Amended Safety Assessment of Lanolin-Derived Ingredients as Used in Cosmetics

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*All interested persons are provided 60 days from the above release date (i.e., **June 15, 2024**) to comment on this safety assessment, and to identify additional published data that should be included or provide unpublished data which can be made public and included. Information may be submitted without identifying the source or the trade name of the cosmetic product containing the ingredient. All unpublished data submitted to CIR will be discussed in open meetings, will be available for review by any interested party, and may be cited in a peer-reviewed scientific journal. Please submit data, comments, or requests to the CIR Executive Director, Dr. Bart Heldreth.*

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ABBREVIATIONS

CIR	Cosmetic Ingredient Review
Council	Personal Care Products Council
CPSC	Consumer Product Safety Commission
DEA	diethanolamine
ECHA	European Chemicals Agency
EDEN	European Dermato-Epidemiology Network
FDA	Food and Drug Administration
HPA	highly-purified anhydrous
HRIPT	human repeated-insult-patch -test
IVDK	Information Network of Department of Dermatology
LLNA	local lymph node assay
NACDG	North American Contact Dermatitis Group
NOAEL	no-observable-adverse-effect level
OECD	Organisation for Economic Co-operation and Development
OTC	over-the-counter
Panel	Expert Panel for Cosmetic Ingredient Safety
PEG	polyethylene glycol
PII	primary irritation index
ROAT	repeated open application test
SPIN	significance-prevalence index
TG	test guideline
VCRP	Voluntary Cosmetic Registration Program
wINCI *Dictionary*	web-based *International Cosmetic Ingredient Dictionary and Handbook*

ABSTRACT

The Expert Panel for Cosmetic Ingredient Safety (Panel) assessed the safety of 9 lanolin-derived ingredients, most of which are reported to function as skin conditioning agents-emollient and hair conditioning agents in cosmetic products. The Panel reviewed the available data to determine the safety of this ingredient. The Panel concluded that these lanolin-derived ingredients are safe in cosmetics in the present practices of use and concentration described in this safety assessment.

INTRODUCTION

The Expert Panel for Cosmetic Ingredient Safety (Panel) previously reviewed the safety of 9 lanolin-derived ingredients in a report that was published in 1980.[1] At that time, the Panel concluded "Lanolin and related Lanolin materials… are safe for topical application to humans in the present practices of use and concentration" (as described in that assessment). The Panel first considered a re-review of this report in February 2003, and the Panel reaffirmed the original conclusion, as published in 2005.[2] In accordance with its Procedures, the Panel evaluates the conclusions of previously-issued reports approximately every 15 years, and it has been at least 15 years since this assessment was last reviewed. This report has been reopened to reassess the safety of the 9 lanolin-derived ingredients (listed below) included in the original report as used in cosmetics. According to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*; see Table 1), most of these ingredients are reported to function in cosmetics as skin conditioning agents-emollient and hair conditioning agents; other cosmetic functions are also reported.[3]

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

The Panel has also reviewed related ingredients. The Panel concluded that polyether lanolin ingredients are safe in the practices of use and concentration described in a safety assessment that was published in 2018.[4] In a report that was published in 2013, the Panel concluded that lanolinamide diethanolamine (DEA) is safe with several qualifications.[5] Additionally, the Panel determined laneth polyethylene glycol (PEG) ethers are safe when formulated to be nonirritating in a report that was published in 2012.[6]

This safety assessment includes relevant published and unpublished data that are available for each endpoint that is evaluated. Published data are identified by conducting an extensive search of the world's literature; a search was last conducted in February 2024. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that the Panel typically evaluates, is provided on the Cosmetic Ingredient Review (CIR) website (https://www.cir-safety.org/supplementaldoc/preliminary-search-engines-and-websites; https://www.cir-safety.org/supplementaldoc/cir-report-format-outline). Unpublished data are provided by the cosmetics industry, as well as by other interested parties.

Some of the data included in this safety assessment were found on the European Chemicals Agency (ECHA) website.[7-12] Please note that the ECHA website provides summaries of information generated by industry, and it is those summary data that are reported in this safety assessment.

Excerpts of data from the original 1980 safety assessment are summarized throughout the text of this document, as appropriate, as are pertinent information from the original re-review document[13] considered by the Panel in February 2003. These data are identified using *italicized text*. (This information is not included in the tables or the summary section.) For complete and detailed information, the original 1980 report can be accessed on the CIR website (https://wwwcir-safety.org/ingredients).

CHEMISTRY

Definition and Structure

The definitions of the lanolin-derived ingredients included in this review are provided in Table 1. Lanolin is a fat-like sebaceous secretion of sheep.

Chemical Properties

Chemical properties of several of the lanolin-derived ingredients are described in Table 2. Lanolin-derived ingredients generally are insoluble in water and have large log P_{ow} values.[7-12]

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.[1] Acetylated Lanolin, therefore, fails to form water/oil emulsions and is soluble in cold mineral oil. Acetylated Lanolin forms a water-resistant film when applied to the skin resulting in the reduction of transepidermal water loss.

Hydrogenated Lanolin

Hydrogenated Lanolin is soluble in ethyl ether and chloroform but insoluble in water.[1] Hydrogenated Lanolin retains the emollient and adhering characteristics of Lanolin but loses odor, taste, color, and tackiness of Lanolin.

Hydroxylated Lanolin

The introduction of highly polar hydroxyl groups renders Hydroxylated Lanolin more hydrophilic than Lanolin.[1] The product becomes more amphoteric resulting in increased inter-facial and surface activities. Hydroxylated Lanolin is superior to Lanolin in forming stable water/oil emulsions.

Lanolin

The raw material Lanolin is referred to as Adeps lanae, wool wax, wool fat, or wool grease.[1] Lanolin comprises 10 to 25% of the weight of sheared wool. 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. 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. 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.

Lanolin Acid

The constituent fatty acids of Lanolin Acid are polar molecules that yield amphoteric properties to this ingredient.[1]

Lanolin Oil

Lanolin Oil, or liquid Lanolin, is less tacky and has less drag than whole Lanolin.[1] 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.

Lanolin Wax

Lanolin Wax is a better water/oil emulsifying agent than whole Lanolin.[1]

Method of Manufacture

Acetylated Lanolin

Lanolin undergoes acetylation when reacted with acetic anhydride.[1] Ester bonds are formed between the acetate moieties and the hydroxyl groups of the Lanolin hydroxyesters. 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% of crude Lanolin. Total acetylation of Lanolin would result, then, in the chemical alteration of over one-third of the original sample.

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.[1] 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.

Hydrogenated Lanolin

Exposing Lanolin to hydrogen at high temperature and pressure in the presence of nickel or chromium catalyst results in a sequence of 4 chemical reactions.[1] 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.

Hydroxylated Lanolin

The hydroxylation of Lanolin involves the addition of 2 hydroxyl groups across a double-bond.[1] 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.

Lanolin

Lanolin is obtained by solvent extraction of wool fleece.[1] It can also be obtained by scouring wool with soap or neutral detergent followed by centrifugation of the resulting emulsion, breaking of the emulsion with acid, or production of foam (with air) and collection of the froth.

Lanolin Acid

Saponification of Lanolin with alcoholic or hydroalcoholic alkali results in the hydrolytic cleavage of its constituent esters.[1] 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 Acid is then dried and further refined.

Lanolin Alcohol

Lanolin Alcohol is derived from Lanolin via hydrolysis followed by extraction.[1]

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.[1] Lanolin Wax is the solid-phase product of this separatory process.

Composition and Impurities

Lanolin and related materials may contain additives and contaminants which may vary widely.[1] These include detergents and the antioxidants butylated hydroxytoluene and alpha-tocopherol. Chlorophyll, pesticides from the fleece, and trace metals such as copper, nickel, and chromium might also be present.

Hydrogenated Lanolin

Hydrogenated Lanolin has never been fully characterized chemically, but its low saponification value indicates the nearly total absence of esters.[1] Additionally, the high hydroxyl value of Hydrogenated Lanolin suggests the presence of a high percentage of free alcohols (94 to 99.8%).

Lanolin

Lanolin is a complex mixture of a large number of compounds.[1] High molecular weight esters make up approximately 87% of a typical Lanolin sample. 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. The approximate typical composition of whole Lanolin is as follows: 35.4% esters of sterols and triterpene alcohols; 23.7% esters of aliphatic alcohols; 20.0% monohydroxyesters of sterols and of triterpene and aliphatic alcohols; 7.9% di- and polyhydroxyesters and free diols; 5.6% free aliphatic alcohols; 4.1% free sterols; 0.6% free hydrocarbons; 0.5% free fatty acids, and 2.2% unknown.

Pesticides were noted to be an impurity of concern in Lanolin products.[13] At least 28 different pesticides have been used to control sheep pests. Detection was claimed at 20 to 97 ng/g. At the time of the study, the European Pharmacopoeia limits were 50 ng/g for individual organochlorine pesticides, 500 ng/g for other individual pesticides, and 1000 ng/g for total pesticides. The authors noted that the limits were higher than the amount determined in 3 of 4 Lanolin samples analyzed.

The allergenic components in Lanolin are mainly the free lanolin alcohols, especially alkane-α,β-diols and alkane-α.ω-diols.[14] According to the *Food Chemicals Codex*, anhydrous Lanolin may not contain more than 3 mg/kg lead.[15] Medical-grade lanolin, produced through process of extraction and distillation, is free of all detergents and reduces free Lanolin Alcohol content to less than 3%.[16] Highly-purified anhydrous (HPA) lanolin is purified by a special proprietary process that removes impurities (including free lanolin alcohols) and allergenic components of Lanolin. HPA lanolin is reported to be free of odors, tastes, bleach, and preservatives.[17] Free lanolin alcohol content in HPA lanolin is reported to be lower than 1.5% and detergent residues are reported at a negligible level.

Lanolin and lanolin-containing nipple care products were analyzed for pesticide contamination.[18] Of the 4 different materials analyzed none were found to have any of the 21 organochloro-pesticides included in the screening protocol. However, trace residues of the diazinon (up to 0.69 mg/kg), ethion (0.27 mg/kg), piperonyl butoxide (up to 1.30 mg/kg), diflubenzuron (0.02 mg/kg), triflumuron (0.02 mg/kg), cypermethrin (0.09 mg/kg), and chlorpyrifos-ethyl (1.50 mg/kg) were detected. The materials were also analyzed for free Lanolin Alcohol, which varied in concentration from 0.61 to 4.50%. Peroxide values, acid values, and anisidine values ranged from 6.60 - 12.63, 0.40 - 0.90, and 2.83 - 8.50, respectively.

Lanolin Acid

Lanolin Acid is a mixture of long-chain fatty acids in which the non-hydroxylated species predominates.[1] Approximately 63% of the Lanolin fatty acids are non-hydroxylated, while 32% are mono--hydroxylated at either the alpha or omega carbon. The predominant non-hydroxylated fatty acids are of the anteiso (containing an isobutyl group) and the iso (containing an isopropyl group) types. The mono-hydroxylated acids (alpha and omega) are mainly of the normal (straight-chain) type. The length of the Lanolin fatty acid chain varies from 7 to 41 carbon atoms. The main fatty acids are palmitic (Cl6), stearic (Cl8) and longer molecules (C20 to C32).

Lanolin Alcohol

Lanolin Alcohol is a mixture of alcohols comprised of about two-thirds sterols and one-fourth aliphatic alcohols.[1] It should be noted that neither squalene nor glycerol is found in Lanolin. Approximately 26% of the Lanolin Alcohols are aliphatic structures: 17% monohydric alcohols and 9% diols. 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 (C16 and greater). Over

68% of the Lanolin Alcohols are sterols: 42% dimethyl sterols (cholesterols) and 26% pentamethyl sterols (lanosterols). The latter group is also referred to as triterpene alcohols.

Lanolin Oil

The approximate typical composition of Lanolin Oil is as follows: 44.0% esters of sterols and triterpene alcohols; 16.0% esters of aliphatic alcohols; 15.0% monohydroxyesters of sterols and of triterpene and aliphatic alcohols; 7.7% di- and polyhydroxyesters and free diols; 10.4% free aliphatic alcohols; 4.4% free sterols; 0.3% free hydrocarbons; 0.7% free fatty acids, and 1.5% unknown.[1]

Lanolin Wax

Lanolin Wax has a similar approximate composition: 28.9% esters of sterols and triterpene alcohols; 13.9% esters of aliphatic alcohols; 16.4% monohydroxyesters of sterols and of triterpene and aliphatic alcohols; 9.3% di- and polyhydroxyesters and free diols; 20.2% free aliphatic alcohols; 5.3% free sterols; 0.4% free hydrocarbons; 1.0% free fatty acids, and 4.6% unknown.[1]

USE

Cosmetic

The safety of the cosmetic ingredients addressed in this assessment is evaluated based on data received from the US Food and Drug Administration (FDA) and the cosmetics industry on the expected use of these ingredients in cosmetics, and does not cover their use in airbrush delivery systems. Data included herein were obtained from the FDA's Voluntary Cosmetic Registration Program (VCRP) database (frequency of use) and in response to a survey conducted by the Personal Care Products Council (Council) (maximum use concentrations). The data were provided by cosmetic product categories, based at that time on 21CFR Part 720. For most cosmetic product categories, 21CFR Part 720 does not indicate type of application and, therefore, airbrush application is not considered. Airbrush delivery systems are within the purview of the US Consumer Product Safety Commission (CPSC), while ingredients, as used in airbrush delivery systems, are within the jurisdiction of the FDA. Airbrush delivery system use for cosmetic application has not been evaluated by the CPSC, nor has the use of cosmetic ingredients in airbrush technology been evaluated by the FDA. Moreover, no consumer habits and practices data or particle size data are publicly available to evaluate the exposure associated with this use type, thereby preempting the ability to evaluate risk or safety.

According to 2023 VCRP survey data, Lanolin has the most reported uses in cosmetic products, with a total of 285 formulations; the majority of the uses are in leave-on products (Table 3).[19] Acetylated Lanolin Alcohol has the second most reported uses in cosmetic products, with a total of 196; the majority of these uses are also in leave-on formulations. The frequencies of use for both of these ingredients have markedly decreased since the Panel last reviewed these ingredients in 2003; Lanolin was reported to have 782 uses, and Acetylated Lanolin Alcohol was reported to have 356 uses.[2] The results of the concentration of use survey conducted by the Council in 2022 indicate Lanolin Oil has the highest maximum concentration of use in a leave-on formulations; it is used at up to 47% in lipsticks.[20] Lanolin is reported to be used at up to 40% in leave-on nail creams and lotions. When the Panel last reviewed these ingredients in 2003, the maximum leave-on use concentration for Lanolin Oil was 65% in lipstick; the maximum leave-on use concentration for Lanolin was 37% in body and hand skin care preparations.[2]

Lanolin-derived ingredients may be used in products that can be incidentally ingested or be used near the eye or mucous membranes. For example, Lanolin has been reported to be used in lipsticks at up to 20.7% and in eyeliners at up to 32%, and Lanolin Oil has been reported to be used in lipsticks at up to 47% and in eye shadows at up to 11.1%.[19,20] Additionally, some of the Lanolin may be used in cosmetic sprays and powders, and could possibly be inhaled; for example, Lanolin is reported to be used at 1.6% in hair sprays and at 0.0099% in face powders, and Lanolin Oil is reported to be used in a fragrance preparation (no reported concentration) and in face powders at 0.3%. In practice, as stated in the Panel's respiratory exposure resource document (https://www.cir-safety.org/cir-findings), most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and tracheobronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount. Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.

Although products containing some of these ingredients may be marketed for use with airbrush delivery systems, this information is not available from the VCRP or the Council survey. Without information regarding the frequency and concentrations of use of these ingredients (and without consumer habits and practices data or particle size data related to this use technology), the data are insufficient to evaluate the exposure resulting from cosmetics applied via airbrush delivery systems.

All of the lanolin-derived ingredients named in the report are not restricted from use in any way under the rules governing cosmetic products in the European Union.[21]

Non-Cosmetic

According to the US FDA, Lanolin is a food additive permitted for direct addition to food for human consumption as a plasticizing material (softener) in chewing gum base (21CFR Part 172.615). It is also an indirect food additive in adhesives and components of coatings (21CFR Part 175.300), in components of paper and paperboard (21CFR Part 176.170, 176.210), in polymers (21CFR Part 177.1200, 177.2600), and in adjuvant, production aids, and sanitizers (21CFR Part 178.3910). In the US, Lanolin may be used as an active ingredient in over-the-counter (OTC) drug products.[3] When used as an active drug ingredient, the established drug name is *Lanolin*. Lanolin is approved for OTC use as an active ingredient in anorectal drug products (21CFR Part 346.14), in skin protectants (21CFR Part 347.10), and in ophthalmic drug products (21CFR Part 349.14). Lanolin is an inactive ingredient for the following approved drug products: ophthalmic ointments (up to 3% w/w); rectal ointments (up to 14% w/w); topical creams, emulsions, lotions, or ointments (up to 10% w/w); shampoos (up to 2% w/w); and vaginal creams (up to 2% w/w).{US Food & Drug Administration (FDA), 2024 #75} Additionally, Lanolin Alcohol and Lanolin Oil are inactive ingredients for ophthalmic ointments (up to 10% w/w) and topical creams, lotions, or ointments (up to 6% w/w). Lanolin has been present as an active ingredient used in over-the-counter hair growers and/hair loss prevention (21CFR Part 310.527), treatments for boils (21CFR Part 310.531), and drug products for poison ivy, poison oak and poison sumac (21CFR Part 310.545); however, there is a lack of adequate data to establish general recognition of the safety and effectiveness of this ingredient for these intended uses.

Several sources have described the use of Lanolin-containing products (especially highly purified materials) for the prevention and treatment of nipple pain in breastfeeding mothers.[17,18,22-26] Lanolin has also been studied for use in coatings and synthetic membranes for drug delivery systems for oral and transdermal drug treatments, respectively.[27-29] Lanolin and Lanolin Alcohol have been evaluated in multiple studies for use in wound treatment[30-36] and barrier cream for barrier deficient skin, such as that found in neonates.[37-39]

TOXICOKINETIC STUDIES

Toxicokinetics studies were not included in the original report and were not found in the updated literature search, and unpublished data were not submitted.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

The acute dermal LD_{50} of Lanolin Oil as applied to the rabbit skin has been determined to be in excess of 10 ml/kg.[1] In a 2-dose (1 or 2 g/kg) study in rats, the LD_{50} of Hydroxylated Lanolin was found to be greater than 2.0 g/kg.

Each of the 9 lanolin ingredients has been tested in rats for acute oral toxicity in a variety of studies.[1] All exhibit low oral toxicity. Only the most pertinent acute oral LD_{50} for each ingredient will be reported: undiluted Lanolin (> 64 ml/kg), undiluted Lanolin Oil (46.5 ml/kg), 50% Lanolin Wax in corn oil (> 32 g/kg), undiluted Lanolin Acid (56.5 ml/kg), 66% Lanolin Alcohol in corn oil (> 42.7 g/kg), undiluted Acetylated Lanolin (> 64 ml/kg), undiluted Acetylated Lanolin Alcohol (> 64 ml/kg), undiluted Hydrogenated Lanolin (> 64 ml/kg), and undiluted Hydroxylated Lanolin > 10 ml/kg).

Acute toxicity studies on lanolin-derived ingredients are summarized in Table 4. In dermal rat studies, the LD_{50}s of Lanolin Acid and Lanolin Alcohol (each tested in arachis oil) were both > 2000 mg/kg (the highest dose tested).[10,11] No dermal irritation was observed in these studies. In oral studies, the LD_{50} for undiluted Hydroxylated Lanolin was > 10 ml/kg in rats.[7] The LD_{50} for Lanolin Alcohol was > 5000 mg/kg.[11]

Subchronic Toxicity Studies

Oral

Lanolin Acid

In a 90-d oral repeated-dose study performed in accordance with OECD TG 408, groups of 10 male and 10 female RccHan™:WIST(SPF) rats received 0, 100, 300, or 1000 mg/kg bw/d Lanolin Acid (purity > 90%) in corn oil via gavage.[10] The animals were observed for clinical signs of toxicity, and body weights and feed consumption were measured. Ophthalmoscopic examinations (control and high dose groups only) were conducted pre-treatment and before study end, and neurobehavioral examinations were conducted at the end of treatment. Blood and urine were collected at the end of the treatment period for hematology and clinical chemistry evaluations. All rats were killed at the end of the study for gross pathology and histopathology examinations.

One rat died in the 300 mg/kg group due to dosing error. No other mortalities were reported. No clinical signs of toxicity were reported. No adverse effects observed in body weight gains, feed consumption, ophthalmology, hematology, clinical biochemistry, or urinalysis. No treatment-related changes were observed with gross pathology or histopathology. The no-observable-adverse-effect level (NOAEL) for Lanolin Acid in this study was greater than 1000 mg/kg bw/d.[10]

Lanolin Alcohol

In another 90-d oral repeated-dose study, groups of 10 male and 10 female Wistar Han™:RccHan™:WIST rats received 0, 100, 300, or 1000 mg/kg bw/d Lanolin Alcohol (purity > 90%) in arachis oil via gavage.[11] This study was performed in accordance with OECD TG 408 in a similar manner as that described above. The animals were observed for clinical signs of

toxicity, and body weights, feed consumption, and water consumption were measured. Ophthalmoscopic examinations (control and high dose groups only) were conducted pre-treatment and before study end, and neurobehavioral examinations were conducted pre-treatment and at weekly intervals thereafter. Blood was collected at the end of the treatment period for hematology and clinical chemistry evaluations. All rats were killed at the end of the study for gross pathology and histopathology examinations.

No mortalities or clinical signs of toxicity were observed. No adverse effects on body weight, feed/water consumption, ophthalmology, hematology, clinical chemistry, or gross pathology were observed. Minimal or mild alveolar macrophages were observed in 300 and 1000 mg/kg dose females, which were attributed to accidental inhalation of the test material during dosing. The NOAEL for Lanolin Alcohol in this study was greater than 1000 mg/kg bw/d.[11]

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

Oral

Lanolin Acid

In an oral developmental toxicity study performed in accordance with OECD TG 414, groups of 22 pregnant RccHan™:WIST(SPF) rats received 0, 100, 300, or 1000 mg.kg bw/d Lanolin Acid in corn oil on days 6-20 of gestation via gavage.[10] The dams were observed for clinical signs of toxicity during the treatment period, and body weights and feed consumption were measured. The dams were killed on gestation day 21 and the ovaries, uterine content, and fetuses were examined.

All dams survived until day 21 termination. No clinical signs of toxicity were observed. No adverse effects on feed consumption or body weights were noted. No effects to relevant reproductive parameters or gross pathological exams were observed. There were no treatment-related effects observed in fetal sex ratio or in the fetuses during examination. The NOAEL for maternal and developmental toxicity for Lanolin Alcohol in this study was ≥ 1000 mg/kg bw/d.[10]

Lanolin Alcohol

In an oral developmental toxicity study performed in accordance with OECD TG 414, groups of 24 pregnant Sprague-Dawley Crl:CD (SD) IGS BR rats received 0, 100, 300, or 1000 mg.kg bw/d Lanolin Alcohol in arachis oil on days 5-19 of gestation via gavage.[11] The dams were observed for clinical signs of toxicity during the treatment period, and body weights, feed consumption, and water consumption were measured. The dams were killed on gestation day 20 and the ovaries, uterine content, and fetuses were examined.

All dams survived until termination. No treatment-related clinical signs of toxicity were observed. No treatment-related effects of feed consumption or body weights were noted. No effects to relevant reproductive parameters or gross pathological exams were observed. There were no treatment-related effects on offspring survival measured by the mean numbers of early or later resorptions, live litter size, and post-implantation losses. There was also no adverse effect in sex ratio. In all dose groups, there were no significant treatment-related trends in the proportion of fetuses or litters with evidence of external, visceral, or skeletal anomalies. There were no findings of known malformations. The NOAEL for maternal and developmental toxicity for Lanolin Alcohol in this study was ≥ 1000 mg/kg bw/d.[11]

GENOTOXICITY STUDIES

In vitro genotoxicity studies on lanolin-derived ingredients are summarized in Table 5. Lanolin Acid and Lanolin Alcohol were not mutagenic in Ames tests when tested at up to 5000 µg/plate, with or without metabolic activation.[10,11] No mutagenicity to Lanolin Acid (at up to 600 µg/ml) or Lanolin Alcohol (at up to 937.5 µg/ml) was observed in mammalian gene mutation tests using mouse lymphoma L5178 cells, with and without metabolic activation. Additionally, Lanolin Acid (at up to 2500 µg/ml) and Lanolin Alcohol (at up to 1250 µg/ml) were not clastogenic in mammalian chromosome aberration tests using human lymphocytes, with and without metabolic activation.

CARCINOGENICITY STUDIES

Carcinogenicity studies were not included in the original report and were not found in the updated literature search, and unpublished data were not submitted.

ANTI-CARCINOGENICITY STUDIES

A study 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.[1] The concentration of 3-methyl-cholanthrene 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. A similar diminution in the carcinogenic potency of methylcholanthrene was observed when Lanolin was used as a diluent. The inhibitory effect was reported even with concentrations that exceeded the concentration of the carcinogen in benzene used as a positive control. Similar results were obtained with another carcinogen, 7,12-dimethylbenz(α)anthracene, on mice.

OTHER RELEVANT STUDIES

Comedogenicity

The acnegenic properties of cosmetics containing Lanolin and Lanolin-related materials were tested in a few studies.[1] Comedogenic effects were described for these ingredients. Concentrations tested were not reported.

Hydroxylated Lanolin

A comedogenicity assay was conducted using 6% w/w Hydroxylated Lanolin solution in cottonseed oil.[7] The right ear of 6 New Zealand White rabbits were treated with the test material and the left ear was dosed with cottonseed oil (positive control) on 5 consecutive d/wk for 3 consecutive wk. The ears were scored for hyperkeratosis and comedone formation each day prior to application of the test material. At study end, the control and treated ears were excised and subsequently subjected to histological examination for comedones. All rabbits appeared active and healthy throughout the test period. No signs of gross toxicity, adverse pharmacologic effects, or abnormal behavior were observed. Transient, mild hyperkeratosis (scores 1 - 2) was noted during the second and third weeks of dosing. The average "in-life" scores for the test and control ears were 0.19 and 0.16, respectively. The total number of visible comedones at test termination was 0 for treated and control ears. Histological examination showed that all ears (treated and control) were negative with respect to comedone formation although hyperkeratosis with scores of 1 - 2 was noted in all but one treated section and in 6 out of 12 control sections. The average group histology scores for treated and control ears were 1.1 and 0.5, respectively. The total number of comedones identified histologically was 0 for both treated and control ears. No further information on the results of the control material was described. Hydroxylated Lanolin was considered to be non-comedogenic in this study.

Efficacy Studies on Wound Healing

In rodent efficacy studies of different compounds used in wound healing, Lanolin was used in vehicle solutions and as a control.[31-35] Concentrations tested were reported to be as high as 30% (anhydrous form) and the rodents were treated with the test materials for as long as 3 wk. No adverse effects to Lanolin as used as a vehicle or control were reported.

DERMAL IRRITATION AND SENSITIZATION STUDIES

With one exception, the Lanolin ingredients are either non-irritating or at most mildly irritating to the skin of experimental animals.[1] The exception is Lanolin Acid which is a moderate skin irritant; it should be noted that Lanolin Acid is seldom, if at all, found in cosmetic formulations as the free acid. In five tests conducted on undiluted Lanolin Acid, the primary irritation index (PII) ranged from 0.78 to 2.2 (maximum of 8). The highest PII values obtained for other undiluted lanolin ingredients are 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).

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.[1]

A skin sensitization study with 8 guinea pigs was done with Acetylated Lanolin Alcohol suspended in physiological saline.[1] Ten intracutaneous injections on alternate days followed by challenge injection 2 wk later showed no sensitization. Hydrogenated Lanolin was not a sensitizer when applied to the skin of guinea pigs 3 times/wk for 7 or more applications. A 2% solution in 1:1:3 acetone:dioxane:corn oil was used. The challenge was applied 2 wk after the last induction dose. The sensitization potential of Lanolin Wax suspended in corn oil was evaluated using 10 guinea pigs; Lanolin Wax had an average score of 0.95 (scores between 0.1 and 2.0 are mild sensitizers). The material was injected intracutaneously 3 times/wk for a total of 10 injections with an eleventh challenge injection 2 wk later.

Numerous patch tests (single and repeated insult) were conducted on volunteers with Lanolin and related cosmetic ingredients.[1] Undiluted Lanolin showed no evidence of primary irritation or sensitization in over 250 subjects. Lanolin Oil has been skin tested in more than 300 volunteers without adverse reactions. Undiluted Lanolin Wax showed extremely low irritation potential and no evidence of sensitization in over 200 subjects. Of the 115 subjects exposed topically to Lanolin Acid, three showed increased reaction not considered sensitization and one showed sensitization. There were no adverse effects noted when 50 volunteers were exposed to undiluted Lanolin Alcohol in a human repeated-insult-patch-test (HRIPT). Questionable evidence of fatiguing was found in 2 of 53 subjects exposed to Acetylated Lanolin. Acetylated Lanolin Alcohol caused an extremely low level of irritation in over 60 individuals. In an HRIPT on 50 subjects, undiluted Hydrogenated Lanolin presented no suggestions of irritation, fatiguing, or sensitization. There were no visible skin changes observed in 53 subjects exposed to Hydroxylated Lanolin at up to 100%.

Dermal irritation and sensitization studies are summarized in Table 6. Lanolin Alcohol (concentration not reported) in mineral oil was irritating in a modified Draize study in New Zealand White rabbits on intact and abraded skin.[11] (This study was disregarded by ECHA as it was not sufficient for use in classifying Lanolin Alcohol.) No irritation was observed in 20 subjects that received nano-emulsions containing 2.0% Acetylated Lanolin.[40] In a dermal tolerance test, Hydrogenated Lanolin did not cause erythema when applied to the palm of the hands of 14 subjects.[8] None of the subjects complained of itching or other signs of intolerance. Lanolin Acid was determined to be non-sensitizing in a local lymph node assay (LLNA) in mice when tested at up to 50% in dimethylformamide.[10]

Photosensitization/Phototoxicity

Human

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.[1] No information on light exposure was reported. There was no evidence of either phototoxicity or photosensitivity.

OCULAR IRRITATION STUDIES

Animal

With one exception, all the Lanolin ingredients were either non-irritating or at most mildly irritating to the eyes of experimental animals.[1] In 3 of 4 ocular irritation studies conducted on rabbits, undiluted Lanolin Acid was found to be a mild or moderately severe irritant (no additional details available). For the other 8 Lanolin ingredients, no or only mild transient reactions were reported.

In a study to determine whether Lanolin-containing ophthalmic materials, applied topically, could be incorporated into the cornea, a series of provocative animal tests were performed.[1] It was concluded that no Lanolin-containing ointment was trapped in the cornea unless the surface of the cornea was directly and repeatedly disrupted and abraded.

Hydroxylated Lanolin

In an ocular irritation study, 3 New Zealand albino rabbits received instillations of 0.1 ml Hydroxylated Lanolin (20%) in mineral oil in the right eye while the left eye was untreated and served as control.[7] The eyes were not rinsed. Changes to the cornea, iris, and conjunctivae were evaluated and scored every 24 h for 4 d and then again on the 7th d. The mean scores for cornea opacity, iris, and conjunctivae chemosis were 0 for all animals at 24, 48, and 72 h. No irritation was observed.

CLINICAL STUDIES

Over the years of its use, Lanolin has been observed to produce allergic or hypersensitivity reactions.[1] The first reports of Lanolin skin sensitization were published in 1930. Since then, numerous reports of Lanolin allergy have been published. The incidence of hypersensitivity among persons exposed has been a matter of great uncertainty.

Three large European retrospective studies of dermatology patients with Lanolin Alcohol hypersensitivity reported incidences of 0.70, 2.38, and 1.82%.[1] Using numerous assumptions, the incidence in the general population was estimated to be no more than 9.7 cases per million people.

For the detection of Lanolin allergy, the use of 30% wool wax alcohol in petrolatum was suggested as the testing agent for Lanolin materials in patch testing.[1] 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.

A study concluded that the greatest allergenic reaction is given by C14-C16 Lanolin Alcohols.[1] A European study group noted that the incidence of hypersensitivity to all topical medicaments was 14% (560/4000) in clinic patients with eczema. Positive test reactions were reported for wool alcohols (3%). The difference between these total values of 12%, and the overall total of 14% was not stated.

The North American Contact Dermatitis Group (NACDG) has issued a series of reports on results of diagnostic patch testing of dermatitis patients using a standard array of test substances.[1] Out of 1200 patients tested over an 18-mo period ending in June 1972, wool wax alcohols (30% in petrolatum) ranked eighth in frequency of reaction with 3% of the patients reacting. In the subsequent 2-yr testing period, wool wax alcohol ranked eleventh, again experiencing a 3% reaction rate in 3165 patients tested. A preliminary report from a testing period of July 1,1975 - June 30, 1976 showed wool alcohol ranking thirteenth with a reaction incidence of 2.9% in 900 - 2000 patients tested. 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.

It has been demonstrated in Lanolin-sensitive patients that the removal of free fatty Lanolin Alcohols and detergents reduced the incidence of detectable hypersensitivity by 96%.[1] An anonymous submission suggested that parabens may increase or be responsible for Lanolin hypersensitivity. Estimates of the extent of hypersensitivity vary 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).[1] It has even been suggested that autoxidation products may contribute to the allergenicity of Lanolin.

The Panel has previously reviewed data on efficacy studies with Lanolin in wound care and skin protective materials.[13] Several multicenter and retrospective studies reported the sensitization rates of Lanolin and Lanolin Alcohol in patients with allergic contact dermatitis.

Lanolin is a weak sensitizer. The "lanolin paradox" is a phenomenon wherein Lanolin may be observed to cause allergic contact dermatitis when it is applied to damaged skin, but allergenicity does not appear in these apparently sensitized patients when it is applied to normal healthy skin, yielding false negative patch tests.[14] Allergic reactions are observed

primarily in patients with stasis dermatitis, leg ulcers, perianal/genital dermatitis, and atopic dermatitis. Children and the elderly have a greater risk of developing contact allergy to Lanolin due to comorbidities.

Clinical Reports

In a study of 10 subjects with history of contact allergy to a trademarked Lanolin product (a Lanolin derivative comprised of 10% Lanolin Alcohol and mineral oil), the subjects were re-tested in a dose-response manner followed by a comprehensive transcriptomic analysis of samples of skin reactions.[41] Concentrations tested were 3, 10, 30, 50, and 100% w/w in pet. Positive reactions were observed in 8 subjects in the re-test. Most of the positive patch tests had an allergy signature with strong activation of gene modules associated with adaptive immunity and down regulation of cornification pathway genes. Gene modulation was correlated with the magnitude of patch test reactions and the concentration applied. Some positive patch reactions to the test material had no or few allergy biomarkers, suggesting induction of an irritant skin inflammation response.

A trademarked Lanolin product was studied to evaluate its ability to serve as a marker for Lanolin allergy in a repeated open application test (ROAT).[42] The ROAT was designed as a double-blind, randomized case-control study. Patch tests were performed with the trademarked Lanolin product at up to 100%, Lanolin products at up to 50% pet., Lanolin Alcohol at up to 30% pet., and "as-is" products prior to the 4-wk ROAT with Lanolin samples and base creams. Irritant dermatitis was induced by sodium lauryl sulfate. Twelve test patients with previous strong reactions and 14 controls completed the study. In the patch test, 11 subjects had a positive reaction with Lanolin at 100% and 5 subjects were positive to Lanolin at 50% pet. Only 3 subjects had positive reaction to patch test preparations other than Lanolin. No positive reactions were observed in controls. In the ROAT, no reactions were observed to any of the cream products containing Lanolin.

In a study of 430 patients with known cosmetic contact dermatitis, female facial melanoderma, cosmetic contact dermatitis anamnesis, and other dermatological diseases, the patients were patch-tested with 24 lanolin-derived substances.[11] These included Acetylated Lanolin, Acetylated Lanolin Alcohol, Hydrogenated Lanolin, Lanolin, Lanolin Acid, and Lanolin Alcohol at either 30% concentration, undiluted, or both. Control subjects (number not reported) were also patch-tested. The patches were either Finn chambers or Torii patch test plaster and the test sites were occluded. The test materials were applied to the upper back of the patients for 48 h. The test sites were observed at 1 and 24 h and 1 wk after the patches were removed. Very mild reactions for Lanolin Alcohol were observed in the subjects that already experienced dermatitis. Various lanolin fractions and derivatives produced different degrees of reaction (+ to greater than ++). Refined Lanolin Acid (30%) had the highest percentage of ++/+++ responses at 11.6% and + responses at 37.5%. Lanolin Alcohol (30%) had the next highest percentage of ++/+++ responses at 2.3% and + responses at 6.8%.

In a randomized study of 60 in-patients with venous leg ulcers in Croatia, 30 patients had allergic contact dermatitis and 30 did not have signs of contact allergy.[43] Patch testing was performed using a standard series of allergens and a special series of allergens that included Lanolin 20% pet. Two positive reactions to Lanolin were recorded in each the allergic contact dermatitis group and the control group. Total positivity was 6.66%.

Clinical trials have been performed evaluating the efficacy of the use of Lanolin for treatment of nipple pain in breastfeeding women.[17,23-26] No adverse effects due to Lanolin were reported.

The efficacy of Lanolin for treatment of side effects on the lips from chemotherapy was also studied.[30] Patients (n = 24) received Lanolin treatment 6 times/d from the beginning of chemotherapy until 2 wk after the end of chemotherapy. No adverse effects from the use of Lanolin were reported.

A clinical trial on the safety of and efficacy of pure Lanolin and another treatment for foot xerosis was performed in a double-blind randomized test.[36] The pure Lanolin was used twice daily on one foot of 67 patients with bilateral conditions for up to 4 wk. The other treatment was used on the opposite foot under the same conditions. Pruritus, burning, and redness were reported in 21 patients; however, the study authors did not provide details as to which treatment was associated with which adverse effects other than to say they were comparable between the 2 study groups.

The effects of topical therapy with an ointment containing Lanolin Alcohol were studied in neonates.[38] This study specifically investigated the prevention of nosocomial infections in infants born before week 33 of gestation. No adverse effects were observed in the 157 neonates that received the ointment that contained Lanolin Alcohol. In another topical therapy study in neonates, 58 infants between the ages of 25 and 36 wk gestation were tested for up to 4 wk with a cream containing 70% Lanolin and 30% olive oil.[39] Application of the cream was well tolerated by the infants.

Retrospective and Multicenter Studies

The results of numerous multicenter and retrospective studies conducted over more than 50 years are summarized in Table 7. These studies were primarily performed using Lanolin Alcohol, with a few on Lanolin or a trademarked Lanolin product. Sensitization to Lanolin and Lanolin Alcohol has been observed around the globe, with sensitization rates in patients with contact dermatitis varying, independent of region or span of time.[8,44-69] Using North America as an example, a multicenter study from the NACDG of patients with suspected allergic contact dermatitis found the positive reactivity rate for to a trademarked Lanolin product (50% pet.; contains 10% Lanolin Alcohol and mineral oil) to be 4.6% from 2011 to 2012 and 3.7% from 2019 to 2020. [47,48] In patients with suspected allergic contact dermatitis, the Netherlands has reported a positivity rate for Lanolin Alcohol (31% pet.) as high as 14.7% (2016 to 2017)[66] and Tunisia reported positivity rates from 52

to 63% over a 7-yr period (dates not reported).[67] Positivity rates in children were notably higher than those observed in adults.[45,51,57,65] The positivity rate of contact allergy to the general population in Europe was determined to be 0.4% in a multicenter study that took place between August 2008 and October 2011.[69]

In addition to the retrospective and multicenter studies, literature review studies of irritant and allergic contact dermatitis have been performed. Lanolin and Lanolin Alcohol were identified as common allergens in wound care-related materials and moisturizers.[70] Lanolin Alcohol is also a common sensitizer in the elderly, with increased sensitization rates observed over adult patients.[71] In a systematic review of patch test results in 34 published studies, from 1997 to 2012, Lanolin was included in the most common allergens in children aged up to 19-yr-old.[72]

Case Reports

In a case report, a 19-yr-old female presented with widely distributed, erythematous, papular, and confluent eruptions on both backs of her hands following dermal exposure to several items, including propolis cream that contained Lanolin Alcohol.[73] The patient also had edema on the left hand with vesicular eruptions and inflammatory, itchy, papular lesions on the cheeks and feet. Patch test results were +++ on days 3 and 5 for Lanolin Alcohol (30%). The patient also had positive patch results for *Myroxylon pereirae*, colophonium, fragrance mix 1 and 2, clove oil, lemon grass oil, sorbitan sesquioleate, farnesol, propolis cream, and unguentum lanalcoli.

Comedogenic Effects

The comedogenicity of a finished product that contained Lanolin (concentration not reported) was assessed in a double-blind randomized controlled trial with 15 subjects.[74] The subjects applied the test material 3 times/wk for up to 4 wk. No adverse effects to the product containing Lanolin were reported. The finished product was non-comedogenic.

Occupational Exposure

No scientific reports of adverse reactions among persons occupationally-exposed during production or use of Lanolin over a 50-yr period have been reported.[1] Similarly, there have been no reported adverse experiences in several studies of multiple year exposure by workers or customers for Lanolin Oil, Lanolin Wax, Lanolin Acid, Lanolin Alcohol, Acetylated Lanolin, or Acetylated Lanolin Alcohol.

SUMMARY

The Panel previously reviewed the safety of 9 lanolin-derived ingredients in a report that was published in 1980. At that time, the Panel concluded "Lanolin and related Lanolin materials… are safe for topical application to humans in the present practices of use and concentration" (as described in that assessment). The Panel first considered a re-review of this report in February 2003, and the Panel reaffirmed the original conclusion, as published in 2005. In accordance with its Procedures, the Panel evaluates the conclusions of previously-issued reports approximately every 15 years, and it has been at least 15 years since this assessment was last reviewed. This report has been reopened to reassess the safety of the 9 lanolin-derived ingredients (listed below) included in the original report as used in cosmetics. According to the *Dictionary*, most of these ingredients are reported to function in cosmetics as skin conditioning agents-emollient and hair conditioning agents; other cosmetic functions are also reported.

According to 2023 VCRP survey data, of the ingredients named in this report, Lanolin has the most reported uses in cosmetic products, with a total of 285 formulations; the majority of the uses are in leave-on products. Acetylated Lanolin Alcohol has the second most reported uses in cosmetic products, with a total of 196; the majority of these uses are also in leave-on formulations. The frequencies of use for both of these ingredients have markedly decreased since the Panel last reviewed these ingredients in 2003; Lanolin was reported to have 782 uses, and Acetylated Lanolin Alcohol was reported to have 356 uses. The results of the concentration of use survey conducted by the Council in 2022 indicate Lanolin Oil has the highest maximum concentration of use in a leave-on formulation; it is used at up to 47% in lipsticks. Lanolin is reported to be used at up to 40% in leave-on nail creams and lotions. When the Panel last reviewed these ingredients in 2003, the maximum leave-on use concentration for Lanolin Oil was 65% in lipstick; the maximum leave-on use concentration for Lanolin was 37% in body and hand skin care preparations.

All of the lanolin-derived ingredients named in the report are not restricted from use in any way under the rules governing cosmetic products in the European Union. In the United States, Lanolin is permitted to be used as direct and indirect food additives. Additionally, Lanolin is approved as active and inactive ingredients in several over-the-counter products.

In acute dermal rat studies, the LD_{50}s of Lanolin Acid and Lanolin Alcohol (each tested in arachis oil) were both > 2000 mg/kg. No dermal irritation was observed in these studies. In acute oral studies, the LD_{50} for undiluted Hydroxylated Lanolin was > 10 ml/kg in rats. The LD_{50} for Lanolin Alcohol was > 5000 mg/kg. In separate 90-d rat studies, the oral NOAEL was determined to be greater than 1000 mg/kg bw/d for Lanolin Acid and Lanolin Alcohol. The NOAEL for maternal and developmental toxicity was also $\geq$ 1000 mg/kg bw/d in separate oral studies in rats for Lanolin Acid and Lanolin Alcohol.

Lanolin Acid and Lanolin Alcohol were not mutagenic in Ames tests when tested at up to 5000 µg/plate, with or without metabolic activation. No mutagenicity to Lanolin Acid (at up to 600 µg/ml) or Lanolin Alcohol (at up to 937.5

μg/ml) was observed in mammalian gene mutation tests using mouse lymphoma L5178 cells, with and without metabolic activation. Additionally, Lanolin Acid (at up to 2500 μg/ml) and Lanolin Alcohol (at up to 1250 μg/ml) were not clastogenic in mammalian chromosome aberration tests using human lymphocytes, with and without metabolic activation.

Hydroxylated Lanolin at 6% in cottonseed oil was considered to be non-comedogenic in a rabbit study. No adverse effects were reported in efficacy studies of wound healing products where Lanolin was used in vehicle solutions and controls.

Lanolin Alcohol (concentration not reported) in mineral oil was irritating in a modified Draize study in New Zealand White rabbits on intact and abraded skin. No irritation was observed in 20 subjects that received nano-emulsions containing 2.0% Acetylated Lanolin. In a dermal tolerance test, Hydrogenated Lanolin did not cause erythema when applied to the palm of the hands of 14 subjects. None of the subjects complained of itching or other signs of intolerance. Lanolin Acid was determined to be non-sensitizing in an LLNA in mice when tested at up to 50% in dimethylformamide. No ocular irritation was observed in a study in rabbits with 20% Hydrogenated Lanolin.

Lanolin is a weak sensitizer. Detection of Lanolin-induced contact dermatitis in diseased skin by patch testing on normal skin may lead to false negative results; this is known as the lanolin paradox. Allergic reactions are observed primarily in patients with stasis dermatitis, leg ulcers, perianal/genital dermatitis, and atopic dermatitis. Children and the elderly have a greater risk of developing contact allergy to Lanolin due to comorbidities.

Clinical studies of Lanolin products observed some positive reactions to these ingredients. No adverse effects were observed in efficacy studies of Lanolin for use in treatment in breastfeeding mothers or topical therapies in neonates. Numerous multicenter and retrospective studies have reported sensitization to Lanolin and Lanolin Alcohol around the globe, with sensitization rates in patients with contact dermatitis varying, independent of region or span of time. In literature review studies, Lanolin and Lanolin Alcohol were identified as common allergens in wound care-related materials and moisturizers. Lanolin and Lanolin Alcohol are common sensitizers in the elderly and in children aged up to 19-yr-old. A case report of a 19-yr-old patient was positive for Lanolin Alcohol 30%. A finished product that contained an unreported concentration of Lanolin was non-comedogenic in a double-blind randomized controlled trial of 15 subjects.

Toxicokinetic and carcinogenicity studies on lanolin-derived ingredients were not included in the original report and were not found in the updated literature search, and unpublished data were not submitted.

DISCUSSION

In accordance with its Procedures, the Panel re-evaluates the conclusions of previously-issued reports approximately every 15 years. In 1980, the Panel published a final report on 9 lanolin-derived ingredients and concluded that the available data supported the safety of these ingredients for topical applications. The conclusion of the report was reaffirmed in a re-review that was published in 2005. This report was reopened in June 2023 to expand the discussion from the original report. The Panel noted that the available data show no systemic toxicity or genotoxicity, and no- to minimal dermal irritation or sensitization in healthy skin. The Panel considered these findings and determined that the data are sufficient to conclude that the lanolin-derived ingredients described in this report are safe in cosmetics in the present practices of use and concentration.

The Panel discussed the “lanolin paradox,” wherein Lanolin may cause allergic contact dermatitis when applied to damaged skin, but allergenicity does not appear in these apparently sensitized patients when Lanolin is applied to normal, healthy skin in patch tests. The rate of allergic reaction to Lanolin is extremely low in the general population, and sensitization can be further reduced when Lanolin is ultra refined to reduce the amount of free Lanolin Alcohol. The Panel cautioned that Lanolin should not be used on damaged skin, especially in high-risk populations for sensitivity (e.g., pediatric and geriatric populations).

The Panel expressed concern regarding heavy metals that may be present in these ingredients. They stressed that the cosmetics industry should continue to use the necessary procedures to minimize impurities in cosmetic formulations according to limits set by the FDA and EPA. The Panel was also concerned with the risks inherent in using animal-derived ingredients, namely the transmission of infectious agents and biologically-derived impurities (e.g., nucleic acids, proteins, endotoxins). The Panel stressed that these ingredients must be free of detectible pathogenic viruses, infectious agents (e.g. prions), and/or biologically-derived impurities. Suppliers and users of these ingredients must accept responsibility for assuring that these ingredients are risk-free. Tests to assure the absence of a pathogenic agent in the ingredients or controls to assure derivation from pathogen-free sources are two approaches that should be considered.

The Panel discussed the issue of incidental inhalation exposure resulting from these ingredients (e.g., Lanolin is used in a hair spray at 1.6% and Lanolin Oil is used in face powders at 0.3%). Inhalation toxicity data were not available. However, the Panel noted that in aerosol products, the majority of droplets/particles would not be respirable to any appreciable amount. Furthermore, droplets/particles deposited in the nasopharyngeal or tracheobronchial regions of the respiratory tract present no toxicological concerns based on the chemical and biological properties of these ingredients. Coupled with the small actual exposure in the breathing zone and the low concentrations at which these ingredients are used (or expected to be used) in potentially inhaled products, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects. A detailed discussion and summary of the Panel’s approach

to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at https://www.cir-safety.org/cir-findings.

The Panel's respiratory exposure resource document (see link above) notes that airbrush technology presents a potential safety concern, and that no data are available for consumer habits and practices thereof. As a result of deficiencies in these critical data needs, the safety of cosmetic ingredients applied by airbrush delivery systems cannot be assessed by the Panel. Therefore, the Panel has found the data insufficient to support the safe use of cosmetic ingredients applied via an airbrush delivery system.

CONCLUSION

The Expert Panel for Cosmetic Ingredient Safety concluded that the following 9 lanolin-derived ingredients are safe in cosmetics in the present practices of use and concentration described in this safety assessment.

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

TABLES

Table 1. Definitions and reported function of the ingredients in this safety assessment.

Ingredient & CAS No.	Definition	Function(s)
Acetylated Lanolin 61788-48-5	Acetylated Lanolin is the acetyl ester of Lanolin.	hair conditioning agent; skin-conditioning agent - emollient; skin-conditioning agents - occlusive
Acetylated Lanolin Alcohol 61788-49-6	Acetylated Lanolin Alcohol is the acetyl ester of Lanolin Alcohol.	hair conditioning agent; skin-conditioning agent - emollient; skin-conditioning agents - occlusive
Hydrogenated Lanolin 8031-44-5	Hydrogenated Lanolin is the end product of controlled hydrogenation of Lanolin.	fragrance ingredient; hair conditioning agent; skin-conditioning agent - occlusive
Hydroxylated Lanolin 68424-66-8	Hydroxylated Lanolin is the product obtained by controlled hydroxylation of Lanolin.	binder; skin-conditioning agent - misc.
Lanolin 8006-54-0 (anhydrous)	Lanolin is a refined derivative of the unctuous fat-like sebaceous secretion of sheep. It consists of a highly complex mixture of esters of high molecular weight aliphatic, steroid or triterpenoid alcohols and fatty acids.	emulsion stabilizer; hair conditioning agent; skin protectant; skin-conditioning agent – emollient; surfactant - emulsifying agent
Lanolin Acid 68424-43-1	Lanolin Acid is a mixture of organic acids obtained from the hydrolysis of Lanolin.	surfactant - cleansing agent
Lanolin Alcohol 8027-33-6	Lanolin Alcohol is a mixture of organic alcohols obtained from the hydrolysis of Lanolin.	binder; emulsion stabilizer; hair conditioning agent; skin-conditioning agent - misc.; viscosity increasing agent - nonaqueous
Lanolin Oil 8038-43-5 70321-63-0	Lanolin Oil is the liquid fraction of lanolin obtained by physical means from whole lanolin.	hair conditioning agent; skin-conditioning agent - emollient
Lanolin Wax 68201-49-0	Lanolin Wax is the semisolid fraction of lanolin obtained by physical means from whole lanolin.	binder; hair conditioning agent; skin-conditioning agent - emollient; viscosity increasing agent - nonaqueous

Table 2. Chemical properties

Property	Value	Reference
Acetylated Lanolin		
Physical Form	Yellow-brown paste	9
Specific Gravity @ 20 ºC)	0.95	9
Melting Point ºC	30 - 40 31 - 55	1 9
Boiling Point ºC	128 (decomposition)	9
Vapor Pressure (mm Hg @ 20 ºC)	9.75×10^{-5}	9
log P_{ow}	> 10.0 (calculated)	9
Water Solubility (g/L @ 20 ºC & pH 6)	$< 1.0 \times 10^{-3}$	9
Acetylated Lanolin Alcohol		
Physical Form	Lemon-yellow to straw-colored, oily hydrophobic liquid with a characteristic bland odor Yellow solid	1 12
Specific Gravity (@ 25 ºC (@ 20 ºC)	0.850 - 0.880 0.904 - 1.00	1 12
Melting Point ºC	45 - 80	12
Boiling Point ºC	220 - 420	12
Vapor Pressure (mm Hg @ 20 ºC)	1.85×10^{-5}	12
log P_{ow}	> 7.2 (calculated)	12
Water Solubility (mg/L @ 20 ºC & pH 8)	< 1.20	12
Refractive Index (@ 20 ºC)	1.4445 - 1.4485	1
Hydrogenated Lanolin		
Physical Form	Light yellow to white tacky solid White, odorless paste	1 8
Specific Gravity (@ 20 ºC)	0.906	8
Vapor Pressure (mm Hg @ 25 ºC)	4.2×10^{-5}	8
Melting Point ºC	48 - 53 27 - 61	1 8
Boiling Point ºC	100 - 315	8
log P_{ow}	7 - 10 (calculated)	8
Water Solubility (mg/L @ 20 ºC & pH 7)	1.24	8

Table 2. Chemical properties

Property	Value	Reference
Hydroxylated Lanolin		
Physical Form	Yellow-brown solid crystalline	7
Specific Gravity (@ 20 ºC)	0.963	7
Vapor Pressure (mm Hg @ 25 ºC)	5.5×10^{-5}	7
Melting Point ºC	39 - 46 32 - 59	1 7
Boiling Point ºC	155 (decomposition)	7
log P_{ow} (@ 40 ºC)	> 10 (calculated)	7
Water Solubility (g/L @ 20 ºC & pH 6)	< 0.001	7
Lanolin		
Physical Form	Ointment-like material with a slight, characteristic odor; in anhydrous form, transparent to yellow, tenacious, unctuous mass	1
Melting Point ºC	36 - 42	1
Lanolin Acid		
Physical Form	Hard, waxy, yellow-tan solid with a mild waxy odor Brown waxy solid	1 10
Specific Gravity (@ 20 ºC)	0.908	10
Vapor Pressure (mm Hg @ 20 ºC)	< 5.25	10
Melting Point ºC	40 - 62 35 - 60	1 10
Boiling Point ºC	320 - 430	10
log P_{ow} (@ 30 ºC)	1.35 to > 6.5 (calculated)	10
Water Solubility (mg/L @ 20 ºC & pH 7)	0.21	10
Lanolin Alcohol		
Physical Form	Firm, waxy, amber solid with a characteristic odor Yellow waxy solid	1 11
Specific Gravity (@ 20 ºC)	0.904 - 0.953	11
Vapor Pressure (mm Hg @ 20 ºC)	2.7	11
Melting Point ºC	47 - 65 45 - 80	1 11
Boiling Point ºC	220 - 420	11
Water Solubility (mg/L @ 20 ºC & pH 7)	0.14 - 0.38	11
Lanolin Oil		
Physical Form	Clear, amber-colored liquid	1
Lanolin Wax		
Physical Form	Odorless, tasteless, ceraceous solid	1
Melting Point ºC	41 - 51	1

Table 3. Frequency (2023/2002) and concentration (2022/2003) of use according to likely duration and exposure and by product category.

	Acetylated Lanolin				Acetylated Lanolin Alcohol				Hydrogenated Lanolin				Hydroxylated Lanolin			
	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	2023[19]	**2002**[2]	**2022**[20]	**2003**[2]	**2023**[19]	**2002**[2]	**2022**[20]	**2003**[2]	**2023**[19]	**2002**[2]	**2022**[20]	**2003**[2]	**2023**[19]	**2002**[2]	**2022**[20]	**2003**[2]
Totals*	**2**	**163**	**7.5-8**	**0.1-7**	**196**	**356**	**0.02-6.3**	**0.002-16**	**6**	**111**	**10.2**	**0.5-10**	**4**	**139**	**3.5-17.5**	**0.5-28**
summarized by likely duration and exposure**																
Duration of Use																
Leave-On	*2*	*144*	*7.5-8*	*0.1-7*	*191*	*328*	*0.02-6.3*	*0.002-16*	*6*	*104*	*10.2*	*1-10*	*4*	*137*	*3.5-17.5*	*0.5-28*
Rinse-Off	*NR*	*19*	*NR*	*0.1-1*	*5*	*28*	*0.61*	*0.01-1*	*NR*	*7*	*NR*	*0.5-1*	*NR*	*2*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type																
Eye Area	NR	6	NR	0.1-0.6	NR	33	0.38-6.3	0.002-0.9	NR	8	10.2	1-10	3	96	3.5-17.5	1-11
Incidental Ingestion	NR	33	7.5-8	5	1	100	1.1	2-3	2	30	NR	3-9	1	18	NR	0.5-28
Incidental Inhalation-Spray	1[a]	62[a]; 26[b]	NR	1-4[a]; 0.5-2[b]	168[a];15[b]	12; 52[a]; 57[b]	0.02-0.07	0.01-0.4; 0.01-5[a]; 0.1-6[b]	1[a]; 3[b]	1; 26[a]; 29[b]	NR	2[a]; 2-10[b]	NR	10[a]; 2[b]	NR	NR
Incidental Inhalation-Powder	NR	2; 1[c]; 26[b]	NR	0.2-0.3; 3[c]; 0.5-2[b]	6; 15[b]	16; 2[c]; 57[b]	0.1[c]	0.01-2; 0.01-16[c]; 0.1-6[b]	3[b]	29[b]	NR	2-10[b]	NR	3; 2[b]	NR	2
Dermal Contact	2	129	NR	0.1-7	195	231	0.02-6.3	0.01-16	4	72	10.2	1-10	3	111	10.8-17.5	2-11
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR	NR	1[a]	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	1	NR	NR	NR	18	NR	0.01-0.02	NR	3	NR	0.5	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	1	NR	NR	NR	NR	NR	1	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	2	0.25-0.61	0.01-0.1	NR	1	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	33	7.5-8	1-5	2	106	1.1	0.1-3	2	30	NR	3-9	1	18	NR	0.5-28
Baby Products	NR	1	NR	3	NR	2	NR	0.01-16	NR	NR	NR	NR	NR	NR	NR	2
as reported by product category																
Baby Products																
Baby Lotions/Oils/Powders/Creams	NR	1	NR	3	NR	2	NR	0.01-16								
Other Baby Products													NR	NR	NR	2
Bath Preparations (diluted for use)																
Bath Oils, Tablets, and Salts																
Bubble Baths																
Other Bath Preparations																
Eye Makeup Preparations																
Eyebrow Pencil					NR	NR	NR	0.1					3	3	NR	NR
Eyeliner					NR	NR	0.38	0.4	NR	2	NR	1	NR	73	10.8	5-10
Eye Shadow					NR	17	6.3	0.9	NR	NR	10.2	NR	NR	7	17.5	3-10
Eye Lotion	NR	1	NR	0.6	NR	1	NR	NR								
Eye Makeup Remover																
Mascara					NR	4	NR	0.002	NR	5	NR	NR	NR	10	3.5	1
Other Eye Makeup Preparations	NR	5	NR	0.1	NR	11	NR	NR	NR	1	NR	7-10	NR	3	11.1	2-11
Fragrance Preparations																
Cologne and Toilet Water					NR	5	0.02	0.07								
Perfumes							0.07									
Powders (dusting/talcum, excl aftershave talc)					NR	6	NR	0.01								
Sachets																
Other Fragrance Preparation					NR	3	NR	0.1-0.4	NR	1	NR	NR				
Hair Preparations (non-coloring)																
Hair Conditioner	NR	1	NR	NR	NR	1	NR	NR	NR	1	NR	0.5				
Hair Spray (aerosol fixatives)					NR	4	NR	0.01								
Hair Straighteners					NR	3	NR	NR								
Permanent Waves																
Rinses (non-coloring)									NR	1	NR	NR				
Shampoos (non-coloring)					NR	1	NR	0.02								
Tonics, Dressings, and Other Hair Grooming Aids					NR	6	NR	0.01	NR	1	NR	NR				

Table 3. Frequency (2023/2002) and concentration (2022/2003) of use according to likely duration and exposure and by product category.

	Acetylated Lanolin				Acetylated Lanolin Alcohol				Hydrogenated Lanolin				Hydroxylated Lanolin			
	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	2023	**2002**	**2022**	**2003**	**2023**	**2002**	**2022**	**2003**	**2023**	**2002**	**2022**	**2003**	**2023**	**2002**	**2022**	**2003**
Wave Sets																
Other Hair Preparations					NR	3	NR	NR								
Hair Coloring Preparations																
Hair Dyes and Colors									NR	NR	NR	1				
Hair Tints																
Hair Rinses (coloring)																
Hair Shampoos (coloring)																
Hair Color Sprays (aerosol)																
Hair Bleaches																
Other Hair Coloring Preparation					NR	1	NR	NR								
Makeup Preparations																
Blushers (all types)					1	9	NR	0.3-0.8					NR	2	NR	3
Face Powders	NR	2	NR	0.2-0.3	6	10	NR	0.01-2					NR	3	NR	2
Foundations	NR	3	NR	3-7	NR	9	NR	1-2	NR	2	NR	NR	NR	2	NR	2
Leg and Body Paints																10
Lipstick	NR	33	7.5-8	5	1	100	1.1	2-3	2	30	NR	3-9	1	18	NR	0.5-28
Makeup Bases					NR	8	NR	NR	NR	1	NR	NR	NR	2	NR	NR
Rouges					NR	1	0.6	NR								
Makeup Fixatives													NR	1	NR	NR
Other Makeup Preparations	1	3	NR	0.5-3	NR	8	NR	0.1-3	NR	1	NR	NR	NR	1	NR	4
Manicuring Preparations (Nail)																
Basecoats and Undercoats																
Cuticle Softeners					NR	NR	0.25	0.1								
Nail Creams and Lotions									NR	1	NR	NR				
Nail Polish and Enamel					NR	2	NR	0.01								
Nail Polish and Enamel Removers					NR	NR	0.61	0.02								
Other Manicuring Preparations																
Personal Cleanliness Products																
Bath Soaps and Detergents	NR	NR	NR	1	1	4	NR	0.4								
Deodorants (underarm)									NR	1	NR	NR				
Feminine Deodorants																
Other Personal Cleanliness Products					NR	2	NR	0.1								
Shaving Preparations																
Aftershave Lotion					NR	2	NR	NR								
Shaving Cream					NR	3	NR	0.02								
Other Shaving Preparations																
Skin Care Preparations																
Cleansing	NR	14	NR	0.1	3	10	NR	< 1	NR	4	NR	NR	NR	2	NR	NR
Depilatories																
Face and Neck (exc shave)	NR	6	NR	1	4	4	NR	0.2-3	1	4	NR	10				
Body and Hand (exc shave)	NR	20	NR	0.5-2	11	53	0.1	0.1-6	2	25	NR	2	NR	2	NR	NR
Moisturizing	1	35	NR	1	167	33	NR	0.5-5	1	16	NR	NR	NR	6	NR	NR
Night	NR	23	NR	4	1	5	NR	0.1	NR	3	NR	NR	NR	3	NR	NR
Paste Masks (mud packs)	NR	4	NR	1	1	3	NR	0.01	NR	1	NR	NR				
Skin Fresheners					NR	2	NR	NR	NR	1	NR	NR				
Other Skin Care Preparations	NR	8	NR	3	NR	14	NR	0.01-0.4	NR	4	NR	2				
Suntan Preparations																
Suntan Gels, Creams, and Liquids									NR	3	NR	2	NR	1	NR	NR
Indoor Tanning Preparations																
Other Suntan Preparations									NR	2	NR	NR				

Table 3. Frequency (2023/2002) and concentration (2022/2003) of use according to likely duration and exposure and by product category.

	Lanolin†				Lanolin Acid				Lanolin Alcohol				Lanolin Oil			
	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	2023[19]	**2002[2]**	**2022[20]**	**2003[2]**	**2023[19]**	**2002[2]**	**2022[20]**	**2003[2]**	**2023[19]**	**2002[2]**	**2022[20]**	**2003[2]**	**2023[19]**	**2002[2]**	**2022[20]**	**2003[2]**
Totals*	**285**	**782**	**0.0099-40**	**0.001-37**	**9**	**44**	**0.04-0.05**	**1-3**	**65**	**358**	**0.01-5**	**0.6-4**	**39**	**521**	**0.25-47**	**0.1-65**
summarized by likely duration and exposure**																
Duration of Use																
Leave-On	*262*	*627*	*0.0099-40*	*0.001-37*	*4*	*34*	*0.04*	*1-3*	*56*	*305*	*0.01-5*	*0.6*	*37*	*462*	*0.25-47*	*0.4-65*
Rinse-Off	*23*	*153*	*0.48-10*	*0.01-16*	*5*	*10*	*0.04-0.05*	*NR*	*9*	*46*	*0.5*	*4*	*2*	*48*	*NR*	*0.3-18*
Diluted for (Bath) Use	*NR*	*2*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*7*	*NR*	*NR*	*NR*	*11*	*NR*	*0.1-3*
Exposure Type*																
Eye Area	10	44	0.018-32	0.1-32	NR	21	NR	3	2	40	0.04-0.8	NR	NR	72	11.1	1-10
Incidental Ingestion	54	133	1.3-20.7	1-33	NR	2	NR	NR	3	18	0.36	NR	21	226	14.3-47	3-65
Incidental Inhalation-Spray	8; 74[a]; 32[b]	4; 176[a]; 114[b]	1.6; 0.5-15[a]	0.001; 0.2-19[a]; 2-37[b]	3[a]	6[a]	NR	NR	1; 18[a]; 8[b]	8; 76[a]; 63[b]	NR	0.6[b]	1; 6[a,b]	5; 54[a]; 31[b]	1[a]	0.8; 0.5-8[a]; 3[b]
Incidental Inhalation-Powder	4; 1[c]; 32[b]	10; 3[c]; 114[b]	0.0099; 0.2-7[c]	1-5; 0.2-4[c]; 2-37[b]	NR	NR	NR	NR	2; 8[b]	7; 2[c]; 63[b]	0.3; 0.01-1[c]	0.6[b]	2; 6[b]	13; 1[c]; 31[b]	0.25; 1-2[c]	2; 1[c]; 3[b]
Dermal Contact	152	507	0.0099-32	0.01-37	NR	21	NR	1	55	323	0.01-1	0.6	14	266	0.25-11.1	0.1-45
Deodorant (underarm)	NR	4[a]	NR	0.2[a]	NR	NR	NR	NR	NR	NR	NR	NR	NR	1[a]	NR	NR
Hair - Non-Coloring	65	124	0.5-15	0.001-19	8	8	0.04-0.05	NR	4	14	NR	NR	4	10	1-2	0.3-2
Hair-Coloring	7	8	0.5-0.91	0.4	1	NR	NR	NR	3	1	NR	4	NR	12	NR	0.8
Nail	3	7	1-40	0.3-20	NR	NR	NR	NR	NR	1	5	NR	NR	6	NR	2-25
Mucous Membrane	55	153	0.48-20.7	0.01-33	NR	2	NR	NR	7	31	0.36	NR	22	246	14.3-47	0.1-65
Baby Products	1	2	0.2	0.2-4	NR	NR	NR	NR	NR	2	0.2	NR	NR	1	NR	1
as reported by product category																
Baby Products																
Baby Lotions/Oils/Powders/Creams	1	3	0.2	0.2-4					NR	2	0.2	NR	NR	1	NR	1
Other Baby Products																
Bath Preparations (diluted for use)																
Bath Oils, Tablets, and Salts	NR	1	NR	NR					NR	7	NR	NR	NR	9	NR	0.1
Bubble Baths													NR	1	NR	NR
Other Bath Preparations	NR	1	NR	NR									NR	1	NR	3
Eye Makeup Preparations																
Eyebrow Pencil	1	16	4.4	6-7					NR	1	NR	NR	NR	2	NR	1
Eyeliner	1	6	32	10-32	NR	3	NR	NR	1	1	NR	NR	NR	8	NR	2-10
Eye Shadow	2	11	0.018-9	5-9	NR	4	NR	NR	NR	27	0.8	NR	NR	55	11.1	3-6
Eye Lotion	1	NR	NR	NR					NR	NR	0.04	NR				
Eye Makeup Remover									NR	3	NR	NR	NR	1	NR	NR
Mascara	4	3	NR	0.1-12	NR	13	NR	3	NR	1	NR	NR	NR	1	NR	1-3
Other Eye Makeup Preparations	1	8	NR	5	NR	1	NR	NR	1	7	NR	NR	NR	5	NR	6
Fragrance Preparations																
Cologne and Toilet Water																
Perfumes	4	NR	NR	NR												
Powders (dusting/talcum, excl aftershave talc)	NR	1	NR	NR									NR	1	NR	NR
Sachets	NR	9	NR	NR												
Other Fragrance Preparation	3	3	NR	NR					1	5	NR	NR	1	4	NR	NR
Hair Preparations (non-coloring)																
Hair Conditioner	12	33	0.9-10	0.2-10	3	4	0.04	NR	NR	8	NR	NR	1	5	NR	0.4-2
Hair Spray (aerosol fixatives)	1	1	1.6	0.001					NR	1	NR	NR				
Hair Straighteners	NR	7	NR	0.3	NR	3	NR	NR								
Permanent Waves	NR	2	NR	NR									NR	1	NR	1
Rinses (non-coloring)					1	NR	NR	NR								
Shampoos (non-coloring)	NR	9	NR	0.5	NR	NR	0.05	NR					NR	4	NR	0.3

Table 3. Frequency (2023/2002) and concentration (2022/2003) of use according to likely duration and exposure and by product category.

	Lanolin†				Lanolin Acid				Lanolin Alcohol				Lanolin Oil			
	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	2023[19]	**2002[2]**	**2022[20]**	**2003[2]**	**2023[19]**	**2002[2]**	**2022[20]**	**2003[2]**	**2023[19]**	**2002[2]**	**2022[20]**	**2003[2]**	**2023[19]**	**2002[2]**	**2022[20]**	**2003[2]**
Tonics, Dressings, and Other Hair	33	69	0.5-15	0.5-19	3	NR	0.04	NR	NR	2	NR	NR	3	NR	1	0.5-2
Wave Sets	NR	2	NR	4												
Other Hair Preparations	19	1	NR	5	1	1	NR	NR	4	3	NR	NR	NR	NR	2	NR
Hair Coloring Preparations																
Hair Dyes and Colors	1	NR	0.91	NR												
Hair Tints	1	NR	NR	NR					1	NR	NR	NR				
Hair Rinses (coloring)	NR	NR	0.5	NR												
Hair Shampoos (coloring)					1	NR	NR	NR								
Hair Color Sprays (aerosol)													NR	1	NR	0.8
Hair Bleaches													NR	11	NR	NR
Other Hair Coloring Preparation	5	8	NR	0.4					2	1	NR	4				
Makeup Preparations																
Blushers (all types)	2	31	9	2-9					13	16	0.3	NR	NR	11	0.25	2-12
Face Powders	4	9	0.0099	1-5					2	7	0.3	NR	2	12	0.25	2
Foundations	1	17	NR	2-9	NR	2	NR	NR	2	28	NR	NR	NR	10	NR	0.7-2
Leg and Body Paints									1	NR	NR	NR				
Lipstick	54	133	1.3-20.7	1-33	NR	2	NR	NR	3	18	0.36	NR	21	226	24.3-47	3-65
Makeup Bases	NR	5	0.4-6	0.4-5					NR	22	NR	NR	NR	10	0.35	0.4
Rouges	NR	4	NR	5												
Makeup Fixatives									NR	4	NR	NR	NR	1	NR	NR
Other Makeup Preparations	24	12	NR	10-17	NR	1	NR	NR	NR	7	NR	NR	NR	8	NR	20-45
Manicuring Preparations (Nail)																
Basecoats and Undercoats													NR	2	NR	NR
Cuticle Softeners	NR	6	1	20					NR	1	NR	NR	NR	2	NR	2
Nail Creams and Lotions	2	1	40	0.3-3									NR	1	NR	5
Nail Polish and Enamel	1	NR	NR	15												
Nail Polish and Enamel Removers																
Other Manicuring Preparations									NR	NR	5	NR	NR	1	NR	3-25
Personal Cleanliness Products																
Bath Soaps and Detergents	NR	11	0.48	0.01-4					1	3	NR	NR	NR	9	NR	NR
Deodorants (underarm)	NR	4	NR	0.2									NR	1	NR	NR
Feminine Deodorants									NR	2	NR	NR				
Other Personal Cleanliness Products	1	7	NR	NR					3	1	NR	NR	1	NR	NR	NR
Shaving Preparations																
Aftershave Lotion	NR	2	NR	0.5					NR	3	NR	NR				
Shaving Cream	2	11	NR	0.5-2	NR	3	NR	NR	1	6	NR	NR	NR	4	NR	2
Other Shaving Preparations									NR	6	0.5	NR				
Skin Care Preparations																
Cleansing	1	48	NR	0.1-3					NR	10	NR	NR	NR	12	NR	3
Depilatories	NR	3	NR	NR					1	1						
Face and Neck (exc shave)	6	26	NR	2-4					4	9	0.08	NR	NR	4	1-2	3
Body and Hand (exc shave)	26	88	7	2-37					4	52	0.01-1	0.6	6	27	1-2	NR
Moisturizing	37	56	0.5-18	0.2-11	NR	4	NR	NR	18	40	0.25	NR	3	37	1	2
Night	4	32	NR	0.5-10	NR	1	NR	NR	NR	19	0.08	NR	NR	6	NR	1
Paste Masks (mud packs)	NR	12	NR	16					NR	7	NR	NR	NR	1	NR	18
Skin Fresheners																
Other Skin Care Preparations	30	51	NR	22	NR	1	NR	1	2	10	NR	NR	1	14	NR	10
Suntan Preparations																
Suntan Gels, Creams, and Liquids	NR	11	NR	NR	NR	1	NR	NR	NR	12	NR	NR	NR	6	NR	8
Indoor Tanning Preparations	NR	7	NR	2					NR	2	NR	NR	NR	1	NR	NR
Other Suntan Preparations	NR	1	NR	NR					NR	3	NR	NR	NR	4	1.1	1

Table 3. Frequency (2023/2002) and concentration (2022/2003) of use according to likely duration and exposure and by product category.

	Lanolin Wax																			
	# of Uses		*Max Conc of Use (%)*																	
	2023[19]	**2002[2]**	**2023[19]**	**2002[2]**																
Totals*	**17**	**97**	**0.4-8.5**	**0.5-23**																
summarized by likely duration and exposure**																				
Duration of Use																				
Leave-On	*15*	*94*	*0.5-8.5*	*0.5-23*																
Rinse-Off	*2*	*3*	*0.4*	*NR*																
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*																
Exposure Type																				
Eye Area	NR	11	NR	2-4																
Incidental Ingestion	NR	56	3.2	20-23																
Incidental Inhalation-Spray	14[a]	14[a]; 3[b]	0.6-8[a]	0.5[b]																
Incidental Inhalation-Powder	NR	1; 3[b]	0.5-2[c]	0.5[b]																
Dermal Contact	8	31	0.5-2	0.5-4																
Deodorant (underarm)	NR	NR	NR	NR																
Hair - Non-Coloring	7	4	0.4-8.5	NR																
Hair-Coloring	2	NR	NR	NR																
Nail	NR	NR	NR	NR																
Mucous Membrane	NR	56	3.2	20-23																
Baby Products	NR	NR	NR	NR																
as reported by product category																				
Baby Products																				
Baby Lotions/Oils/Powders/Creams																				
Other Baby Products																				
Bath Preparations (diluted for use)																				
Bath Oils, Tablets, and Salts																				
Bubble Baths																				
Other Bath Preparations																				
Eye Makeup Preparations																				
Eyebrow Pencil																				
Eyeliner	NR	4	NR	4																
Eye Shadow	NR	1	NR	4																
Eye Lotion																				
Eye Makeup Remover																				
Mascara	NR	6	NR	2																
Other Eye Makeup Preparations																				
Fragrance Preparations																				
Cologne and Toilet Water																				
Perfumes																				
Powders (dusting/talcum, excl aftershave talc)																				
Sachets																				
Other Fragrance Preparation																				
Hair Preparations (non-coloring)																				
Hair Conditioner																				
Hair Spray (aerosol fixatives)																				
Hair Straighteners																				
Permanent Waves																				
Rinses (non-coloring)																				
Shampoos (non-coloring)	NR	NR	0.4	NR																
Tonics, Dressings, and Other Hair Grooming Aids	6	4	0.6-8	NR																
Wave Sets																				
Other Hair Preparations	1	NR	8.5	NR																

Table 3. Frequency (2023/2002) and concentration (2022/2003) of use according to likely duration and exposure and by product category.

	Lanolin Wax			
	# of Uses		*Max Conc of Use (%)*	
	2023[19]	**2002[2]**	**2023[19]**	**2002[2]**
Hair Coloring Preparations				
Hair Dyes and Colors	2	NR	NR	NR
Hair Tints				
Hair Rinses (coloring)				
Hair Shampoos (coloring)				
Hair Color Sprays (aerosol)				
Hair Bleaches				
Other Hair Coloring Preparation				
Makeup Preparations				
Blushers (all types)	NR	2	0.5	4
Face Powders	NR	1	NR	
Foundations	NR	2	NR	4
Leg and Body Paints				
Lipstick	NR	56	3.2	20-23
Makeup Bases	NR	NR	0.5	NR
Rouges				
Makeup Fixatives				
Other Makeup Preparations	NR	1	NR	0.5
Manicuring Preparations (Nail)				
Basecoats and Undercoats				
Cuticle Softeners				
Nail Creams and Lotions				
Nail Polish and Enamel				
Nail Polish and Enamel Removers				
Other Manicuring Preparations				
Personal Cleanliness Products				
Bath Soaps and Detergents				
Deodorants (underarm)				
Feminine Deodorants				
Other Personal Cleanliness Products				
Shaving Preparations				
Aftershave Lotion				
Shaving Cream				
Other Shaving Preparations				
Skin Care Preparations				
Cleansing	NR	2	NR	NR
Depilatories				
Face and Neck (exc shave)			0.5	
Body and Hand (exc shave)	NR	3	2	0.5
Moisturizing	8	6	NR	NR
Night	NR	2	NR	NR
Paste Masks (mud packs)	NR	1	NR	NR
Skin Fresheners				
Other Skin Care Preparations	NR	4	NR	NR
Suntan Preparations				
Suntan Gels, Creams, and Liquids	NR	1	NR	NR
Indoor Tanning Preparations				
Other Suntan Preparations	NR	1	NR	NR

† Includes entries in the VCRP for Lanolin, Anhydrous; † Includes entries in the VCRP for Lanolin, Anhydrous

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

**likely duration and exposure is derived based on product category (see Use Categorization https://www.cir-safety.org/cir-findings)

[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.

Table 4. Acute toxicity studies

Test Article	Vehicle	Animals/Group	Concentration/Dose	Protocol	LD_{50}/LC_{50}/Results	Reference
DERMAL						
Lanolin Acid	arachis oil	5 male and 5 female Wistar rats	2000 mg/kg bw	Acute dermal study performed in accordance with OECD TG 402; test sites clipped and semi-occluded; rats exposed to test material for 24 h, after which test material was wiped off; animals observed for signs of toxicity 0.5, 1, 2, 4 h and once daily for 14 d after dosing	> 2000 mg/kg bw; no clinical signs of toxicity or signs of dermal irritation; no abnormalities at necropsy and no mortalities during observation period	[10]
Lanolin Alcohol	arachis oil	5 male and 5 female Wistar rats	2000 mg/kg bw	Acute dermal study performed in accordance with OECD TG 402; test sites clipped and semi-occluded; rats exposed to test material for 24 h, after which test material was wiped off; animals observed for signs of toxicity 0.5, 1, 2, 4 h and once daily for 14 d after dosing	> 2000 mg/kg bw; no clinical signs of toxicity or signs of dermal irritation; no signs of toxicity at necropsy and no moralities during observation period	[11]
ORAL						
Hydroxylated Lanolin	none	1 male and 1 female Sherman-Wistar rat per dose group	2.5, 5.0, 10.0, 20.0, or 40.0 ml/kg	Acute oral gavage study performed in accordance with OECD TG 401; animals observed for 14 d	> 10 ml/kg bw; no deaths observed in any dose group	[7]
Lanolin Alcohol	sesame oil	5 male and 5 female Sprague-Dawley rats	2000 mg/kg bw	Acute oral gavage study performed in accordance with OECD TG 401; animals observed for 14 d before being killed for complete gross necropsy	> 2000 mg/kg bw; no substance-related findings, gross pathological changes, or mortality observed	[11]
Lanolin Alcohol	not reported	5 male and 5 female albino rats	5000 mg/kg bw	Acute oral study in accordance with OECD TG 401; no further details provided	> 5000 mg/kg bw; 2 females died during study, no further details provided	[11]

Table 5. Genotoxicity studies

Test Article	Vehicle	Concentration/Dose	Test System	Procedure	Results	Reference
IN VITRO						
Lanolin Acid	acetone	50-5000 µg/plate	*S. typhimurium* strains TA98, TA100, TA1535, TA1537 and *E. coli* strain WP2 uvrA	Ames test in accordance with OECD TG 471; with and without metabolic activation	Not mutagenic, with and without metabolic activation	[10]
Lanolin Acid	acetone	up to 600 µg/ml without metabolic activation; up to 400 µg/ml with metabolic activation	mouse lymphoma L5178 cells at the *tk* locus	Mammalian gene mutation test in accordance with OECD TG 476; with and without metabolic activation	Not mutagenic, with and without metabolic activation	[10]
Lanolin Acid	acetone	up to 2500 µg/ml	human lymphocytes	Mammalian chromosome aberration test in human lymphocytes in accordance with OECD TG 473; with and without metabolic activation	Not clastogenic, with and without metabolic activation	[10]
Lanolin Alcohol	acetone	50-5000 µg/plate	*S. typhimurium* strains TA98, TA100, TA1535, TA1537 and *E. coli* strain WP2 uvrA	Ames test in accordance with OECD TG 471; with and without metabolic activation	Not mutagenic, with and without metabolic activation	[11]
Lanolin Alcohol	acetone	up to 937.5 µg/ml	mouse lymphoma L5178 cells at the *tk* locus	Mammalian gene mutation test in accordance with OECD TG 476; with and without metabolic activation	Not mutagenic, with and without metabolic activation	[11]
Lanolin Alcohol	acetone	up to 1250 µg/ml	human lymphocytes	Mammalian chromosome aberration test in human lymphocytes in accordance with OECD TG 473; with and without metabolic activation	Not clastogenic, with and without metabolic activation	[11]

Table 6. Dermal irritation and sensitization studies

Test Article	Vehicle	Concentration/Dose	Test Population/System	Protocol	Results	Reference
IRRITATION						
ANIMAL						
Lanolin Alcohol	mineral oil	0.5 ml; no further details	6 New Zealand White rabbits	Modified Draize study; single application; test sites (2.5 cm^2) clipped, intact and abraded, and occluded for 24 h; animals observed for 72 h	Irritating; mean erythema scores of 3 for intact and abraded skin at 24 and 72 h, mean edema score of 2 and 1 on intact skin and 1.5 and 1 on abraded skin at 24 and 72 h, respectively. This study was disregarded by ECHA as it was not considered sufficient for use in classifying Lanolin Alcohol.	[11]
HUMAN						
nano-emulsion containing 2.0% Acetylated Lanolin,	nano-emulsion contained a mixture of raspberry, passion fruit, and peach oils (1:1:1), sorbitan monooleate, PEGs 15-30-, 36-, 40-, and 54-castor oil	50 µl	20 subjects	Test materials applied to areas of 13.80 cm^2 and evaluated 30-, 60-, 90-, and 150-min post-application. Irritation potential assessed with a Chromameter CR-200.	No irritation reactions observed	[40]
Hydrogenated Lanolin	not reported	25 g	14 subjects	Dermal tolerance test; test material applied to the palm of the hand; covered test site (4 cm^2) checked after 24 and 48 h for possible skin reactions	No erythema observed; none of the subjects complained about itching or other indications of intolerance	[8]
SENSITIZATION						
ANIMAL						
Lanolin Acid	dimethylformamide	10, 25, or 50%	female CBA mice	LLNA in accordance with OECD TG 429	Non-sensitizing; the stimulation indices for 10, 25, and 50% Lanolin Acid were 1.42, 1.77, and 2.35, respectively	[10]

Table 7. Multicenter and retrospective studies on Lanolin and Lanolin Alcohol

# Patients	Clinical Testing Type	Location	Years	Results	Reference
		Multicenter Studies			
		Children			
6708	Multicenter retrospective study of patch test results of children ages 1 to 18-yr old with suspected allergic contact dermatitis. Patients patch tested with basel-ne series.	Europe	2002 through 2010	Approximately 1.8% of patients had positive reactions to Lanolin Alcohol. In a subgroup (n = 210) tested with TRUE test allergens, 1% had positive reactions to lanolin Alcohol.	[46]
		Adults			
491	Multicenter study of patch testing reproducibility using TRUE Test™ system.	Uruguay	not reported	Lanolin Alcohol resulted in 7 positive concordant patch test reactions, 3 positive discordant reactions, and 4 irritant or doubtful reactions either on one or both sides	[44]
43,691	Multicenter study at NACDG clinics of patch test results for patients with suspected allergic contact dermatitis to Lanolin. Allergens in Allergens in testing protocols included a trademarked Lanolin product at 50% in pet. (2011-2018) and Lanolin Alcohol 30% pet. (2001-2010).	North America	2001 through 2018	1431 (3.3%) were allergic to Lanolin, of which 1238 (86.5%) were currently relevant to the patient's dermatitis. Allergic reactions and currently relevant reactions to Lanolin were significantly higher in children (n = 85 (4.5%) and n = 77(4.0%)) than adults (n = 1346 (3.2%) and n = 1161 (2.8%)). Common primary body sites affected by allergic reaction to Lanolin were the hands, scattered generalized distribution, and the face. The most common source of the Lanolin exposure to those with allergic reaction was personal care products (moisturizers/lotions/creams (23%) and lipsticks and lip balms (4%).	[45]
3119	The European Dermato-Epidemiology Network (EDEN) fragrance study performed TRUE Test panels in a multicenter study to determine the prevalence of contact allergy to several allergens; wool alcohols were tested at 1.0 mg/cm^2	Sweden, Germany, Netherlands, Italy, and Portugal	Between August 2008 and October 2011	A total of 14 subjects (5 males and 9 females) had reactions to Lanolin Alcohol. The prevalence in the general population for allergy to Lanolin Alcohol was determined to be 0.4%.	[69]
515 (EDEN) 1684 (IVDK)	Secondary analysis of data obtained from patch test results with a modified European baseline series in a population sample of the EDEN fragrance study (above) and patch test results from the Information Network of Departments of Dermatology (IVDK) documented in the Jena center in Germany. Wool alcohols (Lanolin; 1.0 mg/cm^2) were tested in the EDEN study network and Lanolin Alcohol (30% pet.) was tested in the IVDK study network. The testing occurred during similar time frames.	Germany	Between August 2008 and October 2011/ 2007 through 2012	Lanolin Alcohol produced positive patch test results in 4/515 (1.04%) in the EDEN study and 69/1684 (3.73%) in the IVDK study.	[68]
4238	Multicenter study of patch tests in patients tested with a series of 70 allergens, including Lanolin Alcohol 50% pet.	North America	January 1, 2011 through December 31, 2012	194 (4.6%) reactions to Lanolin Alcohol observed. Compared to 2 previous reporting periods, positive reaction rates increased for Lanolin Alcohol.	[47]
4116	Multicenter study of patients tested at NACDG clinics using standardized patch testing technique with 80 allergens that included a trademarked Lanolin product at 50% in pet.	North America	January 1, 2019 to December 31, 2020	3.7% had positive reactions to Lanolin Alcohol 50% pet. It was ranked 16th in the significance-prevalence index (SPIN 133). For comparison, methylisothiazolinone 0.2% aq ranked 1st with a SPIN of 683.	[48]
499	Multicenter study with patients that underwent a variety of surgical procedures followed by application of a wound healing ointment with Lanolin Alcohol without antibiotics.	United States	2010 (99 patients); 2019 (400 patients)	No allergic contact dermatitis was identified in the patients. Authors opined that the lack of reactions observed may have been due to the highly purified Lanolin Alcohol used in the study formulation.	[49]
		Retrospective Studies			
		Children			
1012	Retrospective analysis of children ages 0-17 yr with suspected contact dermatitis patch tested with the European baseline series or parts thereof and a supplementary series. Lanolin Alcohol 30% pet. and a trademarked Lanolin product at 50% in pet. were included in the tests.	Netherlands	1996 through 2013	Out of all children tested, the positivity rate was 6.2% to Lanolin Alcohol 30% pet and 8.8% to the trademarked Lanolin product. Children with atopic dermatitis had higher positivity rates to these ingredients (7.8% and 12.6%, respectively) than those who did not have atopic dermatitis (4.3% and 5.3%, respectively).	[51]
1634	Retrospective study of NACDG data of children aged less than 18 yr old. Of the 1634 patients, 237 had involvement of the hands. Patch tests included Lanolin Alcohol 50% pet.	North America	2000 through 2016	Lanolin Alcohol was in the top 5 most common currently relevant allergens. In a multivariable logistic regression model of the top 20 relevant allergens, hand eczema was associated with significantly higher odds of currently relevant reactions to Lanolin Alcohol.	[53]

Table 7. Multicenter and retrospective studies on Lanolin and Lanolin Alcohol

# Patients	Clinical Testing Type	Location	Years	Results	Reference
833	Retrospective study of children ages 0-18 patch-tested with 65 or 70 allergen series, including Lanolin Alcohol 50% pet. and Lanolin Alcohol 30% pet.	North America	January 1, 2005 through December 31, 2012	5.5% of patients had positive patch test reactions to Lanolin Alcohol 50% pet. (5.1% relevant patch test reactions). 1.7% patients had positive reactions to Lanolin Alcohol 30% pet. (1.5% relevant patch test reactions). Reactions observed only in ages 6 and up.	[57]
100	Retrospective study of adolescents aged 13-18 yr who were consecutively patch tested. Patch tests performed on symptom-free patients using an environmental contact allergen series (87 patients) and an implantation and dental contact allergen series (13 patients) from the Brial-Allergen D-Greven Panel.	Hungary	January 1, 2007 through December 31, 2016	Contact hypersensitivity was observed in 51 patients. Most common contact allergens included Lanolin Alcohol in boys. Of the 47 patients were atopic dermatitis, 51.1% had contact hypersensitivity: the most common allergen in this group included Lanolin Alcohol (10.6%).	[62]
1142	Retrospective study of patch test cases of children under the age of 18 yr. Patients were patch-tested to assess sensitizations to various allergens	United States	January 1, 2015 through December 31, 2015	Wool alcohol and Lanolin were ranked #8 and #9, respectively, out of the top 21 allergens in children. The relevant positive patch test result was 25 (4.6%) for wool alcohol and 26 (6.0%) for Lanolin.	[65]
		Adults			
756	Retrospective study of individuals tested to anhydrous Lanolin and 2 preparations of Hydrogenated Lanolin on intact skin of patients with contact dermatitis	Japan	January 1972 through June 1973	Individuals with a positive response more than ++ to any of the material were subjected to 2 series of further patch tests. The results showed incidence of skin sensitivity decreased with every stage of purification (no further detail). The results in 1972 showed incidence of sensitivity to Hydrogenated Lanolin was significantly higher than that to anhydrous Lanolin at the 1 % level, while no significant difference was found between both samples in 1973. Contamination by traces of copper, chromium and nickel in hydrogenated preparations may be the source of other possible allergens.	[8]
31,200	Analysis of the NACDG's patch test results for 153 compounds to determined trends over time for positive test reactions	North America	1984 through 2016	From 1994 to 2010, the positive reactivity proportion for Lanolin Alcohol (30% pet.) went from 3.3% to 2.5%	[50]
4094	Retrospective study of patients tested with baseline series, which included Lanolin Alcohol. Results compared to those tested from 1990 to 1994.	Switzerland	2000 through 2004	147 (3.6%) had positive reactions to Lanolin Alcohol. Reactions were more frequent in females (104/2388 (4.4%)) than males 43/1706 (2.5%). The rate of sensitization rose from 1.7% in 1990-1994.	[52]
532	Retrospective study of patients with acute contact dermatitis from topical drugs applied onto the (peri)anal/genital area that were tested with the European baseline series, with some additional series, and the topical medication used along with ingredients.	Belgium	January 2000 through December 10, 2018	44/473 with lesions in the (peri)anal/genital area had positive patch test results to topical drug preparations and/or their ingredients. Lanolin Alcohol (wool alcohol) was among the vehicle components that yielded positive reactions.	[54]
5264	Retrospective study of patients with lower leg dermatitis, chronic venous insufficiency, or chronic leg ulcers. Data compared to 4881 corresponding patients from 1994 to 2003. Control group without diagnoses numbered 55,510. Patch tests included 30% Lanolin Alcohol and a trademarked Lanolin product at 50%	Germany, Switzerland, and Austria	2003 through 2014	Allergic contact dermatitis was diagnosed less frequently in the study group than in the historical control group and contact sensitization to most allergens had declined. Lanolin Alcohol was still considered an important allergen (7.8% of positive reactions). Patch testing with additional series showed sensitization to a trademarked Lanolin product (9.7% of positive reactions).	[55]
9577	Retrospective study of consecutively patch tested dermatitis patients with Lanolin Alcohol 30% pet. and a trademarked Lanolin product at 50% in pet.	Denmark	January 1, 2004 through December 31, 2015	Prevalence of Lanolin allergy increased from 0.45% in 2004 to 1.81% in 2015. In age-adjusted and sex-adjusted analyses, weak, significant associations were found between atopic dermatitis and Lanolin and Lanolin Alcohol allergy, respectively, but no association with the trademarked product allergy was found. Out of 9286 dermatitis patients tested with both allergens, 108 had a positive reaction to either Lanolin Alcohol or the trademarked Lanolin product, whereas only 29 patients had positive reactions to both markers.	[56]
80	Retrospective study of pediatric atopic dermatitis patients. Patients patch tested with European baseline series, which included Lanolin Alcohol 30% pet.	Tunisia	January 2005 through April 2021	Lanolin Alcohol was one of top 5 allergens with 5% of patients having a positive reaction.	[58]

Table 7. Multicenter and retrospective studies on Lanolin and Lanolin Alcohol

# Patients	Clinical Testing Type	Location	Years	Results	Reference
618	Retrospective study of a dermatology clinic of patients with allergic contact dermatitis. Patients were patched with the standard epicutaneous patch series, which included Lanolin	Brazil	January 2006 through December 2011	16 (2.59%) patients had positive reactions to Lanolin. Sensitization rates to Lanolin had a diminished sensitization rate ($p = 0.01$) during the time period.	[59]
94	Retrospective study of patients with chronic leg ulcers and contact dermatitis of the lower leg and foot. Testing performed with the European baseline series.	Lithuania	April 2006 through October 2008	Out of 35 patients with chronic leg ulcers, 6 (17.1%) had positive reactions to 30% Lanolin Alcohol. Out of 59 patients with contact dermatitis to the lower leg/foot, 2 (3.4%) had positive reactions to 30% Lanolin Alcohol.	[60]
10,124	Retrospective analysis of patients patch tested due to suspected intolerance reactions to leave-on cosmetics, including Lanolin Alcohol 30%. Control group without diagnoses numbered 14,728. Additional testing was done with the ointment base series in 7716 patients with a trademarked Lanolin product at 50% in pet. and in 7549 patients with Lanolin Alcohol 30%.	Germany, Switzerland, and Austria	2006 to 2011	246 (2.6%) patients had positive reactions to Lanolin Alcohol. Control group had reactions in 1.8% of the subjects. Results of the ointment base series had positive reactions in 4.1% of patients to the trademarked Lanolin product and positive reactions in 2.4% of patients to Lanolin Alcohol.	[61]
5790	Retrospective study of individuals tested with the European environmental baseline series. Specific analysis was on preservative contact hypersensitivity and atopic dermatitis.	Hungary	2007 through 2021	In preservative contact hypersensitivity, Lanolin Alcohol (30%) was a common concomitant allergen (13/68 patients).	[63]
4355	Retrospective study of individuals tested with the European baseline series and additional trays. A trademarked Lanolin product at 50% in pet. was included in the European cosmetics tray.	Israel	2012 through 2020	The Lanolin product had 27 positive reactions out of 3752 tests performed. The study data indicated that out of the 27 patients, only 74% had a positive reaction to Lanolin. The authors stated that 26% of the reactions would have been missed if extended patch testing was not performed.	[64]
594	Retrospective analysis of patients patch tested with Lanolin Alcohol 30% pet., a trademarked Lanolin product at 50% in pet., and a supplementary series containing other Lanolin derivatives. Lanolin Alcohol and the trademarked product were tested in duplicate	Netherlands	January 1, 2016 through December 31, 2017	28.6% had a positive patch test reaction to at least one Lanolin derivative. Reactions to Lanolin Alcohol (14.7%) and the trademarked product (15.0%) were common in routinely tested series. The addition of the trademarked product to Lanolin Alcohol significantly increased the number of positive cases (odds ratio 1.79, $p < 0.001$).	[66]
1006	Retrospective study of individuals tested with European baseline series. Seasonal variation in patch test reactions analyzed.	Tunisia	7-yr period, yr not specified	63% were positive in winter vs 52% in summer. Lanolin Alcohol reactions varied seasonally, with weak positive reactions increasing in the spring.	[67]

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