Safety Assessment of Fatty Acids & Fatty Acid Salts as Used in Cosmetics

Status:	Draft Report for Panel Review
Release Date:	November 9, 2018
Panel Meeting Date:	December 3-4, 2018

The 2018 Cosmetic Ingredient Review Expert Panel members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A. Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Executive Director is Bart Heldreth, Ph.D. This safety assessment was prepared by Christina L. Burnett, Senior Scientific Analyst/Writer.

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Cosmetic Ingredient Review

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Memorandum

To: CIR Expert Panel Members and Liaisons
From: Christina L. Burnett, Senior Scientific Writer/Analyst
Date: November 9, 2018
Subject: Draft Safety Assessment on Fatty Acids and Fatty Acid Salts

Enclosed is the Draft Report of the Safety Assessment of Fatty Acids and Fatty Acid Salts as Used in Cosmetics. (It is identified as *facids122018rep* in the pdf document.) According to the *Dictionary*, fatty acids and fatty acid salts are reported to function mainly as anticaking agents, emulsion stabilizers, viscosity increasing agents, opacifying agents, and surfactants in cosmetics.

On October 2, 2018, CIR issued the Scientific Literature Review (SLR) of these ingredients. This safety assessment was initiated based on the high frequency of use of Linoleic Acid reported to the VCRP in 2016/2017, which led to its prioritization for review by the Panel. Several previously assessed ingredients, such as Oleic Acid, Myristic Acid, and Stearic Acid, have been included in the report as they fit within this grouping of fatty acids and salts and can be appropriately re-reviewed here within. Each of the ingredients in this report comprises a carboxylic acid functional group and an aliphatic (fatty) chain. Relevant data from the previous reports have been *summarized in italics* in the appropriate sections of this safety assessment.

The Council provided concentration of use survey data (identified as *facids122018data1* through *facids122018data3*). No other unpublished data were provided. Comments on the SLR were received from the Council and addressed (*facids122018pcpc*).

According to 2018 VCRP data, Linoleic Acid has 633 total uses in cosmetic products; the majority of these uses are in leave-on skin care products. Stearic Acid, a previously reviewed ingredient, has the most reported uses of the ingredients in this safety assessment, with a total of 5738; the majority of these uses are in leave-on eye makeup preparations and skin care products. Stearic Acid had a total of 2133 reported uses in 2006; the majority of the uses were also in leave-on eye makeup preparations and skin care products. Palmitic Acid, another previously reviewed ingredient, has the second greatest number of reported uses in this safety assessment with 1240; the majority of the uses were in leave-on eye makeup preparations and skin care products. In 2006, Palmitic Acid had a total of 132 reported uses; the majority of the uses were in rinse-off products such as shampoos, shaving products, and personal cleanliness products.

The results of the concentration of use survey conducted in 2016 by the Council indicate that Linoleic Acid is used at up to 21.8% in rinse-off skin cleansing products and at up to 3.4% in face, neck, body, and hand skin care products. Sodium Laurate/Linoleate/Oleate/Palmitate is used at up to 84.7% in bath soaps and detergents and at up to 74.5% in leave-on baby products. Stearic Acid is reported to be used at up to 37.4% in rinse-off products (bath soaps and detergents) and at up to 21% in leave-on products (eyebrow pencil); Palmitic Acid is reported to be used at up to 21% in both rinse-off and leave-on products (skin cleansing preparations and fragrance products, respectively). In 2006, Stearic Acid was reported to be used at up to 43% in rinse-off products (shaving cream) and 22% in leave-on products (eyeliners); Palmitic Acid was reported to be used at up to 20% in rinse-off products (shaving cream) and 16% in leave-on products (lipsticks).

Currently, the ingredients in this report are presented alphabetically, but a table is included that describes the carbon chain length of the parent fatty acid. The Panel should advise CIR staff on any other ingredient organization that would be helpful in reviewing the safety of these ingredients, or if the current organization is sufficient.

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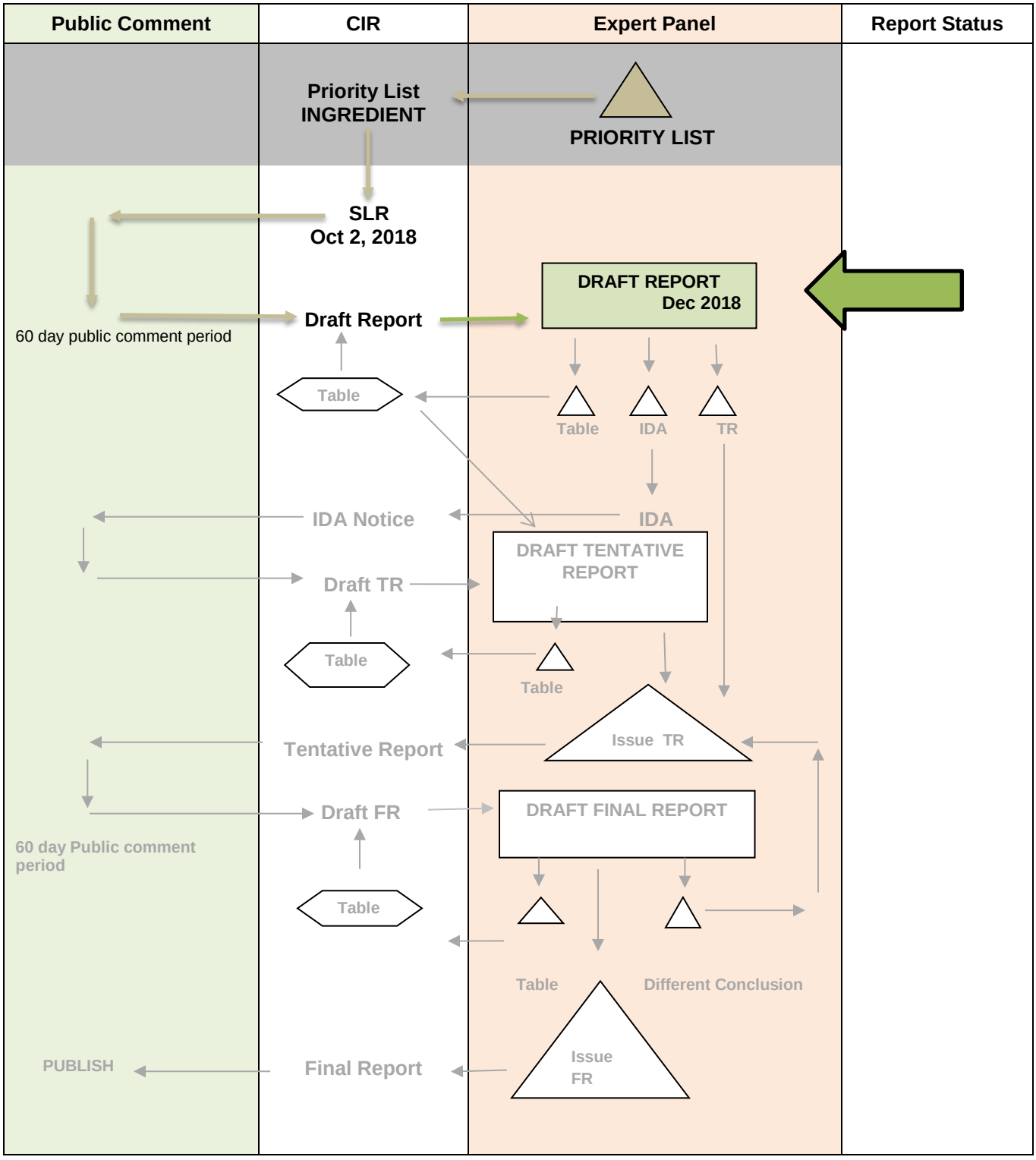
If no further data are needed, the Panel should formulate a Discussion and issue a Tentative Report. However, if additional data are required, the Panel should be prepared to identify those needs and issue an Insufficient Data Announcement.

SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY Fatty Acids and Fatty Acid Salts

MEETING December 2018



Fatty Acids and Fatty Acid Salts History

October 2, 2018 – Scientific Literature Review announced.

Fatty Acids and Fatty Acid Salts Data Profile –December 2018 – Writer, Christina Burnett																
	In-Use	Physical/Chemical Properties	Method of Manufacturing	Composition/Impurities	UV Absorption	Acute Toxicity	Repeated Dose Toxicity	Genotoxicity	Reproductive and Developmental	Carcinogenicity	Toxicokinetics	Irritation/Sensitization - Nonhuman	Irritation/Sensitization - Human	Ocular/Mucosal	Phototoxicity	Clinical/Case Studies
Aluminum Dilinoleate																
Aluminum Distearate	X	X										*		*		
Aluminum Isostearate																
Aluminum Isostearates/Palmitates																
Aluminum Isostearates/Stearates																
Aluminum Isostearates/ Laurates/Palmitates																
Aluminum Isostearates/ Laurates/Stearates																
Aluminum Lanolate																
Aluminum Stearate	X	X				*										
Aluminum Stearates	X															
Aluminum Tristearate	X	X										X				
Ammonium Isostearate																
Ammonium Oleate		X				X		X				X				
Ammonium Stearate		X				*						*	*	*		
Arachidic Acid	X	X														
Beeswax Acid				X												
Behenic Acid	X	X		X		X	X	X	X							
C14-28 Alkyl Acid	X															
C10-40 Isoalkyl Acid	X															
C14-28 Isoalkyl Acid	X															
C32-36 Isoalkyl Acid																
Calcium Behenate	X															
Calcium Laurate																
Calcium Stearate	X	X		X		X	X*	X	X		*					
Calcium Undecylenate		X														
Capric Acid	X	X				X	X	X	X			X				

Fatty Acids and Fatty Acid Salts Data Profile –December 2018 – Writer, Christina Burnett																
	In-Use	**Physical/Chemical Properties**	**Method of Manufacturing**	**Composition/Impurities**	**UV Absorption**	**Acute Toxicity**	**Repeated Dose Toxicity**	**Genotoxicity**	**Reproductive and Developmental**	**Carcinogenicity**	**Toxicokinetics**	**Irritation/Sensitization - Nonhuman**	**Irritation/Sensitization - Human**	**Ocular/Mucosal**	**Phototoxicity**	**Clinical/Case Studies**
Caproic Acid	X	X						X				X		X		
Caprylic Acid	X	X		X		X		X	X			X		X		
Dilinoleic Acid	X	X														
Dierucic Acid																
Eicosatrienoic Acid		X														
Erucic Acid		X														
Hydroxycapric Acid	X	X														
Hydroxycaprylic Acid	X	X														
10-Hydroxydecanoic Acid	X	X														
Hydroxylauric Acid		X														
Hydroxystearic Acid	X	X						*	*	*	*	X	*			X
10-Hydroxystearic Acid		X					*									
Isomerized Linoleic Acid	X	X				X		X								
Isomerized Safflower Acid																
Isostearic Acid	X	X				*					*	X*	*	*	*	
Lauric Acid	X	X	*	X		X*	*	X*	*	*	*	X*	*	X*	X	
Linoleic Acid	X	X		X			X	X				X				
Linolenic Acid	X	X										X				
Lithium Stearate	X	X				X*	X	X	X			X		X		
Magnesium Lanolate																
Magnesium Laurate	X															
Magnesium Palmitate		X														
Magnesium Stearate	X	X		X		*		*	*	*		*		*		
Magnesium Tallowate																
Myristic Acid	X	X	*	X				X	*		*	*	*	*		
Methyl Myristic Acid		X														
Oleic Acid	X	X	*	X		*	*	*	*	*	X*	X*	*	X*	*	
Palmitic Acid	X	X	*	X		X*	*		*	*	*	X*	X*	X*	*	

Fatty Acids and Fatty Acid Salts Data Profile –December 2018 – Writer, Christina Burnett																
	In-Use	**Physical/Chemical Properties**	**Method of Manufacturing**	**Composition/Impurities**	**UV Absorption**	**Acute Toxicity**	**Repeated Dose Toxicity**	**Genotoxicity**	**Reproductive and Developmental**	**Carcinogenicity**	**Toxicokinetics**	**Irritation/Sensitization - Nonhuman**	**Irritation/Sensitization - Human**	**Ocular/Mucosal**	**Phototoxicity**	**Clinical/Case Studies**
Potassium Behenate	X															
Potassium Borageate																
Potassium Camelliate																
Potassium Caprate																
Potassium Caprylate																
Potassium Caprylate/Caprate																
Potassium Castorate	X															
Potassium Hydrogenated Tallowate	X															
Potassium Hydroxystearate																
Potassium Isostearate	X															
Potassium Lanolate																
Potassium Laurate	X	X														
Potassium Linoleate		X														
Potassium Linseedate																
Potassium Oleate	X	X														
Potassium Olivate/Sunflowerseedate																
Potassium Palmitate	X															
Potassium Stearate	X	X														
Potassium Sunflowerseedate																
Potassium Tallate	X															
Potassium Tallowate	X															
Potassium Undecylenate		X														X
Sodium Arganate																
Sodium Beeswax																
Sodium Behenate	X															
Sodium Camellia Japonica Seedate																

Fatty Acids and Fatty Acid Salts Data Profile –December 2018 – Writer, Christina Burnett																
	In-Use	Physical/Chemical Properties	Method of Manufacturing	Composition/Impurities	UV Absorption	Acute Toxicity	Repeated Dose Toxicity	Genotoxicity	Reproductive and Developmental	Carcinogenicity	Toxicokinetics	Irritation/Sensitization - Nonhuman	Irritation/Sensitization - Human	Ocular/Mucosal	Phototoxicity	Clinical/Case Studies
Sodium Caprate											X					
Sodium Caprylate																
Sodium Castorate	X															
Sodium Dilinoleate																
Sodium Hydrogenated Tallowate																
Sodium Hydroxystearate																
Sodium Isostearate	X															
Sodium Lanolate																
Sodium Lardate																
Sodium Laurate	X														X	
Sodium Laurate/Linoleate/ Oleate/Palmitate	X															
Sodium Linoleate																
Sodium Oleate	X	X								X						
Sodium Palmitate	X	X														
Sodium Stearate	X	X				*					*		*			
Sodium Tallowate	X															
Sodium Tamanuseedate																
Sodium Undecylenate		X					X					X		X		
Stearic Acid	X	X	*	X		X*	*	*	*	*	*	*	*	X*	X	
Trilinoleic Acid	X	X										X				
Undecanoic Acid	X	X														
Undecylenic Acid	X	X				X	X	X	X			X		X		X

X indicates that data were available in the category for that ingredient.
* indicates data were available in previous reports for that ingredient.

Fatty Acids & Soaps

Ingredient	CAS #	InfoB	SciFin	PubMed	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	ECETOC	HPVIS	NICNAS	NTIS	NTP	WHO	FAO	NIOSH	FEMA	Web
Aluminum Dilinoleate	53202-37-2	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Aluminum Distearate - RR	300-92-5	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Aluminum Isostearate	72277-75-9	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Aluminum Isostearates/Palmitates		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Aluminum Isostearates/Stearates		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Aluminum Isostearates/Laurates/ Palmitates		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Aluminum Isostearates/Laurates/\ Stearates		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Aluminum Lanolate		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Aluminum Stearate-RR	7047-84-9	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Aluminum Stearates		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Aluminum Tristearate-RR	637-12-7	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Ammonium Isostearate		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Ammonium Oleate	544-60-5	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Ammonium Stearate-RR	1002-89-7	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Arachidic Acid	506-30-9	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Beeswax Acid		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Behenic Acid	112-85-6	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
C14-28 Alkyl Acid		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
C10-40 Isoalkyl Acid		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
C14-28 Isoalkyl Acid		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
C32-36 Isoalkyl Acid		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Calcium Behenate	3578-72-1	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Calcium Laurate	4696-56-4	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Calcium Stearate	1592-23-0	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Calcium Undecylenate	1322-14-1	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Capric Acid	334-48-5	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Caproic Acid	142-62-1	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Caprylic Acid	124-07-2	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√

Ingredient	CAS #	InfoB	SciFin	PubMed	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	ECETOC	HPVIS	NICNAS	NTIS	NTP	WHO	FAO	NIOSH	FEMA	Web
Dilinoleic Acid	26085-09-6; 6144-28-1	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Dierucic Acid	63541-50-4	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Eicosatrienoic Acid	1783-84-2	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Erucic Acid	112-86-7	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Hydroxycapric Acid	5393-81-7	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Hydroxycaprylic Acid	617-73-2	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
10-Hydroxydecanoic Acid	1679-53-4	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Hydroxylauric Acid	2984-55-6	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Hydroxystearic Acid - RR	106-14-9; 1330-70-7	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
10-Hydroxystearic Acid	638-26-6	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Isomerized Linoleic Acid	67701-06-8	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Isomerized Safflower Acid	121250-47-3	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Isostearic Acid-RR	2724-58-5; 30399-84-9	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Lauric Acid	143-07-7	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Linoleic Acid	342889-37-6; 60-33-3	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Linolenic Acid	463-40-1	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Lithium Stearate-RR	4485-12-5	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Magnesium Lanolate		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Magnesium Laurate	4040-48-6	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Magnesium Palmitate	2601-98-1	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Magnesium Stearate-RR	557-04-0	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Magnesium Tallowate	68953-41-3	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Myristic Acid-RR	544-63-8	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Methyl Myristic Acid	73679-18-2	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Oleic Acid-RR	112-80-1; 2027-47-6	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Palmitic Acid-RR	57-10-3	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Potassium Behenate	7211-53-2	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Potassium Borageate		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Potassium Camelliate		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Potassium Caprate	13040-18-1	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√

Ingredient	CAS #	InfoB	SciFin	PubMed	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	ECETOC	HPVIS	NICNAS	NTIS	NTP	WHO	FAO	NIOSH	FEMA	Web
Potassium Caprylate	764-71-6	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Potassium Caprylate/Caprate		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Potassium Castorate	8013-05-6	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Potassium Hydrogenated Tallowate		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Potassium Hydroxystearate	34326-46-0	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Potassium Isostearate	68413-46-7	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Potassium Lanolate		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Potassium Laurate	10124-65-9	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Potassium Linoleate	3414-89-9	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Potassium Linseedate		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Potassium Oleate	143-18-0; 23282-35-1	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Potassium Olivate/ Sunflowerseedate		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Potassium Palmitate	2624-31-9	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Potassium Stearate-RR	593-29-3	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Potassium Sunflowerseedate		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Potassium Tallate-RR	61790-44-1		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Potassium Tallowate	61790-32-7	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Potassium Undecylenate	6159-41-7	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Sodium Arganate		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Sodium Beeswax		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Sodium Behenate	5331-77-1	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Sodium Camellia Japonica Seedate		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Sodium Caprate	1002-62-6	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Sodium Caprylate	1984-06-1	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Sodium Castorate	8013-06-7; 96690-37-8	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Sodium Dilinoleate	67701-20-6	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Sodium Hydrogenated Tallowate		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Sodium Hydroxystearate	13329-67-4	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√

Ingredient	CAS #	InfoB	SciFin	PubMed	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	ECETOC	HPVIS	NICNAS	NTIS	NTP	WHO	FAO	NIOSH	FEMA	Web
Sodium Isostearate	64248-79-9	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Sodium Lanolate		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Sodium Lardate	68605-06-1	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Sodium Laurate	629-25-4	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Sodium Laurate/Linoleate/ Oleate/Palmitate		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Sodium Linoleate	822-17-3	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Sodium Oleate	143-19-1; 166558-02-4	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Sodium Palmitate	408-35-5	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Sodium Stearate-RR	822-16-2	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Sodium Tallowate	8052-48-0	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Sodium Tamanuseedate		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Sodium Undecylenate	3398-33-2	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Stearic Acid-RR	57-11-4	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Trilinoleic Acid	68937-90-6; 7049-66-3	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Undecanoic Acid	112-37-8	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Undecylenic Acid	112-38-9 ; 1333-28-4	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√

Botanical and/or Fragrance Websites (if applicable)

Ingredient	Dr. Duke's	Taxonomy	GRIN	Sigma-Aldrich	AHPA	EMA	AGRICOLA	SSA	IFRA	RIFM
Capric Acid	NA	NA	NA	NA	NA	NA	NA	NA	√	√
Caproic Acid	NA	NA	NA	NA	NA	NA	NA	NA	√	√
Caprylic Acid	NA	NA	NA	NA	NA	NA	NA	NA	√	√
Lauric Acid-RR	NA	NA	NA	NA	NA	NA	NA	NA	√	√
Linoleic Acid	NA	NA	NA	NA	NA	NA	NA	NA	√	√
Linolenic Acid	NA	NA	NA	NA	NA	NA	NA	NA	√	√
Myristic Acid-RR	NA	NA	NA	NA	NA	NA	NA	NA	√	√
Oleic Acid-RR	NA	NA	NA	NA	NA	NA	NA	NA	√	√
Palmitic Acid-RR	NA	NA	NA	NA	NA	NA	NA	NA	√	√
Stearic Acid-RR	NA	NA	NA	NA	NA	NA	NA	NA	√	√
Undecanoic Acid	NA	NA	NA	NA	NA	NA	NA	NA	√	√
Undecylenic Acid	NA	NA	NA	NA	NA	NA	NA	NA	√	√

NA= Not applicable
RR = Re-Review

Search Strategy

SciFinder and **PubMed** tallies are combined. SciFinder was searched by CAS# and INCI names, references were then narrowed by "adverse effects, including toxicity". PubMed returns were limited when needed by "toxicity" or "dermal" or "sensitization" or "irritation".

Aluminum Tristearate (limited to 2000-2018) = 3335 hits, 3 relevant
Ammonium Stearate (limited to 2000-2018) = 3333 hits, 0 relevant
Arachidic Acid OR Eicosenoic Acid = 335 hits, 2 relevant
Calcium Stearate (limited to 2000-2018) = 3346 hits, 1 relevant
Capric Acid = 1012 hits, 5 relevant
Caproic Acid = 1411 hits, 1 relevant
Caprylic Acid = 2240 hits, 14 relevant
Dierucic Acid = 629 hits, 0 relevant
Eicosatrienoic Acid = 1889 hits, 4 relevant
Erucic Acid = 623 hits, 5 relevant
Hydroxystearic Acid (limited 2014-2018 due to RR in 2015) = 38 hits, 0 relevant
Lauric Acid = 1833 hits, 2 relevant
Linoleic Acid = 21,546 hits, 22 relevant
Linolenic Acid = 10,526 hits, 4 relevant
Lithium Stearate = 7 hits, 0 relevant
Magnesium Lanolate = 0 hits
Magnesium Laurate = 6 hits, 0 relevant
Magnesium Palmitate = 70 hits, 0 relevant
Magnesium Stearate (limited to 2000-2018) = 3574 hits, 2 relevant
Magnesium Tallowate = 0 hits
Myristic Acid (limited to 2008-2018 due to review in 2010) = 1046 hits, 0 relevant
Methyl Myristic Acid = 181 hits, 0 relevant
Oleic Acid (limited to 2003-2018 due to RR in 2004/2005) = 10,243 hits, 19 relevant
Palmitic Acid (limited to 2003-2018 due to RR in 2004/2005) = 6653 hits, 7 relevant
Potasssium Behenate = 2 hits, 0 relevant
Potassium Borageate as borageate = 0 hits
Potassium Camelliate as camelliate = 0 hits
Potassium Caprate = 7 hits, 1 relevant
Potassium Caprylate = 7 hits, 2 relevant
Potassium Caprylate/Caprate = 0 hits
Potassium Castorate as castorate = 0 hits
Potassium Hydrogenated Tallowate = 0 hits
Potassium Hydroxystearate = 2 hits, 0 relevant
Potassium Isostearate = 1 hit, 0 relevant
Potassium Lanolate = 0 hits
Potassium Laurate = 1853 hits, 2 relevant
Potassium Linoleate = 301 hits, 0 relevant
Potassium Linseedate as linseedate = 0 hits
Potassium Oleate = 378 hits, 1 relevant

Potassium Olivate/Sunflowerseedate = 0 hits
Potassium Palmitate = 143 hits, 0 relevant
Potassium Stearate (limited to 2000-2018) = 53 hits, 0 relevant
Potassium Sunflowerseedate as sunflowerseedate = 0 hits
Potassium Tallate (limited to 2009-2018) = 0 hits
Potassium Tallowate = 0 hits
Potassium Undecylenate = 4 hits, 1 relevant
Sodium Arganate as arganate = 0 hits
Sodium Beeswax = 26 hits, 0 relevant
Sodium Behenate = 14 hits, 0 relevant
Sodium Camellia Japonica Seedate = 0 hits
Sodium Caprate = 817 hits, 1 relevant
Sodium Caprylate = 1989 hits, 4 relevant
Sodium Castorate = 0 hits
Sodium Dilinoleate = 0 hits
Sodium Hydrogenated Tallowate = 0 hits
Sodium Hydroxystearate = 7 hits, 0 relevant
Sodium Isostearate = 7 hits, 0 relevant
Sodium Lanolate = 1 hit, 0 relevant
Sodium Lardate = 0 hits
Sodium Laurate = 1936 hits, 4 relevant
Sodium Laurate/Linoleate/Oleate/Palmitate = 1 hit, 0 relevant
Sodium Linoleate = 756 hits, 0 relevant
Sodium Oleate = 523 hits, 2 relevant
Sodium Palmitate = 15,433 hits, 0 relevant
Sodium Stearate (limited to 2000-2018) =3477 hits, 0 relevant
Sodium Tallowate = 249,884 hits, 0 relevant
Sodium Tamanuseedate = 0 hits
Sodium Undecylenate = 10 hits, 0 relevant
Stearic Acid (limited to 2003-2018 due to RR in 2004/2005) = 3090 hits, 3 relevant
Trilinoleic Acid = 3 hits, 0 relevant
Undecanoic Acid = 247 hits, 0 relevant
Undecylenic Acid = 237 hits, 3 relevant

Typical Search Terms

- INCI names
- CAS numbers
- chemical/technical names
- additional terms will be used as appropriate

LINKS

Search Engines

- Pubmed (- http://www.ncbi.nlm.nih.gov/pubmed)
- Toxnet (https://toxnet.nlm.nih.gov/); (includes Toxline; HSDB; ChemIDPlus; DART; IRIS; CCRIS; CPDB; GENE-TOX)
- Scifinder (https://scifinder.cas.org/scifinder)

appropriate qualifiers are used as necessary
search results are reviewed to identify relevant documents

Pertinent Websites

- wINCI - http://webdictionary.personalcarecouncil.org
- FDA databases http://www.ecfr.gov/cgi-bin/ECFR?page=browse
- FDA search databases: http://www.fda.gov/ForIndustry/FDABasicsforIndustry/ucm234631.htm;,
- EAFUS: http://www.accessdata.fda.gov/scripts/fcn/fcnnavigation.cfm?rpt=eafuslisting&displayall=true
- GRAS listing: http://www.fda.gov/food/ingredientspackaginglabeling/gras/default.htm
- SCOGS database: http://www.fda.gov/food/ingredientspackaginglabeling/gras/scogs/ucm2006852.htm
- Indirect Food Additives: http://www.accessdata.fda.gov/scripts/fdcc/?set=IndirectAdditives
- Drug Approvals and Database: http://www.fda.gov/Drugs/InformationOnDrugs/default.htm
- http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/UCM135688.pdf
- FDA Orange Book: https://www.fda.gov/Drugs/InformationOnDrugs/ucm129662.htm
- OTC ingredient list: https://www.fda.gov/downloads/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/ucm135688.pdf
- (inactive ingredients approved for drugs: http://www.accessdata.fda.gov/scripts/cder/iig/

- HPVIS (EPA High-Production Volume Info Systems) - https://ofmext.epa.gov/hpvis/HPVISlogon
- NIOSH (National Institute for Occupational Safety and Health) - http://www.cdc.gov/niosh/
- NTIS (National Technical Information Service) - http://www.ntis.gov/
- NTP (National Toxicology Program) - http://ntp.niehs.nih.gov/
- Office of Dietary Supplements https://ods.od.nih.gov/
- FEMA (Flavor & Extract Manufacturers Association) - http://www.femaflavor.org/search/apachesolr_search/

- EU CosIng database: http://ec.europa.eu/growth/tools-databases/cosing/
- ECHA (European Chemicals Agency – REACH dossiers) – http://echa.europa.eu/information-on-chemicals;jsessionid=A978100B4E4CC39C78C93A851EB3E3C7.live1
- ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) - http://www.ecetoc.org
- European Medicines Agency (EMA) - http://www.ema.europa.eu/ema/
- IUCLID (International Uniform Chemical Information Database) - https://iuclid6.echa.europa.eu/search
- OECD SIDS (Organisation for Economic Co-operation and Development Screening Info Data Sets)- http://webnet.oecd.org/hpv/ui/Search.aspx
- SCCS (Scientific Committee for Consumer Safety) opinions: http://ec.europa.eu/health/scientific_committees/consumer_safety/opinions/index_en.htm
- NICNAS (Australian National Industrial Chemical Notification and Assessment Scheme)- https://www.nicnas.gov.au/

- International Programme on Chemical Safety http://www.inchem.org/
- FAO (Food and Agriculture Organization of the United Nations) - http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-additives/en/
- WHO (World Health Organization) technical reports - http://www.who.int/biologicals/technical_report_series/en/

- www.google.com - a general Google search should be performed for additional background information, to identify references that are available, and for other general information

Botanical Websites, if applicable

- Dr. Duke's - https://phytochem.nal.usda.gov/phytochem/search
- Taxonomy database - http://www.ncbi.nlm.nih.gov/taxonomy
- GRIN (U.S. National Plant Germplasm System) - https://npgsweb.ars-grin.gov/gringlobal/taxon/taxonomysimple.aspx
- Sigma Aldrich plant profiler- http://www.sigmaaldrich.com/life-science/nutrition-research/learning-center/plant-profiler.html
- American Herbal Products Association Botanical Safety Handbook (database) - http://www.ahpa.org/Resources/BotanicalSafetyHandbook.aspx
- European Medicines Agency Herbal Medicines - http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/landing/herbal_search.jsp
- National Agricultural Library NAL Catalog (AGRICOLA) https://agricola.nal.usda.gov/
- The Seasoning and Spice Association List of Culinary Herbs and Spices http://www.seasoningandspice.org.uk/ssa/background_culinary-herbs-spices.aspx

Fragrance Websites, if applicable

- IFRA (International Fragrance Association) – http://www.ifraorg.org/
- Research Institute for Fragrance Materials (RIFM)

Note: ChemPortal can be used to search several of the above databases simultaneously - http://www.echemportal.org/echemportal/index?pageID=0&request_locale=en

Safety Assessment of Fatty Acids & Fatty Acid Salts as Used in Cosmetics

Status: Draft Report for Panel Review
Release Date: November 9, 2018
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The 2018 Cosmetic Ingredient Review Expert Panel members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A. Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Executive Director is Bart Heldreth, Ph.D. This safety assessment was prepared by Christina L. Burnett, Senior Scientific Analyst/Writer.

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INTRODUCTION

This report assesses the safety of 102 fatty acid and fatty acid salts (listed below) as used in cosmetics. Most of the fatty acids and fatty acid salts detailed in this safety assessment are reported to function as anticaking agents, emulsion stabilizers, viscosity increasing agents, opacifying agents, and surfactants, according to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*; see Table 1).[1] Additional reported functions included hair and skin conditioning agents, binders, slip modifier, antioxidants, fragrance ingredients, colorants, skin protectants, cosmetic biocide, and film formers. Functions such as oral health care drug (for Isomerized Safflower Acid) and antifungal agent (for Calcium Undecylenate and Undecylenic Acid) are not considered cosmetic functions in the United States (US) and, therefore, do not fall under the purview of the Cosmetic Ingredient Review (CIR).

Aluminum Dilinoleate
Aluminum Distearate
Aluminum Isostearate
Aluminum Isostearates/Palmitates
Aluminum Isostearates/Stearates
Aluminum Isostearates/Laurates/Palmitates
Aluminum Isostearates/Laurates/Stearates
Aluminum Lanolate
Aluminum Stearate
Aluminum Stearates
Aluminum Tristearate
Ammonium Isostearate
Ammonium Oleate
Ammonium Stearate
Arachidic Acid
Beeswax Acid
Behenic Acid
C14-28 Alkyl Acid
C10-40 Isoalkyl Acid
C14-28 Isoalkyl Acid
C32-36 Isoalkyl Acid
Calcium Behenate
Calcium Laurate
Calcium Stearate
Calcium Undecylenate
Capric Acid
Caproic Acid
Caprylic Acid
Dilinoleic Acid
Dierucic Acid
Eicosatrienoic Acid
Erucic Acid
Hydroxycapric Acid
Hydroxycaprylic Acid
10-Hydroxydecanoic Acid
Hydroxylauric Acid
Hydroxystearic Acid
10-Hydroxystearic Acid
Isomerized Linoleic Acid
Isomerized Safflower Acid
Isostearic Acid
Lauric Acid
Linoleic Acid
Linolenic Acid
Lithium Stearate
Magnesium Lanolate
Magnesium Laurate
Magnesium Palmitate
Magnesium Stearate
Magnesium Tallowate
Myristic Acid
Methyl Myristic Acid
Oleic Acid
Palmitic Acid
Potassium Behenate
Potassium Borageate
Potassium Camelliate
Potassium Caprate
Potassium Caprylate
Potassium Caprylate/Caprate
Potassium Castorate
Potassium Hydrogenated Tallowate
Potassium Hydroxystearate
Potassium Isostearate
Potassium Lanolate
Potassium Laurate
Potassium Linoleate
Potassium Linseedate
Potassium Oleate
Potassium Olivate/Sunflowerseedate
Potassium Palmitate
Potassium Stearate
Potassium Sunflowerseedate
Potassium Tallate
Potassium Tallowate
Potassium Undecylenate
Sodium Arganate
Sodium Beeswax
Sodium Behenate
Sodium Camellia Japonica Seedate
Sodium Caprate
Sodium Caprylate
Sodium Castorate
Sodium Dilinoleate
Sodium Hydrogenated Tallowate
Sodium Hydroxystearate
Sodium Isostearate
Sodium Lanolate
Sodium Lardate
Sodium Laurate
Sodium Laurate/Linoleate/Oleate/Palmitate
Sodium Linoleate
Sodium Oleate
Sodium Palmitate
Sodium Stearate
Sodium Tallowate
Sodium Tamanuseedate
Sodium Undecylenate
Stearic Acid
Trilinoleic Acid
Undecanoic Acid
Undecylenic Acid

While most of the fatty acids and fatty acid salts have not been previously review by the CIR Expert Panel (Panel), such as Linoleic Acid (with reported use in 633 cosmetic formulations),[2] several previously assessed ingredients have been included herein (denoted in red above) as they fit within this grouping of fatty acids and salts and can be appropriately re-reviewed here within.[3-11] Each of the ingredients in this report comprises a carboxylic acid functional group and an aliphatic (fatty) chain. Additionally, several related ingredients have also been reviewed and are referred to herein as supplemental information.[12-18] The conclusions of the previously assessed ingredients and a few other related reports have been provided in Table 2. Pertinent data from the reports on the previously reviewed ingredients are summarized in the appropriate sections of this report in *italics*. Note: the Panel has previously reviewed the safety of Arachidonic Acid; however, this ingredient is not included in this assessment because the Panel found the data were insufficient to determine safety.[19] The conclusion was subsequently changed to "Use Not Supported by the Data and Information Submitted to the CIR," per the CIR Procedures.

The fatty acid ingredients described in this safety assessment are ubiquitous in food as dietary fats. The US Food and Drug Administration (FDA) has affirmed that Calcium Stearate, Caprylic Acid, Linoleic Acid, Magnesium Stearate, Sodium Oleate, Sodium Palmitate, and Stearic Acid are generally recognized as safe (GRAS) as direct or indirect food substances. The US FDA has also affirmed that Oleic Acid is GRAS as a substance migrating from food packaging. Additionally, the US FDA has determined that several of the fatty acids and salts of fatty acids are approved as food additives permitted for direct addition to food for human consumption (see the Non-Cosmetic Use section for the complete list). Daily consumption of these ingredients would result in much larger systemic exposures than what is expected from use in cosmetic products, even if there was 100% absorption. A sampling of the systemic toxicity via oral exposure has been included in this report; however, the primary focus of the safety assessment of the ingredients that are approved direct food additives is based on topical exposure and local effects.

The available data in the published literature on fatty acids is voluminous. For this draft report, a representative sampling of the most pertinent data has been included. Additional relevant data may be added in subsequent drafts. This safety assessment includes relevant published and unpublished data that are available for each endpoint that is evaluated. Published data are identified by conducting an exhaustive search of the world's literature. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that CIR typically evaluates, is provided on the CIR website (https://www.cir-safety.org/supplementaldoc/preliminary-search-engines-and-websites; https://www.cir-safety.org/supplementaldoc/cir-report-format-outline). Unpublished data are provided by the cosmetics industry, as well as by other interested parties.

Some chemical and toxicological data on the fatty acids and fatty acid salts included in this safety assessment were obtained from robust summaries of data submitted to the European Chemical Agency (ECHA) by companies as part of the REACH chemical registration process.[20-33] Additionally, some data were obtained from an assessment by the Organisation for Economic Co-Operation and Development Screening Information Data Sets (OECD SIDS).[34-36] These data summaries are available on the ECHA and OECD SIDS websites, respectively, and when deemed appropriate, information from the summaries has been included in this report.

CHEMISTRY

Definitions and Structures

The definitions and structures of the fatty acids and fatty acid salts in this safety assessment are detailed in Table 1. Fatty acids, or aliphatic acids, consist of a carboxylic acid group at the polar end and a non-polar hydrocarbon chain.[36] The general structure for these acids in mono form is:

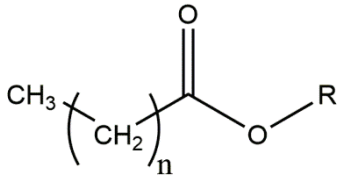


Figure 1. Generic fatty acid/salt structure (wherein R is a hydrogen atom or an ammonium, sodium, potassium, magnesium, or calcium cation. The chain lengths for fatty acids are 4 to 40 carbons in length (i.e. n is 2 to 38)).

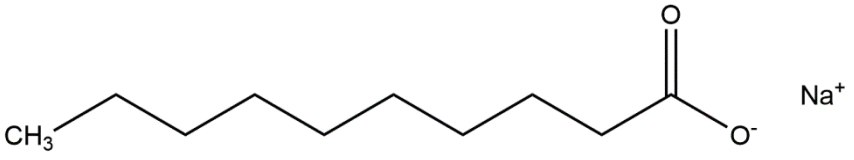


Figure 2. Specific example of a fatty acid salt with a 10 carbon chain length, Sodium Caprate

While some of these ingredients comprise straight (i.e. not branched) alkanes (saturated chains; i.e. no double bonds) like Sodium Caprate (Figure 2), some others comprise varying degrees of unsaturation (alkenes; e.g., Oleic Acid: 1, Linoleic Acid: 2, and Linolenic Acid: 3) and/or branching (e.g., Methyl Myristic Acid). Table 3 lists the parent fatty acid ingredients by increasing carbon chain length, for the straight chain alkanes and alkenes.

Physical and Chemical Properties

The available physical and chemical properties of many of the fatty acids in this report are found in Table 4. Generally, as alkyl chain lengths increase in fatty acids, melting points and boiling points increase, while water solubility and vapor pressure decrease.[36] Additionally, within a given carbon chain length, melting points increase with increasing saturation and decrease with increasing unsaturation.

Method of Manufacturing

Fatty acids occur naturally in animal and plant biochemistry, including synthesis in tissues such as the skin.[37] For example, the essential fatty acid, Linoleic Acid, is essential in mammalian skin for the establishment and maintenance of the epidermal water barrier.[38] Fatty acids are usually produced by the hydrolysis of common animal and vegetable fats and oils followed by fractionation of the resulting fatty acids.[8] Fatty acids that are used in foods, drugs and cosmetics normally exist as mixtures of several fatty acids, depending on the source and manufacturing process.

Lauric Acid

Lauric Acid is produced by the hydrolysis, usually via saponification, of animal or vegetable fats and oils followed by fractional distillation.[8] Lauric Acid is commonly isolated from coconut oil, and several patents describe its chemical synthesis.

Myristic Acid

The following methods have been used in the preparation of Myristic Acid: isolation from tall-oil fatty acids from 9-ketotetradecanoic acid, by electrolysis of a mixture of methyl hydrogen adipate and decanoic acid, by Maurer oxidation of myristanol, and from cetanol.[8] The most common means of preparation is by fractional distillation of hydrolyzed coconut oil, palm kernel oil, or coconut acids.

Oleic Acid

Oleic Acid is produced by the hydrolysis and fractionation (e.g., saponification and distillation) of animal or vegetable fats and oils.[8] Preparation of Oleic Acid from animal tallow and olive has been reported. It is also obtained as a by-product in the manufacture of solid Stearic and Palmitic Acids. Crude (i.e., unpurified, unbleached) Oleic Acid of commerce contains Stearic and Palmitic Acids in varying quantities.

Palmitic Acid

Palmitic Acid is produced by the hydrolysis and fractionation of palm oil, tallow oil, coconut oil, Japan wax, Chinese vegetable tallow, and spermaceti.[8] Fractionation is usually by distillation or crystallization. Palmitic Acid can also be obtained in the manufacturing process for Stearic Acid.

Stearic Acid

Methods of processing for Stearic Acid include hydrolysis of tallow or hydrogenation of unsaturated fatty acids (e.g., Oleic Acid) in cottonseed and other vegetable oils, followed by methods of isolation, such as fractional distillation or crystallization.[8] A successive series of pressing operations has been used to separate the liquid unsaturated fatty acids from the solid saturated fatty acids. The Palmitic Acid/Stearic Acid ratio obtained from tallow hydrolysis and triple-pressing or solvent crystallization is 55%/45%. Concentrations of Stearic Acid as high as 95-99% have been reported from the hydrogenation of unsaturated fatty acids.

Composition/Impurities

Beeswax Acid

Unhydrolyzed beeswax produced by the honeybee, *Apis melifera,* contains 23% hydrocarbons, 45% wax monoesters, 6% diesters of long chain alcohols with Palmitic Acid, 1% free alcohols, and 12% free acids.[39] Palmitic Acid is the major acid found in the ester fraction.

Behenic Acid

The major impurities reported for Behenic Acid (86% pure) are C_{12}-C_{20} fatty acids (~11%).[34]

Calcium Stearate

The *Food Chemicals Codex* describes Calcium Stearate as a compound of calcium with a mixture of solid organic acids obtained from edible sources and consisting chiefly of variable proportions of Calcium Stearate and Calcium Palmitate.[40] Specifications for Calcium Stearate indicate that the chemical should not contain more than 2 mg/kg lead.

Caprylic Acid

The *Food Chemicals Codex* specifies that Caprylic Acid should not contain more than 0.2% unsaponifiable matter.[40]

Lauric Acid

The *Food Chemicals Codex* specifies that Lauric Acid should not contain more than 0.1 mg/kg lead and not more than 0.3% unsaponifiable matter.[40]

Linoleic Acid

The *Food Chemicals Codex* specifies that Linoleic Acid should not contain more than 2 mg/kg lead and not more than 2.0% unsaponifiable matter.[40]

Magnesium Stearate

The *Food Chemicals Codex* describes Magnesium Stearate as a compound of magnesium with a mixture of solid organic acids obtained from edible sources and consisting chiefly of variable proportions of Magnesium Stearate and Magnesium Palmitate.[40] Specifications for Magnesium Stearate indicated that the chemical should not contain more than 5 mg/kg lead.

Myristic Acid

The *Food Chemicals Codex* states Myristic Acid is obtained from coconut oil and other fats.[40] Specifications for Myristic Acid indicated that the chemical should not contain more than 2 mg/kg lead and not more than 1% unsaponifiable matter.

Oleic Acid

The *Food Chemicals Codex* specifies that Oleic Acid should not contain more than 0.1 mg/kg lead and not more than 2.0% unsaponifiable matter.[40]

Palmitic Acid

The *Food Chemicals Codex* describes Palmitic Acid as a mixture of solid organic acids obtained from fats consisting chiefly of Palmitic Acid with varying amounts of Stearic Acid.[40] Specifications for Palmitic Acid indicated that the chemical should not contain more than 0.1 mg/kg lead and not more than 1.5% unsaponifiable matter.

Stearic Acid

The *Food Chemicals Codex* describes Stearic Acid as a mixture of solid organic acids obtained from fats consisting chiefly of Stearic Acid and Palmitic Acid.[40] Specifications for Stearic Acid indicated that the chemical should not contain more than 2 mg/kg lead and not more than 1.5% unsaponifiable matter.

USE

Cosmetic

The safety of the cosmetic ingredients included in this assessment is evaluated based on data received from the US FDA and the cosmetics industry on the expected use of these ingredients in cosmetics. Use frequencies of individual ingredients in cosmetics are collected from manufacturers and reported by cosmetic product category in the FDA Voluntary Cosmetic Registration Program (VCRP) database. Use concentration data are submitted by the cosmetics industry in response to surveys, conducted by the Personal Care Products Council (Council), of maximum reported use concentrations by product category.

While this report comprises in part, a number of previously-reviewed ingredients, it is not a re-review. Instead, this report was prioritized based on the high frequency of use of a previously unreviewed ingredient, Linoleic Acid. According to 2018 VCRP data, Linoleic Acid has 633 total uses in cosmetic products; the majority of the uses are in leave-on skin care products (Table 5).[41] Stearic Acid, a previously reviewed ingredient, has the most reported uses in this safety assessment with a total of 5738 uses; the majority of the uses is in leave-on eye makeup preparations and skin care products (Table 6). The reported frequency of use of this ingredient has more than doubled since it was last reviewed; Stearic Acid had a total of 2133 reported uses in 2006, the majority of which were also in leave-on eye makeup preparations and skin care products.[9] Palmitic Acid, another previously reviewed ingredient, has the second greatest number of reported uses in this safety assessment with 1240 uses; the majority of these uses are in leave-on eye makeup preparations and skin care products.[41] Again use of this

ingredient has increased significantly since it was last reviewed; in 2006, Palmitic Acid had a total of 132 reported uses, the majority of those uses were in rinse-off products.[9]

The results of the concentration of use survey conducted in 2016 by the Council indicate that Linoleic Acid is used at up to 21.8% in rinse-off skin cleansing products and at up to 3.4% in face, neck, body, and hand skin care products.[2] Sodium Laurate/Linoleate/Oleate/Palmitate is used at up to 84.7% in bath soaps and detergents and at up to 74.5% in leave-on baby products.[2] Stearic Acid was reported to be used at up to 37.4% in rinse-off products (bath soaps and detergents) and at up to 21% in leave-on products (eyebrow pencil). Use concentrations have slightly decreased since the last review of Stearic Acid in 2006, where Stearic Acid was reported to be used at up to 43% in rinse-off products (shaving cream) and 22% in leave-on products (eyeliners).[9] In 2016, Palmitic Acid was reported to be used at up to 21% in both rinse-off and leave-on products (skin cleansing preparations and fragrance products, respectively);[2] whereas in 2006, Palmitic Acid was reported to be used at up to 20% in rinse-off products (shaving cream) and 16% in leave-on products (lipsticks), indicating a slight increase in use concentration.[9] Since last reviewed, the highest concentration of use for Sodium Stearate in leave-on products has increased from 25% (in deodorants) to 84% (in fragrance preparations).[2,3] Ingredients with no reported uses in the VCRP or by Council are listed in Table 7.

Many of the ingredients included in this safety assessment may be used in products that can be incidentally ingested or come into contact with mucous membranes; for example, use is reported in lipsticks, bath preparations, and bath soaps and detergents. According to concentration of use survey data from 2016, Behenic Acid is reported to be used at up to 14% in lipstick and Sodium Laurate/Linoleate/Oleate/Palmitate is reported to be used at up to 84.7% in bath soaps and detergents.[2] Additionally, these ingredients are reported to be used in products that may come into contact with the eyes, such as eyebrow pencils, eyeliners, mascara, and eye shadows. According to the 2016 survey, Behenic Acid is reported to be used at up to 22% in eyebrow pencils and Hydroxystearic Acid is used at up to 14% in eyeshadows.

Fatty acids and fatty acid salts were reported to be used in cosmetic sprays and powders, including skin, deodorant, and fragrance products, and could possibly be inhaled. For example, Stearic Acid is reported to be in face and neck sprays at up to 3%, Oleic Acid is reported to be in spray deodorants at up to 1.5%, and Magnesium Stearate is reported to be in face powders at up to 7.2%.[2] In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters > 10 μm with propellant sprays yielding a greater fraction of droplets/particles below 10 μm compared with pump sprays.[42-45] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and bronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.[42,43] There is some evidence indicating that deodorant spray products can release substantially larger fractions of particulates having aerodynamic equivalent diameters in the range considered to be respirable.[42] However, the information is not sufficient to determine whether significantly greater lung exposures result from the use of deodorant sprays, compared to other cosmetic sprays. Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.[46-48]

In regulations on cosmetic products in the European Union, Aluminum Stearate, Calcium Stearate, and Magnesium Stearate are listed on Annex IV: list of colorants allowed in cosmetic products in the EU.[49] Calcium Undecylenate, Potassium Undecylenate, Sodium Undecylenate, and Undecylenic Acid are listed on Annex V: list of preservatives allowed in cosmetic products; the maximum concentration in ready for use preparations is restricted to 0.2% as acid. The remaining fatty acids and fatty acid salts listed in this report are not restricted from use in any way under the rules governing cosmetic products in the European Union.

According to Australia's National Industrial Chemicals Notification and Assessment Scheme (NICNAS), the following ingredients are Tier I chemicals (not considered to pose an unreasonable risk to the health of workers and public health on the basis of the Tier I IMAP assessment): Ammonium Stearate, Arachidic Acid, Behenic Acid, Calcium Behenate, Calcium Laurate, Calcium Stearate, Erucic Acid, Hydroxystearic Acid, Isostearic Acid, Lauric Acid, Linoleic Acid, Linolenic Acid, Magnesium Laurate, Magnesium Palmitate, Magnesium Stearate, Myristic Acid, Oleic Acid, Palmitic Acid, Potassium Caprylate, Potassium Castorate, Potassium Hydrogenated Tallowate, Potassium Laurate, Potassium Oleate, Potassium Palmitate, Potassium Stearate, Potassium Tallate, Potassium Tallowate, Sodium Caprylate, Sodium Castorate, Sodium Hydrogenated Tallowate, Sodium Isostearate, Sodium Laurate, Sodium Oleate, Sodium Palmitate, Sodium Stearate, Sodium Tallowate, Stearic Acid, and Undecylenic Acid.[50] The remaining fatty acids and fatty acid salts listed in this report do not have a NICNAS determination.

Non-Cosmetic

The fatty acid ingredients described in this safety assessment are dietary fats found in both plant and animal food sources.[51] Linoleic Acid and Linolenic Acid are essential fatty acids for biological processes that must be obtained from the diet as they are not synthesized in the human body. The US Department of Agriculture (USDA) recommends that the daily intake of fatty acids (as unsaturated fats) in adults should be 27 g per day based on a 2000 calorie diet, and that saturated fat intake should be limited to less than 10% of daily caloric intake.

Regulations applicable to the use of fatty acids and fatty acid salts in human food, animal feed, drugs, and pesticides in the US are summarized in Table 8. Non-cosmetic uses of the ingredients listed in this report are found in Table 9.

TOXICOKINETICS

Dermal Penetration

Sodium Stearate

Sodium Stearate is absorbed through both rat and human skin.[4]

Penetration Enhancement

Oleic Acid

Oleic Acid has been studied for its ability to act as a penetration enhancer for use in the topical delivery of celecoxib and lumiracoxib.[52,53]

Sodium Caprate

Sodium Caprate is reported to be an oral absorption promoter that has potential for use in oral drug products containing poorly permeable molecules.[54]

Myristic Acid

Myristic Acid enhanced the dermal penetration of several drugs (e.g., bupropion and nitrendipine).[10]

Absorption, Distribution, Metabolism, Distribution

Fatty acids share a common degradation pathway in which they are metabolized to acetyl-Coenzyme A (acetyl-CoA) or other key metabolites that are structurally similar breakdown products.[36] No differences in metabolism are expected between even and odd numbered carbon chain compounds or saturated and unsaturated compounds.

Calcium Stearate

Limited absorption studies indicated that Calcium Stearate is slightly absorbed by isolated dog intestine.[4]

Lauric Acid, Oleic Acid, Palmitic Acid, Stearic Acid

Fatty acids are absorbed, digested, and transported in animals and humans.[8] *Radioactivity from labeled fatty acids administered orally, intravenously, intraperitoneally, and intraduodenally has been found in various tissues and in blood and lymph. P-Oxidation of the fatty acids involves serial oxidation and reduction reactions yielding acetyl-CoA.*

Hydroxystearic Acid

In male rats fed a diet containing hydrogenated castor oil, Hydroxystearic Acid was deposited in abdominal fat, as well as other body lipids, along with its metabolities (hydroxypalmitic acid, hydroxymyristic acid, and hydroxylauric acid).[5] *Hydroxystearic Acid has also been detected in the feces of 12 subjects who presumably ate a normal mixture of foods.*

Isostearic Acid

Studies with rat liver homogenate suggest Isostearic Acid is readily metabolized following ingestion.[6]

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

Acute dermal and oral studies of several fatty acids and fatty acid salts are summarized in Table 10. In dermal studies of Capric Acid, Lithium Stearate, Stearic Acid, and Undecylenic Acid, the LD_{50} values were greater than 2000 mg/kg/bw.[23,28,30,32] The LD_{50} values in oral studies of Ammonium Oleate (up to 64 ml/kg), Behenic Acid (up to 5000 mg/kg bw), Calcium Stearate (2000 mg/kg bw), Capric Acid (up to 5000 mg/kg bw), Caprylic Acid (up to 5000 mg/kg bw), Isomerized Linoleic Acid (2000 mg/kg bw), Lauric Acid (up to 10,000 mg/kg bw), Lithium Stearate (up to 5000 mg/kg bw), Palmitic Acid (5000 mg/kg bw), Stearic Acid (up to 6000 mg/kg bw), and Undecylenic Acid (up to 2000 mg/kg bw) were above the doses tested.[20,22,23,25-30,32,35,55]

Lauric Acid, Oleic Acid, Palmitic Acid, Stearic Acid

Little acute toxicity was observed when Oleic Acid, Lauric Acid, Palmitic Acid, Myristic Acid, or Stearic Acid, or cosmetic formulations containing these fatty acids at concentrations of 2.2 - 13%, were given to rats orally at doses of 15,000 - 19,000 mg/kg body weight.[8]

Results from single topical applications of Oleic Acid (at concentrations up to 50%) to the skin of mice, rabbits, and guinea pigs ranged from no toxicity to signs of erythema, hyperkeratosis, and hyperplasia.[8] *An acute intradermal administration to guinea pigs of up to 25% Oleic Acid resulted in local inflammation and necrosis. A formulation containing 2.2% Palmitic Acid was considered nontoxic to rabbits in an acute dermal study. A single topically applied dose of 5 g/kg commercial grade Stearic Acid was not toxic to rabbits. An acute intradermal administration of 10-100 mM Stearic Acid to guinea pigs and rabbits resulted in mild erythema and slight induration.*

Aluminum Stearate, Ammonium Stearate, Lithium Stearate, Magnesium Stearate, and Sodium Stearate

Acute oral studies with rats showed that Aluminum (5.0 g/kg), Ammonium (5.0 g/kg), Lithium (tested up to 15.0 g/kg, but no effects at up to 3.0 g/kg), Magnesium (up to 10.0 g/kg), and Sodium (up to 5 g/kg) Stearates are practically nontoxic.[4] Studies with guinea pigs demonstrated that 100% Aluminum Stearate and 100% Ammonium Stearate have a low potential for acute dermal toxicity.

Isostearic Acid

In rats, the acute oral LD_{50} of Isostearic Acid is estimated to be greater than 32 ml/kg.[6]

Short-Term and Subchronic Toxicity Studies

Repeated dose short-term and subchronic dermal and oral studies of several fatty acid and fatty acid salt ingredients are summarized in Table 11. The no-observable-adverse effect level (NOAEL) in a dermal study of Lithium Stearate in rats was $\geq$ 1000 mg/kg bw/day for systemic effects, but the NOAEL for local effects was 100 mg/kg bw/day.[28] The NOAELs for Behenic Acid (up to 1000 mg/kg bw/day), Calcium Stearate (up to 2000 mg/kg bw/day), and Capric Acid (up to 1000 mg/kg bw/day) were greater than or equal to the highest doses tested in oral studies.[22,23,35] In oral gavage studies with Sodium Undecylenate, the NOAEL was $\leq$ 50 mg/kg bw/day with adverse effects including dose-dependent clinical signs of toxicity and adverse effects in the forestomaches of high dose groups.[32] Conjugated Linoleic Acid (a technical name for Isomerized Safflower Acid) tested at 1% in feed did not cause adverse effects in rats.[56] An 8-week dietary study of up to 2.5% Undecylenic Acid reported "inhibition of growth" in rats.[55]

Lauric Acid, Oleic Acid, Palmitic Acid, Stearic Acid

No deaths or significant gross or microscopic alterations were observed among New Zealand White rabbits after 4 weeks of topical administration of product formulations containing 2.0% Stearic Acid.[8] No abnormal physiological parameters were noted in a 13-week dermal toxicity study in rats of 2 cosmetic product formulations containing, at most, 5% Stearic Acid.

In subchronic oral toxicity studies, Oleic Acid, Palmitic Acid, and Stearic Acid were fed to rats in diets at concentrations ranging from 5 to 50%.[8] Thrombosis, aortic atherosclerosis, anorexia, and mortality were observed. In a subchronic study, no signs of toxicity were observed in chicks fed 5% dietary Stearic and Oleic Acids.

Calcium Stearate

An emulsion of Calcium Stearate in egg yolk and water applied to the skin of guinea pigs for 14 days caused a significant decrease in body weight.[4] Calcium Stearate (10 or 50 mg in 0.5 ml of saline and 0.01 ml of egg yolk) administered intratracheally to rats for 2 and 4 months caused varying degrees of lung pathology.

Hydroxystearic Acid

Reduced growth rate was noted in rats fed diets containing 8.7% and 17.3% Hydroxystearic Acid, but not in rats fed 4.3% Hydroxystearic Acid, in a 90-day subchronic oral toxicity study.[5] The results of a second 90-day experiment (no reduction in growth rate) confirmed that the reduction in growth rate previously observed was due to the lower caloric density of diets consisting of 8.7% and 17.3% Hydroxystearic Acid. In both experiments, the results of hematologic and microscopic evaluations were unremarkable.

Chronic Toxicity Studies

Oleic Acid

Feeding of 15% dietary Oleic Acid to rats in a chronic study resulted in normal growth and general health.[8]

Calcium Stearate

Calcium Stearate (10 or 50 mg in 0.5 ml of saline and 0.01ml of egg yolk) administered intratracheally to rats for 6 and 8 months caused varying degrees of lung pathology.[4]

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY (DART) STUDIES

Dermal and oral DART studies of several fatty acid and fatty acid salt ingredients are summarized in Table 12. Lithium Stearate caused no treatment-related adverse reproductive or developmental effects at doses up to 1000 mg/kg bw/day in dermal studies where male rats were treated for 43 days and female rats were treated for 33 days until gestation day 19.[28] While non-reproductive effects were noted in parental animals in a few oral studies, no treatment-related adverse effects were observed on the reproductive cycles or development of offspring in rats exposed to Behenic Acid (up to 1000 mg/kg/day; males were treated 42 days and females were treated ~39 days until lactation day 3),[22] Calcium Stearate (up to 1000 mg/kg/day; males were treated 28 days and females were treated ~39 days until lactation day 3),[35] Capric Acid (up to 2000 mg/kg/day; females were treated up to ~33 days until lactation day 4),[23] Caprylic Acid (up to 1000 mg/kg/day; females were

treated for up to 9 days during gestation),[25,57] or Undecylenic Acid (up to 1000 mg/kg/day; males were treated up to 28 days and females were treated up to 40 days until lactation day 4).[32]

Lauric Acid, Myristic Acid, Oleic Acid, Palmitic Acid, Stearic Acid

Although placental transfer of fatty acids has been documented in several species and fetal lipid metabolism has been studied, no studies on the teratogenicity of Oleic, Lauric, Palmitic, Myristic, or Stearic Acids were found.[8] Feeding of 15% dietary Oleic Acid to rats in a chronic study resulted in impairment in the reproductive capacity of female rats. Little or no toxicity to sperm cells in whole semen samples by serial dilutions of Oleic Acid, Palmitic Acid, and Stearic Acid were observed in studies of these ingredients.[9]

Magnesium Stearate

When fed to female rabbits at 8 days post-coitus, a pharmaceutical vehicle containing 5.5% by weight Magnesium Stearate was not teratogenic.[4]

Hydroxystearic Acid

The dermal teratogenicity of two antiperspirant prototype formulations containing 7% Hydroxystearic Acid was evaluated using 2 groups of 30 Charles River Crl:CD VAF/Plus female rats.[5] There were no test article-related or statistically significant differences in the incidence of fetal malformations or fetal developmental variations between experimental and control groups. Skin irritation reactions, however, were observed in greater than 50% of the dams in both experimental groups. No deaths were reported during the study.

GENOTOXICITY STUDIES

Genotoxicity studies of several fatty acid and fatty acid salt ingredients are summarized in Table 13. In vitro bacterial cell and mammalian cell assays were negative for genotoxicity, with and without metabolic activation, in Ammonium Oleate (up to 333 µg/plate),[20] Behenic Acid (up to 5000 µg/plate),[22] Calcium Stearate (up to 312.5 µg/plate),[35] Capric Acid (up to 10, 000 µg/plate),[23,58] Caproic Acid (up to 10,000 µg/plate),[24] Caprylic Acid (up to 3333 µg/plate),[25,58] Isomerized Linoleic Acid (up to 2500 µg/plate),[26] Lauric Acid (up to 2500 µg/plate),[27,58] Linoleic Acid (dose not reported),[59] Lithium Stearate (up to 5000 µg/plate),[28] Myristic Acid (dose not reported),[58] and Undecylenic Acid (up to 750 µg/plate).[32] No genotoxicity was detected in an oral micronucleus assay in mice with up to 4000 mg/kg Undecylenic Acid in 10% gum arabic.[32]

Lauric Acid, Oleic Acid, Stearic Acid

Although Oleic Acid and Lauric Acid induced mitotic aneuploidy in in vitro mutagenicity tests, both have been indicated as inhibitors of mutagenicity produced by positive controls, such as N-nitrosopyrrolidine and sodium azide, in other tests. Stearic Acid was inactive in aneuploidy induction tests and in the Ames test, and it did not inhibit mutagenicity, as did Oleic Acid and Lauric Acid. No increase of mitotic crossing-over events was induced by Oleic Acid, Lauric Acid, or Stearic Acid. Oleic Acid did not increase the number of sister chromatid exchanges over background.

Magnesium Stearate

Magnesium Stearate was not mutagenic in microbial tests with Salmonella typhimurium or Saccharomyces cerevisiae.[4]

Hydroxystearic Acid

Hydroxystearic Acid was not mutagenic in S. typhimurium strainsTA1535, TA100, TA1537, TA1538, and TA98.[5] However, Hydroxystearic Acid was classified as mutagenic in Escherichia coli strain Hs30. Hydroxystearic Acid was not mutagenic in the L5178Y TK +/- mouse lymphoma assay, with or without metabolic activation, nor did it produce chromosome aberrations in Chinese hamster ovary cells, with or without metabolic activation.

CARCINOGENICITY STUDIES

Sodium Oleate

In a 108-week drinking water study, groups of 50 male and 50 female F344 rats received 0%, 2.5%, or 5.0% Sodium Oleate.[60] Water consumption was recorded twice weekly and the rats were weighed every two or four weeks. Blood and urine samples were taken from 10 rats per sex per dose group prior to study termination for biochemical and hematological analyses. A necropsy was performed at study termination to examine for tumors or other lesions in the major organs and tissues.

Survival rates for the treated rats were comparable to the controls. While there was a slight reduction in body weight gains in male rats, there were no significant differences in growth curve of treated and control rats of either sex. Water consumption was slightly, but not significantly, depressed in both female treatment groups. The mean liver weight in the 5% male test group was statistically significantly lower than that of the males in the control and 2.5% test group. The mean thymus weight in the 5% female test group was statistically significantly higher than that of the females in the control and 2.5% test group. No statistically significant differences were observed between the treated rats of either sex and the control rats in

the results of urine and serum analyses, hematology parameters, or in tumor incidences, except for pancreatic tumors. An increase in the incidence of pancreatic tumors was observed in both male dose groups when compared to the control group, but these were not significantly different from reported spontaneous incidences of these tumors in this strain of rat. The authors concluded that Sodium Oleate did not induce tumors in this drinking water study in rats.[60]

Lauric Acid, Oleic Acid, Palmitic Acid, Stearic Acid

In carcinogenicity studies, no malignant tumors were induced by repeated subcutaneous injections of 1 - 16.5 mg Oleic Acid in two strains of mice. Intestinal and gastric tumors were found in mice receiving dietary Oleic Acid at daily doses up to 200 mg/mouse. Treatment of mice with repeated subcutaneous injections of 25 and 50 mg Lauric Acid was not carcinogenic. Low incidences of carcinomas, sarcomas, and lymphomas were observed in mice receiving single or repeated subcutaneous injections of 25 and 50 mg Palmitic Acid and up to 82 mg Stearic Acid. Feeding of up to 50 g/kg/day dietary Stearic Acid to mice was not carcinogenic (duration not reported).

Magnesium Stearate

Mice surviving 30-week implants of Magnesium Stearate pellets in the bladder had a bladder tumor incidence of 5.0%, but the incidence was no different than that caused by glass beads.

Hydroxystearic Acid

In an 18-month carcinogenicity study (subcutaneous study), Hydroxystearic Acid was classified as tentatively carcinogenic in Swiss-Webster mice.[5] Subcutaneous sarcomas were observed at the site of injection in 9 of the 28 mice (14 per dose group) that were alive at 6 months. All of the sarcomas were observed in the low-dose group (total dose of 4 mg delivered in a total of 8 ml tricaprylin for 80 weeks). The high-dose group received a total dose of 80 mg delivered in a total of 8 ml of tricaprylin. In a second study in which 9 A/He male mice received a total intraperitoneal dose of 60 mg Hydroxystearic Acid over a period of 4 weeks, the frequency of lung tumors was within the spontaneous occurrence.

OTHER RELEVANT STUDIES

Comedogenicity

Oleic Acid

Oleic Acid and its UVA-induced peroxides were associated with increased comedo formation on the treated ears of two species of rabbits.[8]

Isostearic Acid

A product formulation both with and without 2.5% Isostearic Acid was tested in a rabbit ear comedogenicity assay. The formulation without Isostearic Acid was irritating but did not produce comedones; however, the formulation with Isostearic Acid was both irritating and comedogenic.

Hepatotoxicity

Hydroxystearic Acid

In an in vitro study, Hydroxystearic Acid interfered with oxidative phosphorylation in rat liver mitochondria.[5] Oxidative phosphorylation was uncoupled and mitochondria were damaged.

DERMAL IRRITATION AND SENSITIZATION STUDIES

Dermal irritation and sensitization studies of several fatty acid and fatty acid salt ingredients are summarized in Table 14. Several in vitro assays and animal irritation studies indicate that Caproic Acid (up to 100%) and Caprylic Acid (up to 100%) are corrosive, and Capric Acid (concentration not reported) Isostearic Acid (100%), Lauric Acid (concentration not reported), Trilinoleic Acid (concentration not reported), and Undecylenic Acid (concentration not reported) may be irritating.[20,24,25,27,29,31,61-65] Aluminum Tristearate, Lauric Acid, Lithium Stearate, however, were predicted to be not irritating and/or corrosive human epidermis models.[21,28,65] In human irritation studies, Lauric Acid at 50% induced erythema, edema, and scaling in a closed epicutaneous test; however, only slight erythema was observed in an open epicutaneous test of Lauric Acid at 80%.[27] No dermal irritation was observed in subjects exposed to Palmitic Acid at 50%.[29]

In vitro direct peptide reactivity assays (DPRAs) predicted that Linoleic Acid (100 mM) and Linolenic Acid (100 mM) were skin sensitizers, while Oleic Acid (100 mM) and Undecylenic Acid (100 mM) were not.[66] In local lymph node assays (LLNAs) and modified LLNAs, Lithium Stearate (up to 10%) was not sensitizing; however, the results of tests with Ammonium Oleate (up to 50%), Hydroxystearic Acid (up to 50%), Linoleic Acid (25%), Linolenic Acid (25%), Oleic Acid (10%), and Undecylenic Acid (25%) indicate that these ingredients may induce sensitization.[20,28,33,66] In guinea pig studies, reactions observed to Ammonium Oleate (up to 50%) and Hydroxystearic Acid (up to 10%) may have been due to irritation.[20,33] No sensitization was observed in guinea pig studies with Capric Acid (up to 40%), Lauric Acid (up to 2.5%), Sodium Undecylenate (up to 0.1%), Trilinoleic Acid (up to 75%), or Undecylenic Acid (up to 100%).[23,27,31,32]

Lauric Acid, Oleic Acid, Palmitic Acid, Myristic Acid, and Stearic Acid

In single insult occlusive patch tests for primary irritation, Stearic Acid at doses of 35-65% in vehicles and Lauric, Oleic, Palmitic, and Myristic Acids at 1-13% in cosmetic product formulations produced no to moderate erythema and slight, if any, edema in the skin of rabbits.[8] Slight increases in irritation were observed in the short-term repeated patch tests (daily for 3-14 days) of Oleic Acid (5%) and Myristic Acid (concentration not reported). Approximately 5% (w/v; 18 mmol%) alcohol solution of the fatty acids topically applied to the skin of the external ear canals of albino rabbits for 6 weeks produced a range of responses, varying from no irritation with Stearic Acid to slight irritation with Myristic Acid and Palmitic Acid to defined erythema, desquamation, and persistent follicular keratosis with Oleic Acid and Lauric Acid. Slight local edema was observed among New Zealand White rabbits after 4 weeks of topical administration of product formulations containing 2.0% Stearic Acid. In 13-week dermal toxicity studies, 2 cosmetic product formulations containing, at most, 5% Stearic Acid produced moderate skin irritation in rats receiving 4.0 ml/kg and 227 mg/kg doses.

In guinea pig maximization studies with 2 cosmetic product formulations containing 5.08% Oleic Acid and 1.0% Stearic Acid, slight reactions were observed to challenge patches.[8] These formulations were considered weak, grade 1, sensitizers. In another maximization study, after intradermal induction and booster injections of a formulation containing 3.5% Stearic Acid, reactions to topical challenge applications of the formulation were few and minimal in intensity.

In clinical primary and cumulative irritation studies, 50% Oleic Acid, 50% Myristic Acid, and 40% Stearic Acid in mineral oil were nonirritating.[8] Mild to intense erythema in single insult occlusive patch tests, soap chamber tests, and 21-day cumulative irritation studies were produced by cosmetic product formulations containing Oleic Acid (up to 30%), Palmitic Acid (2.2%), Myristic Acid (up to 8%), or Stearic Acid (up to 13%). In clinical repeated insult patch tests (open, occlusive, and semi-occlusive), maximization tests, and prophetic patch tests with cosmetic product formulations containing Oleic Acid, Lauric Acid, Palmitic Acid, and Stearic Acid at concentrations ranging from < 1 to 13%, no primary or cumulative irritation or sensitization was reported. Slight, if any, reactions were observed after challenge patching at original or adjacent sites on the upper backs or forearms of some subjects (approximately < 2%). Intensity of observed reactions to the formulations was not directly related to the concentrations of the fatty acid ingredients.

Myristic Acid

Myristic Acid (concentration not reported) was non-irritating in a single insult occlusive patch test and slightly irritating in a repeat open patch test on rabbits.[8,10] In clinical primary and cumulative irritation studies, Myristic Acid at up to 50% was nonirritating.

Aluminum Distearate, Ammonium Stearate, Magnesium Stearate, and Sodium Stearate

Skin irritation studies with rabbits demonstrated that 10% Aluminum Distearate in corn oil and 100% Ammonium Stearate were minimal and slight irritants, respectively, whereas 100% Magnesium Stearate and Sodium Stearate were non-irritating. When tested on rabbit skin at concentrations of 100%, Magnesium Stearate was found to be noncorrosive. In human studies, 7 out of 20 subjects exhibited minimal to mild skin erythema when tested with an aqueous solution of 1.5% Ammonium Stearate in a single-insult, 24 h patch test. In a similar study with 0.5% Sodium Stearate in aqueous solution, 4 out of 20 subjects demonstrated minimal to moderate skin erythema. In a 21 day patch test with 10 subjects, an aqueous bath soap and detergent solution containing 0.1% to 0.25% Sodium Stearate caused minimal skin irritation. An aqueous solution of the same formulation containing 0.3% to 0.75% Sodium Stearate caused no sensitization in 100 subjects. A stick deodorant containing 7% Sodium Stearate demonstrated low potential for human skin irritation and sensitization.

Hydroxystearic Acid

Skin irritation reactions to each of 3 antiperspirant prototype formulations, each containing 7% Hydroxystearic Acid, were observed in a human primary irritation patch test using 35 volunteers.[5] Semi-occluded patches produced reactions in as many as 9 of the subjects, whereas occluded patches produced reactions in as many as 17 individuals. Only 2 reactions were noted in the semi-occluded patch controls and only 1 in the occluded patch controls. Although the formulations reportedly contained the same concentration of Hydroxystearic Acid, there were small differences in the numbers of individuals reacting to each.

Isostearic Acid

Isostearic Acid at up to 100% produced no significant skin irritation in Draize rabbit irritation tests, whereas variable degrees of irritation were produced by product formulations containing Isostearic Acid.[6] In clinical studies, 100 subjects showed no signs of irritation after a 24 h single insult skin patch with undiluted Isostearic Acid, and product formulations containing up to 4% Isostearic Acid produced, at most, minimal irritation when similarly tested on a total of 221 subjects. In another study, 35% Isostearic Acid in mineral oil was neither an irritant nor a sensitizer in 168 subjects. Isostearic Acid at 10% in mineral oil was similarly not irritating or sensitizing to 103 subjects. Product formulations containing 2.5% to 2.85% Isostearic Acid produced no evidence of contact sensitization when tested in repeated insult patch tests on a total of 333 subjects.

PHOTOTOXICITY AND PHOTOSENSITIZATION

In Vitro

Lauric Acid and Sodium Laurate

In a validation study of the in vitro reactive oxygen species (ROS) assay and the 3T3 neutral red uptake phototoxicity test (3T3 NRU PT), Lauric Acid and Sodium Laurate were not predicted to cause phototoxicity or photoallergy.[67] These findings were supported by the results of an ultraviolet/visible light (UV/VIS) spectral analysis.

Animal and Human

Oleic Acid, Palmitic Acid, Stearic Acid

Skin lotion formulations containing 2.8% Stearic Acid were not photosensitizing to the skin of Hartley guinea pigs. Cosmetic product formulations containing 1 - 13% Oleic Acid, Palmitic Acid, or Stearic Acid produced no photosensitization in human subjects. There were slight reactions to a few induction patches.

Isostearic Acid

In a subset population of 25 individuals in an irritation and sensitization study in humans, 35% Isostearic Acid in mineral oil with exposure to UVA + UVB was not a photosensitizer.

OCULAR IRRITATION STUDIES

Ocular irritation studies for several fatty acid and fatty acid salt ingredients are summarized in Table 15. Caproic Acid at 50% was corrosive in bovine corneas, but Lithium Stearate (concentration not reported) was predicted to be non-irritating in a human corneal model.[24,28] In rabbits, Caproic Acid (concentration not reported), Caprylic Acid (70%), Lauric Acid (up to 100%), Lithium Stearate (concentration not reported), Stearic Acid (iso-form; 100%), Sodium Undecylenate (33.2%), and Undecylenic Acid (concentration not reported) were mild to moderate ocular irritants.[23-25,27,28,32,68] Oleic Acid (at up to 0.1%) and Palmitic Acid (concentration not reported) were not ocular irritants.[29,69]

Lauric Acid, Oleic Acid, Palmitic Acid, Myristic Acid, and Stearic Acid

In ocular irritation studies, Oleic Acid, Lauric Acid, Palmitic Acid, Myristic Acid, and Stearic Acid neat and at concentrations ranging from 1 to 19.4% in cosmetic product formulations produced no to minimal irritation after single and multiple (daily, 14-day) instillations into the eyes of albino rabbits. Irritation was primarily in the form of very slight conjunctival erythema. A single instillation of Lauric Acid also produced cornea1 opacity and iritis. In humans, there was no treatment-related ocular irritation in female subjects, some of whom were contact lens wearers, involved in two 3-week exaggerated-use studies of mascara formulations containing 2% and 3% Oleic Acid. These formulations were used in combination with other eye area cosmetics. Myristic Acid in product formulations at a concentration of 1.5% was minimally irritating to the eyes of rabbits.[8,10]

Aluminum Distearate, Ammonium Stearate, and Magnesium Stearate

Eye irritation studies with rabbits showed that 10% Aluminum Distearate in corn oil and undiluted Ammonium Stearate and Sodium Stearate were minimal to mild irritants; 100% Magnesium Stearate was non-irritating.

Isostearic Acid

Undiluted Isostearic Acid produced no significant eye irritation in Draize rabbit irritation tests, whereas variable degrees of irritation were produced by product formulations containing Isostearic Acid.

CLINICAL STUDIES

Case Reports

Hydroxystearic Acid

A patient presented with pruritic edematous erythema and scaling on the lips, and positive patch test reactions were reported with three of her lip gloss formulations.[70] Subsequent patch tests were performed with 21 lip gloss ingredients, and only Hydroxystearic Acid and C18-36 acid triglyceride, both tested at 10% in petrolatum and both present in all three lip gloss formulations, produced positive reactions (+ reaction on day 2 and day 3). Patch tests of these substances in 6 control subjects were negative.

In another case report, a patient presented with severe contact dermatitis from a lip balm and from a solid-stick underarm antiperspirant/deodorant.[71] Patch testing with ingredients from the lip balm resulted in positive results at 10% Hydroxystearic Acid in petrolatum. Subsequent patch testing with serial dilutions of Hydroxystearic Acid (99.7% pure) were positive to 0.001% in petrolatum. (A patch test with hydrogenated castor oil, an ingredient present in the deodorant formulation, was positive at 1% in petrolatum.)

Undecylenic Acid and Potassium Undecylenate

A 52-year-old white male patient presented with intermittent scaling and itching between the toes following application of a therapeutic topical cream containing 10% Undecylenic Acid as free acid and potassium salt on two consecutive days.[72] On the third day, the dorsa of the feet became erythematous, edematous, and exudative. When application of the cream was halted, gradual healing occurred with local therapy. Slight residual erythema and fissuring at the base of the left third toe was apparent on day 10 post-application. When the patient resumed use of the cream on his feet, marked erythema, edema, and pruritus occurred within 24 h on the toes and dorsa of the feet. Pruritus and lesions disappeared three weeks after the second discontinuation of the cream. Patch tests with materials from the patient's shoes were negative. Marked positive reactions were observed to the topical cream and a similar powder formulation. Patch tests with Potassium Undecylenate gave a marked positive reaction, but reactions to other preparations containing Undecylenic Acid, zinc undecylenate, copper undecylenate, potassium chloride, and potassium permanganate were negative

SUMMARY

Most of the 102 fatty acids and fatty acid salts detailed in this safety assessment are reported to function as anticaking agents, emulsion stabilizers, viscosity increasing agents, opacifying agents, and surfactants. Additional functions included hair and skin conditioning agents, binders, slip modifier, antioxidants, fragrance ingredients, colorants, skin protectants, cosmetic biocide, and film formers. While some of these ingredients have not been previously review by the Panel, such as Linoleic Acid, several previously assessed ingredients have been included herein as they fit within this grouping of fatty acids and salts and can be appropriately re-reviewed herewith. Each of the ingredients in this report comprises a carboxylic acid functional group and an aliphatic (fatty) chain.

The fatty acids ingredients described in this safety assessment are ubiquitous in food as components of dietary fats. The US FDA determined that several of the fatty acids and salts of fatty acids are approved as food additives permitted for direct addition to food for human consumption. Daily consumption of these ingredients would result in much larger systemic exposures than what is expected from use in cosmetic products, even if there was 100% absorption. A sampling of the systemic toxicity via oral exposure has been included in this report; however, the primary focus of the safety assessment is the review of safety based on topical exposure and local effects.

Fatty acids occur naturally in animal and plant biochemistry, including synthesis in tissues such as the skin. Fatty acids are usually produced by the hydrolysis of common animal and vegetable fats and oils followed by fractionation of the resulting fatty acids. Fatty acids that are used in foods, drugs and cosmetics normally exist as mixtures of several fatty acids depending on the source and manufacturing process.

According to 2018 VCRP data, Linoleic Acid has 633 total uses in cosmetic products; the majority of these uses is in leave-on skin care products. Stearic Acid, a previously reviewed ingredient, has the most reported uses in this safety assessment with a total of 5738; the majority of these uses is in leave-on eye makeup preparations and skin care products. This ingredient had a total of 2133 reported uses in 2006; the majority of the uses were also in leave-on eye makeup preparations and skin care products. Palmitic Acid, another previously reviewed ingredient, had the second greatest number of reported uses in this safety assessment with 1240; the majority of the uses were in leave-on eye makeup preparations and skin care products. In 2006, Palmitic Acid had a total of 132 reported uses; the majority of the uses were in rinse-off products such as shampoos, shaving products, and personal cleanliness products.

The results of the concentration of use survey conducted in 2016 by the Council indicate that Linoleic Acid is used at up to 21.8% in rinse-off skin cleansing products and at up to 3.4% in face, neck, body, and hand skin care products. Sodium Laurate/Linoleate/Oleate/Palmitate is used at up to 84.7% in bath soaps and detergents and at up to 74.5% in leave-on baby products. Stearic Acid is reported to be used at up to 37.4% in rinse-off products (bath soaps and detergents) and at up to 21% in leave-on products (eyebrow pencil); Palmitic Acid is reported to be used at up to 21% in both rinse-off and leave-on products (skin cleansing preparations and fragrance products, respectively). In 2006, Stearic Acid was reported to be used at up to 43% in rinse-off products (shaving cream) and 22% in leave-on products (eyeliners); and Palmitic Acid was reported to be used at up to 20% in rinse-off products (shaving cream) and 16% in leave-on products (lipsticks).

Fatty acids share a common degradation pathway in which they are metabolized to acetyl-CoA or other key metabolites that are structurally similar breakdown products. No differences in metabolism are expected between even and odd numbered carbon chain compounds or saturated and unsaturated compounds.

In dermal studies of Capric Acid, Lithium Stearate, Stearic Acid, and Undecylenic Acid, the LD_{50} values were greater than 200 mg/kg/bw. The LD_{50} values in oral studies of numerous fatty acid and fatty acid salt ingredients were above the doses tested.

The NOAEL in a dermal study of Lithium Stearate in rats was $\geq$ 1000 mg/kg bw/day for systemic effects, but the NOAEL for local effects was 100 mg/kg bw/day. The NOAELs for Behenic Acid, Calcium Stearate, and Capric Acid were greater than or equal to the highest doses tested in oral studies. In oral gavage studies with Sodium Undecylenate, the NOAEL was $\leq$ 50 mg/kg bw/day with adverse effects including dose-dependent clinical signs of toxicity and adverse effects in the forestomaches of high dose groups. An 8-week dietary study of up to 2.5% Undecylenic Acid reported "inhibition of growth" in rats.

Lithium Stearate caused no treatment-related adverse reproductive or developmental effects at doses up to 1000 mg/kg bw/day in dermal studies. While non-reproductive effects were noted in parental animals in a few oral studies, no treatment-

related adverse effects were observed on the reproductive cycles or development of offspring in rats exposed to Behenic Acid, Calcium Stearate, Capric Acid, Caprylic Acid, or Undecylenic Acid.

In vitro bacterial cell and mammalian cell assays were negative for genotoxicity in Ammonium Oleate, Behenic Acid, Calcium Stearate, Capric Acid, Caproic Acid, Caprylic Acid, Isomerized Linoleic Acid, Lauric Acid, Linoleic Acid, Lithium Stearate, Myristic Acid, and Undecylenic Acid. No genotoxicity was detected in a micronucleus assay in mice with Undecylenic Acid.

Several in vitro assays and animal irritation studies indicate that Caproic Acid (up to 100%) and Caprylic Acid (up to 100%) are corrosive, and Capric Acid (concentration not reported), Isostearic Acid (100%), Lauric Acid (concentration not reported), Trilinoleic Acid (concentration not reported), and Undecylenic Acid (concentration not reported) may be irritating. Aluminum Tristearate, Lauric Acid, and Lithium Stearate, however, were predicted to be not irritating and/or corrosive human epidermis models. In human irritation studies, Lauric Acid at 50% induced erythema, edema, and scaling in a closed epicutaneous test; however, only slight erythema was observed in an open epicutaneous test of Lauric Acid at 80%. No dermal irritation was observed in subjects exposed to Palmitic Acid at 50%. In LLNAs, Lithium Stearate (up to 10%) was not sensitizing; however, the results of tests with Hydroxystearic Acid (up to 50%) and Ammonium Oleate (up to 50%) indicate that these ingredients may induce sensitization. In guinea pig studies, reactions observed to Ammonium Oleate (up to 50%) and Hydroxystearic Acid (up to 10%) may have been due to irritation. No sensitization was observed in guinea pig studies with Capric Acid (up to 40%), Lauric Acid (up to 2.5%), Sodium Undecylenate (up to 0.1%), Trilinoleic Acid (up to 75%), or Undecylenic Acid (up to 100%).

Caproic Acid at 50% was corrosive in bovine corneas, but Lithium Stearate (concentration not reported) was predicted to be non-irritating in a human corneal model. In rabbits, Caproic Acid (concentration not reported), Caprylic Acid (70%), Lauric Acid (concentration not reported), Lithium Stearate (concentration not reported), and Undecylenic Acid (concentration not reported) were ocular irritants of varying severity. Oleic Acid (up to 0.1%) and Palmitic Acid (concentration not reported) were not ocular irritants.

Case reports of reactions to Hydroxystearic Acid in lip products and deodorants and to Potassium Undecylenate in a topical cream have been reported.

PREVIOUS DISCUSSIONS

Lauric Acid, Oleic Acid, Palmitic Acid, Myristic Acid, and Stearic Acid

Although insufficient data were available for Myristic Acid, the Expert Panel included it in this safety assessment due to its structural similarity with the other fatty acids of this group.

Applications of Lauric and Oleic Acids to the skin of rabbits resulted in follicular keratosis and/or formation of comedones. These effects were considered by members of the Expert Panel in their safety assessment of the fatty acids reviewed in this report.

In the re-review summary, the Panel noted that these fatty acids may be plant-derived. In such cases, established limits for pesticide and heavy metal residues should not be exceeded (lead $\leq$ 10 ppm, arsenic $\leq$ 3 ppm, mercury $\leq$ 1 ppm, total PCB/pesticide $\leq$ 40 ppm, with $\leq$ 10 ppm for any specific pesticide residue).

The Panel also noted in the re-review summary that these fatty acids may also be derived from animal sources, including beef. The Panel agrees with the Food and Drug Administration's position that tallow derivatives, including these fatty acids, would not present any risk of transmissible encephalopathies.

Myristic Acid and Related Salts and Esters

The data on Butyl Myristate and the related salts and esters, coupled with the data on the related chemicals (Myristic Acid, Myristyl Myristate, and Isopropyl Myristate), are a sufficient basis for a safety assessment. The CIR Expert Panel believes that there is little toxicological and chemical difference between Myristic Acid and any of its inorganic salts included in this report. The salts are expected to dissociate in any product formulation, independent of whether the salt is aluminum, calcium, magnesium, potassium, sodium, or zinc. For the various esters of fatty alcohols and Myristic Acid, the CIR Expert Panel considers that these fatty acid esters are subject to hydrolysis to Myristic Acid and the component fatty alcohols. It is the experience of the Panel in its review of fatty alcohols of varying length of carbon chains that there is little difference in toxicity. Accordingly, the available data were considered supportive of the safety of the entire group as used in cosmetics.

The Expert Panel recognized that use concentration data are not available for all ingredients in this group and that some ingredients in the group are not in current use. The Expert Panel considered that the use concentrations for the ingredients that are in use are not likely to be different from the use concentrations for other myristates. Were those ingredients not in current use to be used in the future, the Panel expects that they would be used in products and at concentrations similar to those reported.

The Expert Panel recognized that these ingredients can enhance the penetration of other ingredients through the skin. The Panel cautioned that care should be taken in formulating cosmetic products that may contain these ingredients in combination with any ingredients whose safety was based on their lack of dermal absorption data, or when dermal absorption was a concern.

A number of the ingredients in this report—Cetyl Myristate, Octyldodecyl Myristate, and Sodium Myristate—have uses that include sprays. There are no data available on inhalation toxicity for these ingredients or the other ingredients in this

assessment. The Expert Panel determined that there is sufficient inhalation toxicity data on Isopropyl Myristate in its assessment demonstrating no inhalation toxicity. In addition to the inhalation toxicity data, the Panel determined that Butyl Myristate and the salts and esters can be used safely in hair sprays, because the ingredient particle size is not respirable. The Panel reasoned that the particle size of aerosol hair sprays (~38 μm) and pump hair sprays (>80 μm) is large compared with respirable particulate sizes (10 μm).

There are no data on the reproductive or developmental toxicity of Myristic Acid or its component parts for the derivatives. Based on structure-activity relationships, the Expert Panel considered that these chemicals had little potential for such toxicity when used as cosmetic ingredients.

Isopropyl Myristate was not genotoxic in the Ames assay. The Expert Panel determined this to be sufficient carcinogenicity data for the related ingredients in this safety assessment.

Aluminum Distearate, Aluminum Stearate, Aluminum Tristearate, Ammonium Stearate, Calcium Stearate, Lithium Stearate, Magnesium Stearate, Potassium Stearate, and Sodium Stearate

The opinion expressed in the [previous] conclusion is based on a composite of available animal and human data. However, the Panel felt that a number of the reported clinical studies for primary skin irritation and sensitization were suboptimal or inadequate in terms of number of subjects tested, concentrations tested, and/or test protocols employed. Data for the purpose of assessing the human skin sensitization potential of the Stearates were also limited in that only product formulation data were available. Further, no clinical studies relating to phototoxicity or photocontact allergenicity were reported. Despite these limitations and/or deficiencies in the clinical data, it is the Panel's opinion that sufficient animal and human data are available to assess the safety of the Stearates as cosmetic ingredients.

Hydroxystearic Acid

Because of the paucity of information on Hydroxystearic Acid, the Expert Panel considered in its original assessment that the available data on related compounds might be used (e.g. Stearic Acid). Findings on long-chain aliphatic acids were taken from the published CIR report on Oleic Acid, Lauric Acid, Palmitic Acid, Myristic Acid, and Stearic Acid. Slight local edema and no deaths were observed among New Zealand White rabbits after 4 weeks of topical administration (dorsal skin) of product formulations containing 2.0% Stearic Acid. There were no significant gross or microscopic lesions that were considered treatment related. In 13-week dermal toxicity studies, two cosmetic product formulations containing, at most 5% Stearic Acid produced moderate skin irritation (dorsal skin) in rats receiving 4.0 ml/kg and 227 mg/kg doses. All other physiologic parameters were normal. Low incidences of carcinomas, sarcomas, and lymphomas were observed in mice receiving single or repeated subcutaneous injections of 25 and 50 mg Palmitic Acid and up to 82 mg Stearic Acid. Stearic Acid was not carcinogenic in mice fed dietary doses up to 50 g/kg/day. In clinical primary and cumulative irritation studies, Oleic, Myristic, and Stearic Acids at concentrations of 100% or 40 % to 50% in mineral oil were non-irritating. Mild to intense erythema in single insult occlusive patch tests, soap chamber tests, and 21-day cumulative irritation studies were produced by cosmetic product formulations containing 2%-93% Oleic, Palmitic, Myristic, or Stearic Acid and were generally not related to the fatty acid concentrations in the formulations. In clinical repeated insult patch tests, maximization tests, and prophetic patch tests with cosmetic product formulations containing Oleic, Lauric, Palmitic, and Stearic Acids at concentrations ranging from less than 1% to 13%, no primary or cumulative irritation or sensitization was reported. Additionally, cosmetic product formulations containing 1% to 13% Oleic, Palmitic, or Stearic Acid did not induce photosensitization; however, there were slight reactions to some induction patches.

Because of the possible influence of the hydroxyl group on toxicity, however, the Expert Panel determined that these data are not pertinent to the safety assessment of Hydroxystearic Acid. Accordingly, the CIR Expert Panel issued a Final Report in March 1995 concluding that the available data were insufficient to support the safety of Hydroxystearic Acid. The following data were considered necessary to make a safety assessment: (1) concentration of use; (2) chemical characterization; (3) a dermal teratogenicity study; (4) one genotoxicity test using a mammalian system (if the results of the genotoxicity test are positive, a dermal carcinogenicity test by NTP standards will be requested); and (5) skin irritation data.

Subsequently, new data inclusive of all of the above data needs were received. The Expert Panel, with data now available on the use of the ingredient, received the reproduction and developmental toxicity and genotoxicity data that found no significant effects at exposures likely to exceed that seen from expected cosmetic use concentrations. The sarcomas produced by subcutaneous injection of Hydroxystearic Acid were considered to be a physical phenomenon unrelated to the specific material injected and not relevant to the use of this ingredient in cosmetics. Under semi-occluded and occluded patch testing conditions, the Expert Panel recognized irritation was found with antiperspirant prototype formulations. It is the experience of the Expert Panel that such formulations under those exaggerated conditions do produce irritation, but are not generally irritating in actual use.

Isostearic Acid

The Panel expressed concern regarding the production of comedones in the rabbit ear assay by a product formulation containing commercially available Isostearic Acid.[6] The Panel recognized that currently available tests are inadequate to predict the potential for human comedogenicity of an ingredient used in a product formulation. However, it is a potential health effect that should be considered when Isostearic Acid is used in cosmetic formulations.

Tall Oil Acid, Sodium Tallate, Potassium Tallate, and Ammonium Tallate

The CIR Expert Panel recognized that there are limited animal and human toxicity data and dermal irritation/sensitization studies for Tall Oil Acid. Tall Oil Acid is, however, known to be composed of fatty acids for which safety test data were available.

When considered with the subchronic and chronic oral toxicity, reproductive and developmental toxicity, genotoxicity, carcinogenicity, and photosensitization studies available for Oleic Acid, Lauric Acid, Palmitic Acid, Myristic Acid, and Stearic Acid, the available data for Tall Oil Acid itself are a sufficient basis for reaching a conclusion regarding Tall Oil Acid. It is the experience of the Panel in its review of fatty acids of varying carbon chain lengths that there is little difference in toxicity.

The Panel also considered that there is little difference between members of this family of salts of Tall Oil Acid. The salts are expected to be dissociated in any product formulation independent of whether the salt is sodium, potassium, or ammonium. Accordingly, the available data for Tall Oil Acid are considered supportive of the safety of the entire group as used in cosmetics.

The CIR Expert Panel recognized that there are data gaps regarding use and concentration of these ingredients. However, the overall information available on the types of products in which these ingredients are used and at what concentrations indicates a pattern of use, which was considered by the Expert Panel in assessing safety.

TABLES

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment. [1,CIR Staff]

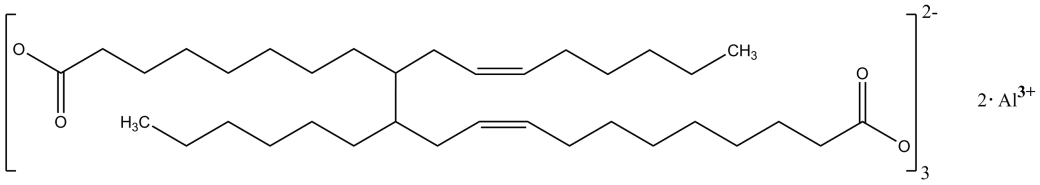
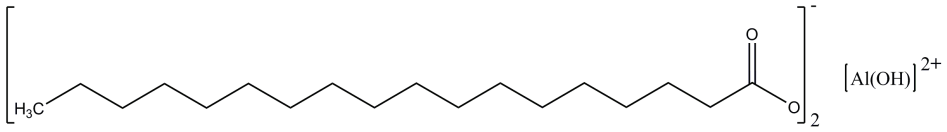
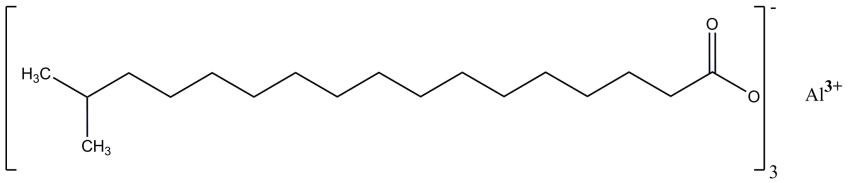
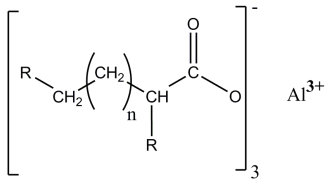
Ingredient & CAS No.	Definition & Structure	Function(s)
Aluminum Dilinoleate 53202-37-2	Aluminum Dilinoleate is the aluminum salt of Dilinoleic Acid 	anticaking agent; emulsion stabilizer; viscosity increasing agent – nonaqueous
Aluminum Distearate 300-92-5	Aluminum Distearate is an aluminum salt of stearic acid that conforms to the formula: 	anticaking agent; emulsion stabilizer; viscosity increasing agent – nonaqueous
Aluminum Isostearate 72277-75-9	Aluminum Isostearate is the aluminum salt of isostearic acid.  [one example of an "iso"]	anticaking agent; emulsion stabilizer; viscosity increasing agent – nonaqueous
Aluminum Isostearates/Palmitates	Aluminum Isostearates/Palmitates is the aluminum salt of a mixture of palmitic acid and isostearic acid.	anticaking agent; emulsion stabilizer; viscosity increasing agent – nonaqueous
Aluminum Isostearates/Stearates	Aluminum Isostearates/Stearates is the aluminum salt of a mixture of stearic acid and isostearic acid.	anticaking agent; emulsion stabilizer; viscosity increasing agent – nonaqueous
Aluminum Isostearates/Laurates/ Palmitates	Aluminum Isostearates/Laurates/Palmitates is the aluminum salt of a mixture of isostearic acid, lauric acid, and palmitic acid.	anticaking agent; emulsion stabilizer; viscosity increasing agent – nonaqueous
Aluminum Isostearates/Laurates/ Stearates	Aluminum Isostearates/Laurates/Stearates is the aluminum salt of a mixture of isostearic acid, lauric acid, and stearic acid.	anticaking agent; emulsion stabilizer; viscosity increasing agent – nonaqueous
Aluminum Lanolate	Aluminum Lanolate is the aluminum salt of lanolin acid. [The length of the Lanolin fatty acid chain varies from 7 to 41 carbon atoms, with the main fatty acids being palmitic (Cl6), stearic (Cl8) and longer molecules (C20 to C32).][14]  [wherein "n" is variable for the fatty acid composition of lanolin acid, and is in the range of 4 to 38; R is, in each case, hydrogen or hydroxyl, wherein at least one R is hydrogen; some fatty acids from lanolin acid may be branched][14]	anticaking agent; emulsion stabilizer; viscosity increasing agent – nonaqueous

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment. [1,CIR Staff]

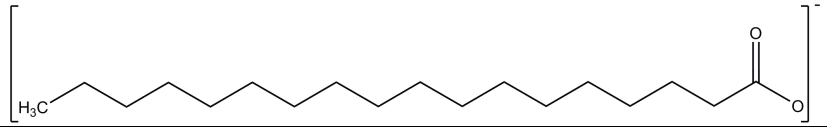
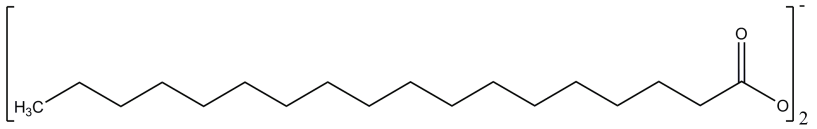
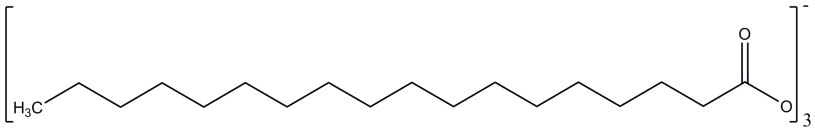
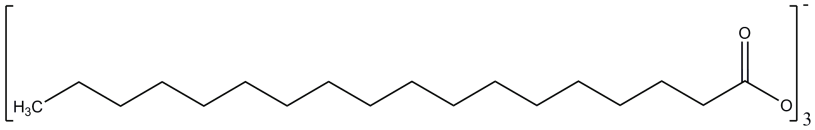
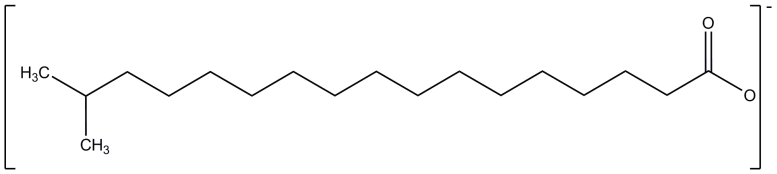
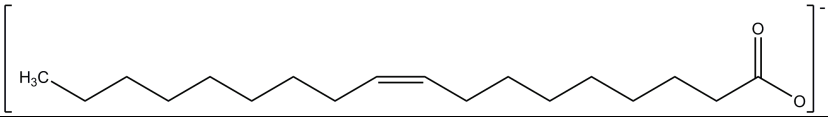
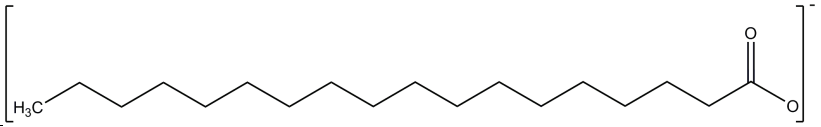
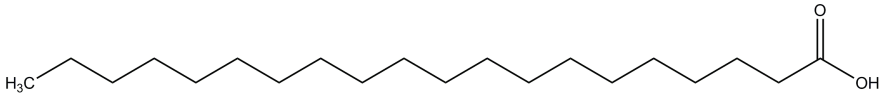
Ingredient & CAS No.	Definition & Structure	Function(s)
Aluminum Stearate 7047-84-9	Aluminum Stearate is the aluminum salt of stearic acid that conforms to the formula: 	anticaking agent; colorants; emulsion stabilizer; viscosity increasing agent – nonaqueous
Aluminum Stearates	Aluminum Stearates is a mixture of equal parts of aluminum distearate and aluminum tristearate.  and 	anticaking agent; emulsion stabilizer; viscosity increasing agent – nonaqueous
Aluminum Tristearate 637-12-7	Aluminum Tristearate is the aluminum salt of stearic acid that conforms generally to the formula: 	anticaking agent; emulsion stabilizer; viscosity increasing agent – nonaqueous
Ammonium Isostearate	Ammonium Isostearate is the ammonium salt of isostearic acid.  one example of an "iso"	surfactant – cleansing agent
Ammonium Oleate 544-60-5	Ammonium Oleate is the ammonium salt of oleic acid that conforms to the formula: 	surfactant – cleansing agent
Ammonium Stearate 1002-89-7	Ammonium Stearate is the ammonium salt of stearic acid. It conforms to the formula: 	surfactant – cleansing agent
Arachidic Acid 506-30-9	Arachidic Acid is the fatty acid that conforms to the formula: 	opacifying agent; surfactant – cleansing agent

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment. [1,CIR Staff]

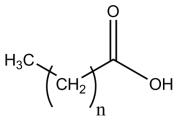
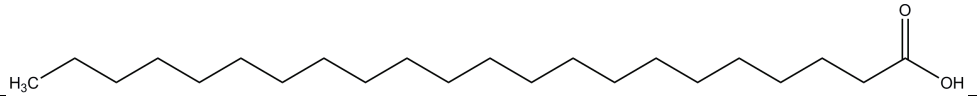
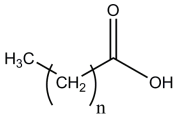
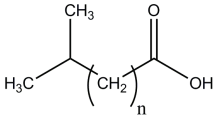
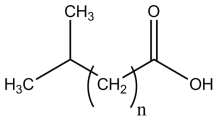
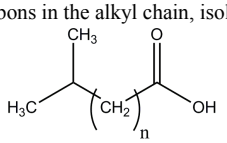
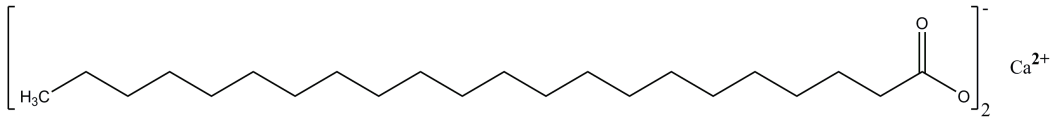
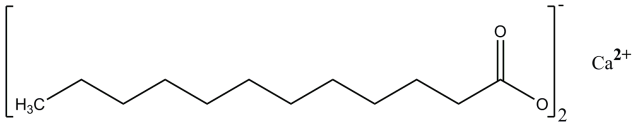
Ingredient & CAS No.	Definition & Structure	Function(s)
Beeswax Acid	Beeswax Acid is the acid portion obtained by the saponification of beeswax. It is composed of C24 to C36 straight-chain acids.  [wherein "n" is 22 to 34]	surfactant- cleansing agent; surfactant – emulsifying agent
Behenic Acid 112-85-6	Behenic Acid is the fatty acid that conforms generally to the formula: 	opacifying agent; surfactant – cleansing agent
C14-28 Alkyl Acid	C14-28 Alkyl Acid is a mixture of saturated fatty acids containing 14 to 28 carbons in the alkyl chain.  [wherein "n" is 12 to 26]	hair conditioning agent
C10-40 Isoalkyl Acid	C10-40 Isoalkyl Acid is a mixture of branched, saturated fatty acids with 10 to 40 carbons in the alkyl chain, isolated from lanolin acid.  [one example of an "iso"; wherein "n" is 7 to 37]	hair conditioning agent; skin-conditioning agent - emollient
C14-28 Isoalkyl Acid	C14-28 Isoalkyl Acid is a mixture of branched chain, saturated fatty acids containing 14 to 28 carbons in the alkyl chain.  [one example of an "iso"; wherein "n" is 11 to 25]	hair conditioning agent
C32-36 Isoalkyl Acid	C32-36 Isoalkyl Acid is a mixture of branched, saturated fatty acids with 32 to 36 carbons in the alkyl chain, isolated from lanolin acid.  [one example of an "iso"; wherein "n" is 29 to 33]	skin-conditioning agent – misc.
Calcium Behenate 3578-72-1	Calcium Behenate is the calcium salt of Behenic Acid. 	anticaking agent; viscosity increasing agent - nonaqueous
Calcium Laurate 4696-56-4	Calcium Laurate is the calcium salt of Lauric Acid. 	anticaking agent; emulsion stabilizer; viscosity increasing agent - nonaqueous

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment. [1,CIR Staff]

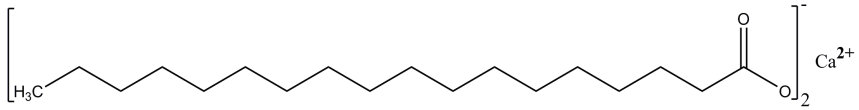
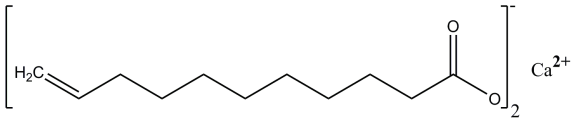
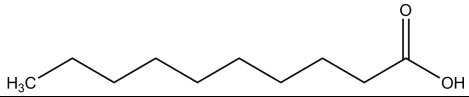
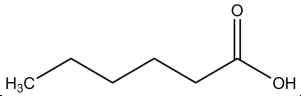
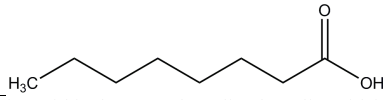
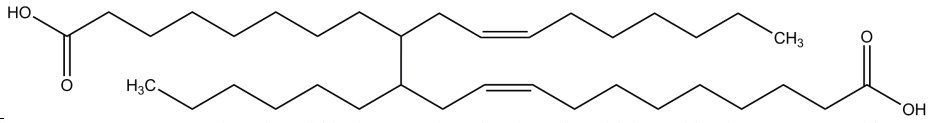
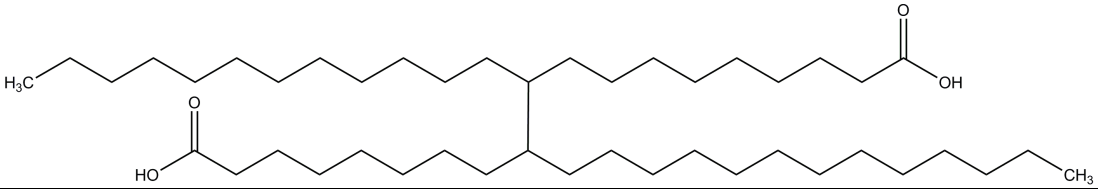
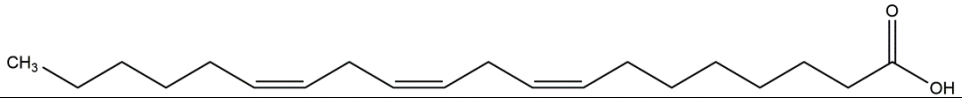
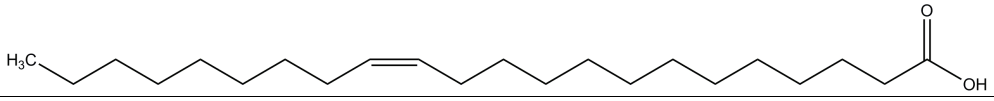
Ingredient & CAS No.	Definition & Structure	Function(s)
Calcium Stearate 1592-23-0	Calcium Stearate is the calcium salt of stearic acid. It conforms to the formula: 	anticaking agent; colorant; emulsion stabilizer; viscosity increasing agent - nonaqueous
Calcium Undecylenate 1322-14-1	Calcium Undecylenate is the organic salt that conforms to the formula: 	antifungal agent; viscosity increasing agent - nonaqueous
Capric Acid 334-48-5	Capric Acid is the fatty acid that conforms to the formula: 	fragrance ingredient; surfactant – cleansing agent
Caproic Acid 142-62-1	Caproic Acid is the aliphatic acid that conforms to the formula: 	fragrance ingredient; surfactant – cleansing agent
Caprylic Acid 124-07-2	Caprylic Acid is the fatty acid that conforms to the formula: 	fragrance ingredient; surfactant – cleansing agent
Dilinoleic Acid 26085-09-6 6144-28-1	Dilinoleic Acid is the 36-carbon dicarboxylic acid formed by the catalytic dimerization of linoleic acid. 	skin-conditioning agent – occlusive
Dierucic Acid 63541-50-4	Dierucic Acid is the 44-carbon dicarboxylic acid formed by the dimerization of Erucic Acid. 	skin-conditioning agent - occlusive
Eicosatrienoic Acid 1783-84-2	Eicosatrienoic Acid is the organic compound that conforms to the formula: 	skin-conditioning agent – misc.
Erucic Acid 112-86-7	Erucic Acid is the fatty acid that conforms to the formula: 	skin-conditioning agent – misc.

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment. [1,CIR Staff]

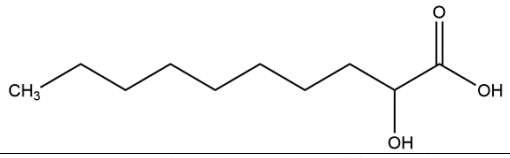
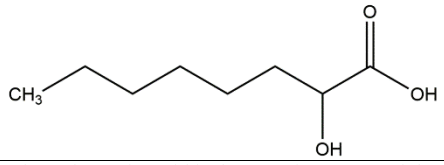
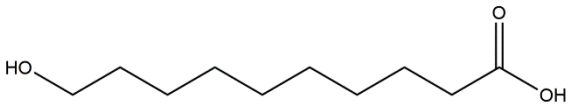
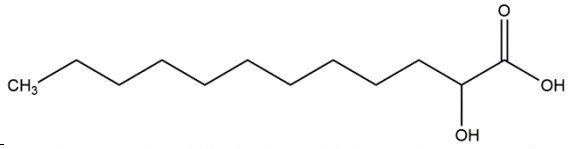
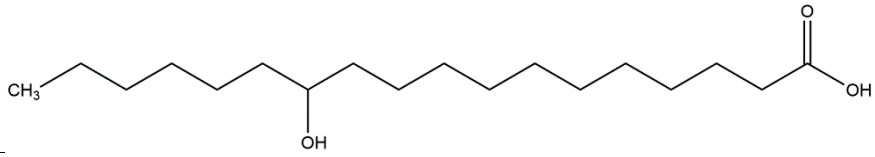
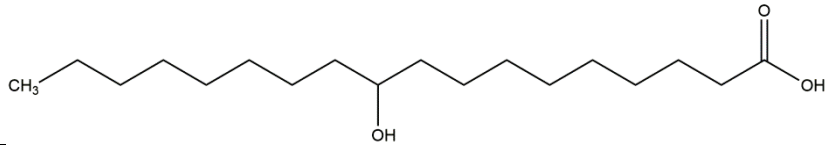
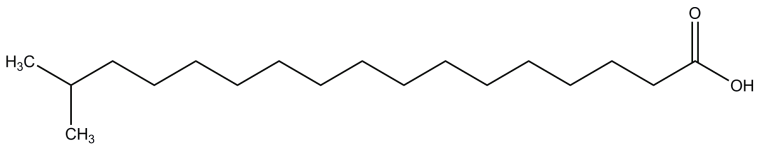
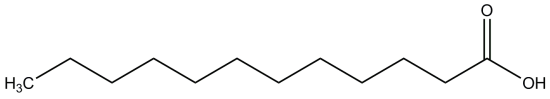
Ingredient & CAS No.	Definition & Structure	Function(s)
Hydroxycapric Acid 5393-81-7	Hydroxycapric Acid is the organic acid that conforms to the formula: 	skin-conditioning agent – misc.
Hydroxycaprylic Acid 617-73-2	Hydroxycaprylic Acid is the organic acid that conforms to the formula: 	skin-conditioning agent – misc.
10-Hydroxydecanoic Acid 1679-53-4	10-Hydroxydecanoic Acid is the organic compound that conforms to the formula: 	skin-conditioning agent - occlusive
Hydroxylauric Acid 2984-55-6	Hydroxylauric Acid is the organic compound that conforms to the formula: 	skin-conditioning agent – misc.
Hydroxystearic Acid 106-14-9 1330-70-7	Hydroxystearic Acid is the fatty acid that conforms generally to the formula: 	surfactant – cleansing agent
10-Hydroxystearic Acid 638-26-6	10-Hydroxystearic Acid is the organic compound that conforms to the formula: 	skin protectant; skin-conditioning agent – misc.
Isomerized Linoleic Acid 67701-06-8	Isomerized Linoleic Acid is the end-product of the controlled isomerization of Linoleic Acid.	film former; skin-conditioning agent – occlusive
Isomerized Safflower Acid 121250-47-3	Isomerized Safflower Acid is the end-product of the controlled isomerization of Safflower Acid. [Carthamus Tinctorius (Safflower) Seed Oil is mainly comprised of C18:2 and C18:1 fatty acids].[12]	oral health care drug; skin-conditioning agent – misc.
Isostearic Acid 2724-58-5 30399-84-9	Isostearic Acid is a mixture of branched chain 18 carbon aliphatic acids.  one example of an "iso"	binder; surfactant – cleansing agent
Lauric Acid 143-07-7	Lauric Acid is the fatty acid that conforms generally to the formula: 	fragrance ingredient; surfactant – cleansing agent

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment. [1,CIR Staff]

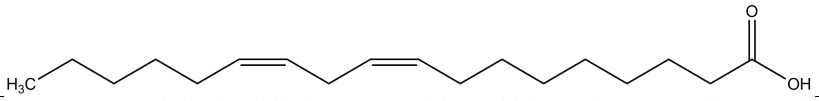
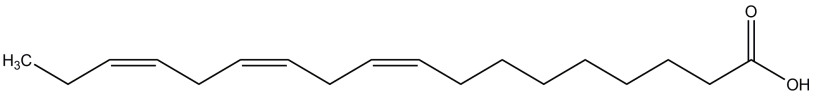
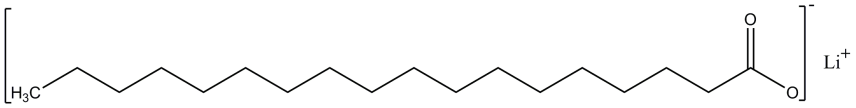
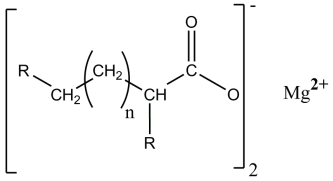
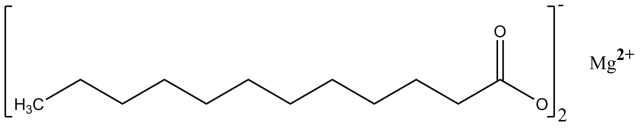
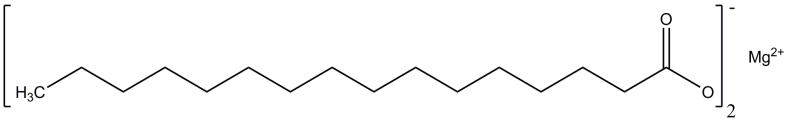
Ingredient & CAS No.	Definition & Structure	Function(s)
Linoleic Acid 342889-37-6 60-33-3	Linoleic Acid is the unsaturated fatty acid that conforms generally to the formula: 	fragrance ingredient; hair conditioning agent; skin-conditioning agent – misc.; surfactant – cleansing agent
Linolenic Acid 463-40-1	Linolenic Acid is the unsaturated fatty acid that conforms generally to the formula: 	fragrance ingredient; hair conditioning agent; skin-conditioning agent – misc.; surfactant – cleansing agent
Lithium Stearate 4485-12-5	Lithium Stearate is the lithium salt of stearic acid. It conforms generally to the formula: 	anticaking agent; binder; opacifying agent; slip modifier; viscosity increasing agent - nonaqueous
Magnesium Lanolate	Magnesium Lanolate is the magnesium salt of Lanolin Acid.  [wherein "n" is variable for the fatty acid composition of lanolin acid, and is in the range of 4 to 38; R is, in each case, hydrogen or hydroxyl, wherein at least one R is hydrogen; some fatty acids from lanolin acid may be branched][14]	anticaking agent; skin-conditioning agent – misc.; viscosity increasing agent - nonaqueous
Magnesium Laurate 4040-48-6	Magnesium Laurate is the magnesium salt of Lauric Acid. It conforms generally to the formula: 	binder
Magnesium Palmitate 2601-98-1	Magnesium Palmitate is the magnesium salt of palmitic acid. It conforms generally to the formula: 	anticaking agent; slip modifier; viscosity increasing agent - nonaqueous

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment. [1,CIR Staff]

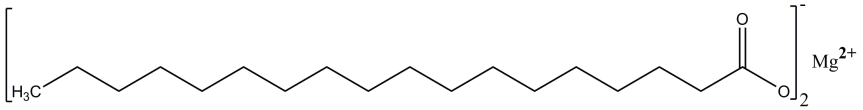
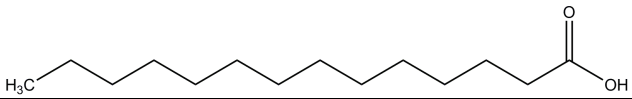
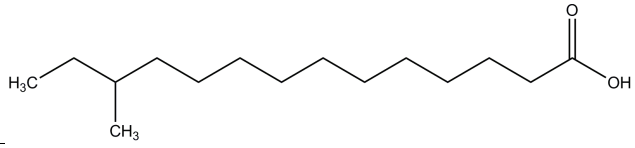
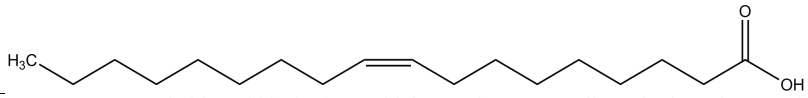
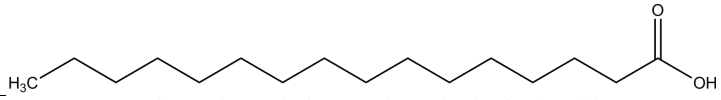
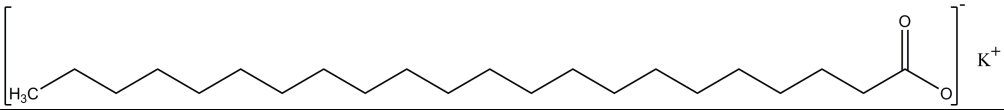
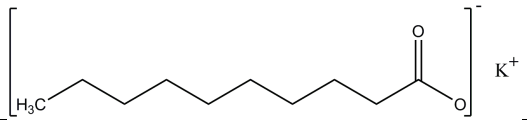
Ingredient & CAS No.	Definition & Structure	Function(s)
Magnesium Stearate 557-04-0	Magnesium Stearate is the magnesium salt of stearic acid. It conforms generally to the formula: 	anticaking agent; bulking agent; colorant; viscosity increasing agent - nonaqueous
Magnesium Tallowate 68953-41-3	Magnesium Tallowate is the magnesium salt of Tallow Acid. [Tallow is mainly comprised of C14, C16, C18, C18:1, and C18:2 fatty acid glycerides].[17]	anticaking agent; bulking agent; viscosity increasing agent - nonaqueous
Myristic Acid 544-63-8	Myristic Acid is the organic acid that conforms generally to the formula: 	fragrance ingredient; opacifying agent; surfactant – cleansing agent
Methyl Myristic Acid 73679-18-2	Methyl Myristic Acid is the organic compound that conforms to the formula: 	antioxidant
Oleic Acid 112-80-1 2027-47-6	Oleic Acid is the unsaturated fatty acid that conforms generally to the formula: 	fragrance ingredient; surfactant – cleansing agent
Palmitic Acid 57-10-3	Palmitic Acid is the fatty acid that conforms generally to the formula: 	fragrance ingredient; opacifying agent; surfactant – cleansing agent; surfactant – emulsifying agent
Potassium Behenate 7211-53-2	Potassium Behenate is the potassium salt of Behenic Acid. 	surfactant – cleansing agent
Potassium Borageate	Potassium Borageate is the potassium salt of the fatty acids derived from Borago Officinalis Seed Oil. [Borago Officinalis Seed Oil is mainly comprised of C16, C18, C18:1, and C18:2 fatty acids].[12]	surfactant – cleansing agent
Potassium Camelliate	Potassium Camelliate is the potassium salt of the fatty acids derived from Camellia Seed Oil. [Camellia Seed Oil obtained from various species of *Camellia* is mainly comprised of C18:1 and C18:2 fatty acids].[12]	surfactant – cleansing agent
Potassium Caprate 13040-18-1	Potassium Caprate is the potassium salt of Capric Acid. 	surfactant – cleansing agent

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment. [1,CIR Staff]

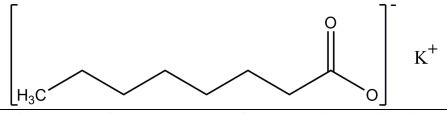
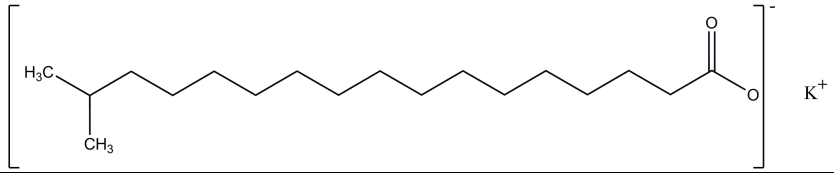
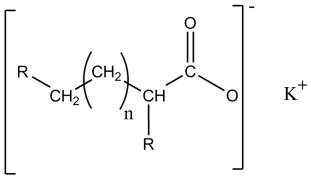
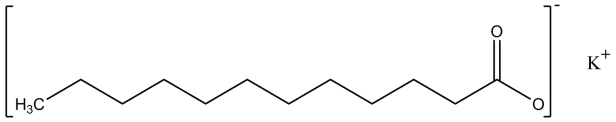
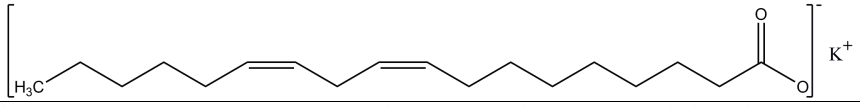
Ingredient & CAS No.	Definition & Structure	Function(s)
Potassium Caprylate 764-71-6	Potassium Caprylate is the potassium salt of Caprylic Acid that conforms to the formula: 	surfactant – cleansing agent; surfactant – emulsifying agent
Potassium Caprylate/Caprate	Potassium Caprylate/Caprate is the potassium salt of a mixture of Caprylic Acid and Capric Acid. 	surfactant – cleansing agent; surfactant - hydrotropes
Potassium Castorate 8013-05-6	Potassium Castorate is the potassium salt of the fatty acids derived from Ricinus Communis (Castor) Seed Oil. [Ricinus Communis (Castor) Seed Oil is mainly comprised of C18:1(OH), C18:1, and C18:2 fatty acids].[16]	surfactant – cleansing agent; surfactant – emulsifying agent
Potassium Hydrogenated Tallowate	Potassium Hydrogenated Tallowate is the potassium salt of Hydrogenated Tallow Acid. [Tallow is mainly comprised of C14, C16, C18, C18:1, and C18:2 fatty acid glycerides].[17]	surfactant – cleansing agent
Potassium Hydroxystearate 34326-46-0	Potassium Hydroxystearate is the potassium salt of Hydroxystearic Acid.	surfactant – cleansing agent
Potassium Isostearate 68413-46-7	Potassium Isostearate is the potassium salt of Isostearic Acid. 	surfactant – cleansing agent
Potassium Lanolate	Potassium Lanolate is the potassium salt of Lanolin Acid.  [wherein "n" is variable for the fatty acid composition of lanolin acid, and is in the range of 4 to 38; R is, in each case, hydrogen or hydroxyl, wherein at least one R is hydrogen; some fatty acids from lanolin acid may be branched][14]	surfactant – cleansing agent
Potassium Laurate 10124-65-9	Potassium Laurate is the potassium salt of lauric acid. It conforms generally to the formula: 	surfactant – cleansing agent; surfactant – emulsifying agent
Potassium Linoleate 3414-89-9	Potassium Linoleate is the potassium salt of Linoleic Acid. 	surfactant – cleansing agent; surfactant – emulsifying agent; viscosity increasing agent - nonaqueous
Potassium Linseedate	Potassium Linseedate is the potassium salt of the fatty acids derived from Linum Usitatissimum (Linseed) Seed Oil.[Linum Usitatissimum (Linseed) Seed Oil is mainly comprised of C16, C18, C18:1, C18:2, and C18:3 fatty acids].[12]	surfactant – cleansing agent

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment. [1,CIR Staff]

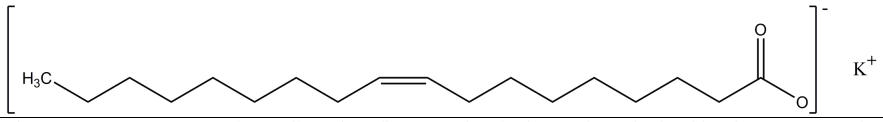
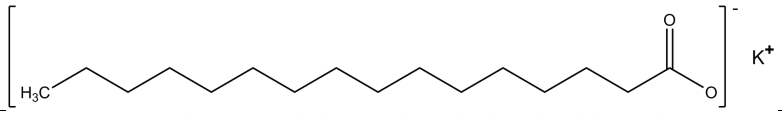
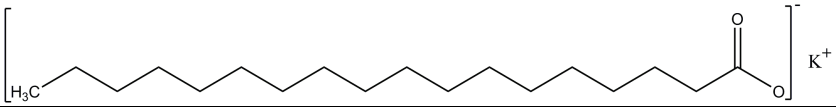
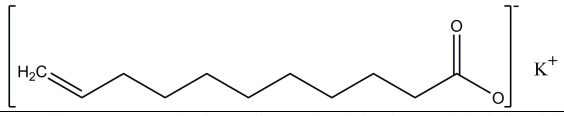
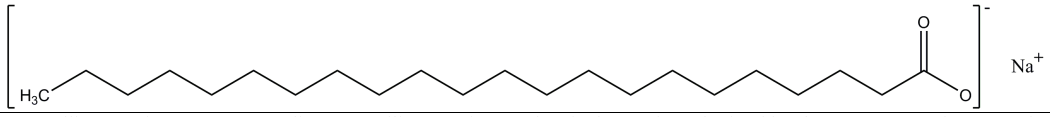
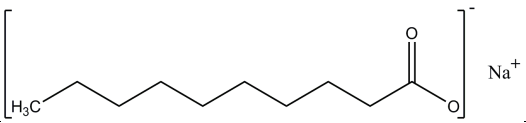
Ingredient & CAS No.	Definition & Structure	Function(s)
Potassium Oleate 143-18-0 23282-35-1	Potassium Oleate is the potassium salt of oleic acid. It conforms generally to the formula: 	surfactant – cleansing agent; surfactant – emulsifying agent
Potassium Olivate/ Sunflowerseedate	Potassium Olivate/Sunflowerseedate is the product obtained by the hydrolysis of a mixture of Olea Europaea (Olive) Fruit Oil and Helanthus Annuus (Sunflower) Seed Oil with potassium hydroxide. [Olea Europaea (Olive) Fruit Oil and Helanthus Annuus (Sunflower) Seed Oil are mainly comprised of C16, C18, C18:1, and C18:2 fatty acids].[12]	surfactant – cleansing agent; surfactant – emulsifying agent
Potassium Palmitate 2624-31-9	Potassium Palmitate is the potassium salt of palmitic acid. It conforms generally to the formula: 	surfactant – cleansing agent; surfactant – emulsifying agent
Potassium Stearate 593-29-3	Potassium Stearate is the potassium salt of stearic acid. It conforms generally to the formula: 	surfactant – cleansing agent; surfactant – emulsifying agent
Potassium Sunflowerseedate	Potassium Sunflowerseedate is the potassium salt of Sunflower Seed Acid. [Sunflower Seed Acid is mainly comprised of C16, C18, C18:1, and C18:2 fatty acids].[12]	surfactant – cleansing agent
Potassium Tallate 61790-44-1	Potassium Tallate is the potassium salt of Tall Oil Acid. [Tall Oil Acid is mainly comprised of C18:1 and C18:2 fatty acids].[11]	surfactant – cleansing agent; surfactant – emulsifying agent
Potassium Tallowate 61790-32-7	Potassium Tallowate is the potassium salt of Tallow Acid. [Tallow is mainly comprised of C14, C16, C18, C18:1, and C18:2 fatty acid glycerides].[17]	surfactant – cleansing agent; surfactant – emulsifying agent
Potassium Undecylenate 6159-41-7	Potassium Undecylenate is the potassium salt of Undecylenic Acid. 	surfactant – cleansing agent; surfactant – emulsifying agent
Sodium Arganate	Sodium Arganate is the sodium salt of the fatty acids derived from Argania Spinosa Kernel Oil. [Argania Spinosa Kernel Oil is mainly comprised of C16, C18, C18:1, and C18:2 fatty acids].[12]	surfactant – cleansing agent
Sodium Beeswax	Sodium Beeswax is the sodium salt of the fatty acids derived from Beeswax. [Beeswax is mainly comprised of even numbered C14 to C32 alcohols].[13]	surfactant – emulsifying agent
Sodium Behenate 5331-77-1	Sodium Behenate is the sodium salt of Behenic Acid. 	surfactant – cleansing agent
Sodium Camellia Japonica Seedate	Sodium Camellia Japonica Seedate is the product obtained by the hydrolysis of Camellia Japonica Seed Oil by sodium hydroxide. [Camellia Japonica Seed Oil is mainly comprised of C18:1 fatty acids].[12]	surfactant – cleansing agent
Sodium Caprate 1002-62-6	Sodium Caprate is the sodium salt of Capric Acid. 	surfactant – cleansing agent

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment. [1,CIR Staff]

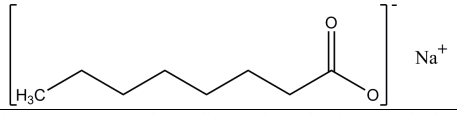
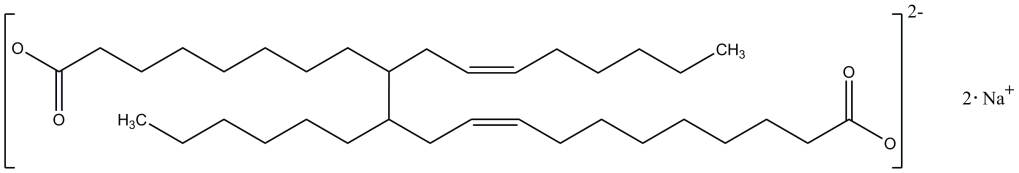
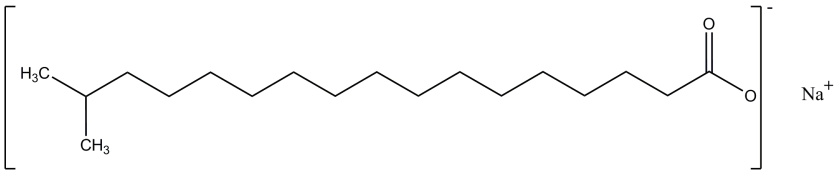
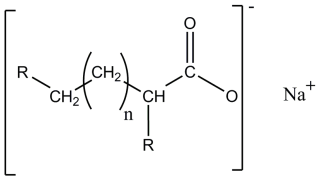
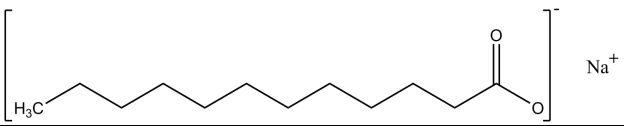
Ingredient & CAS No.	Definition & Structure	Function(s)
Sodium Caprylate 1984-06-1	Sodium Caprylate is the sodium salt of caprylic acid that conforms to the formula: 	surfactant – cleansing agent; surfactant – emulsifying agent
Sodium Castorate 8013-06-7 96690-37-8	Sodium Castorate is the sodium salt of the fatty acids derived from Ricinus Communis (Castor) Seed Oil. [Ricinus Communis (Castor) Seed Oil is mainly comprised of C18:1(OH), C18:1, and C18:2 fatty acids].[16]	surfactant – cleansing agent; surfactant – emulsifying agent
Sodium Dilinoleate 67701-20-6	Sodium Dilinoleate is the sodium salt of Dilinoleic Acid. 	surfactant – cleansing agent
Sodium Hydrogenated Tallowate	Sodium Hydrogenated Tallowate is the sodium salt of Hydrogenated Tallow Acid. [Tallow is mainly comprised of C14, C16, C18, C18:1, and C18:2 fatty acid glycerides].[17]	surfactant – cleansing agent
Sodium Hydroxystearate 13329-67-4	Sodium Hydroxystearate is the sodium salt of Hydroxystearic Acid.	surfactant – cleansing agent
Sodium Isostearate 64248-79-9	Sodium Isostearate is the sodium salt of Isostearic Acid.  one example of an "iso"	surfactant – cleansing agent; surfactant – emulsifying agent
Sodium Lanolate	Sodium Lanolate is the sodium salt of Lanolin Acid.  [wherein "n" is variable for the fatty acid composition of lanolin acid, and is in the range of 4 to 38; R is, in each case, hydrogen or hydroxyl, wherein at least one R is hydrogen; some fatty acids from lanolin acid may be branched][14]	surfactant – cleansing agent
Sodium Lardate 68605-06-1	Sodium Lardate is the sodium salt of the fatty acids derived from Lard. [Lard is mainly comprised of C16, C18, and C18:1 fatty acids].[15]	surfactant – cleansing agent; surfactant – emulsifying agent; surfactant – foam booster
Sodium Laurate 629-25-4	Sodium Laurate is the sodium salt of lauric acid that conforms generally to the formula: 	surfactant – cleansing agent; surfactant – emulsifying agent
Sodium Laurate/Linoleate/ Oleate/Palmitate	Sodium Laurate/Linoleate/Oleate/Palmitate is the sodium salt of a mixture of lauric, linoleic, oleic and pamitic acids.	skin protectant; skin-conditioning agent – emollient; skin-conditioning agent – misc.
Sodium Linoleate 822-17-3	Sodium Linoleate is the sodium salt of Linoleic Acid.	surfactant – cleansing agent; surfactant – emulsifying agent; viscosity increasing agent - nonaqueous

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment. [1,CIR Staff]

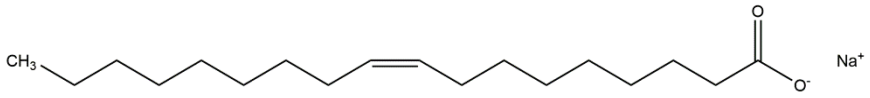
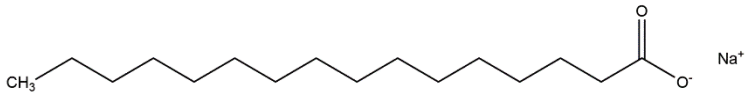
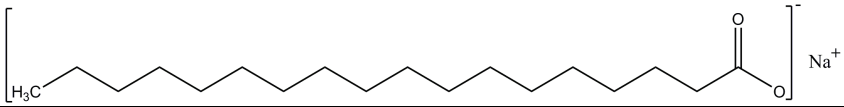
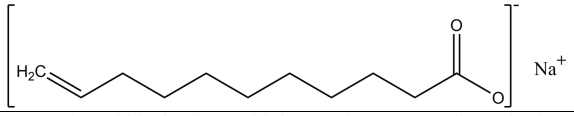
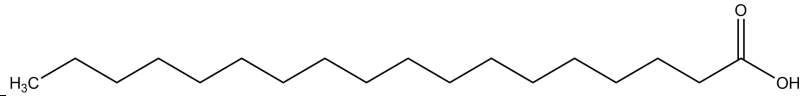
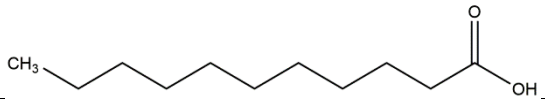
Ingredient & CAS No.	Definition & Structure	Function(s)
Sodium Oleate 143-19-1 166558-02-4	Sodium Oleate is the sodium salt of oleic acid that conforms generally to the formula: 	surfactant – cleansing agent; surfactant – emulsifying agent; viscosity increasing agent - aqueous
Sodium Palmitate 408-35-5	Sodium Palmitate is the sodium salt of palmitic acid that conforms generally to the formula: 	surfactant – cleansing agent; surfactant – emulsifying agent; viscosity increasing agent - aqueous
Sodium Stearate 822-16-2	Sodium Stearate is the sodium salt of stearic acid that conforms generally to the formula: 	surfactant – cleansing agent; surfactant – emulsifying agent; viscosity increasing agent - aqueous
Sodium Tallowate 8052-48-0	Sodium Tallowate is the sodium salt of Tallow Acid. [Tallow is mainly comprised of C14, C16, C18, C18:1, and C18:2 fatty acid glycerides].[17]	surfactant – cleansing agent; surfactant – foam booster; viscosity increasing agent - aqueous
Sodium Tamanuseedate	Sodium Tamanuseedate is the sodium salt of the fatty acids derived from Calophyllum Inophyllum Seed Oil.[Calophyllum Inophyllum Seed Oil is mainly comprised of C18:1, C18:2, C18, and C16 fatty acids].[73]	surfactant – cleansing agent; surfactant – emulsifying agent; viscosity increasing agent - nonaqueous
Sodium Undecylenate 3398-33-2	Sodium Undecylenate is the sodium salt of Undecylenic Acid that conforms generally to the formula: 	surfactant – cleansing agent; surfactant – emulsifying agent
Stearic Acid 57-11-4	Stearic Acid is the fatty acid that conforms generally to the formula: 	fragrance ingredient; surfactant – cleansing agent; surfactant – emulsifying agent
Trilinoleic Acid 68937-90-6 7049-66-3	Trilinoleic Acid is the 54-carbon tricarboxylic acid formed by the catalytic tirmerization of Linoleic Acid.	skin-conditioning agent – occlusive; viscosity increasing agent - nonaqueous
Undecanoic Acid 112-37-8	Undecanoic Acid is the aliphatic acid that conforms to the formula: 	fragrance ingredient; surfactant – cleansing agent; surfactant – emulsifying agent

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment. [1,CIR Staff]

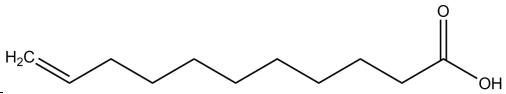
Ingredient & CAS No.	Definition & Structure	Function(s)
Undecylenic Acid 112-38-9 1333-28-4	Undecylenic Acid is the aliphatic acid that conforms generally to the formula: 	antifungal agent; cosmetic biocide; fragrance ingredient; surfactant – cleansing agent; surfactant – emulsifying agent

Table 2. Previously reviewed and related reviewed ingredients

Ingredients	Conclusion	Assessment Publication Status	Reference
Previously Reviewed Ingredients			
Aluminum Distearate	Safe as used	published in1982; re-review published in 2003 – not reopened	[3,4]
Aluminum Stearate	Safe as used	published in1982; re-review published in 2003 – not reopened	[3,4]
Aluminum Tristearate	Safe as used	published in1982; re-review published in 2003 – not reopened	[3,4]
Ammonium Stearate	Safe as used	published in1982; re-review published in 2003 – not reopened	[3,4]
Calcium Stearate	Safe as used	published in1982; re-review published in 2003 – not reopened	[3,4]
Hydroxystearic Acid	Safe as used	published in 1999	[5]
Isostearic Acid	Safe as used	published in 1983; re-review published in 2005 – not reopened	[6,7]
Lauric Acid	Safe as used	published in 1987; re-review published in 2006 – not reopened	[8,9]
Lithium Stearate	Safe as used	published in1982; re-review published in 2003 – not reopened	[3,4]
Magnesium Stearate	Safe as used	published in1982; re-review published in 2003 – not reopened	[3,4]
Myristic Acid	Safe as used	published in 1987; re-review published in 2006 – not reopened; included in expanded report with salts and esters published in 2010	[8-10]
Oleic Acid	Safe as used	published in 1987; re-review published in 2006 – not reopened	[8,9]
Palmitic Acid	Safe as used	published in 1987; re-review published in 2006 – not reopened	[8,9]
Potassium Stearate	Safe as used	published in1982; re-review published in 2003 – not reopened	[3,4]
Potassium Tallate	Safe as used	published in 2009	[11]
Sodium Stearate	Safe as used	published in1982; re-review published in 2003 – not reopened	[3,4]
Stearic Acid	Safe as used	published in 1987; re-review published in 2006 – not reopened	[8,9]
Related Ingredients			
Argania Spinosa Kernel Oil	Safe as used	published in 2017	[12]
Beeswax	Safe as used	published in1984; re-review published in 2005 – not reopened	[7,13]
Borago Officinalis Seed Oil	Safe as used	published in 2017	[12]
Camellia Japonica Seed Oil	Safe as used	published in 2017	[12]
Helianthus Annuus (Sunflower) Seed Oil and Sunflower Seed Acid	Safe as used	published in 2017	[12]
Lanolin and Lanolin Acid	Safe as used	published in 1980; re-review published in 2005 – not reopened	[7,14]
Lard	Safe as used provided established limits on heavy metals and pesticides are not exceeded	published in 2001; re-reviewed in 2017 – not reopened	[15]
Linum Usitatissimum (Linseed) Seed Oil	Safe as used	published in 2017	[12]
Olea Europaea (Olive) Fruit Oil	Safe as used	published in 2017	[12]
Ricinus Communis (Castor) Seed Oil	Safe as used	published in 2007	[16]
Tallow	Safe as used	published in 1990; re-review published in 2008 – not reopened	[17,18]

Table 3. Fatty acid ingredients by carbon chain length

Ingredient	***Carbon Chain Length as Lipid Number***
Caproic Acid	6:0
Caprylic Acid	8:0
Capric Acid	10:0
Undecanoic Acid	11:0
Undecylenic Acid	11:1
Lauric Acid	12:0
Myristic Acid	14:0
Palmitic Acid	16:0
Stearic Acid	18:0
Oleic Acid	18:1
Linoleic Acid	18:2
Linolenic Acid	18:3
Arachidic Acid	20:0
Eicosatrienoic Acid	20:3
Behenic Acid	22:0
Erucic Acid	22:1

Table 4. Physical and chemical properties

Property	Value	Reference
Aluminum Distearate		
Physical Form	White powder	[74]
Molecular Weight Da	610	[4]
Specific gravity	1.009	[4]
Melting Point º C	120-145	[4]
Aluminum Stearate		
Physical Form	White powder	[74]
Molecular Weight Da	344	[4]
Specific gravity	1.010	[4]
Melting Point º C	173	[4]
Aluminum Tristearate		
Physical Form	White powder	[21]
Molecular Weight Da	877.35	[4]
Density g/cm^3 @ 20º C	1.066	[21]
Vapor Pressure mmHg @ 25º C	0	[21]
Melting Point º C at 760 mmHg	179.5	[21]
Boiling Point ºC at 760 mm Hg	250	[21]
Water Solubility mg/L @ 25ºC	0 (insoluble)	[21]
Log P	22.69	[21]
Ammonium Oleate		
Physical Form	Yellow-brown paste	[75]
Molecular Weight Da	299.50	[75]
Melting Point º C	21.1-22.2	[75]
Ammonium Stearate		
Physical Form	Yellow-white powder or tan, wax-like solid	[74,75]
Molecular Weight Da	301.5	[4]
Specific gravity @ 22º C	0.89	[4]
Melting Point º C	73-87	[4]
Arachidic Acid		
Physical Form	Shining, white, crystalline leaflets	[74]
Molecular Weight Da	312.5	[75]
Density g/cm^3 @ 20º C and 760 mmHg	0.884 (estimated)	[76]
Melting Point º C	75.5	[75]
Boiling Point ºC at 760 mm Hg	328	[75]
Behenic Acid		
Physical Form	White to off-white waxy solid	[22]
Molecular Weight Da	340.59	[75]
Density g/cm^3 @ 100º C	0.82	[75]
Vapor Pressure mmHg @ 100º C	$< 4.875 \times 10^{-5}$	[34]
Melting Point º C	79.95	[75]
Boiling Point ºC at 60 mm Hg	306	[75]
Water Solubility mg/L @ 25ºC	0.016	[22]
Log P @ 25ºC	> 5.11	[22]
Calcium Stearate		
Physical Form	Granular, fatty powder	[75]
Molecular Weight Da	607.00	[4]
Melting Point º C	129-180	[4]
Calcium Undecylenate		
Physical Form	Fine, white powder	[74]
Melting Point º C	155	[74]
Capric Acid		
Physical Form	White to pale yellow crystals or needles	[23]
Molecular Weight Da	172.27	[75]
Density g/cm^3 @ 20º C	0.89	[23]
Vapor Pressure mmHg @ 25º C	3.66×10^{-4}	[23]
Melting Point º C at 760 mmg Hg	31.65	[23]
Boiling Point ºC at 760 mm Hg	268.7	[23]
Water Solubility mg/L @ 25ºC	61.8	[23]
Log P @ 20ºC	4.1	[23]
Caproic Acid		
Physical Form	Colorless to light brown liquid	[24]
Molecular Weight Da	116.16	[75]
Density g/cm^3 @ 20º C	0.93	[24]
Vapor Pressure mmHg @ 25º C	0.044	[24]
Melting Point º C at 760 mmg Hg	- 4	[24]
Boiling Point ºC at 760 mm Hg	203	[24]
Water Solubility g/L @ 25ºC	10.3	[24]
Log P_{ow}	1.92	[24]

Table 4. Physical and chemical properties

Property	Value	Reference
	Caprylic Acid	
Physical Form	Colorless liquid	[25]
Molecular Weight Da	144.21	[75]
Density g/cm^3 @ 20º C	0.91	[25]
Vapor Pressure mmHg @ 25º C	0.00368	[25]
Melting Point º C at 760 mmg Hg	16.5	[25]
Boiling Point ºC at 760 mm Hg	237	[25]
Water Solubility mg/L @ 20ºC	680	[25]
Log P @ 20ºC	3.05	[25]
	Dilinoleic Acid	
Physical Form	Light yellow, viscous liquid	[74]
Density g/cm^3 @ 100º C	0.921	[74]
	Eicosatrienoic Acid	
Molecular Weight Da	306.48	[76]
Density g/cm^3 @ 20º C and 760 mmHg	0.917 (estimated)	[76]
Vapor Pressure mmHg @ 25º C	6.77 x 10^{-9} (estimated)	[76]
Boiling Point ºC at 760 mm Hg	438.0 (estimated)	[76]
Log P @ 25ºC	7.541 (estimated)	[76]
	Eruric Acid	
Molecular Weight Da	338.58	[75]
Density g/cm^3 @ 55º C	0.860	[75]
Vapor Pressure mmHg @ 25º C	4.91 x 10^{-7} (estimated)	[76]
Melting Point º C	33.8	[75]
	381.5 (decomp.)	[75]
Log P @ 25ºC	9.459	[76]
Boiling Point ºC at 760 mm Hg	***Hydroxycapric Acid***	
Molecular Weight Da	188.26	[76]
Density g/cm^3 @ 20º C and 760 mm Hg	1.011 (estimated)	[76]
Vapor Pressure mmHg @ 25º C	2.90 x 10^{-5} (estimated)	[76]
Boiling Point ºC at 760 mm Hg	318.9 (estimated)	[76]
Log P @ 25ºC	2.716 (estimated)	[76]
	Hydroxycaprylic Acid	
Molecular Weight Da	160.21	[76]
Density g/cm^3 @ 20º C and 760 mmHg	1.046 (estimated)	[76]
Vapor Pressure mmHg @ 25º C	2.49 x 10^{-4} (estimated)	[76]
Melting Point º C	70	[77]
Boiling Point ºC at 760 mm Hg	289.0 (estimated)	[76]
Log P @ 25ºC	1.697	[76]
	10-Hydroxydecanoic Acid	
Molecular Weight Da	188.26	[76]
Density g/cm^3 @ 20º C and 760 mmHg	1.013 (estimated)	[76]
Vapor Pressure mmHg @ 25º C	1.18 x 10^{-5} (estimated)	[76]
Boiling Point ºC at 760 mm Hg	330.8 (estimated)	[76]
Log P @ 25ºC	1.847 (estimated)	[76]
	Hydroxylauric Acid	
Molecular Weight Da	216.32	[76]
Density g/cm^3 @ 20º C and 760 mmHg	0.987 (estimated)	[76]
Vapor Pressure mmHg @ 25º C	3.05 x 10^{-6} (estimated)	[76]
Boiling Point ºC at 760 mm Hg	348.5 (estimated)	[76]
Log P @ 25ºC	3.735 (estimated)	[76]
	Hydroxystearic Acid	
Molecular Weight Da	300.48	[5]
Density g/cm^3 @ 20 ºC and 760 mmHg	0.944 (estimated)	[76]
Vapor Pressure mmHg @ 25 ºC	1.92 x 10^{-9} (estimated)	[76]
Melting Point ºC	75-82	[5]
Boiling Point ºC at 760 mm Hg	436.3 (estimated)	[76]
Log P @ 20 ºC	5.767 (estimated	[76]
	10-Hydroxystearic Acid	
Molecular Weight Da	300.48	[76]
Density g/cm^3 @ 20º C and 760 mmHg	0.944 (estimated)	[76]
Vapor Pressure mmHg @ 25º C	1.92 x 10^{-9} (estimated)	[76]
Boiling Point ºC at 760 mm Hg	436.3 (estimated)	[76]
Log P @ 25ºC	5.767 (estimated)	[76]
	Isomerized Linoleic Acid	
Physical Form	paste	[26]
Molecular Weight Da	228.291	[78]
Density g/cm^3 @ 20º C	0.84-0.89	[26]
Melting Point º C	44-48	[26]
Boiling Point ºC at 7.5 mm Hg	225	[26]

Table 4. Physical and chemical properties

Property	Value	Reference
	Isostearic Acid	
Physical Form	Clear, oily liquid	[6]
Molecular Weight Da	284.48	[76]
Specific gravity @ 25º C	0.89-0.906	[6]
Vapor Pressure mmHg @ 25º C	1.52 x 10^{-7} (estimated)	[76]
Boiling Point ºC at 760 mm Hg	400.8 (estimated)	[76]
Log P @ 25ºC	7.674 (estimated)	[76]
	Lauric Acid	
Physical Form	White or slightly yellow, somewhat glossy crystalline solid or powder/colorless solid	[8]
Molecular Weight Da	200.32	[8]
Density g/cm^3 @ 50º C	0.8679	[8]
Vapor Pressure mmHg @ 25º C	6.61 x 10^{-4} (estimated)	[76]
Melting Point º C	44 or 48	[8]
Boiling Point ºC	225	[8]
Log P @ 25ºC	4.773 (estimated)	[76]
	Linoleic Acid	
Physical Form	Colorless oil	[75]
Molecular Weight Da	280.45	[75]
Density g/cm^3 @ 15º C	0.905	[74]
Vapor Pressure mmHg @ 25º C	3.54 x 10^{-6} (estimated)	[76]
Melting Point º C	-12	[75]
Boiling Point ºC @ 14 mmHg	228	[74]
Log P @ 25ºC	7.017 (estimated)	[76]
	Linolenic Acid	
Physical Form	Colorless liquid	[75]
Molecular Weight Da	278.44	[75]
Density g/cm^3 @ 20 º C	0.916	[74]
Vapor Pressure mmHg @ 25º C	4.24x 10-9 (estimated)	[76]
Melting Point º C	-11	[74]
Boiling Point ºC @ 17 mmHg	230	[74]
Log P @ 25ºC	6.522 (estimated)	[76]
	Lithium Stearate	
Physical Form	White solid	[28]
Molecular Weight Da	290.41	[4]
Specific gravity	1.025	[4]
Melting Point º C	108	[4]
	Magnesium Palmitate	
Physical Form	Crystalline needles or white lumps	[74]
Melting Point º C	121.5	[74]
	Magnesium Stearate	
Physical Form	White powder	[75]
Molecular Weight Da	591.27	[4]
Specific gravity	1.028	[4]
Melting Point º C	86-132	[4]
	Methyl Myristic Acid	
Molecular Weight Da	242.40	[76]
Density g/cm^3 @ 20º C and 760 mmHg	0.894 (estimated)	[76]
Vapor Pressure mmHg @ 25º C	5.19 x 10^{-6} (estimated)	[76]
Boiling Point ºC at 760 mm Hg	355.5 (estimated)	[76]
Log P @ 25 ºC	6.146 (estimated)	[76]
	Myristic Acid	
Physical Form	Solid	[8]
Molecular Weight Da	228.36	[8]
Density g/cm^3 @ 70º C	0.8528	[8]
Vapor Pressure mmHg @ 25º C	1.39 x 10^{-4} (estimated)	[76]
Melting Point º C	54.4-58.5	[8]
Boiling Point ºC	250.5	[8]
Log P @ 25ºC	5.792 (estimated)	[76]
	Oleic Acid	
Physical Form	Colorless to pale yellow, oily liquid above 5-7 ºC	[8]
Molecular Weight Da	282.45	[8]
Density g/cm^3 @ 25º C	0.895	[8]
Vapor Pressure mmHg @ 25º C	3.70 x 10^{-6} (estimated)	[76]
Melting Point º C	16.3	[8]
Boiling Point ºC at 11 mm Hg	286	[8]
Log P @ 25ºC	7.421 (estimated)	[76]

Table 4. Physical and chemical properties

Property	Value	Reference
	Palmitic Acid	
Physical Form	White or faintly yellow, slightly glossy crystalline solid/white or yellow-white powder/white crystalline scales/colorless crystals	[8]
Molecular Weight Da	256.43	[8]
Density g/cm^3 @ 62º C	0.8527	[8]
Melting Point º C	63-64	[8]
Boiling Point ºC	215	[8]
Water Solubility mg/L @ 20ºC	< 0.05	[29]
	Potassium Laurate	
Physical Form	Light tan paste	[74]
	Potassium Linoleate	
Physical Form	Light tan paste	[74]
	Potassium Oleate	
Physical form	Yellowish or brownish soft mass or gray-tan paste	[74,75]
	Potassium Stearate	
Physical Form	White to pale yellow powder	[75]
Molecular Weight Da	322.58	[4]
Density g/cm^3 @ 75º C	1.037	[75]
	Potassium Undecylenate	
Physical Form	Finely divided, white powder	[74]
	Sodium Oleate	
Physical Form	White powder	[75]
Molecular Weight Da	304.45	[75]
Melting Point º C	232-235	[74]
	Sodium Palmitate	
Physical Form	White to yellow powder	[74]
Melting Point º C	270	[77]
	Sodium Stearate	
Physical Form	White powder	[75]
Molecular Weight Da	306.47	[4]
	Sodium Undecylenate	
Physical Form	White powder	[74]
	Stearic Acid	
Physical Form	White or faintly yellow crystals or leaflets/white or yellow-white powder	[8]
Molecular Weight Da	284.48	[8]
Density g/cm^3 @ 70º C	0.847	[8]
Vapor Pressure mmHg @ 25º C	4.28 x 10^{-8}	[30]
Melting Point º C	69-71.2	[8]
Boiling Point ºC at 760 mmHg	232	[30]
Water Solubility mg/L @ 25ºC	0.597	[30]
Log P @ 25ºC	8.23	[30]
	Trilinoleic Acid	
Physical Form	Dark brown liquid	[31]
Molecular Weight Da	801.036	[78]
Density g/cm^3 @ 19º C	0.967	[31]
Melting Point º C	- 3	[31]
Water Solubility mg/L @ 20ºC	< 0.37	[31]
	Undecanoic Acid	
Molecular Weight Da	186.29	[76]
Density g/cm^3 @ 80 ºC	0.805	[74]
Vapor Pressure mmHg @ 25º C	1.51 x 10^{-3} (estimated)	[76]
Melting Point º C	28.5	[74]
Boiling Point ºC at 760 mmHg	284.0	[74]
Log P @ 25ºC	4.263 (estimated)	[76]
	Undecylenic Acid	
Physical Form	Colorless or white solid	[32]
Molecular Weight Da	184.28	[75]
Density g/cm^3 @ 24.4º C	1.0024	[32]
Vapor Pressure mmHg @ 20º C	0.000143	[32]
Melting Point º C at 760 mmg Hg	26.4	[32]
Boiling Point ºC at 760 mm Hg	293.75	[32]
Water Solubility mg/L @ 20ºC	38.46	[32]
Log P_{ow} @ 20ºC	4.0	[32]

Table 5. Frequency (2018) and concentration of use (2016) according to duration and type of exposure for fatty acids and fatty acid salts[2,41]

	# of Uses	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*
	Aluminum Stearates		**Arachidic Acid**		**Behenic Acid**		**C14-28 Alkyl Acid**	
Totals[†]	**3**	**NR**	**9**	**0.000001-0.065**	**125**	**0.024-22**	**26**	**0.0095-0.075**
Duration of Use								
Leave-On	3	NR	7	0.000001-0.065	89	0.024-22	1	NR
Rinse Off	NR	NR	2	0.0002	36	0.9-6	25	0.0095-0.075
Diluted for (Bath) Use	NR	NR	NR	NR	NR	0.044	NR	NR
Exposure Type								
Eye Area	1	NR	5	0.065	16	0.024-22	NR	NR
Incidental Ingestion	NR	NR	NR	NR	3	0.48-14	NR	NR
Incidental Inhalation-Spray	NR	NR	1[b]	0.000001[a]	2; 8[a]; 9[b]	0.5; 12[a]	NR	NR
Incidental Inhalation-Powder	NR	NR	1[b]	NR	2[c]; 9[b]	0.5-2[c]	NR	NR
Dermal Contact	2	NR	3	0.0002	99	0.042-22	1	NR
Deodorant (underarm)	NR	NR	NR	NR	29[a]	0.75	NR	NR
Hair - Non-Coloring	NR	NR	NR	0.000001	11	2-12	23	0.0095-0.075
Hair-Coloring	NR	NR	NR	NR	1	NR	2	NR
Nail	NR	NR	1	NR	NR	0.5	NR	NR
Mucous Membrane	NR	NR	NR	0.0002	7	0.044-14	NR	NR
Baby Products	NR	NR	NR	NR	2	NR	NR	NR

	C10-40 Isoalkyl Acid		**C14-28 Isoalkyl Acid**		**Calcium Behenate**		**Capric Acid**	
Totals[†]	**NR**	**0.02-0.18**	**25**	**0.029-0.075**	**1**	**NR**	**2**	**0.0036-4**
Duration of Use								
Leave-On	NR	0.18	NR	NR	1	NR	NR	0.01-4
Rinse Off	NR	0.02	25	0.029-0.075	NR	NR	2	0.0036-0.2
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR
Exposure Type								
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	0.18[a]	NR	NR	1	NR	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	NR	NR	0.01[c]
Dermal Contact	NR	NR	NR	NR	NR	NR	2	0.0036-4
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	0.02-0.18	23	0.0.29-0.075	1	NR	NR	NR
Hair-Coloring	NR	NR	2	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	0.07-0.1
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

Table 5. Frequency (2018) and concentration of use (2016) according to duration and type of exposure for fatty acids and fatty acid salts[2,41]

	# of Uses	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*
	Caproic Acid		**Caprylic Acid**		**Dilinoleic Acid**		**Hydroxycapric Acid**	
Totals[†]	**NR**	**0.011**	**6**	**0.0018-4**	**71**	**0.14-2.5**	**1**	**0.7**
Duration of Use								
Leave-On	NR	NR	6	0.23-4	NR	0.14	1	0.7
Rinse Off	NR	0.011	NR	0.0018-0.1	71	2.5	NR	0.7
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR
Exposure Type								
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	0.011	2	NR	NR	0.14	NR	NR
Incidental Inhalation-Spray	NR	NR	3[a]	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	NR	NR	0.7[c]
Dermal Contact	NR	NR	3	0.0018-4	NR	NR	1	0.7
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	1	0.23	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	71	2.5	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	0.011	2	0.0018-0.1	NR	0.14	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	Hydroxycaprylic Acid		**10-Hydroxydecanoic Acid**		**Isomerized Linoleic Acid**		**Linoleic Acid**	
Totals[†]	**4**	**0.076**	**11**	**0.0084-0.1**	**22**	**0.1-0.75**	**633**	**0.00033-21.8**
Duration of Use								
Leave-On	4	0.076	9	0.0084-0.1	19	0.1-0.75	557	0.00085-3.4
Rinse Off	NR	0.076	2	NR	3	NR	76	0.00033-21.8
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	0.0012
Exposure Type								
Eye Area	NR	NR	NR	0.1	7	NR	70	0.01-0.76
Incidental Ingestion	NR	NR	NR	NR	NR	NR	96	0.0075-1
Incidental Inhalation-Spray	1[a]; 2[b]	NR	5[a]; 2[b]	NR	6[a]; 4[b]	NR	210[a]; 105[b]	0.0038-0.25; 0.003-0.67[a]; 0.2[b]
Incidental Inhalation-Powder	2[b]	0.076[c]	2[b]	0.02; 0.1[c]	4[b]	0.1-0.75[c]	8; 105[b]	0.2; 0.0015-3.4[c]; 0.2[b]
Dermal Contact	4	NR	11	0.0084-0.1	22	0.1-0.75	475	0.00085-21.8
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	0.07
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR	52	0.0009-0.67
Hair-Coloring	NR	NR	NR	NR	NR	NR	5	0.00033-0.31
Nail	NR	NR	NR	NR	NR	NR	2	2
Mucous Membrane	NR	NR	NR	NR	1	NR	103	0.001-1.1
Baby Products	NR	NR	NR	NR	NR	NR	NR	0.043

Table 5. Frequency (2018) and concentration of use (2016) according to duration and type of exposure for fatty acids and fatty acid salts[2,41]

	# of Uses	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*
	Linolenic Acid		**Magnesium Laurate**		**Potassium Behenate**		**Potassium Castorate**	
Totals[†]	**205**	**0.000007-1**	**3**	**NR**	**5**	**NR**	**2**	**0.52**
Duration of Use								
Leave-On	170	0.00005-1	NR	NR	NR	NR	NR	NR
Rinse Off	35	0.000007-0.44	3	NR	5	NR	2	0.52
Diluted for (Bath) Use	NR	0.0002	NR	NR	NR	NR	NR	NR
Exposure Type								
Eye Area	17	0.001-0.084	NR	NR	NR	NR	NR	NR
Incidental Ingestion	6	0.0022-0.01	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	81[a]; 36[b]	0.00005-0.25; 0.001-1[a]	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	1; 36[b]	0.003-0.067[c]	NR	NR	NR	NR	NR	NR
Dermal Contact	161	0.000007-0.45	3	NR	5	NR	2	0.52
Deodorant (underarm)	NR	0.0045-0.07	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	36	0.00005-1	NR	NR	NR	NR	NR	NR
Hair-Coloring	1	NR	NR	NR	NR	NR	NR	NR
Nail	1	0.01	NR	NR	NR	NR	NR	NR
Mucous Membrane	10	0.000007-0.2	3	NR	2	NR	2	0.52
Baby Products	NR	0.005	NR	NR	NR	NR	NR	NR

	Potassium Hydrogenated Tallowate		**Potassium Isostearate**		**Potassium Laurate**		**Potassium Oleate**	
Totals[†]	**1**	**NR**	**5**	**1.6-3**	**24**	**0.001-9**	**19**	**0.25-23**
Duration of Use								
Leave-On	1	NR	2	NR	1	0.001-2	1	NR
Rinse Off	NR	NR	3	1.6-3	23	1.3-9	18	0.25-23
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR
Exposure Type								
Eye Area	NR	NR	NR	NR	NR	0.001-0.0019	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	1[a]	NR	2[b]	NR	1[a]	NR	1[a]	NR
Incidental Inhalation-Powder	NR	NR	2[b]	NR	NR	0.0018-2[c]	NR	NR
Dermal Contact	1	NR	5	1.6-3	24	0.001-9	17	0.25-23
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	2	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	3	3	6	2-5.3	10	0.25-3
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

Table 5. Frequency (2018) and concentration of use (2016) according to duration and type of exposure for fatty acids and fatty acid salts[2,41]

	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)
	Potassium Palmitate		**Potassium Tallowate**		**Sodium Behenate**		**Sodium Castorate**	
Totals[†]	**25**	**0.26-21.1**	**3**	**0.2-12.9**	**14**	**NR**	**2**	**NR**
Duration of Use								
Leave-On	6	0.26	NR	0.2	14	NR	NR	NR
Rinse Off	19	0.3-21.1	3	12.9	NR	NR	2	NR
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR
Exposure Type								
Eye Area	4	0.26	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	2[b]	NR	NR	0.2[a]	NR	NR	NR	NR
Incidental Inhalation-Powder	2[b]	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	25	0.26-21.1	3	12.9	14	NR	2	NR
Deodorant (underarm)	NR	NR	NR	NR	14[a]	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	0.2	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	5	0.73	NR	NR	NR	NR	2	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	Sodium Isostearate		**Sodium Laurate**		**Sodium Laurate/Linoleate/Oleate/Palmitate**		**Sodium Oleate**	
Totals[†]	**11**	**3**	**87**	**0.005-14**	**NR**	**74.5-84.7**	**62**	**0.000002-3.7**
Duration of Use								
Leave-On	8	NR	21	0.075-6	NR	74.5	58	0.000002-0.025
Rinse Off	3	3	66	0.005-14	NR	84.7	4	0.000025-3.7
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	0.35-0.38
Exposure Type								
Eye Area	2	NR	NR	NR	NR	NR	9	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	2[a]; 4[b]	NR	2[a]; 3[b]	NR	NR	NR	31[a]; 16[b]	NR
Incidental Inhalation-Powder	4[b]	NR	3[b]	6[c]	NR	NR	16[b]	NR
Dermal Contact	11	3	76	0.005-14	NR	74.5-84.7	62	0.000002-3.7
Deodorant (underarm)	NR	NR	14[a]	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	11	0.005-0.4	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	0.2
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	3	3	45	0.013-8.7	NR	84.7	2	0.000025-3.7
Baby Products	NR	NR	NR	0.01	NR	74.5	NR	NR

Table 5. Frequency (2018) and concentration of use (2016) according to duration and type of exposure for fatty acids and fatty acid salts[2,41]

	# of Uses	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*
	Sodium Palmitate		**Sodium Tallowate**		**Trilinoleic Acid**		**Undecanoic Acid**	
Totals†	**102**	**0.06-55.8**	**110**	**5.1-80**	**4**	**NR**	**NR**	**0.0014-0.14**
Duration of Use								
Leave-On	25	0.06-4.1	4	NR	3	NR	NR	0.0014-0.096
Rinse Off	75	1.3-55.8	106	5.1-80	1	NR	NR	0.016-0.14
Diluted for (Bath) Use	2	NR	NR	NR	NR	NR	NR	NR
Exposure Type								
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	3[a]	NR	1[b]	NR	3[a]	NR	NR	0.0014
Incidental Inhalation-Powder	NR	NR	1[b]	NR	NR	NR	NR	NR
Dermal Contact	102	0.06-55.8	110	5.1-80	NR	NR	NR	0.0014-0.14
Deodorant (underarm)	21[a]	4.1	NR	NR	NR	NR	NR	0.0014-0.096
Hair - Non-Coloring	NR	NR	NR	NR	4	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	58	5.9-55.8	95	9-80	NR	NR	NR	0.016-0.14
Baby Products	1	0.06	2	NR	NR	NR	NR	NR

	Undecylenic Acid	
Totals†	**1**	**0.2-25**
Duration of Use		
Leave-On	1	0.2-25
Rinse Off	NR	NR
Diluted for (Bath) Use	NR	NR
Exposure Type		
Eye Area	NR	NR
Incidental Ingestion	NR	NR
Incidental Inhalation-Spray	1[a]	NR
Incidental Inhalation-Powder	NR	0.2
Dermal Contact	NR	0.2
Deodorant (underarm)	NR	NR
Hair - Non-Coloring	NR	NR
Hair-Coloring	NR	NR
Nail	NR	25
Mucous Membrane	NR	NR
Baby Products	NR	NR

NR = Not reported.

† 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 may be sprays, but it is not specified whether the reported uses are sprays.

[b.] Not specified whether a powder or a spray, so this information is captured for both categories of incidental inhalation.

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

Table 6. Current and historical frequency and concentration according to duration and type of exposure for previously reviewed fatty acids and fatty acid salts

	Aluminum Distearate				Aluminum Stearate			
	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	2018[41]	**2001/2003[3]**	**2016[2]**	**2001/2003[3]**	**2018[41]**	**2001/2003[3]**	**2016[2]**	**2001/2003[3]**
Totals[†]	**23**	**50**	**0.004-5.5**	**0.1-5**	**50**	**3**	**0.00014-3.4**	**0.3-8**
Duration of Use								
Leave-On	*20*	*46*	*0.004-5.5*	*0.1-5*	*49*	*3*	*0.0099-3.1*	*0.3-8*
Rinse Off	*3*	*4*	*0.054-4*	*3*	*1*	*NR*	*0.00014-3.4*	*1-4*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	6	21	0.08-5.2	3	6	1	0.0099-1.8	0.5-7
Incidental Ingestion	1	1	0.36-0.4	5	NR	NR	NR	0.3-1
Incidental Inhalation-Spray	1[a]; 1[b]	1[a]; 1[b]	NR	0.1-0.5[a]	14[a]; 13[b]	1[b]	NR	0.4-8[a]; 0.3-0.4[b]
Incidental Inhalation-Powder	4; 1[b]	3; 1[b]	0.1-4.5; 0.048-1.5[c]	NR	13[b]	1[b]	3.1; 0.0099-1.3[c]	4; 0.3-0.4[b]
Dermal Contact	17	43	0.004-5.5	0.1-3	44	2	0.0099-3.1	0.3-8
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	2	NR	0.00014-0.00016	NR
Hair-Coloring	3	3	4	3	1	NR	3.4	NR
Nail	NR	NR	0.37	NR	1	NR	NR	NR
Mucous Membrane	1	1	0.36-0.4	5	NR	NR	NR	0.3-1
Baby Products	NR	NR	NR	NR	NR	NR	0.53	NR

	Aluminum Tristearate				Calcium Stearate			
	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	2018[41]	**2001/2003[3]**	**2016[2]**	**2001/2003[3]**	**2018[41]**	**2001/2003[3]**	**2016[2]**	**2001/2003[3]**
Totals[†]	**2**	**12**	**NR**	**NR**	**263**	**107**	**0.000098-5**	**0.02-23**
Duration of Use								
Leave-On	*2*	*11*	*NR*	*NR*	*256*	*103*	*0.000098-5*	*0.02-23*
Rinse Off	*NR*	*1*	*NR*	*NR*	*7*	*4*	*0.00089-2.4*	*0.1-2*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	NR	4	NR	NR	211	72	0.01-4	0.2-20
Incidental Ingestion	NR	NR	NR	NR	3	3	0.1-2	1-23
Incidental Inhalation-Spray	1[b]	5[a]; 1[b]	NR	NR	1; 3[b]	1	0.000098-0.05; 0.005-0.025[a]	3
Incidental Inhalation-Powder	1[b]	1[b]	NR	NR	12; 3[b]	12	0.1-5; 0.65-5[c]	0.2-9
Dermal Contact	2	3	NR	NR	254	99	0.00089-5	0.02-20
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	5	0.02[a]
Hair - Non-Coloring	NR	5	NR	NR	NR	NR	0.000098-0.03	NR
Hair-Coloring	NR	NR	NR	NR	5	4	0.09-2.4	1
Nail	NR	NR	NR	NR	1	1	0.03-5	0.09-4
Mucous Membrane	NR	NR	NR	NR	4	3	0.1-2	1-23
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	Hydroxystearic Acid				Isostearic Acid			
	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	2018[41]	**1996[5]**	**2016[2]**	**1995[5]**	**2018[41]**	**2002/2005[7]**	**2016[2]**	**2002/2005[7]**
Totals[†]	**124**	**2**	**0.00011-14**	**2.5-10**	**270**	**119**	**0.004-20**	**0.003-26**
Duration of Use								
Leave-On	122	2	0.005-14	2.5-10	233	113	0.012-16	0.003-16
Rinse Off	2	NR	0.00011-2	NR	37	6	0.004-20	1-26
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR
Exposure Type								
Eye Area	13	NR	0.018-14	NR	80	13	0.013-9.5	0.01-3
Incidental Ingestion	60	NR	0.15-10	2.5	16	6	0.025-0.29	10
Incidental Inhalation-Spray	2; 7[a]; 3[b]	2[b]	NR	NR	39[a]; 47[b]	32[a]; 9[b]	0.032; 0.02-3[a]	0.5-3[a]; 0.3-2[b]
Incidental Inhalation-Powder	3[b]	2[b]	0.5; 0.001-2.6[c]	NR	1[c]; 47[b]	3; 9[b]	0.012-0.3; 0.045-3.8[c]	0.3-3; 0.3-2[b]
Dermal Contact	61	2	0.005-14	5-10	177	96	0.01-9.6	0.003
Deodorant (underarm)	9[a]	NR	NR	5-10[a]	2[a]	2[a]	NR	NR
Hair - Non-Coloring	2	NR	0.8-4	NR	5	4	0.004-2	1
Hair-Coloring	NR	NR	NR	NR	2	NR	0.75-20	18
Nail	1	NR	0.00011-0.038	NR	NR	2	3-16	2
Mucous Membrane	60	NR	0.15-10	2.5	34	6	0.025-0.29	2
Baby Products	NR	NR	NR	NR	1	NR	NR	NR

Table 6. Current and historical frequency and concentration according to duration and type of exposure for previously reviewed fatty acids and fatty acid salts

	Lauric Acid				**Lithium Stearate**			
	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	2018[41]	**2006[9]**	**2016[2]**	**2006[9]**	**2018[41]**	**2001/2003[3]**	**2016[2]**	**2001/2003[3]**
Totals[†]	**517**	**121**	**0.0011-18**	**0.000004-11**	**85**	**17**	**0.1-4**	**2-3**
Duration of Use								
Leave-On	30	11	0.0011-13	0.00002-3	85	17	0.1-4	2-3
Rinse Off	485	90	0.005-18	0.000004-8	NR	NR	NR	NR
Diluted for (Bath) Use	2	20	0.11	2-11	NR	NR	NR	NR
Exposure Type								
Eye Area	1	NR	0.0048-0.8	NR	79	1	NR	2
Incidental Ingestion	3	1	0.0011	0.00003	4	1	NR	NR
Incidental Inhalation-Spray	4[a]; 9[b]	7[a]	0.2; 0.2[a]	0.00002-0.001; 0.00003-1[a]; 0.00006[b]	NR	NR	NR	3[a]
Incidental Inhalation-Powder	9[b]	NR	0.019-10[c]	0.00006[b]	NR	2	3	NR
Dermal Contact	322	70	0.0018-18	0.00002-11	81	16	0.1-4	2
Deodorant (underarm)	5[a]	3[a]	0.3	0.3[a]	NR	NR	NR	NR
Hair - Non-Coloring	35	7	0.005-4.2	0.000004-4	NR	NR	NR	3
Hair-Coloring	156	43	0.01-1.5	NR	NR	NR	NR	NR
Nail	1	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	136	40	0.0011-5	0.00003-11	4	1	NR	NR
Baby Products	1	NR	0.0018-0.31	NR	NR	NR	NR	NR

	Magnesium Stearate				**Myristic Acid**			
	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	2018[41]	**2001/2003[3]**	**2016[2]**	**2001/2003[3]**	**2018[41]**	**2010[10]**	**2016[2]**	**2010[10]**
Totals[†]	**807**	**96**	**0.012-10**	**0.02-8**	**369**	**207**	**0.0005-28.7**	**0.00002-20**
Duration of Use								
Leave-On	754	92	0.012-10	0.02-8	162	61	0.0005-20.2	0.00002-20
Rinse Off	53	4	0.33-5	1	205	146	0.0031-28.7	0.00002-19
Diluted for (Bath) Use	NR	NR	NR	NR	2	NR	1	2
Exposure Type								
Eye Area	420	49	0.5-10	1-5	34	3	0.011-1	0.5
Incidental Ingestion	4	NR	0.012	1	2	5	NR	NR
Incidental Inhalation-Spray	2; 17[a]; 5[b]	6[a]; 8[b]	0.75; 0.15-0.6[a]	0.02-3[a]; 0.1[b]	1; 28[a]; 64[b]	11[a]; 14[b]	2.5; 0.002-7[a]	0.00002; 0.00002-2[a]; 0.8-20[b]
Incidental Inhalation-Powder	132; 5[b]	21; 8[b]	1-7.2; 0.12-1[c]	1-8; 0.1[b]; 2[c]	10; 64[b]	1; 14[b]	0.1-0.66; 0.03-20.2[c]	0.5; 0.8-20[b]
Dermal Contact	748	95	0.03-10	0.02-8	339	171	0.0005-28.7	0.005-20
Deodorant (underarm)	NR	NR	NR	NR	1[a]	1[a]	0.015	2[a]
Hair - Non-Coloring	7	NR	0.15-1	NR	13	29	0.002-7	0.00002-5
Hair-Coloring	44	NR	0.33-5	NR	NR	NR	0.2-0.33	0.00002
Nail	NR	NR	NR	NR	2	NR	0.04	NR
Mucous Membrane	8	5	0.012	1	34	16	0.0031-1.35	0.1-19
Baby Products	NR	NR	NR	2	NR	NR	0.05	NR

	Oleic Acid				**Palmitic Acid**			
	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	2018[41]	**2006[9]**	**2016[2]**	**2006[9]**	**2018[41]**	**2006[9]**	**2016[2]**	**2006[9]**
Totals[†]	**1052**	**1131**	**0.0002-20.9**	**0.000004-20**	**1240**	**132**	**0.000000001-21**	**0.000006-20**
Duration of Use								
Leave-On	294	106	0.0002-17	0.00005-20	924	47	0.000000001-21	0.00003-16
Rinse Off	758	1014	0.0005-20.9	0.000004-19	312	74	0.00082-21	0.00002-20
Diluted for (Bath) Use	NR	11	0.0005-3	NR	2	11	NR	0.000006-2
Exposure Type								
Eye Area	69	49	0.01-5	0.1-5	204	3	0.011-5.3	0.003-4
Incidental Ingestion	87	5	0.0015-0.2	16	99	1	0.00033-1	0.2-16
Incidental Inhalation-Spray	72[a]; 29[b]	6; 14[a]; 2[b]	0.0007-1.5; 0.003-3.8[a]	0.001; 0.02-0.6[a]; 0.2-2[b]	3; 251[a]; 214[b]	1; 16[a]; 5[b]	0.0003-0.8; 0.000000001-8[a]	0.01-3; 0.00003-3[a]; 0.05-7[b]
Incidental Inhalation-Powder	1[c]; 29[b]	1[c]; 2[b]	0.24; 0.04-3.3[c]	0.0001; 1[c]; 0.2-2[b]	14; 2[c]; 214[b]	1; 5[b]	0.12; 0.03-8.6[c]	0.01-1; 0.5-7[b]
Dermal Contact	164	102	0.0002-20.9	0.000004-15	898	99	0.000005-21	0.000006-20
Deodorant (underarm)	3[a]	NR	0.64; 1.5[d]	0.0007-0.6[a]	35[a]	1[a]	0.06-3.5; 0.0021[d]	0.09-3[a]
Hair - Non-Coloring	21	10	0.001-3.8	0.000007-20	43	30	0.000000001-8	0.00002-3
Hair-Coloring	720	974	1.4-17	19	60	1	0.005-2	NR
Nail	7	2	0.0003-0.3	0.0008	4	NR	0.0042-7.5	0.02-0.03
Mucous Membrane	90	40	0.0005-10	0.000004-16	158	22	0.00033-9.7	0.000006-16
Baby Products	1	6	0.1-0.36	1-2	2	NR	0.98-1.7	NR

Table 6. Current and historical frequency and concentration according to duration and type of exposure for previously reviewed fatty acids and fatty acid salts

	Potassium Stearate				**Potassium Tallate**			
	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	2018[41]	**2001/2003[3]**	**2016[2]**	**2001/2003[3]**	**2018[41]**	**2009[11]**	**2016[2]**	**2009[11]**
Totals†	**158**	**NR**	**0.0083-45**	**0.05-12**	**NR**	**9**	**NR**	**NR**
Duration of Use								
Leave-On	76	NR	0.0083-7.5	0.05	NR	NR	NR	NR
Rinse Off	82	NR	0.0097-45	12	NR	9	NR	NR
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR
Exposure Type								
Eye Area	5	NR	0.033-0.8	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	28[a]; 24[b]	NR	0.2-7.5[a]	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	7; 1[c]; 24[b]	NR	0.0083; 0.18-1.8[c]	NR	NR	NR	NR	NR
Dermal Contact	136	NR	0.0083-45	0.05-12	NR	9	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	11	NR	0.0097-7.5	NR	NR	NR	NR	NR
Hair-Coloring	9	NR	3.1	NR	NR	NR	NR	NR
Nail	1	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	19	NR	0.59-3	NR	NR	9	NR	NR
Baby Products	1	NR	NR	NR	NR	NR	NR	NR

	Sodium Stearate				**Stearic Acid**			
	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	2018[41]	**2001/2003[3]**	**2016[2]**	**2001/2003[3]**	**2018[41]**	**2006[9]**	**2016[2]**	**2006[9]**
Totals†	**519**	**184**	**0.000075-84**	**0.0001-25**	**5738**	**2133**	**0.00006-37.4**	**0.000002-43**
Duration of Use								
Leave-On	330	132	0.000075-84	0.0001-25	4616	1580	0.0001-21	0.00005-22
Rinse Off	189	51	0.000075-84	0.3-18	1119	539	0.00006-37.4	0.000002-43
Diluted for (Bath) Use	NR	1	NR	NR	3	14	0.02-1	0.000007-7
Exposure Type								
Eye Area	12	4	0.09-8.4	0.7-8	789	224	0.002-21	0.009-22
Incidental Ingestion	1	NR	7	0.1	103	40	0.0013-12	0.02-9
Incidental Inhalation-Spray	30[a]; 31[b]	6; 5[a]; 11[b]	0.13[a]	5-8; 7[a]	4; 1952[a]; 1180[b]	32; 490[a]; 409[b]	0.00015-3; 0.01-20[a]; 2.3-5.5[b]	1-16; 0.01-10[a]; 0.1-16[b]
Incidental Inhalation-Powder	1; 31[b]	2[c]; 11[b]	0.1-6[c]	NR	27; 28[c]; 1180[b]	6; 11[c]; 409[b]	0.36-2.1; 0.05-20[v]; 2.3-5.5[b]	0.1-1; 2-3[c]; 0.1-16[b]
Dermal Contact	475	170	0.000075-84	0.0001-25	4822	1819	0.0001-37.4	0.000007-43
Deodorant (underarm)	215[a]	101[a]	3.5-10	5-25[a]	54[a]	21[a]	0.05-4.1	0.2-9[a]
Hair - Non-Coloring	2	NR	0.00075-0.1	NR	124	29	0.00006-20	0.000002-7
Hair-Coloring	40	14	0.4-5.5	10-12	240	137	0.08-5	NR
Nail	NR	NR	7.5	NR	8	13	0.021-9.1	0.04-5
Mucous Membrane	106	32	0.001-34.3	0.1-18	331	101	0.0013-37.4	0.000007-19
Baby Products	NR	2	0.033	NR	30	18	0.03-2.1	0.1-3

NR = Not reported.

† 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 may be sprays, but it is not specified whether the reported uses are sprays.

[b] Not specified whether a powder or a spray, so this information is captured for both categories of incidental inhalation.

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

[d] spray deodorant

Table 7. Ingredients not reported in use.

Aluminum Dilinoleate
Aluminum Isostearate
Aluminum Isostearates/Palmitates
Aluminum Isostearates/Stearates
Aluminum Isostearates/Laurates/Palmitates
Aluminum Isostearates/Laurates/Stearates
Aluminum Lanolate
Ammonium Isostearate
Ammonium Oleate
Ammonium Stearate
Beeswax Acid
C32-36 Isoalkyl Acid
Calcium Laurate
Calcium Undecylenate
Dierucic Acid
Eicosatrienoic Acid
Erucic Acid
Hydroxylauric Acid
10-Hydroxystearic Acid
Isomerized Safflower Acid
Magnesium Lanolate
Magnesium Palmitate
Magnesium Tallowate
Methyl Myristic Acid
Potassium Borageate
Potassium Camelliate
Potassium Caprate
Potassium Caprylate
Potassium Caprylate/Caprate
Potassium Hydroxystearate
Potassium Lanolate
Potassium Linoleate
Potassium Linseedate
Potassium Olivate/Sunflowerseedate
Potassium Sunflowerseedate
Potassium Undecylenate
Sodium Arganate
Sodium Beeswax
Sodium Camellia Japonica Seedate
Sodium Caprate
Sodium Caprylate
Sodium Dilinoleate
Sodium Hydrogenated Tallowate
Sodium Hydroxystearate
Sodium Lanolate
Sodium Lardate
Sodium Linoleate
Sodium Tamanuseedate
Sodium Undecylenate

Table 8. FDA and EPA regulations applicable to fatty acids and fatty acid salts

Direct and Indirect Food Substances Affirmed as GRAS from 21 CFR §184.1025, §184.1065, §184.1090, §184.1229, §184.1440, §186.1770, and §186.1771
Calcium Stearate, Caprylic Acid, Linoleic Acid, Magnesium Stearate, Sodium Oleate, Sodium Palmitate, Stearic Acid
GRAS as Substance Migrating from Packaging from 21 CFR §182.70 and §182.90
Oleic Acid
Approved Direct Food Additives from 21 CFR §172.515, §172.615, §172.860, §172.862, and §172.863
Aluminum Distearate, Aluminum Stearate, Aluminum Stearates, Aluminum Tristearate, Calcium Laurate, Calcium Stearate, Capric Acid, Caproic Acid, Caprylic Acid, Lauric Acid, Magnesium Palmitate, Magnesium Stearate, Myristic Acid, Oleic Acid (including that derived from tall oil fatty acids), Palmitic Acid, Potassium Caprate, Potassium Laurate, Potassium Oleate, Potassium Palmitate, Potassium Stearate, Sodium Caprate, Sodium Laurate, Sodium Oleate, Sodium Palmitate, Sodium Stearate, Stearic Acid, Undecylenic Acid
Approved Secondary Direct Food Additives from 21 CFR §173.315 and §173.340
Aluminum Distearate, Aluminum Stearate, Aluminum Tristearate, Calcium Stearate, Capric Acid, Caproic Acid, Caprylic Acid, Lauric Acid, Magnesium Stearate, Myristic Acid, Oleic Acid, Palmitic Acid, Potassium Stearate, Stearic Acid,
Approved Indirect Food Additives from 21 CFR §175.105, §175.210, §175.300, §175.320, §176.170, §176.200, §176.210, §177.1010, §177.1200, §177.2260, §177.2600, §177.2800, §178.1010, §178.2010, §178.3297, §178.3570, §178.3910
Aluminum Dilinoleate, Aluminum Distearate, Aluminum Isostearates/Palmitates, Aluminum Isostearates/Stearates, Aluminum Isostearates/Laurates/Palmitates, Aluminum Isostearates/Laurates/Stearates, Aluminum Lanolate, Aluminum Stearate, Aluminum Stearates, Aluminum Tristearate, Aluminum Isostearate, Ammonium Oleate, Ammonium Stearate, Behenic Acid, Calcium Behenate, Calcium Laurate, Calcium Stearate, Capric Acid, Caproic Acid, Caprylic Acid, Dilinoleic Acid, Erucic Acid, Hydroxystearic Acid, Isostearic Acid, Lauric Acid, Linoleic Acid, Linolenic Acid, Lithium Stearate, Magnesium Lanolate, Magnesium Palmitate, Magnesium Stearate, Magnesium Tallowate, Myristic Acid, Oleic Acid, Palmitic Acid, Potassium Behenate, Potassium Caprate, Potassium Castorate, Potassium Isostearate, Potassium Lanolate, Potassium Laurate, Potassium Linoleate, Potassium Oleate, Potassium Palmitate, Potassium Stearate, Potassium Tallate, Potassium Tallowate, Sodium Behenate, Sodium Caprate, Sodium Caprylate, Sodium Castorate, Sodium Dilinoleate, Sodium Isostearate, Sodium Lanolate, Sodium Lardate, Sodium Laurate, Sodium Linoleate, Sodium Oleate, Sodium Palmitate, Sodium Stearate, Sodium Tallowate, Stearic Acid, Trilinoleic Acid
Approved Over-the-Counter Drug Use from 21 CFR §310.545 and §333.210
Calcium Undecylenate (dandruff/seborrheic dermatitis/psoriasis drug product/topical antifungal: total undecylenate concentration of 10-15%), Sodium Caprylate (topical antifugal drug products for diaper rash drug products), Sodium Oleate (laxative drug products), Undecylenic Acid (dandruff/seborrheic dermatitis/psoriasis drug product/topical antifungal: total undecylenate concentration of 10%-15%)
GRAS for Animals from 21 CFR §582.5065
Linoleic Acid
Approved for Animal Drugs or Feed from 21 CFR §522.1610 and §573.280
Calcium Stearate, Sodium Oleate, Sodium Stearate
Tolerances and Exemptions for Pesticide Chemical Residues in Food from 40 CFR §180.940 and §180.1068
Calcium Stearate (no limit), Capric Acid (end-use concentration not to exceed 100 ppm), Caprylic Acid (end-use concentration not to exceed 52 ppm), Potassium Laurate, Potassium Oleate, Potassium Palmitate, Potassium Stearate

Table 9. Non-cosmetic uses of fatty acid and fatty acid salts[74,75]

Aluminum Distearate	Thickener in paints, inks and greases; water repellent; lubricant in plastics and cordages; in cement production
Aluminum Stearate	Paint and varnish drier; greases; waterproofing agent; cement additive; lubricants; cutting compounds; flatting agents; pharmaceuticals; defoaming agent in beet sugar and yeast processing
Aluminum Tristearate	Waterproofing fabrics and ropes; in paint and varnish driers; thickening lubricating oils; in cements; in light-sensitive photographic compositions
Ammonium Oleate	Detergent; solidifying alcohol; emulsifying agent
Ammonium Stearate	In waterproofing cements, concrete, stucco, paper, textiles, etc.
Arachidic Acid	Organic synthesis; lubricating greases; waxes and plastics, source of arachidyl alcohol; biochemical research
Behenic Acid	In lubricating oils; as solvent evaporation retarder in paint removers; waxes; plasticizers; chemicals; stabilizers
Calcium Stearate	For waterproofing fabrics, cement, stucco and explosives; as a releasing agent for plastic molding powders; as a stabilizer for polyvinyl chloride resins; lubricant in making tablets; in pencils and wax crayons; in food and pharmaceuticals as a conditioning agent; flatting agent in paints
Calcium Undecylenate	Bacteriostat and fungistat in pharmaceuticals
Capric Acid	Manufacture of esters for artificial fruit flavors and perfumes; as an intermediate in other chemical syntheses; base for wetting agents; plasticizer; resins; intermediate for food-grade additives
Caproic Acid	Manufacture of esters for artificial flavors and hexyl derivatives; analytical chemistry; manufacture of rubber chemicals; varnish driers, resins; pharmaceuticals
Caprylic Acid	An intermediate in manufacture of esters used in perfumery; in manufacture of dyes, drugs, antiseptics, and fungicides; ore separations; synthetic flavors
Dilinoleic Acid	Modifier in alkyd and polyamide resins; polyester or metallic soap for petroleum additive; emulsifying agent; adhesives; shellac substitute; to upgrade drying oils
Erucic Acid	Preparation of dibasic acids and other chemicals; polyethylene film additive; water-resistant nylon
Hydroxystearic Acid	Lithium greases; chemical intermediates
Lauric Acid	Alkyd resins; wetting agents; soaps; detergents; insecticides; food additives
Linoleic Acid	Manufacture of paints, coatings, emulsifiers, vitamins; soaps; special driers for protective coatings; feeds, geochemical research; dietary supplement; margarine
Linolenic Acid	Dietary supplement/nutrient; biochemical research; drying oils
Lithium Stearate	Plastics; waxes; greases; lubricant in powder metallurgy; corrosive inhibitor in petroleum; flatting agent in varnishes and lacquers; high-temperature lubricant
Magnesium Palmitate	Varnish drier; lubricant for plastics
Magnesium Stearate	Lubricant in making tablets; drier in paints and varnishes; flatting agent; stabilizer and lubricant for plastics; dietary supplement; in medicines
Myristic Acid	In lubricants; in coatings for anodized aluminum; antifoaming agent in pharmaceutic aids; soaps; synthesis of esters for flavors and perfumes; component of food-grade additives
Oleic Acid	In preparation of Turkey red oil; in polishing compounds; in waterproofing textiles and oiling wool; manufactured driers; thickening lubricating oils; emulsifying and solubilizing agent in pharmaceutic acids and a diagnostic aid for pancreatic function; soap base; manufacture of oleates; ointments; ore flotation; intermediate; surface coatings; food grade additives
Palmitic Acid	Manufacture of metallic palmitates; soaps; lubricating oils; waterproofing; food-grade additives
Potassium Laurate	Emulsifying agent
Potassium Linoleate	Emulsifying agent
Potassium Oleate	Detergent
Potassium Stearate	Anti-tack or release agent for elastomers; binder, emulsifier or anticaking agent in foods; stabilizer for chewing gum; base for textile softeners
Potassium Undecylenate	Bacteriostat and fungistat in pharmaceuticals
Sodium Oleate	Ore flotations; waterproofing textiles; emulsifier of oil-water systems
Sodium Palmitate	Polymerization catalyst for synthetic rubbers; laundry soap; detergents; phamaceuticals; printing inks; emulsifier
Sodium Stearate	Industrial and household soap; emulsifying and stiffening agent in pharmaceutic acids; waterproofing and gelling agent, stabilizer in plastics
Sodium Undecylenate	Bacteriostat and fungistat in pharmaceuticals
Stearic Acid	For suppositories, coating enteric pills, ointments, and for coating bitter remedies; in the manufacture of metal stearate salts, stearin soap for opodeldoc, candles, phonograph records, insulators, and modeling compounds; impregnating plaster of Paris; stearates and stearate driers; lubricants; soaps; accelerator activator; dispersing agent and softener in rubber compounds; shoe and metal polishes; food packaging
Undecanoic Acid	Organic synthesis
Undecylenic Acid	Antifungal therapy; perfumery; flavoring; plastics; modifying agent (plasticizer, lubricant additive, etc.)

Table 10. Acute toxicity studies

Concentration/Vehicle	Dose/Study Protocol	Results	LD_{50}	Reference
		Dermal		
Capric Acid in PEG 300	Acute dermal toxicity study in 5 male and 5 female HanRcc:WIST (SPF) rats; performed in accordance with OECD TG 402; test sites were clipped and semi-occluded; skin was rinsed with water after 24 h; 2000 mg/kg bw	4/5 males and 3/5 females were slightly to moderately sedated on day 2 after patch removal; at same time point, 3/5 males and 2/5 females had deep respiration and 3/5 males and 1/5 females had hunched posture; 1/5 females lost 2.3% body weight in the 1st week after treatment; no adverse effects observed at necropsy; slight to moderate erythema noted in all animals at patch removal; slight to moderate scaling in all animals and slight scabs observed in all but one female, which reversed by day 5	> 2000 mg/kg bw	[23]
Lithium Stearate; no vehicle used	Acute dermal toxicity study in 5 male and 5 female Wistar rats; performed in accordance with OECD TG 402; test sites were clipped and semi-occluded; test material was removed after 24 h; 2000 mg/kg bw	No clinical signs of toxicity or abnormal findings at necropsy were observed	> 2000 mg/kg bw	[28]
Stearic Acid; concentration and vehicle were not reported	Fixed dose dermal toxicity study in 3 male and 3 female New Zealand White rabbits; test sites were occluded; test material was removed after 24 h; 2000 mg/kg bw	Slight to moderate erythema observed at patch removal and remained, becoming severe in one female; 4 animals had slight to moderate desquamation; slight edema and eschar formation was also noted in some animals during the 1st week; slight diarrhea in one female day 3 post-exposure; severe consolidation of the lungs in the only animal that died during the observation period; no other macroscopic abnormalities were observed	> 2000 mg/kg bw	[30]
Undecylenic Acid; concentration not reported, no vehicle used	Acute dermal toxicity study in 5 male and 5 female Sprague-Dawley rats per dose group; performed in accordance with OECD TG 402;test sites were semi-occluded 2000 mg/kg bw	No cutaneous reactions, clinical signs of toxicity, or abnormal findings at necropsy were observed	>2000 mg/kg bw	[32]
		Oral		
Ammonium Oleate; concentration not reported, no vehicle used	Gavage study in male and female rats (strain not reported); performed in accordance with OECD TG 401; 4, 8, 16, 32, 48, or 64 ml/kg; 5 animals per dose	Rats in the 16 mg/kg dose groups and greater experienced nasal hemorrhage, crusted ocular areas, oozed urine, and a debilitated appearance prior to death; mortalities occurred in the "40 ml/kg" dose groups and greater	47.3 ml/kg bw or 42,097 mg/kg bw	[20]
Behenic Acid; 20% in corn oil	Gavage study in 5 male and 5 female Sprague-Dawley rats; performed in accordance with OECD TG 401; 2000 mg/kg bw	No adverse effects observed	> 2000 mg/kg bw	[22]
Behenic Acid; 50% in DMSO	Gavage study in 5 male and 5 female Wistar rats; performed in accordance with OECD TG 401; 5000 mg/kg bw	Ruffled fur and diminished activity approximately 20 min after treatment that cleared within 24 h; stomach mucosa was reddened and swollen, with remnants of test material undigested	> 5000 mg/kg bw	[22]
Calcium Stearate in corn oil	Gavage study in 3 female Sprague-Dawley rats; 2000 mg/kg bw; study performed with a 2nd confirmatory experiment (6 rats total)	Soiled perineal region, inanimation, prone position; no unscheduled deaths; no adverse effects at necropsy	> 2000 mg/kg bw	[35]
Capric Acid; concentration not reported; no vehicle used	Gavage study in 5 male and 5 female Wistar rats; performed in accordance with OECD TG 401; 2000 mg/kg bw	No clinical signs of toxicity; firm and/or small white/greyish patches in the forestomach observed during necropsy	> 2000 mg/kg bw	[23]

Table 10. Acute toxicity studies

Concentration/Vehicle	Dose/Study Protocol	Results	LD_{50}	Reference
Capric Acid in water; concentration not reported	Gavage study in 5 male and 5 female Wistar rats; performed in accordance with OECD TG 401; 5000 mg/kg bw	Ruffled fur and diminished activity approximately 20 min after treatment that cleared within 24 h; slight reddening of gastric mucosa	> 5000 mg/kg bw	[23]
Caprylic Acid; concentration not reported; no vehicle used	Gavage study in 5 male and 5 female Wistar rats; performed in accordance with OECD TG 401; 2000 mg/kg bw	Firm and/or small white/greyish irregular patches in the forestomach observed in all animals	> 2000 mg/kg bw	[25]
Caprylic Acid; 25% in water	Gavage study in 5 male and 5 female Wistar rats; performed in accordance with OECD TG 401; 5000 mg/kg bw	Clinical signs of toxicity included salivation, reduced breathing and activity, and "reduced state" in both sexes, additionally ataxia, lateral position and reduced corneal reflex was observed in females; no abnormal findings were observed at necropsy	> 5000 mg/kg bw	[25]
Isomerized Linoleic Acid; concentration not reported; in propylene glycol	Gavage study in 5 male and 5 female Wistar rats; performed in accordance with OECD TG 401; 2000 mg/kg bw	One female rat had bloody eye encrustation and dacryorrhea; no abnormal findings were observed at necropsy	> 2000 mg/kg bw	[26]
Lauric Acid; concentration not reported; in water	Gavage study in 5 male and 5 female Wistar rats; performed in accordance with OECD TG 401; 5000 mg/kg bw	Slightly ruffled fur within 20 min after dosing that reversed within 24 h; slight reddening of gastric mucosa	> 5000 mg/kg bw	[27]
Lauric Acid; concentration not reported; in water and emulsifying agent	Gavage study with Wistar rats; 3 animals each at 2500 and 5000 mg/kg bw and 10 animals at 10,000 mg/kg bw; no further details provided	No mortality or clinical signs of toxicity noted	> 10,000 mg/kg bw	[27]
Lithium Stearate; concentration not reported, in water	Gavage fixed dose study in Wistar rats;1female at 300 mg/kg bw and 5 females at 2000 mg/kg bw; performed in accordance with OECD TG 420	Hunched posture, piloerection, ataxia, noisy respiration, sneezing, and increased salivation in rats that received 2000 mg/kg bw; no abnormal findings at necropsy	> 2000 mg/kg bw	[28]
Lithium Stearate; 16.66% in carboxymethyl cellulose	Gavage study in 5 or 10 male and 5 or 10 female Sprague-Dawley rats; 2, 3, 4, or 5 g/kg bw	Hemorrhagic lungs and thymus and reduced hemorrhagic and expanded caecum observed a necropsy	> 5000 mg/kg bw	[28]
Palmitic Acid; concentration not reported, in DMSO	Gavage study in 5 male and 5 female Wistar rats; performed in accordance with OECD TG 401; 5000 mg/kg bw	Clinical signs appeared after 20 min and included slightly diminished activity and ruffled fur; swelling of the gastric mucosa observed at necropsy	> 5000 mg/kg bw	[29]
Stearic Acid; concentration not reported, in DMSO	Gavage study in 5 male and 5 female Wistar rats; performed in accordance with OECD TG 401; 5000 mg/kg bw	Clinical signs appeared after 20 min and included ruffled fur, strong salivation and very diminished activity; swelling of the gastric mucosa observed at necropsy	> 5000 mg/kg bw	[30]
Stearic Acid; 20%, vehicle not reported	Gavage study in 5 male and 5 female Wistar rats; performed in accordance with OECD TG 401; 2000 mg/kg bw	Prior to death, 1 female exhibited dyspnea, lethargy, and bloody nose encrustation on dosing day; one other male had bloody eye encrustation; the female that died had petichiae in the thymus	> 2000 mg/kg bw	[30]
Stearic Acid; 20% w/v aqueous solution	Gavage study in 5 male and 5 female Sprague-Dawley rats; performed in accordance with OECD TG 401; 6000 mg/kg bw	No clinical signs of toxicity or abnormalities at necropsy were observed	> 6000 mg/kg bw	[30]
Undecylenic Acid; concentration not reported, in corn oil	Gavage study in 5 male and 5 female Sprague-Dawley rats; performed in accordance with OECD TG 401; 2000 mg/kg bw	Hypoactivity and piloerection was observed in 1 male and 1 female on day 1; no other clinical signs of toxicity or abnormal findings at necropsy were observed	>2000 mg/kg bw	[32]
Undecylenic Acid; concentration not reported, in sesame oil	Gavage study in 3-12 male and 3-12 female Carworth CF1 mice per dose group;0.034-0.29 g	Hyperirritability, spasmodical jumping, shock-like collapse prior to death	8150 mg/kg bw	[32,55]

Abbreviations: DMSO – dimethyl sulfoxide; OECD – Organization for Economic Co-operation and Development; TG – test guideline

Table 11. Repeated dose toxicity studies

Concentration/Dose/Vehicle	Species	Study Protocol/Duration	Results	Reference
		Dermal		
Lithium Stearate; 0, 100, 300, or 1000 mg/kg/ day in water	10 male and 10 female Sprague-Dawley rats per dose group; recovery group had 5 rats per sex per dose	Dermal study in accordance with OECD TG 422;2.5 ml/kg applied daily for 6 h; semi-occluded; males treated for 43 days, started 14 days prior to mating, and females treated for 14 days prior to mating to gestation day 19 test sites washed with distilled water after exposure	NOAEL $\geq$ 1000 mg/kg bw/day in paternal animals for systemic effects ; NOAEL = 100 mg/kg bw/day for local effects; treatment-related increased incidence and/or severity of erosion/ulceration, epidermal hyperplasia and exudate, and acute to subacute/chronic inflammation and edema were observed in the mid- and high-dose groups; no treatment-related systemic adverse effects were observed	[28]
		Oral		
Behenic Acid;0, 100, 300, or 1000 mg/kg bw/day in corn oil	13 male and 13 female Sprague-Dawley rats per dose group	Gavage study in accordance with OECD TG 422; males were treated 42 days and females were treated for 14 days prior to mating to day 3 of lactation	NOAEL $\geq$ 1000 mg/kg bw/day; no treatment-related adverse effects observed	[22]
Calcium Stearate; 0, 500, 1000, or 2000 mg/kg bw/day in corn oil	10 male and 10 female Sprague-Dawley rats in the control and high dose groups and 5 of each sex in the low- and mid-dose groups	28 day gavage study	NOAEL $\geq$ 2000 mg/kg bw/day; no unscheduled deaths; no significant toxicological changes any test parameter	[35]
Capric Acid;0, 50, 150, or 1000 mg/kg bw/day in propylene glycol	5 male and 5 female Wistar rats per dose group	28 day gavage study in accordance with OECD TG 407	NOAEL $\geq$ 1000 mg/kg bw/day; slight to moderate breathing difficulties in several high dose animals only during week 3 of treatment were not considered treatment-related; irregularities in the forestomach were not considered toxicologically relevant	[23]
Capric Acid;0, 50, 250, or 1000 mg/kg bw/day in olive oil	10 male and 10 female Wistar rats per dose group	28 day gavage study in accordance with OECD TG 407	NOAEL $\geq$ 1000 mg/kg bw/day; no treatment-related effects were observed, including in the reproductive organs, some histopathologic edemas and ulcerations were attributed to the vehicle	[23]
Capric Acid; 0, 100, 300, or 1000 mg/kg bw/day in corn oil	13 male and 13 female Sprague-Dawley rats per dose group	Gavage study in accordance with OECD TG 422; males were treated 42 days and females were treated for 14 days prior to mating to day 3 of lactation	NOAEL $\geq$ 1000 mg/kg bw/day; no treatment-related adverse effects observed	[23]
Linoleic Acid (conjugated); 0% or 1% in semi-purified feed	10 and 11 weanling male Fischer 344 rats in the control and treatment groups, respectively	Dietary study for 18 months; rats were observed closely for clinical signs of toxicity; body weight and feed intake were measured weekly and twice a week, respectively; 3 rats from each group were randomly selected to measure body fat after 12 weeks; clinical chemistry and hematological analyses at 72 weeks; necropsy and histopathology performed at study end	Study authors concluded that test material did not cause adverse effects in rats; 4 control and 3 treatment animals died before study completion, these animals were found to have severe chronic renal disease and were observed to have either pituitary or testicular tumors; feed intake was lower in the treatment group than in the control group, but body weight and percent body fat, while lower, were not significantly different than the control group; clinical chemistry and hematology were within normal ranges for the treatment group except for increased blood urea nitrogen and cholesterol, which may be attributed to renal failure and age, respectively; no significant differences were observed in tissue weights at necropsy	[56]

Table 11. Repeated dose toxicity studies

Concentration/Dose/Vehicle	Species	Study Protocol/Duration	Results	Reference
Sodium Undecylenate; 50, 250, or 1000 mg/kg in water	6 male and 6 female Sprague-Dawley rats per dose group;	Gavage study in accordance with OECD TG 407; animals were treated for 14 days	NOAEL < 50 mg/kg bw/day; treatment-related mortality observed in high dose group; dose-dependent clinical signs of toxicity included ptyalism, loud breathing, swollen abdomen, sedation, soiled urogenital area, piloerection, round back and pallor of extremities; body weight gain and feed consumption reduced in dose-dependent manner; elevated urea levels observed in the high dose group along with slightly increased creatinine levels in females; thickened forestomaches due to epithelial cell hyperplasia/hyperkeratosis in high dose group	[32]
Sodium Undecylenate; 0, 20, 60, or180/360 mg/kg in water; high dose increased from 180 to 360 after day 50	10 male and 10 female Sprague-Dawley rats per dose group; included additional group of 10 for high dose recovery	Gavage study in accordance with OECD TG 408; animals were treated for 90 days	NOAEL = 60 mg/kg bw/day; LOAEL = 180 mg/kg bw/day; clinical signs of toxicity included ptyalism, loud breathing/respiratory difficulties and poor clinical condition; body weight gain and feed consumption were reduced in high dose group males, especially after dose increase at day 50; reduced glucose plasma levels (reversible) and reduced triglyceride levels (not reversible) observed in high dose females; high dose group also had reversible cardiomyopathy, forestomach edema/inflammatory cell infiltration; no treatment-related effects observed in low- and mid-dose groups	[32]
Undecylenic Acid; 0.5%, 1%, or 2.5%in feed	7 male Sprague-Dawley rats per dose group	8 week dietary study; bio-physical parameters studied not reported	Authors reported inhibition of growth, especially at 2.5%; no other bio-physical parameters reported	[55]

Abbreviations: LOAEL – lowest observed adverse effect level; NOAEL – no observed adverse effect level; OECD – Organization for Economic Co-operation and Development; TG – test guideline

Table 12. DART studies

Concentration/Dose/Vehicle	Species	Study Protocol/Duration	Results	Reference
		Dermal		
Lithium Stearate; 0, 100, 300, or 1000 mg/kg/ day in water	10 male and 10 female Sprague-Dawley rats per dose group; recovery group had 5 rats per sex per dose	Dermal study in accordance with OECD TG 422 (same as repeated dose study described in Table 10); males treated for 43 days, started 14 days prior to mating, and females treated for 14 days prior to mating to gestation day 19	NOAEL $\geq$ 1000 mg/kg bw/day; no treatment-related adverse reproductive effects in parental animals and no treatment-related adverse effects in development of offspring	[28]
		Oral		
Behenic Acid;0, 100, 300, or 1000 mg/kg bw/day in corn oil	13 male and 13 female Sprague-Dawley rats per dose group	Gavage study in accordance with OECD TG 422 (same as repeated dose study described in Table 10); males were treated 42 days and females were treated for 14 days prior to mating to day 3 of lactation	NOAEL $\geq$ 1000 mg/kg bw/day; no treatment-related adverse effects observed in parental animals or offspring	[22]
Calcium Stearate; 0, 250, 500, or 1000 mg/kg bw/day in corn oil	10 male and 10 female Sprague-Dawley rats per dose group	Gavage study; males were treated 28 days and females were treated for 14 days prior to mating to day 3 of lactation	NOAEL = 1000 mg/kg bw/day for parental animals and for offspring; no treatment-related adverse effects observed	[35]
Capric Acid; 0, 200, 1000, or 2000 mg/kg bw/day in corn oil	10 female Crl:CD (SD)BR rats per dose group	Gavage study in accordance with OECD TG 421 (male rats were not treated or assessed); females were treated for 7 days prior to mating to day 4 of lactation	Maternal NOAEL = 200 mg/kg bw/day and fetal NOAEL $\geq$ 2000 mg/kg bw/day; no treatment-related adverse effects observed in offspring; rales and excessive salivation observed in low-dose dams, ataxia, decreased motor activity, ungroomed and urine-stained coat, and mortalities observed in mid- and high-dose dams; decreased body weights and feed consumption observed in mid- and high-dose dams	[23]
Capric Acid; 0, 1000, or 1500 mg/kg bw/day in corn oil	22 female Crl:COBS, CD (SD) BR rats	Gavage study in accordance with OECD TG 414; dams received test material on gestation days 6 to15	Maternal and fetal NOAEL $\geq$ 1500 mg/kg bw/day; no treatment-related adverse effects observed in parental animals or offspring	[23]
Caprylic Acid; 0 or 1000 mg/kg bw/day in corn oil	22 female Crl:COBS, CD (SD) BR rats	Gavage study in accordance with OECD TG 414; dams received test material on gestation days 6 to 15	Maternal and fetal NOAEL $\geq$ 1000 mg/kg bw/day; no treatment-related adverse effects observed in parental animals or offspring	[25]
Caprylic Acid; 18.75 mmol/kg; undiluted	12 female Sprague-Dawley rats	Gavage teratology study; dams received test material on gestation days 12 to 20	Slight reduction of fetal weight likely due to severe maternal toxicity; no other significant embryotoxicity effects reported; low concentration of test material in maternal plasma	[57]
Undecylenic Acid;0, 50, 150, or 450 mg/kg bw/ day in corn oil	male and female Sprague-Dawley rats	Gavage study in accordance with OECD TG 421; males were treated 2 weeks prior to mating and during mating for a total of 4 weeks; females were treated 2 weeks prior to mating and during mating, pregnancy, and lactation until day 4 post-partum	NOAEL = 150 mg/kg bw/day for parental toxicity; NOEL = 450 mg/kg bw/day for reproductive performance; 2 males died on days 3 and 35 without clinical signs of toxicity and no evident cause of death at necropsy; hypersalivation was observed in both sexes in all dose groups along with respiratory difficulties in males in the high dose group; no treatment-related effects were observed to reproductive performance or in offspring	[32]

Table 12. DART studies

Concentration/Dose/Vehicle	Species	Study Protocol/Duration	Results	Reference
Undecylenic Acid; 0, 150, 450, or 750 mg/kg bw/day in corn oil	24 female Sprague-Dawley rats per dose group	Gavage study in accordance with OECD TG 414; received test material from day 6 to day of gestation	Maternal NOAEL = 150 mg/kg bw/day and maternal LOAEL = 450 mg/kg bw/day; fetal NOAEL = 450 mg/kg bw/day; high dose group treatment was terminated due to high mortality; dams in mid-dose group were observed with hypersalivation and significantly reduced body weight gain compared to control; no treatment-related adverse effects observed in offspring	[32]
Undecylenic Acid; 0, 150, 450, or 1000 mg/kg bw/day in corn oil	7 female Sprague-Dawley rats per dose group	Gavage study in accordance with OECD TG 414; dams received test material from day 6 to day 20 of gestation	Maternal NOEL = 450 mg/kg bw/day; maternal LOAEL = 1000 mg/kg bw/day; hypersalivation was observed from gestation day 12 in all dose groups in a dose-dependent manner; 3 dams in the high dose group died on gestation day 7 without clinical signs of toxicity or adverse effects at necropsy; no treatment-related adverse effects observed in offspring	[32]

Abbreviations: LOAEL – lowest observed adverse effect level; NOAEL – no observed adverse effect level; NOEL – no observed effect level; OECD – Organization for Economic Co-operation and Development; TG – test guideline

Table 13. Genotoxicity

Concentration/Dose	Species/Strain/Cell	Method	Results	Reference
	In Vitro			
Ammonium Oleate; 0.1 to 333 µg/plate with and without metabolic activation	*Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1537	Ames test	Not genotoxic	[20]
Behenic Acid; 156 to 5000 µg/plate with and without metabolic activation in DMSO	*S. typhimurium* strains TA98, TA100, TA1535, and TA1537 and *Escherichia coli* strain WP2 uvr A	Ames test	Not genotoxic	[22]
Behenic Acid; up to 3500 µg/ml with and without metabolic activation in 1% carboxymethylcellulose sodium	Chinese hamster lung cells	Mammalian chromosome aberration test	Not genotoxic	[22]
Calcium Stearate; up to 312.5 µg/plate with and without metabolic activation in tetrahydrofuran	*S. typhimurium* strains TA98, TA100, TA1535, and TA1537 and *E. coli* strain WP2 uvr A	Ames test	Not genotoxic	[35]
Calcium Stearate; up to 2.0 µg/ml with and without metabolic activation in tetrahydrofuran	Chinese hamster lung cells	Mammalian chromosome aberration test	Not genotoxic	[35]
Capric Acid; 500 to 5000 µg/plate with and without metabolic activation in DMSO	*S. typhimurium strains* TA98 and TA100, *E. coli* strain WP2 uvr A pKM 101, and *E. coli strain* – not specified	Ames test	Not genotoxic	[23]
Capric Acid; 1000 to 10,000 µg/plate with and without metabolic activation in DMSO	*S. typhimurium strains* TA98 and TA100 and *E. coli* strain WP2 uvr A pKM 101	Ames test	Not genotoxic	[23]
Capric Acid; concentration and vehicle not reported; with and without metabolic activation	*S. typhimurium* strains TA97, TA98, TA100, TA1535, and TA1537	Ames test	Not genotoxic	[58]
Capric Acid; up to 1.84 mM with metabolic activation for 4 h; up to 1.18 mM without metabolic activation for 4h; up to 0.30 mM without metabolic activation for 24 h; all in RPMI cell culture medium	Mouse lymphoma L5178Y cells	Mammalian cell gene mutation assay at the TK locus	Not genotoxic	[23]
Capric Acid; up to 3500 µg/ml with and without metabolic activation in 1.0% carboxymethylcellulose sodium	Chinese hamster lung cells	Mammalian chromosome aberration test	Not genotoxic	[23]
Capric Acid; 5 to20 µg/ml with metabolic activation and 39 to 156 µg/ml without metabolic activation; vehicle = DMSO	Chinese hamster ovary cells	Mammalian chromosome aberration test	Not genotoxic	[23]
Caproic Acid; 3.1 to 5000 µg/plate with and without metabolic activation in Tween 80/double distilled water	*S. typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538	Ames test	Not genotoxic	[24]
Caproic Acid; 1000 to 10,000 µg/plate with and without metabolic activation in DMSO	*S. typhimurium* strains TA98 and TA100 and *E.coli* strain WP2 uvr A pKM 101	Ames test	Not genotoxic	[24]
Caproic Acid; 10 to 1000 µg/plate with and without metabolic activation in DMSO	*S. typhimurium* strains TA97 and TA102	Ames test	Not genotoxic	[24]
Caprylic Acid; 10 to 3333 µg/plate with and without metabolic activation in DMSO	*S. typhimurium* strains TA97, TA98, TA100, TA1535, and TA1537	Ames test	Not genotoxic	[25]
Caprylic Acid; 4 to 2500 µg/plate with and without metabolic activation in Tween 80/double distilled water	*S. typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538	Ames test	Not genotoxic	[25]
Caprylic Acid; concentration and vehicle not reported; with and without metabolic activation	*S. typhimurium* strains TA97, TA98, TA100, TA1535, and TA1537	Ames test	Not genotoxic	[58]
Isomerized Linoleic Acid; up to 2500 µg/plate with and without metabolic activation in water/Tween 80	*S. typhimurium strains* TA98, TA100, TA1535, TA1537, and TA1538	Ames test	Not genotoxic	[26]
Lauric Acid; 4 to 2500 µg/plate with and without metabolic activation in DMSO	*S. typhimurium strains* TA98, TA100, TA1535, TA1537, and TA1538	Ames test	Not genotoxic	[27]
Lauric Acid; concentration and vehicle not reported; with and without metabolic activation	*S. typhimurium* strains TA97, TA98, TA100, TA1535, and TA1537	Ames test	Not genotoxic	[58]
Linoleic Acid; concentrations and vehicle not reported, with and without metabolic activation	*S. typhimurium strains* TA98, TA100, TA1535, TA1537; may have included TA97	Ames test	Not genotoxic	[59]
Lithium Stearate; 5 to 5000 µg/plate with and without metabolic activation in acetone	*S. typhimurium* strains TA98, TA100, TA1535, and TA1537 and *E. coli* strain WP2 uvr A	Ames test	Not genotoxic	[28]
Lithium Stearate; up to 80 µt/ml without metabolic activation and up to 120 µg/ml with metabolic activation; in acetone	Mouse lymphoma L5178Y cells	Mammalian cell gene mutation assay at the TK locus	Not genotoxic	[28]

Table 13. Genotoxicity

Concentration/Dose	Species/Strain/Cell	Method	Results	Reference
Lithium Stearate; up to 320 µg/ml without metabolic activation and up to 480 µg/ml with metabolic activation; in DMSO	Human lymphocytes	Mammalian chromosome aberration test	Not genotoxic	[28]
Myristic Acid; concentration and vehicle not reported; with and without metabolic activation	*S. typhimurium* strains TA97, TA98, TA100, TA1535, and TA1537	Ames test	Not genotoxic	[58]
Undecylenic Acid; up to 750 µg/ml with and without metabolic activation; in DMSO	*S. typhimurium strains* TA98, TA100, TA1535, TA1537, and TA1538	Ames test	Not genotoxic	[32]
Undecylenic Acid; up to 600 µg/ml with and without metabolic activation; in DMSO	Chinese hamster lung fibroblasts (V79)	Mammalian gene mutation assay	Not genotoxic	[32]
Undecylenic Acid; up to 500 µg/ml without metabolic activation; in DMSO	Primary rat hepatocytes	DNA damage and repair assay (unscheduled DNA synthesis)	Not genotoxic	[32]
Undecylenic Acid; up to 500 µg/ml with and without metabolic activation; in DMSO	Human lymphocytes	Mammalian chromosome aberration test	Not genotoxic	[32]
In Vivo				
Undecylenic Acid; 0, 1000, 2000, or 4000 mg/kg in 10% gum arabic	15 male and 15 female CD-1 mice per dose group	Micronucleus assay; test material administered via gavage in a single treatment	Not genotoxic	[32]

Abbreviations: DMSO – dimethyl sulfoxide; TK – thymidine kinase

Table 14. Dermal irritation and sensitization

Concentration/Dose/Vehicle	Test System/Population	Method	Results	Reference
		Irritation – In Vitro		
Aluminum Tristearate; undiluted	Human epidermis	Mat Tek EpiDerm™ model	Predicted to be not irritating	[21]
Capric Acid; at least 99% pure	Full-thickness Wistar rat dorsal and flank tissue	In vitro corrosivity test	Predicted to be not corrosive	[62]
Capric Acid; at least 99% pure	Full-thickness human mammary tissue; subcutaneous tissue removed	In vitro corrosivity test	Predicted to be not corrosive	[62]
Capric Acid; concentration and vehicle not reported	RHE	SkinEthic™ RHE 42 bis skin irritation model (validation study)	Predicted to be irritating	[65]
Caproic Acid; at least 99% pure	Full-thickness Wistar rat dorsal and flank tissue	In vitro corrosivity test	Predicted to be corrosive	[62]
Caproic Acid; at least 99% pure	Full-thickness human mammary tissue; subcutaneous tissue removed	In vitro corrosivity test	Predicted to be corrosive	[62]
Caproic Acid; 50% to 70% in sesame oil, 50 µl applied	Human epidermis	Mat Tek EpiDerm™ model	Predicted to be corrosive at 70%, non-corrosive at 50% and 60%	[24]
Caproic Acid; 100%	Human epidermis	Episkin™ test	Predicted to be corrosive	[24]
Caproic Acid; 100%	Wistar rat skin disks	TER test	Predicted to be corrosive	[24]
Caproic Acid; 100%	Reconstituted collagen matrix	CORROSITEX™ assay	Predicted to be corrosive in 1 out of 3 laboratories	[24]
Caproic Acid; 100%	Intact human skin equivalent	Skin 2TM ZK1350 assay	Predicted to be corrosive in 2 out of 3 laboratories	[24]
Caprylic Acid; concentration not reported, no vehicle used	Wistar rat disks	TER test	Predicted to be corrosive	[25]
Caprylic Acid; at least 99% pure	Full-thickness Wistar rat dorsal and flank tissue	In vitro corrosivity test	Predicted to be corrosive	[62]
Caprylic Acid; at least 99% pure	Full-thickness human mammary tissue; subcutaneous tissue removed	In vitro corrosivity test	Predicted to be not corrosive	[62]
Caprylic Acid; 99% pure	RHE	SkinEthic™ RHE skin corrosion test	Predicted to be corrosive	[63]
Caprylic Acid; concentration not reported	Human skin keratinocytes	Modified EpiSkin™ full thickness skin model	Predicted to be corrosive	[64]
Caprylic Acid; concentration not reported	Human skin fibroblasts	Modified SkinEthic™ RHE skin model	Predicted to be corrosive	[64]
Isostearic Acid; 99% pure	RHE	SkinEthic™ RHE skin corrosion test	Predicted to be not corrosive	[63]
Lauric Acid; at least 99% pure	Full-thickness Wistar rat dorsal and flank tissue	In vitro corrosivity test	Predicted to be not corrosive	[62]
Lauric Acid; at least 99% pure	Full-thickness human mammary tissue; subcutaneous tissue removed	In vitro corrosivity test	Predicted to be not corrosive	[62]
Lauric Acid; concentration and vehicle not reported	RHE	SkinEthic™ RHE 42 bis skin irritation model (validation study)	Predicted to be not irritating	[65]
Lithium Stearate; concentration not reported, no vehicle used	Human epidermis	Episkin test	Predicted to be not corrosive	[28]
Lithium Stearate; concentration not reported, no vehicle used	Human epidermis	Episkin test	Predicted to be not irritating	[28]
Undecylenic Acid; concentration and vehicle not reported	RHE	SkinEthic™ RHE 42 bis skin irritation model (validation study)	Predicted to be irritating	[65]
		Irritation – Animal		
Ammonium Oleate; concentration not reported, no vehicle, ~ 0.5 ml applied to test site	6 rabbits, strain and sex not reported	Acute dermal irritation study in accordance with OECD TG 404; test sites occluded, with and without abrasion; 4 h exposure on 1.5 in^2 site followed by washing with solvent	PII = 0.04; mean erythema score = 0.04 with effects fully reversed at 48 h; mean edema score = 0	[20]
Caproic Acid; concentration not reported, no vehicle, ~ 0.5 ml applied to test site	5 New Zealand White rabbits; sex not reported	Acute dermal irritation study in accordance with OECD TG 404; test sites shaved and occluded; 4 h exposure on 3 cm^2 site followed by washing	Corrosive; intensive erythema and edema observed after patch removal, edema disappeared after 7 days while erythema persisted and became full thickness necrosis; scar tissue observed after 21 days	[24]

Table 14. Dermal irritation and sensitization

Concentration/Dose/Vehicle	Test System/Population	Method	Results	Reference
Caprylic Acid; 100%	3 New Zealand White rabbits; sex not reported	Acute dermal irritation study in accordance with OECD TG 404; test sites clipped and semi-occluded; 4 h exposure followed by wiping off material with tissue	Corrosive; mean erythema score was 3 and mean edema score was 1.8	[25]
Caprylic Acid; 30%, 50%, 60%, and 70% in PEG 200/water and 100%	6 New Zealand White rabbits; sex not reported	Acute dermal irritation study; test sites clipped and occluded; 3 h exposure on 0.65 in^2	Corrosive at 100%with mean erythema and edema scores of $\geq$ 3.3 and 3.2, respectively; non-irritating at 30% through 70%	[25]
Caprylic Acid; 4%, 7.5%, 10%, and 15% in PEG 200/water and 100%	6 New Zealand White rabbits; sex not reported	Acute dermal irritation study; test sites clipped and occluded; 3 h exposure	Corrosive at 100%with mean erythema and edema scores of 3.3 and 2.5, respectively; non-irritating at 4% through 15%	[25]
Caprylic Acid; 55%, 60%, 65% and 80% in PEG/water	5 New Zealand White rabbits; sex not reported	Acute dermal irritation study; test sites clipped and occluded; 3 h exposure	Non-irritating at 55% and 60%; moderate to severe erythema and slight to moderate edema observed in 2aniamls at 65% and 80%	[25]
Caprylic Acid; 100%	3 rabbits; details not provided	Acute dermal irritation study in accordance with OECD TG 404; 4 h exposure	Necrosis and eschar observed at day 2 and 3; PII = 4.44	[61]
Caprylic Acid/Capric Acid mix (55:45); 100%	3 rabbits; details not provided	Acute dermal irritation study in accordance with OECD TG 404; 4 h exposure	Necrosis and eschar observed at day 2 and 3; PII = 5.11	[61]
Caprylic Acid/ Capric Acid mix (60:40); 100%	3 rabbits; details not provided	Acute dermal irritation study in accordance with OECD TG 404; 4 h exposure	Eschar at day 1 in 2 animals; new skin formation with or without scaliness at day 14 in all animals; PII could not be calculated	[61]
Caprylic Acid/ Capric Acid mix (65:35); 100%	3 rabbits; details not provided	Acute dermal irritation study in accordance with OECD TG 404; 4 h exposure	Eschar at day 1 in 2 animals; new skin formation or scaliness day 14 in all animals; PII could not be calculated	[61]
Caprylic Acid/ Capric Acid mix (65:35); 100%	3 rabbits; details not provided	Acute dermal irritation study in accordance with OECD TG 404; 4 h exposure	Reactions observed outside of test site in all animals starting 4.5 h; PII = 5.33	[61]
Isostearic Acid; 100%	3 rabbits; details not provided	Acute dermal irritation study in accordance with OECD TG 404; 4 h exposure	Reactions outside of test site in all animals starting on day 1; PII = 4.33	[61]
Lauric Acid; concentration not reported; in water	3 New Zealand White rabbits; sex not reported	Acute dermal irritation study in accordance with OECD TG 404; test sites shaved and semi-occluded; 4 h exposure on 10 cm^2 test site followed by wiping off material with tissue	Non-irritating; mean erythema and edema scores were 0.4 and 0, respectively	[27]
Lauric Acid; concentration not reported; no vehicle used	4 Kleinrussen rabbits; sex not reported	Acute dermal irritation study in accordance with OECD TG 404; test sites shaved and occluded; 4 h exposure on 2.5 cm^2 test site	Irritating; mean erythema and edema scores were 3.1 and 2, respectively	[27]
Lauric Acid; 100%	3 rabbits; details not provided	Acute dermal irritation study in accordance with OECD TG 404; 4 h exposure	PII = 0.44	[61]
Oleic Acid; 10% in a formulation with a pharmaceutical	2 groups of 3 rabbits; sex and strain not reported	Primary and cumulative skin irritation; 100 mg test material applied to shaved dorsa that were divided into four quadrants of about 4 cm^2 each and occluded; two quadrants were scarified; one group received test material for only 4 h and the other received test material for 24 h for 5 consecutive days	No primary or cumulative dermal irritation observed	[52]
Palmitic Acid; concentration not reported; no vehicle used	4 Kleinrussen rabbits; sex not reported	Acute dermal irritation study in accordance with OECD TG 404; test sites shaved and occluded; 4 h exposure on 2.5 cm^2 test site	Non-irritating; mean erythema and edema scores were 0 and 0, respectively	[29]
Sodium Undecylenate; 33% aq	3 rabbits; details not provided	Acute dermal irritation study in accordance with OECD TG 404; 4 h exposure	PII = 1.67	[61]
Trilinoleic Acid; concentration not reports; no vehicle used	6 New Zealand White rabbits; sex not reported	Acute dermal irritation study; test sites intact and abraded; occlusive patch for 24 h	Slightly irritating	[31]
Undecylenic Acid; 100%	4 rabbits; details not provided	Acute dermal irritation study in accordance with OECD TG404; 4 h exposure	PII = 2.42	[61]

Table 14. Dermal irritation and sensitization

Concentration/Dose/Vehicle	Test System/Population	Method	Results	Reference
		Irritation – Human		
Lauric Acid; 50%; vehicle not reported	20 volunteers	Closed epicutaneous test; 10 µl applied to the back for 24 h in large Finn chambers	Substance induced erythema, edema, and scaling	[27]
Lauric Acid; 80%; vehicle not reported	10 volunteers	Open epicutaneous test on lower forearm; procedure repeated every 30 sec for 30 min; substance was not washed	3 subjects had erythema (score 1) after 30 min that disappeared after 30 min; no other reactions were observed	[27]
Palmitic Acid; 50%; vehicle not reported	20 volunteers	Closed epicutaneous test; 10 µl applied to the back for 24 h in large Finn chambers	Not irritating; skin scores for erythema, edema, scaling, and fissures were all 0	[29]
		Sensitization – In Vitro		
Linoleic Acid (99% pure);100 mM in acetonitrile (9:1)	Heptapeptides containing cysteine or lysine	DPRA in accordance with OECD TG 442C	Positive	[66]
Linolenic Acid (99% pure); 100 mM in isopropyl alcohol (9:1)	Heptapeptides containing cysteine or lysine	DPRA in accordance with OECD TG 442C	Positive	[66]
Oleic Acid (97% pure); 100 mM in acetonitrile (9:1)	Heptapeptides containing cysteine or lysine	DPRA in accordance with OECD TG 442C	Negative	[66]
Undecylenic Acid (98% pure); 100 mM in acetonitrile (9:1)	Heptapeptides containing cysteine or lysine	DPRA in accordance with OECD TG 442C	Negative	[66]
		Sensitization - Animal		
Ammonium Oleate; 5% in physiological saline for intradermal induction; 25% or 50% in Vaseline® for topical induction; 25% in Vaseline® for topical challenge	10 female Hsd Poc:DH guinea pigs per dose group; 5 females in control	Guinea pig maximization study	All animals, including controls, exhibited grade 1 skin reactions during challenge, only animals with greater than 1 reaction counted as + reaction; 0, 1, and 4 animals had reactions at 24, 48, and 72 h post-challenge, respectively; 2, 3, and 3 animals had reaction at 24, 48, and 72 h post-rechallenge, respectively.	[20]
Ammonium Oleate; 10%, 25%, or 50% in acetone/olive oil (4:1 v/v)	5 female CBA/Ca mice/dose group	LLNA	SI were 2.6, 14.9, and 6.9 for 10%, 25%, and 50%, respectively; according to test standards, the test material was sensitizing at 25% and 50%	[20]
Capric Acid; induction with 40% in distilled water, challenge and re-challenge with 20% in distilled water	10 male and 10 female Dunkin-Hartley albino guinea pigs/dose	Buehler test; occlusive	Not sensitizing; observed effects of confluent or moderate erythema in 6 animals at re-challenge was determined to be due to irritation	[23]
Capric Acid; induction with 5% in ethanol, challenge with 5% in acetone	20 guinea pigs, strain and sex not specified	Buehler test; occlusive	Not sensitizing	[23]
Hydroxystearic Acid; 0%, 10%, or 50% (containing 86% 12-hydroxystearic acid) in dimethyl sulfoxide	5 female CBA mice per group	LLNA	Sensitizing; EC3 value calculated to be 16%	[33]
Hydroxystearic Acid; intradermal induction with 2.5% in corn oil or 50% Freund's complete adjuvant/0.9% saline, topical induction with 10% in corn oil, challenge with 2.5% in corn oil	10 male and 10 female Dunkin-Hartley guinea pigs	Maximization test; occlusive	At 24-h post challenge, discrete or moderate erythema observed in 7/20 animals; at 48- and 72-h readings, increase in incidence and severity of cutaneous reactions at test sites correlated with the flanks being shaved after the 24-h reading; not possible to deter-mine incidence of sensitization due to cutaneous reactions; test concentration used at challenge may have been too high and caused irritation	[33]

Table 14. Dermal irritation and sensitization

Concentration/Dose/Vehicle	Test System/Population	Method	Results	Reference
Hydroxystearic Acid; intradermal induction with 2.5% in corn oil or 50% Freund's complete adjuvant/0.9% saline, topical induction with 10% in corn oil, 1st challenge with 0.5% in corn oil and 2nd challenge with 1% and 5% in acetone	10 male and 10 female Dunkin-Hartley guinea pigs	Maximization test; occlusive	Not sensitizing; at 24-h post challenge, discrete erythema present at the vehicle patch site in 6/10 control animals, the test article patch sites of 4/10 control animals, the vehicle patch site of 7/20 test animals, and the test article patch site of 6/10 test animals; at 48-h reading, the incidences at the same sites were 6/10, 9/10, 4/20, and 6/20 animals, respectively; no cutaneous reactions at the 24-h reading of 2nd challenge and discrete erythema in 2/10 animals at the 48-h reading ; no reactions at the test article patch sites of any of the animals in either group	[33]
Lauric Acid; induction and challenge with 2.5% in ethanol	20 Pirbright white guinea pigs; sex not reported	Maximization test; occlusive	Not sensitizing	[27]
Linoleic Acid (99% pure); 5.0%, 10.0%, 25.0%, and 50% in dose-finding study; 25% in primary study; in acetone:olive oil (4:1, v/v)	Groups of 5 female CBA/J mice	LLNA:DAE	Weak skin sensitizer	[66]
Linolenic Acid (99% pure); 5.0%, 10.0%, 25.0%, and 50% in dose-finding study; 25% in primary study; in acetone:olive oil (4:1, v/v)	Groups of 5 female CBA/J mice	LLNA:DAE	Weak skin sensitizer	[66]
Lithium Stearate; 2.5%, 5%, or 10% in ethanol/distilled water (7:3)	4 female CBA/Ca mice per group	LLNA	Not sensitizing; SI were 0.86, 1.48, and 1.68 for 2.5%, 5%, and 10%, respectively	[28]
Oleic Acid (97% pure); 5.0%, 10.0%, 25.0%, and 50% in dose-finding study; 10% in primary study; in acetone:olive oil (4:1, v/v)	Groups of 5 female CBA/J mice	LLNA:DAE	Weak skin sensitizer	[66]
Sodium Undecylenate; intradermal induction with 0.1%; topical induction and challenge with 0.05%; in physiological saline	10 male and 10 female Dunkin-Hartley guinea pigs	Maximization test; occlusive	Not sensitizing	[32]
Trilinoleic Acid; induction undiluted, challenge with 50% or 75% in corn oil	20 guinea pigs per group, strain and sex not specified	Buehler test; no further details provided	Not sensitizing	[31]
Undecylenic Acid (98% pure); 5.0%, 10.0%, 25.0%, and 50% in dose-finding study; 25% in primary study; in acetone:olive oil (4:1, v/v)	Groups of 5 female CBA/J mice	LLNA:DAE	Weak skin sensitizer	[66]
Undecylenic Acid; intradermal induction with 1%; topical induction with 100%; challenge with 2.5%; in corn oil	10 male and 10 female Dunkin-Hartley guinea pigs	Maximization test; occlusive	Not sensitizing	[32]

Abbreviations: DPRA -direct peptide reactivity assay; EC3 – estimated concentration of a substance expected to produce an SI of 3; LLNA – local lymph node assay; LLNA:DAE – modified local lymph node assay with an elicitation phase; OECD – Organization for Economic Co-operation and Development; PII – primary dermal irritation index; RHE – reconstructed human epidermis; SI – stimulation index; TER – transcutaneous electrical resistance; TG – test guideline;

Table 15. **Ocular irritation studies**

Concentration/Dose	Test System/Population	Method	Results	Reference
In Vitro				
Caproic Acid; 50% in sesame oil	Bovine corneas	Bovine Corneal Opacity and Permeability test	Corrosive	[24]
Lithium Stearate; concentration not reported, no vehicle used	Corneal epithelial tissue reconstruct	Reconstructed Human Corneal model	Predicted to be non-irritating	[28]
Animal				
Caproic Acid; concentration not reported, no vehicle used	6 rabbits; no further details provided	Ocular irritation study; details not provided	Ocular irritant; corneal opacity and moderate conjunctivitis reported that did not reverse within 72 h	[23]
Caprylic Acid; 70% in Vaseline	3 female New Zealand White rabbits	Ocular irritation study; 0.1 ml instilled; eyes were rinsed with physiological saline after 24 h	Ocular irritant; conjunctival redness, chemosis, and discharge observed in all animals; corneal lesions observed in 2/3 animals	[25]
Caprylic Acid; concentration not reported, no vehicle used	6 rabbits; no further details provided	Ocular irritation study; details not provided	Ocular irritant; corneal opacity and moderate conjunctivitis that persisted until 72 h	[25]
Lauric Acid; concentration not reported, no vehicle used	3 New Zealand White rabbits; sex not reported	Ocular irritation study in accordance with OECD TG 405; details not provided	Ocular irritant; lacrimation and corneal epithelial damage in all animals; no corrosion observed	[27]
Lauric Acid; concentration not reported, no vehicle used	3 New Zealand White rabbits; sex not reported	Ocular irritation study in accordance with OECD test guideline 405;0.1 g instilled; eyes were rinsed with physiological saline	Not irritating	[27]
Lauric Acid; concentration not reported, no vehicle used	1 Kleinrussen rabbit; sex not reported	Ocular irritation study in accordance with OECD TG 405; eyes were not rinsed; no further details provided	Ocular irritant; slight to moderate reactions observed on the cornea that did not disappear within 21 days; reversible reactions in the iris and conjunctivae were observed	[27]
Lauric Acid; 100%	3 rabbits; strain and sex not reported	Draize ocular irritation study; 0.1 ml instilled	Modified maximum average score = 38.0; opacity and conjunctival redness was not resolved by day 21	[68]
Lithium Stearate; concentration not reported, no vehicle used	2 New Zealand White rabbits; sex not reported	Ocular irritation study in accordance with OECD TG 405; 0.1 ml instilled; eyes were not rinsed;	Mild ocular irritant; moderate conjunctival irritation observed	[28]
Oleic Acid; 0%, 0.02%, 0.05%, and 0.1% (v/v) in phosphate buffer at pH 7.4 and 1% Tween—80	6 New Zealand White rabbits per dose group; sex not reported	Modified Draize ocular irritation study; 100 µl instilled in left eye every 4 h and 4 times/day for 7 days; right eye received phosphate buffer; observation up to 72-h after last instillations	Not irritating	[69]
Palmitic Acid; concentration not reported, no vehicle used	4 Kleinrussen rabbits; sex not reported	Ocular irritation study in accordance with OECD TG 405; 0.1 ml instilled; eyes were not rinsed	Not irritating	[29]
Sodium Undecylenate; 33.2% in water	1 rabbit; strain and sex not reported	Draize ocular irritation study; 0.1 ml instilled	Moderately irritating; modified maximum average score = 45; corneal opacity and conjunctival redness and chemosis not resolved until day 9	[68]
Stearic Acid (iso-); 100%	3 rabbits; strain and sex not reported	Draize ocular irritation study; 0.1 ml instilled	Minimally irritating; modified maximum average score = 3.3; conjunctival redness resolved by day 3	[68]
Undecylenic Acid; concentration not reported, no vehicle used	3 male New Zealand White rabbits	Ocular irritation study in accordance with OECD TG 405; 100 mg instilled; no further details provided	Irritating; very slight to moderate conjunctival reactions observed in all animals from day 1 that persisted to day 14; slight iritis observed in 2 animals on day 2 that lasted to day 4 or 10, respectively; very slight or slight corneal opacity observed in all animals on day 2 that lasted until day 4 in 2 animals and to day 12 in the other	[32]

OECD = Organization for Economic Co-operation and Development; TG – test guideline

REFERENCES

1. Nikitakis J and Kowcz A. wINCI: International Cosmetic Ingredient Dictionary and Handbook. http://webdictionary.personalcarecouncil.org/jsp/Home.jsp. Washington, DC. Last Updated 2018. Date Accessed 4-3-2018.

2. Personal Care Products Council. 12-14-2016. Concentration of Use by FDA Product Category: Fatty Acids and Soaps. Unpublished data submitted by Personal Care Products Council.

3. Andersen FA (ed.). Annual Review of Cosmetic Ingredient Safety Assessments - 2001/2002. *Int J Toxicol*. 2003;22(Suppl 1):1-35.

4. Elder RL (ed.). Final Report of the Safety Assessment of Lithium Stearate, Aluminum Distearate, Aluminum Stearate, Aluminum Tristearate, Ammonium Stearate, Calcium Stearate, Magnesium Stearate, Potassium Stearate, Sodium Stearate, and Zinc Stearate. *J Am Coll Toxicol*. 1982;1(2):142-177.

5. Andersen FA (ed.). Amended Final Report on the Safety Assessment of Hydroxystearic Acid. *Int J Toxicol*. 1999;18(Suppl 1):1-10.

6. Elder RL (ed.). Final Report on the Safety Assessment of Isostearic Acid. *J Am Coll Toxicol*. 1983;2(7):61-74.

7. Andersen FA (ed.). Annual Review of Cosmetic Ingredient Safety Assessments - 2002/2003. *Int J Toxicol*. 2005;24(Suppl 1):1-102.

8. Elder RL (ed.). Final Report on the Safety Assessment of Oleic Acid, Lauric Acid, Palmitic Acid, Myristic Acid, and Stearic Acid. *J Am Coll Toxicol*. 1987;6(3):321-401.

9. Andersen FA (ed.). Annual Review of Cosmetic Ingredient Safety Assessments - 2004/2005. *Int J Toxicol*. 2006;25(Suppl 2):1-89.

10. Becker LC, Bergfeld WF, Belsito DV, et al. Final Report of the Amended Safety Assessment of Myristic Acid and Its Salts and Esters as Used in Cosmetics. *Int J Toxicol*. 2010;29(Suppl 3):162S-186S.

11. Robinson V, Bergfeld WF, Belsito DV, et al. Amended Safety Assessment of Tall Oil Acid, Sodium Tallate, Potassium Tallate, and Ammonium Tallate. *Int J Toxicol*. 2009;28(Suppl 3):252S-258S.

12. Burnett CL, Fiume MM, Bergfeld WF, et al. Safety Assessment of Plant-Derived Fatty Acid Oils. *Int J Toxicol*. 2017;36(Suppl 3):51S-129S.

13. Elder RL (ed.). Final Report on the Safety Assessment of Candelilla Wax, Carnauba Wax, Japan Wax, and Beeswax. *J Am Coll Toxicol*. 1984;3(3):1-41.

14. Elder RL (ed.). Final Report of the Safety Assessment for Acetylated Lanolin Alcohol and Related Compounds. *J Environ Pathol Toxicol*. 1980;4(4):63-92.

15. Andersen FA (ed.). Final Report on the Safety Assessment of Lard Glyceride, Hydrogenated Lard Glyceride, Lard Glycerides, Hydrogenated Lard Glycerides, Lard, and Hydrogenated Lard. *Int J Toxicol*. 2001;20(Suppl 2):57-64.

16. Andersen FA (ed.). Final Report on the Safety Assessment of Ricinus Communis (Castor) Seed Oil, Hydrogenated Castor Oil, Glyceryl Ricinoleate, Glyceryl RIcinoleate SE, Ricinoleic Acid, Potassium Ricinoleate, Sodium Ricinoleate, Zinc Ricinoleate, Cetyl RIcinoleate, Ethyl Ricinoleate, Glycol Ricinoleate, Isopropyl Ricinoleate, Methyl Ricinoleate, and Octyldodecyl Ricinoleate. *Int J Toxicol*. 2007;26(Suppl 3):31-77.

17. Elder RL (ed.). Final Report on the Safety Assessment of Tallow, Tallow Glyceride, Tallow Glycerides, Hydrogenated Tallow Glyceride, and Hydrogenated Tallow Glycerides. *J Am Coll Toxicol*. 1990;9(2):153-164.

18. Andersen FA (ed.). Annual Review of Cosmetic Ingredient Safety Assessments: 2005/2006. *Int J Toxicol*. 2008;27(Suppl 1):77-142.

19. Andersen FA (ed.). Final Report on the Safety Assessment of Arachidonic Acid. *J Am Coll Toxicol*. 1993;12(5):481-559.

20. European Chemicals Agency. Ammonium Oleate. https://echa.europa.eu/. Last Updated 2018. Date Accessed 6-18-2018.

21. European Chemicals Agency. Aluminum Tristearate. https://echa.europa.eu/. Last Updated 2018. Date Accessed 6-18-2018.

22. European Chemicals Agency. Docosanoic Acid. https://echa.europa.eu. Last Updated 2017. Date Accessed 6-19-2018.

23. European Chemicals Agency. Decanoic Acid. https://echa.europa.eu. Last Updated 2018. Date Accessed 6-19-2018.

24. European Chemicals Agency. Hexanoic Acid. https://echa.europa.eu. Last Updated 2018. Date Accessed 6-20-2018.

25. European Chemicals Agency. Octanoic Acid. https://echa.europa.eu. Last Updated 2018. Date Accessed 6-22-2018.

26. European Chemicals Agency. Fatty Acids, C14-18 and C16-18-Unsatd. https://echa.europa.eu. Last Updated 2018. Date Accessed 6-25-2018.

27. European Chemicals Agency. Lauric Acid. https://echa.europa.eu. Last Updated 2018. Date Accessed 6-25-2018.

28. European Chemicals Agency. Lithium Stearate. https://echa.europa.eu. Last Updated 2018. Date Accessed 6-25-2018.

29. European Chemicals Agency. Palmitic Acid. https://echa.europa.edu. Last Updated 2018. Date Accessed 6-26-2018.

30. European Chemicals Agency. Stearic Acid. https://echa.europa.eu. Last Updated 2018. Date Accessed 6-27-2018.

31. European Chemicals Agency. Fatty Acids, C18-Unsatd., Trimers. https://echa.europa.eu. Last Updated 2018. Date Accessed 6-28-2018.

32. European Chemicals Agency. Undec-10-enoic Acid. https://echa.europa.eu. Last Updated 2018. Date Accessed 6-28-2018.

33. European Chemicals Agency. 12-Hydroxystearic Acid. https://echa.europa.eu. Last Updated 2018. Date Accessed 7-23-2018.

34. OECD SIDS. Docosanoic Acid CAS No: 112-85-6. Bern, Switzerland: UNEP Publications. 2001. http://www.inchem.org/documents/sids/sids/docosanoic.pdf. Date Accessed 7-25-2018.

35. OECD SIDS. Calcium Distearate. Paris, France: UNEP Publications. 2012. https://hpvchemicals.oecd.org/ui/SIDS_Details.aspx?id=7d49842a-206f-41a3-b76a-904c11ef4cf8. Date Accessed 7-10-2018.

36. OECD SIDS. SIDS Initial Assessment Profile: Aliphatic Acids Category. CoCAM 6 September 30-October 3, 2014 Italy/ICCA. 2014. https://hpvchemicals.oecd.org/ui/handler.axd?id=DB963BA2-B206-461D-86FF-755992A63432.

37. Brooks SC, Godefroi VC, and Simpson WL. Specific sites of fatty acid and sterol synthese in isolated skin components. *J Lipid Res*. 1966;7(1):95-102.

38. Vicanová J, Weerheim AM, Kempenaar JA, et al. Incorporation of linoleic acid by cultured human keratinocytes. *Arch Dermatol Res*. 1999;291:405-412.

39. Hargrove JL, Greenspan P, and Hartle DK. Nutritional significance and metabolism of very long chain fatty alcohols and acids from dietary waxes. *Exp Biol Med (Maywood)*. 2004;229(3):215-226.

40. Council of Experts, United States Phamacopeial Convention. Food Chemicals Codex. 8th *ed*. Rockville, MD: United States Pharmacopeia (USP), 2012.

41. U.S. Food and Drug Administration Center for Food Safety & Applied Nutrition (CFSAN). Voluntary Cosmetic Registration Program - Frequency of Use of Cosmetic Ingredients. College Park, MD: 2018. Obtained under the Freedom of Information Act from CFSAN; requested as "Frequency of Use Data" January 3 2018; received February 5 2018).

42. Bremmer HJ, Prud'homme de Lodder LCH, and Engelen JGM. Cosmetics Fact Sheet: To assess the risks for the consumer; Updated version for ConsExpo 4. Bilthoven, Netherlands: Netherlands National Institute for Public Health and the Environment. 2006. http://www.rivm.nl/bibliotheek/rapporten/320104001.pdf. Date Accessed 8-24-2011. Report No. RIVM 320104001/2006. pp. 1-77.

43. Rothe H, Fautz R, Gerber E, et al. Special aspects of cosmetic spray safety evaluations: Principles on inhalation risk assessment. *Toxicol Lett*. 2011;205(2):97-104.

44. Rothe H. Special Aspects of Cosmetic Spray Evalulation. 9-26-2011. Unpublished data presented at the 26 September CIR Expert Panel meeting. Washington, D.C.

45. Johnsen MA. The Influence of Particle Size. *Spray Technology and Marketing*. 2004;14(11):24-27.

46. CIR Science and Support Committee of the Personal Care Products Council (CIR SSC). 11-3-2015. Cosmetic Powder Exposure. Unpublished data submitted by the Personal Care Products Council.

47. Aylott RI, Byrne GA, Middleton J, et al. Normal use levels of respirable cosmetic talc: Preliminary study. *Int J Cosmet Sci*. 1976;1(3):177-186.

48. Russell RS, Merz RD, Sherman WT, et al. The determination of respirable particles in talcum powder. *Food Cosmet Toxicol*. 1979;17(2):117-122.

49. European Union. Regulation (EC) No. 1223/2009 of the European Parliament and of the Council of 30 November 2009 on Cosmetic Products. 2009. http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:342:0059:0209:en:PDFDate Accessed 11-9-2017

50. Australian Government Department of Health. National Industrial Chemicals Notification and Assessment Scheme (NICNAS). https://www.nicnas.gov.au/chemical-information. Last Updated 2018. Date Accessed 7-9-2018.

51. U.S. Department of Health and Human Services and U.S. Department of Agriculture. 2015-2020 Dietary Guidelines for Americans. https://health.gov/dietaryguidelines/2015/resources/2015-2020_Dietary_Guidelines.pdf. Last Updated 2015. Date Accessed 10-22-2018.

52. Moreira TSA, de Sousa VP, and Pierre MBR. A novel transdermal delivery system for the anti-inflammatory lumiracoxib: Influence of oleic acid on *in vitro* percutaneous absorption and *in vivo* potential cutaneous irritation. *AAPS Pharm Sci Tech*. 2010;11(2):621-629.

53. Quiñones OG, Mata dose Santos HA, Kibwila DM, et al. In vitro and in vivo influence of penetration enhancers in the topical application of celecoxib. *Drug Dev Ind Pharm*. 2014;40(9):1180-1189.

54. Wang X, Maher S, and Brayden DJ. Restoration of rat colonic epithelium after in situ intestinal instillation of the absorption promoter, sodium caprate. *Ther Deliv*. 2010;1(1):75-82.

55. Newell GW, Petretti AK, and Reiner L. Studies of the acute and chronic toxicity of undecylenic acid. *J Invest Dermatol*. 1949;13(3):145-149.

56. Park Y, Albright KJ, and Pariza MW. Effects of conjugated linoleic acid on long term feeding in Fischer 344 rats. *Food Chem Toxicol*. 2005;43(8):1273-1279.

57. Scott WJ, Collins MD, and Nau H. Pharmacokinetic determinants of embryotoxicity in rats associated with organic acids. *Environ Health Perspect*. 1994;102(11):97-101.

58. Zeiger E, Anderson B, Haworth S, et al. *Salmonella* mutagenicity tests: IV. Results from the testing of 300 chemicals. *Environ Mol Mutagen*. 1988;11(Suppl 12):1-158.

59. Zeiger E, Anderson B, Haworth S, et al. *Salmonella* mutagenicity tests: III. Results from the testing of 255 chemicals. *Environ Mutagen*. 1987;9(Suppl 9):1-110.

60. Hiasa Y, Konishi N, Kitahori Y, et al. Carcinogenicity study of a commerical sodium oleate in Fischer rats. *Food Chem Toxicol*. 1985;23(6):619-623.

61. European Center for Ecotoxicology and Toxicology of Chemicals (ECETOC). Skin Irritation and Corrosion: Reference Chemicals Data Bank. Brussels, Belgium: ECETOC. 1995. http://www.ecetoc.org/wp-content/uploads/2014/08/ECETOC-TR-066.pdf. Report No. Technical Report No. 66.

62. Whittle E, Barratt D, Carter JA, et al. Skin corrosivity potential of fatty acids: In vitro rat and human skin testing and QSAR studies. *Toxicol In Vitro*. 1996;10(1):95-100.

63. Tornier C, Roquet M, and Brugerolle de Fraissinette A. Adaptation of the validated SkinEthic Reconstructed Human Epidermis (RHE) skin corrosion test method to 0.5 cm^2 tissue sample. *Toxicol In Vitro*. 2010;24(1379):1385

64. Catarino CM, do Nacimento Pedrosa T, Penncchi PC, et al. Skin corrosion test: A comparison between reconstructed human epidermis and full thickness skin models. *Eur J Pharm Biopharm*. 2018;125:51-57.

65. Tornier C, Amsellem C, de Brugerolle de Fraissinette A, et al. Assessment of the optimized SkinEthic™ Reconstructed Human Epidermis (RHE) 42 bis skin irritation protocol over 39 test substances. *Toxicol In Vitro*. 2010;24:245-256.

66. Yamashita K, Shinoda S, Hagiwara S, et al. Unsaturated fatty acids show clear elicitation responses in a modified local lymph node assay with an elicitation phase, and test positive in the direct peptide reactivity assay. *J Toxicol Sci*. 2015;40(6):843-853.

67. Onoue S, Suzuki G, Kato M, et al. Non-animal photosafety assessment approaches for cosmetics based on the photochemical and photobiochemical properties. *Toxicol In Vitro*. 2013;27(8):2316-2324.

68. European Center for Ecotoxicology and Toxicology of Chemicals (ECETOC). Eye Irritation: Reference Chemicals Data Bank (2nd Edition). Brussels: 1998. Report No. 48 (2).

69. Gao XC, Qi HP, Bai JH, et al. Effects of oleic acid on the corneal permeability of compounds and evaluation of its ocular irritation of rabbit eyes. *Curr Eye Res*. 2014;39(12):1161-1168.

70. Kimura M, Kawada A, Ogino M, et al. Simultaneous contact sensitivity to hydroxystearic acid and C18-36 acid triglyceride in lip glosses. *Contact Dermatitis*. 2002;47(2):115

71. Shaw DW. Allergic contact dermatitis from 12-hydroxystearic Acid and hydrogenated castor oil. *Dermatitis*. 2009;20(6):E16-E20.

72. Rogers SI and Shatin H. Dermatitis venenata due to potassium undecylenate. *AMA Arch Derm Syphilol*. 1952;66(2):289-289.

73. Crane S, Aurore G, Joseph H, et al. Composition of fatty acids triacylglycerols and unsaponifiable matter in Calophyllum calaba L. oil from Guadeloupe. *Phytochemistry*. 2005;66(15):1825-1831.

74. Lewis RJ (ed.). Hawley's Condensed Chemical Dictionary. 15 *ed*. New York, NY: John Wiley & Sons, Inc., 2007.

75. O'Neil MJ (ed.). The Merck Index. 15th *ed*. Cambridge, UK: Royal Society of Chemistry, 2013.

76. Advanced Chemistry Development (ACD) Software. 11.02. 2018.

77. SRC, Inc. FatePointers Search Module. http://esc.srcinc.com/fatepointer/results.asp. Last Updated 2013. Date Accessed 7-20-2018.

78. Kim S, Thiessen PA, Bolton EE, et al. PubChem Substance and Compound databases. *Nucleic Acids Res*. 2016;44(D1):D1202-D1213.

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4

Final Report on the Safety Assessment of Isostearic Acid

Isostearic Acid is a mixture of fatty esters consisting mainly of methyl branched isomers of octadecanoic acid and is used at concentrations up to 10% in a wide variety of cosmetic products. In rats, the acute oral LD50 is estimated to be greater than 32 ml/kg. The raw ingredient produced no significant skin or eye irritation in Draize rabbit irritation tests.

In clinical studies, 100 subjects showed no signs of irritation after a 24 h single insult skin patch with undiluted Isostearic Acid. Thirty-four percent Isostearic Acid was neither an irritant nor a sensitizer in 168 subjects, and gave no indication of phototoxicity in a subset of this population.

It is concluded that Isostearic Acid is safe as a cosmetic ingredient in the present practices of use. Consideration for the compound's potential for production of human comedogenicity is noted.

CHEMISTRY

Composition

Isostearic Acid is the Cosmetic, Toiletry and Fragrance Association (CTFA) adopted name for a complex blend of branched-chain saturated isomers of octadecanoic acid. The chemical literature sometimes uses the term Isostearic Acid to refer specifically to the isomer 16-methylheptadecanoic acid (CAS Number 2724-58-5). However, the ingredient which is used in cosmetics is a mixture of the 18 carbon isomers generally branching with the methyl group.[1,2] According to CTFA Specifications, Isostearic Acid consists of approximately 80% branched chain C_{16} and C_{18} acids and 20% straight-chain C_{14}, C_{16}, and C_{18} acids.[3] Approximate values for the distribution of the different types of fatty acids present in Isostearic Acid are listed in Table 1.

Isostearic Acid is prepared by dimerizing the fatty acids of Tall Oil, Soybean Oil, or Tallow in the presence of a catalyst. The reaction mixture is then separated into monomer and dimer fractions by distillation. The monomer fraction which is rearranged during the reaction is further refined by hydrogenation, solvent separation, and an additional distillation.[4,5]

Methods for the laboratory synthesis of 16-methylheptadecanoic acid have also been described.[6-10]

TABLE 1. Fatty Acid Components of Isostearic Acid.

Component	*Level (%)*
Methyl-branched isomers of octadecanoic acid	approx. 80
C14 linear saturated fatty acid (Myristic)	1–10
C18 linear saturated fatty acid (Stearic)	1–10
C16 linear saturated fatty acid (Palmitic)	4–8
C18 Oleic acid	0–2

Data from Ref. 4.

Physical Properties

Isostearic Acid is a clear, oily liquid with little odor. It is insoluble in water but easily soluble in such organic solvents as ethanol, acetone, ethyl ether, carbon tetrachloride, and others. Its alkaline salts are readily soluble in water.[2]

The different isomers are mutually soluble and show virtually identical properties. Since it is a mixture, the melting point of Isostearic Acid is much lower than one would expect for a saturated fatty acid of similar molecular weight.[2] Whereas the melting point of 16-methylheptadecanoic acid has been reported as 69.5°–69.7°C,[7] Isostearic Acid is a liquid at room temperature.

Table 2 presents CTFA specifications for Isostearic Acid[3] as well as measured values for the chemical and physical properties of Isostearic Acid obtained from three different commercial sources.[2]

Studies on the molecular and crystalline structures of 16-methylheptadecanoic acid have been conducted,[11,12] and infrared data are available.[13] The surface chemistry of Isostearic Acid as a cosmetic ingredient has also been studied.[14]

Reactivity

Isostearic Acid should participate in chemical reactions common to long chain, saturated fatty acids.

TABLE 2. Chemical and Physical Properties of Isostearic Acid.

Mol. wt.	*Solid pt.*	*Viscosity*	*Sp. gr.*	*Iodine value*	*Acid value*	*Sapon. value*
284	10 °C max.	50 cps 25 °C	0.89 25 °C	3.0 max.[a]	191.0–201.0[a]	197.0–204.0[a]
			0.906 25 °C	3.0	191.0–201.0	197.0–204.0
				8[b]	180–200	185–205
				8	177	189

[a]CTFA Specification.
[b]Resulting from chain branching, not from double bonds.
Data from Refs. 2,3.

Analytical Methods

Gas chromatography,[15,16] mass spectrometry,[17] infrared spectrometry,[13] and x-ray crystallography[11] have been used in the study of Isostearic Acid or its component isomers.

Impurities

Isostearic Acid typically contains unsaponifiable matter and moisture at levels of 3.0% and 1.0%, respectively.[4] Analysis of one sample of Isostearic Acid revealed unsaponifiables at 4% and moisture at 0.01%.[2]

USE

Purpose in Cosmetics

Isostearic Acid is an emollient[18] which shows some of the same chemical properties as stearic acid and has physical properties similar to those of oleic acid. It is used as a replacement for stearic acid when "smoother and more easily spreading" products are desired without the use of oleic acid. Emulsions using Isostearic Acid have desirable organoleptic properties and resist degradation of color and odor. This ingredient is also employed in synthesizing a wide variety of esters that are used in cosmetic formulations.[2]

Scope and Extent of Use in Cosmetics

Table 3 lists product types and the number of product formulations containing Isostearic Acid as reported by the Food and Drug Administration (FDA) in 1981. It is contained in a wide variety of cosmetic products at concentrations generally less than 5%; one fragrance preparation and one suntan product were reported to contain Isostearic Acid in the 5%–10% range.[19] Unpublished safety data (reviewed elsewhere in this report) on a skin cleansing product containing 35% Isostearic Acid suggest possible use at higher concentrations.[20,21]

The cosmetic product formulation computer printout which is made available by the FDA is compiled through voluntary filing of such data in accordance with Title 21 part 720.4 of the Code of Federal Regulations. Ingredients are listed in prescribed concentration ranges under specific product type categories. Certain cosmetic ingredients are supplied by the manufacturer at less than 100% concentration. The value reported by the cosmetic formulator in such a case may not necessarily reflect the actual concentration found in the finished product; the actual concentration would be a fraction of that reported to the FDA. The fact that data are submitted only within the framework of preset concentration ranges also provides the opportunity for a two- to 10-fold overestimation of the actual concentration of an ingredient in a particular product.

Potential Interactions with Other Ingredients

Chemical interactions of Isostearic Acid with the other ingredients in cosmetic formulations have not been reported.

TABLE 3. Product Formulation Data on Isostearic Acid.

Product category	Total no. of formulations in category	Total no. containing ingredient	No. of product formulations within each concentration range (%)			
			>5-10	>1-5	>0.1-1	≤0.1
Isostearic Acid						
Eyeliner	396	2	–	1	1	–
Eye shadow	2582	17	–	2	14	1
Mascara	397	9	–	9	–	–
Blushers (all types)	819	20	–	10	9	1
Face powders	555	13	–	1	2	10
Makeup foundations	740	12	–	11	1	–
Lipstick	3319	8	1	–	6	–
Makeup bases	831	17	–	11	6	–
Rouges	211	1	–	1	–	–
Bath soaps and detergents	148	3	–	3	–	–
Other personal cleanliness products	227	2	–	–	2	–
Shaving cream (aerosol brushless, and lather)	114	2	–	2	–	–
Other shaving preparation products	29	1	–	–	1	–
Skin cleansing preparations (cold creams, lotions liquids and pads)	680	5	–	3	2	–
Face, body, and hand skin care preparations (excluding shaving preparations)	832	6	–	3	3	–
Moisturizing skin care preparations	747	19	–	8	11	–
Night skin care preparations	219	2	–	1	1	–
Skin lighteners	44	1	–	1	–	–
Suntan gels, creams, and liquids	164	1	1	–	–	–
Other suntan preparations	28	1	–	1	–	–
1981 TOTALS		142	2	68	59	12

Data from Ref. 19.

Surfaces to which Commonly Applied

Products containing Isostearic Acid are applied to all areas of the skin, hair, nails, and mucous membranes (Table 3). They may be applied as many as several times a day and remain in contact with the skin for various periods of time following each application. Daily or occasional use may extend over many years.

BIOLOGICAL PROPERTIES

Although branched chain fatty acids are not usually found in animal tissues,[22] the 16-methylheptadecanoic acid component of Isostearic Acid has been isolated from a number of animal sources. Hydrogenated mutton fat,[23]

wool,[7] and milk fat[15,16,24] have been found to contain trace amounts of 16-methylheptadecanoic acid. Likewise, it appeared in relatively small amounts in the mitochondrial and microsomal fractions of rat pituitary homogenate.[22] It was also detected in bovine muscle, where its relative concentration was significantly correlated with subjective evaluations of tenderness and flavor.[25]

Isostearate and other branched chain fatty acids supported the growth of a sterol requiring Mycoplasma (strain Y) which was unable to synthesize or alter the chain length of either saturated or unsaturated fatty acids.[26]

The incorporation of free fatty acids into myxoviruses was shown through the use of branched chain fatty acids as molecular markers. Gas–liquid chromatography revealed the presence of incorporated 16-methylheptadecanoic acid.[27]

Metabolism

Acyl coenzyme A synthetase of rat liver homogenate was found to activate Isostearic Acid.[28] Iso-fatty acids are metabolized in a way similar to that of straight-chain fatty acids by the mitochondrial and microsomal fractions of rat liver homogenate. In contrast, however, with the straight-chain fatty acids which are successively oxidized at the β carbon to yield two carbon fractions, the iso-fatty acids are also oxidized to a large extent at the ω carbon to ultimately form three carbon dicarboxylic acids. The enzymes catalyzing the ω-hydroxylation are present in the mitochondrial and microsomal fractions of liver homogenate, whereas the enzymes catalyzing the further oxidation into carboxylic acids have been demonstrated in the soluble fraction.[17]

Animal Toxicology

Acute Studies

Oral toxicity

The acute oral toxicity of Isostearic Acid was evaluated in three studies on the undiluted ingredient[29-31] and two studies on product formulations containing the ingredient.[32,33] In each study, young adult albino rats were fasted overnight and administered a single dose of the undiluted ingredient or product formulation by gastric intubation. They were then allowed free access to food and water for two weeks. The results and other details of these studies are summarized in Table 4. From these data, the acute oral LD50 of Isostearic Acid in rats is between 32 and 64 ml/kg.

Primary skin irritation and phototoxicity

The potentials for primary skin irritation caused by undiluted Isostearic Acid,[34] 15% Isostearic Acid in corn oil[30] and three product formulations containing Isostearic Acid[20,32,35] were evaluated using the Draize rabbit skin patch test technique. In each study, 0.5 ml samples were applied and occluded for 24 h, after which time the patch sites were graded for erythema and edema on the Draize scale. The results and other details of these studies are summarized in Table 5. The undiluted ingredient produced minimal irritation of the rabbit skin, whereas no irritation was noted when it was diluted to 15% in corn oil. Product

TABLE 4. Acute Oral Toxicity Tests on Isostearic Acid.

Concentration (%)	*Dose*	*Dose of Isostearic Acid (adjusted for dilution)*	*Animals*	*Results*	*Comments*	*Ref.*
100	2.0–64.0 ml/kg	2.0–64.0 ml/kg	5 rats at each of 6 dose levels	no deaths at doses up to 32 ml/kg; 3 died at 64.0 ml/kg	Slight nasal hemorrhage at 32.0 ml/kg; moderate to severe nasal hemorrhage at 64.0 ml/kg with erratic locomotion prior to death. Two survivors at 64.0 ml/kg were severely debilitated. LD50 between 32.0 and 64.0 ml/kg	29
100	5 g/kg	5 g/kg	10	no deaths		31
100	15.9 g/kg	15.9 g/kg	5 rats	no deaths		30
4.0 (in product formulation)	15.0 g/kg	0.6 g/kg	5 rats	no deaths		32
2.0 (in product formulation)	15.9 g/kg	0.32 g/kg	5 rats	no deaths		33

TABLE 5. Draize Primary Skin Irritation Tests on Isostearic Acid.

Concentration (%)	*Number of rabbits*	*Primary irritation index (max = 8)*	*Comments*	*Refs.*
100	6	0.63	Minimal irritation	34
100	6	0.3	Minimal transient irritation	37
15 (in corn oil)	6	0.0	No signs of irritation	30
35 (in product formulation)	9	1.89	Moderate irritation by product formulation	20
4 (in product formulation)	9	0.39	Minimal irritation by product formulation	32
4 (in product formulation)	9	0.06	Minimal irritation by product formulation	35
1.25 (aqueous solution of product formulation)	9	0.00	No signs of irritation by aqueous solution of product formulation	20

formulations containing Isostearic Acid produced minimal to moderate skin irritation, most probably by virtue of the other ingredients present in the formulations.

In a primary skin irritation and phototoxicity test, 200 mg of 100% Isostearic Acid was applied to the dorsal surface of New Zealand rabbits. The test material was applied for 2 h under gauze patches to 1-in^2 skin areas on both the left- and right-hand sides. The patch on the right-hand side was removed and exposed to 5×10^7 ergs/cm^2 black light (320–450 nm). The nonirradiated areas were shielded with aluminum foil during the light exposure. A positive Oxsoralen control was treated in a similar manner. The investigators concluded that the test material was mildly irritating without light exposure and only moderately irritating following light exposure. The investigator reported that a statistically significant difference was not detected between the nonirradiated and radiated sites.[36]

Eye irritation

The Draize rabbit eye irritation procedure or a modification of the test was used to evaluate undiluted Isostearic Acid[30,37] and four product formulations containing Isostearic Acid.[20,32,33,35] In each study, a 0.1 ml sample was instilled into the conjunctival sac of one eye of each rabbit with no washing; the untreated eye served as a control. Treated eyes were examined and graded on the Draize eye irritation scale at 1, 2, 3, 4, and 7 days. The results and other details of these studies are summarized in Table 6. The undiluted ingredient produced only minimal eye irritation which cleared by 24 h. Some of the product formulations produced moderate eye irritation, which is greater than that produced by the ingredient alone.

Comedogenicity

Comedogenicity* studies were conducted on two sunscreen formulations, one containing 2.5% Isostearic Acid and the other without Isostearic Acid.[38-40]

*Comedones are also known as blackheads.

TABLE 6. Draize Eye Irritation Tests on Isostearic Acid.

Type of product formulation	*Isostearic Acid concentration (%)*	*Number of rabbits*	*Ocular irritation index (max = 110)*					*Comments*	*Ref.*
			24 h	*48 h*	*72 h*	*4 days*	*7 days*		
None	100	3	0	0	0	0	0	Transient conjunctival irritation at 1 h; all eyes normal by 24 h.	30
None	100	6	0.3	0	0	0	0	Eyes unwashed; minimal transient irritation.	37
		3	0	0	0	0	0	Eyes washed with tepid water; no irritation.	
Skin cleanser	35 (in product formulation)	6	34	14	6	4	0	Moderate reversible eye irritation which gradually cleared; all eyes normal by Day 7.	20
Face color	4 (in product formulation)	6	1	0	0	0	0	Transient conjunctival irritation at 24 h; all eyes normal by 48 h.	32
Mascara	4 (in product formulation)	6	8	6	4	1	0	Minimal eye irritation which gradually cleared; all eyes normal by Day 7	35
		retest of same animals	2	1	0	0	0	after initial application and by 72 h after repeat application.	
Face makeup foundation	2 (in product formulation)	3	–	0	0	0	0	Transient conjunctival irritation at 24 h; all eyes normal by 48 h.	33

– No data.

The formulation containing Isostearic Acid was tested in two separate assays;[38,39] 1 ml of the product was applied to the glabrous inner portion of the right ear of each of nine rabbits. The left ear was untreated and served as a control. The test material was applied five days per week for a total of 20 applications. Observations of grossly appearing enlarged pores and hyperkeratosis were made daily, and terminal biopsies were made with histologic comparison of treated and control skin. The product containing Isostearic Acid was significantly comedogenic and irritating to rabbit ears under the conditions of this test. An identical assay on the product without Isostearic Acid[40] showed the formulation to be irritating but not comedogenic to the ears of six rabbits.

Clinical Assessment of Safety

Primary Skin Irritation

A 24 h occlusive patch test procedure was used to evaluate the primary skin irritation caused by undiluted Isostearic Acid[30] and by four product formulations containing Isostearic Acid.[21,33,41,42] The results and other details of these studies are summarized in Table 7. The undiluted ingredient tested "negative" in the single insult patch test; product formulations containing Isostearic Acid produced up to minimal irritation, most probably by virtue of the other ingredients present in the formulations.

A sunscreen formulation containing 2.5% Isostearic Acid was applied to the backs of 10 subjects. Approximately 50–200 mg of the test formulation containing 1.2–5.0 mg Isostearic Acid was used in the test. The test sites were occluded for 48 h before removal. No irritation was reported.[43]

In another study,[44] 19 women participated in a controlled-use test on the skin cleanser formulation containing 35% Isostearic Acid. The product was ap-

TABLE 7. Clinical 24-Hour Single Insult Patch Tests with Isostearic Acid.

Product type	*Isostearic Acid concentration (%)*	*Number of subjects*	*Results*	*Ref.*
None	100	100	"negative"	30
Face color	4 (in product formulation)	19	No signs of irritation	41
Mascara	4 (in product formulation)	18	No signs of irritation	42
Skin cleanser	0.44 (1.25% aqueous solution of product formulation containing 35% Isostearic Acid)	80 (20 each for four versions of the product formulation)	PIIs = 0.13 to 0.18; (max = 4.0) minimal irritation	21
Face makeup foundation	0.2 (10% in peach kernel oil of product formulation containing 2% Isostearic Acid)	104	"negative"	33

plied once on one cheek the first day and twice on the same cheek on Days 2–4 of the study. The other cheek, cleansed with soap, served as a control. None of the 19 participants noted discomfort. Although three reported mild to moderate dryness on the area treated with the cleanser, the product compared favorably to the control soap.

A sunscreen containing 2.5% Isostearic Acid was tested in a 21-day repeated insult patch test on 19 subjects. The test material, 0.2 g of formulation, was placed on nonwoven fabric patches and semioccluded on the backs of the subjects for 24 h. A total of 15 applications of the material were applied over a 21-day test period. A Cumulative Irritation Index (CII) of 0.87 out of a maximum score of 84 was reported. The investigator did not consider this value of CII to be clinically significant.[45]

Irritation/Sensitization

One hundred three subjects completed a repeated insult patch test of 10% Isostearic Acid dissolved in mineral oil. Each subject received a patch to the intact skin of the upper back under semiocclusion. The patches remained in place for 48 h (72 h on weekends) at which time they were removed, the sites were examined for irritation and new patches were applied. These procedures were repeated 10 times, followed by a two-week nontreatment period and rechallenge. The test ingredient had a mean cumulative irritation score of 0.243 ± 0.068. Mineral oil was included in the study as a nonirritating control and had a mean cumulative irritation score of 0.177 ± 0.042. Propylene glycol, a positive control as a known mild irritant, had a mean cumulative score of 0.388 ± 0.071. The investigators reported there were no skin reactions consistent with ingredient-induced sensitization.[46]

A repeated insult patch test was performed on 168 subjects (115F, 53M) using 0.1 ml of a 35% mineral oil solution of Isostearic Acid. The test material was applied at 48 h intervals, three times per week for three weeks on the back of the subjects. The test area was occluded for 24 h before removal, and washed with distilled water. The test sites were read at 48 h, after which fresh test material and the occlusive patch were reapplied. After a three-week nontreatment period, the test area, as well as a previously untreated site, were challenged using the same procedure as previously noted. The sites were scored for sensitization at 24, 48, and 72 h. The investigator noted that only transient reactions were observed during the test and that Isostearic Acid was neither an irritant nor a sensitizer.[47]

A sunscreen containing 2.5% Isostearic Acid was tested in a 21-day repeated insult patch test. Approximately 200 mg of the test formulation, which is equivalent to 5 mg of Isostearic Acid, was applied at 48 h intervals for 10 applications to the backs of 235 Caucasian females. Following a two-week nontreatment period, the subjects were re-exposed for 48 h. There were no reactions during the induction phase of the study, and the investigator concluded that the formulation's potential for sensitization was extremely low, or nonexistent.[48]

A mascara formulation containing 2.85% Isostearic Acid was tested in a repeated insult patch test on 98 subjects.[49] The induction phase of the procedure consisted of 10 consecutive occlusive patch applications to the same site over a period of two weeks. A single occlusive challenge patch was applied to

TABLE 8. Clinical Repeated Insult Patch Tests with Isostearic Acid.

Product Type	*Concentration (%)*	*Number of subjects*	*Results*	*Ref.*
None	35 (mineral oil dil.)	168	No irritation; no sensitization	47
None	10 (mineral oil dil.)	103	None to mild irritation; no sensitization	46
Mascara	2.85	98	1/98 show some irritation; no sensitization	49
Sunscreen	2.5	235	No irritation potential; as sensitizer, extremely low or nonexistent	48

the original contact site and/or a virgin site after a 10- to 14-day nontreatment period. During the induction phase of the experiment, one subject exhibited some skin irritation. There were no reactions at challenge and thus no indications of skin sensitization. The results of all repeated insult patch tests are summarized in Table 8.

Phototoxicity and Photosensitization

Twenty-eight of the 168 subjects tested for irritation and sensitization discussed above were randomly selected to test the ability of 35% Isostearic Acid in mineral oil to induce a phototoxic or photosensitive reaction following ultraviolet exposure. The test protocols were the same except that the forearm was used as a test site. The 28 subjects were divided into two groups; 19 received only UVA and 9 received both UVA and UVB. The UVA (320–400 nm) light was applied for 15 min to the 19 subjects (4.4 $\mu W/cm^2$ at the skin surface measured at a 360 nm wavelength peak). The UVB was applied at two times Mean Erythema Dose (MED) to nine subjects from a 150 watt Xenon Arc Solar Simulator emitting at 280–320 nm. The subjects receiving the UVB exposure were also exposed for 5 min to UVA as previously described. The investigator noted that only transient reactions were observed, and that Isostearic Acid was not a photosensitizer.[47]

SUMMARY

Isostearic Acid is a mixture of fatty esters consisting mainly of methyl branched isomers of octadecanoic acid. It is reported by the FDA to be used at concentrations up to 10% in a wide variety of cosmetic products which may be applied to all areas of the body; data have also been received on a product containing 35% Isostearic Acid.

Studies with rat liver homogenate suggest Isostearic Acid is readily metabolized following ingestion. In rats, the acute oral LD50 is estimated to be greater than 32 ml/kg. The raw ingredient produced no significant skin or eye irritation in Draize rabbit irritation tests, whereas variable degrees of irritation were produced by product formulations containing Isostearic Acid. A product for-

mulation both with and without 2.5% Isostearic Acid was tested in a rabbit ear comedogenicity assay. The formulation without Isostearic Acid was irritating but did not produce comedones; however, the formulation with Isostearic Acid was both irritating and comedogenic.

In clinical studies, 100 subjects showed no signs of irritation after a 24 h single insult skin patch with undiluted Isostearic Acid, and product formulations containing up to 4% Isostearic Acid produced, at most, minimal irritation when similarly tested on a total of 221 subjects. In another study, 35% Isostearic Acid in mineral oil was neither an irritant nor a sensitizer in 168 subjects. A subset population of 25 individuals from this study group, when tested in a similar manner but exposed to UVA + UVB, gave no indication that Isostearic Acid is a photosensitizer. Isostearic Acid at 10% in mineral oil was similarly not irritating nor sensitizing to 103 subjects. Product formulations containing 2.5%–2.85% Isostearic Acid produced no evidence of contact sensitization when tested in repeated insult patch tests on a total of 333 subjects.

DISCUSSION

The Panel expresses concern regarding the production of comedones in the rabbit ear assay by a product formulation containing commercially available Isostearic Acid. The Panel recognizes that currently available tests are inadequate to predict the potential for human comedogenicity of an ingredient as used in a product formulation. However, it is a potential health effect that should be considered when Isostearic Acid is used in cosmetic formulations.

CONCLUSION

On the basis of the available information presented in this report, the Panel concludes that Isostearic Acid is safe as a cosmetic ingredient in the present practices of use.

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REFERENCES

1. ESTRIN, N.F. (ed.). (1977). *CTFA Cosmetic Ingredient Dictionary*, 2nd ed. Washington, DC: Cosmetic, Toiletry and Fragrance Association.
2. PROSERPIO, G. (1974). Isocosmetics with isostearics. Cosmet. Perfum. **89**(7), 45–8.
3. ESTRIN, N.F. (ed.). (1974). *CTFA Standards: Cosmetic Ingredient Specifications, Isostearic Acid.* Washington, DC: Cosmetic, Toiletry and Fragrance Association.

4. COSMETIC, TOILETRY AND FRAGRANCE ASSOCIATION (CTFA). (October, 1980). Submission of unpublished data. CTFA Cosmetic Ingredient Chemical Description.*
5. CTFA. (Sept. 27, 1982). Submission of unpublished data. Isostearic Acid, Method of Manufacture.*
6. FORDYCE, C.R. and JOHNSON, J.R. (1933). Branched-chain aliphatic acids. Isomyristic isopalmitic and isostearic acids. J. Am. Chem. Soc. **55,** 3368–72.
7. HOUGEN, F.W., ILSE, D., SUTTON, D.A., and DE VILLIERS, J.P. (1953). Wool wax. III. Synthesis of some iso acids. J. Am. Chem. Soc. pp. 98–102.
8. MILBURN, A.H. and TRUTER, E.V. (1954). J. Am. Chem. Soc. pp. 3344.
9. STENHAGEN, E. and TAGTSTROM-EKETORP, B. (1945). Ark-Kemi. Min. Geol. A. **19,** 8.
10. WEITKAMP, A.W. (1945). J. Am. Chem. Soc. **67,** 447.
11. ABRAHAMSON, S. and LUNDEN, B.M. (1972). Crystal structure of isostearic acid. Acta Crystallogr. **B28**(Pt. 8), 2562–7.
12. AROSENIUS, K.E., STALLBERG, G., STENHAGEN, E., and TAGTSTROM-EDETORP, B. (1948). Long chain iso-acids. II. Synthesis of acids with 13, 15, 17, 24, 25, 26, and 35 carbon atoms, and an x-ray study of synthetic acids and amines. Arkiv. Kemi., Mineral, Geol. **26A**(19), 20 pp.
13. FISCHMEISTER, I. (1963). Infrared spectra of crystalline long-chain methyl fatty acids. I. The methyl group near the carboxylic acid group. Arkiv. Kemi. Min. Geol. **20**(29), 353–67.
14. VANLERBERGHE, G. and HANDJANI-VILA, R.M. (1978). Surface chemistry as a tool for evaluating cosmetic products. Cosmet. Toiletries **93**(1), 29–30, 32, 34–7, 40–2.
15. KAERKKACINEN, V.J. (1964). Minor fatty acids in milk fat. Kiel. Milchwirtsch. Forschungsber. **16,** 331–9.
16. KURKOVA, M.F. and BELOUSOV, A.P. (1966). Minor fatty acids in milk fat. Izv. Vysshikh Uchebn. Zavedenii, Pishchevaya Tekhnol. **4,** 41–3.
17. BJORKHEM, I. and DANIELSON, H. (1970). Omega-oxidation of branched-chain fatty acids in rat liver homogenates. Eur. J. Biochem. **14**(3), 473–7.
18. BALSAM, M.S. and SAGARIN, E. (eds.). (1972). *Cosmetic Science and Technology,* Vol. 1. New York, NY: Wiley-Interscience.
19. FOOD AND DRUG ADMINISTRATION (FDA). (1981). Cosmetic product formulation data. FDA Computer Printout.
20. CTFA. (October 5, 1979). Submission of unpublished data. Toxicology summary report.*
21. CTFA. (November 1, 1979). Submission of unpublished data. Clinical evaluation report.*
22. HYMER, W.C. and McSHAN, W.H. (1963). Isolation of rat pituitary granules and the study of their biochemical properties and hormonal activities. J. Cel. Biol. **17**(1), 67–86.
23. HANSEN, R.P., SHORLAND, F.B., and COOKE, N.J. (1956). The branched-chain fatty acids of mutton fat. 3. The isolation of 16-methylheptadecanoic acid (isostearic acid). Biochem. J. **64**(2), 214–6.
24. RENNER, E. and MELCHER, F. (1978). Studies on minor fatty acids of milk fats. 3. Saturated fatty acids. Milchwissenschaft **33**(5), 281–5.
25. DRYDEN, F.D. and MARCHELLO, J.A. (1970). Influence of total lipid and fatty acid composition upon the palatability of three bovine muscles. J. Anim. Sci. **31**(1), 36–41.
26. RODWELL, A.W. and PETERSON, J.E. (1971). Effect of straight-chain saturated, monoenoic, and branched-chain fatty acids on growth and fatty acid composition of mycoplasma strain Y. J. Gen. Microbiol. **68**(Pt. 2), 173–86.
27. BLOUGH, H.A. and TIFFANY, J.M. (1969). Incorporation of branched-chain fatty acids into myxoviruses. Proc. Nat. Acad. Sci. U.S. **62**(1), 242–7.
28. LIPPEL, K. (1973). Activation of branched and other long-chain fatty acids by rat liver microsomes. J. Lipid Res. **14**(1), 102–9.
29. CTFA. (June 23, 1970). Submission of unpublished data. Acute oral toxicity assay, Bio-Toxicology Labs.*
30. CTFA. (September, 1980). Submission of unpublished data. CIR Safety data submission.*
31. BIORESEARCH. (November 21, 1980). CTFA submission of unpublished safety data. Acute oral toxicity.*
32. CTFA. (December 12, 1978). Submission of unpublished data. Toxicology summary report.*
33. CTFA. (September, 1980). Submission of unpublished data. CIR safety data submission.*
34. CTFA. (July 3, 1968). Submission of unpublished data. Primary skin irritation studies, Hill Top Research.*
35. CTFA. (June 29, 1979). Submission of unpublished data. Toxicology summary report.*

*Available on request: Administrator, Cosmetic Ingredient Review, 1110 Vermont Avenue, N.W., Suite 810, Washington, DC 20005.

36. FOOD AND DRUG RESEARCH LABS (FDRL). (November 25, 1980). CTFA submission of unpublished safety data. Dermal phototoxicity study.*
37. BIORESEARCH. (November 21, 1980). CTFA submission of unpublished safety data. Primary eye irritation.*
38. CONSUMER PRODUCT TESTING. (December 1, 1980). CTFA submission of unpublished safety data. Final report: comedogenicity assay in rabbits.*
39. MAIBACH, H. (November 19, 1980). CTFA submission of unpublished safety data. Comedogenicity assay.*
40. WILLIGAN, D.A. (November 10, 1980). CTFA submission of unpublished safety data. Histopathologic evaluation of skin of ears from rabbits.*
41. CTFA. (October 26, 1978). Submission of unpublished data. Clinical evaluation report.*
42. CTFA. (August 3, 1979). Submission of unpublished data. Clinical evaluation report.*
43. CTFA. (December 16, 1980). Submission of unpublished data. 48-hour patch test.*
44. CTFA. (October 26, 1979). Submission of unpublished data. Clinical evaluation report.*
45. CONCORDIA RESEARCH LABS. (November 12, 1980). CTFA submission of unpublished safety data. Twenty-one day cumulative irritation test.*
46. CTFA. (March 17, 1982). Submission of unpublished data. Repeat insult sensitization study.*
47. FDRL. (March 31, 1982). CTFA submission of unpublished safety data.*
48. CONCORDIA RESEARCH LABS. (October 29, 1980). CTFA submission of unpublished safety data. Repeat insult patch test.*
49. CTFA. (February 27, 1980). Submission of unpublished data. Contact allergy test report.*

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3

Final Report on the Safety Assessment of Oleic Acid, Lauric Acid, Palmitic Acid, Myristic Acid, and Stearic Acid

Oleic, Lauric, Palmitic, Myristic, and Stearic Acids are fatty acids with hydrocarbon chains ranging in length from 12 to 18 carbons with a terminal carboxyl group. These fatty acids are absorbed, digested, and transported in animals and humans. Little acute toxicity was observed when Oleic, Lauric, Palmitic, Myristic, or Stearic Acid or cosmetic formulations containing these fatty acids were given to rats orally at doses of 15–19 g/kg body weight. Feeding of 15% dietary Oleic Acid to rats in a chronic study resulted in normal growth and health, but reproductive capacity of female rats was impaired. Results from topical application of Oleic, Palmitic, and Stearic Acid to the skin of mice, rabbits, and guinea pigs produced little or no apparent toxicity. Studies using product formulations containing Oleic and Stearic acids indicate that neither is a sensitizer or photosensitizing agent. Animal studies also indicate that these fatty acids are not eye irritants. Lauric, Stearic, and Oleic Acids were noncarcinogenic in separate animal tests. In primary and cumulative irritation clinical studies, Oleic, Myristic, and Stearic Acids at high concentrations were nonirritating. Cosmetic product formulations containing Oleic, Lauric, Palmitic, and Stearic Acids at concentrations ranging up to 13% were not primary or cumulative irritants, nor sensitizers. On the basis of available data from studies using animals and humans, it is concluded that Oleic, Lauric, Palmitic, Myristic, and Stearic Acids are safe in present practices of use and concentration in cosmetics.

INTRODUCTION

Oleic, Lauric, Palmitic, Myristic, and Stearic Acids are long hydrocarbon chain carboxylic acids, known as fatty acids. They are usually produced by hydrolysis of common animal and vegetable fats and oils. Fatty acids are generally used as intermediates in the manufacture of their alkali salts, which

are in turn used as emulsifiers, emollients, and lubricants in a variety of cosmetic creams, cakes, soaps, and pastes.

CHEMISTRY

Structure and Nomenclature

Lauric, Myristic, Palmitic, and Stearic Acids are saturated fatty acids of 12-, 14-, 16-, and 18-carbon lengths. Oleic Acid is an 18-carbon *cis*-mono unsaturated fatty acid. These fatty acids consist of long hydrocarbon chains with a terminal carboxyl group. Synonyms for the fatty acids (Table 1) were obtained from the following sources: Windholz et al.,[1] Estrin et al.,[2] Morrison and Boyd,[3] Lehninger,[4] and Osol.[5] Structural formulae are presented in Figure 1. A summary of some physicochemical properties appears in Table 2. Since the saturated fatty acids bear the carboxyl functional group and basically

TABLE 1. Synonyms for the Fatty Acids

Fatty acid	*Synonyms*
Oleic Acid	*cis*-9-Octadecenoic acid *cis*-Δ^9-Octadecenoic acid 9-Octadecenoic acid Oleinic acid Elaic acid Red oil 18:1Δ^9
Lauric Acid	n-Dodecanoic acid Dodecanoic acid Laurostearic acid Dodecoic acid 12:0
Palmitic Acid	n-Hexadecanoic acid Hexadecanoic acid Hexadecoic acid Hexadecylic acid Cetylic acid 16:0
Myristic Acid	n-Tetradecanoic acid Tetradecanoic acid Tetradecoic acid 14:0
Stearic Acid	n-Octadecanoic acid Octadecanoic acid Cetylacetic acid Stearophanic acid 18:0

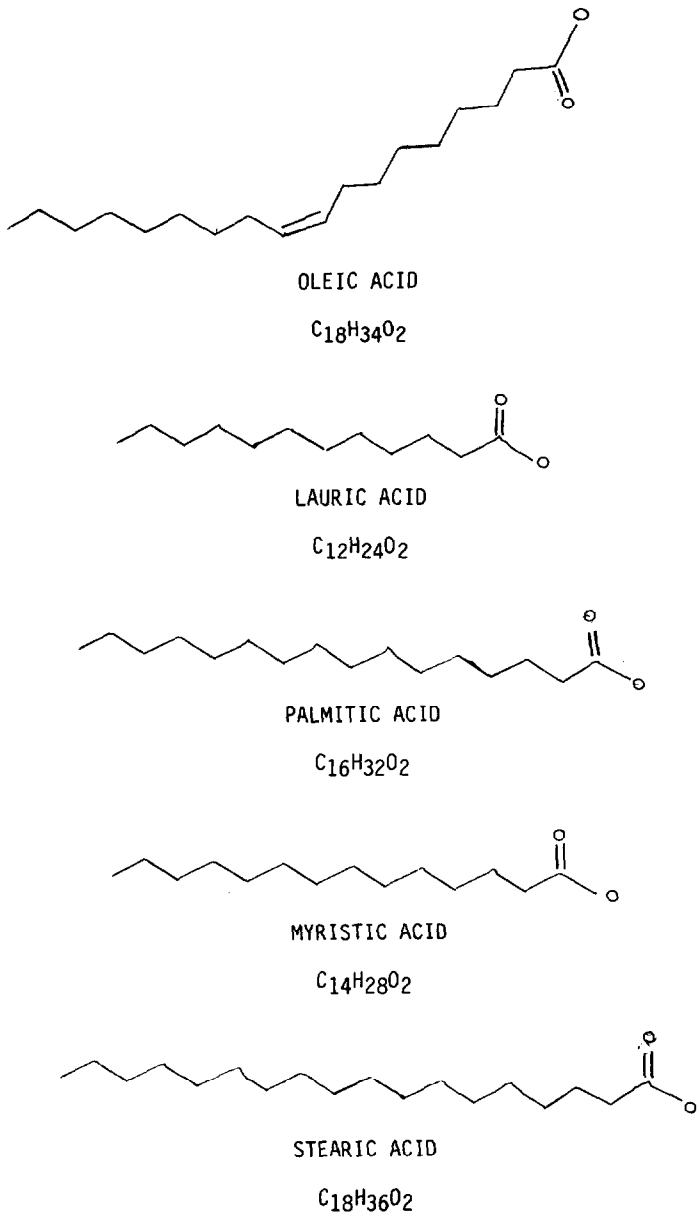

FIG. 1. Structural formulae of fatty acids.

differ from each other by 2–6 methylene groups, their properties are similar. The *cis* double bond of Oleic Acid alters several physical properties relative to those of Stearic Acid.[4]

Description and Source

Fatty acids have been found in marine and freshwater organisms,[6] bacteria,[4] and vegetable oils and animal fats.[3] Although mammalian tissues

TABLE 2. Physicochemical Properties of the Fatty Acids

Property	*Lauric Acid*	*Myristic Acid*	*Palmitic Acid*	*Stearic Acid*	*Oleic Acid*
CAS Registry No.	143-07-7	544-63-8	57-10-3	57-11-4	112-80-1
Empirical formula[a]	$C_{12}H_{24}O_2$	$C_{14}H_{28}O_2$	$C_{16}H_{32}O_2$	$C_{18}H_{36}O_2$	$C_{18}H_{34}O_2$
Molecular weight	200.31[a], 200.33[b]	228.36[a], 228.38[b]	256.42[a], 256.43[b]	284.47[a], 284.50[b]	282.45[a], 282.47[b]
Density (g/ml, °C)	0.8679_4^{50b}	0.8528_4^{70a}	0.8527_4^{62b}	0.847^{70a}	0.895_{25}^{25a}
Melting point (°C)	44, 48[a]	58.5[a], 58[b], 54.4[c]	63–64[a]	69–70[a, c], 71.2[b]	16.3[b]
Boiling point (°C, P in atm)[a]	225_{100}	250.5_{100}	215_{15}	383_1 (decomposes at 360_1)	286_{100}
Solubility[a, b, d]					
Water	Insol.	Insol.	Insol.	Insol.	Insol.
Alcohol	v. sol.—ethanol propanol—1 g/ml	sol.—abs. ethanol v. sol.—methanol	v. sol.—ethanol + heat v. sol.—propanol	sl. sol.—1 g/21 ml ethanol	v. sol.—ethanol
Chloroform	sol.	sol.	v. sol.	sol.—1 g/2 ml	v. sol.
Benzene	v. sol.	v. sol.	sol.	sl. sol.—1 g/5 ml	v. sol.
Ether	v. sol.	sl. sol.	v. sol.	v. sol.	v. sol.
Viscosity (cp, °C)[c]	7.3^{50}	5.06^{75}	7.1^{75}	9.04^{75}	23.01^{30}
Iodine number[a]	—	—	—	—	89.9
Acid value	280.1[c]	245.7[c]	218.0[c]	197.2[c]	198.6[a]

[a]Ref. 1.
[b]Ref. 7.
[c]Ref. 6.
[d]Ref. 8.
Insol., insoluble; sl. sol., slightly soluble; sol., soluble; v. sol., very or freely soluble.

normally contain trace amounts of free fatty acids, conjugated forms can be found in several tissues.[4] Free fatty acids have been found in human sebum and epidermal tissue.[9,10]

Oleic Acid, in esterified form, is found in many vegetable oils and animal fats, frequently constituting greater than 50% of the total fatty acid concentration. Oils rich in Oleic Acid include olive (80%), peanut (60%), teaseed (85%), and pecan (85%) oils; very few fats contain less than 10% Oleic Acid.[6]

Pure Oleic Acid is a colorless to pale yellow, oily liquid at temperatures above 5–7°C. At 4°C, it solidifies to a crystalline mass. Upon exposure to oxygen, it darkens gradually, and it decomposes when heated to 80–100°C at atmospheric pressure.[1,8,11] Oleic Acid has a characteristic lardlike odor and taste.[1,8]

Lauric Acid is one of the three most widely distributed naturally occurring saturated fatty acids; the others are Palmitic and Stearic Acids. Its common name is derived from the laurel family, Lauraceae. The fatty acid content of the seeds is greater than 90% Lauric Acid. Sources of Lauric Acid include coconut and palm kernel oils, babassu butter (approximately 40%) and other vegetable oils, and milk fats (2–8%). Camphor seed oil has a high Lauric Acid content.[1,6,8]

Lauric Acid occurs as a white or slightly yellow, somewhat glossy crystalline solid or powder[1,8] or as a colorless solid[11] with a slight odor of bay oil.[1]

The glyceryl ester of Palmitic Acid is widely distributed, being found in practically all vegetable oils and animal (including marine animal) fats at concentrations of at least 5%. Palmitic Acid is the major component of lard and tallow (25–30%), palm oil (30–50%), cocoa butter (25%), and other vegetable butters. Chinese vegetable tallow is reported to contain 60–70% Palmitic Acid.[1,6]

Palmitic Acid occurs as a mixture of solid organic acids obtained from fats that are primarily composed of Palmitic Acid with varying quantities of Stearic Acid. Its appearance ranges from a hard, white or faintly yellow, slightly glossy crystalline solid to a white or yellow-white powder,[8] white crystalline scales,[1] or colorless crystals.[11]

Myristic Acid is a solid organic acid usually obtained from coconut oil, nutmeg butter (*Myristica fragrans* Houtt), palm seed oils, and milk fats.[1,6] Seed oils of the plant family, Myristaceae, contain the largest amounts of Myristic Acid (up to 80%), but small amounts have been measured in most animal fats and vegetable oils.

Myristic Acid occurs as a hard, white or faintly yellow, glossy crystalline solid, as a white or yellow-white powder,[8] or as colorless leaflets.[11]

Stearic Acid is found primarily as a glyceride in animal fats and oils; lard and tallow contain approximately 10 and 20% Stearic Acid, respectively.[1,6] Most vegetable oils contain 1–5% Stearic Acid; cocoa butter contains about 35%.

Stearic Acid occurs as hard, white or faintly yellow, somewhat glossy crystals or leaflets or as an amorphous white or yellow-white powder.[1,5,8,12] It has a slight odor and taste resembling tallow.[1,8]

Method of Manufacture and Impurities

The fatty acids are usually produced by the hydrolysis of common animal and vegetable fats and oils followed by fractionation of the resulting fatty acids. Fatty acids that are used in foods, drugs, and cosmetics normally exist as mixtures of several fatty acids depending on the source and manufacturing process.

Processing operations in the manufacture of fatty acids from fats are known to alter their chemical compositions. The processes (e.g., distillation, high temperature and pressure hydrolysis, and bleaching) may result in *cis-trans* isomerization, conjugation of polyunsaturates, polymerization, and dehydration.[6]

Cosmetic-grade Oleic, Lauric, Palmitic, Myristic, and Stearic Acids occur as mixtures of fatty acids depending on their method of manufacture and source. The individual fatty acids predominate in the mixture ranging from 74% (Oleic Acid) to 95% (Myristic Acid). All contain varying amounts of unsaponifiable matter, and some grades also contain glyceryl monoesters of fatty acids. Butylated hydroxytoluene may be added to all five fatty acid preparations as an antioxidant.[13–17] In cosmetics containing unsaturated materials, the concentration range for butylated hydroxytoluene should be 0.01 to 0.1%.[18] Butylated hydroxytoluene has been used in some lanolin products containing unsaturated fatty acids, alcohols, esters, sterols, and terpenols, at concentrations ranging from 200 to 500 ppm.[19] Data on the components, impurities, and additives of these cosmetic grade fatty acids are presented in Table 3. Comparisons of specifications for cosmetic, food, and drug grade fatty acids are presented in Tables 4, 5, 6, 7, and 8. Cosmetic grade specifications for fatty acid composition are presented in Table 9.

Fourteen FAPC (Fatty Acid Producers Council of the Soap and Detergent Association) categories of fatty acids are contrasted by titer and iodine value. Typical fatty acid compositions are reported.[6] FDA files contain some composition data on Oleic and Stearic Acids, which were submitted with Food Additive Petitions (Notes from the composition data in CIR files).

Oleic Acid is produced by the hydrolysis and fractionation (e.g., saponification and distillation) of animal or vegetable fats and oils.[1,5,11,16] Preparation of Oleic Acid from animal tallow and olive has been reported.[1,5] It is also obtained as a byproduct in the manufacture of solid Stearic and Palmitic Acids. Crude (unpurified, unbleached) Oleic Acid of commerce, or red oil, contains Stearic and Palmitic Acids in varying quantities.[5,20]

Several commercial grades of Oleic Acid are available, distinguished by varying proportions of saturated fatty acids. The commercial grade contains 7–12% saturated acids and some unsaturated acids and is usually derived from edible sources (internally administered Oleic Acid must be derived from edible sources[5]). Oleic Acid derived from tallow contains varying amounts of linolenic and Stearic Acids and small but significant quantities of elaidic (*trans*-9-octadecenoic) acid, some of which is generated from certain processing operations (e.g., distillation and high-temperature bleaching with clays).[1,5,6]

Hawley[20] reported several technical grades of Oleic Acid: chick edema factor-free grade, U.S. Pharmacopeia (USP) grade, Food Chemicals Codex (FCC) grade, and purified technical grade Oleic Acid. The latter technical

TABLE 3. Components, Impurities, Additives in Cosmetic-Grade Fatty Acids[13–17]

Cosmetic-grade fatty acid	*Components in Mixture (%)*	*Minor Impurities (%)*	*Additives*
Oleic Acid	9-Octadecenoic acid (68–74)[a] 9,12-Octadecadienoic acid (4–12) 9-Hexadecenoic acid (7–11) Hexadecanoic acid (4) Tetradecanoic acid (3) 9-Tetradecenoic acid (1–3) Heptadecanoic acid (1–2) Pentadecanoic acid (0.5–2) Octadecanoic acid (1) Octadecatrienoic acid (1) Decanoic acid Dodecanoic acid	Unsaponifiable material (1.5 max)	Butylated hydroxytoluene[b] (BHT)
Lauric Acid	Dodecanoic acid (90 min) Tetradecanoic acid (6 max) Decanoic acid (5 max) Hexadecanoic acid (2 max)	Unsaponifiable material (0.3 max) (mostly hydrocarbon) Glyceryl monolaurate[b] (0.07 max)	BHT[b]
Palmitic Acid	Hexadecanoic acid (80 min) Octadecanoic acid (11 max) Tetradecanoic acid (7 max) Heptadecanoic acid (4.5 max) Pentadecanoic acid (1 max)	Unsaponifiable material (0.3 max) (mostly hydrocarbon) Glyceryl monopalmitate[b] (0.07 max)	BHT[b]
Myristic Acid	Tetradecanoic acid (95 min) Hexadecanoic acid (4 max) Dodecanoic acid (3 max)	Unsaponifiable material (0.2 max) (mostly hydrocarbon) Glyceryl monomyristate[b] (0.07 max)	BHT[b]
Stearic Acid	Octadecanoic acid (39–95)[a] Hexadecanoic acid (5–50) Tetradecanoic acid (0–3) 9-Octadecenoic acid (0–5) Heptadecanoic acid (0–2.5) Eicosanoic acid (0–2) Pentadecanoic acid (0–1)	9-Hexadecenoic acid 9,12-Octadecadienoic acid Unsaponifiable material (0.3 max) Glyceryl monostearate (0.07 max)	BHT[b]

[a] These are concentration ranges of a typical analysis.
[b] Present in some grades.

grade Oleic Acid contains ≥ 90% Oleic Acid and has a 4% maximum linoleic acid content and a 6% maximum saturated fatty acid content.

Lauric Acid is produced by the hydrolysis, usually via saponification, of animal or vegetable fats and oils followed by fractional distillation.[11,22] Lauric Acid is commonly isolated from coconut oil,[1,11] and several patents describe its chemical synthesis.[1]

Palmitic Acid is produced by the hydrolysis and fractionation of palm oil, tallow oil, coconut oil, Japan Wax, Chinese vegetable tallow, and spermaceti. Fractionation is usually by distillation or crystallization.[1,11,20] Palmitic Acid can also be obtained in the manufacturing process for Stearic Acid.

TABLE 4. Comparison of Specifications: Cosmetic and Food Grades

Oleic Acid	*Cosmetics*[21]	*Foods*[8]
Iodine value	83.0–99.0	83–103
Acid value	190.0–207.0	196–204
Saponification value	198.0–207.0	196–206
Unsaponifiable matter	1.0% max	2% max
Arsenic		3 ppm max
Heavy metals (e.g., Pb)		10 ppm max
Residue on ignition		0.01% max
Titer (solidification point)	2–6°C	< 10°C
Water content		0.4% max

TABLE 5. Comparison of Specifications: Cosmetic and Food Grades

Lauric Acid	*Cosmetics*[13, 14]	*Foods*[8]
Iodine value	0.5 max	3.0 max
Acid value	273–283	252–287
Saponification value	276–284	253–287
Unsaponifiable matter	0.3% max	0.3% max
Arsenic		3 ppm max
Heavy metals (e.g., Pb)		10 ppm max
Residue on ignition		0.1%
Titer (solidification point)	38–44°C	26–44°C
Water content		0.2% max

TABLE 6. Comparison of Specifications: Cosmetic and Food Grades

Palmitic Acid	*Cosmetics*[21]	*Foods*[8]
Iodine value	1.0 max	2.0 max
Acid value	213–221	204–220
Ester value	3.0 max	
Saponification value	216.5–220.5	205–221
Unsaponifiable matter	0.25% max	1.5% max
Arsenic		3 ppm max
Heavy metals (e.g., Pb)		10 ppm max
Residue on ignition		0.1%
Titer (solidification point)	59.4–60.4°C	53.3–62°C
Water content		0.2% max

The following methods have been used in the preparation of Myristic Acid: isolation from tall-oil fatty acids from 9-ketotetradecanoic acid, by electrolysis of a mixture of methyl hydrogen adipate and decanoic acid, by Maurer oxidation of myristanol, and from cetanol.[1] The most common means of preparation is by fractional distillation of hydrolyzed coconut oil, palm kernel oil,[20] or coconut acids.[11]

Commercial Stearic Acid has several crystalline forms and contains varying relative concentrations of other fatty acids depending on the sources and processing methods used.[9] Commercial Stearic Acid is primarily a mixture of

TABLE 7. Comparison of Specifications: Cosmetic and Food Grades

Myristic Acid	*Cosmetics*[13,14]	*Foods*[8]
Iodine value	0.5 max	1.0 max
Acid value	243–249	242–249
Saponification value	243–249	242–251
Unsaponifiable matter	0.2% max	1% max
Arsenic		3 ppm max
Heavy metals (e.g., Pb)		10 ppm max
Residue on ignition		0.1% max
Titer (solidification point)	52–54°C	48–55.5°C
Water content		0.2% max

TABLE 8. Comparison of Specifications: Cosmetic and Food Grades

Stearic Acid	*Cosmetics "95.0%"*[21]	*Foods*[8]
Iodine value	1.0 max	7 max
Acid value		196–211
Ester value	3.0 max	
Saponification value	196.4–200.4	197–212
Unsaponifiable matter	0.25% max	1.5% max
Arsenic		3 ppm max
Heavy metals (e.g., Pb)		10 ppm max
Residue on ignition		0.1% max
Titer (solidification point)	67.2–68.2°C	54.5–69°C
Water content		0.2% max

varying amounts of Stearic and Palmitic Acids. Palmitic Acid/Stearic Acid ratios in commercial preparations depend on several factors, such as source, geographical and climatic influences, genetic uniformity, and fat location site (in animals).[6]

Methods of processing for Stearic Acid include hydrolysis of tallow or hydrogenation of unsaturated fatty acids (e.g., Oleic Acid) in cottonseed and other vegetable oils, followed by methods of isolation, such as fractional distillation or crystallization.[1,5,6,9,11,17] A successive series of pressing operations has been used to separate the liquid unsaturated fatty acids from the solid saturated fatty acids.[6] The Palmitic Acid/Stearic Acid ratio obtained from tallow hydrolysis and triple-pressing or solvent crystallization is 55%/45%. Concentrations of Stearic Acid as high as 95–99%[6,9] have been reported from the hydrogenation of unsaturated fatty acids.

Both double-pressed (two successive pressings to expel unsaturated fatty acids) and triple-pressed Stearic Acid are used by the cosmetic industry.[6,9] Triple-pressed Stearic Acid is a product containing 1.5% 14C (14-carbon), 0.5% 15C, 50% 16C, 1% 17C, and 47% 18C fatty acids, with less than 0.2% Oleic Acid. Double-pressed Stearic Acid typically contains about 2.5% 14C, 50% 16C, 1% 17C, 40% 18C fatty acids, and 6% Oleic Acid.[6]

TABLE 9. Cosmetic-grade Specifications for Fatty Acid Composition (Reported as maximal or minimal acceptable percentage in composition)[21]

Fatty acid chain length[a]	*Oleic Acid*	*Lauric Acid*	*Palmitic Acid*	*Myristic Acid*	*Stearic Acid 37.5%*	*Stearic Acid 42.5%*	*Stearic Acid 95.0%*
8:0–12:0	1.0 max						
10:0		5 max					
12:0		90 min	1.3 max	3 max	0.1 max	0.1 max	Trace (< 0.05)
14:0	5.0 max	6 max	2.5 max	95 min	4.3 max	4.1 max	1.6 max
14:1			Trace (< 0.05)		0.1 max	0.1 max	Trace (< 0.05)
15:0	2.5 max		0.6 max		0.6 max	0.7 max	0.8 max
16:0	7.5 max	2 max	92.5–97.5	4 max	49.0–54.0	49.0–54.0	5.0 max
16:1	4.5–7.5		0.4 max		0.3 max	0.1 max	Trace (< 0.05)
17:0	1.5 max		2.3 max		2.5 max	2.7 max	2.0 max
18:0	3.5 max		5.0 max		35.0–40.0	40.0–45.0	92.5–97.5
18:1	70.0 min		0.4 max		5.5 max	0.6 max	0.6 max
18:2	2.0–12.0 max						
18:3	2.2 max						
16:0 + 18:0					89.0 min	94.0 min	97.5 min
16:0 + 18:0 + 14:0			97.5 min				
20:0			Trace (< 0.05)		0.1 max	0.1 max	Trace (< 0.05)

[a]A form of shorthand notation was used to denote the length of the fatty acid carbon chain and the number of double bonds in the chain (e.g., Myristic Acid—14:0; Oleic Acid—18:1). Information on the position and configuration of double bonds in unsaturated fatty acids was not included (e.g., elaidic acid, the *trans* isomer of Oleic Acid, would also be denoted as 18:1).

Three types of Stearic Acid distinguished by average Stearic Acid concentration, their specifications, and infrared spectra are included in *CTFA's Compendium of Cosmetic Ingredient Composition*.[21] These Stearic Acids, 37.5%, 42.5%, and 95.0%, have minimum Stearic plus Palmitic Acid concentrations of 89.0%, 94.0%, and 97.5%, respectively. Regular pharmaceutical grade Stearic Acid specifies a 40.0% minimum of either Stearic or Palmitic Acid and a 90.0% minimum for their sum.[23] Purified pharmaceutical grade Stearic Acid specifies a 90.0% minimum Stearic Acid content and a 96.0% minimum for the sum.[73] A comparison of these Stearic Acids is presented in Table 9.

Reactivity and Stability

Chemical reactions of the fatty acids are typical of reactions of carboxylic acids and alkanes (or alkenes, in the case of Oleic Acid). Typical reactions of carboxylic acids include reduction to form aldehydes and alcohols, esterification, formation of metal salts, high-pressure hydrogenation, formation of amides and acid halides, alkoxylation, and pyrolysis. Reactions of alkanes and alkenes are dehydrogenation and hydrogenation, halogenation and hydration.[3,6] Halogenation across carbon–carbon double bonds is a useful method for the quantitative titration for relative unsaturation.[4]

Insoluble stearates and oleates are formed in reactions of Stearic Acid and Oleic Acid with heavy metals and calcium. Oxidizing agents, such as nitric acid and potassium permanganate, added to Oleic Acid are known to produce various derivatives of this acid.[5] Other oxidation routes for fatty acids include oxidation via bacterial action, enzyme-catalyzed hydrolysis and oxidation, and autooxidation from atmospheric oxygen.[6]

A significant increase in lipid peroxide concentration has been observed after 18-h UVA-irradiation of Oleic Acid.[24]

Analytical Methods

Two basic methods for the analysis of the fatty acids have been reported by the cosmetic industry. Primarily, gas chromatography (GC) of fatty acid methyl esters, prepared by the boron trifluoride-methanol method, is used for the separation and relative identification of fatty acids in a mixture.[21,25] Infrared spectra of the fatty acids are used for fingerprinting, functional group identification, and impurity screening.[6,13–17,26] Determination of physicochemical properties also aids in positive identification of a specific fatty acid.[6,25]

Basic analysis of the fatty acids by GC[4,25] has evolved by technical advances in methylation procedures[23,27] and development of new derivatization reactants and techniques that allow easier detection of smaller quantities of fatty acids.[28] A method for the GC of nonmethylated fatty acids has been reported.[29]

Flame ionization detection (FID) is usually coupled with the GC of fatty acid methyl esters. Mass spectrometry (MS) has also been used with GC for compound identification.[30]

Thin-layer chromatography[30,31] and high-performance liquid chromatography (HPLC) are also used in fatty acid identification and quantitation. Precolumn chemical derivatization (e.g., forming benzyl, dansyl, phenacyl, and naphthacyl derivatives) of fatty acids is followed by reversed-phase HPLC. Methods of detection include ultraviolet and fluorescence spectroscopic and refractive index detection. The analysis of fatty acids by HPLC has been reviewed.[32,33]

Mass spectrometry with temperature profiling of the chemical ionization source has been reported as a method for initial compound separation. Its coupling with a second MS allows direct analysis of complex lipid sources.[34]

Other separation methods include centrifugal liquid and adsorption chromatography.[35] Identification procedures range from methods, such as gravimetry[25] and histochemical staining,[36] to ultraviolet, infrared, and nuclear magnetic resonance spectroscopy.[6,37,38]

USE

Cosmetic Use

The fatty acids, Oleic, Lauric, Palmitic, Myristic, and Stearic Acids, are primarily used as intermediates in the manufacture of corresponding alkali salts, which are, in turn, used as emulsifiers, emollients, and lubricants in a variety of cosmetic creams, cakes, soaps, and pastes.[5,9,39-41] They may also be used as base components (of the oil phase) of many cosmetic formulations.[38]

Emollient creams containing fatty acids are slightly alkaline, ranging in pH from 7.5 to 9.5. Other ingredients in these creams include sodium, potassium, and ammonium hydroxide, diethanolamine, triethanolamine, isopropanolamines, amino glycol, and borax.[9]

Stearic Acid is contained in 2465 cosmetic products listed by the Food and Drug Administration (FDA) in the 1981 product formulation data table.[41] Oleic Acid is contained in 424, Myristic Acid in 36, Palmitic Acid in 29, and Lauric Acid in 22 cosmetic formulations in several product categories[41] (Table 10).

The reported concentrations of the fatty acids in cosmetic products primarily range from 0.1 to 25%. Stearic Acid is found in cosmetics in all product categories of the FDA table; most products appear in skin care, makeup, and shaving preparation categories. Oleic Acid is found primarily in hair coloring and eye makeup preparation product categories. Lauric, Palmitic, and Myristic Acids are contained in skin care, shaving, and noncoloring hair preparations and personal cleanliness products.

Voluntary filing of product formulation data with FDA by cosmetic manufacturers and formulators conforms to the tabular format listing preset ingredient concentration ranges and product categories in accordance with Title 21 section 720.4 of the Code of Federal Regulations.[42]

Since certain cosmetic ingredients are supplied by the manufacturer at less than 100% concentration, the value reported by the cosmetic formulator may not necessarily reflect the actual concentration found in the finished product; the actual concentration would be a fraction of that reported to the FDA. Data

TABLE 10. Product Formulation Data[41]

Product category	Total no. of formulations in category	Total no. containing ingredient	No. of product formulations within each concentration range (%)					
			> 25–50	> 10–25	> 5–10	> 1–5	> 0.1–1	≤ 0.1
Oleic Acid								
Baby shampoos	35	1	—	1	—	—	—	—
Baby lotions, oils, powders, and creams	56	1	—	—	—	1	—	—
Other baby products	15	2	—	1	—	1	—	—
Bath oils, tablets, and salts	237	1	—	—	1	—	—	—
Eyeliner	396	16	—	1	—	7	8	—
Eye shadow	2582	5	—	—	—	2	3	—
Eye makeup remover	81	2	—	—	—	2	—	—
Mascara	397	41	—	—	23	11	7	—
Other eye makeup preparations	230	1	—	—		1	—	—
Sachets	119	4	—	—	—	—	4	—
Other fragrance preparations	191	8	—	—	—	2	6	—
Hair conditioners	478	1	1	—	—	—	—	—
Permanent waves	474	1	—	—	—	—	—	1
Hair shampoos (noncoloring)	909	9	—	2	—	7	—	—
Tonics, dressings, and other hair grooming aids	290	1	—	—	—	—	1	—
Hair dyes and colors (all types requiring caution statement and patch test)	811	205	—	150	—	49	5	1
Hair tints	15	14	—	13	—	1	—	—
Hair shampoos (coloring)	16	7	—	—	—	6	1	—
Hair lighteners with color	2	1	—	—	—	1	—	—
Hair bleaches	111	8	3	3	1	1	—	—
Blushers (all types)	819	10	—	—	—	10	—	—
Face powders	555	1	—	—	—	—	1	—
Makeup foundations	740	20	—	—	—	15	5	—
Lipstick	3319	1	—	—	1	—	—	—
Makeup bases	831	5	—	—	—	2	2	1
Other makeup preparations (not eye)	530	4	—	3	—	—	1	—

TABLE 10. (Continued)

Product category	Total no. of formulations in category	Total no. containing ingredient	No. of product formulations within each concentration range (%)					
			> 25–50	> 10–25	> 5–10	> 1–5	> 0.1–1	≤ 0.1
Nail basecoats and undercoats	44	1	—	1	—	—	—	—
Bath soaps and detergents	148	5	—	—	—	4	1	—
Other personal cleanliness products	227	3	—	—	1	2	—	—
Aftershave lotions	282	3	—	—	—	—	2	1
Shaving cream (aerosol, brushless, and lather)	114	2	—	—	—	2	—	—
Skin cleansing preparations (cold creams, lotions, liquids, and pads)	680	10	—	—	—	5	5	—
Face, body, and hand skin care preparations (excluding shaving preparations)	832	11	—	1	1	2	7	—
Hormone skin care preparations	10	1	—	—	—	1	—	—
Moisturizing skin care preparations	747	14	—	—	—	4	10	—
Other skin care preparations	349	2	—	—	—	1	1	—
Suntan gels, creams, and liquids	164	2	—	—	—	2	—	—
1981 TOTALS		424	4	176	28	142	70	4
Lauric Acid								
Hair shampoos (noncoloring)	909	3		1		2	—	—
Tonics, dressings, and other hair grooming aids	290	3	—	—	—	—	3	—
Deodorants (underarm)	239	5	—	—	—	—	4	1
Other personal cleanliness products	227	4	—	—	1	—	2	1
Shaving cream (aerosol, brushless, and lather)	114	3	—	—	1	2	—	—

Skin cleansing preparations (cold creams, lotions, liquids, and pads)	680	3	—	—	—	3	—	—
Moisturizing skin care preparations	747	1	—	—	—	—	1	—
1981 TOTALS		22	—	1	2	7	10	2
Palmitic Acid								
Eye shadow	2582	1	—	—	1	—	—	—
Hair shampoos (noncoloring)	909	2	—	—	—	2	—	—
Makeup foundations	740	2	—	—	—	1	1	—
Bath soaps and detergents	148	1	—	—	1	—	—	—
Shaving cream (aerosol, brushless, and lather)	114	4	—	—	3	—	1	—
Skin cleansing preparations (cold creams, lotions, liquids, and pads)	680	8	—	1	1	6	—	—
Face, body, and hand skin care preparations (excluding shaving preparations)	832	3	—	—	—	1	2	—
Moisturizing skin care preparations	747	3	—	—	—	1	2	—
Night skin care preparations	219	3	—	2	—	1	—	—
Other skin care preparations	349	1	—	—	—	1	—	—
Suntan gels, creams, and liquids	164	1	—	1	—	—	—	—
1981 TOTALS		29	—	4	6	13	6	—

Product category	*Total no. of formulations in category*	*Total no. containing ingredient*	*No. of product formulations within each concentration range (%)*						
			> 50	*> 25–50*	*> 10–25*	*> 5–10*	*> 1–5*	*> 0.1–1*	*≤ 0.1*
Myristic Acid									
Mascara	397	2	—	—	—	—	—	2	—
Hair shampoos (noncoloring)	909	2	—	—	—	—	2	—	—
Bath soaps and detergents	148	3	—	—	1	2	—	—	—
Other personal cleanliness products	227	2	—	—	2	—	—	—	—

TABLE 10. (Continued)

Product category	Total no. of formulations in category	Total no. containing ingredient	No. of product formulations within each concentration range (%)						
			> 50	> 25–50	> 10–25	> 5–10	> 1–5	> 0.1–1	≤ 0.1
Beard softeners	4	2	—	2	—	—	—	—	—
Shaving cream (aerosol, brushless, and lather)	114	16	—	—	—	1	15	—	—
Other shaving preparation products	29	1	—	—	—	—	—	1	—
Skin cleansing preparations (cold creams, lotions, liquids, and pads)	680	5	—	—	1	3	1	—	—
Face, body, and hand skin care preparations (excluding shaving preparations)	832	2	—	—	—	—	1	1	—
Moisturizing skin care preparations	747	1	—	—	—	—	—	1	—
1981 TOTALS		36	—	2	4	6	19	5	—
Stearic Acid									
Baby lotions, oils, powders, and creams	56	9	—	—	—	2	5	2	—
Other baby products	15	1	—	—	1	—	—	—	—
Other bath preparations	132	3	—	—	—	—	2	1	—
Eyebrow pencil	145	9	—	—	4	5	—	—	—
Eyeliner	396	55	—	5	6	4	29	11	—
Eye shadow	2582	128	—	—	—	—	111	17	—
Eye lotion	13	1	—	—	—	—	1	—	—
Eye makeup remover	81	1	—	—	—	—	—	1	—
Mascara	397	139	—	5	5	20	83	26	—
Other eye makeup preparations	230	26	—	—	—	2	20	4	—
Colognes and toilet waters	1120	3	—	—	—	—	3	—	—
Perfumes	657	3	—	—	—	—	3	—	—
Sachets	119	32	—	—	—	8	23	1	—
Other fragrance preparations	191	34	—	—	—	3	27	4	—

Hair conditioners	478	18	—	—	—	—	9	7	2
Hair sprays (aerosol fixatives)	265	1	—	—	—	—	1	—	—
Hair straighteners	64	6	—	—	—	2	—	4	—
Hair shampoos (noncoloring)	909	17	—	—	1	9	4	3	—
Tonics, dressings, and other hair grooming aids	290	18	1	—	1	4	7	4	1
Hair dyes and colors (all types requiring caution statement and patch test)	811	76	—	—	—	—	76	—	—
Hair bleaches	111	4	—	—	—	—	1	3	—
Other hair coloring preparations	49	8	—	—	8	—	—	—	—
Blushers (all types)	819	47	—	—	—	2	44	1	—
Face powders	555	2	—	—	—	—	—	2	—
Makeup foundations	740	190	—	—	2	3	179	6	—
Lipstick	3319	27	—	—	6	—	14	7	—
Makeup bases	831	263	—	—	1	1	256	5	—
Rouges	211	9	—	—	—	1	7	1	—
Makeup fixatives	22	1	—	—	—	—	1	—	—
Other makeup preparations (not eye)	530	20	—	—	1	—	18	1	—
Cuticle softeners	32	10	—	—	1	1	5	3	—
Nail creams and lotions	25	6	—	—	—	—	6	—	—
Other manicuring preparations	50	2	—	—	—	1	1	—	—
Bath soaps and detergents	148	13	—	—	9	1	3	—	—
Deodorants (underarm)	239	8	—	—	1	1	6	—	—
Other personal cleanliness products	227	8	—	—	1	—	7	—	—
Aftershave lotions	282	5	—	—	—	—	3	2	—
Shaving cream (aerosol, brushless, and lather)	114	100	—	7	11	63	16	3	—
Shaving soap (cakes, sticks, etc.)	7	1	—	1	—	—	—	—	—
Other shaving preparation products	29	6	—	—	2	—	4	—	—
Skin cleansing preparations (cold creams, lotions, liquids, and pads)	680	173	—	—	18	12	118	24	1

TABLE 10. (Continued)

Product category	*Total no. of formulations in category*	*Total no. containing ingredient*	*No. of product formulations within each concentration range (%)*						
			> 50	*> 25–50*	*> 10–25*	*> 5–10*	*> 1–5*	*> 0.1–1*	*≤ 0.1*
Face, body, and hand skin care preparations (excluding shaving preparations)	832	432	—	2	32	39	325	34	—
Hormone skin care preparations	10	3	—	—	1	1	1	—	—
Moisturizing skin care preparations	747	327	—	2	11	21	259	33	1
Night skin care preparations	219	67	—	—	3	9	48	6	1
Paste masks (mud packs)	171	15	—	—	1	5	9	—	—
Skin lighteners	44	11	—	—	3	—	8	—	—
Skin fresheners	260	4	—	—	4	—	—	—	—
Wrinkle smoothers (removers)	38	4	—	—	—	—	4	—	—
Other skin care preparations	349	55	—	—	13	8	31	3	—
Suntan gels, creams, and liquids	164	48	—	—	1	3	36	8	—
Indoor tanning preparations	15	3	—	—	—	—	—	3	—
Other suntan preparations	28	13	—	—	—	—	12	1	—
1981 TOTALS		2465	1	22	148	231	1826	231	6

submitted within the framework of preset concentration ranges provide the opportunity for overestimation of the actual concentration of an ingredient in a particular product. An entry at the lowest end of a concentration range is considered the same as one entered at the highest end of that range, thus introducing the possibility of a 2- to 10-fold error in the assumed ingredient concentration.

Products containing these fatty acid ingredients may contact the skin, hair, and eyes. Use of Oleic and Stearic Acids in lipstick and manicuring preparations may lead to ingestion of small quantities of these ingredients. Frequency of application of the fatty acids may range from once per week to several times per day, from less than 1 h to several hours, due to the variety of cosmetic products in which they are contained.

Noncosmetic Use

Oleic, Lauric, Palmitic, Myristic, and Stearic Acids are used in foods as plasticizing, lubricating, binding, and defoaming agents and as reagents in the manufacture of other food-grade additives.[8,20,43] Myristic Acid is used as a flavoring agent in foods.[11]

Straight-chain monobasic carboxylic acids from fats and oils derived from edible sources, such as the fatty acids, Oleic, Lauric, Palmitic, Myristic, and Stearic Acids, are accepted as safe for use in food and in the manufacture of food-grade additives providing they meet particular conditions and specifications.[42] The unsaponifiable matter in the fatty acid or fatty acid-derived food additive must not exceed 2%, the food additive must be free of chick-edema factor, and it must be produced and labeled in accordance with good manufacturing practice.[42]

The fatty acids as a group are permitted as direct food additives.[42] Oleic Acid derived from tall oil and Oleic Acid meeting the specifications in Section 172.860 are permitted as direct food additives.[42] Oleic Acid is also allowed as a food additive in preparations of Polysorbate 80 for which it was used as a reagent.[42] Stearic Acid is permitted as a direct food additive in chewing gum base.[42]

Particular salts of fatty acids are allowed as direct food additives.[42] These salts are not reviewed in this report.

There are no limitations other than the observance of current good manufacturing practice[42] on the use of Oleic and Stearic Acids as indirect food additives.[42] These two fatty acids are also listed as substances that are GRAS.[42]

Regulation of Oleic and Stearic Acids as GRAS substances is based on reviews and evaluation by the Select Committee on GRAS Substances (SCOGS).[44,45] Monographs prepared for these evaluations also are available.[46,47] Several additional reports on fatty acid salts and various ester derivatives have been developed by SCOGS.[48]

FDA files contain both published and unpublished data on the Oleic Acid Group fatty acids (and some of their salts) in the form of Flavor and Extract Manufacturers' Association Monographs, Food Additive Safety Profiles, GRAS Monographs, GRAS Petitions, Food Additive Petitions, and Color Additive

Petitions.* The agency's food safety evaluation of these fatty acids and their salts as direct and indirect food additives and as GRAS substances was based on reviews of these data (document dates range from 1928 to 1977).

Unpublished data from industry submissions to FDA include a two-generation feeding and reproduction study in the rat using Oleic Acid derived from tall oil,[49] a 90-day subchronic oral toxicity study of food-grade Oleic Acid in rats,[50] a 52-day subchronic feeding study of rats using Stearic Acid mixed with lactate salts,[51] a 1-month feeding study of control rats using Stearic Acid as a diet supplement,[52] and a 209-day chronic oral toxicity study of control rats fed a diet supplement of Stearic Acid.[53]

Fatty acids have pharmaceutical uses as lubricants in tablet formulations, in the manufacture of their salts for ointment base emulsifiers,[5] and as calorie sources in parenteral and enteral nutrition therapy.[54] Stearic Acid is widely used in the pharmaceutical coating of enteric pills and bitter remedies and in the preparation of suppositories and ointments.[1,5]

None of the five Oleic Acid Group fatty acids are currently on the Over-The-Counter (OTC) Ingredient list of substances currently being reviewed by OTC scientific panels.[55] Several OTC advisory review panels have determined the level of efficacy of Stearic Acid in the (1) miscellaneous external drug product, (2) topical analgesic including antirheumatic, otic, burn, sunburn treatment, and prevention products, (3) antimicrobial II, and (4) contraceptive and other vaginal drug products categories. However, no determination of its safety was made.[56] Sodium Oleate is under review as a stimulant laxative by the OTC Panel for review of laxatives.[55] The ingredients, "fatty acid," "Oleic Acid," and "Stearic Acid" are listed as "inactive ingredients for approved prescription drug products" that are not required in labeling of these products.[57] The "Inactive Ingredient" list also contains common sources for the fatty acids, such as olive, peanut, cottonseed, nutmeg, tall, and coconut oils.

Fatty acids are used in the manufacture of soaps, detergents, metal salts, driers, and rubber; they are used as solvents for water-insoluble compounds, in polishing compounds, lubricating oils, waterproofing, in candles, phonograph records, insulators, modeling compounds, and as intermediates in chemical synthesis.[1,11,20,43]

Recent clinical uses for fatty acids are their conjugation with antibodies to aid incorporation of the proteins into membranes[58] and their conjugation with antigens for immune potentiation.[59] A derivative of Stearic Acid is commonly used as a paramagnetic probe in the measurement of membrane fluidity by electron spin resonance spectroscopy,[60] and radioactive Palmitic Acid is a diagnostic radiotracer in positron emission tomography.[61]

BIOLOGY

Absorption, Distribution, Metabolism, Excretion

The digestion of dietary fatty acids, their absorption in micellar aggregates, and their transport esterified to glycerol in chylomicrons and very low density

*A listing of these documents was obtained through the Freedom of Information Act. Copies of and notes taken from originals have been placed in Cosmetic Ingredient Review (CIR) files.

lipoproteins has been reviewed.[62-65] Oleic, Palmitic, Myristic, and Stearic Acids are primarily transported via the lymphatic system, and Lauric Acid is transported by the lymphatic and (as a free fatty acid) portal systems.[64] Fatty acids originating from adipose tissue stores are either bound to serum albumin or remain unesterified in the blood.[66,67]

Absorption and distribution studies of some fatty acids were reported in GRAS evaluations and scientific literature reviews of Stearic[45,46] and Oleic Acids[44,47] and the sodium salts of oleate and palmitate.[68] Metabolizable energy values and digestibility coefficients were calculated for Oleic and Stearic Acids in rats, pigs, and chickens. Distribution of radioactivity into various lipid classes in lymph from the thoracic duct of rats was followed for Oleic and Palmitic Acids.

Another monograph on Stearic Acid reviewed its digestion, absorption, and metabolism.[69] It was noted that several investigators found that increasing fatty acid chain length slightly decreased their digestibility; Stearic Acid was the most poorly absorbed of the common fatty acids.[70,71]

Oleic Acid has been reported to penetrate the skin of rats.[72] On histological examination, fluorescence from absorbed Oleic Acid was found in epidermal cell layers of skin removed from treated rats within 10 min of its application. The path of penetration was suggested to be via the hair follicles.[73] Only minute amounts of Oleic Acid were visualized in the blood vessels throughout the experiment. Skin permeability was shown to increase with the lipophilic nature of a compound.[74]

Radioactivity has been traced to the heart, liver, lung, spleen, kidney, muscle, intestine, adrenal, blood, and lymph, and adipose, mucosal, and dental tissues after administration of radioactive Oleic, Palmitic, and Stearic Acids.[69,75,76] The sites of the radioactive atoms (^{3}H, ^{14}C, ^{131}I) were not stated in these studies. Radioactive fatty acids were administered orally, intravenously, intraperitoneally, and intraduodenally into rats, dogs, sheep, chicks, frogs, and humans in various physiological states. Uptake and transport of fatty acids into the brain have been observed.[77]

Proposed mechanisms for fatty acid uptake by different tissues range from passive diffusion to facilitated diffusion or a combination of both.[78,79] Fatty acids taken up by the tissues can either be stored in the form of triglycerides (98% of which occurs in adipose tissue depots) or they can be oxidized for energy via the β-oxidation and tricarboxylic acid cycle pathways of catabolism.[80]

The β-oxidation of fatty acids occurs in most vertebrae tissues (except the brain) using an enzyme complex for the series of oxidation and hydration reactions resulting in the cleavage of acetate groups as acetyl-CoA (coenzyme A). An additional isomerization reaction is required for the complete catabolism of Oleic Acid.[63] Alternate oxidation pathways can be found in the liver (ω-oxidation) and in the brain (α-oxidation).[81-83]

Fatty acid biosynthesis from acetyl-CoA takes place primarily in the liver, adipose tissue, and mammary glands of higher animals. Successive reduction and dehydration reactions yield saturated fatty acids up to a 16-carbon chain length. Stearic Acid is synthesized by the condensation of palmitoyl-CoA and acetyl-CoA in the mitochondria, and Oleic Acid is formed via a monooxygenase system in the endoplasmic reticulum.[4,82]

Fatty acid metabolism has been extensively studied under various physiological conditions,[84-86] in mammalian development,[87,88] in various organisms,[89] as affected by xenobiotics, such as ethanol[90,91] and drugs.[92] The regulation of fatty acid metabolism has been reviewed.[93-96]

Simultaneous ingestion of trace amounts of ^{14}C-triolein (10 μCi) and ^{3}H-Oleic Acid (20 μCi) in 42 g of carrier fat by patients with normal fecal fat excretion resulted in estimated fecal excretion of less than 10% of both substances.[97] Gastrointestinal transit times for ^{14}C-triolein, ^{3}H-Oleic Acid, and a nonabsorbable marker, $^{51}CrCl_3$, did not differ significantly.

Fatty acid metabolism has been studied in several tissues. Interest in the correlation between fatty acids, cholesterol, and coronary heart disease has spurred extensive research on myocardial fatty acid metabolism.[98-101] Fatty acid metabolism has also been studied in the liver,[102-104] the intestine and intestinal microflora,[105,106] the lungs,[107] the kidneys,[108-110] skeletal muscle,[111] bone and cartilage,[112] and oral mucosal epithelium.[113]

Maternal–Fetal Transfer

Free fatty acids readily cross the placental barrier in rabbits, guinea pigs, rats, and humans.[114-118] A bolus of 1-^{14}C-Palmitic Acid was injected over 10 sec into the carotid artery of 4 pregnant guinea pigs ranging in gestational age from 48 to 65 days.[119] The fetal side of the placenta was perfused in situ. A rapid decline in maternal plasma radioactivity and a rapid appearance of radioactivity in the perfusate were observed. The disappearance profile of fetal radioactivity essentially paralleled that of maternal radioactivity after a lag time of 1.6 min. Other studies of maternal–fetal transfer of fatty acids were performed primarily with albumin-bound or lipoprotein-emulsified 1-^{14}C-Palmitic Acid.[119,120]

Dietary Fat and Coronary Heart Disease

The Select Committee on GRAS Substances stated its "concern over the role of saturated versus polyunsaturated fatty acids in the etiology of arteriosclerosis and associated vascular diseases" in their review of Stearic Acid.[45] The Committee noted a joint statement by the Food and Nutrition Board of the National Research Council and the Council on Foods and Nutrition of the American Medical Association that acknowledged the importance of reducing the intake of saturated fatty acids and cholesterol.[121] Cholesterol has been reviewed by Cosmetic Ingredient Review.[122]

Current studies and reviews confirm the correlation between dietary saturated fatty acid intake and the incidence of atherosclerosis and thrombosis found in earlier studies and reports.[123,124] Research is now focused on the mechanism(s) of induction and the elucidation of the multifactorial influence of diet on coronary heart disease.[100,101]

TABLE 11. Antimicrobial Activity of Fatty Acids[125, 126]

	Oleic Acid	*Lauric Acid*	*Palmitic Acid*	*Myristic Acid*	*Stearic Acid*
Organism	*Minimal Inhibitory Concentration (mM)*				
Aspergillus niger	—	> 4	—	—	—
Bacillus cereus	—	> 2	—	—	—
Bacillus subtilis	—	> 2, 0.5[b]	—	—	—
Candida albicans	NI[a]	2.49	NI	4.37	NI
Candida utilis	—	4, 1[b]	—	—	—
Micrococcus lysodeikticus	—	> 2	—	—	—
Penicillium citrinum	—	4	—	—	—
Pseudomonas aeruginosa	NI	NI	—	—	—
Streptococcus pneumoniae	NI	0.062	0.48	0.218	NI
Saccharomyces cerevisiae	—	> 4	—	—	—
Staphylococcus aureus	NI	2.49	NI	4.37	NI
Streptococcus Group A	1.77	0.124	3.9	0.547	NI
Streptococcus β-hemolytic type	—	0.249	3.9	2.18	NI

[a]NI, not inhibitory at concentrations tested (1.0 mg/ml or 3–6.0 m*M*).
[b]1st value obtained by agar dilution method, 2nd value obtained by broth dilution method.

Antimicrobial Activity

The antibacterial activities of Oleic, Lauric, Palmitic, Myristic, and Stearic Acids were studied by placing them in liquid broths containing different microorganisms.[125] Minimal inhibitory concentrations at 37°C were determined. Results of this study and of other studies on bacteria and fungi[126] are presented in Table 11.

The effects of Oleic, Lauric, Palmitic, Myristic, and Stearic Acids on aflatoxin B_1 production and growth of the fungus *Aspergillus parasiticus* were studied.[127] Concentrations of 5 m*M* fatty acid were added to liquid medium containing "three drops of the emulsifier, Tween-80." Myristic, Palmitic, and Stearic Acids stimulated and Oleic Acid inhibited toxin synthesis. Lauric Acid inhibited fungal growth.

The antiviral activity of Oleic Acid and other unsaturated fatty acids was studied.[128] These fatty acids inactivated enveloped viruses, such as herpes, influenza, Sendai, and Sindbis viruses at concentrations from 5 to 50 μg/ml. "Naked" viruses, such as polio, SV40, and encephalomyocarditis viruses, were not affected, indicating a direct memebrane effect. Stearic Acid did not inactivate any of the viruses at the concentrations tested.

TOXICOLOGY

Reviews of the literature from 1933 to 1976 were prepared for the safety evaluations of Oleic and Stearic Acids as GRAS substances by FDA[44–47] and of Stearic Acid as a fragrance raw material by Research Institute for Fragrance

Materials (RIFM).[69] RIFM Reviews of Oleic and Myristic Acids have been prepared and are pending publication. A subchronic oral toxicity study of Palmitic Acid was presented in a GRAS monograph on sodium oleate and sodium palmitate.[68]

Oral Toxicity Studies

Acute Oral Toxicity

Oleic, Lauric, Palmitic, Myristic, and Stearic Acids were tested for acute oral toxicity to rats (Table 12).

Administration of doses up to 21.5 ml/kg of Oleic Acid and up to 10.0 g/kg of Palmitic and Myristic Acids (commercial grades) by gavage to albino rats resulted in no deaths and no significant gross lesions at necropsy.[129,130] Doses of 10.0 g/kg of commercial grade Lauric Acid and of 25% (w/v) Stearic Acid in corn oil produced the deaths of 1 rat in each group. At necropsy of these rats, congested lungs and kidneys and advanced autolytic changes were observed. No significant gross lesions were found at necropsy of 2 rats of the 0.464 and 4.64 g/kg triple-pressed Stearic Acid dose groups. Transient signs of toxicity were observed in rats of the higher dose groups of 10.0 and 21.5 ml/kg Oleic Acid, 10.0 g/kg 25% Stearic Acid in corn oil, and the 4.64 and 10.0 g/kg Lauric, Palmitic, Myristic, and triple-pressed Stearic Acids. Signs of toxicity included slight depression, depressed righting and placement reflexes, oily and unkempt fur, mucoid diarrhea, excessive salivation, and sero-sanguineous discharge from the muzzle and eyes.

A cream formulation containing 5% Oleic Acid administered to rats at a dose of 5 ml/kg produced no mortalities. Signs of toxicity included transient weakness in the legs and colored urine and feces.[131]

Oral administration of a 5.0 g/kg dose of a product formulation containing 8.7% Lauric Acid to rats produced slight toxicity and no deaths.[132]

A shave cream formulation containing 2.2% Palmitic Acid administered to rats at a dose of 5 g/kg produced no deaths and was classified as "non-toxic."[133]

White rats were fed a diet containing 50% Stearic Acid.[144] Treated male rats died after an average of 8.2 days and female rats died after 10.2 days. Spasms and paralysis of the extremities of some rats and cardiac irregularities were observed immediately preceding death. With a lower concentration of 15% Stearic Acid in the diet, the rats lived for a much longer period.

In three studies, groups of 5 male albino rats received oral doses of 0.464–10.0 g/kg "eutectic, triple-pressed" Stearic Acid and 25% (w/v) Stearic Acid in corn oil,[130] or approximately 16% Stearic Acid in ethylene oxide and water (65% solution in ethylene oxide diluted 1:3 in water).[134] There were 2 deaths in the 4.64 g/kg dose group of the first study and 1 death in the 10.0 g/kg dose groups of the second and third studies.

A dose of 5 g/kg of a face cream formulation containing 13% Stearic Acid produced no deaths when administered to albino rats by gavage.[135] Skin lotion formulations containing 2.8% Stearic Acid administered at doses of 15 g/kg by gavage to groups of 10 albino rats resulted in 1 death in 1 group.[136,137]

At necropsy of the rat that died, fibrous tissue around the heart and reddish fluid throughout the thoracic cavity were observed. Normal behavior and appearance were observed, and there were no gross alterations in surviving rats. Slight dehydration and depression were observed in 1 rat.

In other studies, testing for acute oral toxicity of skin lotion formulations containing 2.8% Stearic Acid by administration of 5 ml/kg[140-143] and 5 g/kg[138,139] doses of the formulations resulted in few, if any, deaths. At necropsy of the rats that died, fibrous tissue encasing the heart and lungs was observed.

Subchronic and Chronic Oral Toxicity

Feeding of 5% Oleic Acid or 50% Stearic Acid diets to chicks for 4 weeks had no adverse effects (Table 13).[145,146] Decreased clotting time, moderate hyperlipemia, and severe phlebothrombosis following initiation with an intravenous injection of lipopolysaccharide from *Salmonella typhosa* were observed in rats fed high-fat diets containing 5% Stearic Acid.[147,148] Rats fed diets containing 4.6 g/kg/day Palmitic Acid for 6 weeks developed hyperlipemia.[148] A diet containing 50% Stearic Acid fed to rats for 8 weeks resulted in a microscopic "foreign body-type reaction" in adipose tissue.[149] Rats fed high-fat diets containing 6% Stearic Acid for 9 weeks developed severe aortic atherosclerosis and thrombosis induced by *S. typhosa* lipopolysaccharide; high mortality was also observed.[147]

Feeding 15% Oleic Acid diets to rats for 10–16 weeks had no adverse effects on growth or general health.[150] Of 4 female weanling rats fed the diet for 16 weeks, "all 4 were able to become pregnant; however 2 died at parturition, a litter was eaten at birth, and the remaining litter died within 3 days of birth." Mating of 7 adult female rats fed the diet for 16 weeks resulted in production of 52 young, 44 of which survived 1 week and 11 of which survived 3 weeks. Mammary development was retarded, and a few rats had ovarian cysts. No lesions were found in other organs.

A "foreign body-type reaction" in perigonadal fat and the reversible formation of lipogranulomas were observed in rats fed 50 g/kg/day Stearic Acid for 24 weeks.[151] Anorexia, severe pulmonary infection, and high mortality were observed in rats fed diets containing 3000 ppm Stearic Acid for 30 weeks.[152]

Dermal Toxicity Studies

Acute Dermal Toxicity

Oleic, Palmitic, and Stearic Acids were tested for acute dermal toxicity after topical application and intradermal administration to the skin of guinea pigs, rabbits, and mice (Table 14).

In one study, application of commercial grade Oleic Acid to the skin of guinea pigs produced no deaths and no signs of toxicity. The number of applications was not stated.[153] Marked irritation characterized by crusting, ulceration, and thickening of the skin was observed following topical application of commercial grade Oleic Acid to the skin of rabbits, guinea pigs, and

TABLE 12. Acute Oral Toxicity Studies

Fatty acid tested	*Dose*	*Species (No. per group)*	*Results*	*Reference*
Oleic Acid[a]	5.0 g/kg	5 albino rats (bodyweight 193–217 g)	Range of BW after 7 days—235–273 g. No deaths. Signs of toxicity not reported. Oleic Acid classified "slightly toxic by ingestion"	129
Oleic Acid[b]	0.464, 1.00, 2.15, 4.64, 10.0, 21.5 ml/kg	5 male albino rats (BW 214–220 g)	LD_{50} > 21.5 ml/kg. Range in avg. BW gains 65–99. No deaths in any group	130
Oleic Acid—5.0% in cream formulation	5 ml/kg of cream	10 Fischer 344 rats (BW 135–175 g)	No deaths. Transient leg weakness, colored urine and feces	131
Lauric Acid[a]	0.464, 1.00, 2.15, 4.64, 10.0 g/kg	5 male albino rats (BW 221–247 g)	Range, avg. BW gain—73–99 g. One death in group given 10.0 g/kg dose on 1st postdosage day	130
Lauric Acid—8.7% in product formulation	5.0 g/kg of product	5 albino rats (BW 155–160 g)	BW range after 7 days—209–230 g. No deaths. Signs of toxicity not reported. Lauric Acid classified "slightly toxic by ingestion"	132
Palmitic Acid[a]	0.464, 1.00, 2.15, 4.64, 10.0 g/kg	5 male albino rats (BW 209–254 g)	Range, avg. BW gain—65–92 g. No deaths	130
Palmitic Acid—2.2% in shave cream formulation	5 g/kg of cream	≥ 10 albino rats (BW 200–300 g)	Formulation classified "non-toxic." No data or procedures (other than administration by gavage) reported; reference for test method - 16 CFR 1500.3(b)(6)(i)(A)	133
Myristic Acid[a]	0.464, 1.00, 2.15, 4.64, 10.0 g/kg	5 male albino rats (BW 208–211 g)	Range, avg. BW gain—75–95 g. No deaths	130
Stearic Acid (eutectic)[a]	0.464, 1.00, 2.15, 4.64, 10.0 g/kg	5 male albino rats (BW 213–223 g)	Range, avg. BW gain—71–101 g. One death in 4.64 g/kg dose group on day of dosage; one death in 4.64 g/kg dose group on final day of study	130

Stearic Acid—25% (w/v) in corn oil	0.464, 1.00, 2.15, 4.64, 10.0 g/kg	5 male albino rats (BW 216–225 g)	Range, avg. BW gain—90–104 g at lower doses, 77 g at 10.0 g/kg dose. One death in 10.0 g/kg on Day 7 of study	130
Stearic Acid—65% in ethylene oxide, diluted 1 : 3 in water	5 and 10 g/kg	10 male young adult ARS/Sprague-Dawley albino rats (BW 215–239 g)	Final avg. BW 5 g/kg group—317 g; 10 g/kg group—258 g. One death in 10 g/kg dose group on Day 5 following dosage. No pharmacotoxical signs noted. No remarkable alterations at necropsy	134
Stearic Acid—13% in face cream formulation	5 g/kg face cream	≥ 10 albino rats (BW 200–300 g)	Formulation classified "non-toxic." No procedures (other than administration by gavage) or data reported. Reference for test method - 21 CFR 1500.3(b)(6)(i)(A)	135
Stearic Acid—2.8% in skin lotion formulation	15 g/kg skin lotion	10(5M, 5F)albino rats (BW 206–258 g)	Final BW range—228–378 g. One death on Day 2	136
Stearic Acid—2.8% in skin lotion formulation	15 g/kg skin lotion	10(5M, 5F)albino rats (BW 218–254 g)	Final BW range—198–414 g. No deaths	137
Stearic Acid—2.8% in skin lotion formulation	5 g/kg skin lotion	10(5M, 5F)albino rats (BW 184–238 g)	Final BW range—174–386 g. Two deaths on Days 9 and 10	138
Stearic Acid—2.8% in skin lotion formulation	5 g/kg skin lotion	10(5M, 5F)albino rats (BW 202–264 g)	Final BW range—210–430 g. One female rat died on Day 7 postdosage. All rats appeared normal throughout study. At necropsy, fibrous tissue was observed encasing heart and lungs of rat that died and no gross changes were observed in other rats	139
Stearic Acid—2.8% in skin lotion formulation	5.0 ml/kg skin lotion	10 Sprague-Dawley rats (BW 200–254 g)	Range in BW gain—75–127 g. No deaths. All rats appeared normal throughout study. At necropsy, thoracic and abdominal organs appeared normal.	140
Stearic Acid—2.8% in skin lotion formulation	5.0 ml/kg skin lotion	10 Sprague-Dawley rats (BW 174–200 g)	Range in BW gain—85–118 g. No deaths. All rats appeared normal throughout study. At necropsy, thoracic and abdominal organs appeared normal	141
Stearic Acid—2.8% in skin lotion formulation	5.0 ml/kg skin lotion	10 Sprague-Dawley rats (BW 175–189 g)	Range in BW gain—42–118 g. No deaths. All rats appeared normal throughout study. At necropsy, thoracic and abdominal organs appeared normal	142
Stearic Acid—2.8% in skin lotion formulation	5.0 ml/kg skin lotion	6 Sprague-Dawley rats (BW 205–214 g)	Range in BW gain—102–129 g. No deaths. All rats appeared normal throughout study. At necropsy, thoracic and abdominal organs appeared normal	143
Stearic Acid	5 g/kg	rat	No deaths	45

[a]Fatty acid commercially supplied.

[b]These studies were cited in reviews for the safety assessment of particular fatty acids as they are used in foods[44–47, 68] and in fragrances.[69]

TABLE 13. Subchronic and Chronic Oral Toxicity Studies[a]

Study type	*Fatty acid tested*	*Species*	*Results*	*Reference*
Subchronic feeding study (4 weeks)	Stearic Acid—50% in diet	Chick	No adverse effects	145, 146
Subchronic feeding study (4 weeks)	Oleic Acid—5% in diet	Chick	No adverse effects	145
Subchronic feeding study (6 weeks)	Stearic Acid—5% in high-fat diet	Rat	Decreased clotting time, moderate hyperlipemia, severe phlebothrombosis after initiation with *S. typhosa* lipopolysaccharide (LPS)	147, 148
Subchronic feeding study (6 weeks)	Palmitic Acid—4.6 g/kg/day in diet	Rat	Most hyperlipemic of all fatty acids tested (versus Lauric, Myristic, and Stearic Acids). Second to Stearic Acid in thrombogenic effect	148
Subchronic feeding study (8 weeks)	Stearic Acid—50% in diet	Rat	Microscopic foreign body type reaction in excised fat. No reaction in controls	149
Subchronic feeding study (9 weeks)	Stearic Acid—6% in high-fat diet	Rat	Severe aortic atherosclerosis, high mortality, severe thrombosis after *S. typhosa* LPS initiation	147
Subchronic feeding study (10 weeks)	Oleic Acid—15% in diet	Rat	Normal appearance. Mammary gland underdeveloped; few rats with ovarian cysts. No lesions in non-reproductive organs. Production of 52 young by 7 adult females—11/52 survived by 3rd week	150
Chronic feeding study (16 weeks)	Oleic Acid 15% in diet	Rat	No impairment of males' fertility. 4/4 females became pregnant; 2/4 deaths at parturition; 1 litter died within 3 days of birth	150
Chronic feeding study (20 weeks)	Oleic Acid—15% in diet	Rat	Normal growth observed	150
Chronic feeding study (24 weeks)	Stearic Acid—50 g/kg/day in diet	Rat	4/5 rats had foreign body type reaction in perigonadal fat. Lipogranulomas observed. Reversible effects	151
Chronic feeding study (30 weeks)	Stearic Acid—3000 ppm in diet	Rat	Anorexia, severe pulmonary infection, high mortality. No significant pathological lesions	152

[a] These studies were cited in reviews for the safety assessment of particular fatty acids as they are used in foods[44–47, 68] and in fragrances.[69]

TABLE 14. Acute Dermal Toxicity Studies[a]

Fatty acid tested	*Dose*	*Species (No. per group)*	*Results*	*Reference*
Oleic Acid[c]	3.0 g/kg	6 guinea pigs	No deaths. Oleic Acid classified "non-toxic"	153
Oleic Acid[c]	1–2 ml	5 rabbits	Potent depilatory agent. Marked irritation. Microscopic hyper-	154[b]
	1 ml	2 guinea pigs	keratosis, acanthosis. (Observations in all 3 species)	
	0.3 ml	12 mice		
Oleic Acid—50% in mineral oil	1 ml	16 HRS/J mice	Epidermal hyperplasia and hyperkeratosis	155
Oleic Acid—25, 50, 75% in peanut oil	0.1 ml (intradermal)	2 guinea pigs	Local inflammation and necrosis. No alterations in controls given peanut oil	156[b]
Palmitic Acid—2.2% in shave cream formulation	2 g/kg	≥ 10 rabbits	No deaths. Formulation considered "non-toxic"	133
Stearic Acid—10–100 m*M* in olive oil	10–100 m*M* (intradermal)	guinea pigs rabbits	Mild erythema and slight induration of skin	157[b]

[a]Methods of most studies involved topical application of fatty acids. Intradermal administration noted parenthetically.

[b]Data from these studies were obtained from reviews for the safety assessment of particular fatty acids in foods[46, 47, 68] and fragrances.[69]

[c]Fatty acid as commercially supplied.

mice.[154] Microscopically, hyperkeratosis, pronounced acanthosis, follicular keratotic plugs, hyperplasia of sebaceous glands, and loss of hair shafts from follicles were observed. Treated skin returned to normal when treatment was discontinued.

Local skin inflammation and necrosis were observed at sites on the backs of guinea pigs receiving 0.1 ml intradermal injections of 25, 50, and 75% Oleic Acid in peanut oil and Oleic Acid as commercially supplied. No alterations were observed at sites injected with peanut oil alone.[156]

Epidermal hyperplasia and hyperkeratosis were observed in the skin of mice after topical application of 50% Oleic Acid in mineral oil.[155]

Application of a 2 g/kg dose of a shave cream formulation containing 2.2% Palmitic Acid was considered nontoxic to rabbits.[133,158]

Concentrations from 10 to 100 m*M* Stearic Acid in olive oil applied to the skin of guinea pigs and rabbits produced mild erythema and slight induration.[157]

Short-Term Dermal Toxicity

Follicular–keratogenic properties of Oleic, Lauric, Palmitic, Myristic, and Stearic Acids were studied after topical application to the skin of the external ear canal of 4 albino rabbits[159] (Table 15). A 5% (w/v) alcohol solution of Stearic Acid and alcohol solutions of the other fatty acids equimolar with the Stearic Acid solution were prepared [5% (w/v) Stearic Acid ~ 18 mmol% Stearic Acid]. A dose of 3 ml of each of the fatty acid solutions was applied once daily, 5 days per week, for 6 weeks. Controls in one group received similar treatment with absolute alcohol and those in another group received no treatment. Myristic and Palmitic Acids produced transient slight erythema and desquamation in the first 2 weeks of application. No clear alterations were observed after Stearic Acid treatment. One day after treatment with Oleic and Lauric Acids, erythema was observed. The intensity of the redness increased over the following few days and desquamation developed. Distinct follicular keratosis was observed within 1 month. After discontinuation of the applications, the erythema and scaling gradually disappeared, but the keratosis was discernible after 6 weeks.

Follicular epidermal hyperplasia was produced after topical application of undiluted commercial grade Oleic Acid (unspecified dose) to the backs of white mice 6 times per week for 1 month.[160]

In a recent study, no adverse effects were produced from subchronic topical application of Myristic Acid to rabbit skin.[161] One-half milliliter of a 30% preparation of Myristic Acid in ether and propylene glycol (solvents at a 1:1 ratio in concentration) was massaged into the depilated skin of the flanks of 5 rabbits daily for 30 days. The opposite flank of the rabbits was depilated and treated with solvent only. No significant macroscopic changes were observed. Microscopic lesions included thinning of collagen fibers in the superficial layers of the dermis after 10 days and a loose dermal infiltrate of lymphomononuclear cells and histiocytes after 20 and 30 days.

Stearic Acid application had little effect on the epidermis of rats.[72] Hair on the dorsa of albino or Long-Evans rats had been closely clipped before an unspecified dose of Stearic Acid was swabbed on the treatment sites once daily for 5 days to 2 weeks.

TABLE 15. Short-term Dermal Toxicity Studies

Fatty acid tested	*Dose*	*Species*	*Method Notes*[a]	*Results*	*Reference*
Oleic Acid—~ 18 mmol% in alcohol	3 ml	4 rabbits	External ear canal, 6 weeks	Erythema, desquamation, follicular keratosis	159[b]
Oleic Acid		Mice	Dorsa for 1 month	Epidermal hyperplasia	160[b]
Lauric Acid—~ 18 mmol% in alcohol	3 ml	4 rabbits	External ear canal, 6 weeks	Results similar to those after Oleic Acid application. Follicular keratosis persisted after treatment	159[b]
Palmitic Acid—~ 18 mmol% in alcohol	3 ml	4 rabbits	External ear canal, 6 weeks	Slight irritation for first 2 weeks	159[b]
Myristic Acid—~ 18 mmol% in alcohol	3 ml	4 rabbits	External ear canal, 6 weeks	Slight irritation for first 2 weeks	159[b]
Myristic Acid—30% in ether : propylene-glycol	0.5 ml	5 rabbits	Flank, 30 days	Microscopic thinning of dermal collagen. Cellular infiltration	161
Stearic Acid—50% (w/v) in alcohol	3 ml	4 rabbits	External ear canal, 6 weeks	No alterations	159[b]
Stearic Acid—20% in product formulation	2 ml/kg of product	6 rabbits	Abraded/intact sites on back, 4 weeks	No deaths. Slight edema, desquamation	162
Stearic Acid—20% in product formulation	2 ml/kg of product	6 rabbits	Abraded/intact sites on back, 4 weeks	No deaths. Slight edema, desquamation	163

[a]All methods involved repeated topical application to noted sites.
[b]Data from these studies were obtained from reviews for safety assessment of particular fatty acids in foods[46, 47, 68] and fragrances.[69]

Stearic Acid, at a concentration of 2.0% in 2 cosmetic product formulations was tested for subchronic dermal toxicity using groups of 6 New Zealand strain albino rabbits.[162,163] Hair was clipped from the backs of the rabbits, and the skin was either abraded or left intact. Doses of 2 ml/kg of the product formulations were applied to the sites daily, 5 days per week, for a total of 20 applications. The rabbits in the untreated control group had no signs of skin irritation. No mortalities were observed in the 2 groups of rabbits receiving applications of either formulation.

In the first group, the mean percentage gain in body weight was 33%, and the skin of all 6 rabbits was slightly edematous; edema was observed in 3/6 rabbits after the first week, 1/6 rabbits during the third week, and 2/6 rabbits during the fourth week. The skin of 5 of the 6 rabbits remained edematous for the duration of the study. Two of the rabbits had slight local desquamation of the skin that was of irregular duration. The brown color of the product obscured scoring of treatment sites for erythema. Both abraded and intact skin had similar reactions to treatment with the product. Individual fluctuations in hematological values were noted in animals of all groups including controls. Slight differences in serum glutamic-pyruvic transaminase values were observed that were considered unrelated to treatment. At necropsy, organ weights of the treated group were comparable to those of controls, and the pulmonary hemorrhages observed in 1 male were considered unrelated to treatment and common in New Zealand strain rabbits. Discharge from the left eye of 1 male rabbit was noted. No significant microscopic lesions considered to be treatment-related were noted.

In the second group of 6 NZW rabbits that received applications of a product formulation containing 2.0% Stearic Acid for 4 weeks, the mean body weight gain was 18%. The skin of all 6 rabbits was slightly edematous; edema was observed in 1/6 rabbits during the first week, 1/6 rabbits during the second week, and 4/6 rabbits during the fourth week. The edema observed in the skin of the first 2 rabbits disappeared after a few days, recurring in 1 during the fourth week. One rabbit had slight atonia during the second week only. Four rabbits during the second week and 2 rabbits during the third week developed slight desquamation of the skin at treatment sites, which returned to normal. Slight scaling of the skin was observed for the duration of the study. The brown-colored product obscured scoring of treatment sites for erythema. Clinical signs of toxicity included nasal discharge in 2 male rabbits (on days 18–28 and on days 10 and 11) and scabs on the back of a female rabbit (on days 7–28). Both intact and abraded sites had similar reactions to the treatment. No distinct treatment-related effects were noted in hematological, biochemical, or organ weight values. There were no significant gross or microscopic alterations.

A facial skin care product formulation containing 5.0% Stearic Acid was applied to the shaved dorsal skin of 15 female rats of the Crl:COBS CD(SD)BR strain in a 13-week dermal toxicity study.[164] Daily doses of 4.0 ml/kg of the product were applied 5 days per week for a total of 65 applications. The treatment was estimated to provide a dose 100-fold greater than the daily exposure to humans. Controls received no treatment. There were no deaths in the treatment group and one death in the control group. No major changes in

appearance or behavior were observed that were treatment-related, although minimal to moderate skin irritation was observed in all rabbits throughout the study. Statistically significant ($p < 0.05$) changes included decreased glucose and increased serum glutamic-pyruvic transaminase concentrations during the 7th week, and decreased hemoglobin, hematocrit, mean corpuscular volume, and total erythrocyte count during the 13th week. Urinalysis values were within normal limits. At necropsy, increases in absolute weights of the liver, heart, kidneys, and adrenals and in liver/body weight ratios were statistically significant ($p < 0.05$). The apparent statistical significance between hematological, biochemical, and organ weight values of treated and control groups was within normal limits. Subclinical bronchitis and "focal interstitial mononuclear cell infiltration into the kidneys, liver and heart" were noted in an unspecified number of rats. Grade 1 hyperkeratosis was observed in 5 of 15 treated rats.

A concealing cream product formulation containing 2.4% Stearic Acid was applied to the shaved dorsal skin of 15 female Sprague-Dawley rats in a 13-week dermal toxicity study.[165] Daily doses of 227 mg/kg of the product were applied 5 days a week for a total of 65 applications. As in the preceding study,[164] the treatment was estimated to provide a dose 100 times greater than the typical human exposure. Controls received no treatment. There were no deaths or significant differences in growth rates. Sporadic and transient skin irritation was observed in the treatment group throughout the study. Statistically significant ($p < 0.05$) differences between treatment and control groups in mean hematology values (decreased hemoglobin during weeks 7 and 13, decreased hematocrit during week 7, increased mean corpuscular volume during week 13, and decreased total erythrocyte count during weeks 7 and 13) and mean serum chemistry values (decreased serum alkaline phosphatase during week 13) were within normal limits. Urinalysis values were considered normal. At necropsy, changes in mean absolute organ weight (brain) and mean relative organ weights (liver/body, spleen/body) were considered toxicologically insignificant. Minimal hyperkeratosis of the epidermis was observed in some rats.

Administration of subcutaneous Oleic Acid injections at volumes increasing from 0.25 to 0.5 ml for 400 days had no adverse effects in the growth of albino mice. The life duration of mice of both sexes was lower than that expected for normal mice.[166]

Primary Skin Irritation

The fatty acids, Oleic, Lauric, Palmitic, Myristic, and Stearic Acid, were tested for primary skin irritation from topical application to the skin of rabbits (Table 16).

In a single insult occlusive patch test (SIOPT) with 6 albino rabbits, administration of a 0.5 ml dose of Oleic Acid, as commercially supplied, resulted in a primary irritation index (PII) of 0.5 (max PII = 8.0) and mild erythema 24 h after treatment.[130] In a Repeat Open Patch study with 6 rabbits (specific procedure not reported), application of commercial grade Oleic Acid produced mild to moderate erythema after 24 h, mild to marked erythema after 48 h, and moderate to marked erythema after 72 h. Slight to moderate

TABLE 16. Primary Skin Irritation Studies

Fatty acid tested	*Dose*	*No. of Rabbits*	*Method*	*Results*	*Reference*
Oleic Acid, as commercially supplied	0.5 ml	6	SIOPT,[a] I/A[b]	PII[c] 0.50. Minimal erythema at 24 h	130
Oleic Acid, as commercially supplied	~ 0.5 ml	6	Repeat Open Patch, 24, 48, 72 h patches	Cumulative irritation increasing from mild erythema and no edema at 24 h to marked erythema and moderate edema in some rabbits at 72 h	167
Oleic Acid—5.08% in product formulation	0.5 g of product	6	Modified Draize, 3 open patches	Minimal erythema after 72 h	169
Oleic Acid—5.08% in product formulation	0.5 g of product	6	See preceding entry	Minimal erythema in 3 rabbits after 72 h	170
Oleic Acid 5 % in product formulation	0.5 ml of product	6	Daily, 14 d	PII 2.3. Slight irritation after 4–7 days	131
Lauric Acid, as commercially supplied	0.5 ml	6	SIOPT, I/A	PII 1.12. Minimal erythema after 24 h. Minimal edema at few A sites after 72 h	130
Lauric Acid—8.7% in product formulation	0.5% of product in water	6	SIOPT, I/A	PII 0. No irritation	171
Palmitic Acid, as commercially supplied	0.5 ml	6	SIOPT, I/A	PII 0. No irritation	130
Palmitic Acid—74% "plus other fatty acids"	0.5 g	6	SIOPT, I/A 4-h exposure	PII 0.2. Very slight erythema at few I and at all A sites after 4 h	172
Palmitic Acid—4.4% in product formulation	0.5 ml of product	9	SIOPT	PII 1.00. Mild erythema after 2 h. Minimal to mild erythema after 24 h	173
Palmitic Acid—4.4% in product formulation	~ 0.5 ml of product	9	SIOPT	PII 1.00. See preceding entry	174
Palmitic Acid—2.2% in product formulation	0.5 g of product	≥ 6	SIOPT, I/A	"Non-irritating." No other data or specific procedures reported	133
Myristic Acid, as commercially supplied	0.5 ml	6	SIOPT, I/A	PII 0. No irritation	130
Myristic Acid, as commercially supplied	~ 0.5 g	6	Repeat Open Patch	Cumulative irritation increasing from no to mild/moderate erythema from 24 to 72 h	175

Stearic Acid, as commercially supplied	0.5 ml	6	SIOPT, I/A	PII 0. No irritation	130
Stearic Acid (eutectic), as commercially supplied	0.5 ml	6	SIOPT, I/A	PII 0. No irritation	130
Stearic Acid, as commercially supplied	~ 0.5 ml	9	SIOPT, 2-h exposure	PII 0.33. Few rabbits with barely perceptible erythema after 24 h	176
Stearic Acid—65% in ethylene oxide	0.5 g	6	SIOPT, I/A	PII 3.00. Defined erythema and slight edema after 24 and 72 h	134
Stearic Acid—59% "plus other fatty acids"	0.5 g	6	SIOPT, I/A, 4-h exposure	PII 0. No irritation	172
Stearic Acid—45% "plus other fatty acids"	0.5 g	6	SIOPT, I/A, 4-h exposure	PII 0. No irritation	172
Stearic Acid—50% in petrolatum	~ 0.5 ml	9	SIOPT, 2-h exposure	PII 0.56. Few with mild erythema after 2 h; decreased to barely perceptible erythema after 24 h	177
Stearic Acid—35% in water	~ 0.5 ml	9	SIOPT, 2-h exposure	PII 0.33. Few with barely perceptible erythema after 2 h	178
Stearic Acid—13% in product formulation	0.5 g of product	≥ 6	SIOPT, I/A	"Non-irritating." No other data or procedures reported	179
Stearic Acid—2.8% in product formulation	0.5 ml of product	6	SIOPT, I/A	PII 1.00. Transient minimal erythema after 24 h	138
Stearic Acid—2.8% in product formulation	0.5 ml of product	6	SIOPT, I/A	PII 1.05. Transient irritation after 24 h	139
Stearic Acid—2.8% in product formulation	0.5 g of product	6	SIOPT, I/A	PII 0.92. Very slight erythema after 24 and 72 h, persisting at most A sites. Transient minimal edema	140
Stearic Acid—2.8% in product formulation	0.5 ml of product	6	SIOPT, I/A	PII 1.45. Transient minimal to defined erythema and edema after 24 h. Dry skin noted	136
Stearic Acid—2.8% in product formulation	0.5 g of product	4	SIOPT, I/A	PII 0.63. Transient very slight erythema after 24 h	143
Stearic Acid—1.0% in product formulation	0.5 ml of product	6	SIOPT, I/A	PII 2.2. Transient defined erythema and edema after 24 h	180
Stearic Acid—1.0% in product formulation	0.5 ml of product	6	SIOPT, I/A	PII 2.0. Barely perceptible erythema, transient edema after 24 h	180

[a]SIOPT, single insult occlusive patch test, usually 24 h exposure period.
[b]I/A, patches applied to intact and abraded skin sites.
[c]PII, primary irritation index (max = 8.00).

edema was observed after 72 h.[167] In Modified Draize tests,[168] 3 repeated open patch topical applications of cream blush formulations containing 5.08% Oleic Acid produced mild erythema in 6 female NZW rabbits after 72 h. The formulations were not primary skin irritants.[169,170] In a 14-day study with 6 NZW rabbits, the daily topical applications of a red cream formulation containing 5% Oleic Acid produced slight to well-defined erythema and slight

In an SIOPT, commercial grade Lauric Acid applied to intact and abraded sites of the skin of 6 albino rabbits produced slight erythema at both sites after 24 h, which subsided by 72 h, minimal edema after 72 h, and a PII of 1.12. Blanching and some coriaceous tissue were noted at a few abraded sites.[130] In an SIOPT, a 5% aqueous preparation of a product formulation containing 8.7% Lauric Acid applied to intact and abraded skin of 6 albino rabbits resulted in a PII of 0.[171]

A dose of 0.5 ml of commercial grade Palmitic Acid applied to intact and abraded sites on the skin of 6 albino rabbits in an SIOPT resulted in a PII of 0.[130] Administration of product formulations containing 2.2–74% Palmitic Acid produced minimal erythema and no edema 2–24 h after application to the skin of albino rabbits.[133,172–174]

In an SIOPT, commercial grade Myristic Acid was applied to intact and abraded sites on the skin of 6 albino rabbits, and the PII was 0.[130] In a Repeat Open Patch test using commercial grade Myristic Acid, all 6 treated albino rabbits developed mild to moderate erythema from 24 to 72 h. One rabbit developed very slight edema after the 72-h scoring.[175]

No irritation was observed at intact or abraded sites of the skin of albino rabbits in two SIOPT studies involving a commercial grade Stearic Acid.[130] In an SIOPT of commercial grade Stearic Acid, transient minimal erythema and no edema were noted in 9 albino rabbits after a 2-h exposure period.[176]

A preparation of 65% Stearic Acid in ethylene oxide produced erythema and minimal edema 24 and 72 h after application to intact and abraded sites on the skin of 6 NZW rabbits. The PII for this SIOPT was 3.00.[134] No irritation was observed in SIOPT studies involving 4-h exposures of intact and abraded skin of 6 albino rabbits to 45 and 59% Stearic Acid in combination with "other fatty acids."[172] Two-hour exposures of the skin of 9 albino rabbits to 35.0% Stearic Acid in water and 50% Stearic Acid in petrolatum resulted in respective PIIs of 0.33 and 0.56. Transient mild erythema and no edema were observed in both SIOPT studies.[177,178]

SIOPT studies with lotion and cream formulations containing 1.0–13% Stearic Acid resulted in PIIs, ranging from 0.63 to 2.2, that were not directly related to Stearic Acid concentration. A face cream formulation containing 13% Stearic Acid was determined "non-irritating" in a 24-h SIOPT of the fatty acid applied to intact and abraded sites on the skin of at least 6 albino rabbits. The use of a standard procedure was reported,[158] and no additional data were recorded.[179]

In a 24-h SIOPT of a skin lotion formulation containing 2.8% Stearic Acid, the PII was 1.00, and barely perceptible erythema and edema were observed at most intact and abraded sites of 6 NZW rabbits after 24 h. Irritation had subsided after 72 h.[138]

Transient irritation was also observed in a 24-h SIOPT to intact and abraded sites of the skin of 6 NZW rabbits treated with a skin lotion formulation containing 2.8% Stearic Acid. Very slight to well-defined erythema was observed at both sites, and very slight edema was observed at some intact and all abraded sites after 24 h.[139]

A skin lotion formulation containing 2.8% Stearic Acid produced very slight erythema at both intact and abraded treatment sites and transient minimal edema at a few sites 1 day after a 24-h SIOPT.[140]

A skin lotion formulation containing 2.8% Stearic Acid produced minimal to well-defined erythema and edema at both intact and abraded sites of 6 NZW rabbits 24 h after treatment. Very slight erythema was observed at some of the sites after 72 h.[136] Dry skin was noted in all rabbits.

A skin lotion formulation containing 2.8% Stearic Acid produced very slight to well-defined erythema and edema at intact and abraded sites of 6 NZW rabbits 24 h after treatment. Very slight erythema was observed at a few sites, and there was no edema 48 h later.[137] Dry skin was noted at treatment sites of all rabbits.

Intact and abraded sites on the skin of 4 male albino rabbits were treated with a skin lotion formulation containing 2.8% Stearic Acid in a 24-h SIOPT study. Transient minimal erythema was observed after 24 h. One abraded site had very slight edema after 24 h.[143]

Intact and abraded sites on the skin of 6 NZW rabbits were treated with lotion formulations containing 1.0% Stearic Acid in two 24-h SIOPT studies.[180] Treatment with one formulation produced defined erythema and edema at both sites after 24 h, which had subsided by 72 h posttreatment.

Skin Sensitization

A cream blush formulation containing 5.08% Oleic Acid was tested for sensitization using a group of 24 female Hartley guinea pigs weighing 300–500 g.[181] In a maximization test,[182] single intradermal injections of 0.1 ml of 5% Freund complete adjuvant in water, of a 5% solution of the formulation in water, and of a 5% solution of the formulation, water, and Freund adjuvant were administered in rows along the dorsal midline of the guinea pigs. Seven days after the injections, a 10% preparation of sodium lauryl sulfate in petrolatum was topically applied to the clipped dorsal area. Twenty-four hours later, 1 g of the undiluted formulation was applied to the treatment sites under an occlusive patch. The challenge patch, 1 g of the undiluted formulation in a Duhring chamber (aluminum disk with diameter of 18 mm and 2 mm elevated flange), was topically applied under an occlusive wrapping 14 days after topical induction (22 days after the intradermal injection). After a 24-h exposure, the challenge patch was removed. Sites were scored at patch removal and 48 h later. None of the guinea pigs had reactions to the challenge patches. Although no other data were reported, the formulation was considered a weak, grade I, sensitizer.

A suntan lotion formulation containing 1.0% Stearic Acid was tested for sensitization on 22 young adult female Hartley guinea pigs[183] using the same

procedure as in the preceding study.[181] There was one sensitization reaction to the occlusive challenge patch of 1 g of the formulation in a Duhring chamber among the 22 treated guinea pigs. The formulation was considered a weak, grade I, sensitizer.

In a maximization study,[182] a cosmetic product formulation containing 3.5% Stearic Acid was tested for allergic contact sensitization using a group of 10 female guinea pigs.[184] Intradermal injections of 50% aqueous Freund complete adjuvant, 50% formulation in propylene glycol, and 50% formulation in 50% aqueous Freund adjuvant at each of three sites along the upper backs of the guinea pigs were followed 1 week later by a topical booster of a slightly irritating concentration of the formulation in petrolatum. A topical application of 10% sodium lauryl sulfate in petrolatum was made 24 h before the topical booster if the formulation was not sufficiently irritating. Guinea pigs in the control group received induction injections of 50% aqueous Freund complete adjuvant, propylene glycol, and a 1:1 preparation of propylene glycol and 50% aqueous Freund adjuvant along the upper back and topical booster applications of petrolatum. Two weeks after the topical booster application, occlusive challenge patches containing 50 or 100% of the formulation were applied to control and treated guinea pigs. Sites were scored 48 and 72 h later. Five of 10 treatment sites had minimal faint erythema, and 1 of 10 sites had mild erythema 48 h after challenge with the 100% concentration. There were 3 sites with minimal faint erythema after 72 h, 2 of which had signs of desquamation. Other treatment sites had no signs of sensitization. Challenge of the treatment sites with the 50% formulation preparation resulted in minimal faint erythema at 1 of 10 sites after 48 h, which was visible after 72 h. All other treatment sites challenged with the 50% concentration had no signs of sensitization. Two control guinea pigs died, and 4 of the remaining 8 sites challenged with the 100% formulation patch had minimal faint erythema after 48 h. Two of 8 sites challenged with the 50% concentration had minimal faint erythema, and desquamation was observed at another site after 72 h.

Photosensitization

Two skin lotion formulations containing 2.8% Stearic Acid were tested for phototoxicity.[185,186] Aqueous preparations of the formulations, 100, 75, 50, and 25%, were applied to four different sites on the backs of 10 male Hartley albino guinea pigs weighing 324–486 g[185] and 284–452 g.[186] These sites were exposed to UVA radiation. Ten control guinea pigs weighing 268–434 g[185] and 344–464 g[186] received the same topical applications but no UVA irradiation. Sites were evaluated 1 and 24 h after treatment. Neither formulation was considered phototoxic to the guinea pigs under these conditions because the control group had signs of irritation that were comparable to the irradiated test group. One guinea pig in the control group of one study died.[185] The test groups' reactions ranged from questionable to moderate erythema at 6 (50% preparation) to all 10 sites (75%, 100% preparations). The 25% preparations produced no signs of phototoxicity in either study. The control groups in both studies had questionable to moderate (50–100% sites,[185] 50–75% sites[186]) or considerable erythema (100% site[186]). No irritation was observed at control sites treated with the 25% preparations.

Two skin lotion formulations containing 2.8% Stearic Acid were tested for photoallergy using 12 male Hartley albino guinea pigs weighing 378–516 g[186] and 330–404 g.[185] Each guinea pig received 10 topical induction applications of the undiluted formulations. Two weeks after the last application, challenge applications of 10, 20, and 100% (w/v) preparations were made to two separate sites, one of which was irradiated. Control groups of 12 male guinea pigs (360–440 g,[185] 358–492 g[186]) received no induction applications and were treated as test animals in the challenge phase. Induction sites were evaluated daily and challenge sites were evaluated 24 and 48 h after treatment. In one study, 1 test animal died during the induction phase and 2 animals died during the challenge phase.[185] Neither formulation was considered photoallergenic to the guinea pigs under these conditions because the control group had signs of irritation comparable to the test group. Questionable to moderate erythema was observed at up to 11 of 12 sites by the second application of the induction phase. During the challenge phase, no irritation was observed at either irradiated or nonirradiated sites of guinea pigs in control and test groups at the 10 and 20% concentrations. Questionable to minimal erythema was observed at one or two nonirradiated sites and at five irradiated sites of the test group challenged with the undiluted formulation. In the control group, four to seven nonirradiated sites and five to six irradiated sites had questionable to minimal erythema after challenge with the undiluted formulation.

Comedogenicity

The comedogenicity of UVA-irradiated and nonirradiated Oleic Acid was evaluated.[24] A significant increase in lipid peroxide level of Oleic Acid was observed after 18 h of UVA irradiation. Daily applications of the nonirradiated Oleic Acid (approximately 2 ml of 99% Oleic Acid) for 2 weeks were made on the ventral surface of one ear of Japanese and New Zealand White rabbits. An equal volume of irradiated Oleic Acid was applied to the other ear. Both Oleic Acid and its peroxides induced fairly large comedones in both species of rabbit. The lipid peroxide concentration was positively correlated with the degree of comedo formation.

Ocular Irritation Studies

Oleic, Lauric, Palmitic, Myristic, and Stearic Acids were tested for ocular irritation (Table 17).

No or minimal conjunctival irritation was produced in eyes of 6 albino rabbits treated with 0.1 ml of Oleic Acid as commercially supplied. Using the Draize Method,[168] the single instillation was not rinsed from the eyes. Untreated eyes served as controls.[130,187,188] In other Draize studies, 0.1 ml of mascara and cream product formulations containing 2–5% Oleic Acid produced no or slight conjunctival irritation in the eyes of rabbits within 2 days of treatment.[131,191–192] No irritation was observed in eyes that had been irrigated 20 sec after treatment with 20 ml lukewarm water.[190] No irritation was observed in rinsed and unrinsed eyes of rhesus monkeys treated with a mascara formulation containing 6% Oleic Acid.[189]

TABLE 17. Ocular Irritation Studies

Fatty acid tested	*Species (no. per group)*	*Methods*[a]	*Results*	*Reference*
Oleic Acid, as commercially supplied	6 albino rabbits	Draize	Mean score 2 after 24 h; 1 after 48 and 72 h (max = 110). Mild conjunctivitis	130
Oleic Acid, as commercially supplied	3 albino rabbits	Draize	No irritation	187
Oleic Acid, as commercially supplied	3 albino rabbits	Draize	Total mean score 1 after 1 and 2 days; 0 after 3 days. Grade 2 conjunctival irritation	188
Oleic Acid—6% in mascara formulation	3 rhesus monkeys	Draize, ± rinse	No irritation in either group	189
Oleic Acid—5% in cream formulation	6 NZW rabbits	14 daily instillations, no rinse	Intermittent slight conjunctivitis during 1st week	131
Oleic Acid—3% in mascara formulation	3 albino rabbits	Draize, ± rinse	Grade 1 conjunctival erythema in unrinsed treated eyes clearing by 2nd day	190
Oleic Acid—2% in mascara formulation	3 albino rabbits	Draize, ± rinse	No irritation	191
Oleic Acid—2% in mascara formulation	6 albino rabbits	Draize	Mean score 0.66 after 24 h; 0.33 after 48 h. Grade 1 conjunctival erythema in 1 rabbit only	192
Lauric Acid, as commercially supplied	6 albino rabbits	Draize	Mean score 35 after 24 h; 39 after 48 h; 41 after 72 h. Persistent corneal opacity, mild conjunctivitis, iritis	130
Lauric Acid—8.7% in product formulation, 8.0% aqueous dilution tested	6 albino rabbits	Draize	No irritation	193
Lauric Acid—1.95% in soap formulation, 1% aqueous dilution tested	6 NZW rabbits (rinse group) 3 NZW rabbits (no rinse group)	Draize, ± rinse	Max. mean score 0.3 for unrinsed eyes; 0.7 for rinsed eyes. Grade 1 conjunctival erythema	194
Palmitic Acid, as commercially supplied	6 albino rabbits	Draize	No irritation	130
Palmitic Acid—19.4% in product formulation	6 albino rabbits	3 instillations, no rinse	Total mean score 3 after 1 and 2 days. No irritation after 3 days. Primarily conjunctival irritation	195

Palmitic Acid—19.4% in product formulation, 75% solution in corn oil	6 albino rabbits	Draize	Total mean score 1 after 1 day; 6 after 2 days; 1 after 3 days. No irritation after 4 days. Mild irritation of cornea, iris, and conjunctivae	196
Palmitic Acid—4.4% in product formulation	6 albino rabbits	Draize	No irritation	197
Palmitic Acid—4.4% in product formulation	6 albino rabbits	Draize	No irritation	198
Palmitic Acid—2.2% in product formulation	6 albino rabbits	Draize	No irritation	133
Myristic Acid, as commercially supplied	6 albino rabbits	Draize	Grade 1 conjunctival erythema in 3 rabbits after 24 h	130
Myristic Acid—50% in petrolatum	3 albino rabbits	Draize	Total mean score 2 after 1 day; 1 after 2 and 3 days; 0 after 4 days. Grade 2–4 conjunctival irritation	199
Myristic Acid—1.5% in product formulation	6 NZW rabbits (no rinse) 3 NZW rabbits (rinse)	Draize, ±rinse	Max. mean score 1.3 for unrinsed; 0.7 for rinsed treated eyes. Conjunctival erythema up to 72 h later	200
Myristic Acid—1.5% in product formulation	See preceding entry	Draize, ±rinse	Max. mean score 0.7 for unrinsed; 1.3 for rinsed treated eyes. Conjunctival erythema 24–48 h later	201
Stearic Acid, as commercially supplied	6 albino rabbits	Draize	No irritation	130
Stearic Acid (eutectic), as commercially supplied	6 albino rabbits	Draize	Mild conjunctival erythema in 2 rabbits, subsiding by 72 h	130
Stearic Acid—65% in ethylene oxide	6 NZW rabbits	Draize	No irritation	134
Stearic Acid—50% in petrolatum	6 albino rabbits	Draize	Total mean score 4 after 1 day. Conjunctival irritation subsided after 2 days	202
Stearic Acid—35% in corn oil	6 albino rabbits	Draize	Total mean score 1. Mild conjunctival irritation subsided after 2 days	203
Stearic Acid—13% in product formulation	6 albino rabbits	Draize	Iritis in 1 rabbit	179

TABLE 17. (Continued)

Fatty acid tested	*Species (no. per group)*	*Methods*[a]	*Results*	*Reference*
Stearic Acid—2.8% in product formulation	6 NZW rabbits (no rinse) 3 NZW rabbits (rinse)	Draize, ±rinse	Mean total score 0.7 for unrinsed treated eyes after 1 day; conjunctival erythema subsided after 2 days. No irritation in rinsed treated eyes	138
Stearic Acid—2.8% in product formulation	6 NZW rabbits	Draize	No irritation	139
Stearic Acid—2.8% in product formulation	3 NZW rabbits	Draize	Max. mean score 3.3; conjunctival irritation after 1 and 24 h, subsiding after 48 h	140
Stearic Acid—2.8% in product formulation	6 NZW rabbits (no rinse) 3 NZW rabbits (rinse)	Draize, ±rinse	Mean total score 0.7 after 48 h, 0.3 after 72 h and 4 days for unrinsed eyes. Similar scores for rinsed eyes. Slight conjunctival erythema	136
Stearic Acid—2.8% in product formulation	See preceding entry	Draize, ±rinse	Mean total score 0.7 after 24 h in both groups. Slight conjunctival erythema	137
Stearic Acid—2.8% in product formulation	3 NZW rabbits	Draize	Max. mean score 6.0 after 1 h. Conjunctival irritation in all rabbits, subsiding after 24 h	141
Stearic Acid—2.8% in product formulation	3 NZW rabbits	Draize	Max. mean score 6.0 after 1 h. Conjunctival irritation persisting up to 24 h	142
Stearic Acid—2.8% in product formulation	3 NZW rabbits	Draize	Max. mean score 4.0 after 1 h. Slight conjunctival erythema persisting up to 24 h	143
Stearic Acid—1% in product formulation	4 albino rabbits	Draize	Max. mean score 6.0 after 1 h. Slight conjunctival irritation, 2 rabbits had corneal irritation. Subsided by 24 h	204
Stearic Acid—1% in product formulation	6 albino rabbits	Draize	Max. mean score 2.83 after 1 h. Slight conjunctival irritation and iritis in 1–3 rabbits	153

[a]Draize Method[168] used in most studies: usually single instillation of 0.1 ml volume into 1 eye (untreated eye = control). Variant methods (e.g., "rinse" denoting rinsing of treated eyes or "±rinse" denoting that treated eyes of animals in 1 group were rinsed, while those of animals in other group left unrinsed) are noted.

Instillation of commercial grade Lauric Acid into the eyes of 6 albino rabbits produced corneal opacity, mild conjunctivitis, and iritis throughout the 72-h observation period.[130] An aqueous dilution of a product formulation containing 8.7% Lauric Acid produced no ocular irritation in 6 albino rabbits.[193] A 1% aqueous preparation of a soap formulation containing 1.95% Lauric Acid was not irritating to treated unrinsed eyes of rabbits. The preparation was minimally irritating to treated eyes that had been rinsed 30 sec after instillation with 20 ml deionized water at room temperature.[194]

Administration of commercial grade Palmitic Acid to the eyes of 6 albino rabbits produced no irritation.[130] Mild to moderate ocular irritation was produced in rabbits by product formulations containing 19.4% Palmitic Acid. One of these formulations had been diluted to 75% with corn oil.[195,196] Cosmetic product formulations containing 2.2 and 4.4% Palmitic Acid produced no ocular irritation in 6 albino rabbits.[133,197,198]

Slight conjunctival irritation was produced in the eyes of albino rabbits 1 day after instillation of commercial grade Myristic Acid[130] and 50% Myristic Acid in petrolatum.[199] Lotion formulations containing 1.5% Myristic Acid were minimally irritating to rinsed (20 ml ionized water at room temperature, 30 sec after instillation) and unrinsed treated eyes of rabbits.[200,201]

No ocular irritation was produced in 6 albino rabbits by commercial grade Stearic Acid, whereas mild conjunctival erythema was produced in 3 of 6 albino rabbits by commercial grade eutectic (triple-pressed) Stearic Acid.[130] Treatment with 65% Stearic Acid in ethylene oxide resulted in no ocular irritation.[134] Treatment with 35% Stearic Acid in corn oil and 50% Stearic Acid in petrolatum was "practically non-irritating," primarily producing mild conjunctival erythema, which had subsided within 2 days.[202,203]

Iritis was observed in 1 of 6 albino rabbits treated with a face cream formulation containing 13% Stearic Acid.[179] No irritation[139] or mild conjunctival irritation after 1 and 24 h[136–138,141–143,153,204] was observed in the unrinsed eyes of albino rabbits treated with lotion formulations containing 1 and 2.8% Stearic Acid. Mild iritis was also observed in one study.[153] Eyes of rabbits that had been irrigated with water after treatment with a skin lotion formulation containing 2.8% Stearic Acid had no signs of irritation[138] or slight conjunctival erythema after 24 and 48 h.[136,137]

MUTAGENICITY

Oleic, Lauric, and Stearic Acids were assayed for their abilities to induce mitotic aneuploidy and crossing-over of chromosomes in the D_6 strain of *Saccharomyces cerevisiae.(205)* Concentrations of Oleic Acid from 100 to 500 μg/ml and of Lauric Acid from 10 to 200 μg/ml increased aneuploidy, whereas Stearic Acid at concentrations up to 500 μg/ml was inactive. None of the fatty acids tested increased the frequency of mitotic crossing-over events; concentrations of Oleic and Lauric Acids up to 50 μg/ml and of Stearic Acid up to 500 μg/ml were used.

Stearic Acid was tested for mutagenicity using the Ames test[206] with *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538.[207]

Spot tests were performed using 50 mg/ml Stearic Acid suspensions in distilled water (50 μg/plate) with and without microsomal activation from hepatic S9 fractions from rats induced with Aroclor 1254 (50 μg/plate). Positive controls were 2-aminoanthracene and 4-nitro-o-phenylenediamine in dimethyl sulfoxide, 9-aminoacridine in ethanol, and sodium azide in distilled water. Stearic Acid had no mutagenic activity over background in the strains tested with and without metabolic activation.

The genotoxicity of Oleic Acid was studied using V79 Chinese hamster lung fibroblasts.[208] The three tested concentrations of Oleic Acid, 2.5, 5.0, and 10.0 μg/ml, produced a mean number of sister chromatid exchanges per metaphase that was similar to controls. Higher incidences of aneuploidy were observed in cultures at all three concentrations. The 2.5 μg/ml Oleic Acid-treated culture had a higher incidence of tetraploidy when compared to controls.

Isomers of Oleic Acid, *cis*-12- and *cis*-13-octadecenoic acids, produced a greater increase in mitochondrial DNA mutation in *S. cerevisiae* than did Oleic Acid.[209]

Inhibition of Mutagenesis

Oleic, Lauric, Stearic, and Palmitic Acids were tested for their inhibitory action on the mutagenicity of several compounds using two bacterial systems, *Escherichia coli* and *Salmonella typhimurium*. These studies and their results are summarized in Table 18.

In the *S. typhimurium* system, a modified Ames test[206] was used involving preincubation of a mixture containing the mutagen, dimethylsulfoxide (DMSO), fatty acid, S9, and bacteria before plating. A phosphate buffer at pH 6 was used for the preincubation mixture in the *E. coli* system. A significant decrease in the number of revertants compared to negative controls in both tests was interpreted as inhibition by the fatty acid. Positive controls with mutagen alone were done to determine maximum numbers of revertants.

Oleic Acid was toxic to *S. typhimurium* TA 100,[211] and Lauric Acid was toxic to *E. coli* WP2 uvrA/pKM101 in the absence of S9. In the presence of S9, Lauric Acid had a strong inhibitory effect on all N-nitrosodialkylamines tested.[212]

Mechanisms for Oleic and Lauric Acid-inhibition of potent mutagens have been discussed, and results of several bacterial tests for fatty acid inhibition of mutagenesis have been reported.[214]

CARCINOGENICITY

Oleic, Lauric, Palmitic, and Stearic Acids have been tested for carcinogenic activity. The studies were reviewed in the safety assessment of particular fatty acids (and their salts) as they are used in foods[44-47,68] and in fragrances.[69] Data and results from these and additional studies are summarized in Table 19.

TABLE 18. Inhibition of Mutagenicity by Fatty Acids

Fatty acid tested	*Bacterial system used*	*Metabolic activation*	*Results*	*Reference*
Oleic Acid isolated from fecal extract	*Salmonella typhimurium* TA98	S9 from livers of rats induced with poly-chlorinated biphenyl (PCB)	Inhibition of mutagenicity of: 3-amino-1,4-dimethyl-5H-pyrido[4,3-b]indole; 2-amino-6-methyl-dipyrido[1,2-a:3′,2′-d]imidazole; 2-amino-9H-pyrido[2,3-b]indole; 2-amino-3-methyl-imidazo[4,5-d]-quinoline; benzo[a]pyrene (amino acid pyrolysis products) and aflatoxin B_1 Degree of inhibition increased with decreasing pH. I_{50}, 0.02–0.08 mg; I_{95}, 0.05–0.38 mg	210
Oleic Acid	*Escherichia coli* WP2 try, hcr	S9-phenobarbital-induced rat liver	Inhibition: 140 μmol N-nitrosodimethylamine (NDMA); 14 μmol N-nitrosodiethylamine (NDEA); 4 μmol N-nitrosodibutylamine (NDBA); 35 μmol N-nitrosopyrrolidine (NPYR); 35 μmol N-nitroso morpholine (NMOR). Dose-related inhibition observed No inhibition: 2 μmol N-methyl-N′-nitro-N-nitrosoguanidine (NMMG)	211
Oleic Acid	*E. coli* WP2 uvrA/pkM 101	S9-phenobarbital-induced hamster liver	Inhibition: NDMA	212
Lauric Acid	*S. typhimurium* TA100	None reported	Inhibition: sodium azide, 4-nitro-o-phenylene-diamine, N-amino-morpholine, ethylmethane-sulfonate	213
Lauric Acid	*E. coli* WP2 uvrA/pKM 101	S9-phenobarbital-induced hamster liver	Inhibition: NDMA, NDEA, NDBA, N-nitroso-piperidine, NMOR. Cytotoxic in N-methylnitroso-urea cultures	212
		S9-PCB-induced rat liver	Inhibition: benzo[a]pyrene No inhibition: 2-aminoanthracene	
Palmitic Acid	*S. typhimurium* TA98	S9-PCB-induced rat liver	No inhibition: amino acid pyrolysis products, aflatoxin B_1	210
Stearic Acid isolated from fecal extract	*S. typhimurium* TA98	S9-PCB-induced rat liver	No inhibition: amino acid pyrolysis products, aflatoxin B_1	210
Stearic Acid	*E. coli* WP2 try, hcr	S9-phenobarbital-induced rat liver	No inhibition: NDMA	211

I_n, amount of fatty acid needed to produce a percent inhibition.

TABLE 19. Carcinogenicity Studies on Fatty Acids

Fatty acid tested	*Dose*	*Animal*	*Method*	*Results and conclusions*	*Reference*
Oleic Acid in tricaprylin	1–16.5 mg	Mouse (BALB/c, CFW)	Repeated subcutaneous injections. Two experiments: (1) 0.1 mg Oleic Acid in 0.1 ml tricaprylin 3 injections/week, total of 10 injections (2) 0.5 mg Oleic Acid in 0.1 ml tricaprylin 2 injections/week, total of 33 injections	Not carcinogenic (1) 1/15 mice alive at 18 months. No subcutaneous sarcomas (2) 4/16 mice alive at 18 months. No subcutaneous sarcomas, 1 breast carcinoma at 9 months	215[a]
Oleic Acid with linoleic acid in corn oil in diet	150–200 mg/mouse/day of 1.5% fatty acids in in refined corn oil	Mouse (T.M. strain)	Feeding study—dietary supplement. Several groups: (1) Control—chow only ($n = 623$) (2) Refined corn oil supplement ($n = 375$) (3) Refined corn oil + 1.5% free fatty acid supplement (oleic and linoleic acids) ($n = 329$)	(1) Controls— < 20% total tumor incidence mainly lung tumors (2) Incidence of lung and brain nerve cell tumors, lymphosarcomas similar to Group 3. Incidence gastric tumors lower than Group 3. 1 heart tumor found (3) High incidence of lung (48.5%), stomach (27.4% forestomach papillomas, 12.5% pyloric tumors), and brain nerve cell (11%) tumors. Low incidence of mammary carcinomas, myomas, lymphosarcomas. 1 heart tumor found	216
Oleic Acid with linoleic acid in corn oil in diet	200 mg/mouse/day of 1.5% fatty acids in refined corn oil	Mouse	Feeding study—dietary supplement. Several groups (1) Control—chow only ($n = 195$) (2) Refined corn oil supplement ($n = 209$) (3) Crude corn oil supplement ($n = 196$)	Number of tumors Groups: (1) (2) (3) (4) Forestomach papillomas 2 6 49 87 Squamous cell carcinomas 1 1 6 10 Pyloric tumors 0 2 9 41 No intestinal polyps or adenocarcinomas	217

			(4) Refined corn oil + free fatty acid supplement (oleic and linoleic acids) ($n = 328$)		
Oleic Acid in corn oil diet	10 g of 1.5% (w/w) in corn oil in chow	Mouse (C57BL/1 strain)	Feeding study—dietary supplement. 2 groups (1) Control—chow only ($n = 36$) (2) Corn oil + Oleic Acid ($n = 55$)	(1) Incidence of tumorigenesis not reported for controls (2) Metastatic colon adenocarcinomas in 8% of mice. Polycystic kidney in 1 mouse No corn oil in chow group (i.e., treated control) C57BL/1 strain reported to be generally resistant to tumor formation	218
Oleic Acid	Unspecified	Mouse	Unspecified method—biweekly applications for 40 weeks. Series of experiments	No malignant tumors. In 3 experiments: 0/100 mice with tumors 1/200 mice with benign tumor at week 35 1/100 mice with benign tumor at week 15 No change to malignancy	219[a]
Lauric Acid in tricaprylin	25 and 50 mg	Mouse (BALB/c; CFW)	Repeated subcutaneous injections. Two experiments: (1) 1.0 mg Lauric Acid in 0.1 ml tricaprylin. 2 injections/week, total 25 injections (2) 5.0 mg Lauric Acid in 0.1 ml tricaprylin. 3 injections/week, total 10 injections	Not carcinogenic (1) 5/16 mice alive at 18 months. 1 subcutaneous sarcoma, 1 pulmonary tumor, 2 leukemia–lymphomas (4, 5 months) (2) 8/15 mice alive at 18 months. No subcutaneous sarcomas; 1 pulmonary tumor; 1 leukemia-lymphoma (23 months)	215[a]
Palmitic Acid in tricaprylin	25 and 50 mg	Mouse (BALB/c; CFW)	Repeated subcutaneous injections. Two experiments: (1) 1.0 mg Palmitic Acid in 0.1 ml tricaprylin. 2 injections/week, total of 25 injections (2) 5.0 mg Palmitic Acid in 0.1 ml tricaprylin. 3 injections, total of 10 injections	(1) 5/16 mice alive at 18 months. 1 subcutaneous sarcoma (8 months); 2 breast carcinomas (18 months); 1 leukemia -lymphoma (12 months) (2) 6/16 mice alive at 18 months. 1 subcutaneous sarcoma (19 months); 2 pulmonary tumors (19, 22 months); 1 breast carcinoma (22 months)	216[a]
Palmitic Acid in diet	50 g/kg/day	Rat (Holtzman)	Feeding study—dietary supplement	Lipogranulomas observed in fat associated with testis or ovary—reversible upon diet substitution Conclusion: effect due to dietary imbalance	151[a]

TABLE 19. (Continued)

Fatty acid tested	*Dose*	*Animal*	*Method*	*Results and conclusions*	*Reference*
Stearic Acid in olive oil	Unspecified	Mouse	Single subcutaneous injection	No sarcomas observed. Used as a control in study on cholesterol carcinogenicity	220[a]
Stearic Acid in tricaprylin	1.3–82 mg	Mouse (BALB/c and CFW Swiss Webster)	Repeated subcutaneous injections. Series of expts. using 0.05–1.0 mg Stearic Acid in 0.1 ml tricaprylin. 1–3 injections per week, total of 10–114 injections per study	7–90% of mice were alive at 18 months ($n = 10–16$). Only 1 group (0.05 mg, 2x/week, 114 injections) had subcutaneous sarcomas (4 in 4 survivors). 1 adrenal carcinoma, 1 leukemia–lymphoma, 3 pulmonary tumors in total of 92 mice (in entire series)	215[a]
Stearic Acid in tricaprylin	1.3–13 mg	Mouse (ICR/Ha Swiss Millerton and CFW Swiss Webster)	Repeated subcutaneous injections. Series of expts. using 0.05 or 0.5 mg Stearic Acid in 0.1 ml tricaprylin 1 injection per week, 26 weeks	1–3 deaths within 6 months ($n = 15–16$). No sarcomas at injection site. No carcinogenic activity	221[a]
Stearic Acid in diet	0.3%	Rat	Feeding study. Dietary supplement for 209 days	No carcinogenic activity	152[a]
Stearic Acid in diet	50 g/kg/day	Rat (Holtzman)	Feeding study–dietary supplement	Lipogranulomas observed in fat associated with testis or ovary—reversible upon diet substitution. Concluded that effect due to dietary imbalance rather than Stearic Acid-related	151[a]

[a] These studies appeared in reviews for the safety assessment of particular fatty acids as they are used in food[44–47] and in fragrance.[69]

The carcinogenicity of Oleic, Lauric, Palmitic, and Stearic Acids was studied from 1964 to 1967 in a series of experiments with female BALB/c or Swiss-Webster mice.[215] Subcutaneous injections were administered in the inguinal area 3 times per week for 4 weeks. Materials that were administered daily or for longer than 4 weeks were given in inguinal and axillary areas to prevent their accumulation into deposits of unabsorbed oil. The vehicle for the injections was tricaprylin, and the volume per injection was 0.1 ml. One group of control mice was administered tricaprylin alone; the other control group received no treatment. Mice were observed twice weekly for the appearance of subcutaneous neoplasms. Animals with neoplasms or those in poor condition were killed and necropsied.

Oleic Acid was administered to 15 Swiss-Webster mice at a dose of 0.1 mg 3 times per week for a total of 10 injections.[215] The total dose administered in the study was 1.0 mg Oleic Acid per 1 ml tricaprylin. Nine mice were alive after 12 months, and 1 was alive after 18 months. No neoplasms were observed after this treatment. Another group of 16 Swiss-Webster mice received 2 injections of 0.5 mg Oleic Acid per week for a total of 33 injections. The total dose administered was 11.5 mg per 2.3 ml tricaprylin. Eight mice were alive after 12 months, and 4 were alive after 18 months. One mammary gland carcinoma was found after 9 months.

Lauric Acid was administered to 15 Swiss-Webster mice at a dose of 1.0 mg 3 times per week for a total of 12 injections (total dose, 12 mg Lauric Acid/1.2 ml tricaprylin).[215] Thirteen mice were alive after 12 months, and 8 mice were alive after 18 months. One pulmonary neoplasm and 1 "leukemia–lymphoma" were found after 23 months. Another group of 16 Swiss-Webster mice received 2 injections of 5.0 mg weekly for a total of 25 injections (total dose, 125 mg Lauric Acid/2.5 ml tricaprylin). After 12 months, 8 mice were alive, and after 18 months, 5 were alive. One subcutaneous sarcoma and 1 pulmonary neoplasm were found after 18 months. Two "leukemia–lymphomas" were found after the fourth and fifth months.

Palmitic Acid was administered to 16 Swiss-Webster mice at a dose of 1.0 mg 3 times per week for a total of 10 injections (total dose, 10 mg Palmitic Acid/1 ml tricaprylin).[215] Eight mice were alive after 12 months, and 6 were alive after 18 months. One subcutaneous sarcoma was found after 19 months, 2 pulmonary neoplasms were found after 19 and 22 months, and 1 breast carcinoma was found after 22 months. Another group of 16 Swiss-Webster mice received two injections of 5.0 mg weekly for a total of 25 injections (total dose, 125 mg Palmitic Acid/2.5 ml tricaprylin). Eight mice were alive after 12 months, and 5 were alive after 18 months. A subcutaneous sarcoma was found after 8 months, 2 breast carcinomas were found after 18 months, and 1 "leukemia–lymphoma" was found after 12 months.

Stearic Acid was administered to groups of 16 Swiss-Webster mice at doses of 0.05 mg and 0.5 mg weekly for a total of 26 injections.[215] After 18 months, 10 mice were alive in the group given the lower dose, and 6 mice were alive in the group given the higher dose. A third group of 15 Swiss-Webster mice was given injections of 1.0 mg Stearic Acid 3 times per week for a total of 10 injections. Eight mice were alive after 12 months, and 1 was alive after 18 months. A fourth group of 10 BALB/c mice was given injections of 1.0 mg

Stearic Acid twice weekly for a total of 82 injections. Seven mice were alive after 18 months. No neoplasms were found in these four groups.

Neoplasms were found in three other groups of BALB/c mice administered Stearic Acid.[215] The first group of 15 mice was injected with 0.05 mg Stearic Acid twice weekly for a total of 104 injections. Thirteen mice were alive after 18 months, and 1 pulmonary neoplasm was found after 19 months. The second group of 10 mice received injections of 0.05 mg Stearic Acid twice weekly for a total of 114 injections. Four mice were alive after 18 months. Four subcutaneous sarcomas (1 after 6 months, 2 after 10 months, and 1 after 12 months), 1 pulmonary neoplasm (after 19 months), and 1 "leukemia–lymphoma" (after 19 months) were found. The 10 mice in the third group received 0.5 mg Stearic Acid per injection twice weekly for a total of 114 injections. Nine mice were alive after 18 months. After 21 months, 1 pulmonary neoplasm and 1 adrenal carcinoma were found.

In a study modeled after the Swern et al.[215] study, Van Duuren et al.[221] found Stearic Acid to be noncarcinogenic, confirming the previous study's conclusion (see Table 14 for details of study). Investigators in both studies indicated that a compound's carcinogenic activity was assessed by its ability to induce sarcomas at the injection site.

Statistical techniques were used to determine possible associations between dietary fatty acids in triglycerides and the incidence of spontaneous mammary tumors in C3H mice.[222] Eleven natural fats and oils and their mixtures were used to obtain 20 substances with varying concentrations of different fatty acids that were fed to mice. The saturated fatty acids, Lauric, Myristic, and Palmitic Acids, had little effect on tumor incidence or the time needed for a tumor to appear. The concentration of Stearic Acid was calculated to be inversely related to tumor incidence and directly related to the time for tumor appearance. Oleic Acid produced no significant effect on tumor incidence.

The effects of free fatty acids fed as dietary supplement to mice of the T.M. strain were studied.[216] Refined corn oil (free fatty acid content, approximately 1.5%, removed during refining process) fed to the mice at a rate of 150–200 mg/mouse/day contained 1.5% free fatty acids, Oleic and linoleic Acids. Feeding of the refined corn oil plus free fatty acid diet resulted in a high incidence of lung (48.5%), stomach (27.4% forestomach papillomas, 12.5% pyloric tumors), and brain nerve cell (11%) tumors and a low incidence of mammary carcinomas, myomas, and lymphosarcomas. Feeding of the refined corn oil diet resulted in a high incidence of lung and brain nerve cell tumors, lymphosarcomas, and a lower incidence of gastric tumors. One heart tumor was found in each treated group ($n = 329$ in refined corn oil plus free fatty acids group, $n = 375$ in refined corn oil group). Controls fed the standard diet ($n = 623$) had a total tumor incidence of less than 20%; tumors were mainly located in the lung.

A later study was done to determine the types of gastrointestinal tumors induced in the T.M. strain mice fed a standard diet supplemented with refined corn oil, crude corn oil (contains 1.5% free fatty acids), or refined corn oil plus the fatty acids, Oleic Acid and linoleic acid, at concentrations up to 1.5%.[217] These corn oil supplements were given to the mice in daily amounts of 200

mg/mouse. Controls were fed the standard diet. Mice were killed when they began to lose weight rapidly. The average age of the control mice was 645 days, and that of the treated mice was 454–540 days. In the group fed the refined corn oil plus fatty acid diet, 138 gastric tumors were found in 328 treated mice. In the refined corn oil diet group, 9 gastric tumors were found in 209 treated mice. The crude corn oil diet group had 63 gastric tumors in 196 treated mice. Three gastric tumors were observed in the 195 control mice. No intestinal polyps or adenocarcinomas were observed in control or treated mice. The types of induced gastric tumors included papillomas and squamous cell carcinomas.

The carcinogenic activity of a feed supplement of Oleic Acid in corn oil was studied using C57BL/1 black strain mice that were "generally resistant to tumor formation."[218] Control animals from a different supplier were fed chow alone, and the 55 treated mice were fed a diet consisting of 10 g of a mixture of 1.5 g Oleic Acid/100 g corn oil dispersed in 100 g of laboratory chow to which water was added. Throughout the study, randomly selected mice were killed and examined after 6, 12, 18, 21, and 24 months. Colon adenocarcinomas, which metastasized to the lung and muscle, were found in 8% (3/36) of the treated mice. Lipid profiles of the livers and pituitary glands of the mice were obtained. Results for the 2 groups of mice were compared and discussed.

Tumor-Promoting and Cocarcinogenic Activity

In 1932, Twort and Bottomley reported that the induction of nonmalignant skin tumors by chrysene was increased in mice when Oleic Acid was used as the solvent compared to liquid paraffin or benzene. In a later study comparing the induction of skin tumors in mice by carcinogenic hydrocarbons dissolved in various solvents, chrysene induced more tumors when dissolved in Oleic Acid than in chloroform, but benzo(a)pyrene and fractions of synthetic tar induced fewer tumors when dissolved in Oleic Acid.[223] Also, in that study, induction of benign tumors, but not malignant tumors, increased when 1,2,5,6-dibenzanthracene was dissolved in Oleic Acid, compared to liquid paraffin. Use of chloroform as the solvent increased the incidence of malignant tumors.

Shubik[224] tested Oleic Acid as a tumor promoter for 9,10-dimethyl-1,2-benzanthracene-initiated mouse skin. Oleic Acid was administered twice weekly for 20 weeks but did not promote tumors. Gwynn and Salaman[225] also reported negative results for the promotion of 9,10-dimethyl-1,2-benzanthracene-initiated mouse skin tumors when Oleic Acid was administered twice weekly for 12 weeks or weekly for 15 weeks. Holsti[226] demonstrated that more frequent administration of Oleic Acid could promote 9,10-dimethyl-1,2-benzanthracene-initiated skin papillomas in mice; 2 of 40 mice developed papillomas when undiluted Oleic Acid was administered twice weekly, but 27 of 44 mice developed such tumors when Oleic Acid was administered daily for 6 days a week. Oleic Acid or Lauric Acid, but neither Palmitic Acid nor Stearic Acid, dissolved in chloroform also stimulated the

formation of skin papillomas. No malignant tumors were seen in any of the mice treated with any of the fatty acids.

Van Duuren and Goldschmidt[227] tested Oleic Acid and Stearic Acid as cocarcinogens in groups of 50 mice each. Benzo(a)pyrene, administered in acetone, induced 26 papillomas in 16 mice and squamous cell carcinomas in 12 mice. Mice that received the benzo(a)pyrene and 25 mg of Oleic Acid in acetone 3 times a week for 440 days developed no skin tumors, benign or malignant. Benzo(a)pyrene and 4 mg of Stearic Acid, administered 3 times a week for 440 days, resulted in 38 papillomas in 25 mice, but only 7 mice had squamous cell carcinomas, fewer than the controls. The results were considered inconclusive for Stearic Acid but supportive of the possibility that Oleic Acid is not a cocarcinogen.

Hogan and Shamsuddin[228] studied the tumor-promoting properties of *cis*- and *trans*-Oleic Acid on the induction of intestinal cancer by azoxymethane. *cis*-Oleic Acid had no promoting effect; *trans*-Oleic Acid (elaidic acid) had a small promoting effect. Both *cis*- and *trans*-Oleic Acids increased the incidence of nephroblastomas and squamous ear duct tumors from 3/30 to 6/30 rats. No tumors were seen in rats fed a diet containing 25% *cis*-Oleic Acid without azoxymethane for 20 weeks.

Promotion of mammary gland carcinomas has been observed in mice and rats fed diets containing unsaturated fats, particularly polyunsaturated fats.[229]

Several fats, oils, and fatty acids, including Lauric and Oleic Acids, produced acanthosis in guinea pig skin.[230] The acanthosis gradually receded with continued topical application. Oleic Acid has been found to enhance proliferation of both normal and cancer cells in vitro.[231–233] Myristic, Palmitic, and Stearic Acids had an inhibitory effect on normal smooth muscle cell proliferation; ability to inhibit proliferation was observed to increase with increasing chain length.[234] Traul et al.[235] reported that Oleic Acid and Lauric Acid can enhance the transforming ability of 3-methylcholanthrene in Rauscher murine leukemia virus-infected rat embryo cells.

Numerous mechanisms for the role of fatty acids in tumorigenesis have been studied and reviewed. Hypotheses include indirect effects on gene expression, the endocrine system, and the immune system and direct effects on tumor cells, such as alterations in cellular metabolism, membrane fatty acid composition, and intercellular cooperation.[236,237]

Antitumorigenicity

The antitumor activity of Oleic, Lauric, Myristic, Palmitic, and Stearic Acids was studied in vivo using Ehrlich ascites and solid carcinomas implanted into Swiss albino mice of strain ddY.[238] Suspensions of the fatty acids in Tween 80 and distilled water were administered 24 h after tumor implantation and were continued daily for 5 consecutive days. Commercial fatty acid preparations used in the study were not purified, and no analysis of components was performed. Treated mice were killed 30 days after implantation and examined for tumors. Doses of 8 mg/mouse/day of Lauric and Myristic Acids were effective inhibitors against Ehrlich ascites tumor, more than doubling the survival time of treated versus control mice. Similar doses of Palmitic, Stearic,

and Oleic Acids were relatively ineffective against Erhlich ascites tumor. The mode of administration for these fatty acids was not stated.

Several modes of administration were tested using a 1:1 mixture of Oleic and linoleic Acids in the same dosage regimen.[238] Linoleic acid alone was an effective ascites tumor inhibitor. Intraperitoneal administration of the mixture was the most effective against the ascites tumor, and subcutaneous administration inhibited as much as 60% of the weight gain of the solid tumor.

Oleic Acid, at a concentration of 10 μM, inhibited the growth of rat neuroblastoma cells (cell line B104) in serum-free supplemented media.[239] At least a 50% decrease in cell number relative to controls was observed.

The antitumor activity of palmitoleic (*cis*-9-hexadecanoic) acid was compared to that of Oleic Acid using Erhlich ascites tumors in female ICR strain mice.[240] The fatty acids were dissolved in a 0.15 M sodium chloride (NaCl) solution containing 0.2% Tween 80 and, 24 h after tumor inoculation, were injected intraperitoneally once daily for 10 consecutive days. The experiment was terminated on day 60 after tumor inoculation. Control mice received the same volume of the NaCl plus Tween 80 solution. Significant inhibition of tumor growth was observed in Oleic Acid-treated mice at doses ranging from 37.5 to 300 mg/kg/day when compared to control mice. Palmitoleic Acid was more effective than Oleic Acid, inducing complete regression of the tumor in 5 of 10 treated mice at a dose of 75 mg/kg/day.

A diet supplement of Oleic Acid, at a daily dose of 1 mg per rat, failed to protect Sprague-Dawley rats from colon carcinoma caused by 1,2-dimethyl hydrazine (DMH).[241] All rats (22 rats per group) were killed 22 weeks after the first subcutaneous DMH injection and were examined for colon tumors. Control rats fed chow alone and injected with 15 mg/kg DMH weekly for 16 weeks developed 77 colon tumors, whereas those fed chow plus Oleic Acid before and during the DMH injections developed 90 colon tumors.

TERATOGENICITY

Food and fragrance safety evaluation reports on Oleic and Stearic Acids contained no data on their teratogenicity.[44,45,69] Reviews of the scientific literature from 1920 to 1973 were used for the final food safety assessments.[46,47]

Although placental transfer of fatty acids has been documented in several species and fetal lipid metabolism has been studied,[87,242] no studies on the teratogenicity of fatty acids were found.

CLINICAL ASSESSMENT OF SAFETY

A health hazard evaluation report was prepared by the National Institute for Occupational Safety and Health (NIOSH) after environmental and medical observations and examinations of 7 employees exposed to Lauric Acid.[243] Investigators found no significant decreases in pulmonary function, but interviews with workers indicated that Lauric Acid exposure caused local

irritation of moist body surfaces (eye, nose, throat, sweaty skin). Severe irritation was reported by 1 worker after exposure of moist occluded skin areas to Lauric Acid. The suggested reason for the observed irritation was the acidity of Lauric Acid.

Skin Irritation Studies

In a single insult occlusive patch test (SIOPT), commercial grade Oleic Acid produced no irritation in 18 and minimal erythema in 2 of the 20 panelists. The primary irritation index (PII) was 0.05 and Oleic Acid was considered "practically nonirritating"[244] (Table 20).

A 30% preparation of Oleic Acid in water produced barely perceptible erythema in 2, mild erythema in 1, and moderate erythema in 1 of 21 panelists in an SIOPT. There were no signs of irritation in 17 panelists. The PII was 0.19 and Oleic Acid was considered "practically nonirritating."[245]

In a soap chamber test,[251] 0.2 ml of a 50% solution of Oleic Acid in mineral oil was applied to the ventral skin of the forearm of 16 human subjects once daily for 5 days using the Duhring chamber, an aluminum cup with a 12 mm diameter, fitted with nonocclusive tape. The first exposure was usually 24 h long. Successive exposures to the same sites were for 6 h. The erythema score was 0.22 on a scale of 0 to 5. Oleic Acid was considered "non-irritating under conditions of this test."[246]

Several bar soap formulations with concentrations of Oleic Acid ranging from 2.53 to 92.7% were tested for skin irritation using 16 human subjects. A 0.2 ml volume of 8% aqueous preparations was applied to the ventral skin of the forearm under occlusive patches once daily for 5 days using the Frosch and Kligman soap chamber test.[251] The formulations were considered "slightly" to "moderately irritating." The erythema scores ranged from 1.41 to 3.21 on a scale of 0 to 5 and were not directly related to Oleic Acid concentrations in the formulations.[247–249,271]

In a cumulative irritation study, approximately 9.3 ml of each of 2 mascara formulations, a black cream and a brown cream, containing 6% Oleic Acid were applied to the backs of 14 female and 1 male panelist using closed patches.[250] The panelists removed the patches after 23 h and bathed. Reactions were scored 24 h after sample application. The samples were reapplied daily to the same test sites for 21 consecutive days or until irritation scores of 3, corresponding to erythema and papules, were observed.[252] Up to 7 panelists had minimum scores of 1 or slight erythema by the 5th application, and 3 to 4 panelists had maximal scores of 3 and 4 for erythema, papules, or edema by the 14th application. The total irritation scores for the formulations, a summation of the scores over the number of applications and panelists, were 212 and 204 compared with a maximal score of 945. Mean scores were 14.1 and 13.6 compared with a maximal score of 63. The positive control, an aerosol deodorant concentrate, had a total score of 828 and mean score of 55.2. The negative control, a clear liquid baby oil formulation, had a total score of 18 and a mean score of 1.2. The formulations were considered "slightly irritating."

A red paste cosmetic product formulation containing 5% Oleic Acid was tested for cumulative irritation on the skin of 10 human subjects.[255] Each of

TABLE 20. Clinical Skin Irritation Studies

Fatty acid tested	*Concentration*	*No. of subjects*	*Methods*	*Results*	*Reference*
Oleic Acid	As commercially supplied	20	SIOPT[a]	PII[b] 0.05. "Practically non-irritating"	244
	30%	21	SIOPT	PII 0.19. "Practically non-irritating"	245
	0.2 ml of 50% in mineral oil	16	Soap chamber test,[c] 5 daily occlusive patches	Erythema score 0.22. "Non-irritating"	246
	8% (92.7%)[c] in bar soap formulation	16	See preceding entry	Erythema score 2.13. "Moderately irritating"	247
	8% (2.53–41%) in 13 bar soap formulations	16	See preceding entry	Erythema scores ranged from 1.41 to 3.21 (slight to intense erythema). Scores not correlated with Oleic Acid concentration	248, 249
	6% in 2 mascara formulations	15	21-day cumulative irritation test[d]	CIS[e] 204 and 212 (max. 945). Mean irritation score 14 (max. 63). "Irritating"	250
	5% in product formulation	10	See preceding entry	CIS 95 (max. 630). "Probably mild..."	255
	2% in 3 mascara formulations	13	See preceding entry	One faint erythemal reaction to 4th patch of 1 formulation	256
Palmitic Acid	2.2% in shave cream formulation	101	Single patches, open and occlusive	No irritation	257
	2.2% in shave cream formulation	60	4-week controlled use[f]	"Non-irritating"	258
Myristic Acid	As commercially supplied	20	SIOPT	PII 0.2. "Practically non-irritating"	259
	50% in mineral oil	16	Soap chamber test[c]	Erythema score 0.48. "Non-irritating"	260
	8% (10–91%) in 3 bar soap formulations	16	Soap chamber test[c]	Erythema scores ranged from 1.41 to 1.95 (slight to moderate erythema)	261–263
	5% in cleanser lotion formulation	12	21-day cumulative irritation[d]	CIS 609 (max. 756). "Highly irritating"	264

TABLE 20. (Continued)

Fatty acid tested	*Concentration*	*No. of subjects*	*Methods*	*Results*	*Reference*
Stearic Acid	40% in mineral oil	21	SIOPT	No irritation	265
	13% in face cream formulation	101	Single patches, open and occlusive	Mild erythema to occlusive patch in 4 subjects. "Non-irritating"	266
	13% in face cream formulation	105	4-week controlled use[f]	"Non-irritating"	267
	8% in shave cream formulation	100	Single 48-h occlusive patch and 2–4 week daily home use	No reactions to patch. Complaints of minor pruritus from 2 subjects during home use unsubstantiated	268
	2.8% in liquid eyeliner formulation	13	21-day cumulative irritation[d]	CIS 216 (max. 675). "Moderately irritating"	269
	2.6% in 2 moisturizer formulations	12	See preceding entry	CIS 28 and 56. "Basically non-irritating"	270

[a]SIOPT, single insult occlusive patch test.
[b]PII, primary irritation index; maximum possible value 8.00.
[c]In Soap Chamber Test[251] volume of 0.2 ml usually applied; 8% aqueous preparations of bar soap formulations were tested and noted in Concentration column. Erythema scores reported—scale from 0–5.
[d]Ref. 252. Daily 23-h patches to same site. Some studies modified by Ref. 253.
[e]CIS, cumulative irritation scores; maximum possible score noted in parenthesis following CIS.
[f]Ref. 254.

the 21 consecutive closed-patch applications remained in contact with the skin for 23 h. Scoring for irritation and reapplication to the same test site was done 24 h after the preceding application.[252,253] The total irritation score for all subjects for all 21 applications of the formulation was 95 of a maximal possible score of 630. The total scores for the negative and positive controls were 7 and 554, respectively. The formulation was considered "probably mild in normal use."

Three mascara formulations containing 2% Oleic Acid were tested for cumulative irritation on the skin of 13 human subjects.[256] The closed patches were applied for 21 days, but no applications were made on weekends.[253] One of the 13 subjects had a single equivocal erythema reaction (scored ±) after the fourth application of one of the formulations. No other reactions were observed.

Shave cream formulations containing 2.2% Palmitic Acid were considered "non-irritating" to the skin of 101 panelists treated with closed and open patch applications[257] and to facial skin of 60 panelists in a 4-week controlled-use study.[254,258] Although the former skin irritation study was part of a prophetic patch test[272] in which patches usually remain in place for 24 h, no specific procedure was outlined.

In an SIOPT, commercial grade Myristic Acid produced no irritation in 17, mild erythema in 2, and moderate erythema in 1 of 20 panelists. The primary irritation index was 0.2, and Myristic Acid was considered "practically non-irritating."[259]

In a soap chamber test,[251] 0.2 ml of a 50% solution of Myristic Acid in mineral oil was applied to the ventral skin of the forearm of 16 human subjects once daily for 5 days.[260] The erythema score was 0.48 on a scale of 0 to 5. Myristic Acid was considered "non-irritating under conditions of this test."

Several bar soap formulations with concentrations of Myristic Acid of 10,[261] 22.1,[263] and 91%[262] were tested for skin irritation using 16 human subjects. A 0.2 ml volume of an 8% aqueous preparation was applied to the ventral skin of the forearm under occlusive patches once daily for 5 days using the Frosch-Kligman soap chamber test.[251] The formulations were considered "slightly"[261] to "moderately irritating,"[262] and erythema scores were 1.41, 1.73, and 1.95 on a scale of 0 to 5 for the formulations containing 10, 22.1, and 91% Myristic Acid, respectively.

A white cleanser lotion formulation containing 5% Myristic Acid was tested for cumulative irritation on the skin of 12 human subjects using a 21-day consecutive closed-patch test.[252,253] The total irritation score for all subjects for all 21 applications of the formulation was 609 of a maximal possible score of 756. The formulation was considered "highly irritating."[264]

In an SIOPT, 40% Stearic Acid in mineral oil produced no irritation in 21 panelists.[265]

A face cream formulation containing 13% Stearic Acid was considered "non-irritating" to the skin of 101 panelists treated with single 24-h closed and open patch applications. Four of the 101 panelists had mild erythemal reactions to the closed patch application; no other reactions were observed.[266]

A face cream formulation containing 13% Stearic Acid was tested for irritation of the facial skin of 105 panelists in a 4-week controlled-use study.[254] Under these conditions, the formulation was considered "non-irritating."[267]

As part of a Modified Schwartz/Peck prophetic patch study,[272] a shave foam formulation containing 8% Stearic Acid was tested for irritation of the dorsal skin of 100 male subjects.[268] The formulation was applied to subjects' backs for 48 h, then washed from the area. Subjects then used the formulation to shave at least once daily for 2–4 weeks. No irritation was observed after the 48-h occlusive patch, and the complaints of minor pruritus by 2 subjects during the home-use part of the study were not recorded because no clinical signs of erythema or other evidence of itching were noted.

A gray liquid eyeliner formulation containing 2.8% Stearic Acid was tested for cumulative irritation on the skin of 13 human subjects using a 21-day consecutive closed-patch test.[252,253] The total irritation score for all subjects for all 21 applications of the formulation was 216 of a maximal possible score of 675. The formulation was considered "moderately irritating."[269]

Two moisturizer product formulations containing 2.6% Stearic Acid were tested for cumulative irritation on the skin of 12 human subjects.[270] Occlusive patches were applied for 24 h to the skin of the scapular or interscapular area daily for 21 days. Scoring on a scale of 0 to 4 for erythema and edema was done after each patch was removed and before the next application. Markers of results after treatment with 0.5% and 2% sodium lauryl sulfate were used for comparison with sample treatment. Total irritation scores for the formulations from all 12 subjects for all 21 applications were 28 and 56, lower than the score of 67 obtained after treatment with 0.5% sodium lauryl sulfate. The 2% sodium lauryl sulfate score was 298. Both formulations were considered "basically non-irritating."

Skin Sensitization Studies

The maximization test[182] was used to test a black cream mascara formulation containing 6% Oleic Acid for contact sensitization (Table 21).[273] Induction sites on the volar aspect of the 14 subjects' forearms were pretreated with single 24-h occlusive patches of 5% aqueous sodium lauryl sulfate (SLS). Five alternate-day 48-h occlusive induction patches were followed by a 10–14-day nontreatment period. After pretreatment of new sites with single 30-min occlusive patches of 2% aqueous SLS, single 48-h occlusive challenge patches were applied. Results for the sites treated with the formulation were similar to those for control sites treated with petrolatum alone and petrolatum plus SLS, respectively. There was "no significant irritation or evidence of contact sensitization."

In a repeated insult patch test (RIPT), 200 human volunteers were tested for contact sensitization of a purple wax cosmetic formulation containing 5.0% Oleic Acid.[274] Nine 24-h closed induction patches containing 0.3 ml of the formulation were applied to sites on the volar forearm on Mondays, Wednesdays, and Fridays of 3 consecutive weeks during the induction phase of the study. Signs of irritation were scored 48 or 72 h after the application. After a 10–14 day nontreatment period, a single 48-h challenge patch was

made to a separate site, and the site was scored 48-h and 72-h to 96-h after application. Of the 200 subjects, 153 completed the study. Slight irritation was observed in 1 to 3 subjects during the induction phase, and 1 subject reacted slightly to the challenge patch after 48 h. "No contact sensitization" was produced by the formulation under the conditions of this study.

A mascara formulation containing 3.0% Oleic Acid was tested for irritation and sensitization using an RIPT and 222 human subjects, 200 of whom completed the study.[275] Ten occlusive induction patches were applied for 24 h to sites on the upper back on Mondays, Wednesdays, and Fridays. Sites were scored before application of the next induction patch. After a 2-week nontreatment period, 2 48-h challenge patches were applied 1 week apart. Challenge sites were scored after patch removal. Mild erythemal reactions to single induction patches were observed and considered toxicologically insignificant due to their transient nature. Three subjects reacted with mild erythema to the 2nd challenge patch after 48 h. Two different subjects with mild erythemal reactions 72 h after the 2nd challenge patch was applied were challenged again. One of the 2 had a mild reaction to this 3rd challenge patch. The formulation was considered "not irritating or allergenic."

A mascara formulation containing 2.0% Oleic Acid was tested for irritation and sensitization using an RIPT and 222 human subjects, 205 of whom completed the study.[276] The 10 semiocclusive induction patches, applied for 24 h, and the 2-week nontreatment phases were followed by 2 48-h challenge patches applied to a new site, 1 week apart. No irritation or sensitization was observed.

In a modified Draize RIPT[10] with 14 human subjects, there was "no evidence of allergic contact sensitization" produced by a mascara formulation containing 2.0% Oleic Acid.[277] The formulation had been applied to the skin of the upper arms or backs (unspecified) of subjects during the 9 occlusive patch induction phase (3 times weekly for 3 weeks) and after a 2-week nontreatment period during the single patch challenge phase. Induction and challenge patches remained in contact with the skin for 48 h or 72 h. One equivocal reaction to the challenge was observed. There was "no evidence of allergic contact sensitization."

In a modified Shelanski RIPT of a 1% aqueous dilution of a liquid soap formulation containing 1.95% Lauric Acid on intact and abraded skin of the backs of 52 human subjects, no primary or cumulative skin irritation and no sensitization were observed.[278] Approximately 0.2 ml of the preparation was applied to occlusive induction and challenge patches. A total of 12 24-h induction patches were were administered for 3 weeks, 4 times per week from Monday through Thursday. Sites were scored before application of the next patch. No patches were applied from Friday to Sunday of each week. A total of 4 24-h challenge patches were applied to a new site on the 4th week, after a 72-h nontreatment period, from Monday through Thursday. Of the 52 subjects who began the study, 46 subjects were present for the completion of the study.

In a prophetic patch test,[272] a shave cream formulation containing 2.2% Palmitic Acid was tested for irritation and sensitization of the skin of 101 human subjects.[257] Two 24-h closed and open patches are usually applied to

TABLE 21. Clinical Skin Sensitization Studies (Product Formulation Data Only)

Fatty acid tested	*Concentration*	*No. of subjects*	*Methods*	*Results*	*Reference*
Oleic Acid	6% in mascara formulation	23	Maximization	Similar results for treated and control sites. "No significant irritation or evidence of contact sensitization"	273
	5% in product formulation	153	RIPT[a]	Faint reactions to induction in 1–3 subjects. Slight reaction to challenge in 1 subject	274
	3% in mascara formulation	200	RIPT	Isolated irritation reactions. Mild reactions to 2nd challenge patch	275
	2% in mascara formulation	205	RIPT	No irritation or sensitization	276
	2% in mascara formulation	14	RIPT	Equivocal reaction to challenge in 1 subject	277
Lauric Acid	1% (1.95%)[b] in liquid soap formulation	46–48	RIPT, I/A[c]	No irritation or sensitization	278
Palmitic Acid	2.2% in shave cream formulation	101	Prophetic Patch, O/C[d]	Erythema to closed challenge patch in 3 subjects. No other reactions	257
	2.2% in shave cream formulation	52	RIPT, O/C	No irritation or sensitization	257
Stearic Acid	13% in face cream formulation	101	Prophetic Patch, O/C	Mild reactions to closed induction and challenge patch(es) in few subjects	266
	13% in face cream formulation	52	RIPT, O/C	Mild reactions to closed induction patches in few subjects. No reactions to challenge	266
	10% in product formulation	116	RIPT	Mild to moderate erythema to 2 induction patches in 1 subject. No reactions to challenge	279
	10% in mascara formulation	206	RIPT	Reactions to induction and 48–72 h after challenge. Cumulative irritation in 3 subjects	280
	8% in shave foam formulation	101	Prophetic Patch and In-Use Testing	Several reactions 48 h after induction and challenge, fewer 72 h later. No reactions during In-Use phase	22
	8% in shave foam formulation	100	See preceding entry	No reactions to induction or challenge. Complaints of minor pruritis from 2 subjects during In-Use phase	268

7.7% in mascara formulation	101	RIPT	1 subject had reaction to 8th induction patch. No reactions to challenge	281
5% in mascara formulation	205	RIPT, semiocclusive patches	No irritation or sensitization	282
4% in product formulation	48	RIPT	No irritation or sensitization	283
2.8% in hand lotion formulation	51	RIPT	Transient slight induction reactions in 2 subjects. No reactions to challenge at original or untreated site	284
2.8% in 2 skin lotion formulations	57	RIPT, 48-h patches	Reactions to induction in 1–5 subjects. Slight reactions 72 h after challenge	285
2.66% in eyeliner formulation	200	RIPT	Definite erythema to isolated induction patches in few subjects. No reactions to challenge	286
2.6% in moisturizer formulation	204	RIPT	Mild to intense reactions to induction and challenge. "Mild irritant under occlusion patch"	287
2.6% in moisturizer formulation	203	RIPT	Isolated, mild erythema to induction. Few intense reactions to challenge but none to repatching	288
2.6% in sun lotion formulations	208	RIPT, semiocclusive patches	No irritation or sensitization	289
2.6% in sun lotion formulations	208	RIPT, semiocclusive patches	Few subjects with isolated reactions to induction and challenge	290
2.6% in sun block formulations	208	RIPT, semiocclusive patches	Few subjects with isolated reactions to induction. No reactions to challenge	291
1.0% in hand lotion formulation	76	RIPT	Minimal to definite erythema in few subjects to induction and challenge at same site. No reactions to challenge at untreated site	292
1.0% in hand lotion formulation	76	RIPT	Minimal to moderate irritation to induction in few subjects. No reactions to challenge	292
1.0% in suntan lotion formulation	184	RIPT	No reactions to induction or challenge	293
1% (23%)[b] in bar soap formulation	25	Maximization	No contact sensitization	294
0.5% (25%) in product formulation	99	RIPT	Equivocal induction reaction in 1 subject	295

[a]RIPT, repeat insult patch test.
[b]0.5 or 1.0% aqueous dilutions of formulation containing percentage of fatty acid (percentage in parentheses).
[c]I/A, patches applied at intact and abraded sites.
[d]O/C, 2 series of patches, open and closed, applied at separate sites.

the skin 10–14 days apart in the standard Schwartz-Peck procedure. There were 3 reactions of mild to intense erythema to the closed challenge patch and the formulation was considered "nonirritating and nonsensitizing."

A modified Shelanski RIPT[296] in 52 human subjects involved 10 alternate-day 24-h induction patches, a 2- to 3-week nontreatment phase and a single 48-h challenge patch.[257] Closed and open patches with the same shave cream formulation containing 2.2% Palmitic Acid were applied. No irritation or sensitization was observed.

A face cream formulation containing 13% Stearic Acid was tested for photosensitization using a prophetic patch test[272] in 101 subjects and a modified RIPT in 52 subjects.[266] There were mild reactions in a few subjects to closed induction and challenge patches. The formulation was considered "nonirritating and nonsensitizing."

Approximately 0.1 ml of a cosmetic product formulation containing 10% Stearic Acid was tested for irritation and sensitization of sites on the upper back of 116 human subjects with an RIPT involving 9 alternate-day 24-h occlusive induction patches, a 3-week nontreatment period, and a single 24-h challenge patch at a new site.[279] Moderate erythema was observed in 1 subject after the 5th and 6th induction patches and the 7th induction patch at an adjacent site; the remaining 2 induction patches were eliminated. There were no other reactions to induction and no reactions to challenge.

In a modified Draize-Shelanski RIPT,[168,296] approximately 0.1 g of a mascara formulation containing 10% Stearic Acid produced mild to moderate irritation in a few subjects during induction.[280] Signs of erythema, edema, and induration or vesiculation were observed in 1 to 4 subjects 48 and 72 h after challenge application. The 206 subjects had received 10 alternate day 24-h occlusive induction patches and single 48-h occlusive challenge patches following a 2-week nontreatment period.

In a prophetic patch and in-use testing study, application of single 48-h occlusive induction patches was followed by a 4-week period of daily home use and single 48-h occlusive challenge patches of a shave foam formulation containing 8% Stearic Acid.[268] There were no reactions to induction or challenge patches, and 2 of the 100 subjects complained of minor pruritus during the in-use part of the study. However, there was no erythema or itching.

Several 1 + and a few 2 + reactions were observed 48 h after application of induction and challenge patches in another prophetic patch and in-use testing study.[22] Fewer reactions were noted after 72 h. No significant product-related reactions were reported during the in-use phase of the study.

In a modified Draize RIPT,[168] a mascara formulation containing 7.7% Stearic Acid was tested for irritation and sensitization in 101 human subjects.[281] Approximately 0.2 g was applied to upper arm sites with 24-h occlusive patches on Mondays, Wednesdays, and Fridays for 3 weeks during the induction phase and with single 48-h patches during the challenge phase, following a 2-week nontreatment period. One subject had minimal erythema after the 8th induction patch. There were no other reactions to induction and no reactions to challenge patches.

No irritation and no sensitization were noted in RIPTs of cosmetic product formulations containing 4%[283] and 5%[282] Stearic Acid. The 4% formulation

was tested using the 10 alternate-day 24-h occlusive induction patches followed by a single 24-h occlusive challenge patch to a separate site. The 5% formulation involved 10 alternate-day 24-h semiocclusive induction patches and 2 48-h semiocclusive challenge patches 1 week apart. Both studies had a 2-week nontreatment period between induction and challenge phases.

Although slight transient reactions were observed, a hand lotion formulation containing 2.8% Stearic Acid was considered nonirritating and nonsensitizing.[284] In an RIPT, 0.2 ml of the formulation was applied to the skin of 57 human subjects via 10 alternate-day 24-h occlusive induction patches and single 24-h challenge patches to the same site and to a new site following a 10–14-day nontreatment period.

In RIPTs of two skin lotion formulations containing 2.8% Stearic Acid, 9 consecutive 48-h induction patches, followed by a single 48-h challenge patch after a 13-day nontreatment period, were applied to the skin of 57 human subjects.[285] One to five reactions of barely perceptible to mild erythema were observed throughout the induction phase. Application of one lotion produced erythema and minimal edema to the induction patch and 1 reaction to the challenge patch 72 h after its application in 1 subject.

Several cosmetic product formulations containing 0.13% (0.5% aqueous dilution of formulation containing 25%[295]) to 2.66%[286] Stearic Acid were tested for irritation and sensitization in 76 to 208 human subjects. RIPTs involving 9 to 10 alternate-day 24-h occlusive (semiocclusive patches used in 1 study[289]) induction patches, a 13-day to 2-week nontreatment period, and single 48-h challenge patches[286,292,294,295] or 2 48-h challenge patches administered 1 week apart[287–291,293,296] resulted in isolated 1 + irritation reactions in few subjects during the induction phase. These occasional reactions were considered nonspecific; no cumulative irritation was produced. There were no or very few reactions to challenge patches, and the formulations were considered nonsensitizing.

No contact sensitization was produced in 25 human subjects tested with a 1% aqueous dilution of a bar soap formulation containing 23% Stearic Acid in a maximization study.[182] Five 48-h occlusive induction patches applied to volar forearm sites were followed by a single 48-h occlusive challenge patch. Sodium Lauryl Sulfate was used at concentrations of 2% for pretreatment of induction sites and 10% for the 1-h pretreatment of challenge sites.

Photosensitization Studies

Two makeup formulations containing 5.08%[298] and 1.5%[299] Oleic Acid were tested for photosensitization using the skin of the backs of 25 human subjects. A Xenon Arc Solar Simulator (150 W), which was filtered to produce a continuous emission spectrum in the ultraviolet region ranging from 290 to 400 nm (UVA and UVB), was used. Individual minimal erythemal dose (MED) values were determined.[300] Six alternate-day induction patches were applied, each left in place for 24 h, scored, irradiated with 3 MED using the full source spectrum, and scored again 48 h after the application. After a 10-day nontreatment period, single 24-h occlusive challenge patches were applied to new sites. Sites were scored, irradiated for 3 min, using a Schott WG345 filter over the light source, then scored again 15 min and 24, 48, and 72 h after

irradiation. There were no "reactions" to either formulation recorded. The liquid makeup formulation was considered nonphotosensitizing[299] and the blusher formulation nonphotoallergenic.[298] No data were presented to distinguish between "phototoxic reactions" and "photoallergic reactions."

The phototoxicity of a shave cream formulation containing 2.2% Palmitic Acid was tested in 101 human subjects using single 24-h closed and open patches.[257] Sites were UV-irradiated (wavelength and dosage unspecified) after patch removal. Irritation was observed at 1 site tested with a closed patch.

In a photosensitization study with 52 human subjects, sites under 4 induction patches and 1 challenge patch containing the shave cream formulation with 2.2% Palmitic Acid were UV-irradiated (wavelength and dosage unspecified) after patch removal.[257] Both closed and open patches were used. There were no reactions during induction or challenge phases, and the formulation was considered "non-photosensitizing."

No phototoxicity was observed in 101 human subjects exposed to UVA irradiation and single closed or open patches with a face cream formulation containing 13% Stearic Acid.[266]

Minimal to mild erythema was observed at a few sites after treatment with a lotion formulation containing 2.8% Stearic Acid or a 1% aqueous dilution of a bar soap formulation containing 23% Stearic Acid followed by UVA irradiation.[301,302] The lotion formulation was applied via 24-h occlusive patches to the forearm, and treatment sites were irradiated with UVA light for 15 min at a distance of approximately 10 cm, receiving a dose of 4400 $\mu W/cm^2$. The bar soap formulation was applied via 24-h occlusive patches to the infrascapular region of the back, and treatment sites were irradiated with UVA light from Xenon Arc Solar Simulator (150 W) with a Schott WG345 filter for 12 min. Similar results were observed at control sites that had received UVA irradiation alone.

A face cream formulation containing 13% Stearic Acid was tested for photosensitization using 52 human subjects and 4 induction patches and 1 challenge patch.[266] Closed and open 24-h patches were applied, and treated sites were irradiated with the full Xenon UV light spectrum at 3 times the individuals' predetermined MED after removal of each patch and 48 h later. After the 24-h challenge patch, treated sites were irradiated with UVA light (Xenon source plus Schott WG345 filter) for 3 min. There were no reactions observed at sites under closed or open patches at either induction or challenge sites.

No reactions were observed in 100 human subjects of a photosensitization study testing an eyeliner formulation containing 2.66% Stearic Acid.[286] In a 10 induction, 1 challenge occlusive patch RIPT, treated sites were irradiated with UV light from a Hanovia Tanette Mark 1 light source for 1 min at a distance of 1 foot after removal of the 1st, 4th, 7th, and 10th induction patches and after the challenge patch. Approximately 50% of the subjects were designated as "sensitive subjects" because of past experiences of rash or irritation from the use of facial products or because of reaction to a previous patch test with a facial product.

Most of the 30 human subjects tested with 2 lotion formulations had no photosensitization reactions.[303,304] Subjects had been treated with 10 24-h

occlusive induction patches, each patch followed by UVA irradiation of the site for 15 min at a distance of 10 cm from the source for a dosage of 4400 $\mu W/cm^2$. The single 24-h challenge patch was also UVA irradiated. Nonirradiated controls had isolated reactions of minimal erythema.

No reactions were observed in similar photosensitization studies testing suntan lotion,[305,308] moisturizing lotion,[306] and facial lotion[307] formulations containing 1% Stearic Acid in 20–27 human subjects. No other data were included in these studies.

Table 22 summarizes clinical photosensitization studies.

Ocular Irritation Studies

To evaluate ocular irritation produced by eye area cosmetics in contact lens and noncontact lens wearers, female volunteers participated in a 3-week exaggerated-use study. After a brief medical history with emphasis on ocular details (e.g., history of eye diseases, use of contact lenses and eye area cosmetics) and an eye examination, each subject was instructed to use assigned kits of test cosmetics twice daily (morning and early evening) for 3 weeks. The wearers of contact lenses were to handle, wear, and disinfect their contact lenses normally and to apply cosmetics after lens insertion into the eye. Examinations were performed on the 7th, 14th, and 21st days of the study. Eye area cosmetics in the test kits included mascaras containing 2–3% Oleic Acid and eye shadows.[309,310]

There were no product-related findings of irritation in any of the 23 subjects after daily use of a mascara formulation containing 2% Oleic Acid.[309] Investigators considered the "risk of any significant eye area irritation and/or ocular damage minimal, if existent at all."

Similar results were obtained in another 3-week exaggerated use study, with 35 female subjects testing mascara formulations containing 2% and 3% Oleic Acid in combination with eye shadow formulations.[310]

Other Studies

Graded intraduodenal administration of 5–40 ml of Oleic Acid in humans inhibited pentagastrin-stimulated gastric acid secretion.[311,312] Intracolonic infusion of Oleic Acid (117 cal., pH 7.4) into human subjects decreased pancreatic enzyme concentrations and bicarbonate ion output and inhibited biliary secretion.[313]

SUMMARY

Oleic, Lauric, Palmitic, Myristic, and Stearic Acids are fatty acids with hydrocarbon chains ranging in length from 12 to 18 carbons with a terminal carboxyl group. The saturated fatty acids, Lauric(12C), Palmitic(16C), Myristic(14C), and Stearic(18C) Acids, are solids and the *cis*-9,10 monounsaturated Oleic Acid(18C) is a liquid at standard temperature and pressure.

The fatty acids are obtained by the hydrolysis of animal fats and vegetable oils. Cosmetic grade fatty acids occur as mixtures of several fatty acids, the

TABLE 22. Clinical Photosensitization Studies

Fatty acid tested	*Concentration*	*No. of subjects*	*Study type*	*Results*	*Reference*
Oleic Acid	5.08% in blusher formulation	25	Photosensitization	No photoallergic reactions	298
	1.5% in liquid makeup formulation	25	Photosensitization	No indication of photosensitization	299
Palmitic Acid	2.2% in shave cream formulation	101	Phototoxicity	Phototoxic reaction to single closed patch in 1 subject	257
	2.2% in shave cream formulation	52	Photosensitization	No photosensitization reactions to closed or open patches	257
Stearic Acid	13% in face cream formulation	101	Phototoxicity	No phototoxic reactions to closed or open patches	266
	2.8% in lotion formulation	10	Phototoxicity	Minimal erythema after 48 h in 2 subjects similar to control group. No irritation after 1 week	301
	1.0% (23%)[a] in bar soap formulation	10	Phototoxicity	Mild erythema at all irradiated sites—both treated and control	302
	13% in face cream formulation	52	Photosensitization	No photosensitization reactions to closed or open patches	266
	2.66% in eyeliner formulation	200	Photosensitization	No reactions	286
	2.8% in lotion formulation	30	Photoallergy	No photoallergic reactions in most subjects. Non-irradiated control sites had isolated minimal erythema reactions	303
	2.8% in skin lotion formulation	30	Photoallergy	Minimal erythema at irradiated and nonirradiated control sites in 1–2 subjects	304
	1.0% in suntan lotion formulation	25	Photosensitization	No reactions. No other data included	305
	1.0% in moisturizing lotion formulation	27	Photosensitization	No reactions. No other data included	306
	1.0% in facial lotion formulation	27	Photosensitization	No reactions. No other data included	307
	1.0% in suntan lotion formulation	20	Photosensitization	No reactions. No other data included	308

[a] 1.0% aqueous dilution of bar soap formulation containing 23% Stearic Acid tested.

content varying with method of manufacture and source. Fatty acid preparations may include up to 1.5% unsaponifiable matter, glyceryl monoesters of fatty acids, and butylated hydroxytoluene. Gas chromatography is the predominant analytical method for fatty acid identification.

The fatty acids are primarily used as intermediates of fatty acid salts. These salts are used as emulsifiers, emollients, and lubricants in cosmetic creams, cakes, soaps, lotions, and pastes that are slightly alkaline, ranging in pH from 7.5 to 9.5. In product formulation data voluntarily filed in 1981 with FDA by the cosmetic industry, 424 products contained Oleic Acid, 22 contained Lauric Acid, 29 contained Palmitic Acid, 36 contained Myristic Acid, and 2465 contained Stearic Acid at concentrations ranging from 0.1 to 25%.

Fatty acids are absorbed, digested, and transported in animals and humans. Radioactivity from labeled fatty acids administered orally, intravenously, intraperitoneally, and intraduodenally has been found in various tissues and in blood and lymph. β-Oxidation of the fatty acids involves serial oxidation and reduction reactions yielding acetyl-CoA. Although placental transfer of fatty acids has been documented in several species and fetal lipid metabolism has been studied, no studies on the teratogenicity of Oleic, Lauric, Palmitic, Myristic, or Stearic Acids were found. High intake of dietary saturated fatty acids has been associated with the incidence of atherosclerosis and thrombosis.

Little acute toxicity was observed when Oleic, Lauric, Palmitic, Myristic, or Stearic Acid, or cosmetic formulations containing these fatty acids at concentrations of 2.2–13% were given to rats orally at doses of 15–19 g/kg body weight.

In subchronic oral toxicity studies, Oleic, Palmitic, and Stearic Acids were fed to rats in diets at doses ranging from 5 to 50%. Thrombosis, aortic atherosclerosis, anorexia, and mortality were observed. In a subchronic study, no signs of toxicity were observed in chicks fed 5% dietary Stearic and Oleic Acids. Feeding of 15% dietary Oleic Acid to rats in a chronic study resulted in normal growth and general health, but reproductive capacity of female rats was impaired.

Results from topical application of Oleic Acid (at concentrations from 50% Oleic Acid to commercial grade Oleic Acid) to the skin of mice, rabbits, and guinea pigs ranged from no toxicity to signs of erythema, hyperkeratosis, and hyperplasia. Intradermal administration to guinea pigs of 25% Oleic Acid to commercial grade Oleic Acid resulted in local inflammation and necrosis. A formulation containing 2.2% Palmitic Acid was considered nontoxic to rabbits. A topically applied dose of 5 g/kg commercial grade Stearic Acid was not toxic to rabbits. Intradermal administration of 10–100 m*M* Stearic Acid to guinea pigs and rabbits resulted in mild erythema and slight induration.

Eighteen mmol% concentrations of the fatty acids topically applied to the skin of the external ear canals of albino rabbits for 6 weeks produced a range of responses, varying from no irritation with Stearic Acid to slight irritation with Myristic and Palmitic Acids to defined erythema, desquamation, and persistent follicular keratosis with Oleic and Lauric Acids. Slight local edema and no deaths were observed among NZW rabbits after 4 weeks of topical administration of product formulations containing 2.0% Stearic Acid.

In 13-week dermal toxicity studies, 2 cosmetic product formulations containing, at most, 5% Stearic Acid produced moderate skin irritation in rats receiving 4.0 ml/kg and 227 mg/kg doses. All other physiological parameters were normal.

In single insult occlusive patch tests for primary irritation, commercial grades of all 5 fatty acids, at doses of 35–65% in vehicles (Stearic Acid only) and at 1–13% in cosmetic product formulations (other fatty acids), produced no to moderate erythema and slight, if any, edema in the skin of rabbits. Slight increases in irritation were observed in the short-term repeated patch tests (daily for 3–14 days) of Oleic and Myristic Acids.

In maximization studies with 2 cosmetic product formulations containing 5.08% Oleic Acid and 1.0% Stearic Acid, slight reactions were observed to challenge patches. These formulations were considered weak, grade I, sensitizers. In another maximization study, after intradermal induction and booster injections of a formulation containing 3.5% Stearic Acid, reactions to topical challenge applications of the formulation were few and minimal in intensity.

Skin lotion formulations containing 2.8% Stearic Acid were not photosensitizing to the skin of Hartley guinea pigs.

Oleic Acid and its UVA-induced peroxides were associated with increased comedo formation on the treated ears of two species of rabbits.

In ocular irritation studies, the fatty acids alone and at concentrations ranging from 1 to 19.4% in cosmetic product formulations produced no to minimal irritation after single and multiple (daily, 14-day) instillations into the eyes of albino rabbits. Irritation was primarily in the form of very slight conjunctival erythema. A single instillation of Lauric Acid also produced corneal opacity and iritis.

Although Oleic and Lauric Acids induced mitotic aneuploidy in in vitro mutagenicity tests, both have been indicated as inhibitors of mutagenicity produced by positive controls, such as N-nitrosopyrrolidine and sodium azide, in other tests. Stearic Acid was inactive in aneuploidy induction tests and in the Ames test, and it did not inhibit mutagenicity, as did Oleic and Lauric Acids. No increase of mitotic crossing-over events was induced by Oleic, Lauric, or Stearic Acids. Oleic Acid did not increase the number of sister chromatid exchanges over background.

In carcinogenicity studies, no malignant tumors were induced by repeated subcutaneous injections of 1–16.5 mg Oleic Acid in two species of mice. Intestinal and gastric tumors were found in mice receiving dietary Oleic Acid at daily concentrations up to 200 mg/mouse. Treatment of mice with repeated subcutaneous injections of 25 and 50 mg Lauric Acid was not carcinogenic. Low incidences of carcinomas, sarcomas, and lymphomas were observed in mice receiving single or repeated subcutaneous injections of 25 and 50 mg Palmitic and up to 82 mg Stearic Acid. Feeding of up to 50 g/kg/day dietary Stearic Acid to mice was not carcinogenic.

In clinical primary and cumulative irritation studies, Oleic, Myristic, and Stearic Acids at concentrations of 100% or 40–50% in mineral oil were nonirritating. Mild to intense erythema in single insult occlusive patch tests, soap chamber tests, and 21-day cumulative irritation studies were produced by

cosmetic product formulations containing 2–93% Oleic, Palmitic, Myristic, or Stearic Acid and were generally not related to the fatty acid concentrations in the formulations.

In clinical repeated insult patch tests (open, occlusive, and semiocclusive), maximization tests, and prophetic patch tests with cosmetic product formulations containing Oleic, Lauric, Palmitic, and Stearic Acids at concentrations ranging from <1 to 13%, no primary or cumulative irritation or sensitization was reported. A few subjects ($<5\%$ of the approximate 4000 subjects tested) reacted to a few, isolated induction patches. Slight, if any, reactions were observed after challenge patching at original or adjacent sites on the upper backs or forearms of some subjects ($\sim < 2\%$). Intensity of observed reactions to the formulations was not directly related to the concentrations of the fatty acid ingredients.

Cosmetic product formulations containing 1–13% Oleic, Palmitic, or Stearic Acid produced no photosensitization in human subjects. There were slight reactions to a few induction patches.

There was no treatment-related ocular irritation in female subjects, some of whom were contact lens wearers, involved in two 3-week exaggerated-use studies of mascara formulations containing 2 and 3% Oleic Acid. These formulations were used in combination with other eye area cosmetics.

DISCUSSION

Although insufficient data were available for Myristic Acid, the Expert Panel included it in this safety assessment due to its structural similarity with the other fatty acids of this group.

Applications of Lauric and Oleic Acids to the skin of rabbits resulted in follicular keratosis and/or formation of comedones. These effects were considered by members of the Expert Panel in their safety assessment of the fatty acids reviewed in this report.

CONCLUSION

On the basis of available data from studies using animals and humans, the Expert Panel concludes that Oleic, Lauric, Palmitic, Myristic, and Stearic Acids are safe in present practices of use and concentration in cosmetics.

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REFERENCES

1. WINDHOLZ, M., BUDAVARI, S., BLUMETTI, R.F., and OTTERBEIN, E.S. (eds.). (1983). *The Merck Index,* 10th ed. Rahway, NJ: Merck and Co.
2. ESTRIN, N.F., CROSLEY, P.A. and HAYNES, C.R. (1982). *CTFA Cosmetic Ingredient Dictionary*, 3rd ed. Washington, DC: CTFA.
3. MORRISON, R.T. and BOYD, R.N. (1973). *Organic Chemistry*, 3rd ed. Boston, MA: Allyn and Bacon.
4. LEHNINGER, A.L. (1975). *Biochemistry.* New York: Worth Publ.
5. OSOL, A. (ed.). (1980). *Remington's Pharmaceutical Sciences,* 16th ed. Easton, PA: Mack Publ. Co.
6. SWERN, D. (ed.). (1979). *Bailey's Industrial Oil and Fat Products*, 4th ed. New York: John Wiley & Sons, Vol. 1.
7. WEAST, R.C. (ed.). (1982). *CRC Handbook of Chemistry and Physics*, 63rd ed. Boca Raton, FL: CRC Press.
8. FOOD CHEMICALS CODEX (FCC), 3rd ed. (1981). Washington, DC: National Academy Press.
9. BALSAM, M.S. and SAGARIN, E. (1972). *Cosmetics: Science and Technology,* 2nd ed. New York: John Wiley & Sons, Vols. 1, 2, 3.
10. MARZULLI, F.N. and MAIBACH, H.I. (1977). Contact allergy: predictive testing in humans, in *Advances in Modern Toxicology. Dermatology and Pharmacology.* New York: John Wiley & Sons, Vol. 4, Chap. 11, pp. 353–72.
11. FASSETT, D.W. and IRISH, D.D. (eds.). (1963). *Industrial Hygiene and Toxicology*, 2nd ed. *Toxicology.* New York: Interscience Publishers, Vol. 2.
12. UNITED STATES PHARMACOPEIA (USP), 20th rev. (July 1, 1980). Rockville, MD: U.S. Pharmacopeial Convention.
13. COSMETIC, TOILETRY AND FRAGRANCE ASSOCIATION (CTFA). (Feb. 22, 1979). CTFA cosmetic ingredient chemical description. Lauric Acid.*
14. CTFA. (Feb. 23, 1979). CTFA cosmetic ingredient chemical description. Myristic Acid.*
15. CTFA. (Feb. 23, 1979). CTFA cosmetic ingredient chemical description. Palmitic Acid.*
16. CTFA. (Feb. 26, 1979). CTFA cosmetic ingredient chemical description. Oleic Acid.*
17. CTFA. (Feb. 26, 1979). CTFA cosmetic ingredient chemical description. Stearic Acid.*
18. WILKINSON, J.B. and MOORE, R.J. (1982). *Harry's Cosmeticology*, 7th ed. New York: Chemical Publishing, p. 724.
19. ELDER, R.L. (ed.). (1980). Final report of the safety assessment of acetylated lanolin alcohol and related compounds. J. Environ. Pathol. Toxicol. **4**(4), 69.
20. HAWLEY, G.G. (ed.). (1977). *Condensed Chemical Dictionary*, 9th ed. New York: Van Nostrand Reinhold Co.
21. ESTRIN, N.F., HAYNES, C.R., and WHELAN, J.M. (1982). *CTFA Compendium of Cosmetic Ingredient Composition. Specifications/Spectra.* Washington, DC: CTFA.
22. CTFA. (Feb. 1979). Submission of unpublished data. (3-3-93). Clinical skin irritation and sensitization study on 8 percent stearic acid in shave foam.*
23. NATIONAL FORMULARY (NF), 15th ed. (July 1, 1980). Rockville, MD: U.S. Pharmacopeial Convention.
24. MOTOYOSHI, K. (1983). Enhanced comedo formation in rabbit ear skin by squalene and oleic acid peroxides. Br. J. Dermatol. **109**(2), 191–8.
25. HORWITZ, W. (ed.). (1980). *Official Methods of Analysis of the Association of Official Analytical Chemists (AOAC),* 13 ed. Washington, DC: AOAC.
26. SENZEL, A.J. (ed.). (1977). *Newburger's Manual of Cosmetic Analysis,* 2nd ed. Washington, DC: AOAC.
27. ALLEN, K.G., MacGEE, J., FELLOWS, M.E., TORNHEIM, P.A., and WAGNER, K.R. (1984). A new procedure to analyze free fatty acids. Application to 20-mg brain tissue samples. J. Chromatogr. **309**(1), 33–42.
28. GERHARDT, K.O. and GEHRKE, C.W. (1977). Rapid microdetermination of fatty acids in biological materials by gas-liquid chromatography. J. Chromatogr. **143**(4), 335–44.
29. PENTTILA, I., HUHTIKANGAS, A., HERRANEN, J., ESKELINEN, S., and MOILANEN, O. (1984). Simultaneous measurement of free and esterified fatty acids by gas chromatography from normal and type IV hyperlipoproteinaemic sera. Ann. Clin. Res. **16**(1), 13–7.

*Available upon request: Director, Cosmetic Ingredient Review, 1110 Vermont Ave., NW, Suite 810, Washington, DC 20005.

30. TAKATORI, T., TERAZAWA, K., NAKANO, K., and MATSUMIYA, H. (1983). Identification of 10-hydroxy-12-octadecenoic acid in adipocere. Forensic Sci. Int. **23**(2–3), 117–22.
31. VAN DE VAART, F.J., HULSHOFF, A., and INDEMANS, A.W.M. (1983). Analysis of creams. V. Application of thin-layer chromatography. Parts I and II. Pharmaceutisch Weekblad Sci. Ed. **5**(3), 109–18.
32. SMITH, R.M. (1983). Recent advances in the high-performance liquid chromatography of fatty acids. J. Pharm. Biomed. Anal. **1**(2), 143–51.
33. LIE KEN JIE, M.S.F. (1980). The characterization of long-chain fatty acids and their derivatives by chromatography, in Giddings, J.C., Grushka, E., Cazes, J., and Brown, P.R. (eds.). *Advances in Chromatography.* New York: Marcel Dekker, Vol. 18, Chap. 1.
34. DAVIS, D.V. and COOKS, R.G. (1982). Direct characterization of nutmeg constituents by mass spectrometry-mass spectrometry. J. Agric. Food Chem. **30**(3), 495–504.
35. SHIMASAKI, H. and UETA, N. (1983). Fractionation of the neutral lipids of rice-bran oil by centrifugal liquid chromatography. Agric. Biol. Chem. **47**(2), 327–9.
36. CYONG, J. and OKADA, H. (1976). Histochemical studies on fatty acid in lymphocyte-mediated immune reaction. Immunology **30**(5), 763–7.
37. ARUDI, R.L., SUTHERLAND, M.W., and BIELSKI, B.H.J. (1983). Purification of oleic acid and linoleic acid. J. Lipid Res. **24**(4), 485–8.
38. BAILEY, A.V. and PITTMAN, R.A. (1971). Wide-line NMR spectra of some saturated and unsaturated long chain fatty acids. J. Am. Oil Chem. Soc. **48**(12), 775–7.
39. EIERMANN, H.J. Acting Director, Division of Colors and Cosmetics, Food and Drug Administration. (June 12, 1986). Letter to R.L. Elder, Cosmetic Ingredient Review, on Oleic Acid Group, Methylene Chloride, and Glyceryl Ricinoleate.*
40. GREENBERG, L.A. and LESTER, D. (1954). *Handbook of Cosmetic Materials: Their Properties, Uses and Toxic and Dermatologic Actions.* New York: Interscience Publishers.
41. FOOD AND DRUG ADMINISTRATION (FDA). (1981). Cosmetic product formulation data. FDA computer printout.
42. CODE OF FEDERAL REGULATIONS. (1984). Title 21. Food and Drugs. Parts 172.5[a], 172.210, 172.315, 172.340, 172.615, 172.840, 172.860, 172.862, 172.863, 174.5, 175.105, 175.300, 176.200, 182.70, 182.90, 184.1090, 720.4. Washington, DC: U.S. Government Printing Office.
43. PATTY, F.A. (1963). *Industrial Hygiene and Toxicology,* 2nd rev. ed. New York: Interscience Publ.
44. FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY (FASEB). (1977). Evaluation of the health aspects of coconut oil, peanut oil, and oleic acid as they may migrate to food from packaging materials, and linoleic acid as a food ingredient. SCOGS-65. NTIS Doc. no. PB-274-475.
45. FASEB. (1975). Evaluation of the health aspects of tallow, hydrogenated tallow, stearic acid and calcium stearate as food ingredients. SCOGS-54. NTIS Doc. no. PB-262-661.
46. INFORMATICS, INC. (July 1973). Scientific literature reviews on generally recognized as safe (GRAS) food ingredients, tallow and stearic acid. Prepared for FDA under contract no FDA-72-104. NTIS No. PB-223 859.
47. INFORMATICS, INC. (1973). Monograph on vegetable oils, oleic acid, and linoleic acid. Vol. 1. NTIS Doc. no. PB-228 546/8.
48. FASEB. (December 1982). Insights in Food Safety Evaluation. NTIS Doc. no. PB83-154146.
49. FDA. (Dec. 8, 1977). Unpublished industry submission. Two-generation reproduction study in the rat. FDA file FAP 3428, Vol. 1, pp. 52–83.
50. FDA. (Nov. 3, 1969). Unpublished industry submission. Hercules Inc. 90-day subacute oral toxicity of commercial food grade oleic acid (Emersol 6333) in albino rats. FDA file FAP 2504, Vol. 1, pp. 161–72.
51. FDA. (1953). Unpublished industry submission. Pilot feeding studies of rats with sodium lactate (41 percent) + stearic acid (59 percent) or calcium lactate (41 percent) + stearic acid (59 percent). FDA file FAP 215, Vol. 1, pp. 163–299.
52. FDA. (March 13, 1959). Unpublished industry submission. One month feeding studies of vervic acid in rats. Comparison with calcium verv and stearic acid. FDA file FAP 215, Vol. 3, pp. 630–70.
53. FDA. (April 29, 1957). Unpublished industry submission. The chronic toxicity of octadecylamine. Final Report. FDA file FAP 22, Vol. 1, pp. 19–32.
54. AMERICAL MEDICAL ASSOCIATION (AMA). (April 1983). *AMA Drug Evaluations.* Chicago, IL: AMA.
55. FDA. (January 1984). The Division of OTC Drug Evaluation Ingredient Status Report. Rockville, MD.
56. CHECCHI, A.A., INC. (August 1979; December, 1979; March 1982; October 1983). Recommended or final actions of OTC advisory review panels on miscellaneous external drug products, topical analgesic, antirheumatic, otic, burn, sunburn treatment and prevention products, antimicrobial II, and contraceptive and other vaginal drug products, respectively. OTC Drug Ingredient Index and Manual.

57. BROWN, J.L. (1983). Incomplete labeling of pharmaceuticals: A list of "inactive" ingredients. N. Engl. J. Med. **309**(7), 439–41.
58. SHEN, D.-F., HUANG, A., and HUANG, L. (1982). An improved method for covalent attachment of antibody to liposomes. Biochim. Biophys. Acta **689**(1), 31–7.
59. MIGLIORE-SAMOUR, D., FLOC'H, F., MARAL, R., WERNER, G.H., and JOLLES, P. (1977). Adjuvant activities of chemically modified water-soluble substances from *Mycobacterium tuberculosis*. Immunology **33**(4), 477–84.
60. SIEGFRIED, J.A., KENNEDY, K.A., SARTORELLI, A.C., and TRITTON, T.R. (1983). The role of membranes in the mechanism of action of the antineoplastic agent adriamycin. Spin-labeling studies with chronically hypoxic and drug-resistant tumor cells. J. Biol. Chem. **258**(1), 339–43.
61. FOWLER, J.S. and WOLF, A.P. (1981). Special characteristics and potential for radiotracers for positron emission tomography. Acupunct. Electrother. Res. **6**(2–3), 81–108.
62. ELDER, R. (ed.). (1982). Final report on the safety assessment of decyl and isodecyl oleates. J. Am. Coll. Toxicol. **1**(2), 85–95.
63. COSMETIC INGREDIENT REVIEW (CIR). (1985). Tentative report on the safety assessment of Glyceryl Oleate.*
64. BORGSTROM, B. (1974). Fat digestion and absorption. Biomembranes **4B**(0), 555–620.
65. BRINDLEY, D.N. (1974). The intracellular phase of fat absorption. Biomembranes **4B**(0), 621–71.
66. SCOW, R.O., BLANCHETTE-MACKIE, E.J., and SMITH, L.C. (July 1980). Transport of lipid across capillary endothelium. Fed. Proc. **39**(9), 2610–7.
67. WESTERA, G., VAN DER WALL, E.E., VISSER, F.C., DEN HOLLANDER, W., HEIDENDAL, G.A.K., and ROOS, J.P. (1983). The uptake of iodinated free fatty acids in the (ischemic) dog heart. Indications for a dual uptake mechanism. Int. J. Nucl. Med. Biol. **10**(4), 231–6.
68. FASEB. (1977). Evaluation of the health aspects of sodium oleate and sodium palmitate as substances migrating to food from paper and paper-board used in food packaging. SCOGS-86. NTIS Doc. no. PB-276-414.
69. OPDYKE, D.L. (ed.). (1979). Monographs on fragrance raw materials. Stearic Acid. Food Cosmet. Toxicol. **17**(4), 383–8.
70. NUTRITION REVIEWS. (1969). Glyceride structure and fat absorption. Biochem. J. **27**, 18. In Opdyke, 1979, Ref. 69.
71. ANDREWS, R.J. and LEWIS, D. (1970). Utilization of dietary fats by ruminants. II. Effect of fatty acid chain length and unsaturation on digestibility. J. Agric. Sci. Camb. **75**, 55. In Opdyke, 1979, Ref. 69.
72. BUTCHER, E.O. (1951). The effects of application of various substances in the epidermis of the rat. J. Invest. Dermatol. **16**, 88.
73. BUTCHER, E.O. (1953). The penetration of fats and fatty acid into the skin of the rat. J. Invest. Dermatol. **21**, 44.
74. SCHEUPLEIN, R.J. (1965). Mechanism of percutaneous absorption. I. Routes of penetration and influence of solubility. J. Invest. Dermatol. **45**, 334.
75. BEIERWALTES, W.H., ICE, R.D., SHAW, M.J., and RYO, U.Y. (1975). Myocardial uptake of labeled oleic and linoleic acids. J. Nucl. Med. **16**(9), 842–5.
76. GOLDBERG, M. and ESCAIG, F. (1984). An autoradiographic study of the in vivo incorporation of [^{3}H]-palmitic acid into the dentine and enamel lipids of rat incisors, with a comparison of rapid-freezing freeze-substitution fixation and aldehyde fixation. Arch. Oral Biol. **29**(9), 691–5.
77. DHOPESHWARKAR, G.A. and MEAD, J.F. (1973). Uptake and transport of fatty acids into the brain and the role of the blood-brain barrier system. Adv. Lipid. Res. **11**, 109–42.
78. ABUMRAD, N.A., PARK, J.H., and PARK, C.R. (1984). Permeation of long-chain fatty acid into adipocytes. Kinetics, specificity, and evidence for involvement of a membrane protein. J. Biol. Chem. **259**(14), 8945–53.
79. HARRIS, P., GLOSTER, J.A., and WARD, B.J. (1980). Transport of fatty acids in the heart. Arch. Mal. Coeur **73**(6), 593–8.
80. MASORO, E.J. (1977). Lipids and lipid metabolism. Annu. Rev. Physiol. **39**, 301–21.
81. GIBSON, G.G., ORTON, T.C., and TAMBURINI, P.P. (1982). Cytochrome P-450 induction by clofibrate. Purification and properties of a hepatic cytochrome P-450 relatively specific for the 12- and 11-hydroxylation of dodecanoic acid (lauric acid). Biochem. J. **203**(1), 161–8.
82. STUMPF, P.K. (1969). Metabolism of fatty acids. Annu. Rev. Biochem. **38**, 159–212.
83. WAKIL, S.J. and BARNES, E.M. (1971). Pyruvate and fatty acid metabolism, in Florkin, M., and Stotz, E.H. (eds.). *Comprehensive Biochemistry*. New York: Elsevier Publ. Co., Vol. 18S.
84. GELLHORN, A. and BENJAMIN, W. (1966). Fatty acid biosynthesis and RNA function in fasting, aging and diabetes. Adv. Enzyme Regul. **4**, 19–41.

85. OSCAI, L.B. (1981). Exercise and lipid metabolism, in *Nutrition in the 1980's: Constraints on Our Knowledge.* Western Hemisphere Nutrition Congress, 1980. New York: A.R. Liss, pp. 383–90.
86. HULL, F.E., RADLOFF, J.F., and SWEELEY, C.C. (1975). Fatty acid oxidation by ischemic myocardium. Rec. Adv. Stud. Cardiac Struct. Metab. **8**, 153–65.
87. BIEZENSKI, J.J. (1975). Fetal lipid metabolism. Obstet. Gynecol. Annu. **4**, 39–70.
88. KIMURA, R.E. and WARSHAW, J.B. (1983). Metabolic adaptations of the fetus and newborn. J. Pediatr. Gastroenterol. Nutr. **2**(1), S12–S15.
89. GOODWIN, T.W. (ed.). (1977). *International Review of Biochemistry. Biochemistry of Lipids.* Baltimore, MD: University Park Press, Vol. 14, Part 2.
90. REITZ, R.C. (1979). The effects of ethanol ingestion on lipid metabolism. Prog. Lipid Res. **18**(2), 87–115.
91. BARAONA, E. and LIEBER, C.S. (1979). Effects of ethanol on lipid metabolism. J. Lipid Res. **20**(3), 289–315.
92. LECH, J.J., JESMOK, G.J., and CALVERT, D.N. (1977). Effects of drugs and hormones on lipolysis in heart. Fed. Proc. **36**(7), 2000–8.
93. ZAMMITT, V.A. (1983). Regulation of hepatic fatty acid oxidation and ketogenesis. Proc. Nutr. Soc. **42**, 289–302.
94. ZAKIM, D. and HERMAN, R.H. (1969). Regulation of fatty acid synthesis. Am. J. Clin. Nutr. **22**(2), 200–13.
95. NUMA, S. (1974). Regulation of fatty-acid synthesis in higher animals. Ergeb. Physiol. **69**, 54–96.
96. WAKIL, S.J., STOOPS, J.K., and JOSHI, V.C. (1983). Fatty acid synthesis and its regulation. Annu. Rev. Biochem. **52**, 537–79.
97. PEDERSEN, N.T. (1984). Estimation of assimilation of simultaneously ingested ^{14}C-triolein and ^{3}H-oleic acid as a test of pancreatic digestive function. Scand. J. Gastroenterol. **19**(2), 161–6.
98. SCHELBERT, H.R., HENZE, E., SCHON, H.R., KEEN, R., HANSEN, H., SELIN, C., HUANG, S.-C., BARRIO, J.R., and PHELPS, M.E. (1983). C-11 palmitate for the noninvasive evaluation of regional myocardial fatty acid metabolism with positron computed tomography. III. In vivo demonstration of the effects of substrate availability on myocardial metabolism. Am. Heart J. **105**(3), 492–503.
99. SAUER, F.D. and KRAMER, J.K.G. (1980). The metabolism of long-chain monoenoic fatty acids in heart muscle and their cardiopathogenic implications. Adv. Nutr. Res. **24**, 207–30.
100. WHEREAT, A.F. (1971). Fatty acid biosynthesis in aorta and heart. Adv. Lipid Res. **9**, 119–59.
101. KUMMEROW, F.A. (1983). Modification of cell membrane composition by dietary lipids and its implications for atherosclerosis. Ann. NY Acad. Sci. **414**, 29–43.
102. PEARCE, J. (1983). Fatty acid synthesis in liver and adipose tissue. Proc. Nutr. Soc. **42**(2), 263–71.
103. JEFFCOAT, R. (1979). The biosynthesis of unsaturated fatty acids and its control in mammalian liver. Essays Biochem. **15**, 1–36.
104. MAYES, P.A. (1970). Studies on the major pathways of hepatic lipid metabolism using the perfused liver. Horm. Metab. Res. **2**, 186–95.
105. GANGL, A. and OCKNER, R.K. (1975). Intestinal metabolism of lipids and lipoproteins. Gastroenterology **68**(1), 167–86.
106. EYSSEN, H. (1973). Role of the gut microflora in metabolism of lipids and sterols. Proc. Nutr. Soc. **32**(2), 59–63.
107. MIRAS, F., HERNANDEZ, J., DE LA HIGUERA TORRES-P, J., NUNEZ, J., MARTIN, A., and DE LA HIGUERA R., J. (1983). Studies on the fate of labelled almitic acid in rat lung. Comp. Biochem. Physiol. **75C**(1), 179–84.
108. WIRTHENSOHN, G. and GUDER, W.G. (1983). Renal lipid metabolism. Min. Electrolyte Metab. **9**, 203–11.
109. STOFF, J.S., EPSTEIN, F.H., NARINS, R., and RELMAN, A.S. (1976). Recent advances in renal tubular biochemistry. Annu. Rev. Physiol. **38**, 46–68.
110. HOHENEGGER, M. (1975). Lipid metabolism of the kidney: Possible relations to sodium transport. Curr. Probl. Clin. Biochem. **4**, 150–6.
111. ZUURVELD, J.G. and VEERKAMP, J.H. (1984). Palmitate oxidation in suspended skeletal muscle fibers from the rat. Biochim. Biophys. Acta **796**(1), 34–41.
112. DUNHAM, J., DODDS, R.A., NAHIR, A.M., FROST, G.T.B., CATTERALL, A., BITENSKY, L., and CHAYEN, J. (1983). Aerobic glycolysis of bone and cartilage: The possible involvement of fatty acid oxidation. Cell Biochem. Funct. **1**(3), 168–72.
113. HARRIS, R.R. and MACKENZIE, I.C. (1984). Fatty-acid metabolism in oral mucosal epithelium of the hamster. J. Oral Pathol. **13**(4), 394–400.
114. ELPHICK, M.C., HUDSON, D.G., and HULL, D. (1975). Transfer of fatty acids across the rabbit placenta. J. Physiol. **252**, 29–42.

115. HERSHFIELD, M.S. and NEMETH, A.M. (1968). Placental transport of free palmitic and linoleic acids in the guinea-pig. J. Lipid Res. **9**, 460–468.
116. HUMMEL, L., SCHIRRMEISTER, W., and WAGNER, H. (1975). Quantitative evaluation of the maternal fetal transfer of free fatty acids in the rat. Biol. Neonate **26**, 263–7.
117. ELPHICK, M.C., FILSHIE, G.M., and HULL, D. (1978). The passage of fat emulsion across the human placenta. Br. J. Obstet. Gynecol. **85**, 610–8.
118. BOOTH, C., ELPHICK, M.C., HENDRICKSE, W., and HULL, D. (1981). Investigation of ^{14}C-linoleic acid conversion into ^{14}C-arachidonic acid and placental transfer of linoleic and palmitic acids across the perfused human placenta. J. Dev. Physiol. **3**(3), 177–89.
119. THOMAS, C.R. and LOWY, C. (1982). The clearance and placental transfer of free fatty acids and triglycerides in the pregnant guinea-pig. J. Dev. Physiol. **4**, 163–73.
120. HUMMEL, L., SCHINCKMANN, R., and ZIMMERMANN, T. (1983). Maternal–fetal transfer of free fatty acids during late gestation in the rat. Biomed. Biochim. Acta **42**(1), 143–5.
121. AMERICAN MEDICAL ASSOCIATION (AMA). (1972). Diet and coronary heart disease: A joint policy statement of the American Medical Association Council on Foods and Nutrition and the Food and Nutrition Board of the National Academy of Sciences - National Research Council. JAMA **222**, 1647. In FASEB, Refs. 44, 45.
122. COSMETIC INGREDIENT REVIEW (CIR). (Feb. 21, 1985). Final report on the safety assessment of Cholesterol.*
123. REISER, R. (1973). Saturated fat in the diet and serum cholesterol concentration: A critical examination of the literature. Am. J. Clin. Nutr. **26**, 524–55. In FASEB, Ref. 45.
124. OLIVER, M.F. (1982). Diet and coronary heart disease, in *Human Nutrition: Clinical Nutrition.* London: John Libbey, Vol. 36C(6), pp. 413–27.
125. KABARA, J.J. (1978). Structure function relationships of surfactants as antimicrobial agents. J. Soc. Cosmet. Chem. **29**, 733–41.
126. KABARA, J.J. (1984). Antimicrobial agents derived from fatty acids. J. Am. Oil Chem. Soc. **61**(2), 397–403.
127. PRIYADARSHINI, E. and TULPULE, P.G. (1980). Effect of free fatty acids on aflatoxin production in a synthetic medium. Food Cosmet. Toxicol. **18**(4), 367–9.
128. KOHN, A., GITELMAN, J., and INBAR, M. (1980). Unsaturated free fatty acids inactivate animal enveloped viruses. Arch. Virol. **66**(4), 301–7.
129. CTFA. (Sept. 26, 1978). Submission of unpublished data. (3-3-29). Acute oral toxicity data summary sheet on Oleic Acid.*
130. INTERNATIONAL BIO-RESEARCH-U.S., INC. (Jan. 23, 1974). Submission of unpublished data by CTFA. (3-3-2, 3-3-92). Acute toxicity and irritation studies on a series of fatty acids: high purity Stearic Acid, triple pressed Stearic Acid, Lauric Acid, Oleic Acid, Myristic Acid and Palmitic Acid.*
131. CTFA. (July 20, 1981). Submission of unpublished data. (3-3-96). Acute oral toxicity study using rats, dermal toxicity and ocular irritation studies using rabbits: 5 percent Oleic Acid in cream.*
132. CTFA. (Sept. 11, 1973). Submission of unpublished data. (3-3-22). Acute oral toxicity data summary sheet on Lauric Acid.*
133. CTFA. (Aug. 23, 1983). Submission of unpublished data. (3-3-89). Animal oral toxicity, dermal toxicity, skin irritation and ocular irritation studies: data summary sheet on Palmitic Acid in shave cream.*
134. WARF INSTITUTE. (Jan. 13, 1978). Submission of unpublished data by CTFA. (3-3-1). Acute oral toxicity, primary skin irritation, and primary eye irritation of Stearic Acid.*
135. CTFA. (Jan. 23, 1969). Submission of unpublished data. (3-3-85). Oral toxicity study data summary sheet on Stearic Acid in face cream.*
136. CONSUMER PRODUCT TESTING CO., INC. (CPT). (Aug. 7, 1982). Submission of unpublished data by CTFA. (3-3-110). Primary dermal irritation in rabbits, primary ocular irritation in rabbits, and acute oral toxicity in rats of 2.8 percent Stearic Acid in skin lotion.*
137. CPT. (Aug. 7, 1982). Submission of unpublished data by CTFA. (3-3-115). Primary dermal irritation in rabbits, primary ocular irritation in rabbits, and acute oral toxicity in rats of 2.8 percent Stearic Acid in skin lotion.*
138. CPT. (Oct. 10, 1978). Submission of unpublished data by CTFA. (3-3-124; 3-3-125). Primary dermal irritation in rabbits, ocular irritation in rabbits, and acute oral toxicity in rats of 2.8 percent Stearic Acid in skin lotion.*
139. CPT. (Sept. 23, 1980). Submission of unpublished data by CTFA. (3-3-116). Primary dermal irritation in rabbits, primary ocular irritation in rabbits, and acute oral toxicity in rats of 2.8 percent Stearic Acid in hand lotion.*

140. TOX MONITOR LABORATORIES, INC. (TML). (Aug. 28, 1981). Submission of unpublished data by CTFA. (3-3-123). Eye irritation, primary skin irritation and acute oral toxicity testing of 2.8 percent Stearic Acid in lotion.*
141. TML. (March 24, 1983). Submission of unpublished data by CTFA. (3-3-118). Eye irritation and acute oral toxicity testing of 2.8 percent Stearic Acid in lotion.*
142. TML. (March 24, 1983). Submission of unpublished data by CTFA. (3-3-120). Eye irritation and acute oral toxicity testing of 2.8 percent Stearic Acid in lotion.*
143. TML. (April 5, 1983). Submission of unpublished data by CTFA. (3-3-121). Eye irritation and acute oral toxicity testing of 2.8 percent Stearic Acid in lotion.*
144. PRICE, G.E. and BEUTNER, R.H. (1960). Stearic acid as a poison. Fed. Proc. **19**(1 Pt. 1), 388. In: Informatics, Ref. 46.
145. SUNDE, M.L. (1956). The effects of fats and fatty acids in chick rations. Poultry Sci. **35**(2), 362–8. In: Informatics, Refs. 46, 47; FASEB, Ref. 68; Opdyke, Ref. 69.
146. BEILHARZ, R.B. and McDONALD, M.W. (1959). The use of high quality fat and the effect of protein level in broiler diets. Poultry Sci. **38**, 519–26. In: Informatics, Ref. 46.
147. RENAUD, S. (1968). Thrombogenicity and atherogenicity of dietary fatty acids in rat. J. Atheroscler. Res. **8**, 625. In: Opdyke, Ref. 69; Informatics, Refs. 46, 47.
148. RENAUD, S. (1969). Thrombotic, atherosclerotic and lipemic effects of dietary fats in the rat. Angiology **20**, 657. In: Opdyke, Ref. 69; Informatics, Refs. 46, 47.
149. HERTING, D.C. and CRAIN, R.C. (1958). Foreign-body type reaction in fat cells. Proc. Soc. Exp. Biol. Med. **98**(2), 347–8. In: Informatics, Ref. 46.
150. CARROLL, K.K. and NOBLE, R.L. (1957). Influence of a dietary supplement of erucic acid and other fatty acids on fertility in the rat. Sterility caused by erucic acid. Can. J. Biochem. Physiol. **35**(11), 1093–106. In: Informatics, Ref. 47.
151. HERTING, D.C., HARRIS, P.L., and CRAIN, R.C. (1959). Lipogranuloma from dietary saturated fats: Production and reversal. Toxicol. Appl. Pharmacol. **1**, 505–14. In: FASEB, Ref. 68.
152. DEICHMANN, W.B., RADOMSKI, J.L., MacDONALD, W.E., KASCHT, R.L., and ERDMANN, R.L. (1958). The chronic toxicity of octadecylamine. Arch. Industr. Health. **18**, 483–7. In: Informatics, Ref. 46; Opdyke, Ref. 69.
153. CTFA. (Sept. 18, 1978). Submission of unpublished data. (3-3-30). Acute dermal toxicity data summary sheet on Oleic Acid.*
154. FLESCH, P. (1953). Hair loss from sebum. Arch. Dermatol. Syph. **67**, 1–9. In: Informatics, Ref. 47.
155. PUHVEL, S.M. and ERTL, D.C. (1984). Decreased induction of aryl hydrocarbon hydroxylase activity in hyperproliferative hairless mouse epidermis. Br. J. Dermatol. **110**(1), 29–35.
156. BERLIN, B.S. and WYMAN, R. (1971). Fractionation of Arlacel A1. Proc. Soc. Exp. Biol. Med. **136**, 1363–8. In: Informatics, Ref. 47.
157. STILLMAN, M.A., MAIBACH, H.I., and SHALITA, A.R. (1975). Relative irritancy of free fatty acids of different chain length. Contact Dermatitis **1**, 65. In: Opdyke, Ref. 69.
158. CODE OF FEDERAL REGULATIONS. (1982). Title 16. Commercial Practices. Parts 1500.3, 1500.40, 1500.41, 1500.42: Testing Methods. Washington, DC: Government Printing Office.
159. KANAAR, P. (1971). Follicular-keratogenic properties of fatty acids in the external ear canal of the rabbit. Dermatologica **142**, 14–22.
160. SETALA, K., MERENMIES, L., STJERNVALL, L., AHO, Y., and KAJANNE, P. (1959). Mechanism of experimental tumorigenesis. I. Epidermal hyperplasia in mouse caused by locally applied tumor initiator and Dipole-type tumor promoter. J. Natl. Cancer Inst. **23**, 925–51. In: Informatics, Ref. 47.
161. RANTUCCIO, F., SINISI, D., SCARDIGNO, A., and COVIELLO, C. (1981). Histological changes in rabbits after application of medicaments and cosmetic bases (II). Contact Derm. **7**(2), 94–7.
162. CTFA. (Aug. 14, 1974). Submission of unpublished data. (3-3-10). Safety evaluation of 2.0 percent Stearic Acid in 01B/62568-J(6020). Four-week subacute dermal toxicity study in rabbits.*
163. CTFA. (Aug. 14, 1974). Submission of unpublished data. (3-3-16). Four-week subacute dermal toxicity study in rabbits: 2.0 percent Stearic Acid.*
164. CTFA. (July 11, 1980). Submission of unpublished data. (3-3-21). Study project 0135. The safety evaluation of two sun protection products and one facial skin care product. Thirteen-week subchronic dermal toxicity study in albino female rats on 5.0 percent Stearic Acid.*
165. CTFA. (Aug. 18, 1982). Submission of unpublished data. (3-3-15). Study project 0191. The safety evaluation of three make-up products: 2.4 percent Stearic Acid in 03G/18218-12. Thirteen-week subchronic dermal toxicity study using female albino rats.*

166. ROBERTSON, T.B., DAWBARN, M.C., THOMAS, R.G., WALTERS, J.W., and WILSON, J.D.O. (1933). Experiments on the growth and longevity of the white mouse. I. The influence of injections of thorium oleate in oleic acid, and of oleic acid alone, on growth and longevity. Aust. J. Exp. Biol. Med. Sci. **11**, 99–108. In: FASEB, Ref. 68.
167. CTFA. (April 24, 1972). Submission of unpublished data. (3-3-32). Primary skin irritation data summary sheet on Oleic Acid.*
168. DRAIZE, J.H. (1959). In *Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics.* Austin, TX: Association of Food and Drug Officials of the United States.
169. CTFA. (Sept. 30, 1982). Submission of unpublished data. (3-3-51). Dermal irritation assessment data summary sheet on Oleic Acid in cream blusher.*
170. CTFA. (March 17, 1983). Submission of unpublished data. (3-3-50). Dermal irritation assessment data summary sheet on Oleic Acid in cream blush.*
171. CTFA. (May 14, 1973). Submission of unpublished data. (3-3-24). Primary skin irritation data summary sheet on Lauric Acid.*
172. BIO-TOXICOLOGY LABORATORIES. (April 19, 1973). Submission of unpublished data by CTFA. Primary irritation studies on 45 percent Stearic Acid plus other fatty acids and on 74 percent Palmitic Acid plus other fatty acids in two product formulations.*
173. CTFA. (June 4, 1979). Submission of unpublished data. (3-3-37). Primary skin irritation data summary sheet on Palmitic Acid.*
174. CTFA. (June 4, 1979). Submission of unpublished data. (3-3-39). Primary skin irritation data summary sheet on Palmitic Acid.*
175. CTFA. (April 24, 1972). Submission of unpublished data. (3-3-26). Primary skin irritation data summary sheet on Myristic Acid.*
176. CTFA. (Feb. 27, 1978). Submission of unpublished data. (3-3-3). Primary skin irritation data summary sheet on Stearic Acid.*
177. CTFA. (Nov. 15, 1976). Submission of unpublished data. (3-3-5). Primary skin irritation data summary sheet on Stearic Acid.*
178. CTFA. (Jan. 10, 1977). Submission of unpublished data. (3-3-7). Primary skin irritation data summary sheet on Stearic Acid.*
179. CTFA. (Jan. 21, 1983). Submission of unpublished data. (3-3-86). Skin and ocular irritation study: Data summary sheet on Stearic Acid in face cream.*
180. CTFA. (Feb. 3, 1978). Submission of unpublished data. (3-3-82). Skin irritation testing with albino rabbits: Data summary sheet on Stearic Acid in lotion.*
181. CTFA. (Nov. 12, 1982). Submission of unpublished data. (3-3-49). Guinea pig maximization test data summary sheet on Oleic Acid in cream blush.*
182. MAGNUSSON, B. and KLIGMAN, A.M. (1969). The identification of contact allergens by animal assay. The guinea pig maximization test. J. Invest. Dermatol. **52**(3), 268–76.
183. CTFA. (Feb. 3, 1978). Submission of unpublished data. (3-3-55). Guinea pig maximization study data summary sheet on Stearic Acid in suntan lotion.*
184. CTFA. (July 8, 1981). Submission of unpublished data. (3-3-17). Project number GPA-07-81. Guinea pig allergy study protocol for the Magnusson-Kligman procedure on four raw ingredients and one finished product: 3.5 percent Stearic Acid.*
185. CPT. (Jan. 5, 1983). Submission of unpublished data by CTFA. (3-3-113). Phototoxicity and photoallergy testing in guinea pigs of 2.8 percent Stearic Acid in skin lotion.*
186. CPT. (Jan. 5, 1983). Submission of unpublished data by CTFA. (3-3-111). Phototoxicity and photoallergy testing in guinea pigs of 2.8 percent Stearic Acid in skin lotion.*
187. CTFA. (April 24, 1972). Submission of unpublished data. (3-3-4). Eye irritation data summary sheet on Oleic Acid.*
188. CTFA. (Sept. 18, 1972). Submission of unpublished data. (3-3-31). Eye irritation data summary sheet on Oleic Acid.*
189. HAZELTON LABORATORIES, INC. (Dec. 11, 1974). Submission of unpublished data by CTFA. (3-3-66). Eye irritation study in monkeys on mascara EMM-4-120 and mascara EMM-4-122 each containing 6 percent Oleic Acid.*
190. LEBERCO LABORATORIES. (June 14, 1984). Submission of unpublished data by CTFA. (3-3-107). Eye irritation study in rabbits of mascara containing 3 percent Oleic Acid.*
191. LEBERCO LABORATORIES. (June 22, 1982). Submission of unpublished data by CTFA. (3-3-101). Eye irritation study in rabbits of mascara containing 2 percent Oleic Acid.*

192. LEBERCO LABORATORIES. (Oct. 22, 1984). Submission of unpublished data by CTFA. (3-3-105). Eye irritation study in rabbits of mascara containing 2 percent Oleic Acid.*
193. CTFA. (May 15, 1973). Submission of unpublished data. (3-3-23). Eye irritation data summary sheet on Lauric Acid.*
194. STILLMEADOW, INC. (April 1, 1980). Submission of unpublished data by CTFA. (3-3-62). Rabbit eye irritation study on soap containing 1.95 percent Lauric Acid.*
195. CTFA. (Feb. 6, 1985). Submission of unpublished data. (3-3-36). Eye irritation data summary sheet on Palmitic Acid.*
196. CTFA. (Feb. 20, 1985). Submission of unpublished data. (3-3-35). Eye irritation data summary sheet on Palmitic Acid.*
197. CTFA. (June 11, 1979). Submission of unpublished data. (3-3-38). Eye irritation data summary sheet on Palmitic Acid.*
198. CTFA. (June 25, 1979). Submission of unpublished data. (3-3-40). Eye irritation data summary sheet on Palmitic Acid.*
199. CTFA. (April 24, 1972). Submission of unpublished data. (3-3-25). Eye irritation data summary sheet on Myristic Acid.*
200. STILLMEADOW, INC. (March 30, 1982). Submission of unpublished data by CTFA. (3-3-60). Rabbit eye irritation study on lotion containing 1.5 percent Myristic Acid.*
201. STILLMEADOW, INC. (March 30, 1982). Submission of unpublished data by CTFA. (3-3-61). Rabbit eye irritation study on lotion containing 1.5 percent Myristic Acid.*
202. CTFA. (Nov. 15, 1976). Submission of unpublished data. (3-3-6). Eye irritation data summary sheet on Stearic Acid.*
203. CTFA. (Jan. 10, 1977). Submission of unpublished data. (3-3-8). Eye irritation data summary sheet on Stearic Acid.*
204. CTFA. (March 29, 1977). Submission of unpublished data. (3-3-84). Eye irritation testing with albino rabbits: Data summary sheet on Stearic Acid in lotion.*
205. PARRY, J.M., PARRY, E.M., and BARRETT, J.C. (1981). Tumor promoters induce mitotic aneuploidy in yeast. Nature (London) **294**, 263–5.
206. AMES, B.N., McCANN, J., and YAMASAKI, E. (1975). Methods for detecting carcinogens and mutagens with the *Salmonella*/mammalian-microsome mutagenicity test. Mutat. Res. **31**, 347–64.
207. BLEVINS, R.D. and TAYLOR, D.E. (1982). Mutagenicity screening of twenty-five cosmetic ingredients with the *Salmonella*/microsome test. J. Environ. Sci. Health **A17**(2), 217–39.
208. KINSELLA, A.R. (1982). Elimination of metabolic cooperation and the induction of sister chromatid exchanges are not properties common to all promoting or co-carcinogenic agents. Carcinogenesis (London) **3**(5), 499–503.
209. GRAFF, G. and LANDS, W.E.M. (1982). Selective mutational loss of mitochrondrial function can be caused by certain unsaturated fatty acids. Fed. Proc. **41**, 626.
210. HAYATSU, H., ARIMOTO, S., TOGAWA, K., and MAKITA, M. (1981). Inhibitory effect of the ether extract of human feces on activities of mutagens: inhibition by oleic and linoleic acids. Mutat. Res. **81**(3), 287–93.
211. NEGISHI, T., OHARA, Y., and HAYATSU, H. (1982). A sensitive assay for mutagenic activity of N-nitrosamines and its use for detection of modulators of the mutagenicity. IARC Sci. Publ. Iss. N-Nitroso Compd. Occurrence Biol. Eff. Vol. 41, pp. 685–94.
212. NEGISHI, T. and HAYATSU, H. (1984). Inhibitory effect of saturated fatty acids on the mutagenicity of N-nitrosodimethylamine. Mutat. Res. **135**(2), 87–96.
213. PAGANO, D.A. and ZEIGER, E. (1983). Suppressive effects of chemicals in mixture on the *Salmonella* plate test response in the absence of apparent toxicity. Environ. Mutagen. **5**, 473–4.
214. HAYATSU, H. (1982). Modulation of mutagenesis by biological substances. *Environ. Mutagens Carcinog. Proc. 3rd Int. Conf.*, 1981, pp. 521–6.
215. SWERN, D., WIEDER, R., McDONOUGH, M., MERANZE, D.R., and SHIMKIN, M.B. (1970). Investigation of fatty acids and derivatives for carcinogenic activity. Cancer Res. **30**(4), 1037–46.
216. SZEPSENWOL, J. and BOSCHETTI, N.V. (1975). Primary and secondary heart tumors in mice maintained on various diets. Oncology **32**(2), 58–72.
217. SZEPSENWOL, J. (1978). Gastro-intestinal tumors in mice of three strains maintained on fat-enriched diets. Oncology **35**(4), 143–52.
218. EL-KHATIB, S.M. and CORA, E.M. (1981). Role of high-fat diet in tumorigenesis in C57BL/1 mice. J. Natl. Cancer Inst. **66**(2), 297–301.

219. TWORT, C.C. and FULTON, J.D. (1930). Further experiments on the carcinogenicity of synthetic tars and their fractions. J. Pathol. Bacteriol. **33**(1), 119–44. In: Informatics, Ref. 46.
220. HIEGER, I. (1959). Carcinogenesis by cholesterol. Br. J. Cancer **13**, 439–51. In: Informatics, Ref. 45.
221. VAN DUUREN, B.L., KATZ, C., SHIMKIN, M.B., SWERN, D., and WIEDER, R. (1972). Replication of low-level carcinogenic activity bioassays. Cancer Res. **32**(4), 880–1.
222. TINSLEY, I.J., SCHMITZ, J.A., and PIERCE, D.A. (1981). Influence of dietary fatty acids on the incidence of mammary tumors in the C3H mouse. Cancer Res. **41**(4), 1460–5.
223. TWORT, J.M. and TWORT, C.C. (1939). Comparative activity of some carcinogenic hydrocarbons. Am. J. Cancer **35**, 80–5.
224. SHUBIK, P. (1950). Studies on the promoting phase in the stages of carcinogenesis in mice, rats, rabbits and guinea pigs. Cancer Res. **10**, 13–7.
225. GWYNN, R.H. and SALAMAN, M.H. (1953). Studies on cocarcinogenesis. SH-Reactors and other substances tested for cocarcinogenic action in mouse skin. Br. J. Cancer **7**, 482–9.
226. HOLSTI, P. (1959). Tumor-promoting effects of some long chain fatty acids in experimental skin carcinogenesis in the mouse. Acta. Pathol. Microbiol. Scand. **46**, 51–8.
227. VAN DUUREN, B.L. and GOLDSCHMIDT, B.M. (1976). Cocarcinogenic and tumor-promoting agents in tobacco carcinogenesis. J. Natl. Cancer Inst. **56**(6), 1237–42.
228. HOGAN, M.L. and SHAMSUDDIN, A.M. (1984). Large intestinal carcinogenesis. I. Promotional effect of dietary fatty acid isomers in the rat model. J. Natl. Canc. Inst. **73**(6), 1293–6.
229. CARROLL, K.K. (1981). Neutral fats and cancer. Cancer Res. **41**, 3695–9.
230. PRUNIERAS, M. (1979). Carcinogenicity of cosmetic materials, in Cohen, Y. (ed.). *Adv. Pharmacol. Ther., Proc. 7th Int. Congr. Pharmacol.*, 1978. Oxford, England: Pergamon, Vol. 9, pp. 277–87.
231. MORISAKI, N., SPRECHER, H., MILO, G.E., and CORNWELL, D.G. (1982). Fatty acid specificity in the inhibition of cell proliferation and its relationship to lipid peroxidation and prostaglandin biosynthesis. Lipids **17**(12), 893–9.
232. BOOYENS, J., ENGELBRECHT, P., LE ROUX, S., LOUWRENS, C.C., VAN DER MERWE, C.F., and KATZEFF, I.E. (1984). Some effects of the essential fatty acids linoleic acid and alpha-linoleic acid and of their metabolites gamma-linoleic acid, arachidonic acid, eicosapentaenoic acid, docosahexaenoic acid, and of prostaglandins A_1 and E_1 on the proliferation of human osteogenic sarcoma cells in culture. Prostaglandins Leukotrienes Med. **15**(1), 15–33.
233. BARKA, T. and VAN DER NOEN, H. (1982). Culture of A-431 human epidermoid carcinoma cells in serum-free medium: effect of culture conditions on the binding of ^{125}I-epidermal growth factor. Am. J. Anat. **165**(2), 187–98.
234. HUTTNER, J.I., MILO, G.E., PANGANAMALA, R.V., and CORNWELL, D.G. (1978). Fatty acids and the selective alteration of in vitro proliferation in human fibroblast and guinea-pig smooth-muscle cells. In Vitro **14**(10), 854–9.
235. TRAUL, K.A., HINK, R.J., Jr., KACHEVSKY, V., and WOLFF, J.S., III. (1981). Two-stage carcinogenesis in vitro: Transformation of 3-methylcholanthrene-initiated Rauscher murine leukemia virus-infected rat embryo cells by diverse tumor promoters. J. Natl. Cancer Inst. **66**(1), 171–6.
236. WELSCH, C.W. and AYLSWORTH, C.F. (1983). Enhancement of murine mammary tumorigenesis by feeding high levels of dietary fat: A hormonal mechanism? J. Natl. Cancer Inst. **70**(2), 215–21.
237. DIAMOND, L., O'BRIEN, T.G., and BAIRD, W.M. (1980). Tumor promoters and the mechanism of tumor promotion. Adv. Canc. Res. **32**, 1–74.
238. ANDO, K., KATO, A., KIMURA, T., SUZUKI, S., TAMURA, G., and ARIMA, K. (1970). Antitumor activity of fatty acids and their esters. I. Evaluation of antitumor activity of fatty acids. Prog. Antimicrob. Anticancer Chemother. **2**, 136–41.
239. BOTTENSTEIN, J.E. (1980). Serum-free culture of neuroblastoma cells. Prog. Cancer Res. Ther. **12**, 161–70.
240. ITO, H., KASAMA, K., NARUSE, S., and SHIMURA, K. (1982). Antitumor effect of palmitoleic acid on Ehrlich ascites tumor. Cancer Lett. **17**(2), 197–203.
241. NELSON, R.L. and SAMELSON, S.L. (1984). Inability of the mutagen-blocking agent oleic acid to protect against colon carcinogenesis in the rat. Mutat. Res. **140**(2–3), 155–7.
242. HUMMEL, L., SCHIRRMEISTER, W., ZIMMERMAN, T., and WAGNER, H. (1974). Studies of the lipid metabolism using carbon-14-1-palmitate in fetal rats. Biol. Neonate **24**(5–6), 298–305.
243. NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH). (June 1981). Health hazard evaluation report on lauric acid exposure during flaking and bagging operations at Emery Industries, Los Angeles, CA. HHE 80-160-897. NTIS Doc. no. PB82-25694 2.

244. CTFA. (April 5, 1972). Submission of unpublished data. (3-3-33). Skin irritation potential (human patch test) data summary sheet on Oleic Acid.*
245. CTFA. (Oct. 5, 1972). Submission of unpublished data. (3-3-34). Skin irritation potential (human patch test) data summary sheet on Oleic Acid.*
246. CTFA. (January 1984). Submission of unpublished data. (3-3-78). Clinical skin irritation study data summary sheet on Oleic Acid in mineral oil.*
247. CTFA. (January 1985). Submission of unpublished data. (3-3-75). Clinical skin irritation study data summary sheet on Oleic Acid in bar soap.*
248. CTFA. (January 1984). Submission of unpublished data. (3-3-76). Clinical skin irritation study data summary sheet on Oleic Acid in bar soap.*
249. CTFA. (March 1985). Submission of unpublished data. (3-3-74). Clinical skin irritation study data summary sheet on 2.53 to 40 percent Oleic Acid in bar soap.*
250. HILL TOP RESEARCH, INC. (HTR). (Dec. 9, 1974). Submission of unpublished data by CTFA. (3-3-67). Lanman tests of cumulative irritant properties on a series of test materials. A clinical study on black cream mascara EMM-4-120 and brown cream mascara EMM-4-122 containing 6 percent Oleic Acid.*
251. FROSCH, P.J. and KLIGMAN, A.M. (1979). The soap chamber test. J. Am. Acad. Dermatol. **1**, 35–41.
252. LANMAN, B.M., ELVERS, W.B., and HOWARD, C.S. (1968). The role of human patch testing in a product development program. *Proceedings Joint Conference Cosmet. Sci.* Washington, DC: The Toilet Goods Association, Inc., pp. 35–45.
253. PHILLIPS, L., STEINBERG, M., MAIBACH, H.I., and AKERS, W.A. (1972). A comparison of rabbit and human skin response to certain irritants. J. Toxicol. Appl. Pharmacol. **21**, 369–82.
254. HAYNES, C.R. and ESTRIN, N.F. (eds.). (1983). CTFA safety testing guidelines. Guidelines for controlled use studies. *CTFA Technical Guidelines*. Washington, DC: CTFA, Chap. 10.
255. HTR. (Aug. 17, 1982). Submission of unpublished data by CTFA. (3-3-97). Report of a human skin test of cumulative irritation on a red paste formulation containing 5 percent Oleic Acid.*
256. MAIBACH, H.I. (July 21, 1982). Submission of unpublished data by CTFA. (3-3-99; 3-3-102). Study No. 82-A-I-2. 21-Day cumulative irritancy assay of mascara containing 2 percent Oleic Acid.*
257. CTFA. (Oct. 7, 1983). Submission of unpublished data. (3-3-90). Clinical skin irritation, sensitization, and photosensitization studies: Data summary sheet on Palmitic Acid in shave cream.*
258. CTFA. (March 22, 1983). Submission of unpublished data. (3-3-91). Clinical facial skin irritation study: Data summary sheet on Palmitic Acid in shave cream.*
259. CTFA. (April 26, 1972). Submission of unpublished data. (3-3-27). Skin irritation potential (human patch test) data summary sheet on Myristic Acid.*
260. CTFA. (January 1984). Submission of unpublished data. (3-3-70). Clinical skin iritation study data summary sheet on Myristic Acid.*
261. CTFA. (January 1984). Submission of unpublished data. (3-3-72). Clinical skin irritation study data summary sheet on Myristic Acid in bar soap.*
262. CTFA. (January 1985). Submission of unpublished data. (3-3-71). Clinical skin irritation study data summary sheet on Myristic Acid in bar soap.*
263. CTFA. (March 1985). Submission of unpublished data. (3-3-73). Clinical skin irritation study data summary sheet on Myristic Acid in bar soap.*
264. HTR. (Feb. 28, 1979). Submission of unpublished data by CTFA. (3-3-28). The study of cumulative irritant properties of a series of test materials. A clinical study on 5.0 percent Myristic Acid in a cleanser lotion.*
265. CTFA. (Aug. 8, 1972). Submission of unpublished data. (3-3-9). Skin irritation potential (human patch test) data summary sheet on Stearic Acid.*
266. CTFA. (Nov. 11, 1980). Submission of unpublished data (3-3-87). Clinical irritation and photosensitization study: Data summary sheet on Stearic Acid in face cream.*
267. CTFA. (July 2, 1973). Submission of unpublished data. (3-3-88). Clinical controlled use study: Data summary sheet on Stearic Acid in face cream.*
268. LEO WINTER ASSOCIATES. (July 28, 1980). Submission of unpublished data by CTFA. (3-3-94). Final report on prophetic patch and in-use testing on a shave foam containing 8 percent Stearic Acid.*
269. HTR. (July 12, 1978). Submission of unpublished data by CTFA. (3-3-11). Repeated insult patch test of ten test samples. A clinical study on black paste mascara 10229-8 containing 7.7 percent Stearic Acid.*
270. UNIVERSITY OF CALIFORNIA, LOS ANGELES (UCLA). (Oct. 17, 1983). Submission of unpublished data by CTFA. (3-3-42). Twenty-one day cumulative irritation potential of two moisturizers containing 2.6 percent Stearic Acid.*

271. CTFA. (Jan. 1984). Submission of unpublished data. (3-3-77). Clinical skin irritation study data summary sheet on 40 percent Oleic Acid in bar soaps.*
272. SCHWARTZ, L. and PECK, S.M. (1944). The patch test in contact dermatitis. Public Health Rep. **59**, 546–57.
273. CTFA. (Dec. 30, 1974). Submission of unpublished data (3-3-68). Contact sensitizing potential of 6 percent Oleic Acid in humans.*
274. HTR. (Aug. 19, 1983). Submission of unpublished data by CTFA. (3-3-98). Repeated insult patch test on a purple wax formulation containing 5 percent Oleic Acid.*
275. UCLA. (Oct. 19, 1984). Submission of unpublished data by CTFA. (3-3-108). Modified Draize-Shelanski-Jordan repeat insult patch test in humans of a mascara containing 3 percent Stearic Acid.*
276. UCLA. (March 12, 1985). Submission of unpublished data by CTFA. (3-3-106). Modified Draize-Shelanski-Jordan repeat insult patch test in humans of a mascara containing 2 percent Stearic Acid.*
277. MAIBACH, H.I. (Aug. 2, 1982). Submission of unpublished data by CTFA. (3-3-103). Modified Draize skin sensitization study on human subjects of mascara containing 2 percent Oleic Acid.*
278. PRODUCT INVESTIGATORS, INC. (April 30, 1980). Submission of unpublished data by CTFA. (3-3-63). Evaluation of potential hazards by dermal contact (intact and abraded skin) of 1.95 percent Lauric Acid in a liquid soap.*
279. CTFA. (Dec. 16, 1977). Submission of unpublished data. (3-3-19). Allergic contact sensitization test on 10.0 percent Stearic Acid.*
280. CTFA. (Oct. 1980). Submission of unpublished data. (3-3-95). Clinical skin irritation and sensitization study on 10 percent Stearic Acid in a mascara composite.*
281. HTR. (June 22, 1977). Submission of unpublished data by CTFA. (3-3-14). Repeated insult patch test of ten test samples. A clinical study on black paste mascara 10229-8 containing 7.7 percent Stearic Acid.*
282. UCLA. (March 12, 1985). Submission of unpublished data by CTFA. (3-3-41). Modified Draize-Shelanski-Jordan repeat insult patch test in humans of a mascara containing 5 percent Stearic Acid.*
283. CTFA. (Aug. 1, 1980). Submission of unpublished data. (3-3-20). Allergic contact sensitization test on 4.0 percent Stearic Acid.*
284. FOOD AND DRUG RESEARCH LABORATORIES, INC. (FDRL). (Oct. 8, 1980). Submission of unpublished data by CTFA. (3-3-112). Clinical safety evaluation of hand lotion containing 2.8 percent Stearic Acid. Repeat insult patch test.*
285. TKL RESEARCH, INC. (May 24, 1983). Submission of unpublished data by CTFA. (3-3-119). Repeated insult patch test in humans on skin lotion containing 2.8 percent Stearic Acid.*
286. RESEARCH TESTING LABORATORIES. (Dec. 12, 1978). Submission of unpublished data by CTFA. (3-3-12). Patch and usage study 620.0978: 2.66 percent Stearic Acid.*
287. UCLA. (May 20, 1983). Submission of unpublished data by CTFA. (3-3-43). Modified Draize-Shelanski-Jordan patch test in humans of a moisturizer containing 2.6 percent Stearic Acid.*
288. UCLA. (Aug. 10, 1983). Submission of unpublished data by CTFA. (3-3-44). Modified Draize-Shelanski-Jordan patch test in humans of a moisturizer containing 2.6 percent Stearic Acid.*
289. UCLA. (March 16, 1984). Submission of unpublished data by CTFA. (3-3-45). Modified Draize-Shelanski-Jordan repeat insult patch test in humans of a sun lotion containing 2.6 percent Stearic Acid.*
290. UCLA. (March 16, 1984). Submission of unpublished data by CTFA. (3-3-47). Modified Draize-Shelanski-Jordan repeat insult patch test in humans of a sun lotion containing 2.6 percent Stearic Acid.*
291. UCLA. (March 16, 1984). Submission of unpublished data by CTFA. (3-3-48). Modified Draize-Shelanski-Jordan repeat insult patch test in humans of a sun block cream containing 2.6 percent Stearic Acid.*
292. CTFA. (March 1978). Submission of unpublished data. (3-3-81). Clinical skin sensitization testing: data summary sheet on Stearic Acid in hand lotion.*
293. CTFA. (Submission date, Oct. 23, 1985). Submission of unpublished data. (3-3-56). Modified Draize-Shelanski repeat insult patch test data summary sheet on Stearic Acid in suntan lotion.*
294. IVY RESEARCH LABORATORIES, INC. (July 15, 1983). Submission of unpublished data by CTFA. (3-3-64). The appraisal of the contact-sensitizing potential of four (4) materials by means of the maximization study. A clinical study on a bar soap containing 23 percent Stearic Acid.*
295. CTFA. (Dec. 9, 1983). Submission of unpublished data. (3-3-18). Allergic sensitization test on 25.0 percent Stearic Acid.*
296. SHELANSKI, H.A. and SHELANSKI, M.V. (1953). A new technique of human patch tests. Proc. Joint Conf. Cosmet. Sci. Toilet Goods Assoc. **19**, 47–9.

297. UCLA. (March 16, 1984). Submission of unpublished data by CTFA. (3-3-46). Modified Draize-Shelanski-Jordan repeat insult patch test in humans of a sun lotion containing 2.6 percent Stearic Acid.*
298. CTFA. (March 25, 1983). Submission of unpublished data. (3-3-52). Evaluation of photosensitivity potential of topical products data summary sheet on Oleic Acid in blusher.*
299. CTFA. (March 10, 1978). Submission of unpublished data. (3-3-59). Evaluation of photosensitivity potential of topical products data summary sheet on Oleic Acid in liquid makeup.*
300. FEDERAL REGISTER. (Aug. 25, 1978). Sunscreen drug products for over-the-counter human drugs, pp. 28306–69.
301. FDRL. (Dec. 2, 1981). Submission of unpublished data by CTFA. (3-3-114). Clinical safety evaluation of lotion containing 2.8 percent Stearic Acid. Phototoxicity test.*
302. TKL RESEARCH, INC. (May 24, 1983). Submission of unpublished data by CTFA. (3-3-65). Phototoxicity test in humans on soap bar containing 23 percent Stearic Acid.*
303. FDRL. (Dec. 2, 1981). Submission of unpublished data by CTFA. (3-3-117). Clinical safety evaluation of lotion containing 2.8 percent Stearic Acid. Photoallergy test.*
304. FDRL. (Dec. 2, 1981). Submission of unpublished data by CTFA. (3-3-122). Clinical safety evaluation of skin lotion containing 2.8 percent Stearic Acid. Photoallergy test.*
305. CTFA. (May 21, 1979). Submission of unpublished data. (3-3-58). Evaluation of photosensitivity potential of topical products data summary sheet on Stearic Acid in suntan lotion.*
306. CTFA. (Aug. 1, 1979). Submission of unpublished data. (3-3-53). Evaluation of photosensitivity potential of topical products data summary sheet on Oleic Acid in moisturizing lotion.*
307. CTFA. (April 2, 1980). Submission of unpublished data. (3-3-54). Evaluation of photosensitivity potential of topical products data summary sheet on Stearic Acid in facial lotion.*
308. CTFA. (Oct. 22, 1982). Submission of unpublished data. (3-3-57). Evaluation of photosensitivity potential of topical products data summary sheet on Stearic Acid in suntan lotion.*
309. MED CHECK, INC. (June 11, 1982). Submission of unpublished data by CTFA. (3-3-104). Ocular evaluation of eye area cosmetics in humans. Mascara containing 2 percent Oleic Acid.*
310. MED CHECK, INC. (May 1, 1985). Submission of unpublished data by CTFA. (3-3-100, 3-3-109). Ocular evaluation of eye area cosmetics in humans. Mascara formulations containing 2 percent and 3 percent Oleic Acid.*
311. KIHL, B. and OLBE, L. (1981). Inhibition of pentagastrin-stimulated gastric acid secretion by graded intraduodenal administration of oleic acid in man. Scand. J. Gastroenterol. **16**(1), 121–8.
312. KIHL, B., ROKAEUS, A., ROSELL, S., and OLBE, L. (1981). Fat inhibition of gastric acid secretion in man and plasma concentrations of neurotensin-like immunoreactivity. Scand. J. Gastroenterol. **16**(4), 513–26.
313. OWYANG, C., GREEN, L., and RADER, D. (1983). Colonic inhibition of pancreatic and biliary secretion. Gastroenterology **84**(3), 470–5.

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Final Report of the Amended Safety Assessment of Myristic Acid and Its Salts and Esters as Used in Cosmetics

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Abstract

This report addresses the safety of the inorganic salts and esters of various fatty alcohols of myristic acid. Most of the esters are used as skin conditioning agents in many types of cosmetics in a range of concentrations. Myristate esters are readily hydrolyzed to the corresponding alcohols and acids, which are then further metabolized. Myristate salts readily dissociate in any likely cosmetic formulation. The Cosmetic Ingredient Review (CIR) Panel recognized that much of the data supporting the ingredients in this group were previously reviewed in safety assessments for related ingredients. Where specific data did not exist, the Panel considered structure–activity relationships in determining the safety of these ingredients as used in cosmetics. The Panel determined that myristic acid and its salts and esters are safe as cosmetic ingredients in the current practices of use and concentration.

Keywords

safety, cosmetics, myristic acid, salts, esters

Introduction

In 1990, the Cosmetic Ingredient Review (CIR) Expert Panel concluded that butyl myristate is a safe cosmetic ingredient.[1] This safety assessment was re-reviewed in 2006 to consider new safety data and the Expert Panel reaffirmed that myristic acid ester is safe as used in cosmetics. The Expert Panel re-opened this safety assessment to include other esters that are chemically similar to butyl myristate, along with the salts of myristic acid. The Panel determined that the available data in the original safety assessment are sufficient to support the safety of these additional salts and ester of myristic acid.

The Expert Panel also combined this expanded report with other myristates that have already been reviewed. These and other related ingredients that were previously reviewed by the CIR Expert Panel are listed in Table 1.

This amended safety assessment, therefore includes:

- aluminum dimyristate,
- aluminum isostearates/myristates,
- aluminum myristate,
- aluminum myristates/palmitates,
- calcium myristate,
- cetyl myristate,
- decyl myristate,
- ethylhexyl myristate,
- ethyl myristate,
- glyceryl dimyristate,
- glyceryl isostearate/myristate,
- glyceryl myristate,
- isobutyl myristate,
- isocetyl myristate,
- isodecyl myristate,
- isopropyl myristate,
- isostearyl myristate,
- isotridecyl myristate,
- lauryl myristate,
- magnesium myristate,
- methyl myristate,

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- myristic acid,
- myristyl myristate,
- octyldodecyl myristate,
- oleyl myristate,
- potassium myristate,
- propylene glycol myristate,
- sodium myristate,
- tetradecyloctadecyl myristate,
- tridecyl myristate, and
- zinc myristate.

Data from previous safety assessments on butyl myristate, glycerol myristate, myristic acid, isopropyl myristate and myristyl myristate were reviewed and considered during this assessment. For these ingredients, the previous conclusions CIR Panel (as applicable to the ingredients noted) are summarized in the following sections.

Butyl Myristate, JACT, *9(2) 1990*

Butyl myristate is the ester of butyl alcohol and myristic acid. It is a colorless, oily liquid, which is used in cosmetic formulations at concentrations up to 50%. Aliphatic esters such as butyl myristate may be readily hydrolyzed in vivo to the corresponding alcohol and acid, which are then further metabolized. The median lethal dose (LD_{50}) of butyl myristate was greater than 8 g/kg in rats. In animal tests, undiluted butyl myristate was moderately irritating but was not a skin sensitizer. No evidence of eye irritation was noted. On the basis of the available data presented in this report on butyl myristate, as well as other related myristate compounds, the CIR Expert Panel found butyl myristate safe for cosmetic formulation usage.

Glyceryl Myristate, IJT, *23(suppl 2:55-94)2004*

The safety of 43 glyceryl monoesters listed as cosmetic ingredients was reviewed in a safety assessment completed in 2000. Glyceryl myristate was included in this group. Glyceryl monoesters have little, acute or short-term toxicity in animals, and no toxicity was noted following chronic administration of a mixture consisting mostly of glyceryl di- and monoesters. Undiluted glyceryl monoesters may produce minor skin irritation, especially in abraded skin, but in general these ingredients are not irritating at concentrations used in cosmetics. These ingredients are not photosensitizers. Glyceryl monoesters tested failed to produce any significant positive reactions at concentrations used in cosmetics. Based on these data, the CIR Expert Panel found glyceryl myristic safe as a cosmetic ingredient in the current practices of its use and concentration.

Myristic Acid, JACT, *6(3) 1987*

Oleic, lauric, palmitic, myristic, and stearic acids were reviewed as part of a group. These fatty acids are absorbed, digested, and transported in animals and humans. Little acute toxicity was observed when oleic, lauric, palmitic, myristic, or stearic acid or cosmetic formulations containing these fatty acids were given to rats orally at doses of 15 to –19 g/kg body weight. Most of the data in this assessment was oleic, lauric, palmitic, and stearic acids; myristic acid was included in the safety assessment due to its structural similarity. In primary and cumulative irritation clinical studies, oleic, myristic, and stearic acids at high concentrations were nonirritating. Cosmetic product formulations containing oleic, lauric, palmitic, and stearic acids at concentrations ranging up to 13% were not primary or cumulative irritants, nor sensitizers. On the basis of available data from studies using animals and humans, it is concluded that oleic, lauric, palmitic, myristic, and stearic acids are safe in current practices of their use and concentration in cosmetics.

Myristyl Myristate and Isopropyl Myristate, JACT, *1(4) 1982*

Acute oral and dermal toxicity tests indicated that myristyl myristate is nontoxic to rats. This cosmetic ingredient produced minimal-to-mild skin irritation, minimal eye irritation in rabbits, and no sensitization in guinea pigs. Studies with rabbits indicated that undiluted isopropyl myristate was a mild irritant after 24 hours and moderate to severe when applied for3 consecutive days. Isopropyl myristate was minimally irritating to the rabbits' eyes and was not a skin sensitizer in studies with guinea pigs. In limited studies, isopropyl myristate was not carcinogenic on the skin of mice, but a mixture of isopropyl myristate and isopropyl alcohol significantly accelerated the carcinogenic activity of benzo(a)pyrene on the skin.

Human studies with isopropyl myristate indicated that it was not a human skin irritant or sensitizer when applied in a product formulation containing 15% to 58% of the ingredient. A product containing 43% of isopropyl myristate produced no phototoxicity and no photocontact allergenicity in human studies.

From the available information, it is concluded that myristyl myristate and isopropyl myristate are safe as cosmetic ingredients in the current practices of their use.

Summaries of the data from these reports are provided *in italics* where applicable throughout the report.

Chemistry

Definition and Structure

The definitions, structures, and function in cosmetics of myristic acid and the related salt and esters are given in Table 2.

Also, included in Table 2 are the formulas/structures and functions in cosmetics as given in the *International Cosmetic Ingredient Dictionary and Handbook.*[15] The myristates are esters and salts of myristic acid that have the general formula shown in Figure 1.[8]

According to the *International Cosmetic Ingredient Dictionary and Handbook,*[15] myristic acid (CAS No 544-63-8) is an organic acid also known as tetradecanoic acid.

Table 1. Related Ingredients Previously Reviewed by the CIR Expert Panel

Ingredient	Uses	Use Concentrations	Conclusion	Reference
n-Butyl alcohol	112; 29 (addendum)	≤0.1%-10%; 0.000007%-15%	Safe in nail preparations in the current practices of use.	2,3
Cetyl alcohol	2694; 2931 (re-review)	>0.1%-50%; 0.000002%-15%	Safe as cosmetic ingredients in the current practices of use.	4,5
Glyceryl dimyristate	None reported	None reported	Safe as cosmetic ingredients in the practices of use and concentration as described in this safety assessment.	6
Glyceryl isostearate/ myristate	None reported	None reported	Safe as cosmetic ingredients in the current practices of use and concentration.	7
Glyceryl myristate	19	1%-6%	Safe as cosmetic ingredients in the current practices of use and concentration.	7
Isopropyl myristate	2198; 881 (re-review)	≤0.1%->50%; 0.00008%-78%	Safe as cosmetic ingredients in the current practices of use.	6,8
Isostearyl alcohol	41; 16 (re-review)	>0.1%-50%; 0.001%-50%	Safe as cosmetic ingredients in the current practices of use.	5,9
Methyl alcohol	4	0.1%-5%	Safe as used to denature alcohol used in cosmetic products.	10
Myristic acid	36; 73 (re-review)	>0.1%-50%; 0.00001%-38%	Safe in the current practices of use and concentration in cosmetics.	2,11
Myristyl myristate	160; 244 (re-review)	0.1%-25%; 0.01%-20%	Safe as cosmetic ingredients in the current practices of use.	6,8
Oleyl alcohol	1018; 343 (re-review)	≤0.1%->50%; 0.002%-18%	Safe as currently used in cosmetics.	6,12
Propylene glycol myristate	11	None reported	Safe as cosmetic ingredients in the current practices of use.	13

Abbreviation: CIR, Cosmetic Ingredient Review.

Aluminum dimyristate (CAS No 56639-51-1) is also known as aluminum hydroxybis (tetradecanoate) and tetradecanoic acid, aluminum complex.

Aluminum Isostearates/Myristates (no CAS No) is also known as aluminum triisostearate/trimyristate.

Aluminum myristate (CAS No 4040-50-0) is also known as aluminum monomyristate; myristic acid, aluminum salt; and tetradecanoic acid, aluminum salt.

Aluminum myristates/palmitates (no CAS No) is also known as aluminum trimyristate/tripalmitate.

Butyl myristate (CAS No 110-36-1) is also known as butyl n-tetradecanoate; myristic acid, butyl ester, and tetradecanoic acid, butyl ester.

Calcium myristate (CAS No 15284-51-2) is also known as calcium tetradecanoate; myristic acid, calcium salt; and tetradecanoic acid, calcium salt.

Cetyl myristate (CAS No 2599-01-1) is also known as hexadecyl myristate; hexadecyl tetradecanoate: myristic acid, cetyl ester; myristic acid, hexadecyl ester; and palmityl myristate, and tetradecanoic acid, hexadecyl ester.

Decyl myristate (CAS No 41927-71-3) is also known as decyl tetradecanoate; myristic acid, decyl ester; and tetradecanoic acid, decyl ester.

Ethyl myristate (CAS No 124-06-1) is also known as ethyl tetradecanoate and tetradecanoic acid, ethyl ester.

Ethylhexyl myristate (CAS No 29806-75-5) is also known as 2-ethylhexyl myristate; octyl myristate; and tetradecanoic acid, 2-ethylhexyl ester.

Glyceryl dimyristate (CAS No 53563-63-6) is also known as dimyristin; glycerol dimyristate; and tetradecanoic acid, diester with 1,2,3-propanetriol.

Glyceryl isostearate/myristate (no CAS No) is also known as glyceryl monoisostearate monomyristate.

Glyceryl myristate (CAS Nos 589-68-4 and 27214-38-6) is also known as glycerin monomyristate; glycerol monomyristate; glyceryl monomyristate, monomyristin; myristic acid monoglyceride; and tetradecanoic acid, monoester with 1,2,3-propanetriol.

Isobutyl myristate (CAS No 25263-97-2) is also known as 2-methylpropyl tetradecanoate; myristic acid, isobutyl ester; and tetradecanoic acid, 2-methylpropyl ester.

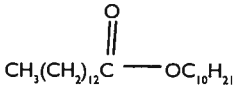
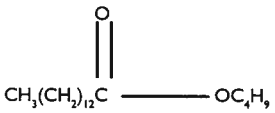
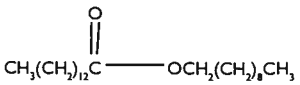
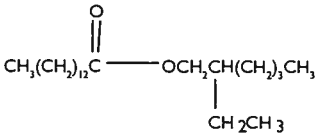
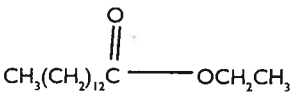
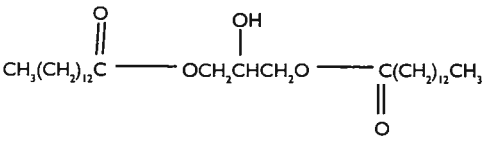
Isocetyl myristate (CAS No 83708-66-1) is also known as myristic acid, isocetyl ester; tetradecanoic acid, isocetyl ester; and tetradecanoic acid, isohexadecyl ester.

Isodecyl myristate (CAS Nos 17670-91-6 and 51473-24-6) is also known as 3,7-dimethyloctyl myristate; isodecyl tetradecanoate; myristic acid, isodecyl ester; tetradecanoic acid, 3,7-dimethyloctyl ester; tetradecanoic acid, isodecyl ester; and tetrahydrogeranyl myristate.

Isopropyl myristate (CAS No 110-27-0) is also known as IPM; isoproylis myristas; isopropyl tetradeconoate; 1-methylethyl tetradecanoate; myristic acid, isopropyl ester; and tetradecanoic acid, 1-methylethyl ester.

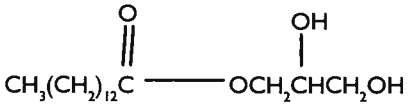
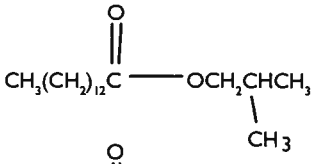
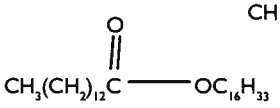
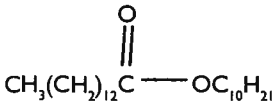
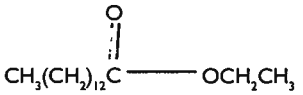
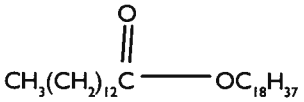
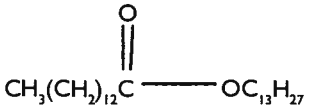
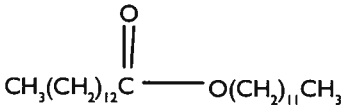
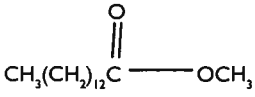
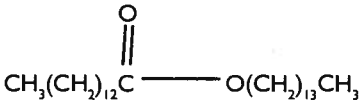
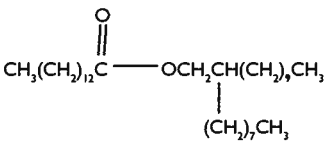
Isostearyl myristate (CAS No 72576-81-9) is also known as tetradecanoic acid, isooctadecyl ester.

Table 2. Definition, Structure, and Function of Myristic Acid and Its Salts and Esters Included in This Report as Given in the International Cosmetic Ingredient Dictionary and Handbook[14]

Ingredient	Definition	Formula/Structure	Function
Myristic acid	Organic acid that conforms generally to the formula:	$CH_3(CH_2)_{12}COOH$	Fragrance ingredient, opacifying agent, surfactant—cleansing agent
Salts			
Aluminum dimyristate	Aluminum salt of myristic acid	$[CH_3(CH_2)_{12}COO]_2AlOH$	Anticaking agent; emulsion stabilizer; viscosity increasing agent—nonaqueous
Aluminum isostearates/ myristates	Aluminum salt of a mixture of isostearic acid and myristic acid	None provided	Anticaking agent; emulsion stabilizer; viscosity increasing agent—nonaqueous
Aluminum myristate	Aluminum salt of myristic acid	$[CH_3(CH_2)_{12}COO]_3Al$	Anticaking agent; emulsion stabilizer; viscosity increasing agent—nonaqueous
Aluminum myristates/ palmitates	Aluminum salt of a mixture of palmitic acid and myristic acid	None provided.	Anticaking agent; emulsion stabilizer; viscosity increasing agent—nonaqueous
Calcium myristate	Calcium salt of myristic acid	$C_{14}H_{28}O_2 \cdot \frac{1}{2}Ca$	anticaking agent; emulsion stabilizer; viscosity increasing agent—nonaqueous
Magnesium myristate	Magnesium salt of myristic acid	$[CH_3(CH_2)_{12}COO^-]_2\ Mg^{+2}$	Anticaking agent; slip modifier; viscosity increasing agent—nonaqueous
Potassium myristate	Potassium salt of myristic acid	$C_3(C_2)_{12}\ COOK$	Surfactant—cleansing agent: surfactant—emulsifying agent
Sodium myristate	Sodium salt of myristic acid	$CH_3(CH_2)_{12}COONa$	Surfactant—cleansing agent; surfactant—emulsifying agent
Zinc myristate	Zinc salt of myristic acid	$[CH_3(CH_2)_{12}COO^-]_2\ Zn^{2+}$	Anticaking agent; slip modifier; viscosity increasing agent—nonaqueous
Esters			
Butyl myristate	Ester of butyl alcohol and myristic acid		skin-conditioning agent—emollient
Cetyl myristate	Ester of cetyl alcohol and myristic acid		Skin-conditioning agent—occlusive
Decyl myristate	Ester of decyl alcohol and myristic acid.		Skin-conditioning agent—occlusive
Ethylhexyl myristate	Ester of 2-ethylhexyl alcohol and myristic acid		Skin-conditioning agent—emollient
Ethyl myristate	Ester of ethyl alcohol and myristic acid		Fragrance ingredient; hair conditioning agent; skin-conditioning agent—emollient
Glyceryl dimyristate	Diester of glycerin and myristic acid		Skin-conditioning agent—emollient

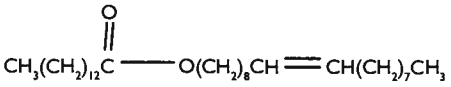
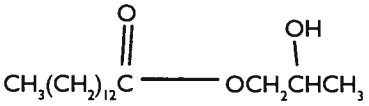
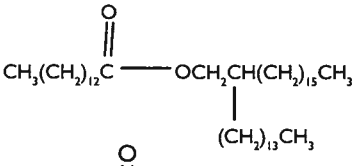
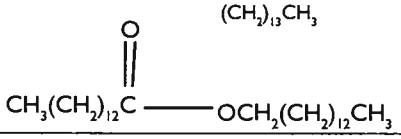
(continued)

Table 2 (continued)

Ingredient	Definition	Formula/Structure	Function
Myristic acid	Organic acid that conforms generally to the formula:	$CH_3(CH_2)_{12}COOH$	Fragrance ingredient, opacifying agent, surfactant—cleansing agent
Glyceryl isostearate/ myristate	Monoester of glyceryn esterfied with a blend of isostearic and myristic acids	None provided.	Skin-conditioning Agent—emollient; surfactant—emulsifying agent
Glyceryl myristate	Monoester of glycerin and myristic acid		Skin-conditioning agent—emollient; surfactant—emulsifying agent
isobutyl myristate	Ester of isobutyl alcohol and myristic acid		Skin-conditioning agent—emollient
Isocetyl myristate	Ester of isocetyl alcohol and myristic acid		Skin-conditioning agent—occlusive
Isodecyl myristate	Ester of branched chain decyl alcohols and myristic acid		Skin-conditioning agent—emollient
Isopropyl myristate	Ester of isopropyl alcohol and myristic acid		Binder; fragrance ingredient; skin-conditioning agent—emollient
Isostearyl mryistate	Ester of Isostearyl Alcohol and myristic acid		Binder; Skin-Conditioning Agent - Emollient
Isotridecyl myristate	Ester of myristic acid and isotridecyl alcohol		Hair conditioning agent; skin-conditioning agent—occlusive
Lauryl myristate	Ester of lauryl alcohol and myristic acid		Hair conditioning agent; skin-conditioning agent—occlusive
Methyl mryistate	Ester of methyl alcohol and myristic acid		Frangrance ingredient; skin-conditioning agent—emollient
Myristyl myristate	Ester of myristyl alcohol and myristic acid		Skin-conditioning agent—occlusive
Octyldodecyl Myristate	Ester of octyldodecanol and myristic acid.		Skin-conditioning agent—occlusive

(continued)

Table 2 (continued)

Ingredient	Definition	Formula/Structure	Function
Myristic acid	Organic acid that conforms generally to the formula:	$CH_3(CH_2)_{12}COOH$	Fragrance ingredient, opacifying agent, surfactant—cleansing agent
Oleyl myristate	Ester of oleyl alcohol and myristic acid		Hair conditioning agent; skin-conditioning agent—occlusive
Propylene glycol myristate	Ester of propylene glycol and myrisitic acid		Skin-conditioning agent—emollient; surfactant—emulsifying agent
Tetradecyloctadecyl myristate	Ester of tetradecyloctadecanol and myristic acid		Binder; emulsion stabilizer; film former; opacifying agent; skin-conditioning agent—occlusive
Tridecyl myristate	Ester of tridecyl alcohol and myristic acid		skin-conditioning agent—occlusive

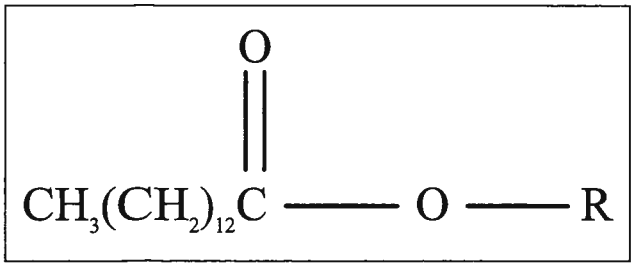


Figure 1. General myristate formula,[1] in which R may be as small as a methyl group for methyl myristate or a potassium ion for potassium myristate.

Isotridecyl myristate (CAS No 96518-24-0) is also known as tetradecanoic acid, isotridecyl ester.

Lauryl myristate (CAS No 2040-64-4) is also known as dodecyl tetradecanoate; myristic acid, dodecyl ester, and tetradecanoic acid, dodecyl ester.

Magnesium myristate (CAS No 4086-70-8) is also known as tetradecanoic acid, magnesium salt.

Methyl myristate (CAS No 124-10-7) is also known as methyl tetradecanoate; myristic acid, methyl ester; and tetradecanoic acid, methyl ester.

Myristyl myristate (CAS No 3234-85-3) is also known as tetradecanoic acid, tetradecyl ester, and tetradecyl tetradecanoate.

Octyldodecyl myristate (CAS Nos 22766-83-2 and 83826-43-1) is also known as myristic acid, 2-octyldodecyl ester; 2-octyldodecyl myristate; tetradecanoic acid, octyldodecyl ester; and tetradecanoic acid, 2-octyldodecyl ester.

Oleyl myristate (CAS No 22393-93-7) is also known as 9-octadecenyl tetradecanoate and tetradecanoic acid, 9-octadecenyl ester.

Potassium myristate (CAS No 13429-27-1) is also known as potassium tetradecanoate and tetradecanoic acid, potassium salt.

Propylene glycol myristate (CAS No 29059-24-3) is also known as propylene glycol monomyristate; propylene glycol monotetradecanoate; and tetradecanoic acid, monoester with 1,2-propanediol.

Sodium myristate (CAS No 822-12-8) is also known as sodium tetradecanoate and tetradecanoic acid, sodium salt.

Tetradecyloctadecyl myristate (no CAS No) is also known as myristic acid, tetradecyloctadecyl ester.

Tridecyl myristate (CAS No 36617-27-3) is also known as tetradecanoic acid, tridecyl ester.

Zinc myristate (CAS No 16260-27-8) is also known as tetradecanoic acid, zinc salt.

Physical and Chemical Properties

Myristic acid. Myristic acid occurs as a hard, white, or faintly yellow, glossy crystalline solid, as a white or yellow-white powder,[16] or as colorless leaflets.[17] Table 3 presents the physical and chemical properties of of myristic acid and octyldodecyl myristate.

Myristic acid is made of tetradecanoic acid (95% minimum), hexadecanoic acid (4% maximum), and dodecanoic acid (3% maximum) Cosmetic, Toiletries and Fragrance Association ([CTFA] Table 4).[25]

Table 3. Physical Properties of Myristic Acid and Octyldodecyl Myristate

Physical Property	Value	Reference
Myristic acid		
Molecular weight	228.36	18
	228.38	19
Density (g/mL) at 70°C	0.8528	18
Melting point (°C)	58.5	18
	58	19
	54.4	20
Boiling point (°C)	250.5	18
Solubility		
Water	Insoluble	16,18,19
Ethanol	Soluble	
Methanol	Very soluble	
Chloroform	Soluble	
Benzene	Very soluble	
Ether	Very soluble	
Viscosity (cp, at 75 (°C)	5.06	20
Acid value	245.7	20
Octyldodecyl Myristate		
Appearance	Oily liquid	21
Test at +8°C	Limpid	21
Odor	Faint	21
Color (Gardner Scale)	<1.5	21
Specific gravity at 20°C	1.435-1.457	21
Viscosity at 20°C	15-45 m.Pa.s	21
Acid value	< 7.00 mg KOH/g	21
Saponification value	90-110 mg KOH/g	21
Iodine value	<7.0 g I_2/100 g	21
Peroxide value	<6.0 meq O_2/kg	21
Alkaline impurities	<30 ppm NaOH	21
Water content	<0.50%	21
Sulphated ashes content	<0.1%	21
Heavy metals content	<10 ppm	21

Table 4. Comparison of Specifications[a]: Cosmetic and Food Grades of Myristic Acid[22]

Myristic acid	Cosmetics[22,23]	Foods[16]
Iodine value	0.5 maximum	1.0 maximum
Acid value	243-249	242-249
Saponification value	243-249	242-251
Unsaponifiable matter	0.2% maximum	1% maximum
Arsenic		3 ppm maximum
Heavy metals (eg, lead)		10 ppm maximum
Residue on ignition		0.1%
Titer (solidification point)	52-54°C	48-55°C
Water content		0.2%

[a] Cosmetic-grade myristic acid specifications for fatty acid composition is as follows: 12:0, 3% maximum; 14:0, 95% minimum; and 16:0, 4% maximum.[25]

Butyl myristate. Butyl myristate is a light, colorless, oily liquid. It is soluble in acetone, castor oil, chloroform, methanol, mineral oil, and toluene and insoluble in water. Other properties of butyl myristate include a freezing point range of 1°C to 7°C, a boiling point range of 167°C to 197°C (at 5 mm Hg), and a specific gravity between 0.850 and 0.858 at 25°C.[26]

Isocetyl myristate. Isocetyl myristate is an oily liquid with practically no odor. It has a density of 0.862, a freezing point of −39°C, and viscosity of 29.0 at 25°C. It is insoluble in water and soluble in most organic solvents. It is combustible.[27]

Nikko Chemicals Co, Ltd, reported that isocetyl myristate is a colorless liquid with a faint characteristic odor.[28] It has a

Table 5. Frequency of Use and Concentration of Myristic Acid and Its Salts and Esters in Cosmetics

Product Category (Total Number of Products in Each Category (FDA 2008))[69]	Frequency of Use[68]	Concentration of Use (%)[70,71]
Myristic Acid		
Bath products		
Soaps and detergents (1329)	9	0.1-19
Other (138)	–	2
Eye makeup		
Eye shadow (1196)	1	0.5
Mascara (463)	2	–
Noncoloring hair care products		
Conditioners (1249)	9	0.00003-0.0002
Shampoos (1403)	10	0.00002-5
Tonics, dressings, etc (1097)	6	0.00002-1
Other (716)	4	–
Hair-coloring products		
Color sprays/aerosol (8)	–	0.00002
Makeup		
Blushers (539)	–	0.3
Face powders (613)	1	0.5
Foundations (635)	15	0.04-0.8
Leg and body paints (29)	2	–
Lipsticks (1912)	5	–
Personal hygiene products		
Underarm deodorants (540)	1	2
Douches (12)	–	4
Other (514)	2	6-9[a]
Shaving products		
Aftershave lotions (395)	3	0.5
Shaving cream (162)	13	0.5-14
Other (107)	2	–
Skin care products		
Skin cleansing creams, lotions, liquids, and pads (1368)	101	0.08-15
Depilatories (62)	–	12
Face and neck creams, lotions, powder and sprays (1195)	1	39497
Body and hand creams, lotions, powder and sprays (1513)	13	0.8-10
Moisturizers (2039)	5	0.8
Night creams, lotions, powder and sprays (343)	–	0.005
Paste masks/mud packs (418)	–	4
Other (1244)	2	8
Suntan products		
Suntan gels, creams, liquids and sprays (156)	–	0.3
Indoor tanning preparations (200)	–	2
Total uses/ranges for myristic acid	207	0.00002-20
Aluminum dimyristate		
Eye makeup		
Eyeliners (684)	1	–
Eye shadow (1196)	133	0.2-3
Eye lotions (177)	–	0.09
Other (288)	1	0.3-2[b]
Makeup		
Blushers (539)	6	0.5-2
Face powders (613)	12	0.5-2
Foundations (635)	1	0.01-2
Makeup bases (164)	1	–
Rouges (99)	13	0.4
Other (406)	4	–

(continued)

Table 5 (continued)

Product Category (Total Number of Products in Each Category (FDA 2008))[69]	Frequency of Use[68]	Concentration of Use (%)[70,71]
Suntan products		
Other (62)	2	–
Total uses/ranges for aluminum dimyristate	174	0.01-3
Aluminum myristate		
Eye makeup		
Eye shadow (1196)	6	0.01-1
Makeup		
Blushers (539)	14	–
Face powders (613)	3	–
Total uses/ranges for aluminum myristate	23	0.01-1
Aluminum myistates/palmitates		
Makeup		
Face powders (613)	2	6
Total uses/ranges for aluminum myristates/ palmitates	2	6
Butyl myristate		
Makeup		
Lipsticks (1912)	16	–
Makeup bases (164)	6	–
Rouges (99)	1	–
Other (406)	2	–
Skin care products		
Moisturizers (2039)	1	–
Total uses/ranges for butyl myristate	26	–
Cetyl myristate		
Eye makeup		
Eye shadow (1196)	1	–
Skin care products		–
Face and neck creams, lotions, powder and sprays (1195)	2	–
Body and hand creams, lotions, powder and sprays (1513)	1	6
Moisturizers (2039)	1	–
Other (1244)	2	–
Total uses/ranges for cetyl myristate	7	6
Glyceryl myristate		
Fragrance products		
Other (399)	1	–
Makeup		
Makeup bases (164)	1	–
Personal hygiene products		
Underarm deodorants (540)	1	–
Skin care products		
Face and neck creams, lotions, powder and sprays (1195)	3	–
Body and hand creams, lotions, powder and sprays (1513)	5	–
Moisturizers (2039)	5	–
Night creams, lotions, powder and sprays (343)	2	–
Paste masks/mud packs (418)	3	–
Other (1244)	2	–
Suntan products		
Suntan gels, creams, liquids and sprays (156)	1	–
Other (62)	1	–
Total uses/ranges for glyceryl myristate	25	–
Isobutyl Myristate		
Skin care products		

(continued)

Table 5 (continued)

Product Category (Total Number of Products in Each Category (FDA 2008))[69]	Frequency of Use[68]	Concentration of Use (%)[70,71]
Body and hand creams, lotions, powder and sprays (1513)	–	30
Paste masks/mud packs (418)	–	10
Suntan products		
Suntan gels, creams, liquids and sprays (156)	–	3
Total uses/ranges for isobutyl myristate	–	3-30
Isocetyl myristate		
Makeup		
Foundations (635)	5	–
Skin care products		
Other (1244)	1	–
Total uses/ranges for isocetyl myristate	6	–
Isodecyl myristate		
Makeup		
Foundations (635)	1	–
Total uses/ranges for isodecyl myristate	1	–
Isopropyl myristate		
Baby products		
Lotions, oils, powders, and creams (132)	4	3
Bath products		
Oils, tablets, and salts (257)	21	39494
Soaps and detergents (1329)	1	0.006-1
Other (239)	2	23
Eye makeup		
Eyebrow pencils (147)	12	0.04-20
Eyeliners (684)	49	39495
Eye shadow (1196)	31	39450
Eye lotions (177)	4	–
Eye makeup remover (131)	3	–
Other (288)	4	–
Fragrance products		
Colognes and toilet waters (1288)	9	39461
Perfumes (569)	3	11
Powders (278)	3	–
Sachets (28)	10	–
Other (399)	39	58
Noncoloring hair care products		
Conditioners (1249)	45	0.5-48
Sprays/aerosol fixatives (371)	1	0.02-10
Straighteners (144)	4	–
Permanent waves (141)	1	–
Shampoos (1403)	4	0.4-1
Tonics, dressings, etc (1097)	39	0.4-23
Other (716)	13	1-10[c]
Hair-coloring products		
Dyes and colors (2481)	1	30[d]
Shampoos (48)	1	–
Color sprays (8)	1	–
Bleaches (152)	2	22
Makeup		
Blushers (539)	36	0.07-2
Face powders (613)	16	0.3-4
Foundations (635)	39	0.001-14
Leg and body paints (29)	1	–
Lipsticks (1912)	49	39472
Makeup bases (164)	8	–
Makeup fixatives (38)	1	–

(continued)

Table 5 (continued)

Product Category (Total Number of Products in Each Category (FDA 2008))[69]	Frequency of Use[68]	Concentration of Use (%)[70,71]
Other (406)	14	2-3[f]
Nail care products		
Basecoats and undercoats (62)	1	–
Cuticle softeners (18)	2	39537
Creams and lotions (17)	1	38
Nail polish and enamel removers (41)	1	–
Other (124)	2	–
Personal hygiene products		
Underarm deodorants (540)	10	0.08-51
Feminine deodorants (21)	5	39579
Other (514)	13	3-60[g]
Shaving products		
Aftershave lotions (395)	11	–
Preshave lotions (27)	8	17
Shaving cream (162)	5	1
Other (107)	6	–
Skin care products		
Skin cleansing creams, lotions, liquids, and pads (1368)	52	39468
Depilatories (62)	2	–
Face and neck creams, lotions, powder and sprays (1195)	48	0.4-5
Body and hand creams, lotions, powder and sprays (1513)	157	2-39
Foot powders and sprays (48)	2	–
Moisturizers (2039)	129	0.2-17
Night creams, lotions, powder and sprays (343)	26	0.1-5
Paste masks/mud packs (418)	10	39521
Skin fresheners (285)	–	3
Other (1244)	61	3-82[h]
Suntan products		
Suntan gels, creams, liquids and sprays (156)	22	39486
Indoor tanning preparations (200)	6	–
Other (62)	6	1-3[i]
Total uses/ranges for isopropyl myristate	1057	0.001-82
Lauryl myristate		
Noncoloring hair care products		
Shampoos (1403)	3	–
Total uses/ranges for lauryl myristate	3	–
Magnesium myristate		
Eye makeup		
Eyeliners (684)	–	0.5
Eye shadow (1196)	76	0.6-7
Eye lotions (177)	1	–
Mascara (463)	1	–
Other (288)	1	6[k]
Fragrance products		
Powders (278)	2	5
Other (399)	1	–
Makeup		
Blushers (539)	6	0.2-5
Face powders (613)	80	0.3-10
Foundations (635)	9	0.05-0.09
Lipsticks (1912)	–	3
Makeup bases (164)	–	0.0001
Rouges (99)	1	–
Makeup fixatives (38)	2	–

(continued)

Table 5 (continued)

Product Category (Total Number of Products in Each Category (FDA 2008))[69]	Frequency of Use[68]	Concentration of Use (%)[70,71]
Other (406)	9	–
Nail care products		
Nail polishes and enamels (17)	1	–
Skin care products		
Body and hand creams, lotions, powder and sprays (1513)	–	5
Other (1244)	1	–
Suntan products		
Indoor tanning preparations (200)	1	–
Other (62)	2	–
Total uses/ranges for magnesium myristate	194	0.0001-10
Myristyl myristate		
Baby products		
Lotions, oils, powders, and creams (132)	14	39448
Other (138)	1	–
Bath products		
Oils, tablets, and salts (257)	5	–
Eye makeup		
Eyebrow pencils (147)	6	6
Eyeliners (684)	8	39611
Eye shadow (1196)	8	39575
Eye lotions (177)	5	0.4-4
Other (288)	7	4-6[j]
Fragrance products		
Perfumes (569)	–	39494
Other (399)	6	–
Noncoloring hair care products		
Conditioners (1249)	8	–
Rinses (47)	1	–
Shampoos (1403)	3	–
Tonics, dressings, etc (1097)	1	–
Other (716)	–	2[l]
Makeup		
Blushers (539)	1	1
Face powders (613)	–	0.5
Foundations (635)	7	0.8-5
Leg and body paints (29)	2	39605
Lipsticks (1912)	18	39607
Makeup bases (164)	3	–
Other (406)	5	3-7[m]
Nail care products		
Cuticle softeners (18)	1	3
Creams and lotions (17)	1	2
Other (124)	2	–
Personal hygiene products		
Underarm deodorants (540)	6	2
Other (514)	–	3
Shaving products		
Aftershave lotions (395)	9	2
Shaving cream (162)	7	0.3
Skin care products		
Skin cleansing creams, lotions, liquids, and pads (1368)	4	2
Face and neck creams, lotions, powder and sprays (1195)	26	0.5-8
Body and hand creams, lotions, powder and sprays (1513)	51	39449
Foot powders and sprays (48)	1	–

(continued)

Table 5 (continued)

Product Category (Total Number of Products in Each Category (FDA 2008))[69]	Frequency of Use[68]	Concentration of Use (%)[70,71]
Moisturizers (2039)	63	0.5-3
Night creams, lotions, powder and sprays (343)	10	2
Paste masks/mud packs (418)	5	0.5
Skin fresheners (285)	1	–
Other (1244)	6	39449
Suntan products		
Suntan gels, creams, liquids and sprays (156)	–	7
Indoor tanning preparations (200)	2	2
Total uses/ranges for myristyl myristate	??	0.3-17
Octyldodecyl Myristate		
Baby products		
Lotions, oils, powders, and creams (132)	2	–
Eye makeup		
Eyebrow pencils (147)	–	0.3
Eyeliners (684)	1	2
Eye shadow (1196)	3	0.3
Eye lotions (177)	1	2
Mascara (463)	1	–
Other (288)	1	–
Fragrance products		
Other (399)	2	–
Noncoloring hair care products		
Tonics, dressings, etc (1097)	1	–
Makeup		
Blushers (539)	2	0.007
Face powders (613)	2	–
Foundations (635)	8	39518
Lipsticks (1912)	10	0.07-21
Shaving products		
Aftershave lotions (395)	4	1
Preshave lotions (27)	2	–
Skin care products		
Skin cleansing creams, lotions, liquids, and pads (1368)	2	–
Face and neck creams, lotions, powder and sprays (1195)	9	39510
Body and hand creams, lotions, powder and sprays (1513)	8	0.9-4
Moisturizers (2039)	16	0.5-2
Paste masks/mud packs (418)	3	–
Skin fresheners (285)	–	0.3
Other (1244)	10	1
Suntan products		
Indoor tanning preparations (200)	7	–
Other (62)	–	1
Total uses/ranges for octyldodecyl myristate	95	0.007-21
Potassium Myristate		
Bath products		
Soaps and detergents (1329)	5	–
Eye makeup		–
Eyeliners (684)	1	–
Other (288)	1	–
Makeup		
Foundations (635)	1	–
Skin care products		
Skin cleansing creams, lotions, liquids, and pads (1368)	18	39574

(continued)

Table 5 (continued)

Product Category (Total Number of Products in Each Category (FDA 2008))[69]	Frequency of Use[68]	Concentration of Use (%)[70,71]
Other (1244)	1	–
Total uses/ranges for potassium myristate	27	5-7
Propylene glycol myristate		
Eye makeup		
Other (288)	1	–
Makeup		
Lipsticks (1912)	2	5
Other (406)	1	–
Skin care products		
Face and neck creams, lotions, powder and sprays (1195)	1	4
Body and hand creams, lotions, powder and sprays (1513)	3	–
Moisturizers (2039)	1	–
Other (1244)	4	–
Suntan products		
Suntan gels, creams, liquids and sprays (156)	2	6
Total uses/ranges for propylene glycol myristate	15	4-6
Sodium myristate		
Bath products		
Soaps and detergents (1329)	3	0.5-6
Noncoloring hair care products		
Conditioners (1249)	1	–
Shampoos (1403)	3	–
Personal hygiene products		
Underarm deodorants (540)	1	0.2
Skin care products		
Skin cleansing creams, lotions, liquids, and pads (1368)	6	–
Face and neck creams, lotions, powder and sprays (1195)	1	–
Total uses/ranges for sodium myristate	15	0.2-6
Zinc myristate		
Eye makeup		
Eyebrow pencils (147)	–	4
Eyeliners (684)	1	5
Eye shadow (1196)	50	0.5-6
Eye lotions (177)	–	0.05
Other (288)	9	–
Fragrance products		
Powders (278)	–	5
Makeup		
Blushers (539)	33	0.3-3
Face powders (613)	18	39526
Foundations (635)	5	0.001-6
Lipsticks (1912)	–	5
Makeup bases (164)	–	5
Other (406)	1	–
Nail care products		
Basecoats and undercoats (62)	–	0.00005
Nail polishes and enamels (419)	5	–
Skin care products		
Face and neck creams, lotions, powder and sprays (1195)	–	5
Suntan products		

(continued)

Table 5 (continued)

Product Category (Total Number of Products in Each Category (FDA 2008))[69]	Frequency of Use[68]	Concentration of Use (%)[70,71]
Suntan gels, creams, liquids and sprays (156)	–	0.1
Total uses/ranges for zinc myristate	122	0.00005-20

[a] 6% in a shower gel; 9% in a body scrub.
[b] 0.3% in a lash powder; 2% in a brow powder wax.
[c] 1% in an aerosol hair shine; 10% in a hair oil treatment.
[d] 5% after dilution.
[e] 11% after dilution.
[f] 4% in a lip liner pencil.
[g] 4% in a body scrub.
[h] 4% in a foot lotion; 82% in a massage oil.
[i] 1% and 3% in tanning oils.
[j] 6% in a lash powder.
[k] 4% in an eye pencil.
[l] 2% in a hairdressing créme conditioner.
[m] 7% in a concealer.
[n] 0.7% in a moisturizing sprays.

maximum acid value of 1 and a saponification value range of 120 to 130.

Isopropyl myristate. Isopropyl myristate is a colorless, almost odorless, mobile liquid with a bland taste. It is soluble in acetone, castor oil, chloroform, cottonseed oil, ethanol, ethyl acetate, mineral oil, and toluene and insoluble in water, glycerol, sorbitan, and propylene glycol. It is miscible with liquid hydrocarbons and fixed oils, and it dissolves lanolin, cholesterol, and many waxes.[29-31]

Octyldodecyl myristate. 2-Octyldodecyl myristate is a colorless, odorless liquid with a maximum acid value of 0.5, saponification value range from 105 to 111, and a maximum hydroxyl value of 5.0. On ignition, the residue has a maximum of 0.5%.[32]

Gattefossé[22] stated that octyldodecyl myristate was slightly soluble in ethanol at 96°C, soluble in chloroform and methylene chloride, insoluble in water, and freely soluble in mineral oils.

Potassium myristate. Potassium myristate is a white-to-pale yellow solid with a faint characteristic odor.[33]

Ultraviolet Absorption

Glyceryl myristate. Glyceryl myristate has UV absorption λ_{max} of 238 nm and λ_{min} of 270 nm.[34]

Reactivity

The myristate esters can be expected to undergo chemical or enzymatic hydrolysis to myristic acid and the corresponding alcohol. Transesterification and other typical ester reactions may also occur. Butyl myristate, if synthesized from a pure, saturated fatty acid, would not significantly autoxidize, discolor, or develop an odor.[35]

Methods of Manufacture

Aluminum dimyristate, aluminum myristate, butyl myristate, calcium myristate, decyl myristate, ethylhexyl myristate, ethyl myristate, glyceryl dimyristate, glyceryl myristate, isobutyl myristate, isocetyl myristate, isodecyl myristate, isopropyl myristate, isotridecyl myristate, lauryl myristate, magnesium myristate, methyl myristate, myristyl myristate, octyldodecyl myristate, potassium myristate, propylene glycol myristate, sodium myristate, tetradecyloctadecyl myristate, tridecyl myristate, and zinc myristate have plant and synthetic sources. Aluminum isostearates/myristates, aluminum myristates/palmitates, cetyl myristate, glyceryl isostearate/myristate, isostearyl myristate, and oleyl myristate have plant, animal, and synthetic sources.[15]

Myristic acid. According to the CTFA (now the Personal Care Products Council [the Council]), myristic acid is produced commercially by the saponification and fractionation of animal or vegetable fats and oils. The isolated acid fraction is hydrogenated to produce the saturated fatty acid.[35]

Myristic acid is a solid organic acid usually obtained from coconut oil, nutmeg butter *(Myristica fragrans* Houtt), palm seed oils, and milk fats.[18,20] Seed oils of the plant family, Myristaceae, contain the largest amounts of myristic acid (up to 80%), but small amounts have been measured in most animal fats and vegetable oils.

The following methods have been used in the preparation of myristic acid: isolation from tail-oil fatty acids, from 9-ketotetradecanoic acid; by electrolysis of a mixture of methyl hydrogen adipate and decanoic acid, by Maurer oxidation of myristanol; and from cetanol.[18] The most common means of preparation is by fractional distillation of hydrolyzed coconut oil, palm kernel oil,[36] or coconut acids.[17]

Butyl myristate. Butyl myristate is derived from the esterification of myristic acid and butyl alcohol in the presence of an

acid catalyst. The product is stripped to remove excess alcohol and alkali refined to neutralize the catalyst. Butyl myristate is obtained through fractional distillation.[35]

Isocetyl myristate. Nikko Chemicals Co, Ltd, reported that isocetyl myristate is produced by the esterification of isocetyl alcohol and myristic acid.[37]

Isopropyl myristate. Isopropyl myristate is commercially produced by distillation, which is preceded by the esterification of myristic acid and isopropanol, in the presence of an acid catalyst. The product is stripped to remove excess isopropanol, alkali refined to neutralize the catalyst, and then the product is distilled to obtain isopropyl myristate.[38]

Methyl myristate. Methyl myristate is derived by the esterification of myristic acid with methanol or alcoholysis of coconut oil with methanol.[27] It is purified by vacuum fractional distillation.

Myristyl myristate. Myristyl myristate is produced by the esterification of myristic acid and myristyl alcohol in the presence of an acid catalyst. The product is stripped to remove excess myristyl alcohol; alkali is used to neutralize the catalyst, and then purified to separate myristyl myristate.[39]

Octyldodecyl myristate. Octyldodecyl myristate is produced by the esterification of myristic acid with 2-octyl dodecanol, manufactured from vegetable sources.[22,40,41]

Potassium myristate. Potassium myristate is produced by the reaction of potassium hydroxide and myristic acid.[42]

Reacting lauric acid, myristic acid, and palmitic acid with water, glycerin, potassium hydroxide, and tetrasodium EDTA produces a product containing potassium myristate (15%) as well as potassium cocoate (23%), EDTA-4Na (0.2%), and water (61.8%).[43]

Analytical Methods

The myristates can be analyzed by thin-layer chromatography (TLC),[44] gas-liquid chromatography,[45] and x-ray powder diffraction.[46]

Two basic methods for the analysis of the fatty acids have been reported by the cosmetic industry. Primarily, gas chromatography (GC) of fatty acid methyl esters, prepared by the boron trifluoride–methanol method, is used for the separation and relative identification of fatty acids in a mixture.[47,48] Infrared spectra of the fatty acids are used for fingerprinting, functional group identification, and impurity screening.[23,49-53] Determination of physicochemical properties also aids in positive identification of a specific fatty acid.[20,47]

Flame ionization detection (FID) is usually coupled with the GC of fatty acid methyl esters. Mass spectrometry (MS) has also been used with GC for compound identification.[54]

Thin-layer chromatography and high-performance liquid chromatography (HPLC) are also used in fatty acid identification and quantitation.[54-57] Methods of detection include UV, fluorescence spectroscopic, and refractive index detection.

Mass spectrometry with temperature profiling of the chemical ionization source has been reported as a method for initial compound separation. Its coupling with a second MS allows direct analysis of complex lipid sources.[58] Other separation methods include centrifugal liquid and adsorption chromatography.[59] Identification procedures range from methods such as gravimetry[47] and histochemical staining[60] to ultraviolet, infrared, and nuclear magnetic resonance spectroscopy.[20,61,62]

Cotte et al[63] used Fourier-transform infrared (FT-IR) microscopy to locate myristic acid in dermal layers.

Impurities

Myristic acid. The myristates used as cosmetic ingredients are mixtures of fatty esters, as the myristic acid and alcohols used in the preparation of these ingredients are themselves mixtures of acids and alcohols, respectively. The CTFA Cosmetic Ingredient Chemical Description[51] for myristic acid lists the following as component acids:

- n-tetradecanoic acid, $CH_3(CH_2)_{12}COOH$ (95% minimum),
- n-hexadecanoic acid, $CH_3(CH_2)_{14}COOH$ (4% maximum),
- and n-dodecanoic acid, $CH_3(CH_2)_{10}COOH$ (3% maximum).

Myristic acid may contain unsaponifiable material, mostly hydrocarbons, at a maximum concentration of 0.2%, and some grades may contain glyceryl monomyristate at a maximum concentration of 0.07%. Butylated hydroxytoluene (BHT) may be present as an added antioxidant.[51]

Butyl myristate. Minor impurities, which may be present, are fatty acids (such as myristic acid) at a maximum of 0.2%.[35]

Glyceryl myristate. Impurities in glyceryl myristate include glycerol (0.3%), diglycerol (0.57%), and free fatty acid (0.14%).[64,65] The ratio of 1,2-(mono)glycerol diester to total (mono)glycerol diester is 27.8. Specifications include monoester content (minimum 90%), free glycerol (maximum 1%), and free fatty acids (maximum 1.5%). The typical value for heavy metals (as lead) in glyceryl myristate is <10 mg/kg.

Isocetyl myristate. Isocetyl myristate is 95% pure with a maximum of heavy metals of 20 ppm and arsenic of 2 ppm.[28]

Isopropyl myristate. Isopropyl myristate may have myristic acid, other free fatty acids are present at a maximum concentration of 1.0%, and unsaponifiable material is present at a maximum concentration of 0.2%. There are no known diluents, solvents, or additives present.[38]

The ester composition is varied according to the specific usage requirement, provided that the specification limits conform to the following: isopropyl myristate, not less than

90.0% (limits, ±5.0%); isopropyl palmitate, not more than 10.0% (limits, ±3.0%); and isopropyl laurate, tridecanoate, pentadecanoate, heptadecanoate, and stearate, none more than 10.0% (limits, 2.0% each).[66]

Methyl myristate. Technical grade methyl myristate is 93% pure and can be purified to >99.8%.[27] Spectrum Chemicals and Laboratory Products[67] stated that a sample of methyl myristate was 99.4% pure. Impurities were not listed.

Myristyl myristate. Myristyl myristate may have free fatty acids, mainly myristic acid, at a maximum concentration of 1.5%. There are no known diluents, solvents, or additives present.[39]

Octyldodecyl myristate. Nikko Chemicals Co, Ltd[32] stated that 2-octyldodecyl myristate has a maximum of 20 ppm heavy metals and 2 ppm arsenic.

Potassium myristate. Nikko Chemicals Co, Ltd[34] stated that potassium myristate has a maximum of 40 ppm heavy metals and 2 ppm arsenic.

Use

Cosmetic

Use information is supplied to the US Food and Drug Administration (FDA) by industry as part of the Voluntary Cosmetic Ingredient Reporting Program (VCRP).[68] Use concentration information is gathered by the Personal Care Products Council (Council) unless noted otherwise. Table 5 presents the use and concentration of myristic acid and its salts and esters in cosmetics.

There were no uses or use concentrations reported for the following:

- aluminum isostearates/myristates,
- calcium myristate,
- decyl myristate,
- ethyl myristate,
- ethylhexyl myristate,
- glyceryl dimyristate,
- glyceryl isostearate/myristate,
- glyceryl myristate,
- isostearyl myristate,
- isotridecyl myristate,
- oleyl myristate,
- tetradecyloctadecyl myristate, or
- tridecyl myristate.

Butyl myristate. Butyl myristate was used in 26 cosmetic products in 2007. Concentration of use data were not reported, although in 1990, concentrations ranged from 1% to 50%.[1]

Glyceryl myristate. Glyceryl myristate was used in 25 cosmetic products in 2007; no use concentrations were reported, although in 1998, its concentrations ranged from 1% to 6%.

Cosmetic Aerosols

Cetyl myristate is used in 2 face and neck creams, lotions, powders, and sprays.

The potential adverse effects of inhaled aerosols depend on the specific chemical species, the concentration, the duration of the exposure, and the site of deposition within the respiratory system.[72] In general the smaller the particle, the farther into the respiratory tree the particle will deposit and the greater the impact on the respiratory system.[73]

Anhydrous hair spray particle diameters of 60 to 80 μm have been reported, and pump hair sprays have particle diameters of ≥80 μm.[74] The mean particle diameter is around 38 μm in a typical aerosol spray.[75] In practice, aerosols should have at least 99% of particle diameters in the 10 to 110 μm range. This means that most aerosol particles are deposited in the nasopharyngeal region and are not respirable.

Noncosmetic

Myristic acid is used in foods as a plasticizing, lubricating, binding, and defoaming agent and as a reagent in the manufacture of other food-grade additives.[16,36,76] Myristic acid is used as a flavoring agent in foods.[17]

Straight-chain monobasic carboxylic acids from fats and oils derived from edible sources, such as the fatty acid myristic acid, are accepted as safe for use in food and in the manufacture of food-grade additives, provided they meet particular conditions and specifications. The unsaponifiable matter in the fatty acid or fatty acid-derived food additive must not exceed 2%, the food additive must be free of chick-edema factor, and it must be produced and labeled in accordance with good manufacturing practice.[77]

Butyl myristate is also used as a plasticizer, as a lubricant for textiles, and in paper stencils.[78]

Both ethyl and methyl myristate are generally recognized as safe food additives by the FDA.[79]

General Biology

Metabolism and Absorption

Myristic acid. Like other higher molecular weight aliphatic esters, the myristates are readily hydrolyzed to the corresponding alcohols and acids, which are then further metabolized.[76] Myristic acid is a digestible constituent of most vegetable and animal fats and is nontoxic when ingested.[80]

Rioux et al[81] incubated cultured Sprague-Dawley rat hepatocytes in radiolabeled myristic acid for 3, 6, 12, and 2 hours. Electrophoresis of the products revealed that myristic acid (4 nmol/L) was metabolized into 18 well-resolved proteins in the 10 to 20 kd range.

Cotte et al[63] used FT-IR to measure the penetration of pre-deuterated myristic acid in pig ear skin using Franz diffusion cells. After 1 day, myristic acid penetrated to the epidermis. For comparison, palmitic acid was detected in the stratum corneum and did not penetrate any further.

Ethyl myristate. Savary and Constantin[82] orally administered ethyl myristate mixed with olive oil in the feed (90% boiled rice, 10% lipid by wet weight) of rats with thoracic-duct fistula. Lymph was collected for 24 to 100 hours. The ester was recovered in small quantities in the thoracic-duct lymph. In the hydrolysis of lymph triglycerides, fatty acid yields from total dietary lipids were 55 mg/h coming from total dietary lipids and 22 mg/h coming from dietary monoalcohol fatty ester.

Ethyl and methyl myristate. Hydrolysis of ethyl myristate (emulsified in buffer) by rat pancreatic juice or pure porcine pancreatic lipase was at a lower relative rate (25% and 31%, respectively) than tetradecyl butyrate (100% and 110%), hexadecyl formate (55% and 80%), hexadecyl propionate (37% and 46%), hexadecyl butyrate (100% and 100%), and *n*-hexyl laurate (110% and 150%). The relative rates of hydrolysis for methyl myristate were 61% and 90%, respectively.[83]

Isopropyl myristate. Four monkeys were exposed for 5 seconds to the spray of an aerosol antiperspirant containing ^{14}C-labeled isopropyl myristate.[84] Two animals were killed immediately after exposure, and the other 2 were killed 24 hours later. The distribution of ^{14}C in the exhaled air and in several tissues indicated that only 0.25% of the dose sprayed at the animals was absorbed; about 10% of this reached the lower respiratory tract. Some 85% of the absorbed isopropyl myristate was eliminated in 24 hours, mainly as exhaled carbon dioxide; very little labeled material reached any tissues other than the lungs.

Suzuki et al[85] reported that ^{14}C-labeled isopropyl myristate penetrated into sebaceous glands, stratum spinosum, hair infundibula, and follicles.

Brinkmann and Müller-Goymann[86] used differential scanning calorimetry, wide-angle x-ray diffraction, and small-angle x-ray diffraction to examine human abdominal and breast skin soaked in isopropyl myristate. The authors reported a slight increase in the short distance of orthorhombically arranged lipids, while that of hexagonally packed lipids decreased. The long distance of the lamellar structure was unaffected. Isopropyl myristate insertion caused a more densely packed lipid order. The authors suggest that isopropyl myristate does a lateral insertion into lipophilic areas of the stratum corneum microstructure with an anchoring of the isopropyl group in the polar region of the layer.

Dermal Penetration Enhancement

Myristic acid has been tested for its ability to enhance the dermal penetration of a number of chemicals. In most cases, skin treated with myristic acid increased dermal penetration.[87-90] Enhanced penetration was also observed by butyl myristate. Testing of isopropyl myristate showed mixed results regarding dermal penetration enhancement.[90-96]

Other Effects

Dermal

Isopropyl myristate. Suzuki et al[85] reported that isopropyl myristate induced acanthosis, edematous degeneration of collagen fibers, and changes in blood vessels when applied to Angora rabbits.

Enzyme

Methyl myristate. Osama et al[97] reported that the half maximal inhibitory concentration (IC_{50}) of methyl myristate for the inhibition of rat brain prostaglandin D synthase and swine brain prostaglandin D_2 dehydrogenase was >200 μmol/L in both cases.

Cytotoxicity

Methyl myristate. Takeara et al[98] used the 3-(4,5-dimethylthiazole-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) test to evaluate the cytotoxicity of methyl myristate on 4 strains of leukemia cells. For acute promyeloblasic leukemia (HL-60) cells, the IC_{50} was 4.68 (1.52-14.44 confidence interval [CI]) μg/mL, >6.25 μg/mL for chronic myelogenic leukemia (K-526) cells, >6.25 μg/mL for lymphoblastic leukemia (CEM) cells, and 4.31 (3.66-5.09 DI) μg/mL for T-cell leukemia (Molt-4) cells.

Animal Toxicology

Acute Oral Toxicity

Data from a previous assessment of myristic acid showed that little acute toxicity was observed at oral doses of 15 to 19 g/kg body weight of 2.2% to 13% myristic acid in rats.[2] In an acute oral toxicity study of butyl myristate in rats, the LD_{50} was >8g/kg. The acute oral LD_{50} for undiluted isopropyl myristate is >16 mL/kg in rats and 49.7 mL/kg in mice.[1]

Butyl myristate. An acute oral toxicity study of butyl myristate was conducted using 10 rats (strain/sex not provided). Daily observations were made over a period of 14 days. The LD_{50} was >8 g/kg. No data on weights of animals tested, ranges of chemical concentration tested, or responses of individual rats were available.[35]

Laboratoire de Recherche et d'Experimentation[99] orally administered butyl myristate (2000 mg/kg) to male NMRI EOPS mice (n = 5). The mice were observed for 6 days. There was no mortality, and no clinical or behavioral signs were observed. Weight gain was satisfactory.

Ethyl myristate. Food and Drug Research Laboratories, Inc,[100] orally treated 10 rats (strain/sex not provided) with 5 g/kg ethyl myristate. Over a 14-day observation period, none of these animals died.

Acute Dermal Toxicity

Butyl myristate (2g/kg) was nontoxic and nonirritating when applied to the skin of rabbits.[101]

Ethyl myristate. Food and Drug Research Laboratories, Inc,[100] dermally treated 10 rabbits with 5 g/kg ethyl myristate. Over a 7-day observation period, 2 of 10 animals died.

Isopropyl myristate. The acute dermal toxicity of undiluted isopropyl myristate and 3 product formulations containing isopropyl myristate were evaluated. Isopropyl myristate was considered nontoxic to the animals tested (rabbits and guinea pigs).

Acute Parenteral Toxicity

Previous safety assessments noted that the intraperitoneal and subcutaneous LD_{20} for isopropyl myristate exceeded 79.5 mL/kg in rats and the intraperitoneal LD_{50} exceeded 50.2 mL/kg in mice.[1]

Sub-Chronic Dermal Toxicity

Previous safety assessments noted that myristic acid produced slight irritation after topical application to the skin of the external ear canal of 4 albino rabbits. No adverse effects were produced from subchronic topical application of myristic acid to rabbit skin.[2]

Subchronic dermal toxicity studies with product formulations containing 16% to 47% isopropyl myristate showed no toxicity over 4 weeks.[1] Butyl myristate and isopropyl myristate were nontoxic when applied to the skin of rabbits. Isopropyl myristate was moderately-to-severely irritiating when applied for 3 consecutive days to the clipped skin of rabbits. Butyl myristate was considered moderately irritating in rabbits in one study and nonirritating in another.

Inhalation Toxicity

Previous safety assessments cited acute inhalation toxicity studies in rats showing no adverse effects from 2 product formulations containing 16% to 20% isopropyl myristate.[1] No toxic effects were observed in subchronic inhalation toxicity studies in guinea pigs and in cynomolgus monkeys.

Chronic Toxicity

No chronic toxicity data were found.

Ocular Irritation

Previous safety assessments cited Draize testing of myristyl myristate and isopropyl myristate at concentrations up to 100% that produced minimum eye irritation in rabbits.[1] Butyl myristate (no concentration provided) was considered nonirritating to the rabbit eye. Undiluted isopropyl myristate produced only minimal eye irritation in rabbits. Myristic acid (1.5%) was minimally irritiating to the eyes of rabbits.[2]

Dermal Sensitization

Previous safety assessments cited data showing that butyl myristate was a moderate skin irritant when intradermaly administered to guinea pigs but was not a sensitizer.[1] Isopropyl myristate did not produce sensitization in guinea pigs. Myristyl myristate produced minimal skin irritation but no sensitization in guinea pigs administered myristyl myristate topically or intracutaneously.

Comedogenicity

Isopropyl and myristyl myristate. Treatment with isopropyl myristate resulted in comedogenic activity in the rabbit ear assay.[102-104]

Nguyen et al[105] applied myristyl myristate (50% in petrolatum; 0.5 g) and isopropyl myristate (50% in various mediums; 0.5 g) to the glabrous inner portion of both ears of New Zealand white rabbits (n = 6; male and female; 6 weeks old) for 5 days per week (Monday to Friday) for 4 consecutive weeks. The ears were then biopsied and scored for comedones through clinical examination and slide biopsy. The control substance was crude coal tar (10%). Isopropyl myristate was found to be comedogenic in all media; myristyl myristate was less comedogenic.

Genotoxicity

Isopropyl myristate. Blevins and Taylor[106] reported that isopropyl myristate tested negative in the *Salmonella*/microsome test in strains TA1538, TA1537, TA1535, TA100, and TA98, with and without activation.

Carcinogenicity

Previous safety assessments noted that isopropyl myristate was not carcinogenic on the skin of mice, but a mixture of isopropyl myristate and isopropyl alcohol significantly accelerated the carcinogenic activity of benzo(a)pyrene on the skin.[1]

Clinical Assessment of Safety

Previous safety assessments on the following ingredients are summarized below:

Isopropyl myristate. [1] Human primary skin irritation studies showed no reactions to isopropyl myristate alone and a mild irritation from product formulations containing 15% to 58% isopropyl myristate. Repeated application of undiluted isopropyl myristate for 21 days produced only slight irritation. Isopropyl myristate was not a human skin sensitizer when in petrolatur or in product formulations at 15% to 58%, although a case report of sensitization was found. A product containing 43% isopropyl myristate produced no phototoxicity and no photocontact allergenicity in human studies.

Myristic acid. [2] In clinical primary and cumulative irritation studies, myristic acid at concentrations of 100% or 40% to 50% in mineral oil were nonirritating. Mild-to-intense erythema in single insult occlusive patch tests, soap chamber tests, and 21-day cumulative irritation studies were produced by cosmetic product formulations containing 2% to 93% myristic acid, and were generally not related to the fatty acid concentrations in the formulations. The Expert Panel also considered data from other fatty acids (oleic, lauric, pamitic, and stearic) due to the structural similarities among these ingredients.

Dermal Sensitization

Ethyl myristate. Kligman[107] applied ethyl myristate for 5 alternate-day 48-hour periods on the volar side of the arm of 25 participants after pretreatment for 24 hours with 2.5% aqueous sodium lauryl sulfate under occlusion. Sodium lauryl sulfate (5%-15%) was applied to the test site for 1 hour before the application of the challenge. There were no signs of sensitization for either the 48- or 72-hour challenge. It was not stated in the text, but according to the Research Institute for Fragrance Materials (RIFM),[108] ethyl myristate was tested at 12%.

Provocative Skin Testing

Isopropyl myristate. Uter et al[109] performed a retroactive study of dermatitis patients patch tested for sensitization to isopropyl myristate. Isopropyl myristate was tested in 20% petrolatum using 8117 patients and 10% petrolatum using 4554 patients between January 1992 and December 2001. The higher concentration had 43 doubtful reactions, 5 irritant reactions, 6 + reactions, and 2 ++/+++ reactions. The lower concentration had 9 doubtful reactions, 2 irritant reactions, 7 + reactions, and 1 ++/+++ reaction. The authors concluded that isopropyl myristate does not need to be tested for during routine patch tests.

Case Reports

Isopropyl myristate. Bharati and King[110] reported a 64-year-old woman who presented with an eczematous rash from a commercial sunscreen. Patch testing of the European standard series gave positive results for formaldehyde, quaternium-15, imidazolidinyl urea, and diazolidinyl urea. A further patch test of the ingredients in the sunscreen resulted in positive reactions for isohexadacane 10% alcohol and isopropyl myristate 10% alcohol.

Summary

This report addressed the safety of the following inorganic salts and esters of various fatty alcohols of myristic acid, including:

- aluminum dimyristate,
- aluminum isostearates/myristates,
- aluminum myristate,
- aluminum myristates/palmitates,
- butyl myristate,
- calcium myristate,
- cetyl myristate,
- decyl myristate,
- ethylhexyl myristate,
- ethyl myristate,
- glyceryl dimyristate,
- glyceryl isostearate/myristate,
- glyceryl myristate,
- isobutyl myristate,
- isocetyl myristate,
- isodecyl myristate,
- isopropyl myristate,
- isostearyl myristate,
- isotridecyl myristate,
- lauryl myristate,
- magnesium myristate,
- methyl myristate,
- myristyl myristate,
- octyldodecyl myristate,
- oleyl myristate,
- potassium myristate,
- propylene glycol myristate,
- sodium myristate,
- tetradecyloctadecyl myristate,
- tridecyl myristate, and
- zinc myristate.

Most of the esters are used as skin conditioning agents in cosmetics, but other functions include the following: anticaking agents, emulsion stabilizers, viscosity increasing agents, surfactants—cleansing agents, surfactants—emulsifying agents, slip modifiers, fragrance ingredients, hair conditioning agents, binders, film formers, and opacifying agents.

Myristic acid is produced by the saponification and fractionation of animal or vegetable fats and oils followed by isolation of the acid fraction that is then hydrogenated.

Analytical methods include TLC, gas-liquid chromatography, x-ray powder diffraction, GC, infrared spectrometry, HPLC, MS, gravimetry, and histochemical staining.

Component fatty acids of myristic acid include *n*-tetradecanoic acid, *n*-hexadecanoic acid, and *n*-dodecanoic acid. Myristic acid and other myristates may contain unsaponifiable material, and some grades may contain glyceryl monomyristate. Impurities in glyceryl myristate include glycerol, diglycerol, and free fatty acid. Other impurities include heavy metals and arsenic.

Isopropyl myristate is the most commonly used ingredient in this assessment and is used in over 1000 products at concentrations of 0.001% to 82%.

Myristic acid, aluminum myristate, aluminum myristates/palmitates, butyl myristate, cetyl myristate, glyceryl myristate, isobutyl myristate, isocetyl myristate, isodecyl myristate, isodecyl myristate, isopropyl myristate, lauryl myristate, magnesium myristate, myristyl myristate, octyldodecyl myristate, potassium myristate, propylene glycol myristate, sodium

myristate, and zinc myristate are also reported as used and/or have reported concentration of use.

No uses or use concentrations were reported for aluminum isostearates/myristate, calcium myristate, decyl myristate, ethyl myristate, ethylhexyl myristate, glyceryl dimyristate, glyceryl isostearate/myristate, isobutyl myristate, isostearyl myristate, isotridecyl myristate, methyl myristate, oleyl myristate, tetradecyloctadecyl myristate, and tridecyl myristate.

Myristic acid is approved as a food reagent and additive. Butyl myristate is also used as a plasticizer, as a lubricant for textiles, and in paper stencils.

The myristates are readily hydrolyzed to the corresponding alcohols and acids, which are then further metabolized. Butyl myristate may be readily hydrolyzed in vivo to its corresponding acid and alcohol, which are then further metabolized.

When isopropyl myristate was aerosolized, 85% of the absorbed isopropyl myristate was eliminated in 24 hours, mainly as exhaled carbon dioxide; very little labeled material reached any tissues other than the lungs in monkeys.

Myristic acid, butyl myristate, and isopropyl myristate enhanced the dermal penetration of several drugs.

The IC_{50} of methyl myristate for the inhibition of rat brain prostaglandin D synthase and swine brain prostaglandin D_2 dehydrogenase was >200 μmol/L.

The acute oral LD_{50} of butyl myristate was >8 g/kg for rats. The acute oral LD_{50} for isopropyl myristate was >16 mL/kg in rats and 49.7 mL/kg in mice.

Acute dermal application of butyl myristate (2 g/kg) was nontoxic and nonirritating to rabbits. When 10 rabbits were treated with a single dermal dose of ethyl myristate (5 g/kg) resulted in the death of 2 over 7 days. The intraperitoneal and subcutaneous LD_{50} for isopropyl myristate exceeded 79.5 mL/kg in rats and the intraperitoneal LD_{50} was >50.2 mL/kg in mice.

No death occurred, and no evidence of systemic toxicity was found at necropsy when the rats were exposed to aerosolized isopropyl myristate.

Myristic acid, isopropyl myristate, and myristyl myristate were minimally irritating to the eyes of rabbits. Butyl myristate was nonirritating to the rabbit eye.

Myristic acid was nonirritating in a single insult occlusive patch test and slightly irritating in a repeat open patch test on rabbits. Butyl myristate was a moderate skin irritant in rabbits and guinea pigs. Isopropyl myristate and myristyl myristate were minimally irritating in several formulations in rabbits and mice.

Isopropyl myristate was nonirritating when injected parenterally in albino rabbits.

Butyl myristate and myristyl myristate were nonsensitizing to guinea pigs.

Isopropyl myristate and myristyl myristate were comedogenic to rabbit ears.

Isopropyl myristate tested negative in the Salmonella/Microsome test in strains TA1538, TA1537, TA1535, TA100, and TA98, with and without activation.

In clinical primary and cumulative irritation studies, myristic acid was nonirritating. Isopropyl myristate can produce slight irritation but is not a human sensitizer at 15% to 50%.

Isopropyl myristate up to 100% was nonirritating, nonirritating in cumulative skin irritation tests, nonphototoxic, and nonphotoallergenic in humans.

Discussion

The data on butyl myristate and the related salts and esters, coupled with the data on the related chemicals (myristic acid, myristyl myristate, and isopropyl myristate), are a sufficient basis for a safety assessment. The CIR Expert Panel believes that there is little toxicological and chemical difference between myristic acid and any of its inorganic salts included in this report. The salts are expected to dissociate in any product formulation, independent of whether the salt is aluminum, calcium, magnesium, potassium, sodium, or zinc. For the various esters of fatty alcohols and myristic acid, the CIR Expert Panel considers that these fatty acid esters are subject to hydrolysis to from myristic acid and the component fatty alcohols. It is the experience of the Panel in its review of fatty alcohols of varying length of carbon chains that there is little difference in toxicity. Accordingly, the available data were considered supportive of the safety of the entire group as used in cosmetics.

The Expert Panel recognized that use concentration data are not available for all ingredients in this group and that some ingredients in the group are not in current use. The Expert Panel considered that the use concentrations for the ingredients that are in use are not likely to be different from the use concentrations for other myristates. Were those ingredients not in current use to be used in the future? The Panel expects that they would be used in products and at concentrations similar to those reported.

The Expert Panel recognized that these ingredients can enhance the penetration of other ingredients through the skin. The Panel cautioned that care should be taken in formulating cosmetic products that may contain these ingredients in combination with any ingredients whose safety was based on their lack of dermal absorption data, or when dermal absorption was a concern.

A number of the ingredients in this report—cetyl myristate, octyldodecyl myristate, and sodium myristate—have uses that include sprays. There are no data available on inhalation toxicity for these ingredients or the other ingredients in this assessment. The Expert Panel determined that there is sufficient inhalation toxicity data on isopropyl myristate in its assessment demonstrating no inhalation toxicity. In addition to the inhalation toxicity data, the Panel determined that butyl myristate and the salts and esters can be used safely in hair sprays, because the ingredient particle size is not respirable. The Panel reasoned that the particle size of aerosol hair sprays ($\sim$38 μm) and pump hair sprays (>80 μm) is large compared with respirable particulate sizes ($\geq$10 μm).

There are no data on the reproductive or developmental toxicity of myristic acid or its component parts for the derivatives. Based on structure–activity relationships, the Expert Panel considered that these chemicals had little potential for such toxicity when used as cosmetic ingredients.

Isopropyl myristate was not genotoxic in the Ames assay. The Expert Panel determined this to be sufficient carcinogenicity data for the related ingredients in this safety assessment.

Conclusion

The CIR Expert Panel finds that myristic acid, aluminum dimyristate, aluminum isostearates/myristates, aluminum myristate, aluminum myristates/palmitates, butyl myristate, calcium myristate, cetyl myristate, decyl myristate, ethyl myristate, ethylhexyl myristate, glyceryl dimyristate, glyceryl isostearate/myristate, glyceryl myristate, isobutyl myristate, isocetyl myristate, isodecyl myristate, isopropyl myristate, isostearyl myristate, isotridecyl myristate, lauryl myristate, magnesium myristate, methyl myristate, myristyl myristate, octyldodecyl myristate, oleyl myristate, potassium myristate, propylene glycol myristate, sodium myristate, tetradecyloctadecyl myristate, tridecyl myristate, and zinc myristate are safe as cosmetic ingredients in the current practices of use and concentration. Were ingredients in this group not in current use to be used in the future? The expectation is that they would be used in product categories and at concentrations comparable to others in the group.

Authors' Note

Unpublished sources cited in this report are available from the Director, Cosmetic Ingredient Review, 1101 17th Street, Suite 412, Washington, DC 20036, USA.

Declaration of Conflicting Interest

No potential conflict of interest relevant to this article was reported. F Alan Andersen, PhD, and Lillian C. Becker are employed by the Cosmetic Ingredient Review.

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References

1. Elder RL. Final report on the safety assessment of butyl myristate. *J Am Coll Toxicol.* 1990;9(2):247-258.
2. Elder RL. Final report on the safety assessment of oleic acid, lauric acid, palmitic acid, myristic acid, and stearic acid. *J Am Coll Toxicol.* 1987;6(3):321-401.
3. Cosmetic Ingredient Review. Safety assessment of glyceryl dilaurate, glyceryl diarachidate, glyceryl dibehenate, glyceryl dierucate, glyceryl dihydroxystearate, glyceryl diisopalmitate, glyceryl diisostearate, glyceryl dilinoleate, glyceryl dimyristate, glyceryl dioleate, glyceryl diricinoleate, glyceryldipalmitate, glyceryl dipalmitoleate, glyceryl distearate, glyceryl palmitate lactate, glyceryl stearate citrate, glyceryl stearate lactate, and glyceryl stearate succinate. Washington, DC: Author; 2005.
4. Elder RL. Final report on the safety assessment of cetearyl alcohol, cetyl alcohol, isostearyl alcohol, myristyl alcohol, and behenyl alcohol. *J Am Coll Toxicol.* 1988;7:359-413.
5. Cosmetic Ingredient Review Cetearyl alcohol, cetyl alcohol, isostearyl alcohol, myristyl alcohol, and behenyl alcohol. Washington, DC: Author; 2006.
6. Andersen FA. Annual review of cosmetic ingredient safety assessments–2002/2003. *Int J Toxicol.* 2005;24(S2):89-98.
7. Final report of the amended safety assessment of glyceryl laurate, glyceryl laurate SE, glyceryl laurate/oleate, glyceryl adipate, glyceryl alginate, glyceryl arachidate, glyceryl arachidonate, glyceryl behenate, glyceryl caprylate, glyceryl caprylate, clyceryl caprylate/caprate, glyceryl citrate/lactate/linoleate/oleate, glyceryl cocoate, glyceryl collagenate, glyceryl erucate, glyceryl hydrogenated rosinate, glyceryl hydrogenated soyate, glyceryl hydroxystearate, glyceryl isopalmitate, glyceryl isostearate, glyceryl isostearate/myristate, glyceryl isostearates, glyceryl lanolate, glyceryl linoleate, glyceryl linoleate, glyceryl montanate, glyceryl myristate, glyceryl isotridecanoate/stearate/adipate, glyceryl oleate SE, glyceryl oleate/elaidate, glyceryl palmitate, glyceryl palmitate/stearate, glyceryl palmitoleate, glyceryl pentadecanoate, glyceryl polyacrylate, glyceryl rosinate, glyceryl sesqioleate, glyceryl/sorbitol/oleate/hydroxystearate, glyceryl stearate/acetate, glyceryl stearate/maleate, glyceryl tallowate, glyceryl thiopropionate and glyceryl undecylenate. *Int J Toxicol.* 2004;23(suppl 2):55-94.
8. Elder RL. Final report on the safety assessment of myristyl myristate and isopropyl myristate. *J Am Coll Toxicol.* 1982;4:5-80.
9. Elder RL. Final report on the safety assessment of Cetearyl Alcohol, Cetyl Alcohol, Isostearyl Alcohol, Myristyl Alcohol, and Behenyl Alcohol. *J Am Coll Toxicol.* 1988;7(3):359-413.
10. Lanigan S. Final report on the safety assessment of methyl alcohol. *Int J Toxicol.* 2001;20(suppl 1):57-85.
11. Andersen FA. Annual Review of Cosmetic Ingredient Safety Assessments–2004/2005. *Int J Toxicol.* 2006;25(S2):73-78.
12. Elder RL. Final report on the safety assessment of Stearyl Alcohol, Oleyl Alcohol, and Octyl Dodecanol. J *Am Coll Toxicol.* 1985;4(5):1-29.
13. Johnson W Sr. Final report on the safety assessment of propylene glycol (PG) dicaprylate, PG dicaprylate/dicaprate, PG dicocoate, PG dipelargonate, PG isostearate, PG laurate, PG myristate, PG oleate, PG oleate SE, PG dioleate, PG dicaprate, PG diisostearate, and PG dilaurate. *Int J Toxicol.* 1999;18(2):35-52.
14. Gottschalck T, Bailey JE. *International Cosmetic Ingredient Dictionary and Handbook 2.* Washington: CTFA 2008.
15. International Cosmetic Ingredient Dictionary and Handbook. 12th ed. Washington, DC: CTFA; 2008.
16. Food Chemicals Codex. 3rd ed. Washington, DC: National Academy Press; 1981.
17. Fassett DW, Irish DD. *Industrial Hygiene and Toxicology.* New York, NY: Interscience Publishers; 1963:2:(2).
18. Windholz M, Budavari S, Blumetti RF, Otterbein ES, eds. *The Merck Index.* Rahway, NJ: Merck and Co; 1983:10.
19. Weast RC. *CRC Handbook of Chemistry and Physics.* Boca Raton, FL: CRC Press; 1982:63.
20. Swern D, ed. *Bailey's Industrial Oil and Fat Products.* New York, NY: John Wiley; 1979:4(1).
21. Gattefossé. *Data sheet.* MOD Unpublished data submitted by the Council, 2008.

22. CTFA. Myristates: summary of unpublished safety data. Unpublished data submitted by CTFA, 1979.
23. CTFA. CTFA cosmetic ingredient chemical description. Lauric acid. Unpublished data submitted by CTFA, 1979.
24. Estrin NF, Haynes CR, Whelan JM, eds. CTFA *Compendium of Cosmetic ingredient Composition. Specifications/Spectra.* Washington, DC: CTFA; 1982.
25. Cosmetic, Toiletries and Fragrance Association. Cosmetic ingredient chemical description: Myristic acid. Unpublished data submitted by CTFA, 1979.
26. Chemline. Online database.Chemical Abstract Society, 1988.
27. Lewis Sr RJ, ed. *Hawley's Condensed Chemical Dictionary.* New York, NY: John Wiley; 1997:13.
28. Nikko Chemicals Co, Ltd. Specification NIKKOL ICR-R (isocetyl myristate). Unpublished data submitted by the Council, 2007.
29. British Pharmaceutical Codex. London, England: The Pharmaceutical Press; 1973.
30. Windholz M, ed. *The Merck Index.* Rahway, NJ: Merck and Co; 1976:9.
31. Wade A, ed. Martindale: *The Extra Pharmacopoeia.* London, England: Pharmaceutical Press; 1977:27.
32. Nikko Chemicals Co, Ltd. Specification NIKKOL ODM-100 (Octyldodecetyl myristate). Unpublished data submitted by the Council, 2007.
33. Nikko Chemicals Co, Ltd. Specification NIKKOL potassium myristate MK-140. Unpublished data submitted by the Council, 2007.
34. Danisco Ingredients. UV-spectra for glycerol monoesters. Unpublished data submitted by CTFA, 1999.
35. CTFA. Myristates: Summary of unpublished data. (31.5a). Unpublished data submitted by CTFA, 1979.
36. Hawley CC, ed. *Condensed Chemical Dictionary.* 9th ed. New York, NY: Van Nostrand Reinhold Co; 1977:10.
37. Nikko Chemicals Co, Ltd. Manufacturing process NIKKOL ICM-R (isocetyl myristate). Unpublished data submitted by the Council, 2008.
38. Cosmetic, Toiletries and Fragrance Association. Cosmetic ingredient chemical description. Isopropyl myristate. Unpublished data submitted by CTFA, 1979.
39. Cosmetic, Toiletries and Fragrance Association. Cosmetic ingredient chemical description. Myristyl myristate. Unpublished data submitted by CTFA, 1979.
40. Personal Care Products Council. Concentration of use—potential additions to the butyl myristate report. Unpublished data submitted by the Council, 2008.
41. Nikko Chemicals Co, Ltd. Manufacturing process NIKKOL ODM-100 (Octyldocetyl myristate). Unpublished data submitted by the Council, 2008.
42. Nikko Chemicals Co, Ltd. Manufacturing process NIKKOL potassium myristate MD-140, 2008.
43. Taiko Oil Chem. Col. Ltd. Manufacturing process MNK-40 (water, postassium cocoate and potassium myristate. Unpublished data submitted by the Council, 2008.
44. Hashimoto A, Hirotani A, Mukai K. Thin-layer chromatography of true wax 8. *Nippon Nogei Kagaku Kaishi.* 1967;41(4): 139-144.
45. Lefort D, Paquot C, Pourchez A. Gas chromatography and lipochemistry. VI. Comparison of the methyl, propyl, and isopropyl esters of fatty acids by gas chromatography. *Oleagineux.* 1962; 17:629-630.
46. Lutz DA, Eddy CR, Hunter JJ. X-ray diffraction study of some normal alkyl esters of long-chain acids. *Lipids.* 1967;2(3):204-207.
47. Horwitz W, ed. *Official Methods of Analysis of the Association of Official Analytical Chemists (AOAC).* 13th ed. Washington, DC: AOAC; 1980: 18.
48. Estrin NF, Haynes CR, Whelan JW. Cosmetic Ingredient Descriptions. CTFA Compedium of Cosmetic Ingredient Composition. Washington, DC: CTFA; 1982.
49. Senzel A, ed. Newburger's Manual of Cosmetic Analysis. Washington DC: AOAC; 1977:2.
50. Cosmetic, Toiletries and Fragrance Association. CTFA cosmetic ingredient chemical description. Myristic acid. Unpublished data submitted by CTFA, 1979.
51. Cosmetic, Toiletries and Fragrance Association. CTFA cosmetic ingredient chemical description. Palmitic acid. Unpublished data submitted by CTFA, 1979.
52. Cosmetic, Toiletries and Fragrance Association. CTFA cosmetic ingredient chemical description. Oleic acid. Unpublished data submitted by CTFA, 1979.
53. Cosmetic, Toiletries and Fragrance Association. CTFA cosmetic ingredient chemical description. Stearic acid. Unpublished data submitted by CTFA, 1979.
54. Takatori T, Terazawa K, Nakano K,. Matsumiya H. Identification of 10-hydroxy-12-octadecenoic acid in adipocere. *Forensic Sci Internat.* 1983;23(2-3):117-122.
55. Van de Vaart FJ, Hulshoff A, Indemans AWM. Analysis of creams. V. Application of thin-layer chromatography. Parts I and II. *Pharm Weekblad Sci.* 1983;5(3):109-118.
56. The characterization of long-chain fatty acids and their derivatrves by chromatography. In: Ciddings JC, Grushka E, Cazes J, Brown PR, eds. *Advances in Chromatography.* New York, NY: Marcel Dekker; 1980.
57. Smith RM. Recent advances in the high-performance liquid chromatography of fatty acids. *J Pharm Biomed Anal.* 1983;1(2): 143-151.
58. Davis DV, Cooks RG. Direct characterization of nutmeg constituents by mass spectrometry-mass spectrometry. *J Agric Food Chem.* 1982;30(3):495-504.
59. Shimasaki H, Ueta N. Fractionation of the neutral lipids of rice-bran oil by centrifugal liquid chromatography. *Agric Biol Chem.* 1983;47(2):327-329.
60. Cyong J, Okada H. Histochemical studies on fatty acid in lymphocyte-mediated immune reaction. *Immunology.* 1976; 30(5):763-767.
61. Bailey AV, Pittmann RA. Wide-line NMR spectra of some saturated and unsaturated long chain fatty acids. *J Am Oil Chem Soc.* 1971;48(12):775-777.
62. Arudi RI, Sutherland MW, Bielski BHJ. Purification of oleic acid and linoleic acid. *J Lipid Res.* 1983;24(4):485-488.
63. Cotte M, Dumas P, Besnard M, Tchoreloff P, Walter P. Synchrotron FT-IR microscopic study of chemical enhancers in

transdermal drug delivery: example of fatty acids. *J Control Release*. 2004;97(2):269-281.
64. Danisco Ingredients. Impurity analysis for glycerol monoesters. Unpublished data submitted by CTFA, 1999.
65. Danisco Ingredients "Impurity analysis" for glcerol monoesters. Unpublished data submitted by CTFA, 1999.
66. Estrin NF, ed. *CTFA Standards: cosmetic Ingredient Specifications, Isopropyl Myristate*. Washington DC: Cosmetic, Toiletry and Fragrance Association; 1974.
67. Spectrum Chemicals and Laboratory Products. Certificate of analysis: Methyl myristate. Unpublished data submitted by the Council, 2008:1 pages.
68. FDA. *Frequency of use of cosmetic ingredients*. FDA Database. Washington, DC: FDA; 2007.
69. Personal Care Products Council. Concentration of use - Potential additions to the butyl myristate report. Unpublished data submitted by the Council, 2008:7 pages.
70. Cosmetic, Toiletries and Fragrance Association. Concentration of use information for proposed additions to the December 2006 re-reviews. Unpublished data submitted by CTFA, 2006.
71. Personal Care Products Council. Concentration of use - Myristic acid. Unpublished data submitted by the Council, 2008:1 page.
72. Industrial hygiene. In: Willeke K, Baron PA, eds. *Aerosol Measurement. Principles, Techniques and Applications*. New York, NY: John Wiley; 1993.
73. Absorption of toxicants by the lungs. In: Klassen CD, ed. *Casarret and Doull's Toxicology: the Basic Science of Poisons*. New York, NY: McGraw-Hill; 2008.
74. Bower D. Unpublished information on hair spray particle sizes provided at the September 9, 1999, CIR Expert Panel meeting. 1999.
75. Johnsen MA. The Influence of Particle Size. *Spray Technol Mark*. 2004;(11): pp. 24-27.
76. In: Patty FA, ed. *Industrial Hygiene and Toxicology*. New York, NY: Interscience Publishers; 1963:2(2).
77. FDA. Food additives permitted for direct addition to food for human consumption: Fatty acids. *Code Federal Regulations*; 2008 21:100-101.
78. In: Hawley CC, ed. *The Condensed Chemical Dictionary*. 8th ed. New York, NY: Van Nostrand Reinhold Company; 1971.
79. FDA. Food additives permitted for direct addition to food for human consumption. *Code of Federal Regulations*. 2003. 172.515.
80. Gosselin RE, Hodge HC, Smith RP, Gleason MN. *Clinical Toxicology of Commercial Products; Acute Poisoning* 1. Baltimore, MD: Williams and Wilkins Co; 1976.
81. Rioux V, Galat A, Vinci G, Jan F, D'Andrea S, Legrand P. Exogenous myristic acid acylates proteins in cultrued rat hepatocytes. *J Nutr Biochem*. 2002;13(2):66-74.
82. Savary P, Constantin J. Intestinal hydrolysis and lymphatic absorption of isopropyl esters of long-chain fatty acids in the rat. *Biochim Biophys Acta*. 1970;218(2):195-200.
83. Savary P. Action of rat pancreatic juice and of purified pig pancreatic lipase upon the esters of short-chain aliphatic monoacids and long-chain primary monoalcohols. *Biochim Biophys Acta*. 1972;270:463-471.
84. Finkelstein P, Wulf RJ. Uptake, distribution, and excretion of a commercial aerosol antiperspirant by the monkey. *J Soc Cosmet Chem*. 1974;25:645-654.
85. Suzuki M, Asaba K, Komatsu H, Mochizuka M. Autoradiographic study on percutaneous absorption of several oils useful for cosmetics. *J Soc Cosmet Chem*. 1978;29:265-282.
86. Brinkmann I, Müller-Goymann CC. An attempt to clarify the influence of glycerol, propylene glycol, isopropyl myristate and a combination of propylene glycol and isopropyl myristate on human stratum corneum. *Pharmazie*. 2005;60(3):215-220.
87. Christy MNA, Bellantone RA, Taft DR, Plakogannis RM. In vitro evaluation of the release of albuterol sulfate from polymer gels: effect of fatty acids on drug transport across biological membranes. *Drug Dev Ind Pharm*. 2002;28(10): 1221-1229.
88. Gwak HS, Kin SU, Chun IK. Effect of vehicles and enhancers on the in vitro permeation of melatonin through hairless mouse skin 6. *Arch Pharm Res*. 2002;25(3):392-396.
89. Gondaliya D, Pundarikakshudu K. Studies in formulation and phamacotechnical evaluation of controlled release transdermal delivery system of bupropion. *AAPS Pharm Sci Tech*. 2003; 4(1):E3.
90. Mittal A, Sara UVS, Ali A, Aqil M. The effect of penetration enhancers on permeation kinetics of nitrendipine in two different skin models. *Biol Pharm Bull*. 2008;31(9):1766-1772.
91. Merino V, Mico-Alinana T, Nacher A, Diez-Sales O, Herraez M, Merino-Sanjuan M. Enhancement of nortriptyline penetration through human peidermis: influence of chemical enhancers and iontophoresis. *Pharm Pharmacol*. 2008;60(4): 415-420.
92. Limpongsa E, Umprayn K. Preparation and evaluation of diltiazem hydrochloride diffuion-controlled transdermal delivery system. *AAPS Pharm Sci.Tech*. 2008;9(2):464-470.
93. Furuishi T, Io T, Fukami T, Suzuki T, Tomono K. Formulation and in vitro evaluation of pentazocine transdermal delivery system. *Biol Pharm Bull*. 2008;31(7):1439-1443.
94. El Maghraby GM, Alanazi FK, Alsarra IA. Transdermal delivery of tadalafil. I. Effect of vehicles on skin permeation. *Drug Dev.Ind.Pharm*. 2009;35(3):329-336.
95. Bounoure F, Skiba ML, Besnard M, Arnaud P, Mallet E, Skiba M. Effect of iontophoresis and penetration enhancers on transdermal absorption of metopimazine. *J Dermatol Sci*. 2008;52(3): 170-177.
96. Ambade KW, Jadhav SL, Gambhire MN, Kurmi SD, Kadam VJ, Jadhav KR. Formulation and evaluation of flurbiprofen microemulsion. *Curr Drug Deliv*. 2008;5(1):32-41.
97. Osama H, Narumiya S, Hayaishi W, Iinuma H, Takeuchi T, Umezawa H. Inhibition of brain prostaglandin D synthetase and prostaglandin D2 dehydrogenase by some saturated and unsaturated fatty acids. *Biochem Biophys Acta*. 1983;752(2): 251-258.
98. Takeara R, Jimenez PC, Wilke DV, et al. Antileukemic effects of Didemnum psammatodes (Tunicata: Ascidiacea) constituents. *Comp Biochem Physiol A Mol Integr Physiol*. 2008;151:(3): 363-369.

99. Laboratoire de Recherche et d'Experimentation. Attestation of biological test. Unpublished data submitted by CTFA, 1994:.
100. Food and Drug Research Laboratories Inc. Report to RIFM. 5-21-1976.
101. CTFA. 1978. Acute Dermal Toxicity in Rabbits. (31.5b. p. 35). Unpublished data submitted by CTFA.
102. Motoyoshi K. Enhanced comedo formation in rabbit ear skin by sqalene and oleic acid peroxides. *Br J Dermatol.* 1983;109: 191-198.
103. Fulton JE, Pay SR. Comedogenicity of current therapeiutic products, cosmetics, and ingredients in the rabbit ear. *J Am Acad Dermatol.* 1984;10:96-105.
104. Tucker SB, Flanigan SA, Dunbar M, Drotman RB. Development of an objective comedogenicity assay. *Arch Dermatol.* 1986; 122:660-665.
105. Nguyen SH, Dang TP, Maibach HI. Comedogenicity in rabbit: some cosmetic ingredients/vehicles. *Cutaneous Ocular Toxicol.* 2007;26:287-292.
106. Blevins RD, Taylor DE. Mutagenicity screening of twenty-five cosmetic ingredients with the Salmonella/microsome test. *J Environ Sci Health Part A.* 1982;17:(2):214-239.
107. Kligman AM. Report to RIFM dated June 1, 1976. Unpublished data submitted by RIFM, 1976:2 pages.
108. Research Institute for Fragrance Materials. Ethyl myristate. *Food and Chem Toxicol.* 1978;16:(4):745-746.
109. Uter W, Schnuch A, Heier J, Lessmann H. Isopropyl myristate recommended for aimed rather than routine patch testing. *Contact Dermatitis.* 2004;50:242-244.
110. Bharati A, King CM. Allergic contact dermatitis from isohexadecane and isopropyl myristate. *Contact Dermatitis.* 2004; 50(256):257.

9

Final Report of the Safety Assessment of Lithium Stearate, Aluminum Distearate, Aluminum Stearate, Aluminum Tristearate, Ammonium Stearate, Calcium Stearate, Magnesium Stearate, Potassium Stearate, Sodium Stearate, and Zinc Stearate

The commercial grade of stearic acid used in cosmetics contains fatty acids that range from C_{18} (stearic) and C_{22} (behenic). The concentrations of these ingredients used in cosmetic products vary from $\leq$ 0.1 to $>$ 50%. Acute oral studies with rats indicated that the Stearates are practically nontoxic, and have a low potential for acute dermal toxicity. Skin irritation studies with rabbits demonstrated that Stearates are only minimal to slight irritants at high concentrations. Pharmaceutical vehicles containing 5.5% Magnesium Stearate were neither teratogenic nor mutagenic. In a limited study, Stearate did not increase bladder tumor incidence.

Seven out of 20 subjects exhibited minimal to mild skin erythema when tested with an aqueous solution of 1.5% Ammonium Stearate. Similar results were obtained with Sodium Stearate at 0.5 percent. In a 21-day patch test with 10 subjects, an aqueous formulation containing 0.1–0.25% Sodium Stearate caused minimal skin irritation. No sensitization was reported in 100 subjects tested with the same formulation.

On the basis of the available information presented in this report, and as qualified in the summary, it is concluded that the Stearate compounds described herein are safe as cosmetic ingredients.

CHEMICAL AND PHYSICAL PROPERTIES

The Stearates reviewed in this report are salts of stearic acid. The commercial stearic acid from which these ingredients are manufactured is a mixture of monocarboxylic acids obtained from a number of animal and vegetable fats; it contains fatty acids that range from C_{12} (lauric) to C_{22} (behenic), and the major components are C_{18} (stearic) and C_{16} (palmitic) acids. The composition of the commercial product depends primarily upon the origin of the fat. Table 1 presents the structural formulas for the 10 Stearate ingredients and stearic acid.[1-4]

The Stearates can be divided into metallic and nonmetallic groups. The metallic Stearates may be further divided into water soluble and water insoluble groups; while the former include both Potassium Stearate and Sodium Stearate, the latter include Aluminum Distearate, Aluminum Stearate, Aluminum Tristearate, Calcium Stearate, Lithium Stearate, Magnesium Stearate, and Zinc Stearate. Ammonium Stearate is non-metallic and slightly soluble in water.[1,2]

Chemical and physical properties for the individual Stearate ingredients are discussed below; additional properties are presented in Table 2.

Aluminum Distearate: Aluminum Distearate is a white to off-white fine powder with a bland fatty odor. It is soluble in hot aromatic and aliphatic hydrocarbons, and is insoluble in water, alcohol, and ether.[5,6] As determined by thermogravimetric analysis, its melting point is 120 °C with endothermic and exothermic maxima of 198 °C and 170 °C, respectively.[7] The melting point has also been reported as 145 °C[6] and 135 °–160 °C.[8]

Aluminum Stearate: Aluminum Stearate is a fine white to yellow-white, bulky powder, with a faint characteristic odor. It is insoluble in water, alcohol, and ether.[8,9]

Aluminum Tristearate: Aluminum Tristearate is a white powder soluble in alkali and petroleum, and practically insoluble in water. When freshly made, it is soluble in alcohol, benzene, oil of turpentine, and mineral oils. It forms gels with aliphatic and aromatic hydrocarbons.[6,10,11]

Ammonium Stearate: Ammonium Stearate is a white to yellowish powder free of ammonia odor. The compound gradually loses NH_3 on exposure to air,

TABLE 1. Structure.[a]

Ingredient	*Structural formula*	*Commercial product*[b]
Aluminum Distearate	$Al(OH)[OOC(CH_2)_{16}CH_3]_2$	$Al(OH)(RCOO)_2$
Aluminum Stearate	$Al(OH)_2OOC(CH_2)_{16}CH_3$	$Al(OH)_2(RCOO)$
Aluminum Tristearate	$Al[OOC(CH_2)_{16}CH_3]_3$	$Al(OH)(RCOO)_3$
Ammonium Stearate	$CH_3(CH_2)_{16}COONH_4$	–
Calcium Stearate	$[CH_3(CH_2)_{16}COO]_2Ca$	$(RCOO)_2Ca$
Lithium Stearate	$CH_3(CH_2)_{16}COOLi$	RCOOLi
Magnesium Stearate	$[CH_3(CH_2)_{16}COO]_2Mg$	$(RCOO)_2Mg$
Potassium Stearate	$CH_3(CH_2)_{16}COOK$	RCOOK
Sodium Stearate	$CH_3(CH_2)_{16}COONa$	RCOONa
Zinc Stearate	$Zn[OOC(CH_2)_{16}CH_3]_2$	$(RCOO)_2Zn$
Stearic Acid	$CH_3(CH_2)_{16}COOH$	–

[a]Data from Refs. 1–4.

[b]In the commercial product, R is a mixture of fatty acids containing predominantly stearic (C_{18}) and palmitic (C_{16}) acids, and lesser amounts of other fatty acids.

TABLE 2. Chemical and Physical Properties.

Ingredient	*Properties*	*Reported value*	*Ref.*
Aluminum Distearate $Al(OH)(C_{18}H_{35}O_2)_2$	Molecular weight	610	
	Melting point	120°C	7
		145°C	6
		135°C	8
	Specific gravity	1.009	6,8
	Separated fatty acids		
	Acid value	198.0–202.0	5
	Titer	54.0–58.0°C	5
	Screen test	20.0% max.	5
	Iodine value on separated fatty acids	2.0 max.	4
Aluminum Stearate $Al(OH)_2(C_{18}H_{35}O_2)$	Molecular weight	344	
	Melting point	173°C	8
	Specific gravity	1.010	8
	Iodine value on separated fatty acids	2.0 max.	4
	Fatty acid titer	53.6°C	8
	Iodine value	2.10	8
Aluminum Tristearate $Al(C_{18}H_{35}O_2)_3$	Percentage composition	C = 73.92%, H = 12.06%, O = 10.94%, Al = 3.08%	10
	Molecular weight	877.35	10
	Melting point	103°C	11
		113°C	8
		115°C	6
		117°–120°C	10
	Specific gravity	1.010	8,11
	Fatty acid titer	52.6°C	8
	Iodine value	5.2	8
Ammonium Stearate $CH_3(CH_2)_{16}COONH_4$	Percentage composition	C = 71.70%, H = 13.04%, N = 4.65%, O = 10.61%	4
	Molecular weight	301.5	4
	Melting point	87°C	8
		73°–75°C	6
	Specific gravity	0.89 (22°C)	6
	pH (3% dispersion)	7.6	6
	Neutralization value	70–80	6
Calcium Stearate $Ca(C_{18}H_{35}O_2)_2$	Percentage composition	C = 71.23%, H = 11.62%, Ca = 6.60%, O = 10.54%	10
	Molecular weight	607.00	10,11
	Melting point	129°C	7
		147–149°C	10
		179–180°C	6,11
	Iodine value on separated fatty acids	3.5 max.	4
	Loss on drying	3.5% max.	13
Lithium Stearate $LiC_{18}H_{35}O_2$	Molecular weight	290.41	11
	Melting point	108°C	7
		220°–221°C	6,8,11
	Specific gravity	1.025	16
Magnesium Stearate $Mg(C_{18}H_{35}O_2)_2$	Percentage composition	C = 73.13%, H = 11.93%, Mg = 4.11%, O = 10.82%	10
	Molecular weight	591.27	10,11
	Melting point	86°–88°C	11
		88.5°C (pure)	6

TABLE 2. (Continued.)

Ingredient	*Properties*	*Reported value*	*Ref.*
		115°C	7
		132°C (technical)	6
	Specific gravity	1.028	6
	Iodine value on separated fatty acids	2.0 max.	4
	Loss on drying	5.0 max.	13
Potassium Stearate $C_{17}H_{35}COOK$	Molecular weight	322.58	11
Sodium Stearate $NaOOC_{17}H_{35}$	Molecular weight	306.47	11
	Iodine value of fatty acids	"not more than 4"	9,17
	Acid value of 1 g of fatty acids	196–211	9,17
Zinc Stearate $Zn(C_{18}H_{35}O_2)_2$	Percentage composition	C = 68.38%, H = 11.16%, O = 10.12%, Zn = 10.34%	10
	Molecular weight	632.33	10,11
	Melting point	120°C	10
		126°C	8
		130°C (pure)	6,11
		132°C	7
	Specific gravity	1.095	6,8
	Iodine value on separated fatty acids	2.5 max.	4
	Loss on drying	0.5% max.	4

and it softens at 2–7 °C. At 27 °C, it is soluble in methanol and ethanol; slightly soluble in water, benzene, xylene and naphtha; and practically insoluble in acetone and carbon tetrachloride. It is soluble in water at 100 °C; in acetone at 57 °C; in ethanol at 78 °C; in methanol at 65 °C; in benzene at 80 °C; in carbon tetrachloride at 77 °C; in xylene at 82 °C; and in naphtha at 71 °C.[8,10] The dry material begins to decompose at 50 °C.[12]

Calcium Stearate: Calcium Stearate is a granular fatty powder soluble in hot pyridine; slightly soluble in hot alcohol, hot vegetable and mineral oils; and practically insoluble in water, ether, chloroform, acetone, and cold alcohol. The commercial preparation, which contains some palmitate salt, is a fine, white bulky powder.[10,13-15] Its melting point as determined by thermogravimetric analysis is 129 °C with endothermic and exothermic maxima of 177 °C and 162.5 °C, respectively.[7] The melting point, as determined by gradient bar, is 147 °–149 °C.[10] It has also been reported that Calcium Stearate melts at 179 °–180 °C.[6,11]

Lithium Stearate: Lithium Stearate is a white crystalline material insoluble in cold or hot water, alcohol, and ethyl acetate. It forms gels with mineral oils.[6] The melting point as determined by thermogravimetric analysis is 108 °C with endothermic and exothermic maxima of 184 °C and 202.5 °C, respectively.[7] The melting point of Lithium Stearate has also been reported as 220 °–221 °C.[6,8,11]

Magnesium Stearate: Magnesium Stearate is a fine, unctuous, white powder with a faint, characteristic odor. It is insoluble in water, alcohol, and ether, and decomposes in dilute acids. The commercial product is a combination of variable proportions of Magnesium Stearate and magnesium palmitate. The

melting point as determined by thermogravimetric analysis is 115 °C. One source reports that the melting point of the pure salt is 88.5 °C, and that the melting point of the technical grade (which may contain small amounts of the oleate salt and 7% magnesium oxide) is 132 °C. Magnesium Stearate has also been reported to melt at 86 °–88 °C.[3,6-10,15]

Potassium Stearate: Potassium Stearate is a white crystalline powder which has a slight fatty odor. It is slowly soluble in cold water, and readily soluble in hot water, alcohol, ether, chloroform, and carbon disulfide. While the aqueous solution is strongly alkaline to litmus or phenolphthalein, the alcoholic solution is only slightly alkaline to phenolphthalein. The commercial product contains a "considerable proportion" of palmitic salt.[6,10,11]

Sodium Stearate: Sodium Stearate is a white powder with a slight tallow-like odor and soapy feel. While it is slowly soluble in cold water or cold alcohol, this salt is freely soluble in hot solvents. In many organic solvents, it is insoluble. As a result of hydrolysis, the aqueous solution is strongly alkaline. The alcohol solution is practically neutral.[5,9-11,17]

Zinc Stearate: Zinc Stearate is a fine, white, hydrophobic powder which has a faint, characteristic odor. It is soluble in benzene, acids, and common solvents and insoluble in water, alcohol, and ether. Zinc Stearate is decomposed by dilute acids and is neutral to moist litmus paper. One hundred percent of the material will pass through a 325 sieve.[6,8-11,13] The melting point as determined by thermogravimetric analysis is 132 °C with an exothermic maximum of 197 °C.[7] The melting point of this Stearate has also been reported as 126 °C[8] and as 130 °C.[6,11]

Reactivity

No information was reported on the chemical reactivity of these ingredients. The low iodine number of stearates indicates a small amount of unsaturated fatty acids; therefore these ingredients would not be expected to undergo significant autoxidation.[13]

Analytical Methods

Analytical methods for the determination of several Stearate compounds and stearic acid are presented below. No information was reported for Aluminum Distearate, Aluminum Tristearate, Ammonium Stearate, or Potassium Stearate.

Stearic Acid: Stearic acid can be separated from these salts by acidification and solvent extraction, and then analyzed by gas chromatography with a flame-ionization detector.[9]

Aluminum Stearate: The United States Pharmacopeia XIX method for identifying Aluminum Stearate requires acid hydrolysis to separate the fatty acids. The quantitative tests for aluminum acetate solutions require acidification and addition of ethylenediamine–tetraacetate, followed by titration with zinc sulfate.[9].

Calcium Stearate: The method for identifying Calcium Stearate reported by *The National Formulary XIV*[14] and *The Food Chemicals Codex II*[15] is the same as that for identifying Aluminum Stearate (discussed above), except insofar as the specific qualitative and quantitative tests for calcium are concerned.

An IR spectrophotometric method was described for the quantitative determination of ≥ 0.5% by weight Calcium Stearate in butyl rubber. The procedure has a relative error of 10%.[18]

A method using flame photometry has been described to determine Calcium Stearate in structural plastics.[19]

Lithium Stearate: Norwitz and Gordon[20,21] described a method for determining Lithium Stearate in sebacate-base semifluid lubricants. The sample is treated with dilute hydrochloric acid and extracted with ethyl ether to remove diisopropyl phosphite. The aqueous extract is then evaporated with perchloric acid, and the lithium determined by atomic absorption.

Magnesium Stearate: The *U.S. Pharmacopeia XIX*[9] and *The Food Chemicals Codex II*[15] report the same tests for Magnesium Stearate as those described above for Aluminum Stearate, except insofar as the specific qualitative and quantitative tests for magnesium are concerned. It is possible to quantify magnesium in an ammonia–ammonium chloride buffer by titrating with disodium ethylenediamine-tetraacetate.

Sodium Stearate: The National Formulary XIII[17] and the *U.S. Pharmacopeia XIX*[9] report a test for qualitatively identifying the stearate portion by means of acid hydrolysis, and a determination of the melting point of the liberated fatty acids. No quantitative tests were found for Sodium Stearate.

Zinc Stearate: The qualitative analytical tests for Zinc Stearate included in the *U.S. Pharmacopeia XIX*[9] are the same as those given for Aluminum Stearate. The zinc content of a fatty acid salt can be quantitatively measured by hydrolysis with 0.1 N sulfuric acid; the fatty acid then is removed by solvent extraction, and the excess sulfuric acid titrated with 0.1 N sodium hydroxide.

A method was reported for determining fatty acids of Zinc Stearate, that involved extraction with acetone, evaporation of the acetone, addition of ethyl alcohol, and titration with 0.05 N KOH. Water-soluble salts were determined as NaCl by extraction with boiling H_2O, passage of the material through a cation-exchange column, and titration with NaOH in the presence of Tashiro's reagent. The moisture content was determined by weighing the material followed by drying at 80 °C to constant weight. The amount of Zinc Stearate was calculated by the difference.[22]

Method of Manufacture and Impurities

The water-soluble metallic stearates are usually manufactured by reacting a selected grade of commercial stearic acid with a strong caustic (either potassium or sodium hydroxide) in an aqueous system, and producing the respective potassium and sodium soap in solution. The solvent is then evaporated off and the solid product milled to a suitable particle size.[1,2]

The insoluble metallic stearates are produced by reacting a selected grade of stearic acid with a caustic (usually sodium hydroxide) in an aqueous system. This produces a solution containing the soluble sodium salt of stearic acid. The insoluble metallic stearate precipitates out when a solution containing the desired metal is added to the sodium stearate solution. The insoluble stearate is then washed free of the water-soluble impurities, dried, milled, and packaged. The packaged compounds are fine, white, fluffy powders with slight fatty odors; the size of particles generally ranges between 0.25 and 10 microns.[1,2]

The method of manufacture and the known impurities for each of the *individual* stearate ingredients are presented below. The manufacturing processes just described and those that follow are not the only ones in use; rather, these are given here as representative examples of major production methods.[1]

Aluminum Distearate: Aluminum Distearate is produced by the reaction of water-soluble aluminum salt and sodium stearate in aqueous media. The precipitate is then filtered, washed, and dried.[4]

The following impurities have been reported:[4,5]

Assay (as Al_2O_3)	8.0–12.0%
Free Fatty Acids (predominantly a mixture of C_{18} and C_{16} fatty acids with minor amounts of other fatty acids)	8.0% max.
Moisture	3.5% max.
Heavy Metals (calculated as Pb)	50 ppm max.
Total Ash	11.5–13.5%
Washed Ash	8.0–10.0%
Soluble Ash (water-soluble salts)	3.5% max.

Aluminum Stearate: Aluminum Stearate is produced by the reaction of sodium stearate and water-soluble aluminum salt in aqueous media. The precipitate is then filtered and dried.[4]

The following impurities have been reported:[4,8]

Assay (as Al_2O_3)	13–17%
Free Fatty Acids (predominantly a mixture of C_{18} and C_{16} fatty acids with minor amounts of other fatty acids)	6.0 percent max.
Moisture	3.5%
Heavy Metals (calculated as Pb)	50 ppm max.
Total Ash	12.6%
Water-soluble Salts	0.5%

Aluminum Tristearate: Aluminum Tristearate is produced by the reaction of water-soluble aluminum salt and sodium stearate in aqueous media. The precipitate is then filtered, washed and dried.[4]

The following impurities have been reported:[4,8]

Assay (as Al_2O_3)	4–8.0 percent max.
Free Fatty Acids (predominantly a mixture of C_{18} and C_{16} fatty acids with minor amounts of other fatty acids)	35 percent max.
Moisture	3.5 percent max.
Heavy Metals (calculated as Pb)	10 ppm max.
Total Ash	5.7 percent
Water-soluble Salts	0.1 percent

Ammonium Stearate: To prepare Ammonium Stearate, stearic acid can be treated with excess 28–30% NH_3 solution. Ammonium Stearate can also be prepared by reacting stearic acid with ammonium carbonate.[1,2,10]

Calcium Stearate: Calcium Stearate is produced by the reaction of water-soluble calcium salt and sodium stearate. The precipitate is then filtered, washed, and dried.[4]

$$CaX_2 + 2(C_{17}H_{35}COONa) \xrightarrow{H_2O} Ca(C_{17}H_{35}COO)_2\downarrow + 2NaX$$

(assuming X is monovalent).

The following impurities have been reported:[4,9]

Assay (as CaO)	7–11%
Free Fatty Acids (predominantly a mixture of C_{18} and C_{16} fatty acids with minor amounts of other fatty acids)	3.5% max.

Composition of Free Fatty Acids:

C_{12}	0.5% max.
C_{14}	10.5% max.
C_{15}	1.5% max.
C_{16}	22.0–35.0%
C_{18}	56.0–71.0%
$C_{18:1}$	2.5% max.
$C_{16} + C_{17} + C_{18}$	90.0% max.
C_{20}	1.0% max.
Moisture	4.0% max.
Arsenic (as As)	3 ppm max.
Lead (as Pb)	10 ppm max.

Lithium Stearate: Lithium Stearate is the reaction product of lithium hydroxide and stearic acid in aqueous media.[4]

$$LiOH + C_{17}H_{35}COOH \xrightarrow{H_2O} (C_{17}H_{35}COO)Li + H_2O$$

The following impurities have been reported:[4]

Free Fatty Acids (predominantly a mixture of C_{18} and C_{16} fatty acids with minor amounts of other fatty acids)	3.5% max.
Moisture	2.0% max.

Magnesium Stearate: Magnesium Stearate is produced by the reaction of water-soluble magnesium salt and sodium stearate. The precipitate is then filtered, washed, and dried.[4]

$$MgX_2 + 2(C_{17}H_{35}COONa) \xrightarrow{H_2O} Mg(C_{17}H_{35}COO)_2\downarrow + 2NaX$$

(assuming X is monovalent).

The following impurities have been reported:[4,13]

Assay (as MgO)	6.4–8.0%
Free Fatty Acids (predominantly a mixture	3.5%

of C_{18} and C_{16} fatty acids with minor amounts of other fatty acids)	

Composition of Free Fatty Acids:

C_{12}	0.4%
$C_{14} + C_{15}$	6.2% max.
C_{16}	24.0–34.0%
C_{18}	58.0–71.0%
$C_{16} + C_{17} + C_{18}$	90.0% max.
C_{20}	4.0% max.
Moisture	5.0% max.
Arsenic (as As)	3 ppm max.
Lead (as Pb)	10 ppm max.

Potassium Stearate: Potassium Stearate is produced by the reaction of potassium hydroxide and stearic acid in aqueous media.[4]

$$KOH + C_{17}H_{35}COOH \xrightarrow{H_2O} C_{17}H_{35}COOK + H_2O$$

The following impurities have been reported:[4]

Free Fatty Acids (predominantly a mixture of C_{18} and C_{16} fatty acids with minor amounts of other fatty acids)	1.0% max.
Moisture	3.0% max.

Other sources report that the commercial product contains a considerable portion of palmitate salt.[6,10]

Sodium Stearate: Sodium Stearate is the reaction product of sodium hydroxide and stearic acid:[4]

$$NaOH + C_{17}H_{35}COOH \xrightarrow{H_2O} C_{17}H_{35}COONa + H_2O$$

The following impurities have been reported:[4]

Free Fatty Acids (predominantly a mixture of C_{18} and C_{16} fatty acids with minor amounts of other fatty acids)	1.3%
Moisture	3.0%

Zinc Stearate: Zinc Stearate is produced by the reaction of water-soluble zinc salt and sodium stearate. The precipitate is then filtered, washed, and dried.[4]

$$ZnX_2 + 2(C_{17}H_{35}COONa) \xrightarrow{H_2O} Zn(C_{17}H_{35}COO)_2\downarrow + 2NaX$$

(assuming X is monovalent).

The following impurities have been reported:[4,8,13]

Assay (as ZnO)	13.0–15.0%
Free Fatty Acids (predominantly a mixture of C_{18} and C_{16} fatty acids with minor amounts of other fatty acids)	0.2–2.0%

Composition of Free Fatty Acids:

C_n ($n \leq 12$)	0.2%
$C_{14} + C_{15}$	6.0% max.
C_{16}	26.0–32.0%
C_{18}	60.0–72.0%
$C_{16} + C_{17} + C_{18}$	91.0% min.
C_{20}	2.0% max.
Moisture	1.5% max.
Arsenic (as As)	3 ppm max.
Cadmium (as Cd)	15 ppm max.
Lead (as Pb)	10 ppm max.
Total Ash	15%
Water-Soluble Salts	0.2%

USE

Purpose in Cosmetics

Although the Stearates perform a number of functions in cosmetic formulations, they are principally used for their lubricating properties. The water-insoluble metallic stearates are widely employed because they are water repellent and adhesive in nature and have good "covering" properties.[1,2] The uses for each of the individual ingredients are discussed below.

Aluminum Distearate: Aluminum Distearate is used in toilet preparations as an emulsifier of water-in-oil and as an agent to increase the viscosity of oils. This compound forms a "medium" gel in oils.[8]

Aluminum Stearate: Aluminum Stearate is used for increasing the viscosity of oils, and for its ability to act as an emulsifier of water-in-oil; it forms a thick gel in oils.[8] In hair grooming products, 7–10% (by weight) Aluminum Stearate has been employed to impart a gel structure to heavy mineral oil. In hair straighteners, the compound functions as a water repellent.[23]

Aluminum Tristearate: Aluminum Tristearate is used in cosmetics for its ability to act as an emulsifier of water-in-oil solutions and for its capacity to increase the viscosity of oils. It forms a thin gel in oils.[8]

Ammonium Stearate: Ammonium Stearate is used as an alcoholic emulsifier in hand creams.[23]

Calcium Stearate: Calcium Stearate is used as an opacifying agent in shampoos and as a water-in-oil emulsifier in hair grooming products.[23]

Lithium Stearate: Lithium Stearate is used as a lubricant in baby powders. It imparts a high degree of water repellency and oil absorbency to the powder, and provides a long lasting film which reportedly prevents chafing and reduces the

possibility of irritation caused by wet diapers.[23] This compound is also used as an emulsifying agent.[6,8]

Magnesium Stearate: Magnesium Stearate is widely used because of its adhesive and waterproofing properties. In powders, it imparts a velvety smoothness to the skin and acts as a dry lubricant which prevents chafing and absorbs moisture. In face powders, it serves as a dry binder. In dentrifices, it functions as a stabilizer to prevent caking, crystal formation, grittiness, and "setting up" of toothpaste and powders. It is used as an opacifying agent in shampoos.[23]

Potassium Stearate: Potassium Stearate serves as an emulsifier in hand creams, and a Potassium Stearate-stearic acid combination serves as a vanishing base for deodorant creams.[23]

Sodium Stearate: Sodium Stearate is used in solid fragrances as a solidifying agent, in hand creams as an anionic emulsifier, and in shampoos as a soluble soap that provides both thickness and opacity.[23]

Zinc Stearate: Zinc Stearate is widely used for its adhesive and water repellent properties, as well as for its "smoothing" qualities. It has been used in baby toiletries and bath powders as a dry lubricant to absorb moisture and prevent chafing. While it acts as a lubricant and improves adhesion in pre-shave preparations, Zinc Stearate serves as an opacifying agent in cleansing creams and shampoos. In hair grooming products, it is used as a water-in-oil emulsifier. In deodorant creams, it functions as an absorbent; and in deodorant powders, it acts as a mild astringent and antiseptic. In face powders, this compound serves as a dry binding agent. When used in "excess", Stearates may create a blotchy effect; but, in "moderate" amounts (4–15%), they (in particular Zinc Stearate) contribute to the adherent qualities of face powder.[8,23]

Scope and Extent of Use in Cosmetics

Table 3 presents FDA product formulation data for each of the Stearate ingredients.[24] Limited product data reported by sources other than FDA are presented in Table 4.[2,6,10,23] Voluntary filing of product-formulation data with the FDA by cosmetic manufacturers and formulators conforms to the prescribed format of present concentration ranges and product categories as described in Title 21 Part 720.4 of the Code of Federal Regulations (21 CFR 720.4). Since certain cosmetic ingredients are supplied by the manufacturer at less than 100% concentration, the concentration reported by the cosmetic formulator may not necessarily reflect the true, effective concentration found in the finished product; the effective concentration in such a case would be a fraction of that reported to the FDA. The fact that data are only submitted within the framework of preset concentration ranges also provides the opportunity for overestimation of the actual concentration of an ingredient in a particular product. An entry at the lowest end of a concentration range is considered the same as one entered at the highest end of that range, thus introducing the possibility of a two- to ten-fold error in the assumed ingredient concentration.

Since there were no petitions requesting their use in 1976, Aluminum, Lithium, Magnesium and Zinc Stearates were deleted from the list of color additives permitted in cosmetics under the Federal Food, Drug and Cosmetic Act.[25]

The Stearates are applied to or come in contact with skin surfaces, eyes, mucous membranes, and respiratory epithelia (see Tables 3 and 4). Small amounts could be ingested in dentrifices and lipsticks.

TABLE 3. Product Formulation Data.[a]

Ingredient/ Cosmetic product type	Concentration (%)	No. of product formulations
Aluminum Distearate		
Eyeliner	>1–5	23
Mascara	>1–5	18
Hair bleaches	>1–5	2
Foundations	>0.1–1	3
Lipstick	>1–5	17
Makeup bases	>0.1–1	1
Cleansing (cold creams, cleansing lotions, liquids, and pads)	>0.1–1	2
Moisturizing	>0.1–1	1
	Total	67
Aluminum Stearate		
Bath oils, tablets, and salts	>1–5	1
Eyeliner	>1–5	14
Eyeshadow	>1–5	2
Eye makeup remover	>1–5	2
Mascara	>1–5	65
	>0.1–1	5
Other eye makeup preparations	>5–10	1
	>1–5	1
Tonics, dressings, and other hair grooming aids	>1–5	2
	>0.1–1	2
Hair bleaches	>1–5	1
Blushers (all types)	>1–5	1
	≤0.1	9
Lipstick	>1–5	1
	≤0.1	11
Makeup bases	>1–5	1
	≤0.1	19
Other personal cleanliness products	>0.1–1	1
	Total	139
Lithium Stearate		
Lipstick	>0.1–1	1
Makeup bases	≤0.1	20
Rouges	≤0.1	2
Makeup fixatives	≤0.1	1
Moisturizing	>0.1–1	2
Other skin care preparations	>0.1–1	1
	Total	98
Magnesium Stearate		
Lotions, oils, powders, and creams	>10–25	1
	>1–5	2
Other bath preparations	>1–5	1
Eyeliner	>5–10	2
Eyeshadow	>10–25	1
	>5–10	30
	>1–5	25
	>0.1–1	1
Mascara	>0.1–1	1
Other fragrance preparations	>0.1–1	4
Shampoos	>0.1–1	2
Blushers	>5–10	1
	>1–5	8

TABLE 3. (Continued.)

Ingredient/ Cosmetic product type	*Concentration (%)*	*No. of product formulations*
Face powders	>5–10	3
	>1–5	59
Foundations	>1–5	1
Makeup bases	>1–5	9
Rouges	>1–5	1
Feminine hygiene deodorants	>0.1–1	1
Other personal cleanliness products	≤0.1	4
Preshave lotions (all types)	>1–5	1
Cleansing (cold creams, cleansing lotions, liquids, and pads)	>1–5	1
Face, body, and hand (excluding shaving preparations)	>1–5	1
	>0.1–1	3
Other skin care preparations	>1–5	1
	>0.1–1	3
	Total	167
Potassium Stearate		
Face, body, and hand (excluding shaving preparations)	>10–25	1
	>0.1–1	1
Moisturizing	>1–5	1
	Total	3
Sodium Stearate		
Colognes and toilet waters	>10–25	1
	>5–10	9
	>1–5	1
Sachets	>5–10	1
Other fragrance preparations	>5–10	12
	>1–5	5
Hair conditioners	>1–5	1
Shampoos (noncoloring)	>10–25	1
	>5–10	6
	>1–5	1
	>0.1–1	1
Shampoos (coloring)	>1–5	1
Hair lighteners with color	>1–5	1
Hair bleaches	>10–25	3
	>1–5	1
Blushers (all types)	>5–10	7
	>1–5	1
Makeup bases	>10–25	2
Other makeup preparations	>5–10	1
Dentifrices (aerosol, liquid, pastes, and powders)	>0.1–1	1
Bath soaps and detergents	>1–5	5
Deodorants (underarm)	>5–10	35
	>1–5	3
Other personal cleanliness products	>5–10	4
Cleansing (cold creams, cleansing lotions, liquids, and pads)	>0.1–1	2
	≤0.1	1
Face, body, and hand (excluding shaving preparations)	>0.1–1	3

TABLE 3. (Continued.)

Ingredient/ Cosmetic product type	*Concentration (%)*	*No. of product formulations*
Moisturizing	>5–10	1
	>1–5	1
	>0.1–1	3
	≤0.1	1
Night cream	>0.1–1	1
Other skin care preparations	>0.1–1	1
Other suntan preparations	>5–10	1
	Total	119
Zinc Stearate		
Lotions, oils, powders and creams	>50	1
	>1–5	1
Bubble baths	>1–5	2
Eyebrow pencil	>10–25	1
	>5–10	11
	>1–5	7
Eyeliner	>10–25	6
	>5–10	8
	>1–5	21
	>0.1–1	1
	Total	59
Aluminum Tristearate		
Eye lotion	>5–10	1
	>0.1–1	6
Makeup bases	>1–5	1
	Total	8
Ammonium Stearate		
Hair straighteners	>5–10	2
Hair bleaches	>10–25	1
	Total	3
Calcium Stearate		
Eyebrow pencil	>25–50	12
Mascara	>1–5	1
	>0.1–1	2
Hair conditioners	>5–10	1
	>1–5	1
Other hair preparations	>0.1–1	1
Hair bleaches	>1–5	1
Face powders	>10–25	1
Other makeup preparations	>25–50	1
	>10–25	1
Cleansing (cold creams, cleansing lotions, liquids, and pads)	≤0.1	1
	Total	23
Lithium Stearate		
Eyeshadow	>1–5	9
	>0.1–1	2
	≤0.1	2
Powders (dusting and talcum) (excluding aftershave talc)	>1–5	6
	>0.1–1	22
Blushers (all types)	≤0.1	1
Face powders	>1–5	2
Foundations	>0.1–1	3
	≤0.1	24
Eyeshadow	>10–25	9
	>5–10	492

TABLE 3. (Continued.)

Ingredient/ Cosmetic product type	*Concentration (%)*	*No. of product formulations*
	>1–5	197
	>0.1–1	8
	≤0.1	1
Eye makeup remover	>1–5	1
Mascara	>1–5	12
	>0.1–1	1
Other eye makeup preparations	>10–25	5
	>5–10	10
	>1–5	4
	>0.1–1	2
Perfumes	>1–5	1
Powders (dusting and talcum)	>5–10	12
	>1–5	109
	>0.1–1	53
	≤0.1	4
Shampoos (noncoloring)	>1–5	1
	>0.1–1	2
Blushers (all types)	>10–25	1
	>5–10	46
	>1–5	45
	>0.1–1	15
Face powders	>10–25	3
	>5–10	99
	>1–5	123
Foundations	>5–10	3
	>1–5	16
	>0.1–1	1
Lipstick	>1–5	2
Makeup bases	>1–5	10
	≤0.1	1
Rouges	>10–25	5
	>5–10	1
	>1–5	8
	>0.1–1	2
	≤0.1	7
Other makeup preparations	>0.1–1	1
Deodorants (underarm)	>10–25	1
Feminine hygiene deodorants	>0.1–1	1
Other personal cleanliness products	>5–10	1
	>1–5	2
Men's talcum	>5–10	1
	>1–5	4
Preshave lotions (all types)	>1–5	1
Cleansing (cold creams, cleansing lotions, liquids, and pads)	>5–10	1
	>0.1–1	1
Face, body, and hand (excluding shaving preparations)	>10–25	1
	>5–10	2
	>1–5	3
Foot powders and sprays	>1–5	2
Moisturizing	>1–5	2
	≤0.1	1
Night cream	>10–25	1
	Total	1,397

[a]Data from Ref. 24.

TABLE 4. Product Data.[a]

Ingredient/ Cosmetic product type	*Concentration (%)*
Aluminum Stearate	
Hair straighteners	5–25
Hair bleaches	5–25
Vanishing creams	5–25
Ammonium Stearate	
Eyeliners	0.1–10
Mascaras	0.1–10
Lipsticks	0.1–10
Blushers	0.1–10
Makeup bases	0.1–10
Shaving creams	–
Vanishing creams	–
Calcium Stearate	
Eyebrow pencils	1–50
Mascaras	1–50
Other makeup preparations	1–50
Lithium Stearate	
Eyeshadows	0.1–5
Blushers	0.1–5
Foundations	0.1–5
Makeup bases	0.1–5
Dusting powders	–
Magnesium Stearate	
Eyeshadows	0.1–5
Dusting and talcum powders	0.1–5
Blushers	0.1–5
Makeup bases	0.1–5
Baby dusting powders	–
Cleansing creams	–
Foundations	–
Potassium Stearate	
Shaving preparations	–
Bath soaps	–
Sodium Stearate	
Shampoos	1.0–25
Underarm stick deodorants	1.0–10
Antiperspirants	1.0–10
Foundations	–
Bath soaps	–
Zinc Stearate	
Eyeliner	0.1–5
Eyeshadows	0.1–5
Eyebrow pencils	0.1–5
Dusting and talcum powders	0.1–5
Blushers	0.1–5
Mascaras	0.1–5
Face powders	0.1–5
Foundations	0.1–5

[a]Data from Refs. 2, 6, 10, and 23.

Product formulations containing one or more of these ingredients may be used from once a week up to several times a day. Many of the products may remain in contact with body surfaces for as briefly as a few minutes to as long as a few days (see Tables 3 and 4). Each product could potentially be applied hundreds of times over the course of several years.

Noncosmetic Uses

Aluminum Distearate: Aluminum Distearate is used as a thickener in paints, inks, and greases, and as a lubricant in plastics and ropes. It is also used in waterproofing fabrics and in producing cement.[6,8]

Aluminum Stearate: Aluminum Stearate is used in paint and varnish driers, and as a waterproofing agent in fabrics and ropes.[8] It is also a direct food additive for which regulations have been issued under the Food, Drug and Cosmetic Act (21 CFR 173.340, 172.863). In this last capacity, Aluminum Stearate functions as a binding, emulsifying, and anticaking agent. In the processing of beet sugar and yeast, it acts as a defoaming agent. No limits are established for the use of this ingredient as a food additive.[26]

Aluminum Tristearate: Aluminum Tristearate is used as a thickener in lubricating oils; as a cement additive, a lubricant, and a "flatting" agent; as a waterproofing agent for fabrics and ropes; and as an additive for chewing gums. It is also used in paint and varnish driers, greases, pharmaceuticals, and in light-sensitive photographic compositions.[6,8,10]

Ammonium Stearate: Ammonium Stearate is used as a waterproofing agent for concrete, cement, stucco, paper, and textiles.[6,8,10]

Calcium Stearate: Calcium Stearate is used for waterproofing fabrics, cements, stucco, and explosives. It is used as a releasing agent for plastic molding powders; a stabilizer for polyvinyl chloride resins; a tablet lubricant in pharmaceuticals; and as a flatting agent in paints. It is also used in pencils and wax crayons.[6,8,10,14]

Calcium Stearate is a direct food additive, for which regulations have been issued under the Food, Drug and Cosmetic Act (21 CFR 169.179, 173.340, 172.863, 573.280). In the processing of beet sugar and yeast, it functions as an antifoaming agent and may be used in accordance with good manufacturing practices. When used as an anticaking agent in vanilla powder, it is restricted to quantities of $\leq 2\%$ by weight. As long as good manufacturing processes are maintained, Calcium Stearate can be employed as an anticaking agent in animal feeds. This compound is also used as a food binder and emulsifer.[15,26]

Calcium Stearate's safety as a food ingredient has recently been reviewed. Concentrations in food range from 0.02% to 1.03%, with average daily intake possibly reaching as much as 38 mg for infants and up to 1500 mg for persons over two years. These are considered "generous estimates"; however, a more realistic estimate of daily intake may be close to 4 mg for people 2–65 years old.[27]

Lithium Stearate: Lithium Stearate is used as a high-temperature lubricant; a plasticizer, an emulsifier, a corrosion inhibitor in petroleum, a flatting agent in varnishes and lacquers, and a lubricant in powder metallurgy. It is also used in waxes and greases.[6,8]

Magnesium Stearate: Magnesium Stearate is used as a flatting agent, a drier in paints and varnishes, a lubricant in pharmaceutical tablets, and a stabilizer and lubricant for plastics.[6,8-10]

Magnesium Stearate is also a GRAS (Generally Recognized As Safe) substance and a direct food additive, for which regulations have been issued under the Food, Drug and Cosmetic Act (21 CFR 172.863, 173.340). It is used in foods as an anticaking agent, binder, emulsifier, stabilizer, and defoaming agent.[6,15,26]

Magnesium Stearate's safety as a food ingredient has recently been reviewed. Its use in food ranges from 0.01% to 1%, and the possible average daily intake

ranges from as much as 1 mg/kg for infants up to 41 mg/kg for persons over two years. These estimates are considered to be of maximum possible intakes; more realistically, a person is likely to take in close to 2.4 mg of Magnesium Stearate as a food additive.[28]

Potassium Stearate: Commonly known as a soap, Potassium Stearate is used in a wide range of household and industrial cleaning products.[1] It is also a direct food additive for which regulations have been issued under the Food, Drug and Cosmetic Act (21 CFR 172.863, 173.340, 172.615, 172.863). In this last capacity, Potassium Stearate functions as a binding, emulsifying, anticaking, or defoaming agent and must be used in accordance with good manufacturing practices.[26] The compound is also used as a water corrective[6] and as a component of chewing gum[26] and of textile softeners.[6,10]

Sodium Stearate: Sodium Stearate is used as a waterproofing and gelling agent, as a stabilizer in plastics, and as an emulsifying and stiffening agent in pharmaceuticals. It is used in the preparation of alcohol pencils for impetigenous dermatoses, in glycerol suppositories, and in toothpastes.[6,8,10] Classified as a soap, Sodium Stearate is used in a variety of household and industrial cleaning products.[1]

Sodium Stearate is also a direct food additive, for which regulations have been issued under the Food, Drug and Cosmetic Act (21 CFR 172.615, 172.863). As a food additive, it functions as a binder, emulsifier or anticaking agent and must be used in accordance with good manufacturing practices.[26]

Zinc Stearate: Zinc Stearate is used as a dry lubricant and dusting agent for rubber; a flatting and sanding agent in lacquers; a waterproofing agent for concrete, rock wool, paper and textiles; a plastic mold releasing agent; a heat and light stabilizer; an antifoamer; and a filler. It is used in powder metallurgy and in pharmaceutical tablets, ointments, and powders. This Stearate is a mild antiseptic and astringent, and it has been used as a local soothing application for inflammatory and irritating skin diseases. Zinc Stearate is also a GRAS food nutrient and/or supplement and is required by law to be free of chick edema factor.[6,8-10,26]

In addition to the *direct* food additive and GRAS status of a number of the ingredients just discussed, suitable grades of fatty acids and their aluminum, ammonium, calcium, magnesium, potassium, sodium, and zinc salts have various approvals for specific *indirect* food additive uses as well.[1]

BIOLOGICAL PROPERTIES

General Effects

Aluminum Stearates: Aluminum Distearate, Stearate, and Tristearate have astringent properties.[8]

Sodium Stearate: Sodium Stearate was added to Novikoff hepatoma cells in culture at concentrations of 0, 25, 50, 75, and 100 μg/ml of growth medium. At concentrations of 50 μg/ml and above, the compound caused a reduction in the rate of cell growth as well as a delay in the time taken to reach maximum cell numbers. The authors suggested that Sodium Stearate exerts its effect on the growth rate of heptoma cells either by acting as a detergent and causing lysis, or by coating the cell surface and thereby reducing the uptake of such essential nutrients as glucose.[29]

Cultures of rat heart muscle and endothelioid cells were treated for 30 minutes with Sodium Stearate in a free fatty acid/albumin ration of 6:1 at concentrations of 5×10^{-6}–$5 \times 10^{-4}M$. Sodium Stearate labilized rat heart muscle at $5 \times 10^{-6}M$. Both endothelioid and rat heart muscle cell mitochondria were significantly labilized by Sodium Stearate at $5 \times 10^{-5}M$.[30]

Sodium Stearate induced a significant increase in fibrinogen biosynthesis in vitro when introduced into the plasma sample of a "young normal subject" at a level of 0.118 microequiv./ml.[31]

Zinc Stearate: Zinc Stearate is reported to be a mild astringent and an antiseptic.[8,23]

Absorption, Metabolism, and Excretion

Calcium Stearate: The influence of bile and bile acid on the absorption of insoluble calcium salts in isolated dog intestine was studied. It was reported that Calcium Stearate "Seems to be slightly absorbed by the supplementation of some bile".[32]

Sodium Stearate: The rate of penetration of 0.5% Sodium Stearate in aqueous solution through human skin was determined to be 0.1 mg/100 ml/min.[33]

The distribution, metabolism, excretion, and storage of radiolabeled ^{14}C-Sodium Stearate were investigated as follows: three rats were injected subcutaneously and three intraperitoneally with 0.1 or 0.5 ml aqueous samples containing 0.18 mg ^{14}C-Sodium Stearate. Negligible amounts (0.1% of the 0.18 mg doses) of the ^{14}C appeared in the urine or feces. Expired CO_2 contained 38 ± 9%, and the carcass retained 56 ± 16% of the applied dose.[34]

Radiolabeled ^{14}C-Sodium Stearate was administered by stomach tube to rats at a dose of 10 μci 100 g of body weight. The animals were sacrificed thereafter at intervals of 1, 2, 4, or 24 hours and their livers were removed. Two phospholipids (phosphatidyl choline and phosphatidyl ethanolamine) of the isolated liver mitochondria had incorporated ^{14}C of the Sodium Stearate.[35]

The results of the studies on percutaneous absorption of radiolabeled ^{14}C-Sodium Stearate through isolated rat skin and human epidermis and in live rats are listed below.

In-Vitro Absorption–Rat Skin: A 0.25 ml sample containing 1.8 mg ^{14}C-labeled Sodium Stearate/ml of aqueous solution was applied over 4.9 cm^2 of excised rat skin. Twenty-four hours after application, the skin surface was rinsed with distilled water and monitored for ^{14}C. Over 24 hours, <0.1 μg/cm^2 had penetrated the skin.[34]

In-Vitro Absorption–Human Epidermis: A 0.1 ml sample containing 1.8 mg of ^{14}C-labeled Sodium Stearate/ml of aqueous solution was applied over 0.78 cm^2 of skin excised from the human abdomen. Twenty-four hours later, the skin was rinsed with distilled water and the epidermal sample monitored for ^{14}C. In 24 hours, 0.1 ± 0.1 μg/cm^2 had penetrated the epidermis.[34]

In-Vivo Absorption–Rat Skin: A 0.1 ml aqueous sample containing 184 μg of ^{14}C-labeled Sodium Stearate was applied over 7.5 cm^2 of clipped rat skin for 15 minutes. After six hours, the treated skin was excised and monitored for ^{14}C. Autoradiographs showed "heavy deposition" (2–5 μg/cm^2) of ^{14}C on the stratum corneum, at the entrances of hair follicles, and in the hair follicles. Traces were also seen in the epidermis, but not in the dermis. The amount of ^{14}C recovered in the expired CO_2, urine, feces, and carcass was 0.53 ± 0.14 μg.[34]

Animal Toxicology

General Studies

Oral toxicity: acute

Aluminum, Ammonium, Lithium, Magnesium, Sodium and Zinc Stearates taken orally were practically nontoxic to rats (see Table 5).[36-46]

Dermal toxicity: acute

Studies with guinea pigs demonstrated that 100% Aluminum and Ammonium Stearates have a low potential for acute dermal toxicity. Studies conducted in rabbits showed that product formulations containing Sodium and Zinc Stearates also have a low potential for dermal toxicity (see Table 6).[38,43-45,47,48]

Dermal corrosion: acute

Magnesium and Zinc Stearates were noncorrosive to the skin of rabbits according to 49 CFR 173.240 (a)(1) (see Table 7).[40,49,50]

Skin irritation: acute

In rabbit studies, 10% Aluminum Distearate in corn oil and 100% Ammonium Stearate were minimal and slight skin irritants, respectively; whereas, 100% Magnesium, Sodium, and Zinc Stearates were nonirritants (see Table 8).[40,44,45,47,49-55]

Eye irritation: acute

In rabbit studies, 10% Aluminum Distearate in corn oil and 100% Ammonium, Sodium, and Zinc Stearates were minimal to mild eye irritants; 100% Magnesium Stearate was a nonirritant (see Table 9).[37,40,44,45,47,49,50,52,53,55-57]

Inhalation toxicity: acute

In studies with albino rats, Magnesium and Zinc Stearates were determined to be nontoxic by inhalation (see Table 10).[39,40]

Miscellaneous toxicity studies

Magnesium Stearate: A commercial Magnesium Stearate powder was introduced into the peritoneal cavity (50 mg) and into skin wounds (10 mg) of kittens, rabbits, guinea pigs, rats, and mice. When the animals were sacrificed six to nine weeks later, none of them showed signs of fibrosis or irritation of the skin or peritoneum.[58]

Sodium Stearate: An aqueous solution containing 0.1% Sodium Stearate (0.97 *M*) produced extensive thrombosis and death when given intravenously to dogs at a dose of 10 ml/kg over a five-minute period.[59,60]

An aqueous suspension of 0.1% Sodium Stearate (pH 7.4) injected intravenously into mice at a dose of 0.01 ml/kg of body weight resulted in generalized thrombosis and sudden death.[61]

An aqueous solution containing 0.66 m*M* Sodium Stearate administered intravenously to rabbits at a dose of 3.5 ml/kg within a 30- to 45-second interval induced reversible thrombopenia.[62]

Intravascular injection into rabbits of 100 mg of a fine colloidal suspension of Sodium Stearate in deproteinized rabbit serum at doses of 28.0 or 32.2 mg/kg caused immediate vascular damage to the vessels nearest the site of injection.[63]

TABLE 5. Acute Oral Toxicity.

Ingredient	*Concentration (%)*	*No. of rats*	*Methods*	*Comments*	*LD50*	*Ref.*
Aluminum Stearate	100	–	–	–	>5.0g/kg	38
Ammonium Stearate	100	–	–	–	>5.0 g/kg	47
Lithium Stearate	Unspec. conc. in propylene glycol vehicle	30 albino	–	Animals fasted for 24 hrs. and then given dosages ranging from 0.05 to 15.0 g/kg. Animals dosed at 0.05, 1.0 and 3.0 g/kg showed no toxic effect; all animals administered 15 g/kg died within 16 hrs. having exhibited unkempt coats, impaired locomotion and lethargy prior to death.	>5.0 g/kg but <15.0 g/kg	39
Magnesium Stearate	25 susp. in corn oil	albino	Hagan; Litchfield and Wilcoxon	Animals fasted overnight and then given doses ranging from 0.05 to 10.0 g/kg. Animals observed daily for 14 days. All animals at 10.0 g/kg exhibited mold diarrhea.	>10 g/kg	40–42
Sodium Stearate	25 in propylene glycol	6	–	Material administered at a dose level of 5.0 g/kg. There were no remarkable clinical or necropsy findings.	>5.0 g/kg	36
Sodium Stearate	7.0 in stick deodorant form	10 albino	–	All animals receiving 10 ml/kg showed moderate or marked depression, labored respiration and "depressed righting and placement reflexes" immediately after intubation. All animals recovered within 24 hrs. and appeared normal during remainder of study. Necropsies performed at day 14 revealed no abnormal gross pathology.	>10 ml/kg (formulation)	43
Sodium Stearate	10–25 in bath soap detergent form	–	–	–	>5 g/kg (formulation)	46

Zinc Stearate	25 susp. in corn oil	albino	Hagan; Litchfield and Wilcoxon	Animals fasted for 24 hrs. and then given doses ranging from 0.05 to 10.0 g/kg. During 14 days of observation, all animals appeared normal; there were no mortalities.	>10 g/kg	41,42,49
Zinc Stearate	100	–	–	–	>5.0 g/kg	37
Zinc Stearate	10 in eye-shadow form	10	–	–	>5.0 g/kg	44,45

TABLE 6. Acute Dermal Toxicity.

Ingredient	*Concentration (%)*	*Animal*	*Comments*	*LD50*	*Ref.*
Aluminum Stearate	100	Guinea pigs	Dermal contact with the test material was maintained for 24 hrs.	>3.0 g/kg	38
Ammonium Stearate	100	Guinea pigs	Dermal contact with the test material was maintained for 24 hrs.	>3.0 g/kg	47
Sodium Stearate	7 in a stick deodorant form.	4 rabbits/ albino	A single application of the undiluted formulation was made to the intact skin for a 24 hr. exposure period. After 24 hrs. all animals showed depression and labored respiration but completely recovered by day three; there were no gross signs of systemic toxicity during remainder of study. Necropsies at day 14 revealed pitted and edematous kidneys in one animal.	>10 ml/kg (formulation)	43
Sodium Stearate	10–25 in a 20% bath and soap and detergent form	Rabbits	–	>3.0 g/kg (formulation)	48
Zinc Stearate	10 in eyeshadow form	10 rabbits	–	>2.0 g/kg (formulation)	44,45

TABLE 7. Acute Dermal Corrosion.

Ingredient	*Concentration (%)*	*No of. Rabbits*	*Method*	*Comments*	*Result*	*Refs.*
Magnesium Stearate	100	6 albino	Draize	Material 0.5 ml (0.5 g) applied in a single dose under occlusive conditions for 4 hrs; one-half test sites abraded and one-half intact. PII = 0.0	Noncorrosive under 49 CFR 173.240(a)(1)	40,50
Zinc Stearate	100	6 albino	Draize	Material 0.5 ml (0.5 g) applied in a single dose under occlusive conditions for four hrs. PII = 0.0.	Noncorrosive under 49 CFR 173.240(a)(1)	49,50

TABLE 8. Skin Irritation.

Ingredient	*Concentration (%)*	*No. of rabbits*	*Method*	*Comments*	*Result*	*Ref.*
Aluminum Distearate	10 susp. in corn oil	–	–	Material applied in a single dose under occlusive conditions. PII = 0.06 (max. = 8)	Minimal irritation	52
Ammonium Stearate	100	–	–	Material applied in a single dose under occlusive conditions. PII = 0.62 (max. = 8)	Slight irritation	47
Magnesium Stearate	100	6 albino	Draize	Material applied under occlusive patch for 24 hrs; one-half test sites abraded and one-half intact. PII = 0.0 (max. = 8)	No irritation	40,50
Sodium Stearate	100	6 albino	–	Material applied in a single dose under occlusive conditions. PII = 0.0 (max. = 8)	No irritation	51
Sodium Stearate	7 in a stick deodorant form	4 albino	Draize	The undiluted formulation (0.5 ml) applied to abraded and intact skin for 24 hr. exposure period. PII of formulation = 2.6 (max. = 8)	Moderate irritation (formulation)	51,53
Sodium Stearate	10–25 in a bath soap and detergent form	6	Draize	PII = 2.2 (max. = 8)	Mild irritation (formulation)	50,55
Zinc Stearate	100	6 albino	Draize	Material applied under occlusive conditions to abraded and intact skin for 24 hr. exposure period. PII = 0.0 (max. = 8)	No irritation	49,50
Zinc Stearate	10 in eye-shadow form	6	–	PII = 0.0 (max. = 8)	No irritation (formulation)	45,54

TABLE 9. Eye Irritation.

Ingredient	*Concentration (%)*	*No. of rabbits*	*Method*	*Comments*	*Result*	*Ref.*
Aluminum Distearate	10 susp. in corn oil	–	Draize	Eyes were unrinsed. Scores were 1, 1, and 0 on Days 1, 2, and 3, respectively	Minimal irritation	50,52
Ammonium Stearate	100	–	Draize	Eyes were rinsed. Scores were 3, 1, and 0 on Days 1, 2, and 3, respectively.	Minimal irritation	47,50
Ammonium Stearate	100	–	Draize	Eyes were unrinsed. Scores were 22, 16, 5, 3, and 1 on Days 1, 2, 3, 4, and 7, respectively.	Mild irritation	47,50
Magnesium Stearate	100	6 albino	Draize	Eyes were unrinsed. The score was 0 on days 1, 2, and 3.	No irritation	40,53
Sodium Stearate	100	6	Draize	On day one, 2/6 conjunctivae appeared necrotic. Scores were 22, 12, 3, 1, and 1 on Days 1, 2, 3, 4, and 7, respectively. This corresponded to moderate irritation initially but was considered negligible by Day 4.	Negligible irritation	56
Sodium Stearate	7 in an undiluted stick deodorant form	5 albino	Draize	Eyes were rinsed. Scores were 29, 27, 21, 16, 13, and 7, at the 1 hr, 1, 2, 3, 4, and 7 day readings, respectively.	–	50,57
Sodium Stearate	7 in an undiluted stick deodorant form	5 albino	Draize	Eyes were unrinsed. Scores were 29, 31, 24, 21, 15, and 8, at the 1 hr, 1, 2, 3, 4, and 7 day readings, respectively.	–	50,57
Sodium Stearate	10–25 in a bath and soap detergent form	–	Draize	Eyes were unrinsed.	Mild irritation (formulation)	50,55
Zinc Stearate	100	6 albino	Draize	Eyes were unrinsed. The score was 0 on Days 1, 2, and 3, respectively.	No irritation	49,53
Zinc Stearate	100	6	Draize	Eyes were unrinsed. Scores were 2 and 0 on Days 1 and 2, respectively.	Minimal irritation	37,50
Zinc Stearate	10 in undiluted eye-shadow form.	6	–	The score was 0 in all animals at 24, 48, and 72 hrs.	No irritation (formulation)	44,45

TABLE 10. Acute Inhalation Toxicity.

Ingredient	*No. of albino rats*	*Chamber conc. (mg/l)*	*Comments*	*LC50*	*Ref.*
Magnesium Stearate	2 groups of 10	200 or 2	At end of single 1-hr. exposure to 200 mg/l, 7/10 rats were dead; an 8th rat died on day 14. In a similar exposure to 2 mg/l, 2/10 deaths occurred in the 2nd week. Material considered nontoxic under Dept. of Transportation regulations.	>2 mg/l	40
Zinc Stearate	10	200	Single 1-hr. exposure; 1/10 rats died during 2-wk. observation period. Material was considered nontoxic by investigators.	>200 mg/l	49

Zinc Stearate: Zinc Stearate was acutely irritating when injected into the lungs of rats and the peritoneum of guinea pigs. When 50 mg suspended in 1 ml of skim milk and saline was injected into the lungs of 50 rats, 20 died in less than 24 hours. Examination of the lungs revealed severe edema, congestion, and small hemorrhages. Animals that survived demonstrated no abnormality of the lungs after 14 or 259 days. When 100 mg Zinc Stearate suspended in 1 ml of tap water was injected into the lungs of six rats, all died as a result of acute edema of those organs. Guinea pigs injected intraperitoneally with either 50 mg (six guinea pigs) or 100 mg (six guinea pigs) Zinc Stearate suspended in 1 ml of tap water developed granulomata of the peritoneum. No permanent fibrosis resulted from the single injection of Zinc Stearate into the lungs of rats or into the peritoneum of guinea pigs.[64]

Subchronic studies

Calcium Stearate: An emulsion of Calcium Stearate (unspecified concentration) in egg yolk and water was applied to the skin of six guinea pigs daily, for 14 days. After only six days of exposure, the body weight of treated animals decreased significantly relative to that of controls. The average body weight change reported on day six for control animals was 56g ± 4.85, while that reported for exposed animals was 29 g ± 10.12 ($p = 0.05$).[65]

Calcium Stearate (50 mg in 0.5 ml of saline and 0.01 ml of egg yolk) administered intratracheally to rats for two months caused severe lesions of blood vessels in the pulmonary tissue. Results for the control animals were not given.[65]

Zinc Stearate: An emulsion of Zinc Stearate (unspecified concentration) in egg yolk and water was applied daily for 14 days to the skin of six guinea pigs. After only four days of exposure, the body weight of treated animals increased significantly over that of controls. The average body weight change reported for animals on day four was 17 g ± 3.84, while that reported for exposed animals was 37 g ± 4.8 ($p = 0.02$).[65]

Chronic studies

Calcium Stearate: Calcium Stearate (50 mg in 0.5 ml of saline and 0.01 ml of egg yolk) administered intratracheally to rats for six months caused "... peribronchial sclerosis, foci of alveolar emphysema, single small areas of

hemorrhage, and pigment aggregations . . .". Results for the control animals were not given.[65]

Calcium Stearate (10 mg in 0.5 ml of saline and 0.01 ml of egg yolk) was administered intratracheally to rats for four or eight months; this caused varying degrees of lung pathology, including peribronchial sclerosis, alveolar atelectasis, and diffuse brochiectasis. Results for the control animals were not given.[65]

Sodium Stearate: A formulation "bath soap and detergent" containing 10–25% Sodium Stearate was used to conduct a dermal toxicity study in rabbits. Formulations for 3 months' doses of 2.0 g/kg were applied to the skin by syringe daily, five days a week. No "untoward reactions" were observed.[66]

Zinc Stearate: Intratracheal administration of Zinc Stearate (50 mg in 0.5 ml of saline and 0.01 ml egg yolk) to rats for two months caused varying degrees of lung pathology, including plasmorrhagia in the walls of arteries, alveolar atelectasis, alveolar emphysema, bronchitis, diffuse bronchiectasis, and hyperplasia of lymphoid tissue. Results for the control animals were not given.[65]

Special Studies

Teratogenesis

Magnesium Stearate: A vehicle used in coated pharmaceutical tablets was assayed for teratogenicity in rabbits. The vehicle consisted of polyethylene glycol 4000, starch, talcum, silica gel and 5.5% Magnesium Stearate. Fourteen females received the vehicle per os at a dose of 2.5 mg/kg 70 hours post coitus whereas 13 females were given the same dose 192 hours post coitus. Compared with anomalies in the fetuses from 16 untreated mothers (12 of 112 offspring had anomalies) the vehicle containing 5.5% Magnesium Stearate induced anomalies in 9 out of 86 and 11 out of 90 fetuses respectively, thus demonstrating the absence of a teratogenic effect.[67]

Mutagenesis

Magnesium Stearate: Magnesium Stearate was not a mutagen in microbial tests with *Salmonella typhimurium* TA-1535, TA-1537, TA-1538, and *Saccharomyces cerevisiae* D4 with or without metabolic activation by liver and lung preparations from rats, mice, and monkeys.[28,68]

Carcinogenesis

Stearic Acid: Ninety-two mice [Swiss Webster female mice and BALB/C (mammary tumor virus-free) female mice, seven test groups of 10–16 animals each] received subcutaneous injections of 0, 0.05, 0.5, and 1.0 mg stearic acid (corresponding to approximate total doses of 0, 2.5, 25, and 50 mg/kg, once, twice, or three times weekly). The number of injections per test group varied from 26 to 114. One mouse in the control group developed a subcutaneous sarcoma during the 18 months of observation. In the test group of 10 mice receiving 0.05 mg twice a week for a total of 114 injections, four subcutaneous sarcomas developed during the 18-month period. No sarcomas developed in the mice in the other six test groups, including those given 0.5 mg twice a week for a total of 114 injections or 1.0 mg twice a week for a total of 82 injections. The occurrence of four sarcomas in the one test group was not explained.[27,69] Clayson[70] regards the induction of localized sarcomas in mice upon repeated subcutaneous injection of test solutions as "notoriously unreliable as an indicator of car-

cinogenicity." Furthermore, he considers "the results of individual experiments as extremely variable."

The foregoing test was repeated in mice; this time the animals were given weekly injections of 0.05 and 0.5 mg for 26 weeks. No sarcomas developed at the site of injection, and it was concluded that stearic acid was not a carcinogen by these procedures.[27,71]

Ten rats fed stearic acid as 0.3% of their diet for 209 days developed no tumors.[27,72]

In a search for carrier materials for introducing potential carcinogens into the urinary bladders of mice, stearic acid and other "inert vehicles" were tested for their ability to produce bladder tumors (See Table 11). Pellets of stearic acid implanted in the bladders of 62 mice for 30 weeks produced a bladder tumor incidence of 13%.[73]

Magnesium Stearate: Pellets of Magnesium Stearate implanted in bladders of 41 mice for 30 weeks produced a 5% incidence of bladder tumors. The incidence of bladder tumors in mice implanted with Magnesium Stearate was similar to that produced by smooth glass beads (See Table 11).[73]

Magnesium Stearate pellets containing different compounds were also implanted into mouse bladders. A significant number of tumors (26%) was produced by 1-methoxy-2-naphthylamine using Magnesium Stearate as a vehicle.

Although Magnesium Stearate pellets containing indoxyl sulfate, hippuric acid, or 3-hydroxyanthranilic acid produced more tumors (the incidence was 19%, 17%, and 19%, respectively) than did Magnesium Stearate alone (5%), the differences according to the authors, were not significant.[73]

Clinical Assessment of Safety

Primary Irritation and Sensitization

Ammonium Stearate: The skin-irritation potential of 1.5% Ammonium Stearate in aqueous solution was determined in 20 subjects using a single insult, 24-hour, occlusive patch test. The test material caused no irritation in 13 subjects, minimal erythema in one, and mild erythema in six. The Primary Irritation Index (PII) was determined to be 0.33, indicating minimal irritation.[74]

TABLE 11. Incidence of Bladder Tumors in Mice Implanted with Inert Materials.[a]

	Numbers of Mice[b]			
Substance	Surviving 30 wks	w/adenoma or papilloma	w/carcinoma	Tumor incidence (%)
Magnesium Stearate	41	1	1	5
Cholesterol	77	4	5	12
Stearic Acid	62	5	3	13
n-Hexadecanol	69	2	6	12
n-Octadecanol	50	7	6	26
Naphthalene	23	0	1	4
Smooth glass	67	–	3	4
Roughened glass	63	–	18	29

[a]Data from Ref. 73.
[b]Stock mice were bred in the Chester Beatty Research Institute.

Sodium Stearate: A single insult, 24-hour, occlusive patch test was conducted on 20 human subjects to determine the skin irritation potential of 0.5% Sodium Stearate in aqueous solution. The test solution produced no irritation in 16 subjects, and minimal to moderate erythema in four. The investigators concluded that Sodium Stearate "exhibited an acceptable and typical soap response."[75]

A stick deodorant containing 7% Sodium Stearate was tested for skin irritation and sensitization potential in 212 subjects. The undiluted formulation was applied to the medial surface of the upper arm of each subject four days a week for two weeks for a total of eight 12-hour patches. After a two-week rest, one 24-hour challenge patch was applied and read at 24, 48, and 72 hours. During the two-week induction period, a total of 61 erythema reactions occurred, 59 of them slight, one moderate, and one severe. The challenge application caused in seven slight erythema reactions by the 24-hour reading and one slight erythema reaction by the 48-hour reading; all eight sites were negative by 72 hours.[76-78]

In a 21-day patch test, a "bath soap and detergent" formulation at a level of 1% in aqueous solution was minimally irritating to 10 subjects. The diluted formulation contained 0.1–0.25% Sodium Stearate.[79] When they were tested with the same formulation at 3% in aqueous solution, 100 subjects showed no sensitization; the diluted formulation contained 0.3–0.75% Sodium Stearate.[80]

Zinc Stearate: Two eyeshadow formulations, each containing 10% Zinc Stearate, were tested by means of the Schwartz–Peck Prophetic Patch Test and the Draize–Shelanski Repeated Insult Patch Test. The former test resulted in "virtually 0 reactions in 202 subjects," whereas the latter one brought about "virtually 0 reactions in 99 subjects."[81,82] One of the formulations was applied twice a day for 28 days to 52 female panelists. Each subject was then examined at baseline and one, two, three, and four weeks after application. "No irritation or sensitization potential was exhibited by the panelists using this product under conditions of this test."[83]

Phototesting: No studies relating to phototoxicity or photo-contact allergenicity were available to the Panel.

Miscellaneous Studies

Sodium Stearate: Nonallergic granulomas of the skin were produced in 9 out of 10 subjects following dermal injections of 0.2 *M* Sodium Stearate at a dose of 0.1 ml. Biopsy specimens of representative areas at the two to four and five week periods revealed a "distinct epithelioid reaction with occasional giant cells and some round cell infiltration"; in some instances there were "fragmentation and degeneration of collagen fibers." The length of duration of the granulomas depended on the time required for the ingestion and metabolism of the compound by reticuloendothelial cells. The authors concluded that the "granulomagenic capacity" of Sodium Stearate was related to its "ability to form colloidal systems composed of micellar particles."[84]

An emulsion of 2.5 *M* Sodium Stearate in NaCl and albumin was given intraduodenally to healthy males and to patients with healed duodenal ulcers in a dose of 0.5 g. The emulsion was administered after a plateau of gastric acid secretion induced by a continuous infusion of pentagastrin had been reached. The test material provoked only a slight inhibition of gastric acid secretion; no vomiting or nausea occurred.[85]

Zinc Stearate: Harding[64] described a case of "pneumoconiosis with probable heart failure" in a rubber factory worker who had been occupationally exposed to Zinc Stearate dust for 29 years. Histological examination of lungs revealed bleeding, a significant increase in connective tissue, and chronic inflammation; likewise, numerous "granules and needles" in the fibrotic tissue that contained zinc were also observed.

Weber et al.[86] described a case of pulmonary fibrosis in a chemical worker who had been occupationally exposed to Zinc Stearate dust for seven years. The amount of zinc retained in the lungs of the deceased worker (6.2 mg/100 g of dry lung tissue) was not significantly different than that retained in the lungs of persons who had not been occupationally exposed. It was the authors' opinion that Zinc Stearate was not the cause of lung fibrosis.

Murray[87] reported that between 1919 and 1924, a Toronto hospital admitted three cases of "drug poisoning" caused by aspiration and ingestion of Zinc Stearate powder. One of the patients, a 14-month old infant, developed diffuse bronchopneumonia and died within two days of the accident.

Heiman and Aschner[88] reported 12 cases in which infants developed fever, rapid respiration, dyspnea, cyanosis, bronchopneumonia, and acute toxemia after incidentally aspiring Zinc Stearate powder. One eight-month-old infant died within 24 hours of the accident. In eight cases, " . . . the initial partial asphyxia was followed by a gradual recovery without definite involvement of the lungs. The rapid respirations and cyanosis which followed immediately on the inhalation of the powder subsided during the course of three days."

The *Handbook of Cosmetic Materials*[8] states that Zinc Stearate is an "extremely tenacious powder which can be harmful when inhaled." Lesions resulting from aspiration of the powder resemble those from aspiration of talc; but the former type of lesions is generally more severe than the latter.[89] *The U.S. Pharmacopeia XIX*[9] reports that the compound is not to be inhaled by or used on infants.

SUMMARY

The Stearates reviewed in this report are salts of stearic acid. They are fine, white powders with a slight fatty odor. The commercial stearic acid from which the Stearates are manufactured is a mixture of monocarboxylic acids obtained from animal and vegetable sources. The commercial grade of stearic acid contains fatty acids that range from C_{12} (lauric) to C_{22} (behenic), and the major components are C_{18} (stearic) and C_{16} (palmitic) acids.

Stearates are generally used for their lubricating properties, but they may also function as emulsifiers, stabilizers, and opacifiers. The range of concentrations of these ingredients in cosmetic products varies from $\leq$ 0.1 to $>$ 50%.

Aluminum, Calcium, Magnesium, Potassium, and Sodium Stearates have been approved for use as food additives, and regulations governing such use have been issued under the Food, Drug and Cosmetic Act. Magnesium and Zinc Stearates are GRAS (Generally Recognized As Safe) compounds.

Limited absorption studies indicated that Calcium Stearate is slightly absorbed by isolated dog intestine, and that Sodium Stearate is absorbed through both rat and human skin.

Acute oral studies with rats showed that Aluminum, Ammonium, Lithium, Magnesium, Sodium, and Zinc Stearates are practically nontoxic. Studies with

guinea pigs demonstrated that 100% Aluminum and Ammonium Stearates have a low potential for acute dermal toxicity. When tested on rabbit skin at concentrations of 100%, Magnesium and Zinc Stearates were found to be noncorrosive. Skin irritation studies with rabbits demonstrated that 10% Aluminum Distearate in corn oil and 100% Ammonium Stearate were minimal and slight irritants, respectively, whereas 100% Magnesium, Sodium, and Zinc Stearates were nonirritants. Eye irritation studies with rabbits showed that 10% Aluminum Distearate in corn oil and 100% Ammonium, Sodium, and Zinc Stearates were minimal to mild irritants; 100 percent Magnesium Stearate was a nonirritant.

An emulsion of Calcium Stearate in egg yolk and water applied to the skin of guinea pigs for 14 days caused a significant decrease in body weight, whereas a similar emulsion containing Zinc Stearate caused a significant increase in body weight.

Zinc Stearate administered intratracheally to rats for two months and Calcium Stearate administered simililarly to rats for two, four, six and eight months, caused varying degrees of lung pathology.

When fed to pregnant rabbits, a pharmaceutical vehicle containing 5.5% by weight Magnesium Stearate was not teratogenic. Magnesium Stearate was not mutagenic in microbial tests with *Salmonella typhimurium* or *Saccharomyces cerevisiae*. Mice surviving 30-week implants of Magnesium Stearate pellets in the bladder had a bladder tumor incidence of 5.0%, but the incidence was no different than that caused by glass beads.

In a clinical study, seven out of 20 subjects exhibited minimal to mild skin erythema when tested with an aqueous solution of 1.5% Ammonium Stearate in a single-insult, 24-hour patch test. In a similar study with 0.5 percent Sodium Stearate in aqueous solution, four out of 20 subjects demonstrated minimal to moderate skin erythema. In a 21-day patch test with 10 subjects, an aqueous "bath soap and detergent" solution containing 0.1–0.25% Sodium Stearate caused minimal skin irritation. An aqueous solution of the same formulation containing 0.3–0.75% Sodium Stearate caused no sensitization in 100 subjects. A stick deodorant containing 7% Sodium Stearate, and eye shadow formulations containing 10% Zinc Stearate demonstrated low potential for human skin irritation and sensitization. There were several reported instances of infant bronchopneumonia and death due to accidental inhalation of Zinc Stearate powder.

The opinion expressed in the conclusion below is based on a composite of available animal and human data. However, the Panel felt that a number of the reported clinical studies for primary skin irritation and sensitization were suboptimal or inadequate in terms of number of subjects tested, concentrations tested and/or test protocols employed. Data for the purpose of assessing the human skin sensitization potential of the Stearates were also limited in that only product formulation data were available. Further, no clinical studies relating to phototoxicity or photocontact allergenicity were reported. Despite these limitations and/or deficiencies in the clinical data, it is the Panel's opinion that sufficient animal and human data are available to assess the safety of the Stearates as comsetic ingredients.

CONCLUSION

On the basis of the available information presented in this report, and as the information is qualified in the summary, the Panel concludes that the Stearate com-

pounds described herein are safe as cosmetic ingredients in the present practices of use and concentration.

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Mr. Jonathon T. Busch, Scientific Analyst and writer, prepared the literature review and technical analysis used by the Expert Panel in developing this chapter.

REFERENCES

1. COSMETIC, TOILETRY AND FRAGRANCE ASSOCIATION (CTFA). (April 17, 1979). Submission of data by CTFA. Stearates. Summary of unpublished safety data. Introduction.*
2. COSMETIC INGREDIENT REVIEW (CIR). (April 27-29, 1979). Minutes of the CIR Expert Panel Meeting.*
3. ESTRIN, N.F. (ed.). (1977). *CTFA Cosmetic Ingredient Dictionary*, 2nd ed. Washington, DC: Cosmetic, Toiletry and Fragrance Association.
4. CTFA. (October 23, 1978). Submission of data by CTFA. CTFA Cosmetic Ingredient Chemical Descriptions.*
5. ESTRIN, N.F. (ed.). (1974). CTFA Standards. Cosmetic Ingredient Descriptions. Washington, DC: Cosmetic, Toiletry and Fragrance Association.
6. HAWLEY, G.G. (ed.). (1971). *The Condensed Chemical Dictionary*, 8th ed. NY: Van Nostrand Reinhold.
7. LORANT, B. (1967). Thermoanalytical and thermogravimetric studies (of metal soaps). Seifen. Ole. Fette. Wachse. **93**(16), 547-51.
8. GREENBERG, L.A., LESTER, D. and HAGGARD, H. (1954). *Handbook of Cosmetic Materials*. NY: Interscience Publishers.
9. UNITED STATES PHARMACOPEIAL CONVENTION. (1975). *The United States Pharmacopeia*, 19th ed. Rockville, MD.
10. WINDHOLZ, M. (ed.). (1976). *The Merck Index*, 9th ed. Rahway, NJ: Merck and Co.
11. WEAST, R.C. (ed). (1978). *CRC Handbook of Chemistry and Physics*, 59th ed. West Palm Beach, FL: CRC Press.
12. KITA, H., OZUKA, W., and SUGAHARA, G. (1956). Mechanism of the preparation of amides and nitriles from fatty acid and ammonia. II. Decomposition properties of ammonium soaps of fatty acids. Kogyo Kagaku Zasshi **59,** 1047-50.
13. ESTRIN, N.F. (ed.). (1974). *CTFA Standards. Cosmetic Ingredient Specifications*. Washington, DC: Cosmetic, Toiletry and Fragrance Association.
14. NATIONAL FORMULARY BOARD. (1975). *The National Formulary*, 14th ed. Washington, DC: American Pharmaceutical Association.
15. NATIONAL ACADEMY OF SCIENCES (NAS). (1972). *Committee of Specifications, Food Chemical Codex*, 2nd ed. Washington, DC: National Academy of Sciences.
16. NATIONAL LIBRARY OF MEDICINE (NLM). (1979). *Chemline*, Computerized Database of the National Library of Medicine, Dept. of Health, Education and Welfare, Bethesda, MD.
17. NATIONAL FORMULARY BOARD. (1970). *The National Formulary*, 13th ed. Washington, DC: American Pharmaceutical Association.
18. RODIONOVA, N.W., ZHUKOVA, V.P. and SHMARLIN, V.S. (1973). Determination of calcium stearate acid in butyl rubber by ir spectroscopy. Prom. Sin. Kauch., Nauch.-Tekhn. Sb. **4,** 3-5.
19. SCHROEDER, E., HAGEN, E., and ZYSIK, M. (1966). Analytical chemistry of plastics. XXXI. Flame photometric determination of calcium and barium stearate in structural plastics. Plaste Kaut. **13**(12), 712-13.
20. NORWITZ, G. and GORDON, H. (1972). Determination of lithium stearate in sebacate-base semifluid lubricants. Establishment of quality assurance requirements for lithium stearate. U.S. Nat. Tech. Inform. Serv. A.D. Rep. No. 751771:2, 21 pp.
21. NORWITZ, G. and GORDON, H. (1973). Determination of lithium stearate in sebacate-based lubricants by atomic absorption. Talanta **20**(9), 905-7.
22. ZLATEVA, P. (1974). Analysis of zinc stearate. Kosh. Obuvna Prom.-St. **15**(5), 26-7.

*Available upon request: Administrator, Cosmetic Ingredient Review, Suite 810, 1110 Vermont Ave., N.W., Washington, DC 20005.

23. BALSAM, M.S. and SAGARIN, E. (eds.). (1974). *Cosmetics. Science and Technology Vol. 2.* NY: John Wiley and Sons.
24. FDA. (Aug. 31, 1976). Cosmetic product formulation data. Washington, DC: Food and Drug Administration.
25. ANONYMOUS. (1976). Termination of provisional listing for color additives. Fed. Reg. **41**(186), 41855–56.
26. FDA. *FDA Inspection Operations Manual,* March 26, 1979; updates Food Additives Status List to Feb. 15, 1979.
27. FASEB. (1975). Select Committee on GRAS Substances. Evaluation of the health aspects of tallow, hydrogenated tallow, stearic acid, and calcium stearate as food ingredients. FDA Contract 233-75-2004. Bethesda, MD: Federation of American Societies for Experimental Biology.
28. FASEB. (1976). Select Committee on GRAS Substances. Evaluation of the health aspects of magnesium salts as food ingredients. FDA Contract 223-75-2004. Bethesda, MD.
29. STEELS, W. and JENSKI, H.M. (1974). Growth of Novikoff hepatoma cells in the presence of long-chain fatty acids. Proc. Soc. Exp. Biol. Med. **146**(3), 885–89.
30. ACOSTA, D. and WEBZEL, D.G. (1974). Injury produced by free fatty acids to lysosomes and mitochondria in cultured heart muscles and endothelial cells. Atherosclerosis **20**(3), 417–26.
31. PILGERAM, L.O. and PICKART, L.R. (1968). Control of fibrogen biosynthesis. The rule of free fatty acid. J. Atheroscler. Res. **8**(1), 155–66.
32. YAMADA, S. (1960). The influence of bile or bile acid on the absorption of insoluble calcium salts in intestinal tract. Eiyo To Shokuryo **12,** 391–403.
33. SZAKALL, A. and SCHULZ, K.H. (1960). The penetration of the human skin by fatty alcohol sulfates and sodium soaps of fatty acids (C_8–C_{18}) and its relation to causes of irritation. Fette. Seifen. Anstrichm. **62,** 170–75.
34. HOWES, D. (1975). Percutaneous absorption of some anionic surfactants. J. Soc. Cosmet. Chem. **26**(1), 47–63.
35. MORIN, R.J. (1966). Incorporation of stearate-1-^{14}C and oleate-1-^{14}C into phosphatidylcholine and phosphatidyethanolamine or rat liver mitochondria. Life Sci. **5**(7), 649–53.
36. AVON PRODUCTS. (Jan. 16, 1973). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate group. Oral toxicity.*
37. AVON PRODUCTS. (Dec. 22, 1976). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate group. Biological Evaluation Summary Report. Zinc Stearate.*
38. AVON PRODUCTS. (June 16, 1978). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate group. Biological Evaluation Summary Report. Aluminum Stearate.*
39. S.B. PENICK and CO. (Aug. 3, 1976). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate group. Bio-Toxicology Laboratories. Acute oral LD50 toxicity study. Lithium Stearate.*
40. S.B. PENICK and CO. (Feb. 9, 1977). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate group. Consumer Product Testing Co., Inc. Final Report. Magnesium Stearate.*
41. HAGAN, E.C. (1959). Acute Toxicity. Appraisal of the safety of chemicals in foods, drugs, and cosmetics. Association of Food and Drug Officials of the U.S., as compiled by the staff of the Div. of Pharmacology, Food and Drug Administration, Dept. of Health, Education and Welfare, Austin, TX, pp. 17–25.
42. LITCHFIELD, J.R. and WILCOXON, F. (1949) J. Pharmacol. Exp. Ther. pp. 96,99.
43. CTFA. (June 16, 1975). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate Group. Acute oral and dermal toxicity, Sodium Stearate. Product Type/In-House Code: DS 5011-55 Stick Deodorant, Test No.: A-4644.*
44. CTFA. (Feb. 9, 1976). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate Group. Acute oral intubation, acute dermal toxicity, primary skin irritation and ocular irritation.*
45. CTFA. (Feb. 6, 1978). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate Group. Acute oral intubation, acute dermal toxicity, primary skin irritation and ocular irritation.*
46. CTFA. (July, 1978). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate Group. Acute oral toxicity, Sodium Stearate. Bath soaps and detergents. Product 78–74.*
47. AVON PRODUCTS. (March 27, 1975). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate group. Biological Evaluation Summary Report. Ammonium Stearate.*
48. CTFA: (March, 1970). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate Group. Acute dermal toxicity, Sodium Stearate. Bath soaps and detergents. Product 78-74.*
49. S.B. PENICK and CO. (Feb. 9, 1977). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate group. Consumer Product Testing Co., Inc. Final Report. Zinc Stearate.*
50. DRAIZE, J.H., WOODARD, G., and CALVERY, H.O. (1944). Methods for the study of irritation and toxicity of substances, applied topically to the skin and mucous membranes. J. Pharmacol. Exp. Ther. **82,** 377.
51. AVON PRODUCTS. (Jan. 4, 1973). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate group. Skin Irritation.*

52. AVON PRODUCTS. (March 4, 1977). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate group. Biological Evaluation Summary Report. Aluminum Distearate.*
53. DRAIZE, J.H. (1959). Dermal Toxicity. Appraisal of the safety of chemicals in foods, drugs, and cosmetics. Assoc. of Food and Drug Officials of the U.S., compiled by the staff of the Div. of Pharmacology, Food and Drug Administration, Dept. of Health, Education and Welfare, Austin, TX, pp. 46–59.
54. CTFA. (May 27, 1975). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate Group. Primary irritancy, Sodium Stearate. Product Type/In-House Code: DS 5011-55 Stick Deodorant, Test No.: A-4644.*
55. CTFA. (May, 1978). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate Group. Eye and lower case primary skin irritation, Sodium Stearate. Bath soaps and detergents. Product 78-74.*
56. AVON PRODUCTS. (Jan. 8, 1973). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate group. Draize eye test.*
57. CTFA. (June 4, 1975). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate Group. Eye irritancy, Sodium Stearate. Product Type/In-House Code: DS 5011-72 Stick Deodorant, Test No.: A-4644.*
58. GRAHAM, J.D.P. and JENKINS, M.E. (1952). Effects of substitutes for surgical talc on wounds. J. Pharm. Pharmacol. **4,** 392–98.
59. CONNOR, W.E., HOAK, J.C., and WARNER, E.D. (1963). Massive thrombosis produced by fatty acid infusion. J. Clin. Invest. **42**(6):860–66.
60. DAY, H.J., FEWELL, W., and SOLOFF, L.A. (1967). Thrombosis in the dog produced by single rapid infusions of long chain saturated fatty acids. Am. J. Med. Sci. **253**(1), 113–23.
61. HOAK, J.C. (1964). Structure of thrombi produced by injection of fatty acids. Brit. J. Exp. Pathol. **45,** 44–7.
62. PROST, R.J., DVOJAKOVIC, M. BARA, L., and SAMAMA, M. (1972). Effects of saturated and unsaturated fatty acids on blood platelet aggregation in vitro and after injection into rabbits. Acta Univ. Carol., Med. Monogr. **53/54,** 403–7.
63. POLLACK, O.J. and WADLER, B. (1951). Experimental atherosclerosis. III. Anatomic alterations induced by intravascular injection of the cholesterol sols into animals. J. Gerontol. **6,** 217–28.
64. HARDING. H.E. (1958). Some inquiries into the toxicology of zinc stearate. Brit. J. Ind. Med. **15,** 130–32.
65. TARASENKO, N.Y., SHABALINA, L.P., and SPIRIDONOVA, V.S. (1976). Comparative toxicity of metal stearates. Int. Arch. Occup. Environ. Health **37**(3), 179–92.
66. CTFA. (May, 1970). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate Group. Three-month dermal toxicity, Sodium Stearate. Bath soaps and detergents. Product 78-74.*
67. GOTTSCHEWSKI, G.H.M. (1967). Can carriers of active ingredients in coated tablets have teratogenic effects? Arzneim. Forsch. **17,** 1100–103.
68. LITTON BIONETICS. (1976). Mutagenic evaluation of compound FDA 75-33, magnesium stearate. Report prepared under DHEW contract no. FDA 223-74-2104, Kensington, MD.
69. SWERN, D., WEIDER, R., MCDONOUGH, M., MERANCE, D.R., and SKIMKIN, M.B. (1970). Investigation of fatty acids and derivatives for carcinogenic activity. Cancer Res. **30,** 1037–46.
70. CLAYSON, D.B. (1962). Chemical Carcinogenesis, p. 341. Boston, MA: Little, Brown and Co.
71. VAN DUUREN, B.L., KATZ, C., SHIMKIN, M.B., SWERN, D., and WIEDER, R. (1972). Replication of low-level carcinogenic activity bioassays. Cancer Res. **32,** 880–81.
72. DEICHMANN, W.B., RADOMSKI, J.L., MACDONALD, W.E., KASCHT, R.L., and ERDMANN, R.L. (1958). The chronic toxicity of octadecylamine. Arch. Industr. Health **18,** 483–87.
73. BOYLAND, E., BUSBY, E.R., DUKES, C.E., GROVER, P.L., and MANSON, D. (1964). Further experiments on implantation of materials into the urinary bladder of mice. Brit. J. Cancer **18**(3), 575–81.
74. AVON PRODUCTS. (March 13, 1975). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate group. Clinical Evaluation Report: Human Patch Test. Ammonium Stearate.*
75. AVON PRODUCTS. (Jan. 16, 1973). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate group. Evaluation of the Irritancy Potential of Sodium Stearate C-6.*
76. CTFA. (June 13, 1978). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate Group. Primary Irritancy/Sensitization, Sodium Stearate. Product Type/In-House Code: DS 5011-0 Stick Deodorant. Test No.: H-1452.*
77. CTFA. (July, 1978). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate Group. Primary Irritancy/Sensitization, Sodium Stearate. Product Type/In-House Code: DS 5011-0 Stick Deodorant. Test No.: H-1478.*
78. CTFA. (Nov., 1978). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate Group. Primary Irritancy/Sensitization, Sodium Stearate. Product Type/In-House Code: DS 5011-0 Stick Deodorant. Test No.: H-1525.*
79. CTFA. (July, 1975). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate Group. Twenty-one day human cumulative irritation, Sodium Stearate. Bath soaps and detergents. Product 78-74.*

80. CTFA. (Oct. and Dec. 1975). Submission of data by CTFA. Unpublished safety data on Lithium Stearate Group. Human skin sensitization, Sodium Stearate. Bath soaps and detergents. Product 78-74.*
81. CTFA. (March 26, 1976). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate Group. Schwartz-Peck Prophetic Patch Test and Draize-Shelanski Repeated Insult Patch Test. Zinc Stearate (10 percent) in eyeshadow 923-100.*
82. CTFA. (March 29, 1978). Submission of data by CTFA. Unpublished safety data on the Lithium Stearate Group. Schwartz-Peck Prophetic Patch Test and Draize-Shelanski Repeated Insult Patch Test. Zinc Stearate (10 percent) in eyeshadow 923-100.*
83. CTFA. (Jan. 24, 1977). Submission of data by CTFA. Unpublished safety data on Lithium Stearate Group. Human usage test. Zinc Stearate (10 percent) in eyeshadow 923-100.*
84. HURLEY, H.J. and SHELLEY, W. (1959). The colloidal state as a stimulus for non-allergic epitheloid granulomas: experimental studies in man with pure sodium stearate and palmitate. J. Invest. Dermatol. **33**(4), 203–19.
85. SCHMIDT-WILCKE, H.A., STEINHAGEN, P., STEINHAGEN, E., and MARTINI, G.A. (1975). Effect of fatty acids on the stimulated gastric secretion in man. Digestion **13**(1–2), 8–14.
86. WEBER, J., EINBRODT, H.J., and WEWER, B. (1976). Can zinc stearate cause lung fibrosis? (Case report). Beitr. Silikoseforsch. **28**(2), 103–16.
87. MURRAY, L.M. (1926). Analysis of sixty cases of drug poisoning. Arch. Pediatrics **43,** 193–96.
88. HEIMAN, H. and ASCHNER, P.W. (1922). The aspiration of stearate of zinc in infancy. A clinical and experimental study. Am. J. Dis. Child. **0,** 503–10.
89. GOSSELIN, R.E., HODGE, H.C., SMITH, R.P., and GLEASON, M.N. (1976). *Clinical Toxicology of Commercial Products,* 4th ed. Baltimore, MD: Williams and Wilkins Co.

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Amended Safety Assessment of Tall Oil Acid, Sodium Tallate, Potassium Tallate, and Ammonium Tallate

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Abstract

Tall oil acid is a mixture of oleic and linoleic acids (fatty acids) and rosin acids derived from tall oil, a by-product of pulp from resinous woods, used in cosmetic products as a surfactant at concentrations up to 8%. Ammonium, potassium, and sodium salts also are listed as cosmetic ingredients. In addition to the studies summarized in this report, extensive toxicity, genotoxicity, and carcinogenicity studies in animals are available for oleic, lauric, palmitic, myristic, and stearic fatty acids as published earlier by the Cosmetic Ingredient Review (CIR). These data may be extrapolated to tall oil acid and its salts. There are no reports of current uses or use concentration data for ammonium tallate, nor are use concentration data available for the other salts. The CIR Expert Panel found tall oil acid, ammonium tallate, potassium tallate, and sodium tallate to be safe cosmetic ingredients in the given practices of use and concentration.

Keywords

safety, cosmetics, Tall Oil Acid, tallates

The Cosmetic Ingredient Review (CIR) Expert Panel previously evaluated the safety of tall oil acid in cosmetics, finding it to be safe for use in cosmetic products.[1] The Expert Panel considered that the available data in that safety assessment were sufficient to also support the safety of the salts of tall oil acid that are used in cosmetics. This report, therefore, is an amended safety assessment of tall oil acid that includes sodium tallate, potassium tallate, and ammonium tallate as used in cosmetics. This safety assessment includes new data on tall oil acid, along with all available data addressing the safety of the sodium, potassium, and ammonium salts.

Because tall oil contains fatty acids, the CIR Expert Panel also considered relevant its earlier safety assessment of oleic, palmitic, myristic, and stearic acids and the finding that these fatty acids were safe for use in cosmetics.[2] In 2006, the Expert Panel considered all newly available data on these fatty acids and reaffirmed that conclusion.[3]

Chemistry

Tall Oil Acid

According to the *International Cosmetic Ingredient Dictionary and Handbook*, tall oil acid (CAS No. 61790-12-3) is the mixture of rosin acids and fatty acids recovered from the hydrolysis of tall oil (Table 1).[4]

Some technical and other names and trade names for tall oil acid given in the *International Cosmetic Ingredient Dictionary and Handbook* include the following[4]:

Technical and other names

- Acids, tall oil
- Fatty acids, tall oil

Trade names

- Actinol EPG
- Actinol FA-1
- Actinol FA-2
- Pamak 4

Sodium Tallate

According to the *International Cosmetic Ingredient Dictionary and Handbook*, sodium tallate (CAS No. 61790-45-2) is the sodium salt of tall oil acid (qv).[4]

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Table 1. Definitions and Functions of Tall Oil Acid and Its Salts as Given in the *International Cosmetic Ingredient Dictionary and Handbook*[4]

Ingredient	Definition	Function(s)
Tall oil acid	Mixture of rosin acids recovered from the hydrolysis of tall oil	Surfactants, cleansing agents Surfactants, emulsifying agents
Ammonium tallate	The ammonium salt of tall oil acid	Surfactants, cleansing agent
Potassium tallate	The potassium salt of tall oil acid	Surfactants, cleansing agents Surfactants, emulsifying agents
Sodium tallate	The sodium salt of tall oil acid	Surfactants, cleansing agents Surfactants, emulsifying agents

Potassium Tallate

According to the *International Cosmetic Ingredient Dictionary and Handbook*, potassium tallate (CAS No. 61790-44-1) is the potassium salt of tall oil acid (qv).[4] A synonym for potassium tallate is tall oil acid, potassium salt. A trade name mixture is Akypogene ZA 97 SP.

The Environmental Protection Agency reported the following synonyms for this chemical[5]:

- Fatty acids, tall-oil, potassium salts
- Tall oil, potassium salt
- Potassium soap of tall oil fatty acids (C18)
- Tall oil acids, potassium salt
- Tall oil fatty acid potassium soap

Ammonium Tallate

According to the *International Cosmetic Ingredient Dictionary and Handbook*, ammonium tallate (CAS No. 68132-50-3) is the ammonium salt of tall oil acid (qv).[4] Some technical and other names for ammonium tallate include fatty acids, tall oil, ammonium salts and tall oil fatty acids, and ammonium salts.

Physical and Chemical Properties and Composition

Tall oil acid, as used in cosmetic products, is a clear, pale-yellow liquid with a characteristic fatty odor and consists mainly of oleic acid (40%), linoleic acid (38%), other fatty acids (13%), and rosin acids (0.6%). Tall oil acid is soluble in most polar and nonpolar organic solvents, but it is insoluble in water.[6]

The chemical and physical properties of tall oil acid, sodium tallate, potassium tallate, and ammonium tallate are presented in Table 2.

Dybdahl[7] reported that the octanol/water partition coefficient (log P_{ow}) for fatty acids in tall oil acid ranged from 4.4 to 8.3 at pH 2 and from 3.6 to 7.4 at pH 7.5. A mixture of 7 materials with known log P_{ow} values was used for reference.[7]

According to Whitman,[8] tall oil acid is composed mainly of palmitic acid, stearic acid, oleic acid, and linoleic acid, which are all natural products derived from the pulping of pine trees. All of these fatty acids are labeled "generally recognized as safe" (GRAS) food additives by the Food and Drug Administration (FDA).[9]

Table 2. Physical and Chemical Properties and Chemical Class of Tall Oil Acid, Sodium Tallate, Potassium Tallate, and Ammonium Tallate

Ingredient and Properties	Value/Description
Tall oil acid	
Chemical class[4]	Fatty acids[4]
Description	Pale color, oily liquid[22]
Iodine value (Wijs)[31]	130
Saponification value[31]	200
Rosin acids (%)[31]	0.5
Unsaponifiables (%)[31]	0.5
Color (Gardner)[31]	1
Flash point, Cleveland Open Cup test[31]	400 °F
Specific gravity at 25°C	0.897
Viscosity (cps, at 25°C)[31]	20
Sodium tallate	
Chemical class[4]	Soaps[4]
Potassium tallate	
Chemical class[4]	Soaps[4]
Ammonium tallate	
Chemical class[4]	Soaps[4]

Taylor and King[10] reported that tall oil is a dark, odorous liquid.[10] Fatty acids, rosin acids, sterols, and other compounds mainly make up this resinous material. The chemical composition of tall oil varies with the age, species, and geographical location of the source coniferous trees. The resin acids are diterpene carboxylic acids based on an alkyl-substituted perhydrophenanthrene ring structure, and the fatty acids are predominantly 18-carbon, straight-chain mono-unsaturated or di-unsaturated fatty acids.

The Pine Chemicals Association[11] reported that the following chemicals are collectively known as tall oil fatty acids and tall oil fatty acid salts:

- CAS No. 61790-12-3, fatty acids, tall-oil (tall oil acid)
- CAS No. 65997-03-7, fatty acids, tall oil, low boiling
- CAS No. 68955-98-6, fatty acids, C16-C18 and C18 unsaturated, branched and linear
- CAS No. 68201-37-6, octadecanoic acid, branched and linear
- CAS No. 61790-44-1, fatty acids, tall oil, potassium salts (potassium tallate)

Table 3. Composition of Typical Tall Oil Fatty Acid[11]

Common Name	Chemical Structure	Percentage of Composition
Palmitic acid	$CH_3(CH_2)_{14}COOH$	1
Stearic acid	$CH_3(CH_2)_{16}COOH$	2
Oleic acid	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	48
Linoleic acid	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	35
Conjugated linoleic acid[a]	$CH_3(CH_2)_xCH{=}CHCH{=}CH{-}(CH_2)_yCOOH$	7
Other acids[b]	—	4
Unsaponifiable matter	—	2

[a] $x + y = 12$; x usually 4 or 5; y usually 7 or 8.
[b] Other acids include 5,9,12-octadecatrienoic acid; linoleic acid; 5,11,14-eicosatrenoic acid; cis,cis-5,9-octadecadienoic acid; eicosadienoic acid; elaidic acid; cis-11 octadecanoic acid; C-20, C-22, C-24 saturated fatty acids.

- CAS No. 61790-45-2, fatty acids, tall oil, sodium salts (sodium tallate)

Tall oil fatty acids and their derivatives are composed of a complex mixture and are often difficult to characterize. Their composition is variable. The melting point cannot be measured because these substances either will not give a sharp melting point when heated or will decompose before they melt. Tall oil fatty acid and all other nonsalts in this category are liquids at room temperature. Boiling points cannot be determined because these substances will decompose before they boil. Under ambient conditions, the vapor pressure of these chemicals is essentially zero, and experimental measurement is not possible. The partition coefficients can yield a range of values representing the various components rather than a single value representing the mixture.

The composition of a given tall oil fatty acid depends on the origin of the tall oil and the fractionation conditions used for its production. The composition of a typical tall oil fatty acid provided by Pine Chemicals Association[11] is shown in Table 3.

According to Waylan et al,[12] modified tall oil (from which tall oil acid is derived) has a high content of conjugated linoleic acid (67.4%) from further processing the fatty acid portion of tall oil.

Use

Cosmetics

Balsam and Sagarin described tall oil acid as a substitute for oleic acid or other fatty acids in formulating cosmetics.[13] According to these authors, tall oil acid is converted to a soap by reaction with bases and then used primarily as a conditioner or emulsifier in hair dyes and bleaches.

The Pine Chemicals Association stated that tall oil fatty acid salts are widely used as surfactants in liquid soaps.[11]

As given in the *International Cosmetic Ingredient Dictionary and Handbook*, tall oil acid functions as a surfactant (cleansing agent and emulsifying agent) in cosmetics.[4] The tall oil acid salts also function as surfactants (cleansing agents and emulsifying agents) in cosmetics.

Manufacturers report current uses of cosmetic ingredients, as a function of product type, to the US FDA under the Voluntary Cosmetic Registration Program (VCRP). Use concentration data are obtained from a survey of the industry done by the industry trade association, formerly the Cosmetic, Toiletry, and Fragrance Association (CTFA) and now the Personal Care Products Council.

Table 4 presents the current product uses reported under the VCRP for tall oil acid, sodium tallate, and potassium tallate in cosmetics along with the total number of products in each category.[14] For example, of a total of 135 shaving cream products, only 1 use of tall oil acid was reported. Clearly, most shaving cream products do not contain tall oil acid. The industry survey done by CTFA reported use concentrations for tall oil acid from 0.6% to 8.0%.[15] No use concentration data were reported for the tall oil acid salts, and no product uses for ammonium tallate were reported under the VCRP.[14-16]

Noncosmetic

As included in the Code of Federal Regulations (CFR), the FDA has approved tall oil acid for use as an indirect food additive and defoaming agent used in the manufacture of paper and paperboard products and coatings of articles intended for use in packaging, transporting, or holding food (21CFR parts 176.200, 176.210, and 720.4).

The use of tall oil acid in preparations of edible oils and edible fat compositions has been patented.[17,18] Tall oil acid is used as a raw material for protective coatings, particularly in alkyd resins, soaps, detergents, and disinfectants.[19]

Pearl[20] stated that large quantities of tall oil acid are used as intermediate chemicals; they are further processed or modified chemically before being incorporated into a product or used in production.

Tall oil acid and its derivatives are used in the manufacturing of rubber, paper, soaps and detergents, printing inks, metalworking fluids, corrosion inhibitors, and plasticizers.[11,21,22]

General Biology

Absorption, Distribution, Metabolism, Excretion

No data are available on absorption, distribution, metabolism, and excretion.

Table 4. Current Uses and Concentrations of Tall Oil Acid, Sodium Tallate, and Potassium Tallate in Cosmetics

Product Category	Ingredient Uses (Total No. of Products in Category)[14]	Use Concentrations, %[15]
Tall oil acid		
Hair coloring preparations		
Hair dyes	NR (1600)[a]	0.6 (0.3 after dilution)
Personal hygiene products		
Other personal hygiene products	3 (390)	NR[a]
Shaving preparations		
Shaving cream	1(135)	NR[a]
Skin care preparations		
Skin cleansing creams, lotions, liquids, and pads	2 (1009)	8
Total uses/ranges for tall oil acid	6	8
Sodium tallate		
Personal hygiene products		
Other personal hygiene products	6 (390)	NR[a]
Total uses/ranges for sodium tallate	6	NR
Potassium tallate		
Personal hygiene products		
Other personal hygiene products	9 (390)	NR[a]
Total uses/ranges for potassium tallate	9	NR

NR, data not reported.

[a] In some cases, ingredient uses were not reported to FDA in the voluntary industry product survey program, but concentrations were provided. In other cases, the uses were reported, but no concentration was provided.

Animal Toxicology

Acute Oral Toxicity

Mallory[23] reported on an acute oral toxicity study in Sprague-Dawley rats (10 males, 10 females). Each animal received a single oral gavage dose of 10 000 mg/kg tall oil acid and were observed for 14 days. Parameters evaluated included clinical signs, mortality, body weight, and gross pathology. None of the animals died. One hour after dosing, piloerection was observed in 1 male, and abnormal stance was observed in 1 male and 1 female. By 4 hours, these effects had resolved. No body weight effects were observed. Gross necropsy revealed no treatment-related effects. The acute oral median lethal dose of tall oil acid was greater than 10 000 mg/kg.

Short-Term Oral Toxicity

An experiment was conducted to study the effect of tall oil acid distillate on the growth of rats. The distillate used in this study was described by the authors as containing 1.8% to 2.2% rosin and 2.8% to 3.2% unsaponifiable matter. It was composed of 42.8% linoleic acid, 38.8% oleic acid, and 17.4% other fatty acids. Male weanling Sprague-Dawley rats, 10 per group and weighing 40 to 60 g, were fed diets containing 15%, 30%, and 60% of the total calories as tall oil acid distillate for 4 weeks. Control groups received diets containing the same percentages of soybean oil. Feed consumption and body weight were measured at least every other day. The growth rate of animals fed a diet with 15% tall oil acid distillate did not differ significantly from that of the control group. Animals in the group receiving 30% of their calories from tall oil acid distillate had a significantly lower growth rate than did the controls, and their feed consumption was slightly more than half that of the control group. One animal in the 15% group died during the experiment. All 10 of the animals in the 60% group died in the first 4 days of the start of the experiment. The author concluded that there was "a growth-retarding or possibly a toxic factor in the tall oil fatty acid distillate."[24]

Subchronic Oral Toxicity Study

Fancher[25] reported on a 90-day subchronic oral toxicity of tall oil fatty acid in albino rats. Tall oil fatty acid was administered to Charles River rats (10 males, 10 females) in the diet at concentrations of 0%, 5%, 10%, or 25% for 90 days. The approximate doses were 0, 2500, 5000, or 12 500 mg/kg/d. Two control rats died during blood sampling. No other deaths occurred and no clinical signs were observed. Body weight and body weight gain were not affected by treatment, but food consumption was slightly decreased at 10% and 25%. No changes in hematology, clinical chemistry, or urinalysis parameters occurred at any dose. At gross pathology, no treatment-related effects were noted at any dose. No consistent organ weight changes and no histopathological effects were reported. Based on these data, the no observed effect level (NOEL) was 5% (approximately 2500 mg/kg/d).

Chronic Toxicity and Irritation

Data on chronic toxicity, ocular irritation, mucosal irritation, and dermal irritation were not available.

Reproductive and Developmental Toxicity

Tall oil acid had no effects when tested for reproductive and developmental toxicity in Sprague-Dawley rats in a full 2-generation study.[26] The test material was administered in the diet at concentrations of 0%, 5%, or 10% to 30 females per group and 15 males per group. The approximate doses were 0, 2500, and 5000 mg/kg/d. Males and females (F0) began treatment at 80 days of age and were mated at 100 days of age. Treatment of the F0 animals continued through the weaning of the first generation (F1). After weaning, the F1 males and females were maintained on the treatment diet. At 100 days of age, they were mated and allowed to deliver pups (F2).

There were no treatment-related effects on reproductive performance or on any parameter measured in either the F1 or F2 pups. No treatment-related changes in fertility, viability, lactation, or gestation indices were observed. Hematology, clinical chemistry, and urinalysis parameters were similarly unchanged, and there were no developmental effects in any F1 or F2 offspring. Tall oil acid did not alter or otherwise affect the reproduction or development of rats in this study at doses as high as 10% (approximately 5000 mg/kg/d).[26]

A 2-generation reproduction study was conducted in which tall oil acid was fed to Charles River CD Sprague-Dawley rats. The rats were classified into 5 groups each consisting of 15 males and 30 females. The experimental groups included negative control, 5% tall oil acid, 10% tall oil acid, 5% oleic acid, and 10% oleic acid. Tall oil acid used in this study was only described as a clear amber-colored liquid with a heavy odor similar to a vegetable oil. The rats (the F0 generation) were fed the test diets for approximately 3 weeks and were then put in mating cages with 1 male and 2 females per cage. The F1 litter was weaned onto the test chemical diets, and 20 female and 20 male rats were carried on to sexual maturity, having been fed the test diet for approximately 180 days, for each of the 5 test groups. These rats were then arranged in mating groups, and the following parameters were measured for the parents and offspring: mating behavior, number of pregnant dams, total number of pups (live born, stillborn, number discarded on day 4, and number alive on day 21), average number of pups per litter (born, day 4, and weaned), and the average weaning weight of the pups. The fertility, viability, lactation, and gestation indices were computed. Clinical chemistry determinations were made for 5 male and 5 female rats from each test group of the F1 generation. Rats from each test group of the F1 generation, 10 males and 10 females, were examined for any abnormalities occurring in hematologic and urinalysis values and organ weights. All rats, whether they died or were killed, were necropsied. No treatment-related effects were found. Several animals had lesions of chronic respiratory and renal diseases, which are endemic in this strain of rat.[27]

Genotoxicity

Godek[28] reported that tall oil fatty acid was not mutagenic in the Ames assay. It was tested for mutagenicity in *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538 at concentrations of 100, 1000, and 10 000 μg per plate, with and without metabolic activation. Information regarding the controls was not provided. No increases in mutation frequency were reported at any concentration, with or without metabolic activation. Tall oil acid was not mutagenic in this assay, and there are no in vivo genotoxicity data using mammalian cells.

Carcinogenicity

No carcinogenicity studies using these cosmetic ingredients were available.

Clinical Assessment of Safety

Dermal Irritation

CTFA[29] reported that tall oil acid in a liquid soap was tested for dermal irritancy potential. The soap contained 12% tall oil acid and was tested at a concentration of 25% in water for a total tested concentration of 3% tall oil acid. The controlled use study was performed according to the CTFA testing guidelines.[30] This type of study is expected to detect adverse reactions under the conditions of expected normal use. The hands and fingers of 54 subjects were examined every week during the 4 weeks of in-use study. No positive reactions occurred during the test, and the soap was nonirritating.

A prophetic patch test also was conducted with a liquid soap containing 12% tall oil acid. The formulation was tested undiluted. The 100 subjects received 2 patches 10 to 14 days apart; both open and closed patches were used. None of the subjects had positive reactions at any of the patch sites. The soap formulation was nonirritating.[29]

Dermal Sensitization and Photosensitization

A liquid soap containing 12% tall oil acid was tested in a repeat-insult patch test. The soap formulation was tested undiluted. A total of 11 patches were applied to the skin of 50 panelists. It was not stated how long the patches stayed in contact with the skin or at what interval the patches were applied. The subjects were exposed to ultraviolet light, of an unspecified wavelength, at patch numbers 1, 4, 7, 10, and 11. No positive reactions were observed at open or closed patch sites. The soap formulation was determined to be nonsensitizing and nonphotosensitizing.[29]

Summary

Tall oil acid is a mixture of oleic and linoleic fatty acids and rosin acids derived from the hydrolysis of tall oil, a by-product of pulp from resinous woods (mainly pine). Safety assessments of the oleic and linoleic acids previously were reported. The salts of tall oil acid also were included in this

safety assessment, including sodium tallate, potassium tallate, and ammonium tallate.

Tall oil acid was reported in 2006 to be used in a small number of formulations at concentrations ranging from 0.6% to 8%. Similar numbers of uses were reported for sodium and potassium tallate, although no use concentration data were available. Ammonium tallate was not reported to be used.

When fed to rats as 15% of total caloric intake, tall oil acid was nontoxic. At 30% and 60% of total caloric intake, tall oil acid had a growth-retarding or toxic effect. Growth was reduced in rats fed tall oil acid at 6% of their diet by mass, equal to 15% of the total calories. The subchronic oral NOEL was 5%.

No treatment-related effects were observed in rats used in a 2-generation feeding study. The rats were fed diets containing 5% and 10% tall oil acid.

Tall oil acid was determined to be nonmutagenic in the Ames assay when tested at concentrations of 100, 1000, and 10 000 μg/plate.

Liquid soap formulations containing up to 12% tall oil acid did not cause dermal irritation, sensitization, or photosensitization in human subjects in a repeat insult patch test.

Discussion

The CIR Expert Panel recognized that there are limited animal and human toxicity data and dermal irritation/sensitization studies for tall oil acid. Tall oil acid is, however, known to be composed of fatty acids for which safety test data were available.

When considered with the subchronic and chronic oral toxicity, reproductive and developmental toxicity, genotoxicity, carcinogenicity, and photosensitization studies available for oleic acid, lauric acid, palmitic acid, myristic acid, and stearic acid, the available data for tall oil acid itself are a sufficient basis for reaching a conclusion regarding tall oil acid. It is the experience of the panel in its review of fatty acids of varying carbon chain lengths that there is little difference in toxicity.

The panel also considered that there is little difference between members of this family of salts of tall oil acid. The salts are expected to be dissociated in any product formulation independent of whether the salt is sodium, potassium, or ammonium. Accordingly, the available data for tall oil acid are considered supportive of the safety of the entire group as used in cosmetics.

The CIR Expert Panel recognizes that there are data gaps regarding use and concentration of these ingredients. However, the overall information available on the types of products in which these ingredients are used and at what concentrations indicates a pattern of use, which was considered by the Expert Panel in assessing safety.

Conclusion

The CIR Expert Panel concluded that tall oil acid, sodium tallate, potassium tallate, and ammonium tallate are safe as cosmetic ingredients in the practices of use and concentration as described in this safety assessment. In the case that ingredients in this group not in current use are used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in the group.

Authors' Note

Unpublished sources cited in this report are available from the Director, Cosmetic Ingredient Review, 1101 17th Street, Suite 412, Washington, DC 20036, USA.

Declaration of Conflicting Interests

No potential conflict of interest relevant to this article was reported. F. Alan Andersen and Valerie Robinson are employed by the Cosmetic Ingredient Review.

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References

1. Elder RL. Final report on the safety assessment of tall oil acid. *J Am Coll Toxicol.* 1989;8:769-776.
2. Elder RL. Final report on the safety assessment of oleic acid, lauric acid, palmitic acid, myristic acid, and stear acid. *J Am Coll Toxicol.* 1987;6:321-402.
3. Andersen FA, ed. Annual review of cosmetic ingredient safety assessments—2004/2005. *Int J Toxicol.* 2006;25(suppl 2):40-47.
4. Gottschalck TE, Bailey J. *International Cosmetic Ingredient Dictionary and Handbook.* 12th ed. Washington, DC: CTFA; 2008.
5. Environmental Protection Agency. Tall oil fatty acids, potassium salts. 2007. Substance Registry System. http://iaspub.epa.gov. Accessed June 6, 2007.
6. Estrin NF, Crosely PA, Haynes CR. *CTFA Cosmetic Ingredient Dictionary.* 3rd ed. Washington DC: CTFA; 1982.
7. Dybdahl HP. Determination of Log Pow for single components in distilled tall oil. Horshplm, Denmark, Water Quality Institute; 1993. GLP Study No. 408335/475. http://www.epa.gov/hpv/pubs/summaries/tofars/c13055rs.pdf.
8. Whitman CT. Comments on HPV test plan and robust summaries for tall oil fatty acids and related substances. 2001. http://www.pcrm.org. Accessed February 13, 2006.
9. Food and Drug Administration. Food additives. *Fed Reg.* 1999;64:48665.
10. Taylor SL, King JW. Fatty and resin acid analysis in tall oil products via supercritical fluid extraction-supercritical reaction using enzymatic catalysis. *J Chromatogr Sci.* 2001;39:269-272.
11. Pine Chemicals Association. *HPV Test Plans and Robust Summaries for Tall Oil and Related Substances and Tall Oil Fatty Acids and Related Substances.* Atlanta, Ga: Pine Chemicals Association; 2001.
12. Waylan AT, O'Quinn PR, Unrah JA, et al. Effects of modified trall oil and vitamin E on growth performance, carcass characteristics, and meat quality of growing-finishing pigs. *J Anim Sci.* 2002;80:1575-1585.
13. Balsam MS, Sagarin E. *Cosmetics: Science and Technology.* New York, NY: John Wiley; 1972.

14. FDA. *Frequency of Use of Cosmetic Ingredients*. Silver Spring, Md: US Food and Drug Administration; 2006.
15. CTFA. *Concentration of Use Information for Proposed Additions to the December 2006 Re-reviews: Potassium Tallate and Sodium Tallate*. Washington, DC: Cosmetic, Toiletry, and Fragrance Association. Unpublished data submitted by CTFA; 2007.
16. Personal Care Products Council. *Concentration of Use: Additional Tall Oil Acid Ingredients*. Washington, DC: Personal Care Products Council. Unpublished data submitted by the Council; 2008.
17. Canada Packers, Ltd. *Edible Oils From Tall Oil Fatty Acids*. 12-16-1964. (978,085):Britain.
18. Canada Packers, Ltd. Edible Fat Compositions Containing Glycerides of Tall Oil Fatty Acids. 12-16-1964. Britain.
19. Swer D. *Bailey's Industrial Oil and Fat Products*. 4th ed. New York, NY: John Wiley; 1979.
20. Pearl I. Utilization of by-products of the pulp and paper industry. *Tappi*. 1982;65:72-73.
21. Mead Westvaco.Tall oil fatty acids. 2006. http://www.meadwestvaco.com. Accessed February 13, 2006.
22. Eastman Chemical Company. Pamak 4 tall oil fatty acid. 2006. http://www.eastman.com. Accessed February 13, 2006.
23. Mallory VT. *Acute Oral Toxicity Study in Rats: Fatty* [product name deleted]. Waverly, Pa: Pharmakon Research International; 1983. Study No. PH 402-AC-009-83.
24. Sappanen R. Studies on the use of tall oil fatty acids in the diet of rats. *Ann Acad Sci Finn*. 1969;[A]:7-85.
25. Fancher OE. *Ninety-Day Subacute Oral Toxicity of* [trade name deleted; tall oil fatty acid] *in Albino Rats*. Northbrook, Ill: Industrial Bio-Test Laboratories; 1969. Study No. PH 301 D-AC-018-83.
26. Tegeris AS. *Tall Oil Fatty Acid: Two-Generation Reproduction Study in the Rat*. Laurel, Md: Pharmacopathics Reserach Laboratories; 1977. Report No. 77-1 24.
27. Pharmacopathics in Research Laboratories. *Two Generation Reproduction Study in the Rat: Tall Oil Fatty Acids*. Laurel, Md: Pharmacopathics in Research Laboratories; 1977. Report No. 7410.
28. Godek EG. *Amee Salmonella/Microsome Plate Test: Fatty Acid* [trade name deleted]. Waverly, Pa: Pharmakon Research International; 1983. Study No. PH 301 D-AC-018-83.
29. CTFA. Washington, DC: Cosmetic, Toiletry, and Fragrance Association. Unpublished data submitted by CTFA; 1982.
30. McEwen GN Jr, Curry AS. Guidelines for Controlled Use Studies. *CTFA Technical Guidelines. Safety Testing Guidelines*. Washington, DC: Cosmetic, Toiletry, and Fragrance Association; 1985.
31. Estrin NF, Haynes CR, Whelan JM. *Cosmetic Ingredient Descriptions*. Washington, DC: Cosmetic, Toiletry, and Fragrance Association; 1982.

2018 FDA VCRP RAW DATA			
03B - Eyeliner	300925	ALUMINUM DISTEARATE	1
03C - Eye Shadow	300925	ALUMINUM DISTEARATE	1
03F - Mascara	300925	ALUMINUM DISTEARATE	2
03G - Other Eye Makeup Preparations	300925	ALUMINUM DISTEARATE	2
06G - Hair Bleaches	300925	ALUMINUM DISTEARATE	3
07A - Blushers (all types)	300925	ALUMINUM DISTEARATE	1
07B - Face Powders	300925	ALUMINUM DISTEARATE	4
07C - Foundations	300925	ALUMINUM DISTEARATE	2
07E - Lipstick	300925	ALUMINUM DISTEARATE	1
07F - Makeup Bases	300925	ALUMINUM DISTEARATE	2
07H - Makeup Fixatives	300925	ALUMINUM DISTEARATE	1
07I - Other Makeup Preparations	300925	ALUMINUM DISTEARATE	1
12C - Face and Neck (exc shave)	300925	ALUMINUM DISTEARATE	1
12F - Moisturizing	300925	ALUMINUM DISTEARATE	1
03B - Eyeliner	7047849	ALUMINUM STEARATE	1
03C - Eye Shadow	7047849	ALUMINUM STEARATE	2
03D - Eye Lotion	7047849	ALUMINUM STEARATE	1
03F - Mascara	7047849	ALUMINUM STEARATE	2
05G - Tonics, Dressings, and Other Hair Grooming Aids	7047849	ALUMINUM STEARATE	2
06G - Hair Bleaches	7047849	ALUMINUM STEARATE	1
07C - Foundations	7047849	ALUMINUM STEARATE	6
07F - Makeup Bases	7047849	ALUMINUM STEARATE	6
08C - Nail Creams and Lotions	7047849	ALUMINUM STEARATE	1
12C - Face and Neck (exc shave)	7047849	ALUMINUM STEARATE	12
12D - Body and Hand (exc shave)	7047849	ALUMINUM STEARATE	1
12F - Moisturizing	7047849	ALUMINUM STEARATE	9
12G - Night	7047849	ALUMINUM STEARATE	2
12J - Other Skin Care Preps	7047849	ALUMINUM STEARATE	3
13A - Suntan Gels, Creams, and Liquids	7047849	ALUMINUM STEARATE	1
03F - Mascara	977165766	ALUMINUM STEARATES	1
12F - Moisturizing	977165766	ALUMINUM STEARATES	1
12G - Night	977165766	ALUMINUM STEARATES	1
12C - Face and Neck (exc shave)	637127	ALUMINUM TRISTEARATE	1
12G - Night	637127	ALUMINUM TRISTEARATE	1
03A - Eyebrow Pencil	1002897	AMMONIUM STEARATE	1

03F - Mascara	1002897	AMMONIUM STEARATE	3
03F - Mascara	506309	ARACHIDIC ACID	5
08E - Nail Polish and Enamel	506309	ARACHIDIC ACID	1
12A - Cleansing	506309	ARACHIDIC ACID	2
12D - Body and Hand (exc shave)	506309	ARACHIDIC ACID	1
01B - Baby Lotions, Oils, Powders, and Creams	112856	BEHENIC ACID	2
03A - Eyebrow Pencil	112856	BEHENIC ACID	4
03D - Eye Lotion	112856	BEHENIC ACID	1
03F - Mascara	112856	BEHENIC ACID	11
04B - Perfumes	112856	BEHENIC ACID	1
04E - Other Fragrance Preparation	112856	BEHENIC ACID	1
05A - Hair Conditioner	112856	BEHENIC ACID	3
05E - Rinses (non-coloring)	112856	BEHENIC ACID	1
05F - Shampoos (non-coloring)	112856	BEHENIC ACID	2
05G - Tonics, Dressings, and Other Hair Grooming Aids	112856	BEHENIC ACID	2
05I - Other Hair Preparations	112856	BEHENIC ACID	3
06D - Hair Shampoos (coloring)	112856	BEHENIC ACID	1
07C - Foundations	112856	BEHENIC ACID	4
07E - Lipstick	112856	BEHENIC ACID	3
07F - Makeup Bases	112856	BEHENIC ACID	3
07G - Rouges	112856	BEHENIC ACID	2
07I - Other Makeup Preparations	112856	BEHENIC ACID	3
10A - Bath Soaps and Detergents	112856	BEHENIC ACID	4
10B - Deodorants (underarm)	112856	BEHENIC ACID	29
11A - Aftershave Lotion	112856	BEHENIC ACID	1
12A - Cleansing	112856	BEHENIC ACID	24
12C - Face and Neck (exc shave)	112856	BEHENIC ACID	5
12D - Body and Hand (exc shave)	112856	BEHENIC ACID	4
12F - Moisturizing	112856	BEHENIC ACID	6
12G - Night	112856	BEHENIC ACID	2
12H - Paste Masks (mud packs)	112856	BEHENIC ACID	1
12J - Other Skin Care Preps	112856	BEHENIC ACID	2
05A - Hair Conditioner	999004013	C14-28 ALKYL ACID	12
05F - Shampoos (non-coloring)	999004013	C14-28 ALKYL ACID	11
06C - Hair Rinses (coloring)	999004013	C14-28 ALKYL ACID	1
06D - Hair Shampoos (coloring)	999004013	C14-28 ALKYL ACID	1
12F - Moisturizing	999004013	C14-28 ALKYL ACID	1

05A - Hair Conditioner	999004012	C14-28 ISOALKYL ACID	12
05F - Shampoos (non-coloring)	999004012	C14-28 ISOALKYL ACID	11
06C - Hair Rinses (coloring)	999004012	C14-28 ISOALKYL ACID	1
06D - Hair Shampoos (coloring)	999004012	C14-28 ISOALKYL ACID	1
05B - Hair Spray (aerosol fixatives)	3578721	CALCIUM BEHENATE	1
03B - Eyeliner	1592230	CALCIUM STEARATE	3
03C - Eye Shadow	1592230	CALCIUM STEARATE	208
04E - Other Fragrance Preparation	1592230	CALCIUM STEARATE	1
06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	1592230	CALCIUM STEARATE	1
06G - Hair Bleaches	1592230	CALCIUM STEARATE	4
07A - Blushers (all types)	1592230	CALCIUM STEARATE	13
07B - Face Powders	1592230	CALCIUM STEARATE	12
07C - Foundations	1592230	CALCIUM STEARATE	5
07E - Lipstick	1592230	CALCIUM STEARATE	3
07F - Makeup Bases	1592230	CALCIUM STEARATE	2
07G - Rouges	1592230	CALCIUM STEARATE	4
07I - Other Makeup Preparations	1592230	CALCIUM STEARATE	1
08G - Other Manicuring Preparations	1592230	CALCIUM STEARATE	1
10E - Other Personal Cleanliness Products	1592230	CALCIUM STEARATE	1
12A - Cleansing	1592230	CALCIUM STEARATE	1
12D - Body and Hand (exc shave)	1592230	CALCIUM STEARATE	2
12E - Foot Powders and Sprays	1592230	CALCIUM STEARATE	1
12A - Cleansing	334485	CAPRIC ACID	2
05G - Tonics, Dressings, and Other Hair Grooming Aids	124072	CAPRYLIC ACID	1
07A - Blushers (all types)	124072	CAPRYLIC ACID	1
07E - Lipstick	124072	CAPRYLIC ACID	2
12F - Moisturizing	124072	CAPRYLIC ACID	2
06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	6144281	DILINOLEIC ACID	71
12J - Other Skin Care Preps	5393817	HYDROXYCAPRIC ACID	1
12C - Face and Neck (exc shave)	92348624	HYDROXYCAPRYLIC ACID	2

12F - Moisturizing	92348624	HYDROXYCAPRYLIC ACID	1
12J - Other Skin Care Preps	92348624	HYDROXYCAPRYLIC ACID	1
07H - Makeup Fixatives	1679534	10-HYDROXYDECANOIC ACID	1
12A - Cleansing	1679534	10-HYDROXYDECANOIC ACID	2
12C - Face and Neck (exc shave)	1679534	10-HYDROXYDECANOIC ACID	1
12D - Body and Hand (exc shave)	1679534	10-HYDROXYDECANOIC ACID	1
12F - Moisturizing	1679534	10-HYDROXYDECANOIC ACID	3
12G - Night	1679534	10-HYDROXYDECANOIC ACID	2
12J - Other Skin Care Preps	1679534	10-HYDROXYDECANOIC ACID	1
03A - Eyebrow Pencil	1330707	HYDROXYSTEARIC ACID	6
03B - Eyeliner	1330707	HYDROXYSTEARIC ACID	3
03C - Eye Shadow	1330707	HYDROXYSTEARIC ACID	2
03G - Other Eye Makeup Preparations	1330707	HYDROXYSTEARIC ACID	2
04B - Perfumes	1330707	HYDROXYSTEARIC ACID	2
05G - Tonics, Dressings, and Other Hair Grooming Aids	1330707	HYDROXYSTEARIC ACID	2
07A - Blushers (all types)	1330707	HYDROXYSTEARIC ACID	3
07C - Foundations	1330707	HYDROXYSTEARIC ACID	1
07D - Leg and Body Paints	1330707	HYDROXYSTEARIC ACID	1
07E - Lipstick	1330707	HYDROXYSTEARIC ACID	60
07I - Other Makeup Preparations	1330707	HYDROXYSTEARIC ACID	20
08G - Other Manicuring Preparations	1330707	HYDROXYSTEARIC ACID	1
10B - Deodorants (underarm)	1330707	HYDROXYSTEARIC ACID	9
12A - Cleansing	1330707	HYDROXYSTEARIC ACID	2
12C - Face and Neck (exc shave)	1330707	HYDROXYSTEARIC ACID	3
12F - Moisturizing	1330707	HYDROXYSTEARIC ACID	4
12G - Night	1330707	HYDROXYSTEARIC ACID	1
12J - Other Skin Care Preps	1330707	HYDROXYSTEARIC ACID	2
03D - Eye Lotion	999001992	ISOMERIZED LINOLEIC ACID	7
07A - Blushers (all types)	999001992	ISOMERIZED LINOLEIC ACID	1
10E - Other Personal Cleanliness Products	999001992	ISOMERIZED LINOLEIC ACID	1
12D - Body and Hand (exc shave)	999001992	ISOMERIZED LINOLEIC ACID	4
12F - Moisturizing	999001992	ISOMERIZED LINOLEIC ACID	4
12G - Night	999001992	ISOMERIZED LINOLEIC ACID	2
12H - Paste Masks (mud packs)	999001992	ISOMERIZED LINOLEIC ACID	2
12J - Other Skin Care Preps	999001992	ISOMERIZED LINOLEIC ACID	1
01B - Baby Lotions, Oils, Powders,	30399849	ISOSTEARIC ACID	1

and Creams			
03B - Eyeliner	30399849	ISOSTEARIC ACID	2
03C - Eye Shadow	30399849	ISOSTEARIC ACID	4
03D - Eye Lotion	30399849	ISOSTEARIC ACID	1
03F - Mascara	30399849	ISOSTEARIC ACID	70
03G - Other Eye Makeup Preparations	30399849	ISOSTEARIC ACID	3
05A - Hair Conditioner	30399849	ISOSTEARIC ACID	1
05F - Shampoos (non-coloring)	30399849	ISOSTEARIC ACID	2
05G - Tonics, Dressings, and Other Hair Grooming Aids	30399849	ISOSTEARIC ACID	2
06B - Hair Tints	30399849	ISOSTEARIC ACID	1
06D - Hair Shampoos (coloring)	30399849	ISOSTEARIC ACID	1
07C - Foundations	30399849	ISOSTEARIC ACID	29
07E - Lipstick	30399849	ISOSTEARIC ACID	16
07F - Makeup Bases	30399849	ISOSTEARIC ACID	6
07H - Makeup Fixatives	30399849	ISOSTEARIC ACID	3
07I - Other Makeup Preparations	30399849	ISOSTEARIC ACID	3
10A - Bath Soaps and Detergents	30399849	ISOSTEARIC ACID	5
10B - Deodorants (underarm)	30399849	ISOSTEARIC ACID	2
10E - Other Personal Cleanliness Products	30399849	ISOSTEARIC ACID	13
11E - Shaving Cream	30399849	ISOSTEARIC ACID	1
12A - Cleansing	30399849	ISOSTEARIC ACID	12
12C - Face and Neck (exc shave)	30399849	ISOSTEARIC ACID	34
12D - Body and Hand (exc shave)	30399849	ISOSTEARIC ACID	13
12F - Moisturizing	30399849	ISOSTEARIC ACID	27
12G - Night	30399849	ISOSTEARIC ACID	5
12H - Paste Masks (mud packs)	30399849	ISOSTEARIC ACID	1
12I - Skin Fresheners	30399849	ISOSTEARIC ACID	1
12J - Other Skin Care Preps	30399849	ISOSTEARIC ACID	7
13B - Indoor Tanning Preparations	30399849	ISOSTEARIC ACID	2
13C - Other Suntan Preparations	30399849	ISOSTEARIC ACID	2
01C - Other Baby Products	143077	LAURIC ACID	1
02B - Bubble Baths	143077	LAURIC ACID	2
03E - Eye Makeup Remover	143077	LAURIC ACID	1
05A - Hair Conditioner	143077	LAURIC ACID	1
05F - Shampoos (non-coloring)	143077	LAURIC ACID	28
05G - Tonics, Dressings, and Other Hair Grooming Aids	143077	LAURIC ACID	4
05I - Other Hair Preparations	143077	LAURIC ACID	2

06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	143077	LAURIC ACID	150
06D - Hair Shampoos (coloring)	143077	LAURIC ACID	1
06G - Hair Bleaches	143077	LAURIC ACID	4
06H - Other Hair Coloring Preparation	143077	LAURIC ACID	1
07E - Lipstick	143077	LAURIC ACID	3
08B - Cuticle Softeners	143077	LAURIC ACID	1
10A - Bath Soaps and Detergents	143077	LAURIC ACID	76
10B - Deodorants (underarm)	143077	LAURIC ACID	5
10E - Other Personal Cleanliness Products	143077	LAURIC ACID	55
11E - Shaving Cream	143077	LAURIC ACID	12
11F - Shaving Soap	143077	LAURIC ACID	3
11G - Other Shaving Preparation Products	143077	LAURIC ACID	4
12A - Cleansing	143077	LAURIC ACID	149
12C - Face and Neck (exc shave)	143077	LAURIC ACID	5
12D - Body and Hand (exc shave)	143077	LAURIC ACID	4
12J - Other Skin Care Preps	143077	LAURIC ACID	5
03C - Eye Shadow	60333	LINOLEIC ACID	7
03D - Eye Lotion	60333	LINOLEIC ACID	48
03F - Mascara	60333	LINOLEIC ACID	3
03G - Other Eye Makeup Preparations	60333	LINOLEIC ACID	12
05A - Hair Conditioner	60333	LINOLEIC ACID	20
05F - Shampoos (non-coloring)	60333	LINOLEIC ACID	12
05G - Tonics, Dressings, and Other Hair Grooming Aids	60333	LINOLEIC ACID	17
05I - Other Hair Preparations	60333	LINOLEIC ACID	3
06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	60333	LINOLEIC ACID	4
06C - Hair Rinses (coloring)	60333	LINOLEIC ACID	1
07A - Blushers (all types)	60333	LINOLEIC ACID	2
07B - Face Powders	60333	LINOLEIC ACID	8
07C - Foundations	60333	LINOLEIC ACID	15
07E - Lipstick	60333	LINOLEIC ACID	96
07F - Makeup Bases	60333	LINOLEIC ACID	6
07G - Rouges	60333	LINOLEIC ACID	1
07I - Other Makeup Preparations	60333	LINOLEIC ACID	5

08B - Cuticle Softeners	60333	LINOLEIC ACID	1
08E - Nail Polish and Enamel	60333	LINOLEIC ACID	1
10A - Bath Soaps and Detergents	60333	LINOLEIC ACID	6
10E - Other Personal Cleanliness Products	60333	LINOLEIC ACID	1
11A - Aftershave Lotion	60333	LINOLEIC ACID	7
12A - Cleansing	60333	LINOLEIC ACID	25
12C - Face and Neck (exc shave)	60333	LINOLEIC ACID	71
12D - Body and Hand (exc shave)	60333	LINOLEIC ACID	34
12F - Moisturizing	60333	LINOLEIC ACID	140
12G - Night	60333	LINOLEIC ACID	38
12H - Paste Masks (mud packs)	60333	LINOLEIC ACID	7
12J - Other Skin Care Preps	60333	LINOLEIC ACID	27
13A - Suntan Gels, Creams, and Liquids	60333	LINOLEIC ACID	6
13B - Indoor Tanning Preparations	60333	LINOLEIC ACID	7
13C - Other Suntan Preparations	60333	LINOLEIC ACID	2
03C - Eye Shadow	463401	LINOLENIC ACID	1
03D - Eye Lotion	463401	LINOLENIC ACID	13
03G - Other Eye Makeup Preparations	463401	LINOLENIC ACID	3
05A - Hair Conditioner	463401	LINOLENIC ACID	14
05F - Shampoos (non-coloring)	463401	LINOLENIC ACID	10
05G - Tonics, Dressings, and Other Hair Grooming Aids	463401	LINOLENIC ACID	8
05I - Other Hair Preparations	463401	LINOLENIC ACID	4
06C - Hair Rinses (coloring)	463401	LINOLENIC ACID	1
07B - Face Powders	463401	LINOLENIC ACID	1
07C - Foundations	463401	LINOLENIC ACID	5
07E - Lipstick	463401	LINOLENIC ACID	6
08E - Nail Polish and Enamel	463401	LINOLENIC ACID	1
10A - Bath Soaps and Detergents	463401	LINOLENIC ACID	4
11A - Aftershave Lotion	463401	LINOLENIC ACID	5
12A - Cleansing	463401	LINOLENIC ACID	5
12C - Face and Neck (exc shave)	463401	LINOLENIC ACID	27
12D - Body and Hand (exc shave)	463401	LINOLENIC ACID	9
12F - Moisturizing	463401	LINOLENIC ACID	50
12G - Night	463401	LINOLENIC ACID	14
12H - Paste Masks (mud packs)	463401	LINOLENIC ACID	1
12J - Other Skin Care Preps	463401	LINOLENIC ACID	14
13A - Suntan Gels, Creams, and	463401	LINOLENIC ACID	6

Liquids			
13B - Indoor Tanning Preparations	463401	LINOLENIC ACID	3
03C - Eye Shadow	4485125	LITHIUM STEARATE	78
03G - Other Eye Makeup Preparations	4485125	LITHIUM STEARATE	1
07A - Blushers (all types)	4485125	LITHIUM STEARATE	2
07E - Lipstick	4485125	LITHIUM STEARATE	4
10A - Bath Soaps and Detergents	4040486	MAGNESIUM LAURATE	3
03A - Eyebrow Pencil	557040	MAGNESIUM STEARATE	1
03B - Eyeliner	557040	MAGNESIUM STEARATE	1
03C - Eye Shadow	557040	MAGNESIUM STEARATE	389
03F - Mascara	557040	MAGNESIUM STEARATE	4
03G - Other Eye Makeup Preparations	557040	MAGNESIUM STEARATE	25
04C - Powders (dusting and talcum, excluding aftershave talc)	557040	MAGNESIUM STEARATE	5
05B - Hair Spray (aerosol fixatives)	557040	MAGNESIUM STEARATE	1
05F - Shampoos (non-coloring)	557040	MAGNESIUM STEARATE	5
05I - Other Hair Preparations	557040	MAGNESIUM STEARATE	1
06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	557040	MAGNESIUM STEARATE	3
06E - Hair Color Sprays (aerosol)	557040	MAGNESIUM STEARATE	1
06G - Hair Bleaches	557040	MAGNESIUM STEARATE	8
06H - Other Hair Coloring Preparation	557040	MAGNESIUM STEARATE	32
07A - Blushers (all types)	557040	MAGNESIUM STEARATE	100
07B - Face Powders	557040	MAGNESIUM STEARATE	126
07C - Foundations	557040	MAGNESIUM STEARATE	46
07E - Lipstick	557040	MAGNESIUM STEARATE	4
07F - Makeup Bases	557040	MAGNESIUM STEARATE	3
07G - Rouges	557040	MAGNESIUM STEARATE	7
07I - Other Makeup Preparations	557040	MAGNESIUM STEARATE	16
10A - Bath Soaps and Detergents	557040	MAGNESIUM STEARATE	3
10D - Feminine Deodorants	557040	MAGNESIUM STEARATE	1
11C - Mens Talcum	557040	MAGNESIUM STEARATE	1
12C - Face and Neck (exc shave)	557040	MAGNESIUM STEARATE	2
12D - Body and Hand (exc shave)	557040	MAGNESIUM STEARATE	2
12F - Moisturizing	557040	MAGNESIUM STEARATE	9
12G - Night	557040	MAGNESIUM STEARATE	2

12H - Paste Masks (mud packs)	557040	MAGNESIUM STEARATE	2
12J - Other Skin Care Preps	557040	MAGNESIUM STEARATE	1
13B - Indoor Tanning Preparations	557040	MAGNESIUM STEARATE	6
02B - Bubble Baths	544638	MYRISTIC ACID	2
03C - Eye Shadow	544638	MYRISTIC ACID	12
03D - Eye Lotion	544638	MYRISTIC ACID	6
03F - Mascara	544638	MYRISTIC ACID	13
03G - Other Eye Makeup Preparations	544638	MYRISTIC ACID	3
05A - Hair Conditioner	544638	MYRISTIC ACID	1
05B - Hair Spray (aerosol fixatives)	544638	MYRISTIC ACID	1
05F - Shampoos (non-coloring)	544638	MYRISTIC ACID	1
05G - Tonics, Dressings, and Other Hair Grooming Aids	544638	MYRISTIC ACID	7
05I - Other Hair Preparations	544638	MYRISTIC ACID	3
07B - Face Powders	544638	MYRISTIC ACID	10
07C - Foundations	544638	MYRISTIC ACID	2
07D - Leg and Body Paints	544638	MYRISTIC ACID	2
07E - Lipstick	544638	MYRISTIC ACID	2
08C - Nail Creams and Lotions	544638	MYRISTIC ACID	1
08G - Other Manicuring Preparations	544638	MYRISTIC ACID	1
10A - Bath Soaps and Detergents	544638	MYRISTIC ACID	22
10B - Deodorants (underarm)	544638	MYRISTIC ACID	1
10E - Other Personal Cleanliness Products	544638	MYRISTIC ACID	8
11A - Aftershave Lotion	544638	MYRISTIC ACID	1
11E - Shaving Cream	544638	MYRISTIC ACID	27
11F - Shaving Soap	544638	MYRISTIC ACID	4
11G - Other Shaving Preparation Products	544638	MYRISTIC ACID	4
12A - Cleansing	544638	MYRISTIC ACID	138
12C - Face and Neck (exc shave)	544638	MYRISTIC ACID	16
12D - Body and Hand (exc shave)	544638	MYRISTIC ACID	48
12F - Moisturizing	544638	MYRISTIC ACID	17
12G - Night	544638	MYRISTIC ACID	2
12J - Other Skin Care Preps	544638	MYRISTIC ACID	12
13A - Suntan Gels, Creams, and Liquids	544638	MYRISTIC ACID	2
01B - Baby Lotions, Oils, Powders, and Creams	112801	OLEIC ACID	1
03A - Eyebrow Pencil	112801	OLEIC ACID	1

03B - Eyeliner	112801	OLEIC ACID	3
03C - Eye Shadow	112801	OLEIC ACID	1
03D - Eye Lotion	112801	OLEIC ACID	5
03F - Mascara	112801	OLEIC ACID	53
03G - Other Eye Makeup Preparations	112801	OLEIC ACID	6
05A - Hair Conditioner	112801	OLEIC ACID	10
05F - Shampoos (non-coloring)	112801	OLEIC ACID	7
05G - Tonics, Dressings, and Other Hair Grooming Aids	112801	OLEIC ACID	2
05I - Other Hair Preparations	112801	OLEIC ACID	2
06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	112801	OLEIC ACID	703
06B - Hair Tints	112801	OLEIC ACID	2
06G - Hair Bleaches	112801	OLEIC ACID	3
06H - Other Hair Coloring Preparation	112801	OLEIC ACID	12
07A - Blushers (all types)	112801	OLEIC ACID	1
07C - Foundations	112801	OLEIC ACID	10
07E - Lipstick	112801	OLEIC ACID	87
07F - Makeup Bases	112801	OLEIC ACID	1
07G - Rouges	112801	OLEIC ACID	1
07I - Other Makeup Preparations	112801	OLEIC ACID	4
08B - Cuticle Softeners	112801	OLEIC ACID	3
08C - Nail Creams and Lotions	112801	OLEIC ACID	1
08F - Nail Polish and Enamel Removers	112801	OLEIC ACID	1
08G - Other Manicuring Preparations	112801	OLEIC ACID	2
10A - Bath Soaps and Detergents	112801	OLEIC ACID	3
10B - Deodorants (underarm)	112801	OLEIC ACID	3
11E - Shaving Cream	112801	OLEIC ACID	2
11G - Other Shaving Preparation Products	112801	OLEIC ACID	2
12A - Cleansing	112801	OLEIC ACID	12
12C - Face and Neck (exc shave)	112801	OLEIC ACID	24
12D - Body and Hand (exc shave)	112801	OLEIC ACID	5
12F - Moisturizing	112801	OLEIC ACID	50
12G - Night	112801	OLEIC ACID	9
12H - Paste Masks (mud packs)	112801	OLEIC ACID	1
12I - Skin Fresheners	112801	OLEIC ACID	1
12J - Other Skin Care Preps	112801	OLEIC ACID	8
13A - Suntan Gels, Creams, and	112801	OLEIC ACID	6

Liquids			
13B - Indoor Tanning Preparations	112801	OLEIC ACID	2
13C - Other Suntan Preparations	112801	OLEIC ACID	2
01B - Baby Lotions, Oils, Powders, and Creams	57103	PALMITIC ACID	2
02D - Other Bath Preparations	57103	PALMITIC ACID	2
03A - Eyebrow Pencil	57103	PALMITIC ACID	1
03B - Eyeliner	57103	PALMITIC ACID	9
03C - Eye Shadow	57103	PALMITIC ACID	16
03D - Eye Lotion	57103	PALMITIC ACID	28
03F - Mascara	57103	PALMITIC ACID	136
03G - Other Eye Makeup Preparations	57103	PALMITIC ACID	14
05A - Hair Conditioner	57103	PALMITIC ACID	8
05B - Hair Spray (aerosol fixatives)	57103	PALMITIC ACID	1
05F - Shampoos (non-coloring)	57103	PALMITIC ACID	7
05G - Tonics, Dressings, and Other Hair Grooming Aids	57103	PALMITIC ACID	22
05I - Other Hair Preparations	57103	PALMITIC ACID	5
06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	57103	PALMITIC ACID	34
06B - Hair Tints	57103	PALMITIC ACID	22
06E - Hair Color Sprays (aerosol)	57103	PALMITIC ACID	2
06G - Hair Bleaches	57103	PALMITIC ACID	2
07A - Blushers (all types)	57103	PALMITIC ACID	14
07B - Face Powders	57103	PALMITIC ACID	14
07C - Foundations	57103	PALMITIC ACID	13
07D - Leg and Body Paints	57103	PALMITIC ACID	2
07E - Lipstick	57103	PALMITIC ACID	99
07F - Makeup Bases	57103	PALMITIC ACID	5
07G - Rouges	57103	PALMITIC ACID	1
07I - Other Makeup Preparations	57103	PALMITIC ACID	18
08C - Nail Creams and Lotions	57103	PALMITIC ACID	1
08E - Nail Polish and Enamel	57103	PALMITIC ACID	2
08G - Other Manicuring Preparations	57103	PALMITIC ACID	1
10A - Bath Soaps and Detergents	57103	PALMITIC ACID	44
10B - Deodorants (underarm)	57103	PALMITIC ACID	35
10E - Other Personal Cleanliness Products	57103	PALMITIC ACID	13
11A - Aftershave Lotion	57103	PALMITIC ACID	5
11E - Shaving Cream	57103	PALMITIC ACID	38

11G - Other Shaving Preparation Products	57103	PALMITIC ACID	47
12A - Cleansing	57103	PALMITIC ACID	87
12C - Face and Neck (exc shave)	57103	PALMITIC ACID	72
12D - Body and Hand (exc shave)	57103	PALMITIC ACID	142
12F - Moisturizing	57103	PALMITIC ACID	196
12G - Night	57103	PALMITIC ACID	23
12H - Paste Masks (mud packs)	57103	PALMITIC ACID	12
12I - Skin Fresheners	57103	PALMITIC ACID	1
12J - Other Skin Care Preps	57103	PALMITIC ACID	35
13A - Suntan Gels, Creams, and Liquids	57103	PALMITIC ACID	7
13B - Indoor Tanning Preparations	57103	PALMITIC ACID	2
10A - Bath Soaps and Detergents	7211532	POTASSIUM BEHENATE	1
10E - Other Personal Cleanliness Products	7211532	POTASSIUM BEHENATE	1
12A - Cleansing	7211532	POTASSIUM BEHENATE	3
10A - Bath Soaps and Detergents	64366241	POTASSIUM CASTORATE	2
12G - Night	999003682	POTASSIUM HYDROGENATED TALLOWATE	1
10A - Bath Soaps and Detergents	68413467	POTASSIUM ISOSTEARATE	3
12D - Body and Hand (exc shave)	68413467	POTASSIUM ISOSTEARATE	2
10A - Bath Soaps and Detergents	10124659	POTASSIUM LAURATE	5
10E - Other Personal Cleanliness Products	10124659	POTASSIUM LAURATE	1
12A - Cleansing	10124659	POTASSIUM LAURATE	17
12F - Moisturizing	10124659	POTASSIUM LAURATE	1
06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	143180	POTASSIUM OLEATE	2
10A - Bath Soaps and Detergents	143180	POTASSIUM OLEATE	4
10E - Other Personal Cleanliness Products	143180	POTASSIUM OLEATE	6
12A - Cleansing	143180	POTASSIUM OLEATE	6
12I - Skin Fresheners	143180	POTASSIUM OLEATE	1
03C - Eye Shadow	2624319	POTASSIUM PALMITATE	3
03G - Other Eye Makeup Preparations	2624319	POTASSIUM PALMITATE	1

10A - Bath Soaps and Detergents	2624319	POTASSIUM PALMITATE	4
10E - Other Personal Cleanliness Products	2624319	POTASSIUM PALMITATE	1
11F - Shaving Soap	2624319	POTASSIUM PALMITATE	4
12A - Cleansing	2624319	POTASSIUM PALMITATE	10
12D - Body and Hand (exc shave)	2624319	POTASSIUM PALMITATE	2
01B - Baby Lotions, Oils, Powders, and Creams	593293	POTASSIUM STEARATE	1
03D - Eye Lotion	593293	POTASSIUM STEARATE	3
03F - Mascara	593293	POTASSIUM STEARATE	1
03G - Other Eye Makeup Preparations	593293	POTASSIUM STEARATE	1
05A - Hair Conditioner	593293	POTASSIUM STEARATE	3
05F - Shampoos (non-coloring)	593293	POTASSIUM STEARATE	3
05G - Tonics, Dressings, and Other Hair Grooming Aids	593293	POTASSIUM STEARATE	4
05I - Other Hair Preparations	593293	POTASSIUM STEARATE	1
06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	593293	POTASSIUM STEARATE	9
07A - Blushers (all types)	593293	POTASSIUM STEARATE	1
07B - Face Powders	593293	POTASSIUM STEARATE	7
07C - Foundations	593293	POTASSIUM STEARATE	2
07I - Other Makeup Preparations	593293	POTASSIUM STEARATE	1
08C - Nail Creams and Lotions	593293	POTASSIUM STEARATE	1
10A - Bath Soaps and Detergents	593293	POTASSIUM STEARATE	12
10E - Other Personal Cleanliness Products	593293	POTASSIUM STEARATE	7
11A - Aftershave Lotion	593293	POTASSIUM STEARATE	3
11E - Shaving Cream	593293	POTASSIUM STEARATE	4
11F - Shaving Soap	593293	POTASSIUM STEARATE	21
11G - Other Shaving Preparation Products	593293	POTASSIUM STEARATE	1
12A - Cleansing	593293	POTASSIUM STEARATE	20
12C - Face and Neck (exc shave)	593293	POTASSIUM STEARATE	3
12D - Body and Hand (exc shave)	593293	POTASSIUM STEARATE	20
12E - Foot Powders and Sprays	593293	POTASSIUM STEARATE	1
12F - Moisturizing	593293	POTASSIUM STEARATE	18
12G - Night	593293	POTASSIUM STEARATE	2
12H - Paste Masks (mud packs)	593293	POTASSIUM STEARATE	2
12J - Other Skin Care Preps	593293	POTASSIUM STEARATE	2
13A - Suntan Gels, Creams, and	593293	POTASSIUM STEARATE	1

Liquids			
13B - Indoor Tanning Preparations	593293	POTASSIUM STEARATE	3
11F - Shaving Soap	61790327	POTASSIUM TALLOWATE	3
10B - Deodorants (underarm)	5331771	SODIUM BEHENATE	14
10A - Bath Soaps and Detergents	8013067	SODIUM CASTORATE	2
03D - Eye Lotion	36111087	SODIUM ISOSTEARATE	1
03G - Other Eye Makeup Preparations	36111087	SODIUM ISOSTEARATE	1
10A - Bath Soaps and Detergents	36111087	SODIUM ISOSTEARATE	3
12C - Face and Neck (exc shave)	36111087	SODIUM ISOSTEARATE	4
12F - Moisturizing	36111087	SODIUM ISOSTEARATE	1
12G - Night	36111087	SODIUM ISOSTEARATE	1
05F - Shampoos (non-coloring)	629254	SODIUM LAURATE	11
07F - Makeup Bases	629254	SODIUM LAURATE	1
10A - Bath Soaps and Detergents	629254	SODIUM LAURATE	36
10B - Deodorants (underarm)	629254	SODIUM LAURATE	14
10E - Other Personal Cleanliness Products	629254	SODIUM LAURATE	9
12A - Cleansing	629254	SODIUM LAURATE	10
12D - Body and Hand (exc shave)	629254	SODIUM LAURATE	3
12F - Moisturizing	629254	SODIUM LAURATE	2
12J - Other Skin Care Preps	629254	SODIUM LAURATE	1
03D - Eye Lotion	143191	SODIUM OLEATE	6
03G - Other Eye Makeup Preparations	143191	SODIUM OLEATE	3
07I - Other Makeup Preparations	143191	SODIUM OLEATE	1
10A - Bath Soaps and Detergents	143191	SODIUM OLEATE	2
12A - Cleansing	143191	SODIUM OLEATE	2
12C - Face and Neck (exc shave)	143191	SODIUM OLEATE	15
12D - Body and Hand (exc shave)	143191	SODIUM OLEATE	1
12F - Moisturizing	143191	SODIUM OLEATE	19
12G - Night	143191	SODIUM OLEATE	10
12I - Skin Fresheners	143191	SODIUM OLEATE	2
12J - Other Skin Care Preps	143191	SODIUM OLEATE	1
01C - Other Baby Products	408355	SODIUM PALMITATE	1
02D - Other Bath Preparations	408355	SODIUM PALMITATE	2

10A - Bath Soaps and Detergents	408355	SODIUM PALMITATE	47
10B - Deodorants (underarm)	408355	SODIUM PALMITATE	21
10E - Other Personal Cleanliness Products	408355	SODIUM PALMITATE	9
11E - Shaving Cream	408355	SODIUM PALMITATE	4
11F - Shaving Soap	408355	SODIUM PALMITATE	4
12A - Cleansing	408355	SODIUM PALMITATE	11
12F - Moisturizing	408355	SODIUM PALMITATE	3
03B - Eyeliner	822162	SODIUM STEARATE	1
03C - Eye Shadow	822162	SODIUM STEARATE	2
03D - Eye Lotion	822162	SODIUM STEARATE	3
03F - Mascara	822162	SODIUM STEARATE	1
03G - Other Eye Makeup Preparations	822162	SODIUM STEARATE	5
05F - Shampoos (non-coloring)	822162	SODIUM STEARATE	1
05G - Tonics, Dressings, and Other Hair Grooming Aids	822162	SODIUM STEARATE	1
06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	822162	SODIUM STEARATE	11
06F - Hair Lighteners with Color	822162	SODIUM STEARATE	5
06G - Hair Bleaches	822162	SODIUM STEARATE	23
06H - Other Hair Coloring Preparation	822162	SODIUM STEARATE	1
07B - Face Powders	822162	SODIUM STEARATE	1
07C - Foundations	822162	SODIUM STEARATE	12
07D - Leg and Body Paints	822162	SODIUM STEARATE	6
07E - Lipstick	822162	SODIUM STEARATE	1
07I - Other Makeup Preparations	822162	SODIUM STEARATE	6
10A - Bath Soaps and Detergents	822162	SODIUM STEARATE	91
10B - Deodorants (underarm)	822162	SODIUM STEARATE	215
10E - Other Personal Cleanliness Products	822162	SODIUM STEARATE	14
11E - Shaving Cream	822162	SODIUM STEARATE	4
11F - Shaving Soap	822162	SODIUM STEARATE	12
11G - Other Shaving Preparation Products	822162	SODIUM STEARATE	1
12A - Cleansing	822162	SODIUM STEARATE	21
12C - Face and Neck (exc shave)	822162	SODIUM STEARATE	23
12D - Body and Hand (exc shave)	822162	SODIUM STEARATE	8
12F - Moisturizing	822162	SODIUM STEARATE	22
12G - Night	822162	SODIUM STEARATE	4

12H - Paste Masks (mud packs)	822162	SODIUM STEARATE	5
12J - Other Skin Care Preps	822162	SODIUM STEARATE	16
13A - Suntan Gels, Creams, and Liquids	822162	SODIUM STEARATE	1
13B - Indoor Tanning Preparations	822162	SODIUM STEARATE	2
01C - Other Baby Products	8052480	SODIUM TALLOWATE	2
10A - Bath Soaps and Detergents	8052480	SODIUM TALLOWATE	85
10E - Other Personal Cleanliness Products	8052480	SODIUM TALLOWATE	10
11A - Aftershave Lotion	8052480	SODIUM TALLOWATE	1
11E - Shaving Cream	8052480	SODIUM TALLOWATE	2
11F - Shaving Soap	8052480	SODIUM TALLOWATE	2
11G - Other Shaving Preparation Products	8052480	SODIUM TALLOWATE	1
12A - Cleansing	8052480	SODIUM TALLOWATE	6
12C - Face and Neck (exc shave)	8052480	SODIUM TALLOWATE	1
01B - Baby Lotions, Oils, Powders, and Creams	57114	STEARIC ACID	28
01C - Other Baby Products	57114	STEARIC ACID	2
02B - Bubble Baths	57114	STEARIC ACID	2
02D - Other Bath Preparations	57114	STEARIC ACID	1
03A - Eyebrow Pencil	57114	STEARIC ACID	28
03B - Eyeliner	57114	STEARIC ACID	82
03C - Eye Shadow	57114	STEARIC ACID	105
03D - Eye Lotion	57114	STEARIC ACID	82
03F - Mascara	57114	STEARIC ACID	441
03G - Other Eye Makeup Preparations	57114	STEARIC ACID	51
04A - Cologne and Toilet waters	57114	STEARIC ACID	1
04E - Other Fragrance Preparation	57114	STEARIC ACID	3
05A - Hair Conditioner	57114	STEARIC ACID	31
05C - Hair Straighteners	57114	STEARIC ACID	2
05E - Rinses (non-coloring)	57114	STEARIC ACID	1
05F - Shampoos (non-coloring)	57114	STEARIC ACID	25
05G - Tonics, Dressings, and Other Hair Grooming Aids	57114	STEARIC ACID	48
05I - Other Hair Preparations	57114	STEARIC ACID	17
06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	57114	STEARIC ACID	106
06B - Hair Tints	57114	STEARIC ACID	131

06D - Hair Shampoos (coloring)	57114	STEARIC ACID	1
06G - Hair Bleaches	57114	STEARIC ACID	2
07A - Blushers (all types)	57114	STEARIC ACID	10
07B - Face Powders	57114	STEARIC ACID	27
07C - Foundations	57114	STEARIC ACID	144
07D - Leg and Body Paints	57114	STEARIC ACID	14
07E - Lipstick	57114	STEARIC ACID	103
07F - Makeup Bases	57114	STEARIC ACID	23
07G - Rouges	57114	STEARIC ACID	1
07H - Makeup Fixatives	57114	STEARIC ACID	3
07I - Other Makeup Preparations	57114	STEARIC ACID	39
08B - Cuticle Softeners	57114	STEARIC ACID	4
08C - Nail Creams and Lotions	57114	STEARIC ACID	3
08G - Other Manicuring Preparations	57114	STEARIC ACID	1
10A - Bath Soaps and Detergents	57114	STEARIC ACID	138
10B - Deodorants (underarm)	57114	STEARIC ACID	54
10E - Other Personal Cleanliness Products	57114	STEARIC ACID	87
11A - Aftershave Lotion	57114	STEARIC ACID	46
11D - Preshave Lotions (all types)	57114	STEARIC ACID	1
11E - Shaving Cream	57114	STEARIC ACID	108
11F - Shaving Soap	57114	STEARIC ACID	15
11G - Other Shaving Preparation Products	57114	STEARIC ACID	47
12A - Cleansing	57114	STEARIC ACID	328
12C - Face and Neck (exc shave)	57114	STEARIC ACID	344
12D - Body and Hand (exc shave)	57114	STEARIC ACID	829
12E - Foot Powders and Sprays	57114	STEARIC ACID	7
12F - Moisturizing	57114	STEARIC ACID	1750
12G - Night	57114	STEARIC ACID	113
12H - Paste Masks (mud packs)	57114	STEARIC ACID	96
12I - Skin Fresheners	57114	STEARIC ACID	3
12J - Other Skin Care Preps	57114	STEARIC ACID	172
13A - Suntan Gels, Creams, and Liquids	57114	STEARIC ACID	10
13B - Indoor Tanning Preparations	57114	STEARIC ACID	19
13C - Other Suntan Preparations	57114	STEARIC ACID	9
05A - Hair Conditioner	999001624	TRILINOLEIC ACID	1
05G - Tonics, Dressings, and Other Hair Grooming Aids	999001624	TRILINOLEIC ACID	3

12F - Moisturizing	112389	UNDECYLENIC ACID	1

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Lillian Gill, D.P.A.
Director - COSMETIC INGREDIENT REVIEW (CIR)

FROM: Beth A. Jonas, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: December 14, 2016

SUBJECT: Concentration of Use by FDA Product Category: Fatty Acids and Soaps

Concentration of Use by FDA Product Category – Fatty Acids and Soaps*

Linoleic Acid
Aluminum Dilinoleate
Aluminum Distearate
Aluminum Isostearate
Aluminum Isostearates/Palmitates
Aluminum Isostearates/Stearates
Aluminum Isostearates/Laurates/Palmitates
Aluminum Isostearates/Laurates/Stearates
Aluminum Lanolate
Aluminum Stearate
Aluminum Stearates
Aluminum Tristearate
Ammonium Isostearate
Ammonium Oleate
Ammonium Stearate
Arachidic Acid
Beeswax Acid
Behenic Acid
C14-28 Alkyl Acid
C10-40 Isoalkyl Acid
C14-28 Isoalkyl Acid
C32-36 Isoalkyl Acid
Calcium Behenate
Calcium Laurate
Calcium Stearate
Calcium Undecylenate
Capric Acid
Caproic Acid
Caprylic Acid
Dierucic Acid
Dilinoleic Acid
Erucic Acid
Isomerized Linoleic Acid
Isomerized Safflower Acid
Isostearic Acid
Lauric Acid
Linolenic Acid
Lithium Stearate
Magnesium Lanolate
Magnesium Laurate
Magnesium Palmitate
Magnesium Stearate
Magnesium Tallowate
Methyl Myristic Acid
Myristic Acid
Oleic Acid
Ozonized Oleic Acid
Palmitic Acid
Potassium Behenate
Potassium Borageate
Potassium Camelliate
Potassium Caprate
Potassium Caprylate
Potassium Caprylate/Caprate
Potassium Castorate
Potassium Hydrogenated Tallowate
Potassium Isostearate
Potassium Lanolate
Potassium Laurate
Potassium Linoleate
Potassium Linseedate
Potassium Oleate
Potassium Olivate/Sunflowerseedate
Potassium Palm Kernelate
Potassium Palmitate
Potassium Stearate
Potassium Sunflowerseedate
Potassium Tallate
Potassium Tallowate
Potassium Undecylenate
Sodium Arganate
Sodium Beeswax
Sodium Behenate
Sodium Camellia Japonica Seedate
Sodium Caprate
Sodium Caprylate
Sodium Castorate
Sodium Dilinoleate
Sodium Hydrogenated Tallowate
Sodium Isostearate

Sodium Lanolate
Sodium Lardate
Sodium Laurate
Sodium Laurate/Linoleate/Oleate/Palmitate
Sodium Linoleate
Sodium Oleate
Sodium Palmitate
Sodium Stearate
Sodium Tallowate
Sodium Tamanuseedate
Sodium Undecylenate
Stearic Acid
Trilinoleic Acid
Undecanoic Acid
Undecylenic Acid
Hydroxystearic Acid
Hydroxycapric Acid
Hydroxycaprylic Acid
10-Hydroxydecanoic Acid
Hydroxylauric Acid
10-Hydroxystearic Acid

Ingredient	**Product Category**	**Maximum Concentration of Use**
Linoleic Acid	Baby lotions, oils and creams Not powder	 0.043%
Linoleic Acid	Bath oils, tablets and salts	0.0012%
Linoleic Acid	Eyebrow pencils	0.15%
Linoleic Acid	Eye shadows	0.05%
Linoleic Acid	Eye lotions	0.2-0.76%
Linoleic Acid	Eye makeup removers	0.2%
Linoleic Acid	Mascara	0.01%
Linoleic Acid	Other eye makeup preparations	0.004-0.2%
Linoleic Acid	Other fragrance preparations	0.0038%
Linoleic Acid	Hair conditioners	0.0009-0.15%
Linoleic Acid	Hair sprays Pump spray	 0.25%
Linoleic Acid	Shampoos (noncoloring)	0.0009-0.1%
Linoleic Acid	Tonics, dressings and other hair grooming aids	0.003-0.67%
Linoleic Acid	Other hair preparations (noncoloring)	0.1%
Linoleic Acid	Hair dyes and colors	0.003-0.31%
Linoleic Acid	Hair rinses (coloring)	0.00033%
Linoleic Acid	Hair shampoos (coloring)	0.003%
Linoleic Acid	Blushers	0.2%
Linoleic Acid	Face powders	0.2%
Linoleic Acid	Foundations	0.00085-0.94%
Linoleic Acid	Lipstick	0.0075-1%
Linoleic Acid	Nail creams and lotions	2%
Linoleic Acid	Bath soaps and detergents	0.0012-0.63%
Linoleic Acid	Deodorants Not spray	 0.07%
Linoleic Acid	Other personal cleanliness products Hand cleaner	0.001% 1.1%
Linoleic Acid	Aftershave lotions	0.0038-0.15%
Linoleic Acid	Shaving cream	0.38%

Linoleic Acid	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.1-21.8%
Linoleic Acid	Face and neck products Not spray	 0.002-3.4%
Linoleic Acid	Body and hand products Not spray Spray	 0.0015-3.4% 0.2%
Linoleic Acid	Foot powders and sprays	0.2%
Linoleic Acid	Moisturizing products Not spray	 0.05-0.5%
Linoleic Acid	Night products Not spray	 0.38-2.3%
Linoleic Acid	Paste masks and mud packs	0.0012-0.57%
Linoleic Acid	Skin fresheners	0.003-0.02%
Linoleic Acid	Other skin care preparations	0.04-0.45%
Linoleic Acid	Suntan products Not spray	 0.2%
Linoleic Acid	Indoor tanning preparations	0.2%
Linoleic Acid	Other suntan preparations	0.2%
Aluminum Distearate	Eyebrow pencils	1-2.9%
Aluminum Distearate	Eyeliners	0.59-5.2%
Aluminum Distearate	Eye shadows	4-4.5%
Aluminum Distearate	Eye lotions	0.08%
Aluminum Distearate	Mascara	2%
Aluminum Distearate	Hair lighteners with color	4%
Aluminum Distearate	Blushers	0.5-5.5%
Aluminum Distearate	Face powders	0.1-4.5%
Aluminum Distearate	Foundations	0.1-3%
Aluminum Distearate	Lipstick	0.36-0.4%
Aluminum Distearate	Makeup bases	0.9%
Aluminum Distearate	Other makeup preparations	4.9%
Aluminum Distearate	Nail creams and lotions	0.37%
Aluminum Distearate	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.054%
Aluminum Distearate	Face and neck products Not spray	 0.048-1%
Aluminum Distearate	Body and hand products Not spray	 0.9-1.5%
Aluminum Distearate	Moisturizing products Not spray	 0.16%
Aluminum Distearate	Other skin care preparations	0.004%
Aluminum Stearate	Baby lotions, oils and creams Not powder	 0.53%
Aluminum Stearate	Eye lotions	0.0099%
Aluminum Stearate	Mascara	0.99-1.8%

Aluminum Stearate	Hair conditioners	0.00014%
Aluminum Stearate	Shampoos (noncoloring)	0.00016%
Aluminum Stearate	Hair bleaches	3.4%
Aluminum Stearate	Face powders	3.1%
Aluminum Stearate	Foundations	0.45-2.8%
Aluminum Stearate	Face and neck products Not spray	 0.0099-1.3%
Aluminum Stearate	Body and hand products Not spray	 1.2%
Aluminum Stearate	Moisturizing products Not spray	 0.66-0.99%
Arachidic Acid	Mascara	0.065%
Arachidic Acid	Tonics, dressings and other hair grooming aids	0.000001%
Arachidic Acid	Bath soaps and detergents	0.0002%
Behenic Acid	Bath oils, tablets and salts	0.044%
Behenic Acid	Eyebrow pencils	15-22%
Behenic Acid	Eyeliners	14-18%
Behenic Acid	Eye shadows	9.7-18%
Behenic Acid	Mascara	0.024-2%
Behenic Acid	Other fragrance preparations Not spray	 0.5%
Behenic Acid	Hair conditioners	6%
Behenic Acid	Tonics, dressings and other hair grooming aids Not spray	12% 2%
Behenic Acid	Foundations	0.042-12%
Behenic Acid	Lipstick	0.48-14%
Behenic Acid	Makeup bases	3%
Behenic Acid	Nail creams and lotions	0.5%
Behenic Acid	Bath soaps and detergents	5.2%
Behenic Acid	Deodorants Not spray	 0.75%
Behenic Acid	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.9-6%
Behenic Acid	Face and neck products Not spray	 0.5-2%
Behenic Acid	Body and hand products Not spray	 2%
Behenic Acid	Moisturizing products Not spray Spray	 4% 0.5%
Behenic Acid	Paste masks and mud packs	2%
Behenic Acid	Other skin care preparations	0.025%
Behenic Acid	Suntan products Not spray	 0.5%

C14-28 Alkyl Acid	Hair conditioners	0.0095%
C14-28 Alkyl Acid	Shampoos (noncoloring)	0.075%
C10-40 Isoalkyl Acid	Shampoos (noncoloring)	0.02%
C10-40 Isoalkyl Acid	Tonics, dressings and other hair grooming aids	0.18%
C14-18 Isoalkyl Acid	Hair conditioners	0.029%
C14-18 Isoalkyl Acid	Shampoos (noncoloring)	0.075%
Calcium Stearate	Eyebrow pencils	3%
Calcium Stearate	Eyeliners	1.5-2%
Calcium Stearate	Eye shadows	0.01-4%
Calcium Stearate	Mascara	0.05%
Calcium Stearate	Perfumes	0.05%
Calcium Stearate	Powders	5%
Calcium Stearate	Hair sprays Aerosol Pump spray	 0.012-0.03% 0.000098%
Calcium Stearate	Tonics, dressings and other hair grooming aids	0.005-0.025%
Calcium Stearate	Hair dyes and colors	2.4%
Calcium Stearate	Hair bleaches	0.09%
Calcium Stearate	Blushers	0.16-4%
Calcium Stearate	Face powders	0.1-5%
Calcium Stearate	Foundations	1-3%
Calcium Stearate	Lipstick	0.5-2%
Calcium Stearate	Makeup bases	0.77%
Calcium Stearate	Nail creams and lotions	0.03%
Calcium Stearate	Nail polish and enamels	5%
Calcium Stearate	Other manicuring preparations	0.03-4.3%
Calcium Stearate	Dentifrices	0.1%
Calcium Stearate	Deodorants Not spray	 5%
Calcium Stearate	Other shaving preparations	0.044%
Calcium Stearate	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.00089-2%
Calcium Stearate	Face and neck products Not spray	 0.65%
Calcium Stearate	Body and hand products Not spray	 5%
Capric Acid	Bath soaps and detergents	0.07-0.1%
Capric Acid	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.0036-0.2%
Capric Acid	Face and neck products Not spray	 0.01%
Capric Acid	Other skin care preparations	4%
Caproic Acid	Dentifrices	0.011%
Caprylic Acid	Other hair preparations (noncoloring)	0.23%

Caprylic Acid	Bath soaps and detergents	0.0018-0.1%
Caprylic Acid	Other skin care preparations	4%
Dilinoleic Acid	Hair dyes and colors	2.5%
Dilinoleic Acid	Lipstick	0.14%
Isomerized Linoleic Acid	Blushers	0.38%
Isomerized Linoleic Acid	Body and hand products Not spray	 0.1-0.75%
Isostearic Acid	Eyebrow pencils	0.3-1%
Isostearic Acid	Eyeliners	0.2-2%
Isostearic Acid	Eye shadows	0.1-1%
Isostearic Acid	Eye lotions	0.013-4%
Isostearic Acid	Eye makeup removers	0.065-2%
Isostearic Acid	Mascara	0.2-9.5%
Isostearic Acid	Other eye makeup preparations	0.5-1.4%
Isostearic Acid	Other fragrance preparations Not spray	 0.3%
Isostearic Acid	Hair conditioners	0.004-1%
Isostearic Acid	Hair sprays Pump spray	 0.032%
Isostearic Acid	Rinses (noncoloring)	0.75%
Isostearic Acid	Shampoos (noncoloring)	0.024-0.3%
Isostearic Acid	Tonics, dressings and other hair grooming aids Not spray	1% 2%
Isostearic Acid	Other hair preparations (noncoloring)	0.03%
Isostearic Acid	Hair dyes and colors	0.75-4.8%
Isostearic Acid	Hair tints	20%
Isostearic Acid	Other hair coloring preparations	3%
Isostearic Acid	Blushers	0.035-1%
Isostearic Acid	Face powders	0.012-0.3%
Isostearic Acid	Foundations	0.28-4%
Isostearic Acid	Lipstick	0.025-0.29%
Isostearic Acid	Makeup bases	1%
Isostearic Acid	Rouges	0.02%
Isostearic Acid	Makeup fixatives	1-2%
Isostearic Acid	Other makeup preparations	1%
Isostearic Acid	Nail creams and lotions	3-16%
Isostearic Acid	Other manicuring preparations	16%
Isostearic Acid	Shaving cream	0.5-4%
Isostearic Acid	Shaving soap	0.051%
Isostearic Acid	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.01-9.6%
Isostearic Acid	Face and neck products Not spray	 0.045-2%
Isostearic Acid	Body and hand products Not spray	 0.051-3.8%

Isostearic Acid	Moisturizing products Not spray	 0.1-3%
Isostearic Acid	Night products Not spray	 0.02-3%
Isostearic Acid	Paste masks and mud packs	0.36%
Isostearic Acid	Other skin care preparations	0.48-1.5%
Isostearic Acid	Suntan products Not spray	 0.48-1%
Isostearic Acid	Other suntan preparations	0.75%
Lauric Acid	Baby shampoo	0.11%
Lauric Acid	Baby lotions, oils and creams Not power	 0.0018%
Lauric Acid	Other baby products	0.31%
Lauric Acid	Bubble baths	0.11%
Lauric Acid	Eyebrow pencils	0.11%
Lauric Acid	Eye lotions	0.8%
Lauric Acid	Eye makeup removers	0.01%
Lauric Acid	Mascara	0.0048%
Lauric Acid	Other eye makeup preparations	0.12%
Lauric Acid	Other fragrance preparations Not spray, rinse-off	 13%
Lauric Acid	Hair conditioners	0.005%
Lauric Acid	Shampoos (noncoloring)	0.06-4.2%
Lauric Acid	Tonics, dressings and other hair grooming aids	0.2%
Lauric Acid	Wave sets	0.027%
Lauric Acid	Other hair preparations (noncoloring) Not spray	 0.1%
Lauric Acid	Hair dyes and colors	0.01-1.5%
Lauric Acid	Hair bleaches	1%
Lauric Acid	Lipstick	0.0011%
Lauric Acid	Makeup fixatives	0.013%
Lauric Acid	Other makeup preparations	0.32%
Lauric Acid	Bath soaps and detergents	0.11-5%
Lauric Acid	Deodorants Not spray	 0.3%
Lauric Acid	Shaving cream	0.1-11.2%
Lauric Acid	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.98-18%
Lauric Acid	Face and neck products Not spray	 0.055-4%
Lauric Acid	Body and hand products Not spray Spray	 0.019-10% 0.2%
Lauric Acid	Moisturizing products Not spray	 0.2%

Lauric Acid	Other skin care preparations	3-9%
Linolenic Acid	Baby lotions, oils and creams Not powder	 0.005%
Linolenic Acid	Bath oils, tablets and salts	0.0002%
Linolenic Acid	Eye lotions	0.001-0.084%
Linolenic Acid	Other fragrance preparations	0.00005%
Linolenic Acid	Hair conditioners	0.0005-0.0006%
Linolenic Acid	Hair sprays Pump spray	 0.25%
Linolenic Acid	Shampoos (noncoloring)	0.00005-0.0005%
Linolenic Acid	Tonics, dressings and other hair grooming aids	0.001-1%
Linolenic Acid	Foundations	0.0001%
Linolenic Acid	Lipstick	0.005-0.01%
Linolenic Acid	Nail creams and lotions	0.01%
Linolenic Acid	Dentifrices	0.0022%
Linolenic Acid	Bath soaps and detergents	0.000007-0.1%
Linolenic Acid	Deodorants Not spray	 0.0045-0.07%
Linolenic Acid	Other personal cleanliness products Hand cleaner	0.0002% 0.2%
Linolenic Acid	Aftershave lotions	0.00005%
Linolenic Acid	Shaving cream	0.12%
Linolenic Acid	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.44%
Linolenic Acid	Face and neck products Not spray or powder Not spray	 0.08% 0.003-0.067%
Linolenic Acid	Body and hand products Not spray or powder Not spray	 0.0002% 0.04-0.067%
Linolenic Acid	Moisturizing products Not spray	 0.001-0.084%
Linolenic Acid	Night products Not spray	 0.01-0.045%
Linolenic Acid	Paste masks and mud packs	0.0002-0.0075%
Linolenic Acid	Skin fresheners	0.02%
Linolenic Acid	Other skin care preparations	0.08-0.45%
Lithium Stearate	Powders (dusting and talcum)	3%
Lithium Stearate	Blushers	4%
Lithium Stearate	Foundations	0.1%
Magnesium Stearate	Eyebrow pencils	0.5%
Magnesium Stearate	Eyeliners	1.1-8%
Magnesium Stearate	Eye shadows	0.57-10%
Magnesium Stearate	Eye lotions	1%
Magnesium Stearate	Other eye makeup preparations	2%

Magnesium Stearate	Powders (dusting and talcum)	2%
Magnesium Stearate	Shampoos (noncoloring)	1%
Magnesium Stearate	Tonics, dressings and other hair grooming aids	0.15-0.6%
Magnesium Stearate	Hair dyes and colors	0.33-5%
Magnesium Stearate	Hair color sprays	0.75%
Magnesium Stearate	Hair bleaches	1.2-1.7%
Magnesium Stearate	Other hair coloring preparations	3%
Magnesium Stearate	Blushers	2-8%
Magnesium Stearate	Face powders	1-7.2%
Magnesium Stearate	Foundations	0.03-6%
Magnesium Stearate	Lipstick	0.012%
Magnesium Stearate	Makeup fixatives	2%
Magnesium Stearate	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.8%
Magnesium Stearate	Face and neck products Not spray	0.12-1%
Magnesium Stearate	Body and hand products Not spray	0.9%
Magnesium Stearate	Other skin care preparations	0.14-1%
Myristic Acid	Baby lotions, oils and creams Not powder	0.05%
Myristic Acid	Bath oils, tablets and salts	1%
Myristic Acid	Other bath preparations	1%
Myristic Acid	Eyeliners	0.1%
Myristic Acid	Eye shadows	0.2%
Myristic Acid	Eye lotions	0.042%
Myristic Acid	Mascara	0.011-1%
Myristic Acid	Other fragrance preparations Not spray, rinse-off	5%
Myristic Acid	Hair conditioners	0.02-0.8%
Myristic Acid	Hair sprays Aerosol	2.5%
Myristic Acid	Shampoos (noncoloring)	0.1-0.33%
Myristic Acid	Tonics, dressings and other hair grooming aids	0.002-7%
Myristic Acid	Hair dyes and colors	0.2%
Myristic Acid	Other hair coloring preparations	0.33%
Myristic Acid	Blushers	0.1-0.77%
Myristic Acid	Face powders	0.1-0.66%
Myristic Acid	Foundations	0.03-0.92%
Myristic Acid	Rouges	0.16%
Myristic Acid	Nail creams and lotions	0.04%
Myristic Acid	Bath soaps and detergents	0.0031-1.35%
Myristic Acid	Deodorants Not spray	0.015%

Myristic Acid	Other personal cleanliness products Hand cleaner	 0.2%
Myristic Acid	Aftershave lotions	0.0005-0.045%
Myristic Acid	Shaving cream	0.26-12%
Myristic Acid	Other shaving preparations	0.09%
Myristic Acid	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	3-28.7%
Myristic Acid	Face and neck products Not spray	 0.03-5.4%
Myristic Acid	Body and hand products Not spray	 0.053-20.2%
Myristic Acid	Night products Not spray	 0.015%
Myristic Acid	Other skin care preparations	3.9%
Myristic Acid	Indoor tanning preparations	2%
Oleic Acid	Baby shampoo	0.1%
Oleic Acid	Baby lotions, oils and creams Not powder	 0.36%
Oleic Acid	Bath oils, tablets and salts	0.0005-3%
Oleic Acid	Eyebrow pencils	0.25-0.75%
Oleic Acid	Eyeliners	2-5%
Oleic Acid	Eye lotions	0.01-0.14%
Oleic Acid	Mascara	0.01-2.4%
Oleic Acid	Other fragrance preparations Not spray, rinse-off	0.0007% 17%
Oleic Acid	Hair conditioners	0.001-1%
Oleic Acid	Rinses (noncoloring)	0.4%
Oleic Acid	Shampoos (noncoloring)	0.001-0.006%
Oleic Acid	Tonics, dressings and other hair grooming aids	0.01-3.8%
Oleic Acid	Wave sets	1%
Oleic Acid	Hair dyes and colors	1.5-17%
Oleic Acid	Hair tints	4%
Oleic Acid	Hair bleaches	1.4-14.2%
Oleic Acid	Face powders	0.24%
Oleic Acid	Foundations	0.0002-2%
Oleic Acid	Lipstick	0.0015-0.2%
Oleic Acid	Makeup bases	0.6%
Oleic Acid	Nail creams and lotions	0.3%
Oleic Acid	Nail polish and enamel	0.0003%
Oleic Acid	Bath soaps and detergents	0.012-3.7%
Oleic Acid	Deodorants Not spray Aerosol	 0.64% 1.5%
Oleic Acid	Other personal cleanliness products Hand cleaner	0.0005% 10%

Oleic Acid	Aftershave lotions	0.0007%
Oleic Acid	Shaving cream	0.014-0.72%
Oleic Acid	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.5-20.9%
Oleic Acid	Face and neck products Not spray	 0.1-3.3%
Oleic Acid	Body and hand products Not spray or powder Not spray	 0.0005% 0.04-3.3%
Oleic Acid	Moisturizing products Not spray	 0.015-0.05%
Oleic Acid	Night products Not spray	 0.1-2.2%
Oleic Acid	Paste masks and mud packs	0.0005-0.11%
Oleic Acid	Skin fresheners	0.003%
Oleic Acid	Other skin care preparations	0.0005-0.05%
Oleic Acid	Suntan products Not spray	 0.3%
Palmitic Acid	Baby lotions, oils and creams Not powder	 0.98-1.7%
Palmitic Acid	Eyeliners	0.11-5.3%
Palmitic Acid	Eye shadows	0.047-1%
Palmitic Acid	Eye lotions	0.065-1.8%
Palmitic Acid	Mascara	0.011-5%
Palmitic Acid	Other fragrance preparations Not spray, leave-on Not spray, rinse-off	0.0003% 0.0094% 21%
Palmitic Acid	Tonics, dressings and other hair grooming aids Not spray	0.000000001-8% 2%
Palmitic Acid	Hair dyes and colors	1.1-2%
Palmitic Acid	Hair color sprays	0.005%
Palmitic Acid	Other hair coloring preparations	0.23%
Palmitic Acid	Blushers (all types)	0.0001-0.52%
Palmitic Acid	Face powders	0.12%
Palmitic Acid	Foundations	0.0045-1.5%
Palmitic Acid	Lipstick	0.00033-1%
Palmitic Acid	Makeup bases	2%
Palmitic Acid	Makeup fixatives	0.5%
Palmitic Acid	Other makeup preparations	0.000005-0.5%
Palmitic Acid	Nail creams and lotions	2.2%
Palmitic Acid	Nail polish and enamel	0.0042%
Palmitic Acid	Nail polish and enamel removers	0.02%
Palmitic Acid	Other manicuring preparations	7.5%
Palmitic Acid	Dentifrices (aerosol, liquid, pastes and powders)	0.5%

Palmitic Acid	Bath soaps and detergents	0.00082-9.7%
Palmitic Acid	Deodorants Not spray Aerosol	 0.06-3.5% 0.0021%
Palmitic Acid	Other personal cleanliness products Hand soap	0.5-0.73% 0.4%
Palmitic Acid	Aftershave lotions	0.0003-1.7%
Palmitic Acid	Shaving cream	3.5-15.6%
Palmitic Acid	Shaving soap	3.9%
Palmitic Acid	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.2-21%
Palmitic Acid	Face and neck products Not spray Spray	 0.065-8.6% 0.8%
Palmitic Acid	Body and hand products Not spray or powder Not spray	 0.67-1% 0.03-8.6%
Palmitic Acid	Moisturizing products Not spray	 1.7-4%
Palmitic Acid	Night products Not spray	 0.065-0.56%
Palmitic Acid	Paste masks and mud packs	0.049-2.3%
Palmitic Acid	Skin fresheners	0.0005%
Palmitic Acid	Other skin care preparations	0.05-9%
Palmitic Acid	Suntan products Not spray	 0.34-2.4%
Palmitic Acid	Indoor tanning preparations	1.8%
Potassium Castorate	Bath soaps and detergents	0.52%
Potassium Isostearate	Bath soaps and detergents	3%
Potassium Isostearate	Shaving soap	1.6%
Potassium Laurate	Eye lotions	0.001-0.0019%
Potassium Laurate	Bath soaps and detergents	2-5.3%
Potassium Laurate	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	1.3-9%
Potassium Laurate	Face and neck products Not spray	 0.0018-2%
Potassium Oleate	Bath soaps and detergents	0.25-3%
Potassium Oleate	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	23%
Potassium Palm Kernelate	Shaving soap	9.9%
Potassium Palm Kernelate	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	29%
Potassium Palmitate	Eye shadows	0.26%
Potassium Palmitate	Bath soaps and detergents	0.73%
Potassium Palmitate	Shaving cream	0.3-21.1%
Potassium Palmitate	Skin cleansing (cold creams, cleansing	3%

	lotions, liquids and pads)	
Potassium Stearate	Eye shadows	0.8%
Potassium Stearate	Mascara	0.033%
Potassium Stearate	Hair conditioners	0.0097-0.066%
Potassium Stearate	Shampoos (noncoloring)	0.7%
Potassium Stearate	Tonics, dressings and other hair grooming aids	0.28-7.5%
Potassium Stearate	Hair dyes and colors	3.1%
Potassium Stearate	Blushers	0.4%
Potassium Stearate	Face powders	0.0083%
Potassium Stearate	Foundations	1%
Potassium Stearate	Bath soaps and detergents	0.59-3%
Potassium Stearate	Aftershave lotions	0.2-5%
Potassium Stearate	Shaving cream	45%
Potassium Stearate	Shaving soap	9.9-10.8%
Potassium Stearate	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.5-18%
Potassium Stearate	Face and neck products Not spray	 0.5-1.8%
Potassium Stearate	Body and hand products Not spray	 0.18-0.2%
Potassium Stearate	Moisturizing products Not spray	 0.075-0.55%
Potassium Stearate	Paste masks and mud packs	0.13%
Potassium Stearate	Indoor tanning preparations	0.2%
Potassium Tallowate	Tonics, dressings and other hair grooming aids	0.2%
Potassium Tallowate	Shaving cream	12.9%
Sodium Isostearate	Bath soaps and detergents	3%
Sodium Laurate	Baby shampoo	0.01%
Sodium Laurate	Shampoos (noncoloring)	0.005-0.4%
Sodium Laurate	Foundations	0.075%
Sodium Laurate	Bath soaps and detergents	6.7-7.4%
Sodium Laurate	Other personal cleanliness products Hand soap	0.013% 8.7%
Sodium Laurate	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.005-14%
Sodium Laurate	Body and hand products Not spray	 6%
Sodium Laurate/Linoleate /Oleate/Palmitate	Other baby products Body soap	 74.5%
Sodium Laurate/Linoleate /Oleate/Palmitate	Bath soaps and detergents	84.7%
Sodium Oleate	Bath oils, tablets and salts	0.35-0.38%
Sodium Oleate	Hair dyes and colors	0.2%
Sodium Oleate	Foundations	0.000002%

Sodium Oleate	Bath soaps and detergents	0.000025-3.7%
Sodium Oleate	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.5%
Sodium Oleate	Other skin care preparations	0.00001-0.025%
Sodium Palmitate	Other baby products	0.06%
Sodium Palmitate	Bath soaps and detergents	5.9-55.8%
Sodium Palmitate	Deodorants Not spray	 4.1%
Sodium Palmitate	Shaving cream	1.3%
Sodium Palmitate	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	5%
Sodium Stearate	Other baby products	0.033%
Sodium Stearate	Eyeliners	7.5-8.4%
Sodium Stearate	Eye shadows	6-8.4%
Sodium Stearate	Mascara	0.09-0.15%
Sodium Stearate	Other fragrance preparations Not spray, rinse-off	 84%
Sodium Stearate	Hair conditioners	0.00075%
Sodium Stearate	Tonics, dressings and other hair grooming aids Not spray	 0.1%
Sodium Stearate	Hair dyes and colors	0.4%
Sodium Stearate	Hair lighteners with color	4%
Sodium Stearate	Hair bleaches	0.55-5.5%
Sodium Stearate	Foundations	0.1-7%
Sodium Stearate	Leg and body paints	6%
Sodium Stearate	Lipstick	7%
Sodium Stearate	Makeup bases	7%
Sodium Stearate	Other manicuring preparations	7.5%
Sodium Stearate	Bath soaps and detergents	0.001-34.3%
Sodium Stearate	Deodorants Not spray	 3.5-10%
Sodium Stearate	Shaving cream	0.64-17.6%
Sodium Stearate	Shaving soap	8.9%
Sodium Stearate	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.000075-84%
Sodium Stearate	Face and neck products Not spray or powder Not spray	 0.000075% 0.1-0.5%
Sodium Stearate	Body and hand products Not spray	 4-6%
Sodium Stearate	Other skin care preparations	0.000075%
Sodium Stearate	Suntan products Not spray	 0.1%
Sodium Stearate	Indoor tanning preparations	0.13%
Sodium Tallowate	Bath soaps and detergents	9-80%

Sodium Tallowate	Other personal cleanliness products	44.9%
Sodium Tallowate	Shaving cream	5.1%
Sodium Tallowate	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	27-68.3%
Stearic Acid	Baby shampoos	0.03-0.52%
Stearic Acid	Baby lotions, oils and creams Not powder	 1.4-2.1%
Stearic Acid	Other baby products	0.52%
Stearic Acid	Bath oils, tablets and salts	0.5%
Stearic Acid	Bubble baths	0.02-1%
Stearic Acid	Eyebrow pencils	0.75-21%
Stearic Acid	Eyeliners	0.002-18%
Stearic Acid	Eye shadows	0.002-3%
Stearic Acid	Eye lotions	0.25-5.5%
Stearic Acid	Eye makeup removers	1.5%
Stearic Acid	Mascara	1-12%
Stearic Acid	Other eye makeup preparations	0.77-11.5%
Stearic Acid	Colognes and toilet waters	0.16%
Stearic Acid	Perfumes	0.27%
Stearic Acid	Other fragrance preparations Not spray, rinse-off	0.00015% 4%
Stearic Acid	Hair conditioners	0.00006-6%
Stearic Acid	Hair sprays Aerosol Pump spray	 0.6% 0.9%
Stearic Acid	Hair straighteners	1%
Stearic Acid	Rinses (noncoloring)	0.5%
Stearic Acid	Shampoos (noncoloring)	0.014-1%
Stearic Acid	Tonics, dressings and other hair grooming aids Not spray	0.01-20% 6%
Stearic Acid	Wave sets	3%
Stearic Acid	Other hair preparations (noncoloring)	0.27-7%
Stearic Acid	Hair dyes and colors	0.08-2%
Stearic Acid	Hair tints	5%
Stearic Acid	Hair rinses (coloring)	1.5%
Stearic Acid	Other hair coloring preparations	0.8%
Stearic Acid	Blushers	0.0001-0.9%
Stearic Acid	Face powders	0.36-2.1%
Stearic Acid	Foundations	0.0045-8%
Stearic Acid	Lipstick	0.0013-12%
Stearic Acid	Makeup bases	0.18-3%
Stearic Acid	Makeup fixatives	0.27-1.5%
Stearic Acid	Other makeup preparations	0.44-2%
Stearic Acid	Nail creams and lotions	0.2-1.8%
Stearic Acid	Nail polish and enamel	0.021%

Stearic Acid	Nail polish and enamel removers	0.021%
Stearic Acid	Other manicuring preparations Rinse-off	 9.1%
Stearic Acid	Dentifrices	2%
Stearic Acid	Bath soaps and detergents	0.009-37.4%
Stearic Acid	Deodorants Not spray	 0.05-4.1%
Stearic Acid	Other personal cleanliness products	0.1-4%
Stearic Acid	Aftershave lotions	0.00015-3%
Stearic Acid	Preshave lotions	18%
Stearic Acid	Shaving cream	0.1-35%
Stearic Acid	Shaving soap	10.1%
Stearic Acid	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	1.2-23.4%
Stearic Acid	Depilatories	0.53%
Stearic Acid	Face and neck products Not spray Spray	 0.05-20% 3%
Stearic Acid	Body and hand products Not spray Spray	 0.05-20% 0.1%
Stearic Acid	Foot powders and sprays	2.3-5.5%
Stearic Acid	Moisturizing products Not spray Spray	 0.32-8% 2%
Stearic Acid	Night products Not spray	 0.055-2%
Stearic Acid	Paste masks and mud packs	0.023-4%
Stearic Acid	Other skin care preparations	0.028-8%
Stearic Acid	Suntan products Not spray	 0.55-2.4%
Stearic Acid	Indoor tanning preparations	1.8-2%
Stearic Acid	Other suntan preparations	1%
Undecanoic Acid	Bath soaps and detergents Hand soap	0.016-0.03% 0.14%
Undecanoic Acid	Deodorants Not spray Aerosol	 0.096% 0.0014%
Undecylenic Acid	Powders (dusting and talcum)	0.2%
Undecylenic Acid	Nail creams and lotions	25%
Hydroxystearic Acid	Eyeliners	0.5-4.2%
Hydroxystearic Acid	Eye shadows	0.8-14%
Hydroxystearic Acid	Eye lotions	0.018-5.8%
Hydroxystearic Acid	Mascara	0.2%
Hydroxystearic Acid	Rinses (noncoloring)	0.8%
Hydroxystearic Acid	Tonics, dressings and other hair grooming	

	aids Not spray	4%
Hydroxystearic Acid	Blushers	2-10.1%
Hydroxystearic Acid	Face powders	0.5%
Hydroxystearic Acid	Foundations	0.055-2.6%
Hydroxystearic Acid	Lipstick	0.15-10%
Hydroxystearic Acid	Makeup bases	3%
Hydroxystearic Acid	Nail creams and lotions	0.038%
Hydroxystearic Acid	Nail polish and enamel removers	0.00011%
Hydroxystearic Acid	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	2%
Hydroxystearic Acid	Face and neck products Not spray	0.032-0.72%
Hydroxystearic Acid	Body and hand products Not spray	0.01-2.6%
Hydroxystearic Acid	Moisturizing products Not spray	0.06%
Hydroxystearic Acid	Night products Not spray	0.005%
Hydroxycapric Acid	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.7%
Hydroxycapric Acid	Face and neck products Not spray	0.7%
Hydroxycaprylic Acid	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.076%
Hydroxycaprylic Acid	Face and neck products Not spray	0.076%
10-Hydroxydecanoic Acid	Other eye makeup preparations	0.1%
10-Hydroxydecanoic Acid	Face powders	0.02%
10-Hydroxydecanoic Acid	Foundations	0.1%
10-Hydroxydecanoic Acid	Face and neck products Not spray	0.1%
10-Hydroxydecanoic Acid	Moisturizing products Not spray	0.0084%
10-Hydroxydecanoic Acid	Other skin care preparations	0.014-0.1%

*Ingredients included in the title of the table but not found in the table were included in the concentration of use survey, but no uses were reported

Information collected in 2016

Table prepared December 14, 2016

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Carol Eisenmann, Ph.D.
Personal Care Products Council

DATE: April 2, 2018

SUBJECT: Concentration of Use by FDA Product Category: Eicosatrienoic Acid

Eicosatrienoic Acid was included in the February 2018 concentration of use survey. No uses of this ingredient were reported.

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review (CIR)

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: October 12, 2018

SUBJECT: Scientific Literature Review: Safety Assessment of Fatty Acids and Soaps As Used in Cosmetics (posted October 2, 2018)

The Council has no suppliers listed for the following ingredients included in this report.

Aluminum Dilinoleate
Aluminum Isostearate
Aluminum Isostearates/Laurates/Palmitates
Aluminum Isostearates/Laurates/Stearates
Aluminum Isostearates/Palmitates
Aluminum Isostearates/Stearates
Ammonium Isostearate
Beeswax Acid
Calcium Behenate
Calcium Laurate
C32-35 Isoalkyl Acid
Dierucic Acid
Magnesium Lanolate
Magnesium Tallowate
Potassium Caprate
Potassium Castorate
Potassium Hydrogenated Tallowate
Potassium Hydroxystearate
Potassium Isostearate
Potassium Lanolate
Potassium Olivate/Sunflowerseedate
Potassium Tallate
Potassium Tallowate
Potassium Undecylenate
Sodium Arganate
Sodium Behenate
Sodium Castorate
Sodium Dilinoleate
Sodium Hydrogenated Tallowate
Sodium Lanolate
Sodium Lardate
Sodium Linoleate
Sodium Tamanuseedate
Trilinoleic Acid

The Council respectfully submits the following comments on the Scientific Literature Review: Safety Assessment of Fatty Acids and Soaps as Used in Cosmetics.

Key Issues

"Soap" has a specific regulatory definition in the United States (see 21CFR701.20 and https://www.fda.gov/cosmetics/productsingredients/products/ucm115449.htm). If a product meets the regulatory definition of "soap" it is regulated by the Consumer Product Safety Commission. Rather than using the term "soaps" in the title, please use "salts". If

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"soaps" is used in the title, the US regulatory definition of soaps should be stated in the report.

In addition to presenting the ingredients alphabetically, somewhere in the report it would be helpful if the ingredients were grouped by structure, e.g., saturated and unsaturated fatty acids and salts.

It would be helpful to state that this report was started because of the relatively high number of uses of Linoleic Acid reported to the VCRP. More information about Linoleic Acid, such as major sources, method of manufacture and the *Food Chemical Codex* specifications should be added to the CIR report.

Introduction - The CIR Expert Panel conclusion of insufficient data for Arachidonic Acid has not changed. According to CIR procedures, after 2 years the insufficient data conclusion was "classified" as "Use Not Supported by the Data and Information Submitted to CIR."

Additional Considerations

Chemistry, Definitions and Structures - If the chain lengths of fatty acids are in the range of "4 to 22 carbons in length", please explain why an ingredient such as C10-40 Isoalkyl Acid is included in this CIR report (other examples of ingredients with carbon chain lengths longer than 22 can be found in Table 1). It would be helpful if the Chemistry section included a discussion of the variation in structure among the ingredients found in this report, e.g., saturated vs unsaturated, straight chained vs branched.

Method of Manufacturing, Myristic Acid, old report summary - "tail-oil" needs to be corrected to "tall-oil" (pine oil)

Composition/Impurities - It would be helpful to list all of the fatty acids that are included in the *Food Chemical Codex* and provide their specifications.

Cosmetic Use - As there is more than one ingredient in this report, "ingredient" needs to be corrected to "ingredients". It would be helpful if information about ingredients not previously reviewed by CIR with relatively high uses, e.g., Linoleic Acid, was discussed in the text and the Summary.

The NICNAS Assessment does not belong in the Cosmetic Use section.

Non-Cosmetic Use - Please add some information about the normal dietary intakes of fatty acids (especially the essential fatty acids such as Linoleic Acid).

Penetration Enhancement - As the ability to enhance penetration of drugs also depends on structure/properties of the drug, please identify the drug(s) for which penetration was enhanced by a fatty acid or fatty acid salt.

ADME, Lauric Acid, Oleic Acid, Palmitic Acid, Stearic Acid, old report summary - The following sentence does not belong in the ADME section: "High intake of dietary saturated fatty acids has been associated with the incidence of atherscleroses and thrombosis."

Acute - In the description of the dermal studies, please correct "200 mg/kg/bw" to "2000 mg/kg bw" (as stated in Table 9). Please state the range of doses tested in the oral studies (state the compound with each dose tested).

Acute, Aluminum Stearate, Ammonium Stearate, Lithium Stearate, Magnesium Stearate, and Sodium Stearate, old report summary - Please give some indication of the doses used in these studies.

Short-Term and Subchronic - Please state the highest doses of Behenic Acid, Calcium Stearate and Capric Acid that were tested. It should be noted that the Dictionary lists conjugated Linoleic Acid as a technical name for Isomerized Safflower Acid. Please state the species in which the 8-week dietary study of Undecylenic Acid was completed.

Short-Term and Subchronic; Chronic Calcium Stearate, old report summaries - What doses were used in the intratracheal studies of Calcium Stearate?

DART - What species was used in the study of Lithium Stearate? As the time during gestation the animals were treated will determine the type of effects observed, the time of treatment in relation to gestation needs to be stated for all DART studies.

DART, Lauric Acid, Myristic Acid, Oleic Acid, Palmitic Acid Stearic Acid, re-review - Were the effects on sperm cells observed in *in vitro* or *in vivo* studies?

DART, Magnesium Stearate, old report summary - The following is not clear: "When fed to female rabbits 8 days post-coitus..". Were the rabbits treated starting at 8 days post-coitus? or were they treated for 8 days post-coitus?

Carcinogenicity - Please correct: "in growth curved of treated and control rats"

Carcinogenicity, Lauric Acid, Oleic Acid, Palmitic Acid, Stearic Acid, old report study - Rather than 2 "species" of mice, it was likely 2 "strains". Units of mg/mouse should be called a "dose" rather than "concentration". What was the duration of the dietary study of Stearic Acid in mice?

Dermal Irritation and Sensitization - Which compounds were irritating and which were corrosive? What concentrations were tested? Is there any association of dermal irritation with fatty acid structure?

Dermal Irritation and Sensitization, Lauric Acid, Oleic Acid, Palmitic Acid, Myristic Acid and Stearic Acid, old report summaries - Please correct "mmol%" and "topically applied to the of the external ear canal". In what species were the maximization studies of 2 cosmetic products completed?

Summary - As fatty acids are ingredients that are being reviewed in this report, it does not make sense to state: "fatty acids that are used to derive the ingredients described in this safety assessment".

How was it determined that "LD_{50} values in oral studies of numerous fatty acid and soap ingredients were <u>well</u> above the doses tested"?

Rather than saying a study was "dated", please state the year it was completed.

Which fatty acids salts were negative in genotoxicity assays.

Previous Discussions, Lauric Acid, et al. - Please correct "Laurie"

Previous Discussions, Myristic Acid - Please correct: "to from"

Table 1, Aluminum Stearates - Please correct "tristate"

Table 1, Aluminum Tristearate - Please correct "slat"

Table 1, Sodium Tamanuseedate - The chain lengths of fatty acids found in Calophyllum Inophyllum Seed Oil should be stated.

Table 3, Ammonium Oleate - For Melting Point, the Property column says "°C" while the Value column says "F"

Table 7 - This "Table" would be easier to read if was a two column table (column 1 the regulation; column 2 the ingredients listed in the regulation).

Table 9 - As there are no LC_{50} studies currently in the table, LC_{50} should be deleted from the column title.

Table 9 , Oral - Please correct: "and greater experiences nasal hemorrhage". The results column of the first oral study suggests that there was dose of 40 ml/kg, but this dose is not listed in the study protocol column. Many of the oral studies state the number of rats "per dose group" when only one dose was used. This is not necessary for single dose studies. In the study of 25% Caprylic Acid, it is not clear what is meant by "reduced state". In the results column of the last study, please correct: "spamodical"

Table 11, Oral, Capric Acid - OECD 421 does not appear to be the correct guideline as it also includes males.

Table 13 - Did the studies from reference 58 really use "full-thickness human mammary tissue" - if so this study does not belong in the skin irritation section. It is more likely that they used skin from breast reduction surgery, not "mammary tissue".