FINAL REPORT OF THE SAFETY ASSESSEMENT FOR ACETYLATED LANOLIN ALCOHOL AND RELATED COMPOUNDS

The results of tests on animals and humans with Acetylated Lanolin and its related cosmetic ingredients are reviewed.

This group of ingredients is used extensively in cosmetics as well as in many other consumer products. They have low acute toxicity and are nonsensitizing to animal skin. However, extensive clinical experience indicates that there is a low incidence of sensitivity to these materials among exposed persons. This experience would seem to involve mainly the lanolin alcohols.

Based on the available animal data and human experience, it is concluded that lanolin and related lanolin materials described in the report are safe for topical application to humans in the present practice of use and concentration.

CHEMICAL AND PHYSICAL PROPERTIES

This report covers the following group of related compounds:

Lanolin
Lanolin Oil
Lanolin Wax
Lanolin Acid
Lanolin Alcohol
Acetylated Lanolin
Acetylated Lanolin Alcohol
Hydrogenated Lanolin
Hydroxylated Lanolin

Structure

Lanolin Lanolin is the purified secretory product of the sheep sebaceous gland. The raw material is referred to as *Adeps lanae*, wool wax, wool fat or wool grease. Lanolin comprises 10 to 25% of the weight of sheared wool (Schlossman and McCarthy, 1977).

Lanolin is a complex mixture of a large number of compounds. High molecular weight esters make up aproximately 87% of a typical Lanolin sample (Table 1) (Chemtob, *et al.*, 1975; Fawaz *et al.*, 1973a). The remainder of the mixture is comprised of 11% free compounds (aliphatic alcohols, sterols, fatty acids and hydrocarbons) and of 2% unidentified compounds. Since Lanolin is composed predominantly of high molecular weight esters, it is classified chemically as a wax and not as a fat. The esters have not been characterized (Schlossman and McCarthy, 1977).

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

Crude Lanolin can be separated into Lanolin Wax and Lanolin Oil (Liquid Lanolin) by solvent fractionation or crystallization (Schlossman and McCarthy, 1977; Chemtob *et al.*, 1974, 1975). Lanolin Oil, Wax and Crude (Whole) Lanolin can be modified chemically to produce a large number of substances of interest to the cosmetic chemist. The constituent esters and free compounds of Lanolin Wax and Oil are listed in Table 1 for comparison with those of Whole Lanolin.

Although the exact chemical nature of the Lanolin esters still remains unknown, most of the constituent fatty acids and alcohols of these esters have been identified through the works of Fawaz, Chemtob and associates (Chemtob *et al.*, 1974, 1975; Fawaz *et al.*, 1973a, b; 1974a, b, c). Lanolin esters can be hydrolyzed by saponification. The saponification products of a typical sample of Lanolin are seen in Table 2 (Schlossman and McCarthy, 1977; Chemtob *et al.*, 1974, 1975; Fawaz *et al.*, 1973a, b; 1974a, b, c). The predominant ester acid is of the unsubstituted, saturated, aliphatic type. However, the predominant ester alcohol is the sterol. Further delineations of the component fatty acids and alcohols of Lanolin are found in Table 3 (Fawaz *et al.*, 1973b; 1974a) and Table 4 (Fawaz *et al.*, 1974b, c), respectively.

TABLE 1. Typical Compositions of Whole Lanolin, Lanolin Wax and Lanolin Oil (Chemtob *et al.*, 1975; Fawaz *et al.*, 1973a)

Group	Whole Lanolin (%)	Lanolin Wax (%)	Lanolin Oil (%)
Esters of sterols and triterpene alcohols	35.4	28.9	44.0
Esters of aliphatic alcohols	23.7	13.9	16.0
Monohydroxyesters of sterols and of triterpene and aliphatic alcohols	20.0	16.4	15.0
Di- and polyhydroxyesters and free diols	7.9	9.3	7.7
Free aliphatic alcohols	5.6	20.2	10.4
Free sterols	4.1	5.3	4.4
Free hydrocarbons	0.6	0.4	0.3
Free fatty acids	0.5	1.0	0.7
Unknowns	2.2	4.6	1.5
TOTAL	100.0	100.0	100.0

Approximately 63% of the Lanolin fatty acids are nonhydroxylated, while 32% are monohydroxylated at either the alpha or omega carbon (Table 3). The predominant nonhydroxylated fatty acids are of the anteiso (containing an isobutyl group) and the iso (containing an isopropyl group) types. The monohydroxylated acids (alpha and omega) are mainly of the normal (straight-chain)

TABLE 2. Typical Saponification Products of Lanolin (Schlossman and McCarthy, 1977; Chemtob *et al.*, 1974, 1975; Fawaz *et al.*, 1973a, b; 1974a, b, c)

Group	Subgroup	Percentage	
Fatty acid	Aliphatic	31.1	
	Alpha-hydroxy	13.8	
	Omega-hydroxy	2.6	
	Unsaturated	2.4	
	Others	1.1	Subtotal = 51%
Alcohols	Cholesterols	19.6	
	Lanosterols	12.6	
	Aliphatic	8.0	
	1,2 diols	4.1	
	Others	2.7	Subtotal = 47%
Unspecified	• • •	2.0	

type. The length of the Lanolin fatty acid chain varies from 7 to 41 carbon atoms. The main fatty acids are palmitic (C_{16}), stearic (C_{18}) and longer molecules (C_{20} to C_{32}) (Fawaz *et al.*, 1973b, 1974a).

Approximately 26% of the Lanolin Alcohols are aliphatic structures: 17% monohydric alcohols and 9% diols (Table 4). The anteiso and iso forms are the predominant types of mono- and di-hydric alcohols found in Lanolin. Most of the aliphatic alcohols are long-chain molecules (C_{16} and greater). Over 68% of the Lanolin alcohols are sterols: 42% dimethyl sterols (cholesterols) and

TABLE 3. Typical Fatty Acid Composition of Lanolin (Fawaz *et al.*, 1973b, 1974a)

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}(17), C_{16}(16.5), C_{26}14.6)
	ante	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)
	ante	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)
	ante	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.

26% pentamethyl sterols (lanosterols). The latter group is also referred to as the triterpene alcohols (Fawaz *et al.*, 1974b, c).

Lanolin Oil and Lanolin Wax Lanolin Oil is the liquid-phase resulting from solvent fractionation (such as with ethyl acetate) of crude Lanolin via vacuum distillation or solvent crystallization. Lanolin Wax is the solid-phase product of this separatory process (Schlossman and McCarthy, 1977; Chemtob *et al.*, 1974, 1975; CTFA, 1978).

TABLE 4. Typical Alcohol Composition of Lanolin (Fawaz *et al.*, 1974b, c)

Class	Group	Subgroup	Percentage (%)	Carbon Chain Length Range	Predominant Constituents of Subgroup
Aliphatics	mono-OH	nor	1.59	14-34	C_{24}(41.1[1]), C_{26}(33.8)
		iso	6.46	14-36	C_{26}(34.6), C_{20}(34.3)
		ante	9.05	13-35	C_{21}(42), C_{27}(31), C_{25}(15)
	1,2 diol	nor	0.39	12-25	C_{16}(43), C_{20}(24), C_{18}(18)
		iso	5.87	12-30	C_{22}(32.4), C_{18}(30), C_{20}(17.5), C_{24}(17)
		ante	2.44	13-29	C_{23}(50), C_{21}(36.4)
Sterols	dimethyl	cholesterol	38.00		
		dihydrocholesterol	Trace		
		7-keto cholesterol	3.60		
	pentamethyl	lanosterol	14.80		
		dihydrolanosterol	10.30		
		7-keto lanosterol	1.60		
Others	polyols and unknowns	• • •	5.90		
TOTAL			100.00		

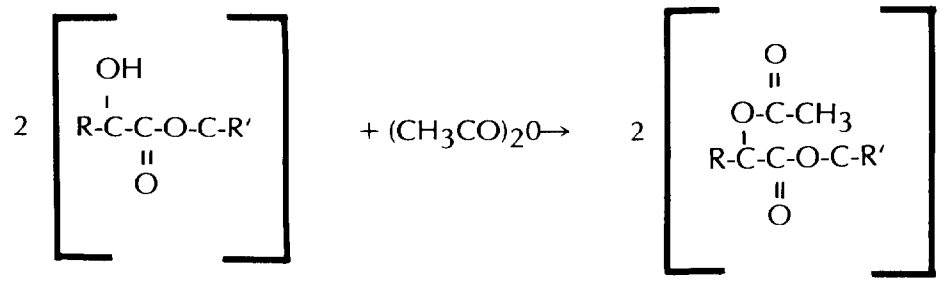
[1]Percent of all within specified subgroup.

Lanolin Acid Saponification of Lanolin with alcoholic or hydroalcoholic alkali results in the hydrolytic cleavage of its constituent esters. The reaction product is a mixture of alkaline soaps of fatty acids and unsaponifiable alcohols. The fatty alcohols can be extracted (such as with ethyl acetate, trichloroethane or aliphatic hydrocarbon solvents) from the acid-alcohol mixture leaving behind the lanolin soaps. These alkali soaps are reacted with sulfuric or phosphoric acid and then water washed to remove excess mineral acid and resultant salts. The Lanolin Acids are then dried and further refined. Lanolin Acid is a mixture of long-chain fatty acids in which the nonhydroxylated species predominates (Tables 2, 3) (Schlossman and McCarthy, 1977; Fawaz *et al.*, 1973b, 1974a, CTFA, 1978).

Lanolin Alcohol Lanolin Alcohol is derived from Lanolin via hydrolysis followed by extraction as described above. Lanolin Alcohol is a mixture of alcohols comprised of about two-thirds sterols and one-fourth aliphatic al-

cohols. It should be noted that neither squalene nor glycerol is found in Lanolin (Tables 2, 4) (Schlossman and McCarthy, 1977; Fawaz *et al.*, 1974b, c; CTFA, 1978).

Acetylated Lanolin Lanolin undergoes acetylation when reacted with acetic anhydride. Ester bonds are formed between the acetate moieties and the hydroxyl groups of the Lanolin hydroxyesters as seen below (Schlossman and McCarthy, 1977):



Lanolin ester Acetic anhydride Acetylated Lanolin

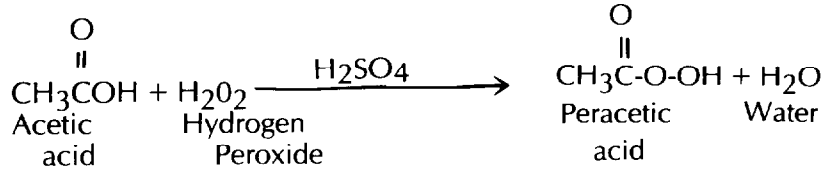
where *R* is hydroxyacid and R' is alcohol.

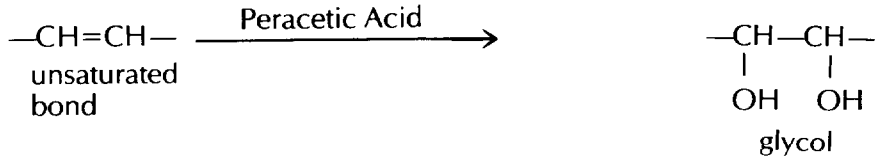
The free alcohols in a Lanolin sample may also undergo esterification with acetic anhydride. These two reactive groups (hydroxyesters and free alcohols) make up nearly 38% (Table 1) of crude Lanolin. Total acetylation of Lanolin would result, then, in the chemical alteration of over one-third of the original sample (Schlossman and McCarthy, 1977; CTFA, 1978).

Acetylated Lanolin Alcohol Once Lanolin has been fractionated into its alcohol and fatty acid components, the former group can be further processed by reacting it with acetic anhydride. Each free hydroxyl group can potentially form an ester linkage with acetate. Since Lanolin Alcohol is a mixture of mono-, di- and polyols, Acetylated Lanolin Alcohol will contain mono-, di- and polyacetates (Schlossman and McCarthy, 1977; CTFA, 1978).

Hydrogenated Lanolin Exposing Lanolin to hydrogen at high temperature and pressure in the presence of nickel or chromium catalyst results in a sequence of four chemical reactions. First, most unsaturated double-bonds become saturated with hydrogen. Second, the Lanolin esters undergo hydrogenolysis. Third, the resulting free fatty acids are reduced to fatty alcohols. Fourth, some of these alcohols, as well as some of those resulting from the ester cleavage step, are further reduced to simple hydrocarbons. Hydrogenated Lanolin has never been fully characterized chemically, but its low saponification value indicates the nearly total absence of esters. Additionally, the high hydroxyl value of Hydrogenated Lanolin suggests the presence of a high percentage of free alcohols (94 to 99.8%) (Schlossman and McCarthy, 1977; CTFA, 1978).

Hydroxylated Lanolin The hydroxylation of Lanolin involves the addition of two hydroxyl groups across a double-bond. The resulting compound is a glycol (diol). Lanolin is mixed with acetic acid, hydrogen peroxide and sulfuric acid (catalyst). The active reactant, peracetic acid (acetyl hydroperoxide), is formed *in situ* in the reaction medium and is consumed immediately as it is generated. Peracetic acid mediates the opening of the unsaturated bond and the concomitant addition of two hydroxyl groups as indicated below (Schlossman and McCarthy, 1977, CTFA).





Properties

Lanolin is an ointment-like material which has a slight, characteristic odor. When heated in a steam bath, Lanolin separates into two layers with the lower layer being water. Additional heating drives off this water phase; if not more than 0.25% water remains, the material is classified as anhydrous Lanolin. While still warm, the Lanolin material is transparent. Upon cooling, it becomes a yellow, tenacious, unctous mass. Lanolin is not soluble in water or mineral oil but is miscible without phase separation with about twice its weight of water. It is sparingly soluble in cold alcohol and more so in hot alcohol. Lanolin is highly soluble in chloroform and ether (Schlossman and McCarthy, 1977). The melting range of Lanolin is 36.0 to 42.0°C (CTFA, 1978). Lanolin displays strong emollient, penetrating and emulsifying properties. It blends well with nearly all other substances used in cosmetic formulations. Lanolin possesses adhesive and tackifying characteristics as well (Schlossman and McCarthy, 1977).

Lanolin Oil Lanolin Oil is a clear, amber-colored liquid which is less tacky and has less drag than Whole Lanolin. However, it retains the emollient characteristics of Lanolin and displays a high spreading coefficient. Liquid Lanolin is soluble in mineral and vegetable oils and in silicone fluids (Schlossman and McCarthy, 1977).

Lanolin Wax Lanolin Wax is an odorless, tasteless, ceraceous solid which is a better water/oil (w/o) emulsifying agent than Whole Lanolin. The melting range is 41 to 51°C (Schlossman and McCarthy, 1977; CTFA, 1978).

Lanolin Acid Lanolin Acid is a hard, waxy, yellow-tan solid with a mild waxy odor. The melting range is 40 to 62°C. The constituent fatty acids are polar molecules giving amphoteric properties to Lanolin Acid (CTFA, 1978; Amerchol, 1976).

Lanolin Alcohol Lanolin Alcohol is a firm, waxy, amber solid with a characteristic odor. The melting range is 47 to 65°C (CTFA, 1978).

Acetylated Lanolin Acetylated Lanolin is more hydrophobic than Lanolin since many of the hydrophilic hydroxyl groups in the latter substance have been esterified to acetate. Acetylated Lanolin, therefore, fails to form w/o emulsions, is soluble in cold mineral oil and has a slightly lower melting range (30 to 40°C) than Lanolin. Acetylated Lanolin forms a water resistant film when applied to the skin resulting in the reduction of transepidermal water loss (Schlossman and McCarthy, 1977; CTFA, 1978).

Acetylated Lanolin Alcohol Acetylated Lanolin Alcohol is a lemon-yellow to straw-colored, oily, hydrophobic liquid with a characteristic bland odor. It has a refractive index of 1.4445 to 1.4485 at 20°C and a specific gravity of 0.850 to 0.880 at 25°C (CTFA, 1978).

Hydrogenated Lanolin Hydrogenated Lanolin is a light yellow to white tacky solid which is soluble in ethyl ether and chloroform but insoluble in water. Its melting range is 48 to 53°C. Hydrogenated Lanolin retains the emollient and adhering characteristics of Lanolin but loses the latter's odor, taste, color, and tackiness (Schlossman and McCarthy, 1977; CTFA, 1978).

Hydroxylated Lanolin The introduction of highly polar hydroxyl groups renders Hydroxylated Lanolin more hydrophilic than Lanolin. The product becomes more amphoteric resulting in increased interfacial and surface activities. Hydroxylated Lanolin is superior to Lanolin in forming stable w/o emulsions. Its melting range is 39 to 46°C (Schlossman and McCarthy, 1977; CTFA, 1978).

Reactivity

Since Lanolin products contain unsaturated fatty acids, alcohols, esters, sterols and terpenols, autoxidation may occur during storage and especially during exposure to sunlight. At present, the chemical nature of such autoxidation products is unknown; however, peroxides and epoxides have been suggested as likely structures (Stutsman, 1977). The addition of stabilizing agents such as alpha-tocopherol and BHT prevents the autoxidation of Lanolin products (Stutsman, 1977; Sugai and Higashi, 1975). BHT has been used in some preparations at the 200 to 500 ppm level. Some brands of Acetylated Lanolin Alcohol contain 4% by weight oleyl acetate and/or BHT (CTFA, 1978).

Analytical Methods

Spilker and Richey (1948) have described a number of analytic methods useful for Lanolin and Lanolin derivatives. These generally involve hydrolysis, fractionation, separation by chromatography and identification.

Manufacturing Methods

Lanolin is obtained by one of the following methods (Gillespie, 1948; Clark, 1971):

1. Solvent extraction of wool fleece.
2. Scouring of wool with soap or neutral detergent followed by:
   a. Centrifugation of the resulting emulsion. This may introduce small amounts of detergents as impurities in the Lanolin.
   b. Breaking of the emulsion with acid, or
   c. Production of foam (with air) and collection of the froth.

Impurities

Lanolin and related materials may contain additives and contaminants which may vary widely. These include detergents and the antioxidants BHT and alpha-tocopherol. Chlorophyll, pesticides from the fleece, and trace metals such as copper, nickel, and chromium might also be present.

Purpose and Extent of Use in Cosmetics

Cosmetic uses of Lanolin are discussed by a number of authors. Lanolin and its derivatives have been used as w/o emulsifiers and as emollients for skin protection and relief of dryness of the skin. They serve as vehicles for external (topical) use on skin, lips, nails, and hair, which may bring them into the proximity of mucous membranes and eyes (Fr. Demande, 1976; Bolderson, 1976; Bradner, 1976; Chalmers, 1972, 1976; Chen, 1976; Clark, 1974; Courtin, 1976; Kelly and Ritter, 1976; Mayer, 1976; McCarthy, 1976; McCarthy *et al.*, 1976; McCarthy and Schlossman, 1975; Moeller and Osberghaus, 1976; Mores and McCarthy, 1976; Roney, 1976; Scott, 1976; Tentsova *et al.*, 1977). Lanolin materials are used in over 5,000 formulations. For each of the materials, the approximate extent of use and concentrations used are summarized in Table 5 (FDA, 1976).

BIOLOGICAL PROPERTIES

General Effects

Lanolin and its derivatives are used for their emollient properties on the skin, nails, and hair. The principal emollient of the skin and nails is water, contained particularly in the stratum corneum. Hydration of the stratum corneum depends, in part, upon the rate at which water reaches the horny layer from the deeper dermal and epidermal layers and upon the rate of evaporation of water from the surface layers. It is thought that this water-binding capacity of

the stratum corneum depends upon the presence of hygroscopic water-soluble substances. Emollients act to decrease the rate of evaporation by forming a barrier or occlusive material on the skin surface permitting hydration or rehydration from the deeper layers (Kammerau *et al.*, 1976). Sebaceous gland excretions provide an emollient effect, presumably by virtue of the lipids they contain. The composition of the skin surface lipids varies considerably from site to site. A similar water-binding capacity effect is observed in the cuticle of the hair (Anonymous, 1973; Peter *et al.*, 1969).

TABLE 5. Product Formulation Data (FDA, 1976)

Ingredient	Cosmetic Product Type	Concentration (%)	Number of Product Formulations
Lanolin	Baby products (skin, hair, mucous membranes)	>0.1 to 10	9
	Bath preparations (skin, mucous membranes)	>0.1 to 5	4
	Eye makeup preparations (eye)	≤0.1 to >50	243
	Colognes and toilet waters (skin)	>0.1 to 10	37
	Hair preparations (noncoloring) (hair)	≤0.1 to 50	137
	Hair coloring preparations (hair)	>0.1 to >50	7
	Makeup preparations (not eye) (skin, lips)	≤0.1 to >50	1318
	Manicuring preparations (nails)	>0.1 to 50	18
	Personal cleanliness (mucous membranes, skin)	>0.1 to 5	23
	Shaving preparations (skin)	≤0.1 to 5	31
	Skin care preparations (creams, lotions, powders, and sprays) (skin)	≤0.1 to >50	531
	Suntan and sunscreen preparations (skin)	>0.1 to 50	31
Lanolin Oil	Baby products (skin, hair mucous membranes)	>0.1 to 5	6
	Bath preparations (skin, mucous membranes)	≤0.1 to 25	44
	Eye makeup preparations (eye)	≤0.1 to 50	135
	Colognes and toilet waters (skin)	>0.1 to 5	9
	Hair preparations (noncoloring) (hair)	≤0.1 to 5	17
	Hair coloring preparations (hair)	≤0.1 to 5	9

TABLE 5. (continued) Product Formulation Data (FDA, 1976)

Ingredient	Cosmetic Product Type	Concentration (%)	Number of Product Formulations
	Makeup preparations (not eye) (skin, lips)	>0.1 to >50	887
	Manicuring preparations (nails)	>0.1 to 50	10
	Personal cleanliness (mucous membranes, skin)	>1 to 5	3
	Shaving preparations (skin)	>0.1 to 5	2
	Skin care preparations (creams, lotions, powder, and sprays) (skin)	≤0.1 to 50	218
	Suntan and sunscreen preparations (skin)	>0.1 to 10	16
Lanolin Acid	Eye makeup preparations (eye)	>0.1 to 10	23
	Hair preparations (noncoloring) (hair)	>1 to 5	2
	Makeup preparations (not eye) (skin, lips)	>0.1 to 10	13
	Manicuring preparations (nails)	>1 to 5	2
	Shaving preparations (skin)	>0.1 to 1	1
	Skin care preparations (creams, lotions, powders and sprays) (skin)	>0.1 to 10	10
Lanolin Alcohol	Baby products (skin, hair, mucous membranes)	>0.1 to 5	2
	Bath preparations (skin, mucous membranes)	>0.1 to 10	28
	Eye makeup preparations (eye)	>0.1 to 25	120
	Colognes and toilet waters (skin)	>0.1 to 25	13
	Hair preparations (noncoloring) (hair)	≤0.1 to 25	15
	Hair coloring preparations (hair)	>0.1 to 1	4
	Makeup preparations (not eye) (skin, lips)	≤0.1 to 25	422
	Personal cleanliness (mucous membranes, skin)	≤0.1 to 5	6
	Shaving preparations (skin)	>0.1 to 5	7
	Skin care preparations (creams, lotions, powders, and sprays) (skin)	>0.1 to >50	115
	Suntan and sunscreen preparations (skin)	>0.1 to 5	6
Acetylated Lanolin	Baby products (skin, hair mucous membranes)	>0.1 to 1	2
	Bath preparations (skin, mucous membranes)	>1 to 5	2

TABLE 5. (continued) Product Formulation Data (FDA, 1976)

Ingredient	Cosmetic Product Type	Concentration (5)	Number of Product Formulations
	Eye makeup preparations (eye)	>0.1 to 50	5
	Colognes and toilet waters (skin)	>0.1 to 1	4
	Hair preparations (noncoloring) (hair)	>0.1 to 5	3
	Makeup preparations (not eye) (skin, lips)	>0.1 to 50	57
	Shaving preparations (skin)	≤0.1 to 1	6
	Skin care preparations (creams, lotions, powders, and sprays) (skin)	>0.1 to 25	50
Acetylated Lanolin Alcohol	Bath preparations (skin, mucous membranes)	>1 to 5	4
	Eye makeup preparations (eye)	>0.1 to 10	31
	Colognes and toilet waters (skin)	>0.1 to 25	16
Acetylated Lanolin Alcohol (cont'd)	Hair preparations (noncoloring) (hair)	>0.1 to 5	4
	Makeup preparations (not eye) (skin, lips)	>0.1 to 25	133
	Manicuring preparations (nails)	≤0.1 to 5	2
	Skin care preparations (creams, lotions, powders, and sprays) (skin)	≤0.1 to 50	105
	Suntan and sunscreen preparations (skin)	>0.1 to 5	11
Hydrogenated Lanolin	Eye makeup preparations (eye)	>5 to 10	1
	Colognes and toilet waters (skin)	>1 to 5	1
	Makeup preparations (not eye) (skin, lips)	>1 to 25	58
	Manicuring preparations (nails)	>1 to 5	1
	Shaving preparations (skin)	>0.1 to 1	1
	Skin care preparations (creams, lotions, powders, and sprays) (skin)	>0.1 to 10	15
	Suntan and sunscreen preparations (skin)	>0.1 to 5	4
Hydroxylated Lanolin	Makeup preparations (not eye) (skin, lips)	>5 to 25	7
	Skin care preparations (creams, lotions, powders, and sprays) (skin)	>0.1 to 5	5
Lanolin Wax	Suntan and sunscreen preparations (skin)	>10 to 25	2
	Colognes and toilet waters (skin)	>1 to 25	11

TABLE 5. (continued) Product Formulation Data (FDA, 1976)

Ingredient	Cosmetic Product Type	Concentration (5)	Number of Product Formulations
	Manicuring preparations (nails)	>1 to 5	1
	Shaving preparations (skin)	>1 to 5	1
	Eye makeup preparations (eye)	>0.1 to 25	41
	Skin care preparations (creams, lotions, powders, and sprays) (skin)	>0.1 to 5	9
	Hair preparations (noncoloring) (hair)	>0.1 to 1	3
	Makeup preparations (not eye) (skin, lips)	≤0.1 to 50	69

Emollient preparations are often chosen, in part, because of their compatability with normal skin surface lipids. Lanolin and its derivatives are not chemically similar to human sebum. Sebum contains approximately 50% glycerides; Lanolin contains none. The variations among derivatives of Lanolin lead to variations in properties from hydrophilic, water-soluble and nonocclusive to hydrophobic, oil-soluble and occlusive (Kammerau *et al.*, 1976).

Animal Toxicology

General Studies

Acute Oral Toxicity (Tables 6—14) Each of the nine Lanolin ingredients has been tested in rats for acute oral toxicity in a variety of studies. All exhibit low oral toxicity. Only the most pertinent acute oral LD50 for each ingredient will be reported: undiluted Lanolin (>64 cc/kg), undiluted Lanolin Oil (46.5 cc/kg), 50% Lanolin Wax in corn oil (>32 g/kg), undiluted Lanolin Acid (56.5 cc/kg), 66% Lanolin Alcohol in corn oil (>42.7 g/kg), undiluted Acetylated Lanolin (>64 cc/kg), undiluted Acetylated Lanolin Alcohol (>64 cc/kg), undiluted Hydrogenated Lanolin (>64 cc/kg), and undiluted Hydroxylated Lanolin (>10 cc/kg) (CTFA: Amerchol a,b,c,d,e; CTFA: Avon; CTFA: Croda a,b,c,d,e,f,g; CTFA: Malmstrom a,b,c,d,e,f,g,h; CTFA: R.I.T.A.; CTFA: Robinson-Wagner a,b,c,d; CTFA: Westbrook a,b,c,d,e,f,g).

Acute Dermal Toxicity The acute dermal LD50 of Lanolin Oil as applied to the rabbit skin has been determined to be in excess of 10 ml/kg (CTFA: R.I.T.A.). In a two-dose (1 or 2 g/kg) study in rats, the LD50 of Hydroxylated Lanolin was found to be greater than 2.0 g/kg (CTFA: Avon).

Acute Skin Irritation (Tables 6—14) With one exception, the Lanolin ingredients are either nonirritating or at most mildly irritating to the skin of experimental animals. The exception is Lanolin Acid which is a mild skin irritant. It should be noted that Lanolin Acid is seldom, if at all, found in cosmetic formulations as the free acid. In the five tests conducted on undiluted

Lanolin Acid, the Primary Irritation Index (PII) ranged from 0.78 to 2.2 (maximum of 8) (CTFA: Amerchol, b; CTFA: Croda, c; CTFA: Malmstrom, d; CTFA: Westbrook, c). The highest PII value obtained for each of the other undiluted Lanolin ingredients is as follows: Lanolin (0.71), Lanolin Oil (1.0), Lanolin Wax (0.67), Lanolin Alcohol (1.5), Acetylated Lanolin (1.62), Acetylated Lanolin Alcohol (2.3), Hydrogenated Lanolin (0.6), and Hydroxylated Lanolin (0.0) (CTFA: Amerchol a,c,d; CTFA: Avon; CTFA: Croda a,b,d,e,f,g; CTFA: Malmstrom a,b,c,e,f,g,h; CTFA: R,I.T.A.; CTFA: Robinson-Wagner a,b,c,d; CTFA: Westbrook a,b,d,e,f,g).

Acute Eye Irritation (Tables 6—14) With one exception, all the Lanolin ingredients were either nonirritating or at most mildly irritating to the eyes of experimental animals. In three of four ocular irritation studies conducted on rabbits, undiluted Lanolin Acid was found to be a mild or moderately severe irritant (CTFA: Amerchol, b; CTFA: Croda, c; CTFA: Malmstrom, d; CTFA: Westbrook, c). For the other eight Lanolin ingredients, no or only mild transient reactions were reported (CTFA: Amerchol, a,c,d,e; CTFA: Avon; CTFA: Croda a,b,d,e,f,g; CTFA: Malmstrom a,b,c,e,f,g,h; CTFA: R.I.T.A.; CTFA: Robinson-Wagner a,b,c,d; CTFA: Westbrook a,b,d,e,f,g).

Subchronic Skin Irritation/Sensitization A skin sensitization study with eight guinea pigs was done with Acetylated Lanolin Alcohol suspended in physiological saline. Ten intracutaneous injections on alternate days followed by challenge injection two weeks later showed no sensitization (CTFA: Amerchol, d).

Hydrogenated Lanolin was not a sensitizer when applied to the skin of guinea pigs three times a week for seven or more applications. A 2% solution in 1:1:3 acetone:dioxane:corn oil was used. The challenge was applied two weeks after the last induction dose (CTFA: R.I.T.A.)

Neither Lanolin Oil applied 15 times to the rabbits skin at concentrations of 5, 15, or 50% nor 50% Hydroxylated Lanolin applied 65 times to the rat skin caused any local skin irritation effects (CTFA: R.I.T.A.; CTFA: Avon).

Lanolin Wax suspended in corn oil was a mild skin sensitizer in 10 guinea pigs as indicated by an average score of 0.95 (scores between 0.1 and 2.0 are mild sensitizers). The material was injected intracutaneously three times/week for a total of 10 injections with an eleventh challenge injection two weeks later (CTFA: Robinson-Wagner, c).

Special Studies Simpson *et al.* (1945) reported that 3-methylcholanthrene dissolved in anhydrous Lanolin was less carcinogenic when painted on the skin of mice as compared to its carcinogenic effect when benzene was the vehicle. The concentration of 3-methylcholanthrene in Lanolin applied in these studies was one-half that of the compound in benzene. However, the volume of the benzene solution applied was twice that of the Lanolin solution. Berenblum and Schoental (1947) observed a similar diminution in the carcinogenic potency of methylcholanthrene when Lanolin was used as a diluent. They reported the inhibitory effect even with concentrations that exceeded the concentration of the carcinogen in benzene used as a positive control. They obtained similar results with another carcinogen, 7,12-dimethylbenz(a)anthracene, on mice.

TABLE 6. Acute Animal Toxicity — Lanolin

		Acute Oral				Skin Irritation		Draize Woodard Calvery	Eye Irritation Draize		
Sample Number	Reference	LD50	Conc.	Dosage	Animals	Conc.	Animals	Irritation Index	Conc.	Animals	Comment
1	CTFA: Westbrook, a	>16 g/kg	40% in arachis oil	2 @ 10 and 16 g/kg	10 rats/ dose	undiluted	6 rabbits	0	undiluted	6 rabbits	no irritation
2	CTFA: Malmstrom, a	>32 g/kg	1:1 in corn oil	6 @ 2.0 — 64.0 cc/kg	5 rats/ dose	undiluted	6 rabbits	0	undiluted	9 rabbits	mild transient irritation
3	CTFA: Malmstrom, a	• • •	• • •	• • •	• • •	undiluted	6 rabbits	0	• • •	• • •	• • •
4	CTFA: Malmstrom, a	>32 g/kg	1:1 in corn oil	6 @ 2.0 — 64.0 cc/kg	5 rats/ dose	undiluted	6 rabbits	0	undiluted	9 rabbits	mild transient irritation
5	CTFA: Malmstrom, a	>32 g/kg	1:1 in corn oil	6 @ 2.0 — 64.0 cc/kg	5 rats/ dose	undiluted	6 rabbits	0.58 mild irritant	undiluted	9 rabbits	mild transient irritation
6	CTFA: Malmstrom, a	>64 cc/kg	undiluted	6 @ 4.0 — 64.0 cc/kg	5 rats/ dose	undiluted	6 rabbits	0	undiluted	9 rabbits	no damage
7	CTFA: Malmstrom, a	>32 g/kg	1:1 in corn oil	6 @ 2.0 — 64.0 cc/kg	5 rats/ dose	undiluted	6 rabbits	0	undiluted	9 rabbits	mild transient irritation

8	CTFA: Malmstrom, a	>64 cc/kg	undiluted	6 @ 4.0 — 64.0 cc/kg	5 rats/ dose	undiluted	6 rabbits	0.1 no irritation	undiluted	9 rabbits	no damage
9	CTFA: Robinson-Wagner, a	>5.0 g/kg	25% in corn oil	1 @ 5.0 g/kg	10 rats/ dose	undiluted	6 rabbits	0.38 mild irritant	undiluted	9 rabbits	no damage
10	CTFA: Croda, a	>20.0 g/kg	25% in corn oil	5 @ 1.25 — 20 g/kg	5 rats/ dose	undiluted	6 rabbits	0.71 mild irritant	undiluted	9 rabbits	mild transient irritation

TABLE 7. Acute Animal Toxicity — Lanolin Oil

		Acute Oral				Skin Irritation		Draize Woodard Calvery	Eye Irritation Draize		
Sample Number	Reference	LD50	Conc.	Dosage	Animals	Conc.	Animals	Irritation Index	Conc.	Animals	Comment
1	CTFA: Westbrook, b	>16 ml/ kg	undiluted	1 @ 16 ml/kg	10 rats/ dose	undiluted	3 rabbits	0.5 mild irritant	undiluted	3 rabbits	no irritant
2	CTFA: Croda, b	>20 ml/ kg	undiluted	5 @ 1.25 — 20.0 ml/kg	5 rats/ dose	undiluted	6 rabbits	1.0	undiluted	6 rabbits	mild transient irritant
3	CTFA: Robinson-Wagner, b	>21.5 ml/kg	undiluted	5 @ 1.0 — 21.5 ml/kg	5 rats/ dose	undiluted	6 rabbits	0.17	undiluted	6 rabbits	mild in 1 animal
4	CTFA: Malmstrom, b	46.5 cc/kg	undiluted	5 @ 8.0 — 64.0 cc/kg	5 rats/ dose	undiluted undiluted	3 rabbits 6 rabbits	1.4 mild 0.30 slight	undiluted	9 rabbits	no irritant

TABLE 7. (Continued) Acute Animal Toxicity — Lanolin Oil

5	CTFA: Malmstrom, b	24.8 g/kg	propylene glycol vehicle	7 @ 2.0 — 32.0 g/kg	5 rats/ dose	undiluted	6 rabbits	0.13 slight	undiluted	9 rabbits	irritant to unwashed eye
6	CTFA: R.I.T.A.	>10 ml/ kg	undiluted	1 @ 10 ml/kg	10 rats/ dose	10% in mineral oil	6 rabbits	0	undiluted	9 rabbits	not irritating

TABLE 8. Acute Animal Toxicity — Lanolin Wax

		Acute Oral				Skin Irritation		Draize Woodward Calvery	Eye Irritation Draize		
Sample Number	Reference	LD50	Conc.	Dosage	Animals	Conc.	Animals	Irritation Index	Conc.	Animals	Comment
1	CTFA: Malmstrom, c	48-64 cc/kg	1:1 in corn oil	6 @ 4.0— 64.0 cc/kg	5 rats/ dose	undiluted	6 rabbits	0.28 mild irritant	undiluted	9 rabbits	no damage
2	CTFA: Malmstrom, c	>42.7 g/kg	66% in corn oil	6 @ 2.0— 64 cc/kg	5 rats/ dose	undiluted	6 rabbits	0	undiluted	9 rabbits	no damage
3	CTFA: Robinson-Wagner, c	>32 g/kg	1:1 in corn oil	6 @ 2.0— 64 cc/kg	5 rats/ dose	undiluted	3 rabbits	0	undiluted	6 rabbits	no damage
4	CTFA: Amerchol , a	• • •	• • •	• • •	• • •	undiluted	3 rabbits	0.67 mild irritant	• • •	• • •	• • •

TABLE 9. Acute Animal Toxicity — Lanolin Acid

Sample Number	Reference	Acute Oral				Skin Irritation		Draize Woodward Calvery	Eye Irritation Draize		
		LD50	Conc.	Dosage	Animals	Conc.	Animals	Irritation Index	Conc.	Animals	Comment
1	CTFA: Westbrook, c	• • •	• • •	• • •	• • •	undiluted	6 rabbits	2.2 moderately irritating	undiluted	6 rabbits	moderately severe irritant
2	CTFA: Amerchol , b	>10 ml/kg	undiluted	5 @ 2.5—40.0 ml/kg	2 rats/dose	undiluted	6 rabbits	1.60 mild irritant	undiluted	6 rabbits	mild transient irritant
3	CTFA: Amerchol , b	>20 ml/kg <40 ml/kg	undiluted	5 @ 2.5—40.0 ml/kg	2 rats/dose	undiluted	6 rabbits	0.78 slight irritant	20% in mineral oil	6 rabbits	non-irritating
4	CTFA: Malmstrom, d	56.5 cc/kg	undiluted	7 @ 4.0—80.0 cc/kg	5 rats/dose	undiluted	6 rabbits	1.05 mild irritant	undiluted	9 rabbits	minimal irritant
5	CTFA: Croda, c	>5 g/kg	undiluted	1 @ 5 g/kg	10 rats/dose	undiluted	6 rabbits	2 moderate irritant	undiluted	6 rabbits	moderately severe irritant

TABLE10 Acute Animal Toxicity — Lanolin Alcohol

Sample Number	Reference	Acute Oral				Skin Irritation		Draize Woodard Calvery	Eye Irritation Draize		
		LD50	Conc.	Dosage	Animals	Conc.	Animals	Irritation Index	Conc.	Animals	Comment
1	CTFA: Westbrook, d	>16 g/kg	40 % in arachis oil	1 @ 16 g/kg	10 rats/dose	• • •	• • •	• • •	• • •	• • •	• • •
2	CTFA: Westbrook, d	• • •	• • •	• • •	• • •	undiluted	3 rabbits	0	undiluted	3 rabbits	very slight irritant
3	CTFA: Robinson-Wagner, d	27 g/kg	propylene glycol vehicle	8 @ 1.0—32.0 g/kg	5 rats/dose	undiluted	6 rabbits	0	undiluted	6 rabbits	no irritation
4	CTFA: Croda, d	>20.0 ml/kg	50% in mineral oil w/ 5% propylene glycol	5 @ 1.25—20.0 ml/kg	5 rats/dose	50% in mineral oil	6 rabbits	1.5 mild irritant	50% in mineral oil	6 rabbits	mild transient irritant
5	CTFA: Malmstrom, e	12.1 mg/kg	2 mg/cc corn oil w/5% propylene glycol	6 @ 8.0—64.0 cc/kg	5 rats/dose	undiluted	6 rabbits	1.5 mild irritant	undiluted	9 rabbits	no damage
6	CTFA: Malmstrom, e	23.3 mg/kg	2 mg/cc of corn oil	5 @ 16.0—64.0 cc/kg	5 rats/dose	undiluted	6 rabbits	1.05 mild irritant	undiluted	9 rabbits	no damage
7	CTFA: Malmstrom, e	>42.7 g/kg	66% in corn oil	6 @ 2.0—64.0 cc/kg	5 rats/dose	undiluted	6 rabbits	0	undiluted	9 rabbits	no damage

8	CTFA: Malmstrom, e	>32 g/kg	50% in corn oil	6 @ 2.0—64.0 cc/kg	5 rats/dose	undiluted	6 rabbits	0	undiluted	9 rabbits	no damage
9	CTFA: Malmstrom, e	21.1g/kg	propylene glycol vehicle	7 @ 2.0—32.0 g/kg	5 rats/dose	undiluted	6 rabbits	0	undiluted	9 rabbits	no damage
10	CTFA: Malmstrom, e	21.3 g/kg	1:2 w/v in corn oil	6 @ 2.0—64.0 cc/kg	5 rats/dose	• • •	• • •	• • •	• • •	• • •	• • •
11	CTFA: Malmstrom, e	21.3 cc/kg	1:2 w/v in corn oil	6 @ 2.0—64.0 cc/kg	5 rats/dose	• • •	• • •	• • •	• • •	• • •	• • •

TABLE11 Acute Animal Toxicity — Acetylated Lanolin

		Acute Oral				Skin Irritation		Draize Woodard Calvery	Eye Irritation Draize		
Sample Number	Reference	LD50	Conc.	Dosage	Animals	Conc.	Animals	Irritation Index	Conc.	Animals	Comment
1	CTFA: Westbrook, e	>16 g/kg	undiluted	1 @ 16 g/kg	10 rats/dose	undiluted	6 rabbits	0.3 mild irritant	undiluted	8 rabbits	marginal irritant
2	CTFA: Croda, e	>15 ml/kg	50% in oil	1 @ 15 ml/kg	20 mice/dose	undiluted	3 rabbits	0	undiluted	3 rabbits	no irritation
3	CTFA: Malmstrom, f	>64 cc/kg	undiluted	6 @ 4.0—64.0 cc/kg	5 rats/dose	undiluted	6 rabbits	0.5 mild irritant	undiluted	9 rabbits	no irritation
4	CTFA: Amerchol , f	>10 ml/kg	undiluted	5 @ 2.5—40.0 ml/kg	2 rats/dose	undiluted	6 rabbits	Avg. 1.62 mild irritant	undiluted	6 rabbits	mild transient irritation

TABLE12 Acute Animal Toxicity — Acetylated Lanolin Alcohol

		Acute Oral				Skin Irritation		Draize Woodard Calvery	Eye Irritation Draize		
Sample Number	Reference	LD50	Conc.	Dosage	Animals	Conc.	Animals	Irritation Index	Conc.	Animals	Comment
1	CTFA: Malmstrom, g	64 cc/kg	undiluted	6 @ 4.0—64.0 cc/kg	5 rats/dose	undiluted	6 rabbits	0	undiluted	9 rabbits	no irritation
2	CTFA: Amerchol , d	40.0 ml/kg	undiluted	5 @ 2.5—40 ml/kg	2 rats/dose	undiluted	6 rabbits	1.3 mild irritant	undiluted	6 rabbits	mild transient irritant
3	CTFA: Westbrook, f	16 g/kg	40% in arachis oil	1 @ 16 g/kg	10 rats/dose	undiluted	6 rabbits	2.3 mod. irritant	undiluted	6 rabbits	not an irritant
4	CTFA: Westbrook, g	16 ml/kg	undiluted	1 @ 16 ml/kg	10 rats/dose	undiluted	6 rabbits	2.1 mod. irritant	undiluted	8 rabbits	marginal irritant
5	CTFA: Croda, f	40 g/kg	undiluted	5 @ 2.5—40.0 g/kg	5 rats/dose	undiluted	3 rabbits	0	undiluted	3 rabbits	not an irritant

TABLE13 Acute Animal Toxicity — Hydrogenated Lanolin

Sample Number	Reference	Acute Oral				Skin Irritation		Draize Woodard Calvery	Eye Irritation Draize		
		LD50	Conc.	Dosage	Animals	Conc.	Animals	Irritation Index	Conc.	Animals	Comment
1	CTFA: Malmstrom, h	>64.0 cc/kg	undiluted	6 @ 4.0— 64 occ/kg	5 rats/ dose	undiluted	6 rabbits	0.1 mild irritant	undiluted	9 rabbits	no damage
2	CTFA: Malmstrom, h	>42.7 g/kg	66% in corn oil	6 @ 2.0— 64 occ/kg	5 rats/ dose	undiluted	6 rabbits	0	undiluted	9 rabbits	no damage
3	CTFA: Croda, g	>5 g/kg	undiluted	1 @ 5 g/kg	10 rats/ dose	undiluted	6 rabbits	0.6 mild irritant	undiluted	6 rabbits	no damage
4	CTFA: R.I.T.A.	8.12 g/kg	25% in propylene glycol	2 @ 5 & 10g/kg	5 rats/ dose	undiluted	6 rabbits	0	50% aqueous paste	9 rabbits	no irritation

TABLE14 Acute Animal Toxicity — Hydroxylated Lanolin

Sample Number	Reference	Acute Oral				Skin Irritation		Draize Woodard	Eye Irritation Draize		
		LD50	Conc.	Dosage	Animals	Conc.	Animals	Irritation Index	Conc.	Animals	Comment
1	CTFA: Avon	2.0 g/kg	undiluted	2 @ 1.0— 2.0 g/kg	5 rats/ dose	undiluted	9 rabbits	0	undiluted	6 rabbits	mild transient irritation
2	CTFA: Amerchol , e	>10 ml/ kg	undiluted	5 @ 2.5— 40.0 ml/kg	2 rats/ dose	• • •	• • •	• • •	undiluted	3 rabbits	no irritation

Clinical Assessment of Safety

General Assessment No scientific reports of adverse reactions among persons occupationally exposed during production or use of Lanolin over a 50-year period have been reported (Table 15) (CTFA: Westbrook, a). Similarly there have been no reported adverse experiences in 22, 22, 25, 30, 6 and 14 years of use by workers or customers for Lanolin Oil (CTFA: Westbrook, b), Lanolin Wax (CTFA: Westbrook, h), Lanolin Acid (CTFA: Westbrook, c), Lanolin Alcohol (CTFA: Westbrook, d), Acetylated Lanolin (CTFA: Westbrook, e), and Acetylated Lanolin Alcohol (CTFA: Westbrook, f,g), respectively.

Skin Irritation Numerous patch tests were conducted on volunteers with Lanolin and related cosmetic ingredients. These studies are summarized in Table 15. Undiluted Lanolin showed no evidence of primary irritation or sensitization in over 250 subjects (CTFA: Malmstrom, a; CTFA: Croda, a). Lanolin Oil has been skin tested in more than 300 volunteers without adverse reactions (CTFA: Croda, b; CTFA: Malmstrom, b). Undiluted Lanolin Wax showed extremely low irritation potential and no evidence of sensitization in over 200 subjects (CTFA: Malmstrom, c). Of the 115 subjects exposed topically to Lanolin Acid, three showed increased reaction not considered sensitization and one showed sensitization (CTFA: Westbrook, c; CTFA: Amerchol, b; CTFA: Croda, c). There were no adverse effects noted when 50 volunteers were exposed to undiluted Lanolin Alcohol in a repeated insult patch test (CTFA: Croda, d). Questionable evidence of fatiguing was found in 2 of 53 subjects exposed to Acetylated Lanolin (CTFA: Amerchol, c). Acetylated Lanolin Alcohol caused an extremely low level of irritation in over 60 individuals (CTFA: Malmstrom, g; CTFA: Amerchol, d). In a repeated insult test on 50 subjects, undiluted Hydrogenated Lanolin presented no suggestions of irritation, fatiguing, or sensitization (CTFA: Croda, g). There were no visible skin changes observed in 53 volunteers exposed to Hydroxylated Lanolin (CTFA: Amerchol, e).

Skin Sensitization Over the years of its use, Lanolin has been observed to produce allergic or hypersensitivity reactions. The first reports of Lanolin skin sensitization were published in 1930 (Ramirez and Eller, 1930). Since then, numerous reports of Lanolin allergy have been published, several of which will be elaborated upon below. The incidence of hypersensitivity among persons exposed has been a matter of great uncertainty (Anonymous, 1971; Clark *et al.*, 1977; Clark, 1975; DeBeukelaar, 1968; Epstein 1972; Fisher *et al.*, 1971; Hannuksela *et al.*, 1976; Schorr, 1974, 1975; Taub, 1976; Wilson, 1973).

Clark (1975) has summarized three large European retrospective studies of dermatology patients with Lanolin Alcohol hypersensitivity with a reported incidence of 0.70, 2.38, and 1.82%. Using numerous assumptions, the incidence in the general population was estimated to be no more than 9.7 cases per million people.

Epstein (1972) and Breit and Bandmann (1973) suggested for detection of Lanolin allergy the use of 30% wool wax alcohol in petrolatum as the testing agent for Lanolin materials in patch testing. With this Lanolin fraction, Lanolin

sensitivity was successfully identified. It was noted that addition of salicylic acid to the Lanolin fraction produced false-positive reactions (Epstein, 1972).

Peter *et al.*, (1969) concluded from his studies that the greatest allergenic reaction is given by C_{14}-C_{16} Lanolin Alcohols.

A European study group noted that the incidence of hypersensitivity to topical medicaments was 14% (560/4000) in clinic patients with eczema. Positive test reactions were reported for neomycin (4%), wool alcohols (3%), iodochlorohydroxyquin (2%), parabens (2%), and chlorquianaldol (1%). The difference between these total values of 12%, and the overall total of 14% was not stated (Bandman *et al.*, 1972).

The North American Contact Dermatitis Group has issued a series of reports on results of diagnostic patch testing of dermatitis patients using a standard array of test substances. Out of 1200 patients tested over an 18-month period ending in June 1972, wool wax alcohols (30% in petrolatum) ranked eighth in frequency of reaction with 3% of the patients reacting (North American Contact Dermatitis Group, 1973). In the subsequent two-year testing period, wool wax alcohol ranked eleventh, again experiencing a 3% reaction rate out of 3165 patients tested (North American Contact Dermatitis Group, 1975). A preliminary report of a more recent testing period (July 1, 1975—June 30, 1976) showed wool alcohol ranking thirteenth with a reaction incidence of 2.9% of 900-2000 patients tested (Rudner, 1977). An unpublished tabulation of 1976-1977 data from the groups shows a sensitivity index of 2% for wool alcohol and 1% for 100% hydrous Lanolin (North American Contact Dermatitis Group, 1976-77).

Clark *et al.*, (1977) demonstrated in Lanolin-sensitive patients that the removal of free fatty Lanolin Alcohols and detergents reduced the incidence of detectable hypersensitivity by 96%. An anonymous submission suggests that parabens, alkyl esters of p-hydroxybenzoic acid, cosmetic preservatives, may increase or be responsible for Lanolin hypersensitivity (Anonymous, 1971; DeBeukelaar, 1968).

Estimates of the extent of hypersensitivity vary apparently according to the type of provocative patch test applied or according to the populations tested. Salicylic acid as a keratolytic agent has been used to increase the sensitivity to Lanolin in patch testing systems with differing results according to the type of Lanolin material used (Lanolin esters or alcohols). It has even been suggested that autoxidation products may contribute to the allergenicity of Lanolin Alcohols (Stutsman, 1977; DeBeukelaar, 1968).

Photosensitivity Two product formulations, each containing 0.75% Lanolin Acid, 3.0% Lanolin Alcohol, and 0.5% Hydroxylated Lanolin, were tested for phototoxicity on 20 human subjects and for photosensitization on 25 human subjects. There was no evidence of either phototoxicity or photosensitivity (CTFA Task Force).

TABLE 15. Clinical Adverse Reactions — Clinical Trials

Ingredient/ Brand Number	Reference	Human Response						
		Test	No. of Subjects	No. of Applications	Concentration	Incubation Period	Final Challenge	Comment
Lanolin								
1	CTFA: Westbrook, a	• • •	• • •	• • •	• • •	• • •	• • •	no reported adverse experiences in 50 yrs of use by workers or customers
2	CTFA: Malmstrom, a	Draize	200	10, 3x's/wk	undiluted	duration not given	yes	no evidence of sensitization
3	CTFA: Croda, a	repeated insult patches	50	every other day for 10 applications	undiluted	10-14 days	yes	no evidence of primary irritation, fatiguing or sensitization
Lanolin Oil								
1	CTFA: Westbrook, b	• • •	• • •	• • •	• • •	• • •	• • •	no reported adverse experiences in 22 yrs of use by workers or customers
2	CTFA: Croda, b	repeated insult patches	50	every other day for 10 applications	undiluted	10-14 days	yes	no evidence of fatiguing, primary irritation or sensitization
3	CTFA: Malmstrom, b	21-day cumulative irritancy assay	8	daily for 21 days	undiluted	• • •	• • •	extremely low irritancy potential
4	CTFA: Malmstrom, b	repeated insult	50	daily for 15 days	undiluted	21 days	yes	no evidence of irritancy, fatiguing or sensitization
5	CTFA: Malmstrom, b	Draize	200	10, 3x's/wk	undiluted	duration not given	yes	no evidence of sensitization
Lanolin Acid								
1	CTFA: Westbrook, c	applied to skin	12	single	undiluted	3 wks	yes	3 subjects showed increased reactions not considered sensitization

2	CTFA: Westbrook, c	• • •	• • •	• • •	• • •	• • •	• • •	no reported adverse experiences in 25 yrs of use by workers or customers
3	CTFA: Amerchol , b	induction	53	4x's/wk for 3 wks	100 & 20-80% in petrolatum	18 days	yes	nothing observed in 53 subjects
4	CTFA: Croda, c	repeated insult patches	50	every other day for 10 applications	undiluted	10-14 days	yes	fatiguing and sensitization in 1 subject
Lanolin Alcohol								
1	CTFA: Westbrook, d	• • •	• • •	• • •	• • •	• • •	• • •	no reported adverse experiences in 30 yrs of use by workers or customers
2	CTFA: Croda, d	repeated insult patches	50	every other day for 10 applications	undiluted	10-14 days	yes	no evidence of primary irritation, fatiguing, or sensitization
Acetylated Lanolin								
1	CTFA: Westbrook, e	• • •	• • •	• • •	• • •	• • •	• • •	no reported adverse experience 6 yrs of use by workers or customers
2	CTFA: Amerchol , d	induction	53	4x's/wk for 3 wks	100 & 20-80% in petrolatum	18 days	yes	questionable evidence of fatiguing in 2 subjects
Acetylated Lanolin Alcohol								
1	CTFA: Malmstrom, g	21-day cumulative irritancy assay	8	daily for 21 days	undiluted	• • •	• • •	extremely low irritancy potential
2	CTFA: Amerchol , d	induction	53	4x's/wk for 3 wks	10-50% in petrolatum	18 days	yes	evidence of fatiguing in 3 subjects
3	CTFA: Westbrook, f	• • •	• • •	• • •	• • •	• • •	• • •	no reported adverse experiences in 7 yrs of use by workers or customers
4	CTFA: Westbrook, g	• • •	• • •	• • •	• • •	• • •	• • •	no reported adverse experiences in 14 yrs of use by workers or customers

Table 15 (continued). Clinical Adverse Reactions — Clinical Trials

Hydrogenated Lanolin								
1	CTFA: Croda, g	repeated insults	50	every other day for 10 applications	undiluted	10-14 days	yes	no evidence of fatiguing, irritation or sensitization
Hydroxylated Lanolin								
1	CTFA: Amerchol , e	induction	53	4x's/wk for 3 wks	100 & 20-80% in petrolatum	18 days	yes	no visible skin damage
Lanolin Wax								
1	CTFA: Malmstrom, c	21-day cumulative irritancy assay	8	daily for 21 days	undiluted	• • •	• • •	extremely low irritancy potential
2	CTFA: Malmstrom, c	Draize	200	10,3 times/ week	undiluted	not specified	yes	no evidence of sensitization
3	CTFA:	• • •	• • •	• • •	• • •	• • •	• • •	no reported adverse experiences in 22 yrs of use by workers or customers

Comedone Formation (Acnegenic Effect) Kligman and Mills (1972) and Fulton *et al.*, (1976) have studied the acnegenic properties of cosmetics including those containing Lanolin and Lanolin related materials. Their papers described the comedogenic effects of these ingredients. Other ingredients in cosmetics that were indicated as comedogenic included petrolatum, certain vegetable oils, butyl stearate, lauryl alcohol, oleic acid, isopropyl myristate, and sodium lauryl sulfate.

Effect on the Eyes Fraunfelder *et al.*, (1973) attempted to determine whether Lanolin-containing ophthalmic materials, applied topically, could be incorporated into the cornea. It is their conclusion, following a series of provocative animal tests, that no Lanolin-containing ointment was trapped in the cornea unless the surface of the cornea was directly and repeatedly disrupted and abraded. These findings further substantiate the animal toxicity data reported previously in Tables 6-14.

SUMMARY

The results of tests on animals and humans with Acetylated Lanolin, its related cosmetic ingredients, and with numerous cosmetic formulations containing these materials attest to the safety of these ingredients as presently used.

These ingredients, as a group, are used extensively in cosmetics as well as in many other consumer products, and there has been ample opportunity for a large proportion of the population to be exposed to some of these materials. The acute toxicity of these materials is low, and the animal tests for skin sensitization are negative. However, extensive clinical experience indicates that there is a low incidence of sensitivity to these materials among exposed persons. This appears to be mainly due to the Lanolin Alcohols. There was no evidence of photosensitization induced by these ingredients. Comedogenic effects from cosmetics incorporating Lanolin and related materials have been reported.

The safety assessment of these ingredients rests on the information at hand and on the considerable usage in various concentrations in a variety of cosmetic formulations. Additional biological assessment of these ingredients might reasonably be expected to include more extended studies in the areas of percutaneous absorption, cutaneous hypersensitivity, chronic toxicity, and mutagenicity.

CONCLUSIONS

Based on the available animal data and human experience, the Panel concludes that Lanolin and related Lanolin materials described herein are safe for topical application to humans in the present practice of use and concentration.

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CTFA.: Amerchol , c Acetylated Lanolin[1].

CTFA.: Amerchol , d Acetylated Lanolin Alcohol[1].

CTFA.: Amerchol , e Hydroxylated Lanolin[1].

CTFA.: Avon Products, Inc. Hydroxylated Lanolin[1].

CTFA.: Croda, Inc., a Lanolin[1].

CTFA.: Croda, Inc., b Lanolin Oil[1].

CTFA.: Croda, inc., c Lanolin Acid[1].

CTFA.: Croda, Inc., d Lanolin Alcohol[1].

CTFA.: Croda, Inc., e Acetylated Lanolin[1].

CTFA.: Croda, Inc., f Acetylated Lanolin Alcohol[1].

CTFA.: Croda, Inc., g Hydrogenated Lanolin[1].

CTFA.: Malmstrom Chemicals., a Lanolin[1].

CTFA.: Malmstrom Chemicals., b Lanolin Oil[1].

CTFA.: Malmstrom Chemicals., c Lanolin Wax[1].

CTFA.: Malmstrom Chemicalss, d Lanolin Acid[1].

CTFA.: Malmstrom Chemicals., e Lanolin Alcohol[1].

CTFA.: Malmstrom Chemicals., f Acetylated Lanolin[1].

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

CTFA.: Malmstrom Chemicals., g Acetylated Lanolin Alcohol[1].
CTFA.: Malmstrom Chemicals., h Hydrogenated Lanolin[1].
CTFA.: R.I.T.A. Chemical Co. Hydrogenated Lanolin; Lanolin Oil[1].
CTFA.: Robinson-Wagner Co., a Lanolin[1].
CTFA.: Robinson-Wagner Co., b Lanolin Oil[1].
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CTFA.: Robinson-Wagner Co., d Lanolin Alcohol[1].
CTFA Task Force: Submission of data in support of the safety of acetylated lanolin alcohol and related materials. Lanolin and its derivatives. Products containing: lanolin acid, hydroxylated lanolin, lanolin alcohol[1].
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