixatives	22	1	–	–	–	–	–	–	–	1
Other makeup preparations (not eye)	530	2	–	–	–	–	–	–	1	1
Cuticle softeners	32	2	–	–	–	–	–	–	2	–
Nail creams and lotions	25	1	–	–	–	–	–	1	–	–
Deodorants (underarm)	239	3	–	–	3	–	–	–	–	–

Other personal cleanliness products	227	10	–	–	–	9	–	1	–	–
Beard softeners	4	1	–	–	–	–	1	–	–	–
Shaving cream (aerosol, brushless, and lather)	114	6	–	–	–	–	–	1	5	–
Other shaving preparation products	29	2	–	–	–	–	–	–	1	1
Skin cleansing preparations (cold creams, lotions, liquids, and pads)	680	39	–	–	–	–	4	15	17	3
Depilatories	32	6	–	–	–	–	–	6	–	–
Face, body, and hand skin care preparations (excluding shaving preparations	823	36	–	–	–	–	1	14	19	2
Moisturizing skin care preparations	747	49	–	–	–	–	1	22	24	2
Night skin care preparations	219	12	–	–	–	–	–	6	4	2
Paste masks (mudpacks)	171	2	–	–	–	–	–	1	1	–
Skin lighteners	44	6	–	–	–	–	1	4	1	–
Skin fresheners	260	1	–	–	–	–	–	–	1	–
Wrinkle smoothers (removers)	38	1	–	–	–	–	–	1	–	–
Other skin care preparations	349	9	–	–	–	–	1	6	1	1
Suntan gels, creams, and liquids	164	2	–	–	–	–	1	–	1	–
Indoor tanning preparations	15	1	–	–	–	–	–	1	–	–
TOTAL 1981 DATA		425	–	–	3	13	16	109	224	60
TOTAL 1979 DATA		414	23	–	–	12	16	101	208	54
Oleyl Alcohol										
Bath oils, tablets, and salts	237	17	–	–	–	5	2	8	1	1
Bubble baths	475	1	–	–	–	–	–	1	–	–
Bath capsules	3	1	–	–	–	–	1	–	–	–
Other bath preparations	132	3	–	–	–	–	–	3	–	–
Eyebrow pencil	145	1	–	–	–	–	1	–	–	–
Eyeliner	369	15	–	–	–	7	7	1	–	–
Eye shadow	2582	124	–	–	–	36	60	19	7	2
Mascara	397	26	–	–	–	–	–	26	–	–
Other eye makeup preparations	230	8	–	–	–	3	2	2	1	–

TABLE 2. (Continued)

Product Category*	Total Formulations in Category	Total No. Containing Ingredient	No. Product Formulations Within Each Concentration Range (%)*							
			Unreported Concentration	>50	>25–50	>10–25	>5–10	>1–5	>0.1–1	≤0.1
Colognes and toilet waters	1120	2	–	–	–	–	–	–	2	–
Perfumes	657	5	–	–	–	3	–	1	–	1
Sachets	119	2	–	–	–	–	–	2	–	–
Other fragrance preparations	191	9	–	–	–	–	–	8	1	–
Hair conditioners	478	9	–	–	–	–	–	3	6	–
Hair straighteners	64	4	–	–	–	–	–	4	–	–
Tonics, dressings, and other hair grooming aids	290	4	–	–	–	–	–	1	3	–
Other hair preparations (noncoloring)	177	1	–	–	–	–	–	1	–	–
Hair dyes and colors (all types requiring caution statement and patch test)	811	63	–	–	–	13	–	50	–	–
Hair tints	15	13	–	–	–	13	–	–	–	–
Hair bleaches	111	2	–	–	–	–	–	2	–	–
Blushers (all types)	819	13	–	1	2	1	7	2	–	–
Face powders	555	1	–	–	–	–	–	1	–	–
Makeup foundations	740	5	–	–	–	–	–	3	2	–
Lipstick	3319	633	–	2	6	236	225	138	19	7
Makeup bases	831	2	–	–	–	1	–	1	–	–
Rouges	211	3	–	–	–	2	–	1	–	–
Other makeup preparations (not eye)	530	10	–	–	–	7	3	–	–	–
Nail polish and enamel remover	41	1	–	–	–	–	–	1	–	–
Deodorants (underarm)	239	2	–	–	–	–	–	2	–	–
Feminine hygiene deodorants	21	1	–	–	1	–	–	–	–	–
Other personal cleanliness products	227	2	–	–	–	–	–	1	1	–
Aftershave lotions	282	2	–	–	–	–	–	2	–	–
Preshave lotions (all types)	29	1	–	–	–	–	–	–	1	–
Skin cleansing preparations (cold creams, lotions, liquids, and pads)	680	2	–	–	–	–	–	2	–	–

Face, body, and hand skin care preparations (excluding shaving preparations)	823	6	–	–	–	–	1	4	–	1
Hormone skin care preparations	10	1	–	–	–	1	–	–	–	–
Moisturizing skin care preparations	747	8	–	–	–	1	–	4	2	1
Night skin care preparations	219	2	–	–	–	1	–	1	–	–
Paste masks (mudpacks)	171	2	–	–	–	–	–	1	–	1
Skin fresheners	260	2	–	–	–	–	–	–	1	1
Other skin care preparations	349	4	–	–	–	1	–	2	–	1
Suntan gels, creams, and liquids	164	5	–	–	–	–	1	3	1	–
TOTAL 1981 DATA		1018	–	3	9	331	310	301	48	16
TOTAL 1979 DATA		1069	138	1	11	267	313	294	32	13
Octyl Dodecanol										
Bath oils, tablets, and salts	237	4	–	–	–	–	4	–	–	–
Eyebrow pencil	145	1	–	–	–	–	1	–	–	–
Eyeliner	369	14	–	–	–	–	11	1	2	–
Eye shadow	2582	82	–	–	–	6	60	16	–	–
Eye lotion	13	1	–	–	1	–	–	–	–	–
Eye makeup remover	81	3	–	–	–	2	–	1	–	–
Mascara	397	1	–	–	–	–	–	1	–	–
Other eye makeup preparations	230	4	–	–	–	2	2	–	–	–
Perfumes	657	3	–	–	3	–	–	–	–	–
Fragrance powders (dusting and talcum, excluding aftershave talc)	483	4	–	–	–	–	–	–	4	–
Sachets	119	6	–	–	6	–	–	–	–	–
Other fragrance preparations	191	1	–	–	–	–	1	–	–	–
Hair conditioners	478	3	–	–	–	–	–	2	1	–
Hair sprays (aerosol fixatives)	265	2	–	–	–	–	–	1	1	–
Hair rinse (noncoloring)	158	2	–	–	–	–	–	–	2	–
Hair dyes and colors (all types requiring caution statement and patch test)	811	41	–	–	–	1	40	–	–	–
Blushers (all types)	819	6	–	–	–	3	2	1	–	–
Face powders	555	6	–	–	–	–	3	1	2	–

TABLE 2. (Continued)

Product Category*	Total Formulations in Category	Total No. Containing Ingredient	No. Product Formulations Within Each Concentration Range (%)*							
			Unreported Concentration	>50	>25–50	>10–25	>5–10	>1–5	>0.1–1	≤0.1
Lipstick	3319	112	–	1	5	46	54	5	1	–
Makeup bases	831	1	–	–	–	–	–	–	1	–
Rouges	211	1	–	–	–	1	–	–	–	–
Makeup fixatives	22	1	–	–	–	–	1	–	–	–
Other makeup preparations (not eye)	530	2	–	–	–	–	1	1	–	–
Bath soaps and detergents	148	1	–	–	–	–	–	–	–	1
Deodorants (underarm)	239	1	–	–	–	1	–	–	–	–
Other personal cleaniness products	227	1	–	–	–	–	–	1	–	–
Preshave lotions (all types)	29	1	–	–	–	–	–	–	1	–
Shaving cream (aerosol, brushless, and lather)	114	1	–	–	–	–	–	–	1	–
Skin cleansing preparations (cold creams, lotions, liquids, and pads)	680	9	–	–	–	–	3	5	–	1
Face, body, and hand skin care preparations (excluding shaving preparations)	823	23	–	–	3	2	7	9	2	–
Moisturizing skin care preparations	747	14	–	–	–	1	1	6	4	2
Night skin care preparations	219	3	–	–	–	2	–	1	–	–
Skin lighteners	44	4	–	–	–	–	–	3	1	–
Wrinkle smoothers (removers)	38	1	–	–	–	–	–	1	–	–
Other skin care preparations	349	7	–	–	–	2	2	3	–	–
Suntan gels, creams, and liquids	164	3	–	–	–	1	2	–	–	–
Other suntan preparations	28	1	–	–	–	–	–	1	–	–
TOTAL 1981 DATA		371	–	1	18	70	195	60	23	4
TOTAL 1979 DATA		295	294	–	–	–	–	1	–	–

*Preset product categories and concentration ranges in accordance with federal filing regulations (21 CFR 720.4); see Scope and Extent of Use in Cosmetics.

ter, 27 percent fatty alcohol, 16 percent monoglyceride, 6 percent free fatty acid, and 5 percent diglyceride. Oleyl Alcohol deposition in liver was manifested as 7 percent wax ester, 11 percent triglyceride, 3 percent free fatty acid, 6 percent free fatty alcohol, and 72 percent phospholipid.[41]

Two additional studies investigated the metabolism of orally administered Oleyl Alcohol in rats. The intragastric administration to rats of 200 mg/day of Oleyl Alcohol for 14 days increased the relative concentration of alkyl and alky-1-enyl moieties in alkoxylipids in the small intestine.[42] In another study, the incoporation of long-chain alcohols and acyl glycerols into hepatic tissues of rat was studied. A group of 4 rats were fed a basic diet (control), and a second group of 4 were fed the basic diet plus 100 mg/day of cis-9-octadecenyl alcohol (Oleyl Alcohol) for 28 days. Experimental compounds were fed by stomach tube, and the animals were killed 10 hours after the last feeding. The alcohol produced no abnormalities in the rats and did not effect the distribution of lipid classes or fatty acid composition of the phosphoglycerides in the liver. Pronounced changes did occur in both the alkyl and alkyl-1-enyl moieties of the phosphoglycerides of the liver. Metabolites of long-chain alcohols become incorporated into the phosphoglycerides of the liver.[43]

Miscellaneous Effects

Microbial Effects

Yanagi and Onishi[44] found that Oleyl and Stearyl Alcohol can be utilized as the sole source of carbon by some species of *Penicillium, Candida,* and *Pseudomonas.*

Cellular and Subcelluar Effects

Stearyl Alcohol, a known tobacco smoke constituent, was studied for its effect on the plasma membrane of cultured human lung fibroblasts. The fibroblasts, labeled with ^{3}H-uridine, were incubated for 30 minutes at 37°C with 25 mM alcohol in Tris-buffered saline. The leakage of radiolabeled intracellular substances was used to indicate plasma membrane damage. Stearyl Alcohol was inactive in inducing significant cellular damage.[45]

The differential effects of Oleyl Alcohol on the osmotic fragility of erythrocytes were studied using heparinized adult male human blood. The erythrocytes from venous blood were washed, prepared as a 50 percent cell suspension, and then mixed with varying concentrations of saline solution. The alcohol was dissolved in methanol and added to the cells for 10 minutes. The cells were then centrifuged, and hemolysis was determined by measuring the supernatant hemoglobin absorbance at 540 nm. At high saline concentrations, those at which hemolytic activity was greatest, the alcohol did not stabilize the erythrocytes against hypotonic hemolysis.[46]

Raz and Goldman[47] studied the effect of Oleyl Alcohol on the osmotic fragility of lysosomes. Rat livers were removed and homogenized, and their lysosomal fraction was extracted. To this fraction, Oleyl Alcohol was added in varying concentrations. Damage to lysosomes was determined by using the extent of leakage of lysosomal acid phosphatase. At 2×10^{-5} M, Oleyl Alcohol had significant stabilizing effect, and 5×10^{-5} M caused extensive damage to the lyso-

somes. The interaction of Oleyl Alcohol with lysosomes was biphasic; it was stabilizing at low concentrations and labilizing at high concentrations.

Animal Toxicology

Oral Toxicity

Acute Studies

Egan and Portwood[7] reported the LD_{50} of Stearyl Alcohol was not reached even at doses of 8 g/kg given orally to male and female Holtzman albino rats. Stearyl Alcohol is classified as "nontoxic" by the Federal Hazardous Substances Labelling Act (FHSLA) and "practically non-toxic" by the criteria of Hodge and Sterner. Other sources reported that Stearyl Alcohol had a low order of toxicity.[29,48]

Undiluted Octyl Dodecanol was administered orally as a single dose to 5 rats at 5 g/kg, with no evident toxicity.,[49]

Product formulations containing Oleyl Alcohol or Octyl Dodecanol have been tested for acute oral toxicity in rats. Products containing 8.0 percent or 20 percent Oleyl Alcohol administered by gastric intubation at doses up to 10 g/kg caused no deaths and no toxic effects.[50-52] A lipstick containing 10.2 percent Octyl Dodecanol was diluted to 50 percent and administered to 10 rats at a dose of 25 g/kg. The total dose of Octyl Dodecanol was 1.28 g/kg. There were no deaths.[53]

Percutaneous Toxicity

Acute Studies

An acute percutaneous toxicity study was conducted with 100 percent Octyl Dodecanol on 6 guinea pigs. A single dose of 3.0 g/kg was applied under occlusion to each animal on abraded and intact skin. No deaths occurred, all animals appeared normal throughout the study, and there were no gross lesions at necropsy on the seventh day.[54]

Subchronic Studies

A subchronic percutaneous toxicity study was conducted for 3 months on a cream product formulation containing 8.0 percent Stearyl Alcohol. In 2 groups of 10 rabbits each, animals received topical applications of the product at doses of 8.8 mg/cm^2 per 8.4 percent body surface area (BSA) or 13.2 mg/cm^2 per 11.2 percent BSA 3 days a week during a 3-month period. A third group of 10 rabbits served as an untreated control. The product caused very slight to well-defined erythema and mild desquamation during the first month of treatment, and mild inflammation at the site of application was noted at necropsy. The results of hematological and blood chemistry determinations, urinalyses, organ weight measurements, and necropsy indicated no treatment-related effects. No evidence of systemic toxicity attributable to topical application of the product was found.[55]

Ocular Irritation

Studies of irritation to the rabbit eye were conducted on samples of undiluted Stearyl Alcohol from 4 separate commercial sources. Each of the samples

was instilled full strength into 1 eye of each of 6 rabbits. Minimal irritation was noted on Day 1 for 3 of the samples (maximum score of 5, scale 0 to 110), and there was no irritation from the remaining sample. Scores decreased to 0 by Day 4 in all cases.[56]

An irritation test of 100 percent Oleyl Alcohol using 6 rabbits gave an ocular irritation score of 1 (max, 110) on Day 1; all scores were 0 by the second day.[57] The ocular toxicity of 4 lots of Oleyl Alcohol was tested in a modified version of the Official French Method.[58] The undiluted ingredient in a 0.1 ml volume was applied to 1 eye of each of 6 rabbits, and readings were made at 1, 24, and 48 hours. The scores were 7.17 (max, 110) at 1 hour, 0.33 at 24 hours, and 0.0 at 48 hours.[59]

In an ocular irritation test 100 percent Octyl Dodecanol with 6 rabbits had an average irritation score of 4 (max, 110) on Day 1, with a score of 0 by Day 4.[60] In an identical test, 100 percent Octyl Dodecanol had scores of 1 on Days 1 and 2 and 0 on Day 3.[61]

Several ocular irritation studies using rabbits were conducted on product formulations containing 8.0 to 20 percent Oleyl Alcohol or 3.0 to 10.2 percent Octyl Dodecanol. In every case, there was either no or only minimal, transient ocular irritation induced by these products.[52,62-67]

A Draize ocular irritation test was conducted on a hairdressing formulation containing 1.5 percent Oleyl Alcohol after several complaints of ocular irritation were reported from its use. A 0.1 ml volume of the undiluted product was instilled into the eyes of 3 albino rabbits both with and without tapwater rinse. The product was practically nonirritating. The product was also tested undiluted and in a 25 percent diluted form and caused no ocular irritation in squirrel monkeys. Furthermore, exposure of the hairdressing formulation to oxygen, UV irradiation, and 0.01 N sulfuric acid caused no increase in product-induced irritation. Instillation of the hairdressing did not potentiate the ocular irritancy of a saturated solution of NaCl, 4 percent Formosaline, or 15 percent Teepol. Irritation did occur after the instillation into the eyes of rabbits of rinsings taken from the human head after use of the hairdressing.[68]

Skin Irritation

Acute Studies

Cutaneous irritation tests using rabbits were conducted on 4 samples of Stearyl Alcohol obtained from separate commercial sources. When each sample was applied full strength under occlusion to the clipped skin of 9 rabbits for 24 hours, irritation scores of 0.4, 0.5, 1.42, and 1.5 were recorded (scale 0 to 4). These scores were indicative of minimal to mild primary skin irritation.[69]

Many studies on the irritant properties to the skin of Oleyl Alcohol have been reported. According to Drill and Lazar[70] 25 percent Oleyl Alcohol in mineral oil caused no to low skin irritation. Four lots of Oleyl Alcohol were tested for acute skin irritation according to a modified version of the Official French Method.[58] Samples were fixed for 24 hours under occlusion to the backs of rabbits. Irritation was evaluated according to a modification of the French Method scale of 0 to 8: nonirritant, less than 0.5; slight irritant, 0.5 to 2; moderate irritant, 2–5; severe irritant 5–8. The four lots were each tested in undiluted form and in a 10 percent aqueous dispersion, and 2 samples were assayed twice. Each assay was per-

formed on at least 6 animals. By this assay, Oleyl Alcohol was slightly irritating when undiluted and nonirritating when in a 10 percent aqueous dilution (Table 3).[59]

A skin irritation test with 9 rabbits gave an irritation index of 0.17 (scale 0 to 4) for 100 percent Oleyl Alcohol applied for 24 hours under occlusion. This score was indicative of minimal primary skin irritation.[71] When undiluted Oleyl Alcohol was applied to the skin of rabbits for 4 consecutive days, the greatest average irritation score was 2.33 (scale 0 to 4). This result was interpreted as mild primary skin irritation.[72]

Three separate cutaneous irritation tests using rabbits were conducted on 100 percent Octyl Dodecanol or a 30 percent aqueous dilution of Octyl Dodecanol in which the test material was applied under occlusion to the backs of 9 rabbits for 24 hours. The ingredient produced skin irritation indices (scale 0 to 4) of 1.13,[73] 0.5,[74] and zero[75] for the alcohol full strength and zero[75] for the 30 percent aqueous dilution.

Technical grade Oleyl Alcohol and 2-octyl dodecanol were tested for skin irritation using rabbits, guinea pigs, rats, miniature swine, and man.[76] In the rabbit studies, the hair on 6 areas of each of 6 albino rabbits was shaved, and test materials were applied 24 hours later. Undiluted samples were applied in 0.1 g amounts to the test areas for 24 hours. The sites were graded for irritation, and the compounds were reapplied 30 minutes later. Second gradings were made 48 hours later (72 hours after the initial application), after which Evans blue solution was injected intravenously into each animal. One hour after injection, the animals were killed and the skin sampled. In guinea pig and rat studies, 2 dorsal areas of each of 6 male Hartley guinea pigs and 6 Wistar rats were clipped free of hair, and testing began 24 hours later. One site received a dose of 0.1 g of the test compound, and the other site was left untreated. Other test parameters were identical to the rabbit test procedure. In the swine test, the entire dorsal area of groups of 6 miniature Pitman-Moore improved strain swine was clipped free of

TABLE 3. Oleyl Alcohol, Acute Skin Irritation[59]

		Irritation		
Lot	*Compound Concentration*	*Assay No.*	*Score*	*Interpretation*
1	Undiluted	1	1.71	Slight irritant
		2	1.58	Slight irritant
	10%	1	0.17	Nonirritant
		2	0.33	Nonirritant
2	Undiluted	1	1.67	Slight irritant
		2	1.75	Slight irritant
	10%	1	0.04	Nonirritant
		2	0.25	Nonirritant
3	Undiluted	1	1.50	Slight irritant
	10%	1	0.29	Nonirritant
4	Undiluted	1	1.33	Slight irritant
	10%	1	0.42	Nonirritant

hair, and testing began 24 hours later. The test compounds (0.05 g) were applied under occlusion for 48 hours and scored on a scale of (−), no reddening, to (+++), severe reddening. The results of these assays were expressed as scores of 0 (negative) to 3 (severely irritating) and compared to the results of human skin patch testing of these compounds by the same investigators. Although irritation was moderate to severe in the rabbit, guinea pig, and rat, no irritation occurred in swine or human skin. The two compounds were comparable in their ability to produce irritation (Table 4). Skin samples from the rabbit, guinea pig, and rat following exposure to the 2 alcohols had changes of acanthosis, hyperkeratinization, swelling of cells, and proliferation of basal cells. Vasodilatation, edema, alteration of collagenous fibers, and mononuclear and polymorphonuclear leukocyte infiltration were observed in the dermis. In the case of Oleyl Alcohol, edema of the epidermis developed into spongiosis, causing an "eruption" of the epidermis and "crust and ulcer" formation. Both the erupted epidermis and the infundibulum of the hair follicles were infiltrated by inflammatory cells.

Several primary skin irritation studies have been conducted on product formulations containing various concentrations of Oleyl Alcohol or Octyl Dodecanol.[52,62,58,77–80] Single applications under occlusion for 24 hours of products containing 8.0 to 20 percent Oleyl Alcohol or 4.0 percent Octyl Dodecanol produced no to mild irritation with primary irritation indices (scale 0 to 4) of 0.0 to 1.08.[52,77–79] Product formulations containing 12.7 percent Oleyl Alcohol or 10.2 percent Octyl Dodecanol applied to the skin of rabbits for 3 to 4 consecutive days produced minimal to mild irritation.[62,80] A product containing 1.5 percent Oleyl Alcohol was tested for primary skin irritation undiluted and diluted 1:4 with water. Test materials were applied to the intact and abraded skin of rabbits and to the ears of female CF/1 mice, for 4 daily 0.01 ml applications. The product, both diluted and undiluted, was irritating to the skin of rabbits and mice.[68] The degree of irritation in these studies did not correlate with the concentration of Oleyl Alcohol or Octyl Dodecanol present.

Subchronic Studies

A 60-day modified cumulative irritation test as outlined in *Journal Officiel de la Republique Francaise*[58] was conducted on 4 lots of Oleyl Alcohol in undiluted form and in 10 percent dilutions. Materials were applied every day. Scoring

TABLE 4. Comparative Irritation of Oleyl Alcohol and 2-Octyl Dodecanol in Several Species[76]

Species	Concentration (%)	Dose (g)	Irritation Score*	
			Oleyl Alcohol	2-Octyl Dodecanol
Rabbit	100	0.1	3	3
Guinea pig	100	0.1	3	2
Rat	100	0.1	2	2
Swine	100	0.05	0	0
Human	100	0.05	0	0

*0, negative; 2, moderately irritating; 3, severely irritating.

was expressed as a weekly average of daily observations. After 8 weeks, microscopic examinations of 2 samples of skin were conducted. A study of recovery from cutaneous injury was performed by interrupting application for 7 days and examining the skin thereafter. The results indicated that undiluted Oleyl Alcohol was poorly tolerated, with thickening and drying of skin and eschar formation. Microscopic changes were thinning of stratum corneum, acanthosis, and orthokeratosis. The 10 percent dilutions were "relatively well tolerated," with only slight exfoliation. Hyperplasia, moderate hypercanthosis, vascular congestion of superficial dermis, and slight erythema and edema were present.[59]

Guinea Pig Skin Sensitization

Two guinea pig sensitization studies were conducted on a deodorant containing 24.0 percent Stearyl Alcohol using the Draize repeated topical application method.[81,82] In one study,[81] 25 animals received 9 induction applications of the deodorant, diluted to 50 percent in petrolatum, under occlusion for 24 hours on abraded skin sites. This was followed by a 2-week nontreatment period and then challenge applications to both intact and abraded untreated sites. Groups of 5 animals served as petrolatum and untreated controls. At challenge, 1 of 25 treated animals and 1 of 5 petrolatum controls gave a ± (equivocal) score at 24 hours on the intact skin sites; all other test sites were nonreactive. In the second similar experiment,[82] no evidence of reaction at challenge was noted, although 2 of the 10 test animals died during the experiment. Under these test conditions, Stearyl Alcohol was not a contact sensitizer.

Comedogenicity

Stearyl Alcohol was not comedogenic when applied to the ear canal of 2 rabbits 5 days per week, for 2 weeks.[83]

Special Studies

Mutagenicity

Stearyl Alcohol was tested for mutagenic activity in an Ames assay using 4-histidine-requiring mutants of *Salmonella typhimurium* (TA98, TA100, TA1535, TA1537). The compound was tested both with and without metabolic activating S-9 fractions from the livers of rats pretreated with Aroclor 1254 or methylcholanthrene. Stearyl Alcohol was not mutagenic.[84]

Tumorigenicity

Sice[85] studied the tumor-promoting activity of alkanes and 1-alkanols. Thirty female Swiss strain mice received an initiating dose of 7,12-dimethylbenz[a]anthracene to the shaved skin of the back. Beginning 1 week after the initiating dose, 1 drop (20 μl) of a solution of Stearyl Alcohol in cyclohexane (20 g/100 ml) was applied 3 times weekly for 60 weeks over the initiated area. Twenty-three of the 30 mice survived the study, and 1 tumor appeared on the initiated area of one mouse at 30 weeks.[85]

Clinical Assessment of Safety

Eye Irritation

Ten human volunteers used 3 ml of a hairdressing product containing 1.5 percent Oleyl Alcohol daily for 5 days. The head was rinsed daily with 50 ml of water. One drop of the rinse water was instilled 4 times daily for 5 days into the same eye. No irritation occurred in any volunteers.[68]

Skin Irritation and Sensitization

Patch Testing

In 24-hour single insult occlusive patch tests, mild irritation was produced by 100 percent Stearyl Alcohol in 1 of 80 subjects[86] and by 100 percent Octyl Dodecanol in 1 of 40 subjects (Table 5).[87]

Occlusive 48-hour patches using undiluted technical grade Oleyl Alcohol and Octyl Dodecanol in 0.05 g amounts were applied to randomized sites on the skin of the back of 50 adult male volunteers.[76] The patches were removed, and 30 minutes later the sites were evaluated. Observations also were made at 72 and 96 hours and, if necessary, at 120 hours. There were no signs of skin irritation.

The North American Contact Dermatitis Group reported results of 48- and 96-hour screening patch tests of 30 percent Stearyl Alcohol in petrolatum from several 1-year intervals. Allergic reactions occurred in 2 of 172 individuals tested during the year ending in June 1976,[88] 1 of 446 during the year ending June 1977,[89] 6 of 824 during the year ending June 1979,[90] and 6 of 634 during the year ending June 1980[91] (Table 5).

Hjorth and Trolle-Lassen[92] studied allergic skin reactions to ointment bases. Out of a test population of 1664 panelists, each tested with all 3 ingredients, Stearyl Alcohol (30 percent in liquid paraffin) caused 4 positive reactions, Oleyl Alcohol (30 percent in petrolatum) produced 10 positive reactions, and Octyl Dodecanol (30 percent in petrolatum) caused 6 positive reactions (Table 5). Of the 10 patients sensitive to Oleyl Alcohol, 3 were also sensitive to Stearyl Alcohol, and the investigators suggest that cross-sensitization may have occurred.

Lanette-0 (20 percent in petrolatum) is a mixture of Cetyl and Stearyl Alcohols. Lanette-0 was patch tested on 21 patients, and Stearyl Alcohol (50 percent in petrolatum) was tested on those patients who were sensitive to the Lanette-0. Of 7 individuals who were sensitive to the Lanette-0, 4 were sensitive to the Stearyl Alcohol.[93]

Calnan and Connor[94] reported 4 positive reactions to carbon paper among 40,000 subjects tested. One of the four had dermatitis and a positive reaction to Oleyl Alcohol.

A number of product formulations containing various alcohols at concentrations of 2.5 to 24 percent have also been tested for human skin irritation (Table 6). Single insult occlusive patch tests on lipstick formulations containing 20 percent Oleyl Alcohol and a moisturizing cream containing 4.0 percent Octyl Dodecanol produced no or only minimal irritation.[95-97] Daily patch testing of 5 product formulations containing 8.0 to 24 percent Stearyl Alcohol, 2.5 percent Oleyl Alcohol, or 3.0 percent Octyl Dodecanol for 21 days produced ratings of "essentially nonirritating" or "slightly irritating."[98-102] Controlled use of a lipstick containing 8.0 percent Oleyl Alcohol for 4 weeks produced no irritation.[103] Re-

TABLE 5. Clinical Skin Patch Tests with Stearyl Alcohol, Oleyl Alcohol, or Octyl Dodecanol

Test Method	*Material Tested*	*Concentration of Alcohol (%)*	*No. of Subjects*	*Results*	*Reference*
24-hour single insult occlusive patch	Stearyl Alcohol	100	80	Mild irritation in 1 subject	86
	Octyl Dodecanol	100	40	Mild irritation in 1 subject	87
Single insult screening patch for contact sensitization	Stearyl Alcohol	30 in petrolatum	172	2 positive reactions; 1.2 %	88
	Stearyl Alcohol	30 in petrolatum	446	1 positive reaction; 0.22 %	89
	Stearyl Alcohol	30 in petrolatum	824	6 positive reactions; 0.73 %	90
	Stearyl Alcohol	30 in petrolatum	634	6 positive reactions; 0.95 %	91
Single insult screening patch for contact sensitization	Stearyl Alcohol	30 in liquid paraffin	1664	4 positive reactions; 0.24 %	92
	Oleyl Alcohol	30 in petrolatum	1664	10 positive reactions; 0.60 %	92
	Oleyl Dodecanol	30 in petrolatum	1664	6 positive reactions; 0.36 %	92

TABLE 6. Clinical Skin Patch Tests with Product Formulations Containing Stearyl Alcohol, Oleyl Alcohol, or Octyl Dodecanol

Test Method	*Material Tested*	*Concentration of Alcohol (%)*	*No. of Subjects*	*Results*	*Reference*
24-hour single insult occlusive patch	Lipstick	20 Oleyl Alcohol	19	No signs of irritation	95
	Lipstick	20 Oleyl Alcohol	16	No signs of irritation	96
	Moisturizing cream	4.0 Octyl Dodecanol	20	PII, 0.03 (max 4.0); minimal irritation in 1 subject	97
21-day cumulative irritancy (23-hour occlusive patch for 21 consecutive days)	Deodorant	24 Stearyl Alcohol	12	Slightly irritating; total composite score was 128/630 max	98
	Antiperspirant	17 Stearyl Alcohol	27	Essentially nonirritating	99
	Cream	8.0 Stearyl Alcohol	9	Essentially nonirritating; total composite score was 36/630 max	100
	Moisturizer	2.5 Oleyl Alcohol	10	Slightly irritating; total composite score was 59/630 max	101
	Eye pencil	3.0 Octyl Dodecanol	16	Essentially nonirritating; total composite score was 7.5/630. Patches applied 5 days/week for 21 total patches	102
Controlled use (4 weeks of daily use)	Lipstick	8.0 Oleyl Alcohol	52	No irritation	103
Schwartz-Peck prophetic patch test (open and closed 48-hour patches, repeated after 2 weeks)	Lipstick	8.0 Oleyl Alcohol	308	Mild irritation with closed patch in 3 subjects at first exposure; no evidence of sensitization. Supplemental UV exposure after second insult produced no reactions	104
Modified repeated insult patch test (12- or 24-hour patches 4 days/week for 8 induction patches; challenge patch after 2-week rest)	Antiperspirant	17 Stearyl Alcohol	52	Minimal irritation; no sensitization	105
	Antiperspirant	17 Stearyl Alcohol	45	Minimal to mild irritation with evidence of fatigue; no evidence of sensitization	106
	Antiperspirant	14 Stearyl Alcohol	50	No irritation; no sensitization	107

TABLE 6. (Continued)

Test Method	*Material Tested*	*Concentration of Alcohol (%)*	*No. of Subjects*	*Results*	*Reference*
Draize-Shelanski repeated insult patch test (24- or 48-hour patches 3 days/ week for 10 induction patches; challenge after 2-week rest)	Deodorant	24 Stearyl Alcohol	176	Minimal irritation; no sensitization	108
	Deodorant	24 Stearyl Alcohol	150	Minimal irritation; no sensitization	109
	Antiperspirant	17 Stearyl Alcohol	50	Minimal irritation; 1 subject demonstrated reaction indicative of allergic contact dermatitis at challenge; however, rechallenge at untreated site was negative	110
	Antiperspirant	14 Stearyl Alcohol	100	No irritation; no sensitization	111
	Hand cream	12 Stearyl Alcohol	205	Minimal irritation; no sensitization	112
	Deodorant	12 Stearyl Alcohol	48	Mild irritation; no sensitization	113
	Deodorant	12 Stearyl Alcohol	154	Minimal irritation; no sensitization	114
	Cream	8.0 Stearyl Alcohol	213	Minimal irritation; no sensitization	115
	Cream	12.7 Oleyl Alcohol	102	No irritation; no sensitization	116
	Lipstick	8.0 Oleyl Alcohol	154	Minimal irritation; no sensitization. Supplemental UV exposure after induction patches 1, 4, 7, and 10 and after challenge showed no photosensitization	104
	Cream	2.5 Oleyl Alcohol	210	Mild irritation in 1 subject during induction and 1 at challenge; none thought to be indicative of sensitization	117
	Cream	2.5 Oleyl Alcohol	205	Minimal to mild irritation during induction and at challenge; none were thought to be indicative of sensitization	118
	Lipstick	10.2 Octyl Dodecanol	197	No irritation; no sensitization	119
	Unspecified product formulation	3.0 Octyl Dodecanol	210	Isolated mild induction reactions in 2 subjects; no reactions at challenge	120

sults indicative of irritation from product formulations are difficult to interpret with respect to a single ingredient.

Several product formulations containing the alcohols have been tested for skin sensitization on a total of 2629 subjects using a variety of test methods. These studies included: 1 Schwarz-Peck prophetic patch test on a product formulation containing 8.0 percent Oleyl Alcohol, 3 modified repeated insult patch tests on antiperspirant formulations containing 14 or 17 percent Stearyl Alcohol, and 14 Draize-Shelanski repeated insult patch tests on products containing 8.0 to 24 percent Stearyl Alcohol, 2.5 to 12.7 percent Oleyl Alcohol, or 3.0 or 10.2 percent Octyl Dodecanol. Of the 2629 subjects in these studies, there were no reactions indicative of sensitization (Table 6).

Case Reports

Contact sensitization to Stearyl Alcohol has been reported in 3 individuals: 2 had an urticarial-type reaction, and 1 of these reactions was thought to be due to impurities in the Stearyl Alcohol sample.[9,121,122]

Photoreactivity

A phototoxicity study was conducted on a cream product formulation containing 2.5 percent Oleyl Alcohol using 10 subjects. A single 24-hour skin patch of the product with 1X Minimal Erythema Dose (MED) exposure to a Krohmeyer Hot Quartz Lamp produced no reactions.[123] The same product was tested for photoallergenicity with 25 subjects. Five daily 24-hour induction patches with exposure for 30 seconds to a windowglass-filtered Krohmeyer Hot Quartz Lamp were followed by a 12-day nonexposure period and then a single 24-hour challenge with the same UV light exposure. No signs of photosensitivity were present.[123]

A repeated insult photosensitization test using 23 subjects was conducted on a lipstick formulation containing 10.2 percent Octyl Dodecanol. Each subject had applied a 24-hour occlusive patch of the test material followed by UV irradiation of the test site with 3 times the individual's MED. The light source was a filtered 150W Xenon Arc Solar Simulator that produced a continuous emission spectrum in the UVA and UVB region (290 to 400 nm). Patches and irradiation were repeated twice weekly for a total of 6 exposures. Following a 10-day nonexposure period, patches and irradiation were repeated on a previously untreated site. There were no reactions and thus no evidence of phototoxicity or photoallergenicity.[124]

Schwartz-Peck and Draize-Shelanski skin sensitization tests on a lipstick formulation containing 8.0 percent Oleyl Alcohol (summarized in Table 6) also included supplemental UV light exposure, with no resultant reactions.[104]

SUMMARY

Stearyl Alcohol, Oleyl Alcohol, and Octyl Dodecanol are long-chain saturated or unsaturated (Oleyl) fatty alcohols. The materials of commerce are mixtures of fatty acids, with the predominant species being the named compound.

These alcohols have a wide variety of uses in pharmaceutical, food, and other industries. Stearyl Alcohol is approved for use in certain over-the-counter drugs, and Stearyl and Oleyl Alcohols are approved for some food additive appli-

cations. They are used in numerous cosmetic product categories at concentrations of less than 0.1 percent to greater than 50 percent. They are chiefly used at concentrations less than 25 percent.

The metabolism of Stearyl Alcohol and Oleyl Alcohol in rats is well described. They are used in the biosynthesis of lipids and other naturally occurring cellular constituents or enter metabolic pathways for energy production.

Stearyl Alcohol was not mutagenic in the Ames Assay, and it did not promote tumor formation when tested with DMBA. Oleyl Alcohol and Octyl Dodecanol were not tested in these assays. Due to the chemical nature and benign biological activity of these compounds, they are not suspected of significant potential for carcinogenesis.

The results of acute oral toxicity studies in rats of undiluted Stearyl Alcohol and Octyl Dodecanol and of products containing Oleyl Alcohol and Octyl Dodecanol at concentrations up to 20 percent indicate a very low order of toxicity. Results of percutaneous toxicity studies with 100 percent Octyl Dodecanol and with products containing 8.0 percent Stearyl Alcohol or 8.0 percent Oleyl Alcohol also indicate a low order of toxicity. In rabbit irritation tests, these alcohols produced minimal ocular irritation and minimal to mild primary cutaneous irritation. In 1 assay system, the skin irritancy of technical grade Oleyl Alcohol and Octyl Dodecanol was moderate to severe in rabbits, guinea pigs, and rats, whereas no irritation was seen in swine and human skin. Observations made in a subchronic skin irritation study indicated that 100 percent Oleyl Alcohol was "poorly tolerated" when applied to the skin of rabbits daily for 60 days, whereas 10 percent dilutions were "relatively well tolerated." A product containing 24 percent Stearyl Alcohol produced no evidence of contact sensitization in the guinea pig. A rabbit ear comedogenicity test on Stearyl Alcohol was negative.

The results of single insult clinical patch testing indicate a very low order of skin irritation potential for undiluted Stearyl Alcohol and Octyl Dodecanol. Several studies of screening patch testing for contact sensitization in large populations had rates of 19 of 3740 (0.51 percent) for Stearyl Alcohol, 10 of 1664 (0.60 percent) for Oleyl Alcohol, and 6 of 1664 (0.36 percent) for Octyl Dodecanol. Reports of isolated cases of contact dermatitis from Stearyl Alcohol are available. Tests of product formulations in humans demonstrated low potentials for significant skin irritation or sensitization from the alcohols in formulation. Photoreactivity studies on products containing 2.5 percent Oleyl Alcohol or 10.2 percent Octyl Dodecanol were negative for phototoxicity or photosensitization. A hairdressing product containing 1.5 percent Oleyl Alcohol was nonirritating to the human eye.

CONCLUSION

Based on the available data, Stearyl Alcohol, Oleyl Alcohol, and Octyl Dodecanol are safe as currently used in cosmetics.

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