Safety Assessment of Isopropyl Lanolate as Used in Cosmetics

Status:	Re-Review for Panel Consideration
Release Date:	August 22, 2019
Panel Meeting Date:	September 16-17, 2019

The 2019 Cosmetic Ingredient Review Expert Panel members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.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 Monice Fiume, Senior Director.

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Cosmetic Ingredient Review

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Memorandum

To: CIR Expert Panel Members and Liaisons
From: Monice M. Fiume MMF
Senior Director, CIR
Date: August 22, 2019
Subject: Re-Review of the Safety Assessment of Isopropyl Lanolate

The CIR Expert Panel first published the safety assessment of Isopropyl Lanolate in 1980. The Panel concluded that "On the basis of the information available, which the Expert Panel believes to have been accumulated in a reasonable manner, it is concluded that Isopropyl Lanolate is safe as currently used in cosmetic products." The original report is included for your use (identified as *isolan092019orig* in the pdf). In 2003, after considering new studies and updated use data, the Panel determined to not re-open the safety assessment (*isolan092019RR1sum*). The minutes from the Panel deliberations of that re-review are included (*isolan092019min_RR1*). Minutes from the deliberations of the original review are unavailable.

Because it has been at least 15 years since the first re-review summary was published, in accord with CIR Procedures, the Panel should again consider whether the safety assessment of Isopropyl Lanolate should be re-opened. An exhaustive search of the world's literature was performed for studies dated 1995 forward, but no relevant new data were found. However, a data profile is included with this submission that identifies information summarized in the original (1980) report (*isolan092019prof_orig*).

Included for your review are current and historical (2001) use data (*isolan092019use tbl*). The frequency and maximum concentrations of use have decreased significantly since the initial re-review was considered. According to VCRP data, Isopropyl Lanolate was reported to be used in 415 formulations in 2001, but is only reported to be used in 122 formulation in 2019. The maximum reported concentration of use decreased from 26% in 2001 to 14.5% in 2019. It should be noted, however, that the maximum concentration of use in products that could result in incidental ingestion (lipsticks) has remained basically the same (~14%), but for products that result in dermal contact, that concentration has decreased from 26% (in foundations) in 2001 to 6% (in eyeliners) in 2019. It should also be noted that when compared to the use data included in the 1980 assessment, the decreases are even more significant; at that time, Isopropyl Lanolate was reported to be used in 1194 formulations at concentrations up to 50%. The 2019 FDA VCRP data and the results of the 2019 concentration of use survey conducted by the Council are included with this submission (*isolan092019FDA*; *isolan2019conc, respectively*).

The Panel has reviewed the safety of lanolin and numerous lanolin-containing ingredients. In 1980, the Panel concluded that lanolin and eight related ingredients "are safe for topical application to humans in the present practices of use and concentration" as described in that report; the conclusion was reaffirmed in 2005. In 2018, the Panel published a safety assessment on 39 polyether lanolins (which included previously-reviewed polypropylene glycol lanolins and polyethylene glycol lanolins), concluding that these ingredients are "safe in the present practices of use and concentration" described in the safety assessment.

If the Panel determines that a re-review is warranted, a full draft amended report will be presented at an upcoming meeting.

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Isopropyl Lanolate Re-review - Data Profile (original 1980 report)* – September 2019 – Monice Fiume

	Use				Toxico-kinetics			Acute Tox			Repeated Dose Tox			DART		Genotox		Carci		Dermal Irritation			Dermal Sensitization				Ocular Irritation		Clinical Studies	
	Current Info	Old Reports	Method of Mfg	Impurities	log P/log K_{ow}	Dermal Penetration	ADME	Dermal	Oral	Inhalation	Dermal	Oral	Inhalation	Dermal	Oral	In Vitro	In Vivo	Dermal	Oral	In Vitro	Animal	Human	In Vitro	Animal	Human	Photosensitization	In Vitro	Animal	Retrospective/ Multicenter	Case Reports
Isopropyl Lanolate	122 uses	414 uses (2001) 1194 uses (1976)							X		X										X	X		X	X	X		X		

* "X" indicates data included in the original assessment

Isopropyl Lanolate RR

Ingredient	CAS #	PubMed	FDA	EU	ECHA	SIDS	NICNAS	NTIS	NTP	WHO	FAO	NIOSH	Web
Isopropyl Lanolate	63393-93-1	3 hits	---	---	yes, but old data	---	---	---	---	---	---	---	---

Isopropyl Lanolate – published in 1982; RR sum published in 2003

Search Strategy/PubMed – 7/16/19 - from 1995 on

((isopropyl lanolate) OR 63393-93-1[EC/RN Number]) AND ("1995"[Date - Publication] : "3000"[Date - Publication]) - 3 hits2 useful

LINKS

Search Engines

- Pubmed (- http://www.ncbi.nlm.nih.gov/pubmed)

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 – not as a scientific source, purely for informational reasons

June 2001 – Minutes from Original Re-Review Deliberations

Isopropyl Lanolate

Dr. Schroeter noted that the original Final Report on this ingredient was published in 1979 with a safe as used conclusion, and, after reviewing the new data, that his Team concluded that the Panel's original conclusion should not be changed. He added that any information on the re-review of this ingredient that is published should include USP limitations and guidelines on pesticides and infectious agents.

Dr. Schroeter acknowledged that other lanolins are included on the CIR priority list, and recommended that these ingredients be reviewed in the order in which they appear on this list or grouped for review in the future.

For Isopropyl Lanolate as well as all ingredients in this category (i.e., no change in original conclusion) that will be considered for re-review in a given year, Dr. Schroeter recommended an annual journal publication in the form of a brief communication (abstract included) that addresses each re-review.

Dr. Belsito stated that if the safety of Isopropyl Lanolate were reevaluated, any new data on lanolin (which would also include any data on transmissible spongiform encephalopathies) would have to be included in the safety assessment. He agreed that the Panel's safety assessment of Isopropyl Lanolate should not be reopened.

Dr. Bergfeld asked Dr. Andersen to comment on any specific plans/procedures relating to the re-review process.

Dr. Andersen emphasized the importance of due process, and noted that due process has already begun. Specifically, the list of ingredients to be considered for re-review in 2001 was announced at the December 4-5, 2000 Panel meeting, and the opportunity for any interested party to provide information to the Panel was stated clearly. Use concentration data were received in response to this announcement. Dr. Andersen noted that any decisions that are reached at today's meeting (i.e., simple reaffirmation of safety, small addendum, large addendum with new ingredients, or an amended conclusion), will be included in the announcement of meeting results, which will be followed by a 90-day comment period.

Ms. Fise recommended that CIR develop a document that describes the re-review process in its entirety, exactly what all of the possible outcomes will entail, and exactly how the Panel will function in a general re-review. She also said that it should be emphasized very clearly that, at any stage, the Panel is willing to receive information, and that a statement to that effect should appear in any re-review document that is published. In other words, it should be made clear that anyone can submit new information for the Panel's review at any time.

Dr. McEwen expressed concern over the amount of time that may be spent by the CIR staff in searching for information on ingredients that have relatively little or no use, or by the Panel in reviewing this information and determining the content of an addendum or amendment. He noted that there are many ingredients on the CIR priority list that have not been reviewed.

Dr. Andersen said that the re-review process is a purposeful exercise on the part of the Panel to review old safety assessments. Furthermore, based on today's discussion, the expectation is that the Panel will state positively that there are no new test data that would warrant a change in the Panel's original conclusion on Isopropyl Lanolate. Dr. Andersen added that the Panel's decision needs to be captured in some form and made available to the public, insuring that it can be accessed easily and cited.

Dr. McEwen suggested that the report on the re-review (or brief communication) consist of the following: (1) Statement of exactly what was done. Example: These databases were searched for additional information on the toxicity of _____. The Panel reviewed that information and determined that no change in the conclusion(s) in its previous report was necessary (See *Journal of the American College of Toxicology*). A list of the ingredients, on a yearly basis, that this statement applies to would also be included. Appropriate changes that the Panel has considered to be of a generic nature (e.g., pesticide residues, heavy metals, etc.) could be captured in a similar fashion.

Dr. Belsito agreed with Dr. McEwen's suggestion, and that such a document would need to be published so that it could be referenced.

Dr. Bergfeld said that she would suspect that by the next Panel meeting, outlines of various models relating to the re-review process would be available. These models would indicate the different paths that ingredients would take in this process.

Ms. Fise confirmed that the brief communication on Isopropyl Lanolate will contain a note concerning limitations on pesticide residues.

Dr. Andersen asked that the Panel consider expanding its thinking on reaffirming the safety of Isopropyl Lanolate to the CIR Final Report on the following ingredients (published in 1980): Acetylated Lanolin Alcohol, Lanolin, Lanolin Oil, Lanolin Acid, Lanolin Alcohol, Lanolin Wax, Acetylated Lanolin, Hydrogenated Lanolin, and Hydroxylated Lanolin. He noted that the issues that were considered in the safety assessments were all focused on Lanolin, and that the Panel could reaffirm the safety of these ingredients as well at this Panel meeting.

Dr. Bergfeld said that unlike the other ingredients that are being considered for re-review at this meeting, the Acetylated Lanolin Alcohol ingredient family was not included on the meeting agenda that was announced. Thus, it is not possible to

move forward with a decision on these ingredients today. Dr. Bergfeld asked that the Panel, at its September 10-11, 2001 meeting, consider revising the proposed brief communication on Isopropyl Lanolate to incorporate this group of ingredients. However, she emphasized that the Panel will arrive at a decision on the re-review of Isopropyl Lanolate at today's meeting.

Dr. Schroeter said that the minutes should reflect that, in the future, other lanolins will be reviewed in the order in which they appear on the CIR priority list.

Dr. Andersen said that CIR can announce that the Panel is also considering the re-review of the Acetylated Lanolin Alcohol ingredient family (CIR Final Report published in 1980). He also said that the announcement will also contain a caveat indicating that the Panel is not undertaking a review of any new Lanolate ingredients that have been added to the International Cosmetic Ingredient Dictionary and Handbook and are being used in cosmetics. These ingredients will be addressed after they have been added to the CIR Priority List.

The Panel unanimously concluded that the Panel's original safety assessment of Isopropyl Lanolate does not need to be reopened for a complete review and that the safe as used conclusion on this ingredient does not need to be changed.

Dr. Bergfeld said that a public announcement of the Panel's decision on Isopropyl Lanolate will follow and that a model for the publication of this decision, along with any accompanying information, will be developed.

Dr. Andersen said that, based on the recommendation made by Ms. Fise, CIR will also proceed to develop a document that describes the re-review process in its entirety.

Current (2019) and historical (2001) frequency and maximum concentration of use of Isopropyl Lanolate according to duration and exposure

	# of Uses		*Max Conc of Use (%)*	
	2019[1]	**2001[2]**	**2019[3]**	**2001[2]**
Totals*	**122**	**415**	**0.005 – 14.5**	**0.4 – 26**
Leave-On	*118*	*393*	*0.05 – 14.5*	*1 – 26*
Rinse-Off	*4*	*21*	*NR*	*0.4 – 6*
Diluted for (Bath) Use	*NR*	*1*	*NR*	*NR*
Eye Area	35	41	6	2 – 10
Incidental Ingestion	19	183	2.7 – 14.5	2 – 14
Incidental Inhalation-Spray	3; 4[a]; 13[b]	27[a]; 25[b]	4[a]	10; 1-15[a]; 1-5[b]
Incidental Inhalation-Powder	11; 13[b]	13; 25[b]; 1[c]	1.5[c]	3-6; 1-5[b]
Dermal Contact	100	226	0.5 – 6	1 – 26
Deodorant (underarm)	1[a]	NR	NR	NR
Hair - Non-Coloring	1	4	4	2
Hair-Coloring	NR	NR	NR	0.4
Nail	1	2	NR	1 – 9
Mucous Membrane	19	188	2.7 – 14.5	2 – 14
Baby Products	NR	1	NR	NR

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

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

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

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

NR – no reported use

1. US Food and Drug Administration (FDA) Center for Food Safety & Applied Nutrition (CFSAN). 2019. Voluntary Cosmetic Registration Program (VCRP) - Frequency of Use of Cosmetic Ingredients. College Park, MD Obtained under the Freedom of Information Act from CFSAN; requested as "Frequency of Use Data" January 3 2019; received February 13, 2019.

2. Andersen F.A. (ed). Annual Review of Cosmetic Ingredient Safety Assessments - 2001/2001. Isopropyl Lanolate. *Int J Toxicol*. 2003;22:17-19.

3. Personal Care Products Council. 2019. Concentration of Use by FDA Product Category: Isopropyl Lanolate. Unpublished data submitted by the Personal Care Products Council on April 11, 2019.

FINAL REPORT OF THE SAFETY ASSESSMENT FOR ISOPROPYL LANOLATE

Isopropyl Lanolate is used in many types of cosmetic products which contact the skin, mucous membranes, and respiratory tract daily and over long periods of time.

Isopropyl Lanolate had an acute oral LD50 >40g/kg in the rat; a very mild, transient primary irritant effect on the skin of the rabbit and guinea pig; and a slight promptly reversible, irritant action on the conjunctivae of the rabbit. Skin sensitization and photosensitization tests were negative in the white guinea pig.

Skin irritation studies in humans were negative, with the exception of one study in which six out of 53 subjects showed some irritation at high concentrations. Two of 53 subjects classed as hyper-reactive by the investigator indicated sensitivity at high concentrations of Isopropyl Lanolate. Human patch tests with cosmetic formulations containing 6 and 14 percent Isopropyl Lanolate were "very slightly irritating." None of the three formulations tests produced contact allergy sensitization.

On the basis of the information available, it is concluded that Isopropyl Lanolate is safe as currently used in cosmetic products.

CHEMICAL AND PHYSICAL PROPERTIES

Structure and Properties

Isopropyl Lanolate is a mixture of isopropyl esters of lanolin acids. The lanolin acids are derived from natural lanolin by hydrolysis. After purification the acids are esterified with isopropanol using a suitable catalyst system. Lanolin fatty acids are a mixture of normal and branched chain and hydroxy acids, ranging in length from C_{12} to C_{34}. Therefore, Isopropyl Lanolate is a mixture of isopropyl esters of these acids. Their average composition is given in Table 1.

The following properties characterize Isopropyl Lanolate (CTFA, 1978a):

Property	Range
Melting point	26°C - 39°C
Specific gravity 25°/25°	0.850 - 0.865
Acid value	20 maximum
Saponification value	135 - 165
Iodine value	6 - 20
Hydroxyl value	35 - 65
Moisture	0.2% maximum
Ash	0.2% maximum

TABLE 1. Typical Fatty Acid Composition of Lanolin

Group	Subgroup	Percentage	Carbon Chain Length Range	Predominant Constituents of Subgroup
Non-hydroxylated	nor	12.69	8-38	C_{24} (18.7%)[1], C_{16} (18), C_{26} (15.5)
	iso	22.08	8-38	C_{20} (1.7), C_{16} (16.5), C_{26} (14.6)
	anteiso	26.23	7-41	C_{25} (14.7), C_{19} (13.5), C_{27} (13.4)
	unsat.	2.10	-	mostly C_{16} and C_{18}
Alpha-hydroxylated	nor	21.71	10-32	C_{16} (88.3)
	iso	4.48	12-34	C_{18} (71.9)
	anteiso	0.81	11-33	C_{23} (40.9), C_{25} (19.8)
Omega-hydroxylated	nor	3.05	22-36	C_{30} (45), C_{32} (21.8), C_{28} (16.1)
	iso	0.81	22-36	C_{30} (39.6), C_{32} (32.6)
	anteiso	1.34	23-35	C_{31} (36), C_{25}(26.9), C_{33} (16.3)
Poly-hydroxylated	all	4.70	-	not characterized
TOTAL		100.00%		

[1]Percent of all within specified subgroup.

Analytical Methods

Spilker and Richey (1973) have described a number of methods for the analysis of lanolin derivatives involving hydrolysis, fractionation, chromatographic separation and identification.

USE

Purpose and Extent of Use in Cosmetics

Isopropyl Lanolate is one of the more versatile of the lanolin derivatives because of its surfactant properties and pigment dispersing ability. It is used in combination with mineral oil and isopropyl palmitate for pigments such as titanium dioxide, oxy red and red #9. In lipsticks, creams, lotions and aerosol emulsions, it acts as a lubricant and gives a high gloss (Conrad, 1962; Conrad *et al.*, 1965; Synyer, 1975; Murphy and Lieberman, 1976).

Isopropyl Lanolate has been used in cosmetics and topical pharmaceuticals for over 20 years. Its current use in cosmetic formulations reported to FDA is shown in Table 2 (FDA, 1976). About 5 percent of these formulations contain this ingredient at 10 to 25% by weight.

BIOLOGICAL PROPERTIES

Animal Toxicology

General Studies

Acute

Oral The acute oral LD50 of Isopropyl Lanolate is greater than 40 g/kg in the rat. Single-dose oral toxicity tests of this ingredient, undiluted or in various

TABLE 2. Prduct Formulation Data (FDA, 1976)

Ingredient	Cosmetic Product Type	Concentration (%)	Number of Product Formulations
Isopropyl Lanolate	Bath oils, tablets, and salts	> 0.1 to 1	3
	Other bath preparations	> 1 to 5	1
		> 0.1 to 1	1
	Eyeliner	> 10 to 25	1
		> 5 to 10	1
		> 1 to 5	61
		> 0.1 to 1	6
	Eye shadow	> 10 to 25	7
		> 5 to 10	62
		> 1 to 5	57
		> 0.1 to 1	58
	Eye makeup remover	> 1 to 5	1
	Mascara	> 5 to 10	1
		> 1 to 5	4
	Other eye makeup preparations	> 10 to 25	4
		> 1 to 5	7
	Eyebrow pencil	> 1 to 5	10
	Sachets	> 1 to 5	3
	Other fragrance preparations	> 0.1 to 1	4
	Hair conditioners	> 0.1 to 1	4
	Hair sprays (aerosol fixatives)	≤ 0.1	2
	Tonics, dressings, and other hair grooming aids	> 1 to 5	2
	Other hair preparations	> 1 to 5	1
	Blushers (all types)	> 10 to 25	1
		> 5 to 10	16
		> 1 to 5	32
		> 0.1 to 1	27
		≤ 0.1	8
	Face powders	> 1 to 5	16
		> 0.1 to 1	31
	Foundations	> 10 to 25	7
		> 5 to 10	19
		> 1 to 5	45
		> 0.1 to 1	17
	Lipstick	> 25 to 50	1
		> 10 to 25	30
		> 5 to 10	231
		> 1 to 5	64
		> 0.1 to 5	21
		≤ 0.1	1
	Makeup bases	> 10 to 25	3
		> 5 to 10	15
		> 1 to 5	43
		> 0.1 to 1	104
		≤ 0.1	11

TABLE 2. Continued

Ingredient	Cosmetic Product Type	Concentration (%)	Number of Product Formulations
Isopropyl Lanolate	Rouges	> 10 to 25	3
		> 1 to 5	5
		> 0.1 to 1	3
	Makeup fixatives	> 0.1 to 1	2
	Other makeup preparations	> 10 to 25	3
		> 5 to 10	3
		> 1 to 5	3
		> 0.1 to 1	10
	Deodorants (underarm)	> 1 to 5	1
		≤ 0.1	1
	Aftershave lotions	> 1 to 5	3
	Beard softeners	> 0.1 to 1	1
	Preshave lotions (all types)	> 0.1 to 1	4
		≤ 0.1	1
	Shaving creams (aerosol, brushless, and lather)	> 0.1 to 1	2
	Other shaving preparation products	> 1 to 5	1
	Cleansing (cold creams, cleansing lotions, liquids and pads)	> 5 to 10	1
		> 1 to 5	1
		> 0.1 to 1	3
	Face, body, and hand (excluding shaving preparations)	> 10 to 25	1
		> 1 to 5	20
		> 0.1 to 1	27
	Hormone	> 0.1 to 1	1
	Moisturizing	> 5 to 10	2
		> 1 to 5	24
		> 0.1 to 1	11
		≤ 0.1	4
	Night	> 5 to 10	1
		> 1 to 5	3
	Skin lighteners	> 1 to 5	1
	Skin fresheners	> 1 to 5	1
		> 0.1 to 1	1
	Wrinkle smoothing (removers)	> 5 to 10	2
	Other skin care preparations	> 1 to 5	4
	Suntan gels, creams, and lotions	> 5 to 10	1
		≤ 0.1	2
	Other suntan preparations	> 1 to 5	1
		> 0.1 to 1	1

vehicles, have been carried out on young adult white rats. The designs and results of these studies are summarized in Table 3. The administration in all cases was by intragastric intubation. No deaths occurred in two tests in which as much as 42.7 g/kg of Isopropyl Lanolate was administered.

TABLE 3. Acute Oral Toxicity

Test Material	Species	Dose/kg	Mortality (%)	LD50/kg	References
Distilled Isopropyl Lanolate	Rat (5M & F)	2 ml	0		CTFA, 1977
		4 ml	0		
		8 ml	0	>64 ml	
		16 ml	0		
		32 ml	0		
		64 ml	0		
Isopropyl Lanolate	Rat (5M & F)	as above	0	>64 ml >42.7 g	Bio-Tox. Labs., 1970
Isopropyl Lanolate (50% solution in vegetable oil)	Rat (1M, 1F)	2.5 g	0		
		5.0 g	0		
		10.0 g	0	>40 g	Bio-Tox. Labs., 1974
		20.0 g	0		
		40.0 g	0		
Isopropyl Lanolate (100%)	Rat (1M, 1F)	as above	0	>40 ml	Food and Drug Res. Labs., 1974
Isopropyl Lanolate (40% suspension in arachis oil)	Rat (5M, 5F)	0	0	>16 g	Food and Drug Res. Labs., 1973
		10 g	0		
		16 g	10 (1F)		
Isopropyl Lanolate (2%)[1]	Rat (5M, 5F)	92.9 g (of mixture)	0	...	CTFA, 1978
Isopropyl Lanolate (6% in makeup concealer)	Rat	...	...	>15.9 g	CTFA, 1978

[1]Two percent Isopropyl Lanolate "in a soft, non-pourable cream with a low pH in a non-ionic oil-in-water emulsion."

Skin Irritation Table 4 shows the results of ten tests on six different preparations of Isopropyl Lanolate. These tests were all performed by standardized procedures involving the application of 0.5 ml of the test material to each of two areas (one abraded and the other intact) on the clipped back of each experimental animal. The test animal was the rabbit in all cases except one in which the guinea pig was used. The Primary Irritation Index (PII) score did not exceed 2.0 in any test out of a maximum possible score of 8. The scores ranged from 0.2 to 1.9 in seven tests, and were zero in the other three. It was concluded that Isopropyl Lanolate has a mild irritant action in tests for primary skin irritancy in the rabbit and guinea pig (Bio-Tox. Labs., 1970).

Eye Irritation The designs and results of eight rabbit eye irritation tests of various preparations of Isopropyl Lanolate, and of three tests on products containing 2, 6, and 20% Isopropyl Lanolate, respectively, are summarized in Table 5. It is noted that the application of the undiluted ingredient resulted in mean scores ranging from 0 to 7.7 out of a maximum possible score of 110, reflecting no irritation to "slight," "mild," "minimal," or "marginal" transient irritation, affecting only the conjunctiva. At a concentration of 20 percent in mineral oil, there was no irritation. Two formulations containing 2 and 6 percent Isopropyl Lanolate produced a minimal, transient irritation affecting

TABLE 4. Primary Skin Irritation

Test Material	Animal and No.	Concentration	Method	PII Score	Conclusion	References
Distilled Isopropyl Lanolate	Rabbit 3	Undiluted	Draize *et al.* Skin intact and abraded	0	Non-irritating.	CTFA, 1977
Distilled Isopropyl Lanolate	Guinea Pig 6	Undiluted	Draize *et al.* Skin intact and abraded	0	Non-irritating.	CTFA, 1977
Isopropyl Lanolate	Rabbit 6	Undiluted	Draize *et al.* Skin intact and abraded	0	Non-irritating.	Bio-Tox. Labs., 1970
Isopropyl Lanolate	Rabbit 6	Undiluted	Dept. of Transportation	0.2	Mild primary irritant. Erythema-eschar at 4 hrs. only	Bio-Tox. Labs., 1970
Isopropyl Lanolate	Rabbit 6	Undiluted	Draize *et al.*	1.54	Mild irritant. Erythema and eschar only; no edema.	Bio-Tox. Labs., 1974
Isopropyl Lanolate	Rabbit 6	Undiluted	Draize *et al.*	0.54	Mild irritant. Erythema and eschar only; no edema.	Food and Drug Res. Labs., 1974
Isopropyl Lanolate	Rabbit 6	Undiluted	Draize *et al.*	1.3	Mild irritant. Both erythema and edema at 24 & 72 hrs.	Food and Drug Res. Labs., 1973
Isopropyl Lanolate	Rabbit 6	Undiluted	Draize *et al.*	0.5	Mild irritant.	Food and Drug Res. Labs., 1973
Isopropyl Lanolate	Rabbit 6	Undiluted	Draize *et al.*	1.9	Mild irritant. Both erythema and edema at 24 & 72 hrs.	Food and Drug Res. Labs., 1973
Isopropyl Lanolate	Rabbit 6	Undiluted	Draize *et al.*	1.9	Mild irritant. Both erythema and edemat at 24 & 72 hrs.	Food and Drug Res. Labs., 1973

TABLE 5. Acute Eye Irritation

Test Material	No. of Rabbits	Methodology	Times of Observation	Mean Score	Conclusion	References
Distilled Isopropyl Lanolate	3, unwashed	Draize, undiluted	1 hr daily for 7 days	0	No irritation.	CTFA, 1977
	3, washed 2 sec.			0	No irritation.	
	3, washed, 4 sec.			0	No irritation	
Isopropyl Lanolate	3, unwashed	Draize, undiluted	1 hr & daily for 7 days	2.7 (at 1 day)	Slight hyperemia of conjunctiva.	Bio-Tox. Labs., 1970
	3, washed, 2 sec.			0	No irritation.	
	3, washed, 4 sec.			0	No irritation.	
Isopropyl Lanolate	6, unwashed	16 CFR 1500.42 undiluted	1, 2, 3, 7 days	7.7 (at 1 day)	Mild transient irritant, conjunctiva only; 7-day recovery.	Bio-Tox. Labs., 1974
Isopropyl Lanolate	6, unwashed	16 CFR 1500.42 undiluted	1, 2, 3, 7 days	7.0 (at 1 day)	Mild transient irritant, conjunctiva only; 7-day recovery.	Food and Drug Res. Labs., 1974
Isopropyl Lanolate (20% in mineral oil)	6, unwashed	16 CFR 1500.42 20%	1, 2, 3, 7 days.	0	No irritation.	Food and Drug Res. Labs., 1974
Isopropyl Lanolate	5, washed, 5 min.	Fed. Reg. 37, No. 83,	1 hr; 1,2,3,4,	1	"Marginal irritant."	Food and Drug Res. Labs., 1973
	3, washed, 24 hr.	1972; 0.1 ml each eye undiluted	7 days	1	Conjunctival redness, chemosis 1hr-1 dayonly.	
Isopropyl Lanolate	5, washed, 5 min.	Fed. Reg. 37, No. 83,	1 hr; 1,2,3,4,	1	"Marginal irritant."	Food and Drug Res. Labs., 1973
	3, washed, 24 hr.	1972; 0.05g in each eye undiluted	7 days	1	Conjunctival redness, chemosis 1hr-1day only.	Food and Drug Res. Labs., 1973
Isopropyl Lanolate	6, washed, 24 hr.	Fed. Reg., Sept. 17, 1964;(S191.12);0.1 ml undiluted	1, 2, 3 days	...	No Irritation	Food and Drug Res. Labs., 1973
Isopropyl Lanolate	6, washed, 24 hr.	Fed. Reg., Sept. 17, 1964;(S191.12); 100 mg	1, 2, 3 days	...	No irritation	Food and Drug Res. Labs., 1973
Skin care Cream Moisturizer 2% Isopropyl Lanolate)	6, unwashed	16 CFR 1500.42 0.1 ml 2%	1, 2, 3, 4, 7 days	...	Minimal irritation. Conjunctiva of 1 rabbit, at 24-48 hrs.	CTFA, 1978b.
	3, washed, 30sec.			...	Same, in 1 rabbit at 24hrs	
Makeup Concealer (6% Isopropyl Lanolate)	3-6	Draize 0.1 ml 6%	1 hr, daily for 3 days	...	Minimal irritation. Conjunctiva only, 1hr-1day.	CTFA, 1978b

only the conjunctiva. When the eyes were washed two to four seconds after application of Isopropyl Lanolate, no irritation resulted. If the eyes remained unwashed or if the washing was delayed for five minutes or 24 hours, some irritation usually occurred with the undiluted Isopropyl Lanolate. In one test on the unwashed eye, no evidence of irritation was seen (Bio-Tox. Labs., 1970, 1974; Food and Drug Res. Labs., 1974, 1973; CTFA, 1977, 1978b).

The results of these tests indicate that Isopropyl Lanolate has a very mild and transient irritation potential affecting the conjunctiva in the eye of the rabbit.

Subchronic

Dermal A 13-week dermal toxicity study of a cosmetic foundation product containing 5 percent Isopropyl Lanolate was conducted using female rats. In this test, 2000 mg/kg of the undiluted product was applied to the clipped backs of 15 rats once daily, 5 days a week, for 13 weeks (65 applications). Throughout this study, the test animals showed no adverse effects which could be attributed to the test material in the areas of behavior, appearance, body weight, hematology, skin condition, mortality, or histology (CTFA, 1977).

Special Studies

Skin Sensitization Distilled Isopropyl Lanolate was tested by the Landsteiner and Jacobs procedure in ten white male guinea pigs. A 0.1 percent solution of the test material in corn oil was injected intracutaneously on the shaved backs of the animals three times weekly for a total of 10 injections. the first injection was 0.05 ml and subsequent injections were 0.1 ml. Two weeks after the tenth injection, a challenge dose of 0.05 ml was administered. Corn oil was used in 10 control animals following the same procedure. As a result, a score of 1, indicating very slight erythema, was recorded for both experimental and control animals. The degree of sensitization was recorded as 0 for both corn oil and test material. It was concluded that distilled Isopropyl Lanolate was nonsensitizing in the guinea pig under these conditions (Bio-Tox. Labs., 1970).

Photosensitization Distilled Isopropyl Lanolate was tested for its photosensitization potential in 10 white male guinea pigs. First, the dose of ultraviolet light radiation was determined that had a sub-erythemal effect on the clipped backs of guinea pigs. The test material was applied daily for ten days and after each application the skin area was exposed for six hours to the pre-established intensity of ultraviolet light. Three control animals treated with distilled water were similarly irradiated. No evidence of photosensitization was observed in the experimental animals (Bio-Tox. Labs., 1970).

Clinical Assessment of Safety

Fifty-three human subjects, 18 years or older (race and sex not reported), were patch tested with Isopropyl Lanolate at concentrations of 20, 40, 60, and 80 percent in petrolatum, and at 100 percent in groups of 9, 13, 12, 8, and 11 individuals, respectively. Occlusive patches carrying the test material were

applied for 24 hours, four days per week for one week. At the end of the first week, all 53 subjects began to receive the 100 percent concentration which they continued to receive during the subsequent two weeks of testing. Throughout the three-week test period, a total of 12 applications and readings were scheduled for each individual. Skin irritation was scored on a scale from 0 to 4 and if any patch site developed a reaction of 2 or greater, the investigator could at his discretion, continue subsequent application on that same site or on a new site. Hence, in some individuals, more than four readings per week were taken. In application number 1, the test material did not elicit any visible evidence of irritation in any of the 53 individuals tested. In application numbers two through 12, the test material elicited evidence of irritation in six of the 53 individuals in the experiment.

Positive Subject #1: The subject scored a 1 reaction on the fifth application with 100 percent Isopropyl Lanolate with no recurrence of irritation on subsequent applications. All other scores prior to this were 0.

Positive Subject #2: The second subject scored a solitary minimal erythema (score = 1) following the twelfth application with 100 percent Isopropyl Lanolate. The erythema disappeared within 24 hours; all scores for this individual prior to this were 0.

Positive Subject #3: This subject showed a solitary minimal erythema (score = 1) after the fourth application; previous scores were 0 with 40 percent Isopropyl Lanolate. This disappeared within 24 hours with no recurrence of irritation on subsequent applications.

Positive Subject #4: This individual showed reactions during the first and third week which were suggestive of fatiguing. Scores recorded in the first week with 20 percent Isopropyl Lanolate were 0, 0, 1, and 2. Scores in the second week with 100 percent Isopropyl Lanolate were all 0, while scores in the third week, again with 100 percent Isopropyl Lanolate, were recorded as 0, 0, 0, 3, 1, 1.

Positive Subject #5: This subject scored 0 during the first week with 60 percent Isopropyl Lanolate and 0, 0, 1, 1, 0, 2, 2 during the second week with 100 percent Isopropyl Lanolate. During the third week at 100 percent Isopropyl Lanolate, three sites were scored; one site showed scores of 2, 2, 2, 1, 1, 0, a second site showed scores of 0, 3, 3, 3, and the third site indicated scores of 0, 3, 3, 3.

Positive Subject #6: This individual scored 0, 1, 1, 1, 1, 0 during the first week with 100 percent Isopropyl Lanolate. In the second week with 100 percent Isopropyl Lanolate, one site showed scores of 0, 2, 2, 1, 1, and a second site showed scores of 0, 2, 2, 1, 1. For the third week, the concentration was reduced from 100 to 80 percent at one site and to 40 percent at

another. The site at which 80 percent Isopropyl Lanolate was used showed scores of 0, 1, 0, 3, 3, and the second site using a 40 percent concentration of the test material resulted in scores of 0, 1, 2, 0.

Thirty six days after the first application of Isopropyl Lanolate, all 53 subjects received a challenge test with 100 percent Isopropyl Lanolate. Two out of 53 subjects showed reactions suggestive of sensitization. These reactions were confirmed following second and third challenges. The investigator noted that these two individuals were hyper-reactive to many skin contactants, and he concluded that ". . .sensitization by this material under actual conditions of use would be a remote possibility, especially at lower concentrations" (CTFA, 1976a).

Another patch-test study of 16 human subjects was performed in which undiluted Isopropyl Lanolate was applied daily for 21 days. Fifteen of the 16 subjects completed the test with scores of zero. One of the 16 developed a reaction to the tape used to apply the patches. It was concluded that the material was non-irritating (CTFA, 1976b).

Three manufacturers of Isopropyl Lanolate in business for 12, 41, and 20 years, respectively, have no reports of adverse effects on employees nor have these firms received any reports of problems from customers (CTFA, 1978c).

The Schwartz-Peck prophetic patch test was performed on 104 humans (age, race and sex not given) using an oil treatment stick containing 14% Isopropyl Lanolate. Zero reactions occurred in all the first and second insult closed and open patch tests and after ultraviolet light exposure (CTFA, 1977).

The Draize-Shelanski repeated insult patch test elicited zero reactions in 50 subjects (not otherwise described) following the open, closed patch test and ultraviolet exposure using the same oil treatment stick. It was concluded that this product produced no irritation or sensitization reactions (CTFA, 1977).

A skin care cream moisturizer containing 2 percent Isopropyl Lanolate was applied five days a week to the backs of one male and 12 female subjects (aged 19 to 60 years) for 21 days. The test sites were observed and scored from 0 to 3 immediately prior to applying a fresh patch. One female, age 47, was scored 3 after the sixth patch and was not further exposed but was scored 3 throughout the remainder of the test. Total score for this individual was 49. The total skin irritation score for the remaining 12 individuals was 11. Six of these 12 individuals scored 0, three scored 1, one scored 2, and two individuals scored 3 (CTFA, 1977).

Human maximization tests were conducted with the same moisturizer on 25 subjects. The test procedures were conducted according to those described in the *Journal of Investigative Dermatology* 47(5):393-409, 1966. The test group consisted of 18 white females, aged 20-43; four white males, aged 21-38; and three black females, aged 20-25. No instance of allergic contact sensitization was noted (CTFA, 1977).

Non-occlusive patch tests were performed on 101 humans using a make-up concealer containing 6 percent Isopropyl Lanolate. No irritation was observed (CTFA, 1977).

SUMMARY

Isopropyl Lanolate is a mixture of the isopropyl esters of the lanolin fatty acids ranging from C_{12} through C_{34}. It is used in many types of cosmetic products which contact the skin, mucous membranes, and respiratory tract daily and over long periods of time.

Isopropyl Lanolate had an acute oral LD50 >40 g/kg in the rat, a very mild, transient primary irritant effect on the skin of the rabbit and guinea pig, and a slight promptly reversible irritant action on the conjunctiva of the eye of the rabbit. Skin sensitization and photosensitization tests were negative in the white guinea pig. The application of 2 g/kg of a formulation containing 5 percent Isopropyl Lanolate to the skin of rats five times a week for 13 weeks produced no harmful behavioral, systemic, or local effects on the skin.

Skin irritation studies in six humans were negative, with the exception of one study in which six out of 53 subjects showed some irritation at high concentrations. Human patch tests with formulations containing 6 and 14 percent Isopropyl Lanolate showed no irritation; one formulation containing 2 percent Isopropyl Lanolate "was very slightly irritating." None of the three formulations tested produced contact allergy sensitization. Results of one skin sensitization study indicated that 100 percent Isopropyl Lanolate was capable of acting in a manner consistent with that of a sensitizer in two individuals out of 53.

Though not critical to the assessment of its safety as currently used in cosmetics, it would be desirable to have information on the absorption and metabolism of Isopropyl Lanolate in rats both when given orally and when applied to the skin. Since Isopropyl Lanolate is used in aerosol form in some cosmetic formulations, tests for irritation of the respiratory tract should be conducted. In addition, the Panel expresses some concern about the occurence in one study of skin sensitization in two out of 53 subjects tested, and believes that further human studies for skin sensitization may be warranted.

CONCLUSION

On the basis of the information available, which the Expert Panel believes to have been accumulated in a reasonable manner, it is concluded that Isopropyl Lanolate is safe as currently used in cosmetic products.

REFERENCES

Bio-Toxicology Laboratories. Isopropyl Lanolate, Distilled, 1970.

Bio-Toxicology Laboratories. Isopropyl Lanolate, 1974.

Conrad, L.I.: The versatility of lanolin derivatives. Chem. Products & Aerosol News. November, 1962.

Conrad, L.I., Maso, H.F. and DeRagon, S.A.: Influence of lanolin derivatives on dispersed systems. I. The dispersion of pigments in nonaqueous liquids. J. Soc. Cosmet. Chem. *16*:617-36, 1965.

CTFA[1]: Submission of data by CTFA. Unpublished toxicological report, 1976a[2].

CTFA: Submission of data by CTFA. Data on products containing isopropyl lanolate. Feb. 10, 1977.[2]

CTFA: Cosmetic Ingredient Description: Isopropyl Lanolate, Cosmetic, Toiletry and Fragrance Association, Washington, D.C., 1978a.

CTFA: Isopropyl Lanolate. Information for CTFA Task Force for submission to CIR, March 1978b.[2]

CTFA: Submission of data by CTFA. Aug. 22, 1978c[2].

FDA: Cosmetic product formulation data, Washington, D.C. Food and Drug Admin., August 31, 1976.
Food and Drug Research Laboratories: Isopropyl Lanolate, 1973.
Food and Drug Research Laboratories: Isopropyl Lanolate, 1974.
Hilltop Research: Submission of Data by CTFA. Research Report 76-156-70, 1976[2].
Murphy, J.H. and Lieberman, G.: Lipstick containing microencapsulated oils. (U.S. Patent). Chem. Abst. *84*:169559J, 1976.
Spilker, C.W. and Richey, T.B.: Analytical procedures for lanolin and lanolin derivatives. Cosmet. Perfum. *88*:43-8, 1973.
Synyer, W.E.: Skin conditioner composition (German Patent). Chem. Abst. *84*:155512B, 1975.

[1]Cosmetic, Toiletry and Fragrance Association.
[2]Available upon request. Administrator, Cosmetic Ingredient Review, Suite 212, 1133 15th St., NW, Washington, DC 20005.

was 1% (CTFA 2001). Table 12 presents the available use information for Imidazolidinyl Urea.

REFERENCES

Amouroux, I., D. Pesando, H. Noel, and J.-P. Girard. 1999. Mechanisms of cytotoxicity by cosmetic ingredients in sea urchin eggs. *Arch. Environ. Contam. Toxicol.* 36:28–37.

Andersen, K. E., A. Boman, K. Hamann, and J. E. Wahlberg. 1984. Guinea pig maximization test with formaldehyde releasers. Results from two laboratories. *Contact Dermatitis* 10:257–266.

Becker, D., U. Kuhn, U. Lempertz, A. Enk, J. Saloga, and J. Knop. 1997. Flow-cytometric screening for the modulation of receptor-mediated endocytosis in human dendritic cells: Implications for the development of an in vitro technique for predictive testing of contact sensitizers. *J. Immunol. Methods.* 203:171–180.

Broeckx, W., A. Bondeel, A. Dooms-Goossens, et al. 1987. Cosmetic intolerance. *Contact Dermatitis* 16:189–194.

Cosmetic, Toiletry, and Fragrance Association (CTFA). 2001. Ingredient use data—Imidazolidinyl Urea. Unpublished data submitted by CTFA.[2]

de Groot, A. C., D. P. Bruynzeel, B. A. Jagtaman, et al. 1988. Contact allergy to diazolidinyl Urea (Germall II). *Contact Dermatitis* 18:202–205.

de Groot, A. C., and J. W. Weyland. 1987. Hidden contact allergy to formaldehyde in imidazolidinyl urea. *Contact Dermatitis* 17:124–125.

de Groot, A. C., J. W. Weyland, J. D. Bos, et al. 1986. Contact allergy to preservatives I. *Contact Dermatitis* 14:120–122.

Dickel, H., J. S. Taylor, P. Evey, et al. 2001, Comparison of patch test results with a standard series among white and black racial groups. *Am. J. Contact Dermatitis* 12:77–82.

Dooms-Goossens, A., K. de Boulle, M. Dooms, et al. 1986. Imidazolidinyl urea dermatitis. *Contact Dermatitis* 14:322–324.

Elder, R. E., ed. 1980. Final report on the safety assessment for imidazolidinyl urea. *J. Environ. Pathol. Toxicol.* 4:5–17.

Food and Drug Administration (FDA). 2001. 2001 frequency of use of cosmetic ingredients. *FDA database.* Washington, DC: FDA.

Ford, G. P., and M. H. Beck. 1986. Reactions to quaternium 15, bronopol and germall 115 in a standard series. *Contact Dermatitis* 14:271–274.

Foussereau, J., and C. Cavelier. 1989. Water versus petrolatum for testing imidazolidinyl urea. *Contact Dermatitis* 21:54–55.

Frosch, P. J., A. Lahti, M. Hannuksela, et al. 1995. Chloromethylisothiazolone/methylisothiazolone(CMI/MI) use test with a shampoo on patch-test-positive subjects. Results of a multicentre double-blind crossover trial. *Contact Dermatitis* 32:210–217.

Goossens, A., M. H. Beck, E. Haneke, et al. 1999. Adverse cutaneous reactions to cosmetic allergens. *Contact Dermatitis* 40:112–113.

Guin, J. D. 1997. Contact dermatitis and other contact reactions. In *Current clinical practice: Allergic diseases: Diagnosis and treatment*, ed. P. Lieberman and J. Anderson, 233–254. Totowa, NJ: Humana Press.

Hectorne, K. J., and A. F. Fransway. 1994. Diazolidinyl urea: Incidence of sensitivity, patterns of cross-reactivity. *Contact Dermatitis* 30:16–19.

Jacobs, M. C., I. R. White, R. J. Rycroft, et al. 1995. Patch testing with preservatives at St. John's from 1982 to 1993. *Contact Dermatitis* 33:247–254.

Marks, J. G. 1990. Cosmetics. *Occupational skin disease*, 2nd ed, ed. R. M. Adams, 326–348. Philadelphia: W. B. Saunders.

Marks, J. G., Jr., D. V. Belsito, V. A. DeLeo, et al. 1995. North American Contact Dermatitis Group standard tray patch test results (1992 to 1994). *Am. J. Contact Dermatitis* 6:160–165.

Marks, J. G., Jr., D. V. Belsito, V. A. DeLeo, et al. 1998. North American Contact Dermatitis Group patch test results for the detection of delayed-type hypersensitivity to topical allergens. *J. Am. Acad. Dermatol.* 38:911–918.

Marks, J. G., Jr., D. V. Belsito, V. A. DeLeo, et al. 2000. North American Contact Dermatitis Group patch-test results. *Arch. Dermatol.* 136:272–273.

Marzulli, F., and H. C. Maguire, Jr. 1983. Validation of guinea pig tests for skin hypersensitivity. In *Dermatotoxicology*, 2nd ed, ed. F. N. Marzulli and H. I. Maibach, 237–250. Washington, DC: Hemisphere Publishing Corporation.

O'Brien, T. J. 1987. Imidazolidinyl Urea (germall 115) causing cosmetic dermatitis. *Aust. J. Dermatol.* 28:36–37.

Pepe, R. C., J. A. Wenninger, and G. N. McEwen, Jr., eds. 2002. *International cosmetic ingredient dictionary and handbook*, 9th ed. Washington, DC: CTFA.

Perrenoud, D., A. Bircher, T. Hunziker, et al. 1994. Frequency of sensitization to 13 common preservatives in Switzerland. *Contact Dermatitis* 30:276–279.

Rivalland, P., K. Vie, L. Coiffard, and Y. De Roeck-Holtzhauer. 1994. Cytotoxicity tests of antibacterial agents on human fibroblast cultures. *Pharm Acta Helv.* 69:159–162.

Schnuch, A., J. Geier, W. Uter, et al. 1998. Patch testing with preservatives, antimicrobials and industrial biocides. Results from a multicentre study. *Br. J. Dermatol.* 138:467–476.

Sherertz, E. F., and P. W. Ayers. 1999. Physician, heed thy self. *J. Am. Acad. Dermatol.* 40:112–114.

Stephens, T. J., K. D. Drake, and R. D. Drotman. 1987. Experimental delayed contact sensitization to diazolidinyl Urea (Germall II) in guinea pigs. *Contact Dermatitis* 16:164–168.

Tosti, A., S. Restani, and M. Lanzarini. 1990. Contact sensitization to diazolidinyl Urea report of 3 cases. *Contact Dermatitis* 22:127–128.

van Neer, P., and A. van der Kley. 1991. Imidazolidinyl Urea (Germall 115) should be patch tested in water. *Contact Dermatitis* 24:302.

Ziegler, V., B. Ziegler, and D. Kipping. 1988. Dose-response sensitization experiments with imidazolidinyl urea. *Contact Dermatitis* 19:236–237.

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

ISOPROPYL LANOLATE

A safety assessment of Isopropyl Lanolate was published in 1980 with the conclusion that this ingredient is "safe as currently used in cosmetic products" (Elder 1980). New studies, along with the updated information below regarding types and concentrations of use, were considered by the CIR Expert Panel. The Panel determined to not reopen this safety assessment.

The CIR Expert Panel did note that a safety assessment of Lanolin itself and eight derivatives were completed in 1980 (Elder 1980) and safety assessments of polyethylene glycol lanolins were published in 1982 (Elder 1982) and 1996 (Andersen 1996). In all cases, the lanolin ingredients were found safe as used in cosmetic formulations.

As with plant-derived cosmetic ingredients, the CIR Expert Panel has a long history of reviewing animal-derived cosmetic ingredients. It is now common to remind manufacturers that cosmetic products containing any animal-derived ingredient should be formulated to limit the presence of pesticide/heavy metal residues as follows: lead $\leq$0.1 ppm; arsenic $\leq$3 ppm; mercury $\leq$1ppm; total PCB/pesticide contamination $\leq$40 ppm with $\leq$10 ppm for any specific residue (Andersen 1998). Likewise, the Panel has concluded that cosmetic products containing any animal-derived ingredient should be formulated to be free of detectable pathogenic viruses or infectious agents (CIR 1999).

In 1976, Isopropyl Lanolate was used in 1194 cosmetic products, with the largest single use in lipsticks. In 2001, there were 415 reported uses (FDA 2001), again with the largest single use in lipstick products in a concentration range of 2% to 14% (CTFA 2001). Table 13 presents the available use information for Isopropyl Lanolate.

TABLE 13
Isopropyl Lanolate use

Product category	1976 use (CIR 1980)	2001 use (FDA 2001)	1976 concentrations (CIR 1980)	2001 concentrations (CTFA 2001)
Baby lotions, oils, powders, etc.	—	1	—	—
Bath oils, tablets, and salts	3	—	>0.1%–1%	—
Other bath preparations	2	1	>0.1%–5%	—
Eyeliner	69	6	>0.1%–25%	4%–6%
Eye shadow	184	11	>0.1%–25%	2%–10%
Eye makeup remover	1	—	>1%–5%	6%
Mascara	5	—	>1%–10%	4%–5%
Other eye makeup preparations	11	24	>1%–25%	3%–8%
Eyebrow pencil	10	—	>1%–5%	—
Other fragrance preparations	4	—	>0.1%–1%	10%
Hair conditioners	4	4	>0.1%–1%	2%
Hair sprays (aerosol fixatives)	2	—	>0.1%–1%	—
Hair tonics, dressings, etc.	2	—	>1%–5%	—
Other hair preparations	1	—	>1%–5%	—
Other hair-coloring preparations	—	—	—	0.4%
Blushers (all types)	84	13	≤0.1%–25%	3%–13%
Face powders	47	13	>0.1%–5%	3%–6%
Foundations	88	32	>0.1%–25%	1%–26%
Lipstick	348	183	≤0.1%–50%	2%–14%
Makeup bases	176	32	≤0.1%–25%	6%
Rouges	11	—	>0.1%–25%	8%
Makeup fixatives	2	—	>0.1%–1%	—
Other makeup preparations	19	13	>0.1%–25%	—
Cuticle softeners	—	2	—	1%–9%
Nail creams and lotions	—	—	—	1%
Other manicuring preparations	—	—	—	1%
Bath soaps and detergents	—	4	—	—
Deodorants (underarm)	2	—	≤0.1%–5%	—
Aftershave lotions	3	6	>1%–5%	1%
Shaving cream	2	3	>0.1%–1%	—
Other shaving preparation products	1	—	>1%–5%	—
Skin cleansing preparations	5	7	>0.1%–10%	4%
Face and neck skin care preparations[a]	48	2	>0.1%–25%	2%–5%
Body and hand skin care preparations[a]		22		1%–2%
Hormone	1	—	>0.1%–1%	—
Foot powders and sprays	—	1	—	2%
Moisturizing preparations	41	16	≤0.1%–10%	1%–5%
Night creams, lotions, etc.	4	8	>1%–10%	—
Paste masks (mud packs)	—	3	—	2%
Skin lighteners	1	—	>1%–5%	—
Skin fresheners	2	—	>0.1%–5%	—
Wrinkle smoothing (removers)	2	—	>5%–10%	—
Other skin care preparations	4	5	>1%–5%	4%–7%
Suntan gels, creams, and liquids	3	2	≤0.1%–10%	—
Other suntan preparations	2	1	>0.1%–5%	15%
Totals/ranges	1194	415	≤0.1%–50%	0.4%–26%

[a]Originally, Face and Neck and Body and Hand were combined as one category, but now they are separated.

REFERENCES

Andersen, F. A., ed. 1996. Addendum to the final report on PEGs Lanolin to include PEG-5, -10, -24, -25, -35, -55, -100 and -150 Lanolin; PEG-5, -10, -20, -24, -30 and -70 Hydrogenated Lanolin; PEG-75 Lanolin Oil; and PEG-75 Lanolin Wax. *Int. J. Toxicol.* 18(Suppl. 1):61–68.

Andersen, F. A., ed. 1998. Final report on the safety assessment of Mink Oil. *Int. J. Toxicol.* 17(Suppl. 4):71–82.

CIR. 1999. Safety assessment of Human Placental Protein, Hydrolyzed Human Placental Protein, Human Placental Enzymes, Human Placental Lipids, Human Umbilical Extract, Placental Protein, Hydrolyzed Placental Protein, Placental Enzymes, Placental Lipids and Umbilical Extract. March, 1999. Washington, DC: CIR.[2]

Cosmetic, Toiletry, and Fragrance Association (CTFA). 2001. Ingredient use data—Imidazolidinyl Urea. Unpublished data submitted by CTFA.[2]

Elder, R. L., ed. 1980. Final report for Acetylated Lanolin Alcohol, Lanolin, Lanolin Oil, Lanolin Acid, Lanolin Alcohol, Lanolin Wax, Acetylated Lanolin, Hydrogenated Lanolin, and Hydroxylated Lanolin. *J. Environ. Pathol. Toxicol.* 4:63–92.

Elder, R. L., ed. 1982. Final report of the safety assessment for PEG-75 Lanolin, PEG-20 Lanolin, PEG-27 Lanolin, PEG-30 Lanolin, PEG-40 Lanolin, PEG-50 Lanolin, PEG-60 Lanolin, and PEG-85 Lanolin. *J. Am. Coll. Toxicol.* 1:91–102.

Food and Drug Administration (FDA). 2001. 2001 frequency of use of cosmetic ingredients. *FDA database*. Washington, DC: FDA.

Katoh, J., T. Sugai, A. Shoji, T. Nakanishi, and A. Kuwano. 1994. Contact allergy from lanolin: The incidence of hypersensitivity and clinical features of lanolin dermatitis these 10 years. *Skin Res.* 36:115–125.

Goossens, A., M. H. Beck, E. Haneke, J. P. McFadden, S. Nolting, G. Durupt, and G. Ries. 1999. Adverse cutaneous reactions to cosmetic allergens. *Contact Dermatitis* 40:112–113.

Hoppe U., ed. 1999. *The Lanolin book*. Hamburg, Germany: Beiersdorf AG.

Pepe, R. C., J. A. Wenninger, and G. N. McEwen, Jr., eds. 2002. *International cosmetic ingredient dictionary and handbook*, 9th ed. Washington, DC: CTFA.

LITHIUM STEARATE, ALUMINUM DISTEARATE, ALUMINUM STEARATE, ALUMINUM TRISTEARATE, AMMONIUM STEARATE, CALCIUM STEARATE, MAGNESIUM STEARATE, POTASSIUM STEARATE, SODIUM STEARATE, AND ZINC STEARATE

A safety assessment of Lithium Stearate, Aluminum Stearate, Aluminum Distearate, Aluminum Tristearate, Ammonium Stearate, Calcium Stearate, Magnesium Stearate, Potassium Stearate, Sodium Stearate, and Zinc Stearate was published in 1982 with the conclusion that these ingredients "are safe as cosmetic ingredients in the present practices of use and concentration" (Elder 1982). New studies, along with updated information regarding types and concentrations of use, were considered by the CIR Expert Panel. The Panel determined to not reopen this safety assessment.

Lithium Stearate

Lithium Stearate was reported to be used in 98 cosmetic preparations in 1976, with the greatest use occurring in powders and foundations at concentrations that ranged from less than 0.1% to 5%. In 2001, Lithium Stearate was reported to be used in 17 preparations (FDA 2001), but concentration of use data were not given (CTFA 2001). Note that a transposition occurred in the original 1982 published safety assessment and the product information for Lithium Stearate is incorrect in that report. Table 14 presents the available use information with the correct data from 1976.

TABLE 14
Lithium Stearate use

Product category	1976 use[a]	2001 use (FDA 2001)	1976 concentrations (Elder 1982)	2001 concentrations (CTFA 2001)
Eyeliner	—	—	—	2%
Eye shadow	13	—	>0.1%–5%	—
Other eye makeup preparations	—	1	—	—
Powders	28	—	>0.1%–5%	—
Hair tonics, dressings, etc.	—	—	—	3%
Blushers (all types)	1	5	≤0.1%	—
Face powders	2	2	>1%–5%	—
Foundations	27	8	>0.1%–1%	—
Lipstick	1	1	>0.1%–1%	—
Makeup bases	20	—	≤0.1%	—
Rouges	2	—	≤0.1%	—
Makeup fixatives	1	—	≤0.1%	—
Moisturizing preparations	2	—	>0.1%–1%	—
Other skin care preparations	1	—	>0.1%–1%	—
Totals/ranges	98	17	≤0.1%–5%	2%–3%

[a]Note that a transposition occurred in the original 1982 published report and the product information for Lithium Stearate is incorrect. This column presents the correct information.

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

Isopropyl Lanolate – 2019 VCRP

03B - Eyeliner	3
03C - Eye Shadow	28
03F - Mascara	1
03G - Other Eye Makeup Preparations	3
04E - Other Fragrance Preparation	3
05A - Hair Conditioner	1
07A - Blushers (all types)	15
07B - Face Powders	11
07C - Foundations	8
07E - Lipstick	19
07I - Other Makeup Preparations	7
08B - Cuticle Softeners	1
10B - Deodorants (underarm)	1
11E - Shaving Cream	1
12A - Cleansing	2
12C - Face and Neck (exc shave)	6
12D - Body and Hand (exc shave)	7
12F - Moisturizing	3
12G - Night	1
12J - Other Skin Care Preps	1

Concentration of Use by FDA Product Category – Isopropyl Lanolate

Product Category	Maximum Concentration of Use
Eyeliners	6%
Tonics, dressings and other hair grooming aids	4%
Lipstick	2.7-14.5%
Rouges	2.8%
Body and hand products Not spray	 1.5%
Moisturizing products Not spray	 0.05%
Other skin care preparations	4.7%

Information collected in 2019

Table prepared April 11, 2019