Amended Safety Assessment of Octyldodecyl Stearoyl Stearate as Used in Cosmetics

Status:	Draft Amended Report for Panel Review
Release Date:	November 10, 2022
Panel Meeting Date:	December 5-6, 2022

The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; David E. Cohen, M.D.; Curtis D. Klaassen, Ph.D.; Allan E. Rettie, Ph.D.; David Ross, Ph.D.; Thomas J. Slaga, Ph.D.; Paul W. Snyder, D.V.M., Ph.D.; and Susan C. Tilton, Ph.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D. This safety assessment was prepared by Regina Tucker, M.S., Scientific Analyst/Writer,

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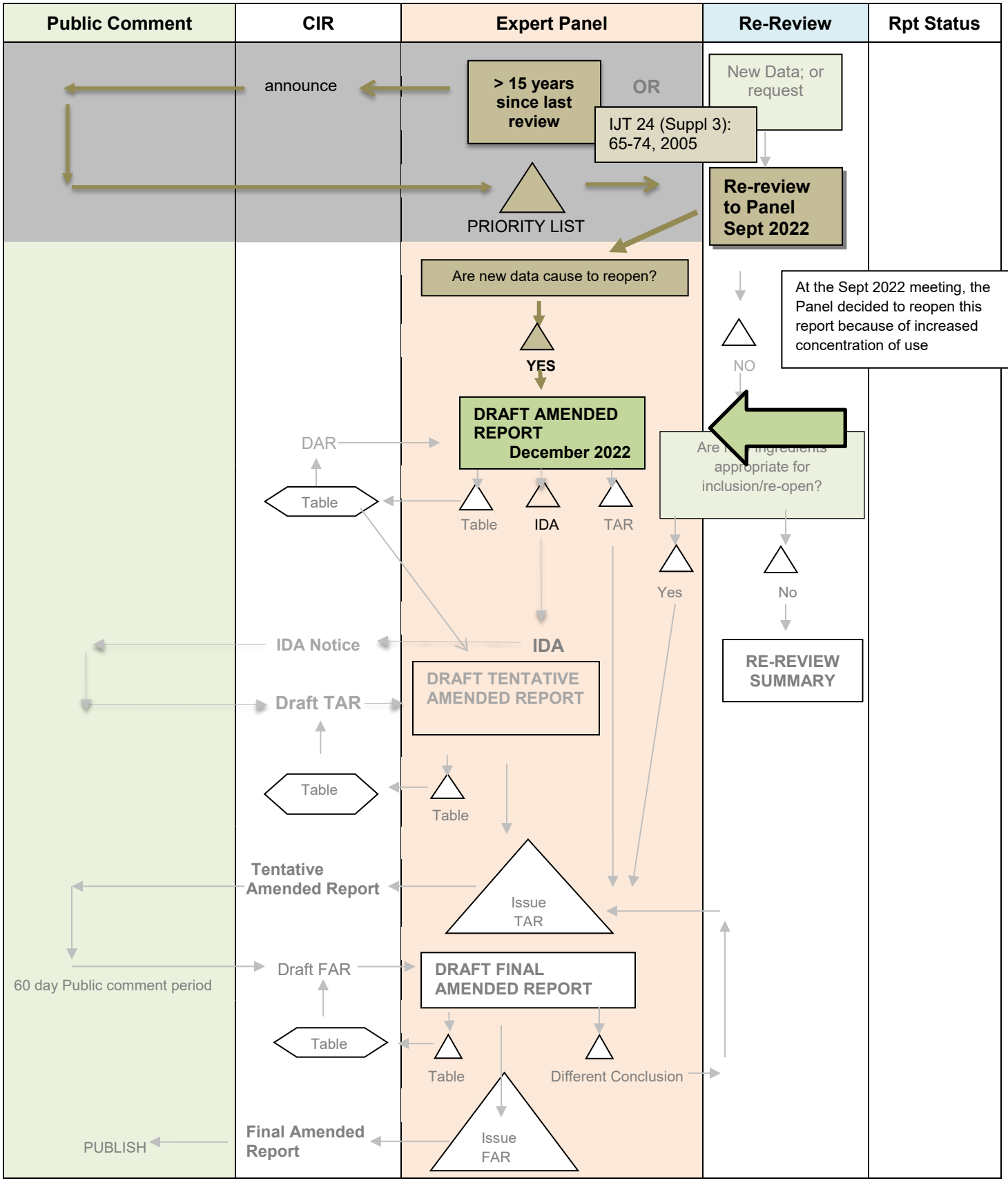
RE-REVIEW FLOW CHART

INGREDIENT/FAMILY Octyldodecyl Stearoyl Stearate

MEETING December 2022



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Memorandum

To: CIR Expert Panel Members and Liaisons
From: Regina Tucker, MS, Scientific Analyst/Writer CIR
Monice Fiume, Senior Director, CIR
Date: November 10, 2022
Subject: Amended Safety Assessment of Octyldodecyl Stearoyl Stearate as Used in Cosmetics

Enclosed is the Draft Amended Report on the Safety Assessment of Octyldodecyl Stearoyl Stearate as Used in Cosmetics. (It is identified as *report_OctyldodecylStearoylStearate_122022* in the pdf document). In its initial assessment of Octyldodecyl Stearoyl Stearate, the Panel found that the data were insufficient to determine safety, and a final report with such conclusion was published in 2001 (*originalreport1_OctyldodecylStearoylStearate_122022*). Subsequently, the Panel's data needs were met, and a final amended report with the following conclusion was published in 2005: Octyldodecyl Stearoyl Stearate is safe for use in cosmetic products in the practices of use and concentration described in this safety assessment (*originalreport2_OctyldodecylStearoylStearate_122022*). In September 2022, the Panel re-opened the safety assessment of this ingredient. In its decision to reopen the assessment, the Panel cited updated usage data and significant increases in concentration of use.

The reported frequency of use of this ingredient has increased since it was last reviewed. According to 2022 VCRP data, the ingredient is reported to be used in 605 formulations *(VCRP_OctyldodecylStearoylStearate_122022)*; according to the 2005 amended report, the reported frequency of use was 106 (2001 VCRP data). Of note, the frequency of use for formulations resulting in incidental ingestion and mucous membrane contact (lipsticks) increased from 1 to 48 uses, and use in products applied near the eye area increased from 35 uses in 2001 to 322 uses in 2022. Additionally, concentrations of use have increased since the last review. The highest reported use concentration in 2022 is in lipstick (28%) *(data1_OctyldodecylStearoylStearate_122022);* in 2001, the maximum concentration of use reported for lipsticks was 10%. Use concentrations in the eye area also increased; the maximum concentration reported in eye shadow was 10% in 2001, and is now 18.5% in 2022.

At the September 2022 Panel meeting, a change to the current Use Table format was discussed. At that time, the Panel requested that both Use Table formats (i.e., the existing and the proposed format) be included in a Draft Report to provide a side-by-side comparison. That has been presented in this document to impart an example for an amended report, which has current and historical use values. It should be noted that while most of the descriptors in the body of the report highlighting the types of use of the ingredients (i.e., eye area, mucous membrane, inhalation, etc.) will remain if the new format is adopted, reference to the highest leave-on/rinse-off concentrations of use will not be included, in that it is not definitively known what the duration of exposure is for all formulations. (This is one of the driving issues behind the consideration of a new Use Table format.) **CIR is asking that you compare the tables and provide your preference as to which format should be used in all future safety assessments.**

Since the September meeting, the following unpublished data have been submitted:

- use study summary – lip balms containing 28% Octyldodecyl Stearoyl Stearate *(data2_OctydodecylStearoylStearate_122022)*
- repeated insult patch test (makeup base containing 21.0112% Octyldodecyl Stearoyl Stearate) *(data3_OctydodecylStearoylStearate_122022)*

Additional supporting documents for this report package include a flow chart (*flow_OctyldodecylStearoylStearate_122022*), report history (*history_OctyldodecylStaroylStearate_122022*), search

strategy (*search_OctyldodecylStearoylStearate_122022*), a data profile (*dataprofile_OctyldodecylStearoylStearate_122022*), the minutes from all the past meetings at which Octyldodecyl Stearoyl Stearate was originally discussed (*originalminutes_OctydodecylStearoylStearate_122022*),and the transcripts from the meeting at which the re-review was discussed (*transcripts_OctydodecylStearoylStearate_122022*).

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

Octydodecyl Stearoyl Stearate History

2001– The Expert Panel for Cosmetic Safety (Panel) published a Final Report with an insufficient data conclusion on Octyldodecyl Stearoyl Stearate.

2005 - The Panels data needs were met, and a Final Amended Report with the following conclusion was published: Octydodecyl Stearoyl Stearate is safe as a cosmetic ingredient in the practices of use and concentration described in this safety assessment.

September 2022 – Review of the available published literature since 2005 was conducted in accordance to CIR Procedures regarding re-review of ingredients after ~15 years. The Panel re-opened the safety assessment for this ingredient, due to reported use frequency increasing from 105 formulations in 2005 to 605 formulations in 2022. An increase in incidental ingestion and mucus membrane contact. The Panel also noted reported uses in two new use categories Hair-(Coloring) and (Non-Coloring).

Octyldodecyl Stearoyl Stearate Data Profile* – December 2022 – Regina Tucker																														
				Toxicokinetics			Acute Tox			Repeated Dose Tox			DART		Genotox		Carci		Dermal Irritation			Dermal Sensitization				Ocular Irritation		Clinical Studies	
	Reported Use	Method of Mfg	Impurities	log P/log K_{ow}	Dermal Penetration	ADME	Dermal	Oral	Inhalation	Dermal	Oral	Inhalation	Dermal	Oral	In Vitro	In Vivo	Dermal	Oral	In Vitro	Animal	Human	In Vitro	Animal	Human	Phototoxicity	In Vitro	Animal	Retrospective/ Multicenter	Use Study
Octyldodecyl Stearoyl Stearate	XO	O	O		0			O			O				O	O				O	XO			XO			O		O

* "X" indicates the new data were available in a category for the ingredient. "O" indicates data were reported in the orginal safety assessment.

Octyldodecyl Stearoyl Stearate

Ingredient	CAS #	PubMed	FDA	HPVIS	NIOSH	NTIS	NTP	FEMA	EU	ECHA	ECETOC	SIDS	SCCS	AICIS	FAO	WHO	Web
Octyldodecyl Stearoyl Stearate	90052-75-8	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√

Search Strategy (from 2000 on)

PubMed

((("Octyldodecyl Stearoyl Stearate") OR (90052-75-8[EC/RN Number])) AND (("2000"[Date - Publication]: "3000"[Date - Publication])) – 2 hits; none useful

Internet searches using trade names and other technical names. No relevant hits.

LINKS

Search Engines

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

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

Pertinent Websites

- wINCI - http://webdictionary.personalcarecouncil.org
- FDA databases http://www.ecfr.gov/cgi-bin/ECFR?page=browse
- FDA search databases: http://www.fda.gov/ForIndustry/FDABasicsforIndustry/ucm234631.htm;,
- Substances Added to Food (formerly, EAFUS): https://www.fda.gov/food/food-additives-petitions/substances-added-food-formerly-eafus
- GRAS listing: http://www.fda.gov/food/ingredientspackaginglabeling/gras/default.htm
- SCOGS database: http://www.fda.gov/food/ingredientspackaginglabeling/gras/scogs/ucm2006852.htm
- Indirect Food Additives: http://www.accessdata.fda.gov/scripts/fdcc/?set=IndirectAdditives
- Drug Approvals and Database: http://www.fda.gov/Drugs/InformationOnDrugs/default.htm
- FDA Orange Book: https://www.fda.gov/Drugs/InformationOnDrugs/ucm129662.htm
- (inactive ingredients approved for drugs: http://www.accessdata.fda.gov/scripts/cder/iig/
- HPVIS (EPA High-Production Volume Info Systems) - https://iaspub.epa.gov/oppthpv/public_search.html_page
- NIOSH (National Institute for Occupational Safety and Health) - http://www.cdc.gov/niosh/
- NTIS (National Technical Information Service) - http://www.ntis.gov/
  - technical reports search page: https://ntrl.ntis.gov/NTRL/
- NTP (National Toxicology Program) - http://ntp.niehs.nih.gov/
- Office of Dietary Supplements https://ods.od.nih.gov/
- FEMA (Flavor & Extract Manufacturers Association) GRAS: https://www.femaflavor.org/fema-gras
- EU CosIng database: http://ec.europa.eu/growth/tools-databases/cosing/
- ECHA (European Chemicals Agency – REACH dossiers) – http://echa.europa.eu/information-on-chemicals;jsessionid=A978100B4E4CC39C78C93A851EB3E3C7.live1
- ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) - http://www.ecetoc.org
- European Medicines Agency (EMA) - http://www.ema.europa.eu/ema/
- OECD SIDS (Organisation for Economic Co-operation and Development Screening Info Data Sets)- http://webnet.oecd.org/hpv/ui/Search.aspx
- SCCS (Scientific Committee for Consumer Safety) opinions: http://ec.europa.eu/health/scientific_committees/consumer_safety/opinions/index_en.htm
- AICIS (Australian Industrial Chemicals Introduction Scheme)- https://www.industrialchemicals.gov.au/
- International Programme on Chemical Safety http://www.inchem.org/
- FAO (Food and Agriculture Organization of the United Nations) - http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-additives/en/
- WHO (World Health Organization) technical reports - http://www.who.int/biologicals/technical_report_series/en/
- www.google.com - a general Google search should be performed for additional background information, to identify references that are available, and for other general information

SEPTEMBER 2022 PANEL MEETING-REREVIEW CONSIDERATION

Belsito's Team Meeting – September 26, 2022

[Due to technical difficulties, transcripts were not available for the Belsito team meeting.]

Cohen's Team - September 26, 2022

Dr. David Cohen - OK. Octyldodecyl stearoyl steer rate. The panel issued an insufficient data conclusion in 2001. Subsequently, data needs were met. And in 2005 it was determined safe as used. I'm going back more than 20 years. No new information has been noted in the literature. It's frequency of use has increased considerably. The highest concentration currently reported is at 28%. From the original report. The steering did was non-irritating at up to 100%. And non-sensitizing or photosensitizing it's 13%. What are the thoughts of the team?

Dr. Tom Slaga - Uh, do not reopen.

Dr. David Cohen - So Tom, the one issue I just wanted to discuss was the highest concentration of use was at 28% and our irritates and sensitization was at 13%. Well, that was for stearic acid that I'm sorry. That was for stearic acid and octal steroid at 7.6%. I'm sorry.

Dr. Tom Slaga - Yeah.

Dr. David Cohen - Any other thoughts? David.

Dr. David Ross - Yeah, I had this down as a plus or minus, but going veering towards a negative. You don't really. I didn't see the increased ocular concentration as being a problem and see the increased oral incidental concentration being a problem based on the oral tox data.

Dr. David Cohen – Susan?.

Susan Tilton - I'm also agreeing towards not reopening. Yeah.

Dr. Wilma Bergfeld - Go ahead. Like to comment didn't 2001 document was insufficient. And the

increase is increase in use this ingredient. What happened when we call this insufficient Monice?

In 2001? Did it not go to?

Monice Fiume (CIR) – Ummm.

Dr. David Cohen - I thought it got data needs were met in 2005. Yeah.

Monice Fiume (CIR) - Yes.

Dr. Wilma Bergfeld - Was there too?

Dr. Tom Slaga - Yeah, they were.

Dr. Wilma Bergfeld - Was it 2005 that they met? OK, thank you.

Dr. David Ross - Yeah.

Monice Fiume (CIR) - It was it was published in 2005, yes.

Dr. Wilma Bergfeld - OK. OK, 2005. No, no. Real OK.

Monice Fiume (CIR) - Because they were looking for the dermal absorption. And then dependent then if the ingredient or if significant quantities of the ingredient has contact with mucous membranes or ingested, then dart were needed, that was the original request.

Dr. Wilma Bergfeld – (*inaudible).

Monice Fiume (CIR) - And see what the discussion says.

Thomas Gremillion (CFA) - Yeah.

Dr. David Cohen – Tom?

Monice Fiume (CIR) - Then they receive skin permeation data.

Thomas Gremillion (CFA) - Yeah.

Dr. Wilma Bergfeld - Yeah. I see it. I have it here.

Thomas Gremillion (CFA) - Doctor Cohen, if I my it sounded like you said the, the concentration of use is increased and there is an ocular irritation study. But was it not as the concentration of use not increased past the Noel or yeah, OK.

Dr. David Cohen - Yeah, I'm. I want to come back to that because, the other question I had was the information provided for sensitization and irritation were for stearic acid and octal stearate so, how close are those to octyldodecyl sterile stearate? And how much can we bridge from that?

Monice Fiume (CIR) - David, there, were data I believe on Octyldodecyl stearoyl stearate itself. If you look at PDF page 20.

Dr. David Cohen - Was it like 5%? Let me go 20.

Monice Fiume (CIR) - I see I do see a test with 10.4.

Dr. David Cohen - Ah OK 10.4. But now Max uses a 28. And it's in the lipstick, so. You know the lips are they're they're easy to create contact dermatitis on the lips. Particularly because the exposures so prolonged and the stratum corneum is so thin. My comment was no new data, but the information was below Max use and I had a plus minus on this. We'll know what's your gut telling you on this?

Dr. Wilma Bergfeld - I said not to reopen.

Dr. David Cohen - Still, even with that difference, you're it's true we don't hear much about this chemical.

Rest of the team?

Dr. Tom Slaga - Do not reopen I'm I don't. I don't think.

Dr. David Ross - Yeah. I think, not reopening going forward.

Dr. David Cohen - You know, I present this tomorrow. I'm going to ask for a bit of a conversation on it. If that's OK? I just like to hear what some of the other team has to say on this and I'll try to look a little deeper in with the Max use and any other report. But Regina, you didn't find any case reports on this? Yeah.

Regina Tucker (CIR) - No.

Dr. David Cohen - OK. OK, OK. To move on, I'll, go with the team on this, but I'll, I'll just bring it up for discussion.

Full Panel – September 27, 2022

Dr. Wilma Bergfeld - The next ingredients. Doctor Cohen again the Octyldodecyl Stearoyl Stearate.

Dr. David Cohen - Yes, so we the Panel previously issued an insufficient data conclusion on Octyldodecyl stearoyl stearate. In 2001, subsequently, the panels data needs were met and in 2005 issued a safe is used statement. A literature review back to 2000 did not reveal any new information. There was some updated usage data. The highest concentration of use is 28% in lipstick. We ultimately moved to not reopen, but I really did want some input from Don and his team about the HRIPT in the original report being at 10% and the Max use now with 28%, although I haven't really seen much trouble from this. Just wanted your thoughts.

Dr. Don Belsito - Yeah, we haven't. Yeah, I haven't seen any much trouble, but we felt there was a fourfold increase in use and significant increase in concentration of use and we really needed to look at all the data based upon that. We might not change our conclusion, but there have been significant changes and the use of this ingredient material. So, we wanted to reopen it.

Dr. David Cohen - I'll move to reopen.

Dr. Wilma Bergfeld - OK. So, we'll assume that's a first and a second motion? And any other discussion? I think the discussion points have already been stated. Calls a question, although it's opposing? Abstaining? This ingredient will be reopened.

DECEMBER 1997 PANEL MEETING

The Panel voted unanimously in favor of issuing an Insufficient Data Announcement with the following data requests:

(1) Current concentration of use
(2) Method of manufacture and impurities
(3) Chemical and physical properties, particularly the physical state
(4) Gross pathology and histopathology in skin and other major organ systems associated with repeated exposures[1], depending on the results, sensitization, and irritation data may be needed
(5) If significantly absorbed through the skin, reproductive and developmental toxicity data may be needed[1]
(6) 2 genotoxicity assays, at least one in a mammalian system; if positive, then a 2-year dermal carcinogenicity assay performed using NTP methods may be needed
(7) Ocular toxicity, if available

[1]Gross pathology and histopathology in skin and other major organ systems, along with certain other toxicity parameters, associated with repeated exposures are data that would be expected from what is commonly referred to as a A28-day dermal toxicity study.@ The CIR Expert Panel is concerned that specifying a type of study may inhibit those who want to gather data using other study designs. For example, the Expert Panel would consider a dermal reproductive and developmental toxicity study in which gross pathology and histopathology data are gathered on the F_0 generation to be sufficient if done at or above current concentrations of use of the ingredient. Stated another way, done properly, one study could meet the data needs in items 4 and 5.

During the Panel's discussion on Octyldodecyl Stearoyl Stearate, Dr. Andersen said that CIR will develop language that can be consistently used in each case where the need for 28-day dermal toxicity data on a cosmetic ingredient has been determined. The language used will present the idea that the results of alternative tests may satisfy the Panel's specific need for data that could be derived from a 28-day dermal toxicity test. Dr. Andersen also said that this language could be incorporated into all data requests approved at this meeting in which 28-day dermal toxicity data was initially included as an item. **[The Panel determined that the specific language developed by Dr. Andersen, included in the preceding list of data requests (see footnote 1), will be included in other Insufficient Data Announcements and data requests in Tentative and Final Reports with an insufficient data conclusion (issued at this meeting) in which the need for 28-day dermal toxicity data was initially determined.]**

MAY 1998 PANEL MEETING

Dr. Belsito stated that an Insufficient Data Announcement on this ingredient was issued at the December 8-9, 1997, Panel meeting. He noted that, since that time, current concentration of use data were received. These are the only data that were received in response to the Insufficient Data Announcement.

The Panel voted unanimously in favor of issuing a Tentative Report with an insufficient data conclusion on this ingredient. The data needed[1] in order for the Panel to complete its safety assessment are listed in the discussion section of the report as follows:

(1) Method of manufacture and impurities
(2) Chemical and physical properties, particularly the physical state
(3) Gross pathology and histopathology in skin and other major organ systems associated with repeated dermal exposures[2]; depending on the results, sensitization and irritation data may be needed
(4) If significantly absorbed through the skin, reproductive and developmental toxicity data may be needed
(5) 2 genotoxicity assays, at least one in a mammalian system; if positive, then a 2-year dermal carcinogenicity assay performed using NTP methods may be needed
(6) Ocular toxicity, if available

[1]If information requested in 1 and 2 were available, then data in items 3, 4, and 5 may not be needed.
[2]These are data that would be expected from what is commonly referred to as a 28-day dermal toxicity study.

DECEMBER 1998 PANEL MEETING

Dr. Schroeter stated that a Tentative Report with an insufficient data conclusion was issued at the May 18-19, 1998 Panel Meeting. The data needed in order for the Panel to complete its safety assessment of Octyldodecyl Stearoyl Stearate are stated in the report discussion as follows[1]:

(1) Method of manufacture and impurities
(2) Chemical and physical properties, particularly the physical state
(3) Gross pathology and histopathology in skin and other major organ systems associated with repeated dermal exposures[2]; depending on the results, sensitization and irritation data may be needed
(4) If significantly absorbed through the skin, reproductive and developmental toxicity data may be needed
(5) 2 genotoxicity assays, at least one in a mammalian system; if positive, then a 2-year dermal carcinogenicity assay performed using NTP methods may be needed
(6) Ocular toxicity, if available

[1]If information requested in 1 and 2 were available, then data in items 3, 4, and 5 may not be needed.
[2]These are data that would be expected from what is commonly referred to as a 28-day dermal toxicity study.

Dr. Schroeter recalled that two genotoxicity studies, received on December 30, 1998, were submitted in response to the preceding request for data. He noted that his Team has not reviewed the data, but that if these data are found to be negative, many of the data needs enumerated by the Panel (items 1 and 3, and reproductive and developmental toxicity data in item 4 above) may be eliminated.

Dr. Schroeter also recalled that data on physical properties, skin irritation and sensitization, and ocular toxicity were received along with the genotoxicity data. He noted that the two latter studies satisfy the Panel's specific requests in items 3 (skin irritation and sensitization data) and 6 (ocular toxicity data) above, respectively. Dr. Schroeter also said that the Panel's request for data on physical properties should remain, even though some data on physical properties were submitted.

Dr. Schroeter recommended that the review of Octyldodecyl Stearoyl Stearate be tabled until the Panel has had an opportunity to review the genotoxicity data in detail.

Dr. Bergfeld asked for clarification of the data that are still needed.

Dr. Schroeter said that the following data are needed[1]:

1. Method of manufacture and impurities
2. Chemical and physical properties, particularly the physical state
3. Gross pathology and histopathology in skin and other major organ systems associated with repeated dermal exposures using cosmetic grade material[2]; depending on the results, if significantly absorbed through the skin, reproductive and developmental toxicity data may be needed
4. 2 genotoxicity assays (may or may not be needed, depending on the Panel's review of the genotoxicity data recently submitted); if positive, then a 2-year dermal carcinogenicity assay performed using NTP methods may be needed

[1]If information requested in 1 and 2 were available, then data in items 3, 4, and 5 may not be needed.
[2]These are data that would be expected from what is commonly referred to as a 28-day dermal toxicity study.

Dr. Andersen noted that the two genotoxicity studies have been received and, because the data were received late, an adequate amount of time for a serious review of these studies by the Panel prior to the meeting was not feasible. He said that these data will be provided to the Panel for review prior to the next Panel meeting.

Dr. Andersen also said that the genotoxicity data may help address some of the data needs, but that there are still specific data needs that these data could not possibly address, namely, chemical and physical properties, and skin absorption (if significantly absorbed through the skin, reproductive and developmental toxicity data may be needed).

Dr. Bergfeld acknowledged that it is possible that all of the data needed for completion of the Panel's safety assessment of Octyldocecyl Stearoyl Stearate will not be available for review at the March 3-4, 1999, Panel meeting and that the report will be declared insufficient.

The Panel voted unanimously in favor of tabling the report on Octyldodecyl Stearoyl Stearate to allow an adequate amount of time for review of the two genotoxicity studies that were submitted.

MARCH 1999 PANEL MEETING

Dr. Schroeter recalled that the Tentative Report (with insufficient data conclusion) on this ingredient was tabled at the December 2-3, 1998, Panel meeting because the Panel needed to review the two unpublished genotoxicity studies that were received. He noted that because data on positive controls were not included, other genotoxicity studies may be needed.

Dr. Belsito recalled that the Panel reviewed data from a micronucleated polychromatic erythrocyte genotoxicity study.

Dr. Schroeter indicated that the study referred to by Dr. Belsito does not contain data on positive controls, and, therefore, is insufficient.

Dr. Shank clarified that positive control data are included in the genotoxicity study; however, it is not stated in the CIR report that the positive control yielded positive results. Therefore, the CIR report needs to be amended to include this statement.

Dr. Schroeter said that because the genotoxicity data requested have been received, only the following three items are needed for completion of the Panel's safety assessment: (1) Methods of manufacture and impurities; (2) chemical and physical properties, particularly the physical state, and (3) gross pathology and histopathology of the skin; if positive, then reproductive and developmental toxicity data may be needed.

Dr. Belsito noted that his Team determined that the following data are still needed: (1) Method of manufacture and impurities and (2) If significantly absorbed through the skin, reproductive and developmental toxicity data may be needed.

The Panel voted unanimously in favor of issuing a Final Report with an insufficient data conclusion on Octyldodecyl Stearoyl Stearate. The data needed in order for the Panel to complete its safety assessment of this ingredient will be listed in the report discussion as follows:

1. Chemical properties, including octanol/water partition coefficient
2. If there is significant dermal absorption or if significant quantities of the ingredient may contact mucous membranes or be ingested, reproductive and developmental toxicity data may be needed.

NOVEMBER 2001 PANEL MEETING

Dr. Marks stated that the Panel issued a Final Report with an insufficient data conclusion on this ingredient in 1999. The data needs at that time were as follows:

1. Chemical properties, including octanol/water partition coefficient
2. If there is significant dermal absorption or if significant quantities of the ingredient may contact mucous membranes or be ingested, reproductive and developmental toxicity data may be needed.

Dr. Marks noted that data addressing the dermal absorption of Octyldodecyl Stearoyl Stearate have been received, and that his Team determined that the earlier conclusion should be changed to indicate that this ingredient is safe as used in cosmetic products. Dr. Mark's Team also agreed that the existing report should be revised to include the new skin penetration data as well as current ingredient frequency and concentration of use data.

Dr. Belsito said that the Panel would like to receive data from CTFA indicating the types of products in which Octyldodecyl Stearoyl Stearate is being used along with current use concentrations. He added that the safe as used

conclusion is predicated on data that would indicate no substantial new uses or substantial changes in prior concentrations of use.

Dr. Snyder recalled that Dr. Shank had requested the control data for the genotoxicity study that is included in the Final Report and noted that these data should be incorporated into the revised document.

The Panel voted unanimously in favor of issuing a Tentative Amended Report with a safe as used conclusion on Octyldodecyl Stearoyl Stearate.

Dr. Bergfeld noted that an appropriate report discussion will be included along with other additions to the report that were mentioned, and that the conclusion issued refers to this amended report.

JUNE 2002 PANEL MEETING

In 1999, the Panel issued a Final Report with an insufficient data conclusion on Octyldodecyl Stearoyl Stearate. The data needs at that time were as follows: (1) Chemical properties, including octanol/water partition coefficient and (2) If there is significant dermal absorption or if significant quantities of the ingredient may contact mucous membranes or be ingested, reproductive and developmental toxicity data may be needed.

Data addressing the dermal absorption of Octyldodecyl Stearoyl Stearate were subsequently received, and the Panel voted unanimously in favor of issuing a Tentative Amended Report with a safe as used conclusion at the November 2001 Panel meeting.

At today's meeting, the Panel voted unanimously in favor of issuing an Amended Final Report with the following conclusion: The CIR Expert Panel concludes that Octyldodecyl Stearoyl Stearate is safe as used in cosmetic products.

Dr. Belsito made the observation that any restrictions regarding the use of Octyldodecyl Stearoyl Stearate in cosmetic products marketed in the European Union should be stated in the report text.

Dr. Shank recommended editorial changes for the report discussion.

Dr. Marks stated that the date on which the re-review document was reviewed by the Panel should be included in the report introduction.

Dr. Bergfeld said that the preceding recommendation by Dr. Marks should be applicable to all re-review documents.

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The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; David E. Cohen, M.D.; Curtis D. Klaassen, Ph.D.; Allan E. Rettie, Ph.D.; David Ross, Ph.D.; Thomas J. Slaga, Ph.D.; Paul W. Snyder, D.V.M., Ph.D.; and Susan C. Tilton, Ph.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D. This safety assessment was prepared by Regina Tucker, M.S., Scientific Analyst/Writer,

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ABBREVIATIONS

CIR	Cosmetic Ingredient Review
Council	Personal Care Products Council
CPSC	Consumer Product Safety Commission
Da	Daltons
Dictionary	web-based *International Cosmetic Ingredient Dictionary and Handbook*
FDA	Food and Drug Administration
HPLC	high performance liquid chromatography
HRIPT	human repeated-insult patch test
IARC	International Agency for Research on Cancer
MPCE	micronucleated polychromatic erythrocyte
NR	none reported
Panel	Expert Panel for Cosmetic Ingredient Safety
QRA	quantitative risk assessment
SCCNFP	Scientific Committee on Cosmetic and Non-Food Products
US	United States
UV	ultraviolet
VCRP	Voluntary Cosmetic Registration Program

INTRODUCTION

According to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*), Octyldodecyl Stearoyl Stearate is reported to function in cosmetics as a skin conditioning agent-occlusive and viscosity increasing agent-nonaqueous.[1] This ingredient was first reviewed by the Expert Panel for Cosmetic Ingredient Safety (Panel) in a safety assessment that was published in 2001.[2] At that time, the Panel issued a Final Report with an insufficient data conclusion; in that report, the Panel considered assessments on related ingredients (i.e., Octyl Dodecanol, Stearic Acid, and Octyl Stearate), but those data also did not provide a sufficient basis to make a determination of safety. Subsequently, the data needs were met, and in 2005, the Panel published a Final Amended Report with a conclusion of safe for use in cosmetic products in the practices of use and concentration described in that safety assessment.[3]

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 has been issued. In September 2022, the Panel determined that this safety assessment should be re-opened for re-evaluation due to updated usage data and significant increases in concentration of use.

Stearic acid, octyldodecanol, and octyldodecyl hydroxystearate are part of the composition of Octyldodecyl Stearoyl Stearate.[3] The safety of stearic acid was last reviewed in 2019 in the report on fatty acid and fatty acid salts; the Panel concluded that the fatty acid and fatty acid salts, including stearic acid, are safe in the present practices of use and concentration described in the safety assessment when formulated to be non-irritating and non-sensitizing, which may be based on a quantitative risk assessment (QRA).[4] The Panel originally published a safety assessment of octyl dodecanol in 1985, with the conclusion that octyl dodecanol is safe as currently used in cosmetics. This decision was reaffirmed, as published in 2006.[5] The safety of octyldodecyl hydroxystearate was reviewed as part of the safety assessment of alkyl esters; in 2015, the Panel published the report with the conclusion safe in the present practices of use and concentration described in this safety assessment when formulated to be nonirritating.[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 exhaustive search of the world's literature. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that 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.

Excerpts from the summaries of the previous report on Octyldodecyl Stearoyl Stearate are disseminated throughout the text of this re-review document, as appropriate, and are identified by *italicized text*. (This information is not included in the tables or the summary section.) It should be noted that only information on Octyldodecyl Stearoyl Stearate, and not the related ingredients, is included herein.

CHEMISTRY

Definition and Structure

According to the *Dictionary*, Octyldodecyl Stearoyl Stearate (CAS No. 90052-75-8) is the ester that conforms generally to the formula in Figure 1.[1] This ingredient comprises a branched fatty carboxyl diester.

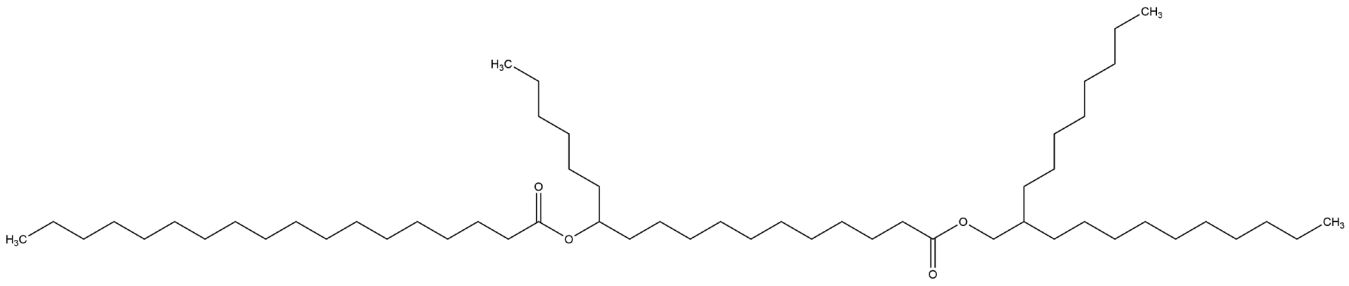

Figure 1. Octyldodecyl Stearoyl Stearate

Chemical Properties

Octyldodecyl Stearoyl Stearate occurs as an amber, yellow liquid with a mild, characteristic odor.[3] It has a molecular weight of 846.87 Da. Octyldodecyl Stearoyl Stearate is partly soluble in 95% ethanol, propylene glycol, glycerin, 70% sorbitol and PEG 400. It is insoluble in water

Method of Manufacture

Octyldodecyl Stearoyl Stearate is manufactured by an inorganic acid-catalyzed, high-temperature (150°C to 160°C) esterification reaction of guerbet alcohol.[3] (Guerbet alcohol is comprised of a mixture of alcohols (primarily C-20) and a

mixture of fatty acids (primarily C-18) with no impurities.) The product is neutralized to a water-soluble soap, washed to purity, dried, and filtered.

Composition/Impurities

Octyldodecyl Stearoyl Stearate is composed of stearic acid (2.5% max), octyldodecanol (5.0% max), octyldodecyl hydroxystearate (5.0% max), and Octyldodecyl Stearoyl Stearate (88.0% max).[3]

USE

Cosmetic

The safety of the cosmetic ingredient 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 this ingredient in cosmetics and does not cover its use in airbrush delivery systems. Data are submitted by the cosmetic industry via 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 are provided by cosmetic product categories, based 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 2022 VCRP survey data, Octyldodecyl Stearoyl Stearate is reported to be used in 605 total formulations, (601 leave-on and 4 rinse off; Table 1).[7] This is a significant increase since the last review; in 2001, VCRP survey data reported 106 uses (102 leave-on and 4 rinse-off).[3] The results of the concentration of use survey conducted by the Council in 2020 indicate Octyldodecyl Stearoyl Stearate is used at up to 28% in leave-on products; in 2001, the maximum reported concentration of use was 15%. The product category with the highest use concentration in 2020 is lipsticks, 28%; in 2001, the maximum concentration of use reported for lipstick was 10%. [For comparison, Table 2 provides the frequency and concentration of use data (both current and historical) by product category.]

Cosmetic products containing Octyldodecyl Stearoyl Stearate may be applied near the eyes, (e.g., at up to 18.5% in eye shadows; this is compared to 10% reported for products applied near the eye in 2001). Octyldodecyl Stearoyl Stearate is also used in cosmetic products that could possibly be inhaled; e.g., it is reported to be used in in face powders (at concentrations up to 7.5%,) 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 cosmetics 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.

Octyldodecyl Stearoyl Stearate is not restricted from use in any way under the rules governing cosmetic products in the European Union. [8]

TOXICOKINETIC STUDIES

Dermal Penetration

In Vitro

An in vitro study of skin penetration and permeation of Octyldodecyl Stearoyl Stearate was conducted.[3] *Permeation at 48 h was 0.023 ± 0.005 µg/cm^2, representing 0.005% ± 0.001% of the applied dose. Permeation at 24 h was higher, but the researchers cautioned that the actual scintillation counts measured in the receptor fluid were very close to background levels. A total of 4% to 5% of the label was found in the tape strips and remaining epidermis combined.*

Additional toxicokinetic studies were not were not found in the updated literature search, and unpublished data were not submitted.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

Octyldodecyl Stearoyl Stearate, tested as a trade compound, had an oral LD_{50} of >20 g/kg in albino rats.[3]

Additional acute toxicity studies were not found in the updated literature search, and unpublished data were not submitted

Short-Term, Subchronic, and Chronic Toxicity Studies

Octyldodecyl Stearoyl Stearate, tested as a trade compound at an oral dose of 5.0 g/kg in 10 rats (5 of each sex) for 14 d, produced no deaths.[3] (No additional details were provided.)

Additional repeated-dose toxicity studies were not were not found in the updated literature search, and unpublished data were not submitted.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

Developmental and reproductive toxicity studies of Octyldodecyl Stearoyl Stearate were not included in the original reports and were not found in the updated literature search, and unpublished data were not submitted.

GENOTOXICITY STUDIES

In a Salmonella typhimurium gene mutation assay with up to 100 µl/plate Octyldodecyl Stearoyl Stearate, there was no positive increase in the number of revertant colonies for any of the tester strains (TA98, TA100, TA1535, TA1537, and TA1538) with or without S-9 activation [3] In vivo, a micronucleus assay was used to determine the genotoxicity of Octyldodecyl Stearoyl Stearate. A single dose of 2.0, 5.0 or 10.0 ml/kg Octyldodecyl Stearoyl Stearate was given to CD-1 mice. No significant increases occurred in the proportion of micronucleated polychromatic erythrocytes (MPCEs) in the test groups compared to the concurrent negative control groups.

Additional genotoxicity studies were not were not found in the updated literature search, and unpublished data were not submitted.

CARCINOGENICITY STUDIES

Carcinogenicity studies of Octyldodecyl Stearoyl Stearate were not included in the original reports and were not found in the updated literature search, and unpublished data were not submitted.

DERMAL IRRITATION AND SENSITIZATION

Irritation

An eyeshadow containing 7.5% Octyldodecyl Stearoyl Stearate was tested on 9 rabbits, in a single insult occlusive patch test and was moderately irritating to the skin.[3] A concealer containing 7.8% Octyldodecyl Stearoyl Stearate was similarly tested on 9 rabbits; no signs of irritancy were observed at 24 h, but erythema was observed at 2 h. A lipstick containing 7.8% Octyldodecyl Stearoyl Stearate was tested similarly to the previous studies in a 4-d cumulative study on 9 rabbits; the lipstick was "essentially non-irritating." Octyldodecyl Stearoyl Stearate, tested as a trade compound, was applied (0.5 ml) under a 24-h occlusive patch to abraded and intact skin on the backs of 6 rabbits. It was considered to have a "potential for slight irritation—rarely irritating to people." A single dermal application of 0.5 ml of Octyldodecyl Stearoyl Stearate, at a 10% w/w dilution in corn oil, was applied to one abraded and one intact site on 6 New Zealand white rabbits. Each test site was observed for erythema and edema 24 and 72 h after application, and the test compound was found to be non-irritating to the skin. A cumulative irritation study of an eyeshadow having 10.4% Octyldodecyl Stearoyl Stearate was completed in 10 subjects. The test material was applied with occlusive patches to the skin 21 times for 23-h intervals. Scoring and reapplication occurred every 24 h. The eyeshadow was classified as a mild irritant. The human irritancy potential of an eyeshadow pencil containing 10.4% Octyldodecyl Stearoyl Stearate was evaluated in a single insult patch test using 19 subjects. No differences in irritancy were observed between subjects of the test and control groups. A concealer containing 5.0% Octyldodecyl Stearoyl Stearate was tested for primary irritation using 20 subjects. No significant differences in irritancy were observed between test subjects and controls. A lipstick having 15.0% Octyldodecyl Stearoyl Stearate was similarly tested using 18 subjects. No differences in irritancy were observed between test subjects and control groups

Human

Under dermatological control, use tests were completed on 4 lip balms containing 28% Octyldodecyl Stearoyl Stearate, each tested on 12-13 subjects.[9] Subjects used the products for 14 d, 3 to 5 times each day. It was concluded that the subjects had good dermatological tolerance for each lip balm.

Sensitization

An eyeshadow containing 10.4% Octyldodecyl Stearoyl Stearate was evaluated in a human repeated insult patch test (HRIPT) using 107 subjects.[3] Applications were made under a closed patch three times weekly during the 22-d induction period, and scored 48 or 72 h after application. Challenge applications were made using 24-h occlusive patches. No evidence of contact sensitization was observed in any of the test subjects. The contact sensitization potential of a concealer containing 5.0% Octyldodecyl Stearoyl Stearate was determined using a maximization test. The test material was evaluated with an occlusive patch. During the induction phase, sodium lauryl sulfate (SLS, 1%) was applied to a different site and examined after 48 or 72 h. The procedure was repeated for 5 induction exposures. None of the 27 subjects had adverse

reactions, and no contact sensitization was observed. A lipstick containing 7.8% Octyldodecyl Stearoyl Stearate was tested in an HRIPT using 85 subjects. Occlusive patches with the test material were applied to the upper back for 24 h, three times weekly, for 3 wk. Challenge applications were made 3 wk after the last induction treatment, and scored 24 and 48 h after patch removal. None of the subjects had erythematous responses during induction or challenge, and the investigators concluded that the lipstick did not have allergic sensitization potential.

Human

An HRIPT with a makeup base containing 21.0112% Octyldodecyl Stearoyl Stearate was performed in 107 subjects.[10] Two-tenths (0.2) g of the test material, or an amount sufficient to cover the contact surface, was applied to the treatment site using occlusive patches. During the induction phase, 24-h patches were applied 3 times per week, for a total of 9 applications. Approximately 2 wk after the final induction application, a challenge patch was applied for 24 h to a previously untreated site, and the site was scored on day 1 and day 3 post-application. No visible skin reactions were observed throughout the test interval. Under the conditions of the study, the test material indicated no potential for dermal irritation or allergic contact sensitization.

OCULAR IRRITATION STUDIES

An EYETEX in vitro irritation assay was performed on a nail cuticle pencil containing 20.6% Octyldodecyl Stearoyl Stearate; the test material produced minimal to mild irritation.[3] In animal studies, an eyeliner containing 7.5% Octyldodecyl Stearoyl Stearate was applied 3 times to the eyes of 6 rabbits; the eyes were not rinsed. The investigators concluded that the eye liner was moderately irritating under the conditions of this study. A concealer containing 12.7% Octyldodecyl Stearoyl Stearate was applied once to the eyes of 6 rabbits, and the eyes were not rinsed; the formulation was classified as mildly irritating. In a third study, none of the 6 rabbits tested had signs of ocular irritation from a lipstick containing 7.8% Octyldodecyl Stearoyl Stearate. Octyldodecyl Stearoyl Stearate, tested as a trade compound, instilled (0.1 ml) into the right conjunctival sac of six rabbit, was scored on days 1 to 4, and 7, and no reactions were observed. A single application of 0.1 ml of Octyldodecyl Stearoyl Stearate, at a 10% w/w dilution in corn oil, was instilled into one eye each of 6 rabbits. No reactions were observed.

Additional ocular irritation studies were not found in the updated literature search, and unpublished data were not submitted.

CLINICAL STUDIES

A clinical use study was performed using a lipstick containing 7.8% Octyldodecyl Stearoyl Stearate with 62 female subjects.[3] The women applied the lipstick at least twice daily for 3 wk. No clinical changes were observed after use of the lipstick.

SUMMARY

Octyldodecyl Stearoyl Stearate is reported to function in cosmetics as a skin conditioning agent-occlusive and viscosity increasing agent-nonaqueous. Octyldodecyl Stearoyl Stearate was previously reviewed by the Panel in a safety assessment that was published in 2001. At that time, the Panel issued an insufficient data conclusion. Subsequently, the data needs were met, and in 2005, the Panel published a Final Amended Report with a conclusion of safe for use in cosmetic products in the practices of use and concentration described in that safety assessment. 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 has been issued. In June 2022, the Panel determined that this safety assessment should be re-opened for re-evaluation due to a four-fold increase in use and significant increase in concentration of use.

According to 2022 VCRP survey data, Octyldodecyl Stearoyl Stearate is reported to be used in 605 total formulations, (601 leave-on and 4 rinse off). The results of the concentration of use survey provided by the Council in 2020, indicate Octyldodecyl Stearoyl Stearate is used at up to 28% in leave-on products, with the highest maximum concentration of use reported for lipstick. When the final amended safety assessment was published in 2005, Octyldodecyl Stearoyl Stearate reported use was in 106 formulations (2001 VCRP data). The highest maximum concentration of use at that time were at up to 15% in body and hand creams, lotions, etc. (excluding shaving).

Under dermatological control, use tests were completed on 4 lip balms containing 28% Octyldodecyl Stearoyl Stearate on 12-13 subjects per formulation. It was concluded that the subjects had good dermatological tolerance for each lip balm. An HRIPT using 24-h occlusive patches of a makeup base containing 21.0112% Octyldodecyl Stearoyl Stearate was completed in 107 subjects. No visible skin reactions were observed throughout the test interval. Under the conditions of the study, the test material indicated no potential for dermal irritation or allergic contact sensitization.

No acute or repeated-dose toxicity, developmental and reproductive, or carcinogenicity studies on Octyldodecyl Stearoyl Stearate were found in an updated search of the published literature, and data were not submitted.

PREVIOUS DISCUSSION

The Expert Panel had previously considered the available data on Octyldodecyl Stearoyl Stearate to be insufficient; the data needed were chemical properties, including the octanol/water partition coefficient, the extent of dermal absorption, and whether significant quantities of the ingredient may contact mucous membranes or be ingested.[3] If a significant penetration or ingestion would occur, the Panel considered the possibility that reproductive and developmental toxicity data may be needed. Dermal absorption data were provided.

Skin permeation and penetration data using isolated human skin indicated that only a small portion of the applied dose permeates the skin (0.005%), only 4% to 5% actually enters the skin, and that almost 95% remained in the material applied to the skin. Based on these data, the Panel does not expect any significant amount of Octyldodecyl Stearoyl Stearate to be available to create a systemic exposure. Although few data are available on the systemic toxicity of Octyldodecyl Stearoyl Stearate, there is no systemic toxicity associated with any of the structurally related chemicals reviewed in previous safety assessments.

None of the available toxicology or clinical data suggest a concern about adverse skin reactions to Octyldodecyl Stearoyl Stearate. Only a mild, transient ocular irritation was associated with Octyldodecyl Stearoyl Stearate.

This ingredient is reportedly used in some product categories, but the concentrations of use are not available. In other cases, information regarding use concentration for a specific product category is provided, but the number of such products is not known. Although there are gaps in knowledge about product use, the overall information available on the types of products in which this ingredient is used and at what concentration indicate a pattern of use. Within this overall pattern of use, the Panel considers this ingredient to be safe.

DISCUSSION

To be determined.

CONCLUSION

To be determined.

TABLES

Table 1.Current and historical frequency and concentration of use according to duration and exposure for Octyldodecyl Stearoyl Stearate

	# of Uses		*Max Conc of Use (%)*	
	2022[7]	**2001[3]**	**2020[11]**	**2001[3]**
Totals*	**605**	**106**	**0.50-28**	**2-15**
Duration of Use				
Leave-On	*601*	*102*	*0.5-28*	*2-15*
Rinse-Off	*4*	*4*	*3.3-3.5*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*
Exposure Type				
Eye Area	322	35	0.5-18.5	4-10
Incidental Ingestion	48	1	3.4-28	5-10
Incidental Inhalation-Spray	7[a];5[c]	1;5[a];2[c]	NR	8[a]; 4-15[c]
Incidental Inhalation-Powder	105; 5[c]	34; 2[c]	1.9-7.5; 1[b]	2-7; 4-15[c]
Dermal Contact	556	103	0.5-25.4	2-15
Deodorant (underarm)	NR	NR	NR	NR
Hair – Non-Coloring	1	NR	NR	NR
Hair-Coloring	NR	NR	3.3-3.5	NR
Nail	NR	2	NR	NR
Mucous Membrane	48	1	3.4-28	5-10
Baby Products	NR	NR	NR	NR

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

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

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

[c] 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

NR – no reported use

Table 2. Current and historical frequency and concentration of use by product category for Octyldodecyl Stearoyl Stearate

	# of uses		**Max conc of use**		**Likely Exposure Site**	
Product Category	**2022[7]**	**2001[3]**	**2020[11]**	**2001[3]**	**2022**	**2001**
Eyebrow Pencil	2	2	0.75%	NR	eye area	eye area
Eyeliner	3	1	NR	4%	eye area	eye area
Eye Shadow	306	30	1.4-18.5%	4-10%	eye area	eye area
Other Eye Makeup Preparations	11	2	0.5-3.2%	NR	eye area	eye area
Powders (dusting and talcum – exc face)	NR	2	NR	4%	NR	skin
Other Fragrance Preparations	NR	1	NR	NR	NR	skin
Hair Conditioner	1	NR	NR	NR	hair	NR
Hair Tints	NR	NR	3.3%	NR	hair	NR
Other Hair Coloring Preparations	NR	NR	3.5%	NR	hair	NR
Blushers (all types)	72	8	1.8-24%	2-7%	skin	skin
Face Powders	105	32	1.9-7.5%	2-7%	skin	skin
Foundations	12	5	0.5-6.7%	4-9%	skin	skin
Lipstick	48	1	3.4-28%	5-10%	skin; mucous membrane	skin; mucous membrane
Makeup Bases	2	5	6.1-24%	10%	skin	skin
Rouges	7	1	25.4%	NR	skin	skin
Other Makeup Preparations	18	1	1.9-3%	5%	skin	skin
Cuticle Softeners	NR	1	NR	NR	NR	nail
Nail Creams and Lotions	NR	1	NR	NR	NR	nail
Cleansing	2	3	NR	NR	skin	skin
Face and Neck (exc shaving)	NR	1	1% (not spray)	4%	skin	skin
Body and Hand (exc shaving)	5	1	NR	15%	skin	skin
Moisturizing	7	4	2-9% (not spray)	NR	skin	skin
Night	NR	1	2.5% (not spray)	NR	skin	skin
Paste Masks (mud packs)	1	1	NR	NR	skin	skin
Other Skin Care Preps	3	2	NR	NR	skin	skin
Suntan Gels, Creams, and Liquids	NR	NR	NR	8%	NR	skin
Totals	**605**	**106**	**0.5-28%**	**2-15%**	**skin; mucous membrane; eye area; hair**	**skin; mucous membrane; eye area; nail**

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Final Report on the Safety Assessment of Octyldodecyl Stearoyl Stearate[1]

Octyldodecyl Stearoyl Stearate functions as an occlusive skin-conditioning agent and as a nonaqueous viscosity-increasing agent in many cosmetic formulations. Current concentrations of use are between 0.7% and 23%, although historically higher concentrations were used. The chemical is formed by a high-temperature, acid-catalyzed esterification reaction of long-chain alcohols (primarily C-20) and a mixture of primarily C-18 fatty acids. Levels of stearic acid, octyldodecanol, and octylydocecyl hydroxystearate in the final product are 5% or less—no other residual compounds are reported. Only limited safety test data were available on Octyldodecyl Stearoyl Stearate, but previous safety assessments of long-chain alcohols and fatty acids found these precursors to be safe for use in cosmetic formulations. Octyldodecyl Stearoyl Stearate produced no adverse effects in acute exposures in rats. The chemical was mostly nonirritating to animal skin at concentrations ranging from 7.5% to 10%; one study did find moderate irritation in rabbit skin at a concentration of 7.5%. Clinical tests at a concentration of 10.4% confirmed the absence of significant irritation in humans. An ocular toxicity study in rabbits found no toxicity. No evidence of genotoxicity was found in either a mammalian test system or in the Ames test system, with or without metabolic activation. The available data on Octyldodecyl Stearoyl Stearate and the previously considered data on long-chain alcohols and fatty acids, however, did not provide a sufficient basis to make a determination of safety. Additional data needs include (1) chemical properties, including the octanol/water partition coefficient; and (2) if there is significant dermal absorption or if significant quantities of the ingredient may contact mucous membranes or be ingested, then reproductive and developmental toxicity data may be needed. Until such time as these data are received, the available data do not support the safety of Octyldodecyl Stearoyl Stearate as used in cosmetic formulations.

INTRODUCTION

Octyldodecyl Stearoyl Stearate is an ester that functions as a skin-conditioning agent—occlusive and a viscosity-increasing agent—nonaqueous in cosmetic product formulations. Only limited data on Octyldodecyl Stearoyl Stearate were found. The safety of the following related ingredients has been reviewed, with the conclusions listed below:

Stearyl Alcohol, Oleyl Alcohol, and Octyl Dodecanol are safe as currently used in cosmetics (Elder 1985a).

Oleic Acid, Lauric Acid, Palmitic Acid, Myristic Acid, and Stearic Acid are safe in the present practices of use and concentration in cosmetics (Elder 1987).

Butyl, Cetyl, Isobutyl, Isocetyl, Isopropyl, Myristyl and Octyl, Stearate are safe as cosmetic ingredients in the present practices of use (Elder 1985b).

Pertinent data from these reports have been added to this review (*italicized text*) as a further basis for the assessment of safety of Octyldodecyl Stearoyl Stearate.

CHEMISTRY

Definition and Structure

Octyldodecyl Stearoyl Stearate (CAS No. 90052-75-8) is an ester that conforms generally to the formula presented in Figure 1. Synonyms for Octyldodecyl Stearoyl Stearate include Octadecanoic Acid, 12-[(1-Oxooctadecyl)Oxy]-, 2-Octyldodecyl Ester; Octadecanoic Acid, 12-[(1-Oxooctadecyl)Oxy]-2-Octyldodecyl Ester; and 12-[(1-Oxooctadecyl)Oxy]Octadecanoic Acid, 2-Octyldodecyl Ester (Wenninger, Canterbery, and McEwen 2000).

Related Ingredients

Octyl Dodecanol is the long-chain saturated fatty alcohol that conforms to the structure presented in Figure 2 (Elder 1985a).

Stearic Acid is found primarily as a glyceride in animal fats and oils; lard and tallow contain approximately 10% and 20% Stearic Acid, respectively. Most vegetable oils contain 1% to 5% Stearic Acid; cocoa butter contains approximately 35%. Cosmetic grade Stearic Acid occurs as a mixture of fatty acids, depending on the method of manufacture and source. Commercial Stearic Acid is primarily a mixture of varying amounts of Stearic and Palmitic Acids. Components of Stearic Acid are octadecanoic acid (39% to 95%), hexadecanoic acid (5% to 50%), tetradecanoic acid (0% to 3%), 9-octadecenoic acid (0% to 5%), heptadecanoic acid (0% to 2.5%), eicosanoic acid (0% to 2%), and pentadecanoic acid (0% to 1%). Butylated hydroxytoluene can be added to preparations containing fatty acids as an antioxidant at concentrations of 0.01% to 0.1% for unsaturated materials (Elder 1987).

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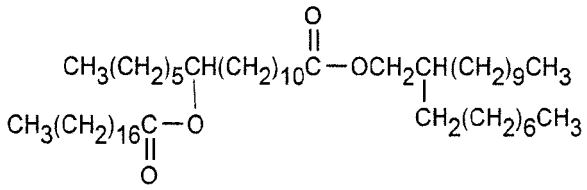

FIGURE 1
Octyldodecyl Stearoyl Stearate.

The Stearates are esters of stearic acid; Octyl Stearate conforms generally to the formula in Figure 3 (Elder 1985b).

Chemical and Physical Properties

The physical form of Octydodecyl Stearoyl Stearate, as the trade compound, occurs as an amber, yellow liquid with a mild, characteristic odor. Its specifications include saponification number of 115.0 to 135.0; specific gravity (25°C) range 0.86 to 0.88; and a refractive index (25°C) of 1.45 to 1.47 (ISP Van Dyke, Inc. 1997).

Octydodecyl Stearoyl Stearate is soluble in silicones; esters; mineral oil; vegetable oils; alcohols; aliphatic, aromatic, and chlorinated hydrocarbons; and is insoluble in water. It has a theoretical molecular weight of 846 Da, a freezing point of −15°C, and a flash point of over 180°C (Alzo, Inc. 1998). Octyldodecyl Stearoyl Stearate is partly soluble in 95% ethanol, propylene glycol, glycerine, 70% sorbitol, and PEG 400 (Trivent Chemical Company, Inc. 1998).

Related Ingredients

Stearic Acid occurs as a hard, white or faintly yellow, glossy crystals or leaflets or as an amorphous white or yellow-white powder. It has a slight odor and tallow-like flavor. Stearic Acid is water insoluble, slightly soluble in alcohol and benzene, soluble in chloroform, and very soluble in ether. The molecular weight is ~284.5 Da (Elder 1987).

Octyl Stearate and the other Stearates are either oily liquids or waxy solids that typically are soluble in organic solvents such as chloroform and acetone. The molecular weight of Octyl Stearate is 396 Da, the ester value is 144 to 154, the acid value and iodine value each have a maximum of 1.0. The Stearates can undergo conversion into stearic acid and the corresponding alcohol by chemical or enzymatic hydrolysis, conversion into amides by ammonolysis, and conversion into different esters by alcoholysis or transesterification. Purer grades of the saturated Stearates are not expected to autoxidize readily (Elder 1985b).

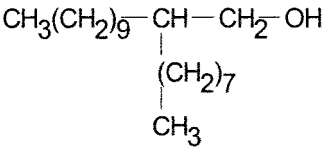

FIGURE 2
Octyl Dodecanol.

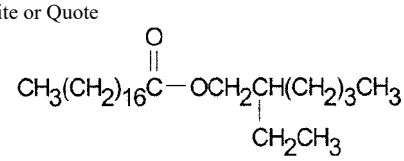

FIGURE 3
Octyl Stearate.

Method of Manufacture

Octyldodecyl Stearoyl Stearate is manufactured by an inorganic acid catalyzed, high temperature (150°C to 160°C) esterification reaction of guerbet alcohol. Guerbet alcohol is comprised of a mixture of guerbet alcohols (primarily C-20) and no other impurity and a mixture of fatty acids (primarily C-18) and no other impurities. The product is neutralized to a water-soluble soap, washed to purity, dried, and filtered (Alzo, Inc. 1998).

Related Ingredients

Octyl Dodecanol is produced by the condensation of two molecules of decyl alcohol, and occurs naturally in small quantities as components of wax esters in plants (Elder 1985a).

Methods of processing Stearic Acid include hydrolysis of tallow or hydrogenation of unsaturated fatty acids in cottonseed and other vegetable oils, followed by fractional distillation or crystallization. Concentrations of Stearic Acid as great as 95% to 99% have been reported from the hydrogenation of unsaturated fatty acids (Elder 1987).

The Stearates are prepared by esterification of stearic acid with the appropriate alcohol in the presence of an acid catalyst. The reaction products are refined either by catalyst neutralization, vacuum distillation, or various decolorization-deoderization techniques to remove residual traces of alcohol (Elder 1985b).

Impurities

Octyldodecyl Stearoyl Stearate is composed of Stearic Acid (2.5% maximum), Octyldodecanol (5.0% maximum), Octyldodecyl Hydroxystearate (5.0% maximum), and Octyldodecyl Stearoyl Stearate (88.0% maximum) (Alzo, Inc. 1998).

Related Ingredients

Stearic Acid contains varying amounts of unsaponifiable matter (0.3% maximum), and can contain glyceryl monostearate (0.07% maximum). Typical impurities are glyceryl monomyristate (0.07% maximum), 9-hexadecanoic acid, 9,12-octadecadienoic acid (Elder 1987).

USE

Cosmetic

Octyldodecyl Stearoyl Stearate functions as a skin-conditioning agent—occlusive and viscosity increasing agent—nonaqueous in cosmetic product formulations (Wenninger, Canterbery, and McEwen 2000).

In 1998, industry reported to the Food and Drug Administration (FDA) that Octyldodecyl Stearoyl Stearate was used in 86 cosmetic formulations (FDA 1998). Table 1 gives the number of formulations in each cosmetic product category containing Octyldodecyl Stearoyl Stearate, along with the total number of formulations in each category. Concentration of use data provided by industry, ranging from a low of 0.7% in makeup preparations to 20% in lipstick, are also included in Table 1. Table 2 gives the historical (FDA 1984) concentration and frequency of use of Octyldodecyl Stearoyl Stearate. For comparison purposes, historical concentration and frequency of use data for Stearic Acid and Octyl Stearate, as reported to FDA in 1984, are included in Table 2.

International

Octyldodecyl Stearoyl Stearate is listed in the *Japanese Comprehensive Licensing Standards of Cosmetics by Category (CLS)* (Santucci 1999). Octyldodecyl Stearoyl Stearate has precedent for use without restriction in all *CLS* categories. According to Notification 990 of the Pharmaceutical and Medical Safety Bureau of the Japan Ministry of Health and Welfare, issued September 29, 2000, Octyldodecyl Stearoyl Stearate is not prohibited or restricted in its use beyond a basic obligation of manufacturers to use all ingredients in a manner which guarantees safety (Japan Ministry of Health and Welfare 2000).

GENERAL BIOLOGY

No data on absorption, distribution, metabolism, or excretion of Octyldodecyl Stearoyl Stearate were available.

Related Ingredients

Stearic Acid and other fatty acids are digested from the diet, absorbed in micellar aggregates, and transported after

TABLE 1
Product formulation data

Product category (total formulations in category) (FDA 1998)	Total no. of formulations containing Octyldodecyl Stearoyl Stearate (FDA 1998)	Current concentration of use (CTFA 1998a, 1998c, 1999) %
Bubble baths (200)	1	—
Eyebrow pencil (91)	2	0.8
Eyeliner (514)	1	4–12
Eye shadow (506)	20	11.7
Other eye makeup preparations (120)	2	5
Powders (fragrance) (247)	2	3–3.4
Other fragrance preparations (148)	1	4–4.3
Hair tints	—	0.8
Blushers (all types) (238)	5	2–7.4
Face powders (250)	29	7
Foundations (287)	5	5–6.3
Lipstick (790)	1	4–20
Makeup bases (132)	4	—
Rouges (12)	1	—
Other makeup preparations	—	0.7–15
Cuticle softeners (19)	1	21
Nail creams and lotions (17)	1	—
Shaving cream	—	3
Cleansing preparations (653)	2	—
Face and neck (excluding shaving) (263)	1	—
Moisturizing preparations (769)	3	—
Night preparations (188)	1	—
Paste masks (mud packs) (255)	1	—
Other skin care preparations (692)	2	—
1998 total for Octyldodecyl Stearoyl Stearate	**86**	

TABLE 2

Historical concentrations and frequencies of use (FDA 1984)

	Concentration of use (%)							
Ingredient	≤0.1	>0.1–1	>1–5	>5–10	>10–25	>25–50	>50	1984 Total
Octyldodecyl Stearoyl Stearate	2	2	7		9			20
Octyl Dodecanol	4	23	60	195	70	18	1	371
Stearic Acid	6	231	1826	231	148	22	1	2465
Octyl Stearate		7	2		1			10

esterification to glycerol in chylomicrons and very-low-density lipoproteins. Stearic Acid is primarily transported via the lymph system. Fatty acids originating from adipose tissue stores are either bound to serum albumin or remain unesterified in the blood. Stearic Acid was the most poorly absorbed of the common fatty acids; the digestibility of fatty acids decreased with increased fatty acid chain length. Radioactivity has been traced to the heart, liver, lungs, spleen, kidneys, muscles, intestines, adrenal glands, blood, and lymph, and to adipose, mucosal, and dental tissues after administration of radioactive Stearic Acid to rats, dogs, sheep, chicks, frogs, and humans. Uptake and transport of fatty acids into the brain has been observed, and free fatty acids readily cross the placental barrier in rabbits, guinea pigs, rats, and humans. Fatty acids that are taken up by tissues are either stored in the form of triglycerides or oxidized for energy (Elder 1987).

ANIMAL TOXICOLOGY

Octydodecyl Stearoyl Stearate, tested as a trade compound at an oral dose of 5.0 mg/kg in 10 rats (5 of each sex) for 14 days, produced no deaths (Wells Laboratories, Inc. 1993). Octydodecyl Stearoyl Stearate, tested as a trade compound, had an oral LD50 of >20 g/kg in albino rats (Food and Drug Research Labs, Inc. 1983). No additional animal toxicology data were available. No data on the carcinogenicity and reproductive and developmental toxicity of Octyldodecyl Stearoyl Stearate were available.

Related Ingredients

No deaths were observed during acute oral toxicity studies when 5 to 10 rats were treated with 5 g/kg of undiluted Octyl Dodecanol or with a lipstick (25 g/kg, diluted to 50%) containing 10.2% Octyl Dodecanol (1.28 g/kg total dose). In an acute dermal toxicity study, intact and abraded skin sites of six guinea pigs were treated with 3.0 g/kg of the undiluted alcohol under occlusive patches. No deaths occurred as a result of treatment, and no gross lesions were observed at necropsy (Elder 1985a).

Little acute toxicity was observed when Stearic Acid or cosmetic formulations containing Stearic Acid at concentrations up to 13% were given orally to rats at doses of 15 to 19 g/kg. In subchronic oral studies, Stearic Acid (5% to 50%) caused thrombosis, aortic atherosclerosis, anorexia, and mortality in rats. Chicks fed 5% Stearic Acid had no signs of toxicity. Topical applications of 5 g/kg Stearic Acid to rabbits did not cause adverse effects. Intradermal administration of 10 to 100 mM Stearic Acid caused mild erythema and slight induration in guinea pigs and rabbits (Elder 1987).

Octyl Stearate generally had "very low" acute oral toxicity in rats and mice. Undiluted Octyl Stearate at a dose of 8 ml/kg did not cause deaths in five rats per sex. Body weight gain averaged 25.7% during the 2-week observation period (Elder 1985b).

Ocular Irritation

An EYETEX in vitro irritation assay was performed on a nail cuticle pencil containing 20.6% Octyldodecyl Stearoyl Stearate. The test material produced scores consistent with minimal to mild irritation (CTFA 1998b).

An undiluted eyeliner containing 7.5% Octyldodecyl Stearoyl Stearate was applied three times to the unrinsed eyes of six rabbits. One rabbit had conjunctival scores of 6, 2, and 2 on days 1, 3, and 4, respectively, and a corneal score of 5 on day 1. Another had a conjunctival score of 4 on day 1. None of the rabbits had signs of ocular toxicity on days 2 or 7. The total Draize scores were 4/110 on day 1 and 1/110 on days 3 and 4. The investigators concluded that the eyeshadow was moderately irritating under the conditions of this study.

A concealer containing 12.7% Octyldodecyl Stearoyl Stearate was applied once to the unrinsed eyes of six rabbits. One rabbit each had conjunctival scores of 2 on days 1 and 2. None of the rabbits had signs of irritancy on days 3, and 4, or 7. The total Draize scores were 1/110 on days 1 and 2 and the formulation was classified as mildly irritating.

In a third study, none of the six rabbits had signs of ocular irritation after treatment with a lipstick containing 7.8% Octyldodecyl Stearoyl Stearate. The lipstick was classified as nonirritating (CTFA 1998b).

Octydodecyl Stearoyl Stearate, tested as a trade compound, was instilled (0.1 ml) into the right conjunctival sac of six rabbits. The contralateral eye served as the control. Eyes were not rinsed. Reactions were scored on days 1 to 4, and 7 according to the Draize scale. No reactions were observed (Consumer Product Testing 1978).

A single application of 0.1 ml of Octydodecyl Stearoyl Stearate, at a 10% *w/w* dilution in corn oil, was instilled into one eye each of six rabbits. The contralateral eye served as the control and the eyes were not rinsed. Reactions were scored on days 1 to 3, and 4 and 7 if irritation persisted. No reactions were observed (Wells Laboratories, Inc. 1993).

Related Ingredients

Six rabbits were treated with 100% Octyl Dodecanol. The average ocular irritation scores were 4/110 at day 1 and 0/110 by day 4. In a second study using the same procedure, the scores were 1/110 at day 1 and 0/110 by day 4. Cosmetic formulations containing 3% to 10.2% Octyl Dodecanol caused either no ocular irritation or minimal, transient irritation in the eyes of rabbits (Elder 1985a).

Undiluted Octyl Stearate caused slight, transient ocular irritation in rabbits (Elder 1985b).

Skin Irritation and Sensitization

An undiluted eyeshadow containing 7.5% Octyldodecyl Stearoyl Stearate was moderately irritating to the skin in a single insult occlusive patch test using nine rabbits. Erythema and edema were observed at 2 and 24 hours after application of the test material. The primary irritation index (PII) for the group was 3.89/8.00.

In a similar study, a concealer containing 7.8% Octyldodecyl Stearoyl Stearate was tested using nine rabbits. The skin sites were evaluated 2 and 24 hours after application of the test material. No signs of irritancy were observed at 24 hours, but erythema was observed at 2 hours. The PII for the group was 0.67/8.00, and the formulation was classified as minimally irritating.

A lipstick containing 7.8% Octyldodecyl Stearoyl Stearate was tested similarly using nine rabbits. None of the animals had erythema or edema 2 or 24 hours after application of the test material, and the PII was 0.00/8.00. In a 4-day cumulative study, the lipstick was "essentially non-irritating" (CTFA 1998b).

Octydodecyl Stearoyl Stearate, tested as a trade compound, was applied (0.5 ml) under a 24-hour occlusive patch to abraded and intact sites on the backs of six rabbits. Sites were examined for erythema and edema at 24 and 72 hours. The maximum possible score was 8. The PII for Octydodecyl Stearoyl Stearate was 0.38. It was considered to have a "potential for slight irritation—rarely irritating to people" (Consumer Product Testing 1978).

A single dermal application of 0.5 ml of Octyldodecyl Stearoyl Stearate, at a 10% *w/w* dilution in corn oil, was applied to one abraded and one intact site on six New Zealand white rabbits. Each test site was observed for erythema and edema 24 and 72 hours after application. The PII for this product was 0.0 (Wells Laboratories, Inc. 1993).

In a rabbit dermal irritation test Octyldodecyl Stearoyl Stearate had a PII of 0.38. No additional details were available (International Specialty Products 1998).

Related Ingredients

Octyl Dodecanol was applied for 24 hours under occlusive patches to the skin of six rabbits during three studies. The irritation scores for a concentration of 100% were 1.13/4, 0.5/4, and 0/4. At a concentration of 30%, it produced scores of 0/4 for all three studies.

Techical grade Octyl Dodecanol (0.1 to 0.5 g) caused severe irritation (+++) to the skin of six albino rabbits and moderate irritation (++) to the skin of six Hartley guinea pigs and six Wistar rats. The compound was nonirritating (−) when applied to the skin of six Pitman-Moore miniature swine. For the study using rabbits, 0.1 g Octyl Dodecanol was applied for 24 hours, the skin sites were graded, and the compound was reapplied for another 24 hours. The treated skin sites were graded after Evans blue solution was injected intravenously. The rabbits were killed 1 hour later, and skin samples were prepared. For the guinea pig study, two dorsal areas were clipped free of hair. One site was treated with 0.1 g for 24 hours and the other was left untreated. The remainder of the study was identical to the one using rabbits. For the swine, the dorsal area was clipped free of hair, and 0.5 g Octyl Dodecanol was applied under occlusive patches for 48 hours. Skin of the rabbits, guinea pigs, and rats had acanthosis, hyperkeratinization, swelling of cells, and proliferation of basal cells. Vasodilatation, edema, alteration of collagenous fibers, and mononuclear and polymorphonuclear leukocytes infiltration of the dermis were also observed.

A formulation containing 4% Octyl Dodecanol was nonirritating to mildly irritating (0/4 to 1.08/4) during primary skin irritation studies. Minimal to mild irritation was observed when a formulation containing 10.2% of the alcohol was applied to the skin of rabbits for 3 to 4 consecutive days. In these studies, the degree of irritation observed did not increase with the concentration tested (Elder 1985a).

No irritation was observed when Stearic Acid was applied (18 mmol %) to the skin of the external ear canals of albino rabbits over a period of 6 weeks. Slight local edema was observed when New Zealand white rabbits were treated with 2% Stearic Acid in formulation for 4 weeks. During a 13-week study, cosmetic formulations containing up to 5% Stearic Acid caused moderate skin irritation in rats (4.0 mg/kg, 227 mg/kg). In single-insult patch tests, 35% to 65% Stearic Acid caused no to moderate erythema and slight, if any, edema to the skin of rabbits. In maximization studies, 1% Stearic Acid caused weak reactions at challenge, and was considered a grade 1 sensitizer. Stearic Acid at a concentration of 2.8% did not cause photosensitization in guinea pigs (Elder 1987).

Undiluted Octyl Stearate produced at most minimal or moderate skin irritation in rabbits. Application of the stearate to the skin of rabbits caused irritation after 60 days of treatment; vesicles and slight epidermal exfoliation were observed, and Octyl Stearate was considered "poorly tolerated." Microscopic changes in the treated skin included epidermal acanthosis and "congestive" dermatitis. Application of 10% aqueous Octyl Stearate daily for 60 days caused irritation (vesicles) in the skin

of rabbits, but was "relatively well tolerated." No significant lesions were observed at microscopic examination of the treated skin (Elder 1985b).

GENOTOXICITY

A micronucleated polychromatic erythrocyte (MPCE) assay was used to determine the genotoxicity of Octyldodecyl Stearoyl Stearate tested under a trade name. CD-1 mice (5/sex/group) were gavaged with a single dose of 2.0, 5.0, or 10.0 ml/kg Octyldodecyl Stearoyl Stearate. One negative-control group was designated for each of the three runs of each treatment group. One group was designated as the positive control. Five male and five female mice were killed from each dose and vehicle control at 24, 48, and 72 hours after the initiation of treatment. Five mice from each sex were killed from the positive-control group 24 hours after treatment. The positive control depressed the polychromatic erythrocyte/normochromatic erythrocyte (PCE/NCE) ratio and showed a statistically significant increase in MPCEs. The mean numbers of MPCEs in 1000 PCEs were 58.8 and 65.2 for the male and female mice, respectively, which fulfilled the criteria for a valid assay. No significant increases occurred in the proportion of MPCEs in the test groups compared to the concurrent negative-control groups (Sitek Research Laboratories 1994a).

A *Salmonella typhimurium* gene mutation assay was used to evaluate Octyldodecyl Stearoyl Stearate for its ability to induce mutations in strains TA98, TA100, TA1535, TA1537, and TA1538. Octyldodecyl Stearoyl Stearate was dosed at concentrations of 1.0, 5.0, 10.0, 50.0, and 100.0 μl/plate. The positive controls and Octyldodecyl Stearoyl Stearate were tested with and without S-9 activation. All test concentrations, including the positive and negative controls, were tested in triplicate and a confirmation assay was performed. Octyldodecyl Stearoyl Stearate and control treatments were performed under ultraviolet (UV)-filtered lights to avoid photoinactivation. Positive controls were considered acceptable because the treated strains had reversion frequencies three times or greater than the mean reversion frequency of the solvent control plates in all positive-control cultures with and without S-9 activation. Octyldodecyl Stearoyl Stearate did not induce any positive increase in the number of revertant colonies for any of the tester strains with or without S-9 activation (Sitek Research Laboratories 1994b).

Related Ingredients

Stearic Acid did not induce an increase of mitotic crossovers during in vitro mutagenicity assays. It was inactive during aneuploidy induction tests, and was nonmutagenic in the Ames test (Elder 1987).

CARCINOGENICITY

No data on the carcinogenicity of Octyldodecyl Stearoyl Stearate were available.

Related Ingredients

Mice that received single or repeated subcutaneous (SC) injections of Stearic Acid (up to 82 mg) had low incidences of carcinomas, sarcomas, and lymphomas. Mice fed up to 50 g/kg/day Stearic Acid did not develop neoplasms (Elder 1987).

CLINICAL ASSESSMENT OF SAFETY

The human irritancy potential of an eyeshadow pencil having 10.4% Octyldodecyl Stearoyl Stearate was evaluated in a single-insult patch test using 19 subjects. The PII was 0/8, and no differences in irritancy were observed between subjects of the test and control groups.

A concealer containing 5.0% Octyldodecyl Stearoyl Stearate was tested for primary irritation using 20 subjects. The PII was 0.08, and no significant differences in irritancy were observed between test subjects and controls. A lipstick having 15.0% Octyldodecyl Stearoyl Stearate was similarly tested using 18 subjects. The PII was 0.00/8.00, and no differences in irritancy were observed between groups (CTFA 1998b).

Thirteen volunteers, 10 of whom completed the study, were used in a cumulative irritation study of an eyeshadow having 10.4% Octyldodecyl Stearoyl Stearate. The test material was applied to the skin of the back 21 times for 23-hour intervals. Scoring for cumulative irritation and reapplication of the eyeshadow occurred every 24 hours. The test sites were covered with closed Parke-Davis patches with Webril. The total score was 1/630, and the eyeshadow was classified as a mild irritant (Hill Top Research 1983a).

The same eyeshadow (10.4%) was evaluated in a repeat-insult patch test using 107 subjects. Applications were made three times weekly during the 22-day induction period. The test material was applied for 24 hours to the skin of the back under a closed patch, and the skin sites were scored 48 or 72 hours after application. Challenge applications were made using 24-hour occlusive patches. No evidence of contact sensitization was observed in any of the test subjects (Hill Top Research 1983b).

A lipstick containing 7.8% Octyldodecyl Stearoyl Stearate was tested in a repeat-insult patch test using 87 panelists, 85 of whom completed the study. Occlusive patches containing the test materials were applied to the skin of the upper back for 24 hours, three times weekly, for 3 weeks. Challenge applications were made 3 weeks after the last induction treatment, and the skin sites were scored 24 and 48 hours after patch removal. None of the subjects had erythematous responses during induction or challenge, and the investigators concluded that the lipstick did not have allergic sensitization potential (CTFA 1998b).

The contact sensitization potential of a concealer containing 5.0% Octyldodecyl Stearoyl Stearate was determined using a maximization test. Patches were applied to the outer arm throughout three phases: pretesting, induction, and challenge. In the pretesting phase, approximately 0.1 g of the material was applied to a skin site under a 15-mm Webril patch, which was fixed to the skin with occlusive tape (Blenderm) and covered with Scanpor tape. The patch was removed after 48 hours and the skin site was examined for signs of irritation. During the induction phase, ~0.1 ml of aqueous sodium lauryl sulfate (SLS,

1%) was applied to a different site and similarly covered for 24 hours. After removal of the SLS patch, 0.1 g of the test material was applied to the same site and covered with an occlusive patch. This patch was removed after 48 or 72 hours, when the site was examined for irritation. This procedure was repeated for a total of five induction exposures. If irritation developed during induction, the 24-hour SLS patch was eliminated and only the test material was administered, after a 24-hour period, during which no patch was applied. After a 10-day nontreatment period, a new skin site on the opposite arm was treated with 0.1 ml of 10.0% SLS under an occlusive patch. The site was then challenged with a single application of the test material, and this patch was removed after 48 hours. The treatment site was examined for irritation 1 and 24 hours after patch removal. None of the 27 subjects had adverse reactions, and no contact sensitization was observed (Ivy Laboratories 1991).

A clinical use study was performed using the same lipstick and 62 female subjects. The women applied the lipstick at least twice daily for 3 weeks. No clinical changes were observed after use of the lipstick (CTFA 1998b).

Related Ingredients

Octyl Dodecanol at a concentration of 100% caused mild irritation in 1 of 40 subjects during a 24-hour single-insult patch test; in a similar test, a moisturizing cream (4.0%) was nonirritating or minimally irritating. Occlusive patches containing 0.05 g (undiluted) Octyl Dodecanol were affixed to the backs of 50 adult males. The patches were removed at 48 hours and the treated sites were evaluated 30 minutes later and at 72 to 120 hours. No signs of irritation were observed. When 3% Octyl Dodecanol was patch tested daily for 21 consecutive days, the alcohol was "essentially nonirritating" or "slightly irritating."

No signs of sensitization were observed when 3% to 10.2% Octyl Dodecanol was tested in a Draize-Shelanski repeat-insult patch test. In other studies, no signs of phototoxicity or photosensitization were observed when a lipstick containing 10.2% Octyl Dodecanol was tested using 23 subjects (Elder 1985a).

Stearic Acid was nonirritating in clinical primary or cumulative irritation studies at concentrations of 100% or 40% to 50% in mineral oil. Cosmetic formulations containing up to 93% Stearic Acid and other fatty acids caused mild to intense erythema, but the reactions were not considered related to the fatty acid content of the products. Stearic Acid at concentrations up to 13% was not a sensitizer, and formulations containing 1% to 13% Stearic Acid were not photosensitizing (Elder 1987).

A suntan lotion and protective facial cream containing 7.6% Octyl Stearate were applied to the skin of 56 subjects daily under 24-hour closed patches for a total of 10 induction applications; after a 10- to 14-day nontreatment period, a 24-hour challenge patch was applied. No signs of irritation or sensitization were observed. In a phototoxicity study using the same formulations (10 subjects), no significant reactions were noted. In a photosensitization study on the same formulations (27 subjects), slight reactions were observed in 4 subjects during induction. One had erythema at challenge, and three subjects only reacted during induction. The investigator concluded that the formulations did not produce photosensitization (Elder 1985b).

SUMMARY

Octyldodecyl Stearoyl Stearate is an ester that functions as a skin-conditioning agent and viscosity-increasing agent in cosmetic products. In 1998, it was reported used in 86 cosmetic formulations. Data submitted by industry indicated that Octyldodecyl Stearoyl Stearate historically was used at concentrations in the 10% to 25% range, but in current data the maximum concentration is in the 5% to 23% range.

Little acute toxicity was reported in animal tests of Octyldodecyl Stearoyl Stearate, Stearic Acid, and Octyl Stearate.

A formulation having 20.6% Octyldodecyl Stearoyl Stearate was classified as minimally to mildly irritating in an in vitro ocular irritation assay. Rabbits treated three times with a formulation having 7.5% of the ingredient had moderate irritation. Formulations having 7.8%, 10.0%, and 12.7% Octyldodecyl Stearoyl Stearate were nonirritating to mildly irritating in the Draize ocular irritation test.

An eyeshadow having 7.5% Octyldodecyl Stearoyl Stearate was moderately irritating to the skin of rabbits, with a PII of 3.89/8. In two primary irritation studies and a 4-day cumulative irritation study, however, formulations having 7.8% Octyldodecyl Stearoyl Stearate were nonirritating to minimally irritating, with PIIs of 0 to 0.67/8, and a single application of the ingredient at 10% produced no irritation.

In clinical single-insult patch tests using up to 20 subjects, formulations having 5.0% to 15.0% Octyldodecyl Stearoyl Stearate were nonirritating to mild (PIIs 0 to 0.08/8). In a cumulative irritation study, a formulation having 10.4% Octyldodecyl Stearoyl Stearate caused mild irritation when tested using 10 subjects. Formulations having 5.0% to 10.4% Octyldodecyl Stearoyl Stearate were nonsensitizing in two repeat-insult patch tests using 27 to 85 panelists and a maximization test using 107 subjects. No adverse effects were observed in 62 women who took part in a 3-week in-use study of a formulation having 7.8% Octyldodecyl Stearoyl Stearate.

As a further basis for the assessment of safety of Octyldodecyl Stearoyl Stearate, data on related ingredients (Octyl Dodecanol, Stearic Acid, and Octyl Stearate) were included in this review.

Related Ingredients

Fatty acids are digested from the diet and esterified to glycerol. Stearic Acid is the most poorly absorbed of the common fatty acids. Free fatty acids readily cross the placental barrier and are stored in the tissues or oxidized for energy.

Undiluted Octyl Dodecanol was nontoxic during acute oral and dermal studies using rats and guinea pigs. Stearic Acid was nontoxic during acute oral studies using rats, but caused toxicity during subchronic studies. Rabbits treated topically with the acid were not affected adversely, and mild erythema and slight

induration were observed when Stearic Acid was administered intradermally to guinea pigs and rabbits. Octyl Stearate had very low acute oral toxicity in rats and mice.

Octyl Dodecanol caused no to minimal ocular irritation in rabbits when administered at concentrations up to 100%. Octyl Dodecanol (100%) caused primary skin irritation scores of 0/4 to 1.13/4 in studies using rabbits, and a concentration of 30% was nonirritating. Technical grade Octyl Dodecanol, however, caused moderate to severe irritation in the skin of rabbits, guinea pigs, and rats, but was nonirritating in the skin of miniature swine. A formulation containing 4% Octyl Dodecanol was not to mildly irritating in the skin of rabbits. Stearic Acid was not to moderately irritating in studies using rabbits and rats, and did not cause photosensitization in guinea pigs. In studies using rabbits, undiluted Octyl Stearate caused slight, transient ocular irritation and, at most, minimal to moderate skin irritation.

Stearic Acid did not induce mitotic crossovers and aneuploidy, and was nonmutagenic in the Ames test. In an MPCE genotoxicity assay Octyldodecyl Stearoyl Stearate produced no significant increases in the proportion of MPCE in the test groups compared to the concurrent negative-control groups. In a Salmonella typhimurium *gene mutation assay Octyldodecyl Stearoyl Stearate did not induce any positive increase in the number of revertant colonies for any of the tester strains with or without S-9 activation. In a feeding study using mice, Stearic Acid was noncarcinogenic at doses up to 50 g/kg/day. Mice given SC injections of the acid had low incidences of carcinomas, sarcomas, and lymphomas.*

In clinical studies, concentrations of up to 100% Octyl Dodecanol were not to mildly irritating, nonsensitizing, nonphototoxic, and nonphotosensitizing. Stearic Acid was nonirritating at concentrations up to 100%, and at concentrations up to 13% it was nonsensitizing and nonphotosensitizing. Octyl Stearate (7.6%) in formulation was nonirritating, nonsensitizing, and nonphotosensitizing.

DISCUSSION

Section 1, paragraph (p) of the Cosmetic Ingredient Review (CIR) Procedures states that "a lack of information about an ingredient shall not be sufficient to justify a determination of safety." In accordance with Section 30(j)(2)(A) of the Procedures, the Expert Panel informed the public of its decision that the data on Octyldodecyl Stearoyl Stearate were not sufficient for determining whether the ingredients, under relevant conditions of use, were either safe or unsafe.

In response to specific requests for data, current concentration of use, dermal irritation and sensitization, and ocular toxicity data were received. In addition, genotoxicity, skin irritation/sensitization, ocular irritation, animal toxicity, cosmetic use, and chemical and physical properties data were provided. These data support the absence of any significant acute or chronic toxicity associated with this ingredient, and demonstrate that skin irritation or sensitization is unlikely. The CIR Expert Panel reviewed the two genotoxicity studies, one micronucleated polychromatic erythrocyte assay and one Ames assay, and concluded that these data support the absence of a carcinogenesis risk. The Panel, however, did not find data that described or even predicted the skin penetration of Octyldodecyl Stearoyl Stearate. Absent such data, the Panel concluded that the following additional data are needed:

1. Chemical properties, including the octanol/water partition coefficient
2. If there is significant dermal absorbtion or if significant quantities of the ingredient may contact mucous membranes or be ingested, reproductive and developmental toxicity data may be needed.

In accordance with Section 45 of the CIR Procedures, the Expert Panel has issued a Final Safety Evaluation Report—Insufficient Data. When the requested new data are available, the Panel will reconsider the Final Report in accordance with Section 46 of the CIR Procedures, Amendment of a Final Report.

CONCLUSION

The CIR Expert Panel concludes that the available data are insufficient to support the safety of Octyldodecyl Stearoyl Stearate for use in cosmetic products.

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Final Amended Report on the Safety Assessment of Octyldodecyl Stearoyl Stearate[1]

Octyldodecyl Stearoyl Stearate is an ester that functions as a skin-conditioning agent and viscosity-increasing agent. It is reported to be used in 105 cosmetic products at concentrations from 2% to 15%. In an isolated human skin permeation and penetration study, 0.005% of the applied dose permeated the skin, around 3% was found in the epidermis, around 1.5% was in tape stripped skin layers, and around 95% stayed in the material applied to the skin. A formulation having 20.6% Octyldodecyl Stearoyl Stearate was classified as minimally to mildly irritating in an in vitro ocular irritation assay. Several tests of products containing from 7.5% to 12.7% Octyldodecyl Stearoyl Stearate using rabbits produced minimal to mild ocular irritation. One test of 100% Octyldodecyl Stearoyl Stearate (a trade compound) and another of 10% Octyldodecyl Stearoyl Stearate in corn oil using rabbits produced no ocular irritation. Tests using rabbits demonstrated that Octyldodecyl Stearoyl Stearate at use concentrations was non- to mildly irritating to skin; only one study reported moderate irritation. Octyldodecyl Stearoyl Stearate was not mutagenic, with or without S-9 activation, in an Ames test and did not produce a significant increase in micronucleated cells in a mouse in vivo study. In clinical single-insult patch tests at use concentrations, Octyldodecyl Stearoyl Stearate was nonirritating to mildly irritating; in a cumulative irritation study, it caused mild irritation. Octyldodecyl Stearoyl Stearate was nonsensitizing in clinical tests. Because few toxicity data were available on Octyldodecyl Stearoyl Stearate, summaries of data from existing safety assessments of related ingredients (Octyl Dodecanol, Stearic Acid, and Octyl Stearate) were included. Undiluted Octyl Dodecanol was nontoxic during acute oral and dermal studies using rats and guinea pigs. Stearic Acid was nontoxic to rats during acute oral studies, but caused toxicity during subchronic studies. Rabbits treated topically with the acid were not affected adversely, and mild erythema and slight induration were observed when Stearic Acid was administered intradermally to guinea pigs and rabbits. Octyl Stearate had very low acute oral toxicity in rats and mice. Octyl Dodecanol produced only transient mild ocular irritation in rabbits when administered at concentrations up to 100%. Octyl Dodecanol (30% and 100%) was nonirritating to skin in one study using rabbits. In another study using multiple species, 100% Octyl Dodecanol (described as technical grade) caused severe skin irritation in rabbits, moderate irritation in guinea pigs and rats, and no irritation in swine. Stearic Acid was non- to moderately irritating in animal studies, and did not cause photosensitization. In studies using rabbits, undiluted Octyl Stearate caused slight, transient ocular irritation, and minimal skin irritation. Stearic Acid did not induce mitotic crossovers and aneuploidy in *Saccharomyces cerevisiae*, and was nonmutagenic in the Ames test. In a feeding study using mice, Stearic Acid was noncarcinogenic at doses up to 50 g/kg/day. Mice given subcutaneous injections of the acid had low incidences of carcinomas, sarcomas, and lymphomas. In clinical studies, concentrations of up to 100% Octyl Dodecanol were non- to mildly irritating, nonsensitizing, nonphototoxic, and nonphotosensitizing. Stearic Acid was nonirritating at concentrations up to 100%, and at concentrations up to 13% it was nonsensitizing and nonphotosensitizing. Octyl Stearate (7.6%) in formulation was nonirritating, nonsensitizing, and nonphotosensitizing. Based on skin permeation and penetration data, the Panel does not expect any significant amount of Octyldodecyl Stearoyl Stearate to be systemically available. There is no evidence of systemic toxicity associated with any of the related chemicals reviewed in previous safety assessments. None of the available toxicology or clinical data suggest a concern about adverse skin reactions to Octyldodecyl Stearoyl Stearate, or to any of the related chemicals. There is no evidence of ocular toxicity, except for a mild, transient ocular irritation associated with Octyldodecyl Stearoyl Stearate and the related chemicals. Overall, Octyldodecyl Stearoyl Stearate was considered safe as used in cosmetics.

INTRODUCTION

This amended safety assessment updates and supersedes an earlier Cosmetic Ingredient Review (CIR) safety assessment of Octyldodecyl Stearoyl Stearate (CIR 1999). New data from human skin penetration and permeation studies have been incorporated in this report.

It remains true that there are only limited data on Octyldodecyl Stearoyl Stearate. Summaries of pertinent data from related ingredients have been added to this review as a further basis for the assessment of safety of Octyldodecyl Stearoyl Stearate. The CIR Expert Panel found that Stearyl Alcohol, Oleyl Alcohol, and Octyl Dodecanol are safe as currently used in cosmetics (Elder 1985a); Oleic Acid, Lauric Acid, Palmitic Acid, Myristic Acid, and Stearic Acid are safe in the present practices of use and concentration in cosmetics (Elder 1987); and that Butyl, Cetyl, Isobutyl, Isocetyl, Isopropyl, Myristyl, and Octyl Stearate are safe as cosmetic ingredients in the present practices of use (Elder 1985b).

On the basis of the available data, including these additional data, the CIR Expert Panel is issuing this amended safety assessment.

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[1]Reviewed by the Cosmetic Ingredient Review Expert Panel.

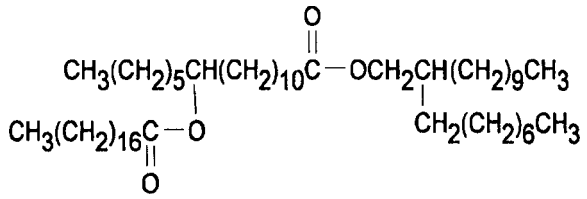

FIGURE 1
Octyldodecyl Stearoyl Stearate.

CHEMISTRY

Definition and Structure

Octyldodecyl Stearoyl Stearate

Octyldodecyl Stearoyl Stearate (CAS no. 90052-75-8) is an ester that conforms generally to the structure presented in Figure 1. Synonyms for Octyldodecyl Stearoyl Stearate include

- Octadecanoic Acid, 12-[(1-Oxooctadecyl)Oxy]-, 2-Octyldodecyl Ester;
- Octadecanoic Acid, 12-((1-Oxooctadecyl)Oxy)-2-Octyldodecyl Ester; and
- 12-[(1-Oxooxradecyl) Oxy]Octadecanoic Acid, 2-Octyldodecyl Ester (Pepe et al. 2002).

The formula for Octyldodecyl Stearoyl Stearate is given as $C_{56}H_{110}O_4$. Another synonym is 2-Octyldodecyl-12-Stearoyl Stearate (International Specialty Products 1998).

Summaries of Related Ingredients

Octyl Dodecanol. Octyl Dodecanol is the long-chain saturated fatty alcohol that conforms to the structure presented in Figure 2 (Elder 1985a).

Stearic Acid. Stearic Acid is found primarily as a glyceride in animal fats and oils. Lard and tallow, for example, contain approximately 10% and 20% Stearic Acid, respectively. Most vegetable oils contain 1% to 5% Stearic Acid. Cocoa butter contains approximately 35% Stearic Acid. Cosmetic grade Stearic Acid occurs as a mixture of varying amounts of Stearic and Palmitic Acids (Elder 1987).

Octyl Stearate. The stearates are esters of stearic acid; Octyl Stearate conforms generally to the formula in Figure 3 (Elder 1985b).

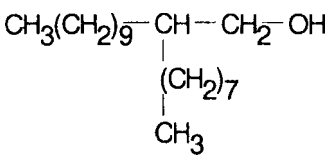

FIGURE 2
Octyl Dodecanol.

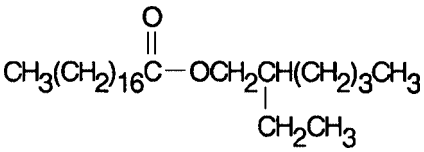

FIGURE 3
Octyl Stearate.

Chemical and Physical Properties

Octyldodecyl Stearoyl Stearate

The physical form of Octyldodecyl Stearoyl Stearate occurs as an amber, yellow liquid with a mild, characteristic odor. Its specifications include; saponification number of 115.0 to 135.0, specific gravity (25°C) range 0.86 to 0.88 and a refractive index (25°C) of 1.45 to 1.47 (ISP Van Dyke, Inc. 1997). In their material safety data sheet (MSDS), International Specialty Products (1998) describes Ceraphyl 847 (trade name for Octyldodecyl Stearoyl Stearate) as a straw white to yellow colored liquid with a fatty odor, a specific gravity of 0.872, and a molecular weight of 846.87. The MSDS also notes that carbon dioxide and monoxide may be formed when this material is heated to decomposition.

Octyldodecyl Stearoyl Stearate is soluble in silicones, esters, mineral oil, vegetable oils, alcohols, aliphatic, aromatic and chlorinated hydrocarbons and is insoluble in water. It has a theoretical molecular weight of 846, a freezing point of −15°C, and a flash point of over 180°C (Alzo, Inc. 1998). Octyldodecyl Stearoyl Stearate is partly soluble in 95% ethanol, propylene glycol, glycerine, 70% sorbitol and PEG 400 (Trivent Chemical Company, Inc. 1998).

Summaries of Related Ingredients

Stearic Acid. Stearic Acid occurs as hard, white or faintly yellow, glossy crystals or leaflets or as an amorphous white or yellow-white powder. It has a slight odor and tallow-like flavor. Stearic Acid is water-insoluble, slightly soluble in alcohol and benzene, soluble in chloroform, and very soluble in ether. The molecular weight is ~284.5 (Elder 1987).

Octyl Stearate. Octyl Stearate and the other Stearates are either oily liquids or waxy solids that typically are soluble in organic solvents such as chloroform and acetone. The molecular weight of Octyl Stearate is 396, the ester value is 144 to 154, the acid value and iodine value each have a maximum of 1.0. The Stearates can undergo conversion into stearic acid and the corresponding alcohol by chemical or enzymatic hydrolysis, conversion into amides by ammonolysis, and conversion into different esters by alcoholysis or transesterification. Purer grades of the saturated Stearates are not expected to autoxidize readily (Elder 1985b).

Method of Manufacture

Octyldodecyl Stearoyl Stearate

Octyldodecyl Stearoyl Stearate is manufactured by an inorganic acid catalyzed, high temperature (150°C to 160°C)

esterification reaction of guerbet alcohol. Guerbet alcohol is comprised of a mixture of alcohols (primarily C-20) and a mixture of fatty acids (primarily C-18) with no impurities. The product is neutralized to a water-soluble soap, washed to purity, dried, and filtered (Alzo, Inc. 1998).

Summaries of Related Ingredients

Octyl Dodecanol. Octyl Dodecanol is produced by the condensation of two molecules of decyl alcohol, and occurs naturally in small quantities as components of wax esters in plants (Elder 1985a).

Stearic Acid. Methods of processing Stearic Acid include hydrolysis of tallow or hydrogenation of unsaturated fatty acids in cottonseed and other vegetable oils, followed by fractional distillation or crystallization. Concentrations of Stearic Acid as great as 95 to 99% have been reported from the hydrogenation of unsaturated fatty acids (Elder 1987).

Octyl Stearate. The Stearates are prepared by esterification of stearic acid with the appropriate alcohol in the presence of an acid catalyst. The reaction products are refined either by catalyst neutralization, vacuum distillation, or various decolorization-deodorization techniques to remove residual traces of alcohol (Elder 1985b).

Impurities

Octyldodecyl Stearoyl Stearate

Octyldodecyl Stearoyl Stearate is composed of Stearic Acid (2.5% max.), Octyldodecanol (5.0% max.), Octyldodecyl Hydroxystearate (5.0% max.), and Octyldodecyl Stearoyl Stearate (88.0% max.) (Alzo, Inc. 1998).

Summaries of Related Ingredients

Stearic Acid. Stearic Acid contains varying amounts of unsaponifiable matter (0.3% max.), and can contain glyceryl monostearate (0.07% max.). Typical impurities are glyceryl monomyristate (0.07% max.), 9-hexadecanoic acid, 9,12-octadecadienoic acid (Elder 1987).

USE

Cosmetic

Octyldodecyl Stearoyl Stearate

Octyldodecyl Stearoyl Stearate functions as a skin conditioning agent—occlusive and viscosity increasing agent—nonaqueous in cosmetic product formulations (Pepe et al. 2002). In 2001, Octyldodecyl Stearoyl Stearate was reported to the Food and Drug Administration (FDA) by industry to be used in 105 cosmetic formulations, representing a range of product types, as shown in Table 1 (FDA 2001). Table 1 also shows product types in which Octyldodecyl Stearoyl Stearate is reported to be used at the given concentrations (CTFA 2001). This ingredient is reportedly used in some product categories, but the concentrations of use are not available. In other cases, information regarding use concentration for a specific product categories is provided, but the number of such products is not known.

The European Commission (EC) has not restricted the use of Octyldodecyl Stearoyl Stearate in cosmetic products (EC 2002).

Octyldodecyl Stearoyl Stearate had been included in the list of ingredients for which there is precedence for use in all cosmetics in Japan (Elder 1999). Japan no longer maintains a list of ingredients for which there is precedence for use. In the current Ministry of Health, Labor and Welfare (MHLW) regulations, Octyldodecyl Stearoyl Stearate is not included on a negative list (MHLW 2000a), on a list of ingredients for which there are restrictions to use in cosmetics (MHLW 2000b), or on a list of quasi-drugs for which listing is required (MHLW 2000c).

ABSORPTION, DISTRIBUTION, METABOLISM, AND EXCRETION

Octyldodecyl Stearoyl Stearate

An-eX Analytical Services, Ltd. (An-eX 2001) conducted an in vitro study of skin penetration and permeation of Octyldodecyl Stearoyl Stearate. [^{14}C]Octyldodecyl Stearoyl Stearate at a concentration of 10% in a safflower oil vehicle with a target activity level of 200 μCi/g was used in the study. Skin samples were obtained from cosmetic reduction surgery (site not identified) from four human female donors. Subcutaneous fat was removed by dissection and the skin was heated (60°C for 45 s) to and separate the dermis from the epidermis. The epidermis was dried, frozen, and thawed immediately prior to mounting in a Franz-type diffusion cell. The temperature of the skin layer was maintained at 32.0°C $\pm$ 1°C by placing the apparatus in a water bath. Samples (200 μl) were taken at 4, 8, 12, 24, and 48 h and the presence of ^{14}C determined by liquid scintillation counting. The skin was removed from the diffusion cell, and tape stripped. The total recovery of the radioactivity was 98.7% $\pm$ 1.1% of the applied dose. The distribution of the ^{14}C radiolabel at 48 h is shown in Table 2. Permeation at 48 h was 0.023 $\pm$ 0.005 μg/cm^2, representing 0.005% $\pm$ 0.001% of the applied dose. Permeation at 24 h was higher, but the authors cautioned that the actual scintillation counts measured in the receptor fluid were very close to background levels. A total of 4% to 5% of the label was found in the tape strips and remaining epidermis combined.

Summaries of Related Ingredients

Octyl Dodecanol. No data on absorption, distribution, metabolism, or excretion of Octyl Dodecanol were available (Elder 1985a).

Stearic Acid. Stearic Acid and other fatty acids are digested from the diet, absorbed in micellar aggregates, and transported after esterification to glycerol in chylomicrons and very low density lipoproteins. Stearic Acid is primarily transported via the lymph system. Fatty acids originating from adipose tissue stores are either bound to serum albumin or remain unesterified in the blood. Stearic Acid was the most poorly absorbed of the common fatty acids; the digestibility of fatty acids decreased

TABLE 1
Use of Octyldodecyl Stearoyl Stearate in Cosmetic Products

Product category (total no. formulations in category) (FDA 2001)	Total no. of formulations containing ingredient (FDA 2001)	Current concentration of use (CTFA 2001) (%)
Eyebrow pencil (99)	2	—
Eyeliner (533)	1	4
Eye shadow (551)	30	4–10
Other eye makeup preparations (151)	2	—
Powders (dusting and talcum)—excluding face (272)	2	4
Other fragrance preparations (173)	1	—
Blushers—all types (243)	8	2–7
Face powders (301)	32	2–7
Foundations (319)	5	4–9
Lipstick (942)	1	5–10
Makeup bases (136)	5	10
Rouges (16)	1	—
Other makeup preparations (186)	1	5
Cuticle softeners (19)	1	—
Nail creams and lotions (15)	1	—
Cleansing preparations (733)	3	—
Face and neck creams, lotions, etc.—excluding shaving (304)	1	4
Body and hand creams, lotions, etc.—excluding shaving (827)	1	15
Moisturizing preparations (881)	4	—
Night preparations (200)	1	—
Paste masks/mud packs (269)	1	—
Other skin care preparations (715)	2	—
Suntan gels, creams, and liquids	—	8
2001 total uses/ranges for Octyldodecyl Stearoyl Stearate	105	2–15

with increased fatty acid chain length. Stearic Acid metabolites are detected in the heart, liver, lungs, spleen, kidneys, muscles, intestines, adrenal glands, blood, and lymph, and in adipose, mucosal, and dental tissues after administration of radioactive Stearic Acid to rats, dogs, sheep, chicks, frogs, and humans. Uptake and transport of fatty acids into the brain has been observed, and free fatty acids readily cross the placental barrier in rabbits, guinea pigs, rats, and humans. Fatty acids that are taken up by tissues are either stored in the form of triglycerides or oxidized for energy (Elder 1987).

TABLE 2
Forty-eight-hour distribution of ^{14}C radiolabel in penetration/permeation study (An-eX 2001)

Site	% applied dose	Octyldodecyl Stearoyl Stearate ($\mu g/cm^2$)
48-Hour rinse	94.18 ± 1.39	477.4 ± 16.1
Tape strips 1–4	1.051 ± 0.162	5.33 ± 0.82
Tape strips 5–12	0.433 ± 0.101	2.18 ± 0.50
Remaining epidermis	3.021 ± 0.406	15.12 ± 1.90
Permeated	0.005 ± 0.001	0.023 ± 0.005
Total recovery	98.69 ± 1.12	

Octyl Stearate. No data on absorption or distribution of Octyl Stearate were available. These esters are generally metabolized to the corresponding alcohol and fatty acid, oxidized to carbon dioxide and water, and excreted (Elder 1985b).

ANIMAL TOXICOLOGY

Octyldodecyl Stearoyl Stearate

Octyldodecyl Stearoyl Stearate, tested as a trade compound at an oral dose of 5.0 g/kg in 10 rats (5 of each sex) for 14 days, produced no deaths (Wells Laboratories, Inc. 1993). Octyldodecyl Stearoyl Stearate, tested as a trade compound, had an oral LD_{50} of >20 g/kg in albino rats (Food and Drug Research Labs, Inc. 1983).

Summaries of Related Ingredients

Octyl Dodecanol. No deaths were observed during acute oral toxicity studies when 5 to 10 rats were treated with 5 g/kg of undiluted Octyl Dodecanol or with a lipstick (25 g/kg, diluted to 50%) containing 10.2% Octyl Dodecanol (1.28 g/kg total dose of Octyl Dodecanol). In an acute dermal toxicity study, intact and abraded skin sites of six guinea pigs were treated with 3.0 g/kg of the undiluted alcohol under occlusive patches. No deaths occurred as a result of treatment, and no gross lesions were observed at necropsy (Elder 1985a).

Stearic Acid. No signs of acute toxicity were observed when Stearic Acid or cosmetic formulations containing Stearic Acid at concentrations up to 13% were given orally to rats at doses of 15 to 19 g/kg. In subchronic oral studies, Stearic Acid (5% to 50%) caused thrombosis, aortic atherosclerosis, anorexia, and mortality in rats. Chicks fed 5% Stearic Acid had no signs of toxicity. Topical applications of 5 g/kg Stearic Acid to rabbits did not cause adverse effects. Intradermal administration of 10 to 100 mM Stearic Acid caused mild erythema and slight induration in guinea pigs and rabbits (Elder 1987).

Octyl Stearate. Octyl Stearate generally had "very low" acute oral toxicity in rats and mice. Undiluted Octyl Stearate at a dose of 8 ml/kg did not cause deaths in five rats per sex (Elder 1985b).

Ocular Irritation

Octyldodecyl Stearoyl Stearate

An EYETEX in vitro irritation assay was performed on a nail cuticle pencil containing 20.6% Octyldodecyl Stearoyl Stearate. The test material produced scores consistent with minimal to mild irritation (CTFA 1998).

An undiluted eyeliner containing 7.5% Octyldodecyl Stearoyl Stearate was applied three times to the unrinsed eyes of six rabbits. One rabbit had conjunctival scores of 6, 2, and 2 on days 1, 3, and 4, respectively, and a corneal score of 5 on day 1. Another had a conjunctival score of 4 on day 1. None of the rabbits had signs of ocular toxicity on day 2 or 7. The total Draize scores were 4/110 on day 1 and 1/110 on days 3 and 4. The investigators concluded that the eye shadow was moderately irritating under the conditions of this study.

A concealer containing 12.7% Octyldodecyl Stearoyl Stearate was applied once to the unrinsed eyes of six rabbits. One rabbit each had conjunctival scores of 2 on days 1 and 2. None of the rabbits had signs of irritancy on days 3, 4, or 7. The total Draize scores were 1/110 on days 1 and 2 and the formulation was classified as mildly irritating.

In a third study, none of the six rabbits had signs of ocular irritation after treatment with a lipstick containing 7.8% Octyldodecyl Stearoyl Stearate. The lipstick was classified as nonirritating (CTFA 1998).

Octyldodecyl Stearoyl Stearate, tested as a trade compound, was instilled (0.1 ml) into the right conjunctival sac of six rabbits. The contralateral eye served as control. Eyes were not rinsed. Reactions were scored on days 1 to 4 and 7 according to the Draize scale. No reactions were observed (Consumer Product Testing 1978).

A single application of 0.1 ml of Octyldodecyl Stearoyl Stearate, at a 10% *w/w* dilution in corn oil, was instilled into one eye each of six rabbits. The contralateral eye served as the control and the eyes were not rinsed. Reactions were scored on days 1 to 3, and 4 and 7 if irritation persisted. No reactions were observed (Wells Laboratories, Inc. 1993).

Summaries of Related Ingredients

Octyl Dodecanol. Six rabbits were treated with 100% Octyl Dodecanol. The average ocular irritation scores were 4/110 at day 1 and 0/110 by day 4. In a second study using the same procedure, the scores were 1/110 at day 1 and 0/110 by day 4. Cosmetic formulations containing 3% to 10.2% Octyl Dodecanol caused either no ocular irritation or minimal, transient irritation in the eyes of rabbits (Elder 1985a).

Stearic Acid. In Draize tests, reactions ranged from "none" to mild, transient irritation, but there was no apparent relationship with the concentration of the Stearic Acid tested (Elder 1987).

Octyl Stearate. Undiluted Octyl Stearate caused slight, transient ocular irritation in rabbits (Elder 1985b).

Skin Irritation and Sensitization

Octyldodecyl Stearoyl Stearate

An undiluted eyeshadow containing 7.5% Octyldodecyl Stearoyl Stearate was moderately irritating to the skin in a single insult occlusive patch test using nine rabbits. Erythema and edema were observed at 2 and 24 h after application of the test material. The primary irritation index (PII) for the group was 3.89/8.00.

In a similar study, a concealer containing 7.8% Octyldodecyl Stearoyl Stearate was tested using nine rabbits. The skin sites were evaluated 2 and 24 h after application of the test material. No signs of irritancy were observed at 24 h, but erythema was observed at 2 h. The PII for the group was 0.67/8.00, and the formulation was classified as minimally irritating.

A lipstick containing 7.8% Octyldodecyl Stearoyl Stearate was tested similarly using nine rabbits. None of the animals had erythema or edema 2 or 24 h after application of the test material, and the PII was 0.00/8.00. In a 4-day cumulative study, the lipstick was "essentially non-irritating" (CTFA 1998).

Octyldodecyl Stearoyl Stearate, tested as a trade compound, was applied (0.5 ml) under a 24-h occlusive patch to abraded and intact sites on the back of six rabbits. Sites were examined for erythema and edema at 24 and 72 h. The maximum possible score was 8. The PII for OSS was 0.38. It was considered to have a "potential for slight irritation—rarely irritating to people" (Consumer Product Testing 1978).

A single dermal application of 0.5 ml of Octyldodecyl Stearoyl Stearate, at a 10% *w/w* dilution in corn oil, was applied to one abraded and one intact site on six New Zealand white rabbits. Each test site was observed for erythema and edema

24 and 72 h after application. The PII for this product was 0.0 (Wells Laboratories, Inc. 1993).

Summaries of Related Ingredients

Octyl Dodecanol. Octyl Dodecanol was applied for 24 h under occlusive patches to the skin of six rabbits during three studies. The irritation scores for a concentration of 100% were 1.13/4, 0.5/4, and 0/4. At a concentration of 30%, it produced scores of 0/4 for all three animals (Elder 1985a).

Technical grade Octyl Dodecanol (0.1 to 0.5 g) caused severe irritation (+++) to the skin of six albino rabbits and moderate irritation (++) to the skin of six Hartley guinea pigs and six Wistar rats. The compound was nonirritating (−) when applied to the skin of six Pitman-Moore miniature swine. For the study using rabbits, 0.1 g Octyl Dodecanol was applied for 24 h, the skin sites were graded, and the compound was reapplied for another 24 h. The treated skin sites were graded after Evans blue solution was injected intravenously. The rabbits were killed 1 h later, and skin samples were prepared. For the guinea pig study, two dorsal areas were clipped free of hair. One site was treated with 0.1 g for 24 h and the other was left untreated. The remainder of the study was identical to the one using rabbits. For the swine, the dorsal area was clipped free of hair, and 0.5 g Octyl Dodecanol was applied under occlusive patches for 48 h. Skin of the rabbits, guinea pigs, and rats had acanthosis, hyperkeratinization, swelling of cells, and proliferation of basal cells. Vasodilatation, edema, alteration of collagenous fibers, and mononuclear and polymorphonuclear leukocyte infiltration of the dermis were also observed (Elder 1985a).

A formulation containing 4% Octyl Dodecanol was nonirritating to mildly irritating (0/4 to 1.08/4) during primary skin irritation studies. Minimal to mild irritation was observed when a formulation containing 10.2% of the alcohol was applied to the skin of rabbits for 3 to 4 consecutive days. In these studies, the degree of irritation observed did not increase with the concentration tested (Elder 1985a).

Stearic Acid. No irritation was observed when Stearic Acid was applied (18 mmol %) to the skin of the external ear canals of albino rabbits over a period of 6 weeks. Slight local edema was observed when New Zealand white rabbits were treated with 2% Stearic Acid in formulation for 4 weeks. During a 13-week study, cosmetic formulations containing up to 5% Stearic Acid caused moderate skin irritation in rats (4.0 mg/kg, 227 mg/kg). In single-insult patch tests, 35% to 65% Stearic Acid caused no to moderate erythema and slight, if any, edema to the skin of rabbits. In maximization studies, 1% Stearic Acid caused weak reactions at challenge, and was considered a grade 1 sensitizer. Stearic Acid at a concentration of 2.8% did not cause photosensitization in guinea pigs (Elder 1987).

Octyl Stearate. Undiluted Octyl Stearate produced at most minimal or moderate skin irritation in rabbits. Application of the stearate to the skin of rabbits caused irritation after 60 days of treatment; vesicles and slight epidermal exfoliation were observed, and Octyl Stearate was considered "poorly tolerated." Microscopic changes in the treated skin included epidermal acanthosis and "congestive" dermatitis. Application of 10% aqueous Octyl Stearate daily for 60 days caused irritation (vesicles) in the skin of rabbits, but was "relatively well tolerated." No significant lesions were observed at microscopic examination of the treated skin (Elder 1985b).

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

No data on the reproductive and developmental toxicity of Octyldodecyl Stearoyl Stearate, Octyl Dodecanol, Stearic Acid, or Octyl Stearate were available. Female rats fed diets with 6.25% Butyl Stearate for 10 weeks were mated—no adverse effects on fertility, litter size, or survival of offspring were noted, although reduced fetal growth during both the preweaning and postweaning periods (up to 21 days) was found (Elder 1985b).

GENOTOXICITY

Octyldodecyl Stearoyl Stearate

A micronucleus assay was used to determine the genotoxicity of Octyldodecyl Stearoyl Stearate. A single dose of 2.0, 5.0 or 10.0 ml/kg Octyldodecyl Stearoyl Stearate was given to CD-1 mice (5/sex/group) by gavage. One negative-control group was designated for each of the three runs of each treatment group. A positive-control group received triethylenemelamine via intraperitoneal injection at a dose of 1 mg/kg. Five male and five female mice were killed from each dose and vehicle control at 24, 48, and 72 h after the initiation of treatment. Five mice from each sex were killed from the positive control group 24 h after treatment. The positive-control depressed the polychromatic erythrocyte to normochromatic erythrocyte (PCE/NCE) ratio and showed a statistically significant increase in micronucleated polychromatic erythrocytes (MPCEs). The mean numbers of MPCEs in 1000 PCEs were 58.8 and 65.2 for the male and female mice, respectively, which fulfilled the criteria for a valid assay. No significant increases occurred in the proportion of MPCEs in the test groups compared to the concurrent negative-control groups (Sitek Research Laboratories 1994a).

A *Salmonella typhimurium* gene mutation assay was used to evaluate Octyldodecyl Stearoyl Stearate using strains TA98, TA100, TA1535, TA1537, and TA1538. Octyldodecyl Stearoyl Stearate was used at concentrations of 1.0, 5.0, 10.0, 50.0, and 100.0 μl/plate. The positive controls and Octyldodecyl Stearoyl Stearate were tested with and without S-9 activation. All test concentrations, including the positive and negative controls, were tested in triplicate and a confirmation assay was performed. Octyldodecyl Stearoyl Stearate and control treatments were performed under ultraviolet (UV)-filtered lights to avoid photoinactivation. Positive controls were considered acceptable because the treated strains had reversion frequencies three times or greater than the mean reversion frequency of the solvent control plates in all positive control cultures with and without S-9 activation. Octyldodecyl Stearoyl Stearate did not induce any positive increase in the number of revertant colonies for any of

the tester strains with or without S-9 activation (Sitek Research Laboratories 1994b).

Summaries of Related Ingredients

Octyl Dodecanol. No genotoxicity tests were available on Octyl Dodecanol, but Stearyl Alcohol was nonmutagenic in the Ames test (Elder 1985a).

Stearic Acid. Stearic Acid did not increase mitotic aneuploidy and chromosome crossovers during in the D_6 strain of *Saccharomyces cerevisiae* in an vitro mutagenicity assay. It was nonmutagenic in the Ames test (Elder 1987).

Octyl Stearate. No genotoxicity tests were available on Octyl Stearate (Elder 1985b).

CARCINOGENICITY

Carcinogenicity data were not available for Octyldodecyl Stearoyl Stearate, or for Octyl Dodecanol or Octyl Stearate. Mice that received single or repeated subcutaneous (s.c.) injections of 0.05 to 1.0 mg Stearic Acid two times per week for up to 57 weeks had subcutaneous sarcomas at the injection site in only the low-dose group—no neoplasms were found in high-dose animals. Mice fed up to 0.3% Stearic Acid, in one study, or 50 g/kg/day Stearic Acid in another, did not develop neoplasms (Elder 1987).

CLINICAL ASSESSMENT OF SAFETY

Octyldodecyl Stearoyl Stearate

Thirteen volunteers, 10 of whom completed the study, were used in a cumulative irritation study of an eyeshadow having 10.4% Octyldodecyl Stearoyl Stearate. The test material was applied to the skin of the back 21 times for 23-h intervals. Scoring for cumulative irritation and reapplication of the eyeshadow occurred every 24 h. The test sites were patched. The total score was 1/630, and the eyeshadow was classified as a mild irritant (Hill Top Research 1983a).

The same eyeshadow (10.4%) was evaluated in a repeat insult patch test using 107 subjects. Applications were made three times weekly during the 22-day induction period. The test material was applied for 24 h to the skin of the back under a closed patch, and the skin sites were scored 48 or 72 h after application. Challenge applications were made using 24-h occlusive patches. No evidence of contact sensitization was observed in any of the test subjects (Hill Top Research 1983b).

The contact sensitization potential of a concealer containing 5.0% Octyldodecyl Stearoyl Stearate was determined using a maximization test. Patches were applied to the outer arm throughout three phases: pretesting, induction, and challenge. In the pretesting phase, approximately 0.1 g of the material was applied to a skin site under a 15-mm Webril patch, which was fixed to the skin with occlusive tape (Blenderm) and covered with Scanpor tape. The patch was removed after 48 h and the skin site was examined for signs of irritation. During the induction phase, ~0.1 ml of aqueous sodium lauryl sulfate (SLS, 1%) was applied to a different site and similarly covered for 24 h. After removal of the SLS patch, 0.1 g of the test material was applied to the same site and covered with an occlusive patch. This patch was removed after 48 or 72 h, when the site was examined for irritation. This procedure was repeated for a total of five induction exposures. If irritation developed during induction, the 24-h SLS patch was eliminated and only the test material was administered, after a 24-h period during which no patch was applied. After a 10-day nontreatment period, a new skin site on the opposite arm was treated with 0.1 ml of 10.0% SLS under an occlusive patch. The site was then challenged with a single application of the test material, and this patch was removed after 48 h. The treatment site was examined for irritation 1 h and 24 h after patch removal. None of the 27 subjects had adverse reactions, and no contact sensitization was observed (Ivy Laboratories 1991).

The human irritancy potential of an eyeshadow pencil having 10.4% Octyldodecyl Stearoyl Stearate was evaluated in a single-insult patch test using 19 subjects. The PII was 0/8, and no differences in irritancy were observed between subjects of the test and control groups (CTFA 1998).

A concealer containing 5.0% Octyldodecyl Stearoyl Stearate was tested for primary irritation using 20 subjects. The PII was 0.08, and no significant differences in irritancy were observed between test subjects and controls. A lipstick having 15.0% Octyldodecyl Stearoyl Stearate was similarly tested using 18 subjects. The PII was 0.00/8.00, and no differences in irritancy were observed between test subjects and control groups (CTFA 1998).

A lipstick containing 7.8% Octyldodecyl Stearoyl Stearate was tested in a repeat insult patch test using 87 panelists, 85 of whom completed the study. Occlusive patches containing the test materials were applied to the skin of the upper back for 24 h, three times weekly, for 3 weeks. Challenge applications were made 3 weeks after the last induction treatment, and the skin sites were scored 24 and 48 h after patch removal. None of the subjects had erythematous responses during induction or challenge, and the investigators concluded that the lipstick did not have allergic sensitization potential (CTFA 1998).

A clinical use study was performed using the same lipstick and 62 female subjects. The women applied the lipstick at least twice daily for 3 weeks. No clinical changes were observed after use of the lipstick (CTFA 1998).

Summaries of Related Ingredients

Octyl Dodecanol. Octyl Dodecanol at a concentration of 100% caused mild irritation in one of 40 subjects during a 24-h single-insult patch test. In a similar test, a moisturizing cream (4.0%) was nonirritating or minimally irritating. Occlusive patches containing 0.05 g (undiluted) Octyl Dodecanol were affixed to the backs of 50 adult males. The patches were removed at 48 h and the treated sites were evaluated 30 min later and at 72 to 120 h. No signs of irritation were observed. When 3% Octyl Dodecanol was patch-tested daily for 21 consecutive days, the

alcohol was "essentially nonirritating" or "slightly irritating" (Elder 1985a).

No signs of sensitization were observed when 3% to 10.2% Octyl Dodecanol was tested in a Draize-Shelanski repeat-insult patch test. In other studies, no signs of phototoxicity or photosensitization were observed when a lipstick containing 10.2% Octyl Dodecanol was tested using 23 subjects (Elder 1985a).

Stearic Acid. Stearic Acid was nonirritating in clinical primary or cumulative irritation studies at concentrations of 100% or 40% to 50% in mineral oil. Cosmetic formulations containing up to 93% of Stearic Acid and other fatty acids caused mild to intense erythema, but the reactions were not considered related to the fatty acid content of the products. Stearic Acid at concentrations up to 13% was not a sensitizer, and formulations containing 1% to 13% Stearic Acid were not photosensitizing (Elder 1987).

Octyl Stearate. A suntan lotion and protective facial cream containing 7.6% Octyl Stearate were applied to the skin of 56 subjects daily under 24-h closed patches for a total of 10 induction applications. After a 10 to 14-day nontreatment period, a 24-h challenge patch was applied. No signs of irritation or sensitization were observed. In a phototoxicity study using the same formulations (10 subjects), no significant reactions were noted. In a photosensitization study on the same formulations (27 subjects), slight reactions were observed in 4 subjects during induction. One had erythema at challenge, and three subjects only reacted during induction. The investigator concluded that the formulations did not produce photosensitization (Elder 1985b).

SUMMARY

Octyldodecyl Stearoyl Stearate is an ester of fatty alcohols and fatty acids that functions as a skin-conditioning agent and viscosity-increasing agent reported to be used in 105 cosmetic products. Data submitted by industry indicated that Octyldodecyl Stearoyl Stearate is used at concentrations from 2% to 15%.

In an isolated human skin permeation and penetration study, 0.005% of the applied Octyldodecyl Stearoyl Stearate permeated the skin, around 3% was found in the epidermis, around 1.5% was in tape stripped skin layers, and around 95% stayed in the material applied to the skin.

A formulation having 20.6% Octyldodecyl Stearoyl Stearate was classified as minimally to mildly irritating in an in vitro ocular irritation assay. Rabbits treated three times with a formulation having 7.5% of the ingredient had moderate irritation. Formulations having 7.8% and 12.7% Octyldodecyl Stearoyl Stearate were nonirritating to mildly irritating in the Draize ocular irritation test using rabbits. Octyldodecyl Stearoyl Stearate neat (a trade name product) and at 10% in corn oil produced no ocular irritation in rabbits.

An eyeshadow having 7.5% Octyldodecyl Stearoyl Stearate was moderately irritating to the skin of rabbits with a PII of 3.89/8. In two primary irritation studies and a 4-day cumulative irritation study, all using rabbits, formulations having 7.8% Octyldodecyl Stearoyl Stearate were nonirritating to minimally irritating, with PIIs of 0/8 to 0.67/8. A single application of Octyldodecyl Stearoyl Stearate at 10% produced no irritation in rabbits.

In clinical single insult patch tests using up to 20 subjects, formulations having 5.0% to 15.0% Octyldodecyl Stearoyl Stearate produced reactions that ranged from nonirritating to mild irritation (PIIs 0/8 to 0.08/8). In a cumulative irritation study, a formulation having 10.4% Octyldodecyl Stearoyl Stearate caused mild irritation when tested using 10 subjects. Formulations having 5.0%–10.4% Octyldodecyl Stearoyl Stearate were nonsensitizing in two repeat-insult patch tests using 27 to 85 panelists and a maximization test using 107 subjects. No adverse effects were observed in 62 women who took part in a 3-week in-use study of a formulation having 7.8% Octyldodecyl Stearoyl Stearate.

Because few toxicity data were available on Octyldodecyl Stearoyl Stearate, summary data from earlier safety assessments of Octyl Dodecanol, Stearic Acid, and Octyl Stearate were included in this review as a further basis for the assessment of safety.

Undiluted Octyl Dodecanol was nontoxic during acute oral and dermal studies using rats and guinea pigs. Stearic Acid was nontoxic during acute oral studies using rats, but caused toxicity during subchronic studies. Rabbits treated topically with the acid were not affected adversely, and mild erythema and slight induration were observed when Stearic Acid was administered intradermally to guinea pigs and rabbits. Octyl Stearate had very low acute oral toxicity in rats and mice.

Octyl Dodecanol caused no to minimal ocular irritation in rabbits when administered at concentrations up to 100%. Octyl Dodecanol (100%) caused primary skin irritation scores of 0/4 to 1.13/4 in studies using rabbits, and a concentration of 30% was nonirritating. Technical grade Octyl Dodecanol, however, caused moderate to severe irritation in the skin of rabbits, guinea pigs, and rats, but was nonirritating in the skin of miniature swine. A formulation containing 4% Octyl Dodecanol ranged from not irritating to mildly irritating in the skin of rabbits. Stearic Acid was nonirritating to moderately irritating in studies using rabbits and rats, and did not cause photosensitization in guinea pigs. In studies using rabbits, undiluted Octyl Stearate caused slight, transient ocular irritation, and, at most, minimal to moderate skin irritation.

Stearic Acid did not induce mitotic crossovers and aneuploidy, and was nonmutagenic in the Ames test. In an micronucleus assay, Octyldodecyl Stearoyl Stearate produced no significant increases in micronucleated erythrocytes in the test groups compared to the concurrent negative-control groups. In a *Salmonella typhimurium* gene mutation assay, Octyldodecyl Stearoyl Stearate did not induce any positive increase in the number of revertant colonies for any of the tester strains with or without S-9 activation. In a feeding study using mice, Stearic Acid was noncarcinogenic at doses up to 50 g/kg/day. Mice given s.c. injections of the acid had low incidences of carcinomas, sarcomas, and lymphomas.

In clinical studies, Octyl Dodecanol at concentrations of up to 100% produced reactions that ranged from nonirritating to mildly irritating, and were nonsensitizing, nonphototoxic, and nonphotosensitizing. Stearic Acid was nonirritating at concentrations up to 100%, and at concentrations up to 13% it was nonsensitizing and nonphotosensitizing. Octyl Stearate (7.6%) in formulation was nonirritating, nonsensitizing, and nonphotosensitizing.

DISCUSSION

The CIR Expert Panel had previously considered the available data on Octyldodecyl Stearoyl Stearate to be insufficient; the data needed were chemical properties, including the octanol/water partition coefficient, the extent of dermal absorption, and whether significant quantities of the ingredient may contact mucous membranes or be ingested. If a significant penetration or ingestion would occur, the Panel considered the possibility that reproductive and developmental toxicity data may be needed. Dermal absorption data were provided.

Skin permeation and penetration data using isolated human skin indicated that only a small portion of the applied dose permeates the skin (0.005%), only 4% to 5% actually enters the skin, and that almost 95% remained in the material applied to the skin. Based on these data, the Panel does not expect any significant amount of Octyldodecyl Stearoyl Stearate to be available to create a systemic exposure. Although few data are available on the systemic toxicity of Octyldodecyl Stearoyl Stearate, there is no systemic toxicity associated with any of the structurally related chemicals reviewed in previous safety assessments.

None of the available toxicology or clinical data suggest a concern about adverse skin reactions to Octyldodecyl Stearoyl Stearate. Only a mild, transient ocular irritation was associated with Octyldodecyl Stearoyl Stearate.

This ingredient is reportedly used in some product categories, but the concentrations of use are not available. In other cases, information regarding use concentration for a specific product categories is provided, but the number of such products is not known. Although there are gaps in knowledge about product use, the overall information available on the types of products in which this ingredient is used and at what concentration indicate a pattern of use. Within this overall pattern of use, the Panel considers this ingredient to be safe.

CONCLUSION

The CIR Expert Panel concludes that Octyldodecyl Stearoyl Stearate is safe for use in cosmetic products in the practices of use and concentration described in this safety assessment.

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Concentration of Use by FDA Product Category - Octyldodecyl Stearoyl Stearate

Product Category	Maximum Concentration of Use
Eyebrow pencils	0.75%
Eye shadows	1.4-18.5%
Other eye makeup preparations	0.5-3.2%
Hair tints	3.3%
Other hair coloring preparations	3.5%
Blushers	1.8-24%
Face powders	1.9-7.5%
Foundations	0.5-6.7%
Lipstick	3.4-28%
Makeup bases	6.1-24%
Rouges	25.4%
Other makeup preparations	1.9-3%
Face and neck products Not spray	 1%
Moisturizing products Not spray	 2-9%
Night products Not spray	 2.5%

Information collected in 2020

Table prepared October 7, 2020

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Carol Eisenmann, Ph.D.
Personal Care Products Council

DATE: September 29, 2022

SUBJECT: Octyldodecyl Stearoyl Stearate

Anonymous. 2022. Use Study Summary – Lip Balms Containing 28% Octyldodecyl Stearoyl Stearate.

September 2022

Use Study Summary – Lip Balms Containing 28% Octyldodecyl Stearoyl Stearate

Use tests under dermatological control were completed on 4 lip balms containing 28% Octyldodecyl Stearoyl Stearate (each lip balm was tested on 12 or 13 volunteers). The subjects used the product for 14 days, with a frequency of 3 to 5 times each day.

The conclusion was a good dermatological tolerance for each lip balm.

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Carol Eisenmann, Ph.D.
Personal Care Products Council

DATE: September 30, 2022

SUBJECT: Octyldodecyl Stearoyl Stearate

Anonymous. 2019. Repeated Insult Patch Test (makeup base containing 21.0112% Octyldodecyl Stearoyl Stearate).

[redacted]

FINAL REPORT

CLIENT: [redacted]

ATTENTION: [redacted]

Makeup base containing 21.0112% Octyldodecyl Stearoyl Stearate

TEST: Repeated Insult Patch Test
Protocol No.: [redacted]
Protocol Date: [redacted]

TEST MATERIAL: [redacted]

STUDY NUMBER: [redacted]

Reviewed by: [redacted], M.D.
Medical Director
Board Certified Dermatologist

Approved by: [redacted], Ph.D., CCRA, CCRC
Vice President, Clinical Evaluations

Approved by: [redacted]
Executive Vice President, Clinical Evaluations

[redacted]

[redacted]

[redacted]

[redacted]

QUALITY ASSURANCE UNIT STATEMENT

[redacted]

Study Number: [redacted]

[redacted] is responsible for auditing the conduct, content and reporting of all clinical trials that are conducted at [redacted]

This trial has been conducted in accordance with the Declaration of Helsinki, the ICH Guideline E6 for *Good Clinical Practice*, the requirements of 21 CFR Parts 50 and 56, other applicable laws and regulations, [redacted] Standard Operating Procedures, and the approved protocol.

The [redacted] has reviewed all data, records, and documents relating to this trial and also this Final Report. The following [redacted] representative signature certifies that all data, records, and documents relating to this trial and also this Final Report have been reviewed and are deemed to be acceptable, and that the trial conforms to all of the requirements as indicated above.

All records and documents pertaining to the conduct of this trial shall be retained in the [redacted] archives for a minimum of ten (10) years. At any time prior to the completion of the tenth archival year, a Sponsor may submit a written request to the [redacted] to obtain custody of trial records once the [redacted] archive period has been completed. This transfer shall be performed at the Sponsor's expense. In the absence of a written request, trial-related records shall be destroyed at the end of the [redacted] archive period with no further notice in a manner that renders them useless.

[redacted]

Quality Assurance Representative

4-26-19

Date

[redacted]

[redacted]

[redacted]

Objective:

To determine by repetitive epidermal contact the potential of a test material to induce primary or cumulative irritation and/or allergic contact sensitization.

Participants:

One hundred twelve (112) qualified subjects, male and female, ranging in age from 18 to 79 years, were selected for this evaluation. One hundred seven (107) subjects completed this study. The remaining subjects discontinued their participation for various reasons, none of which were related to the application of the test material.

Inclusion Criteria:

a. Male and female subjects, age 16[a] to 79 years.
b. Absence of any visible skin disease which might be confused with a skin reaction from the test material.
c. Prohibition of use of topical or systemic steroids and/or antihistamines for at least seven days prior to study initiation.
d. Completion of a Medical History Form and the understanding and signing of an Informed Consent Form.
e. Considered reliable and capable of following directions.

Exclusion Criteria:

a. Ill health.
b. Under a doctor's care or taking medication(s) which could influence the outcome of the study.
c. Females who are pregnant or nursing.
d. A history of adverse reactions to cosmetics or other personal care products.

Test Material:

[redacted]

Study Schedule:

Panel #	Initiation Date	Completion Date
[redacted]	March 4, 2019	April 12, 2019
	March 4, 2019	April 12, 2019

[a]With parental or guardian consent

[redacted]

Methodology:

The upper back between the scapulae served as the treatment area. Approximately 0.2 g of the test material, or an amount sufficient to cover the contact surface, was applied to the 3/4" x 3/4" absorbent pad portion of an adhesive dressing. This was then applied to the appropriate treatment site to form an occlusive patch.

Induction Phase:

Patches were applied three (3) times per week (e.g., Monday, Wednesday, and Friday) for a total of nine (9) applications. The site was marked to ensure the continuity of patch application. Following supervised removal and scoring of the first Induction patch, participants were instructed to remove all subsequent Induction patches at home, twenty-four hours after application. The evaluation of this site was made again just prior to re-application. If a participant was unable to report for an assigned test day, one (1) makeup day was permitted. This day was added to the Induction period.

With the exception of the first supervised Induction Patch reading, if any test site exhibited a moderate (2-level) reaction during the Induction Phase, application was moved to an adjacent area. Applications were discontinued for the remainder of this test phase, if a moderate (2-level) reaction was observed on this new test site. Applications would also be discontinued if marked (3-level) or severe (4-level) reactivity was noted.

Rest periods consisted of one day following each Tuesday and Thursday removal, and two days following each Saturday removal.

Challenge Phase:

Approximately two (2) weeks after the final Induction patch application, a Challenge patch was applied to a virgin test site adjacent to the original Induction patch site, following the same procedure described for Induction. The patch was removed and the site scored at the clinic Day 1 and Day 3 post-application.

[redacted]

Methodology (continued):

Evaluation Criteria (Erythema and additional Dermal Sequelae):

0	=	No visible skin reaction	E	=	Edema
0.5	=	Barely perceptible	D	=	Dryness
1	=	Mild	S	=	Staining
2	=	Moderate	P	=	Papules
3	=	Marked	V	=	Vesicles
4	=	Severe	B	=	Bullae
			U	=	Ulceration
			Sp	=	Spreading

Erythema was scored numerically according to this key. If present, additional Dermal Sequelae were indicated by the appropriate letter code and a numerical value for severity.

Adverse Events: On 3/26/19, Subject #35 on Panel [redacted] informed the clinical staff that she took one dose of Promethazine for a cough on 3/20/19. The Principal Investigator permitted her to continue participation in this clinical trial.

[redacted]

Amendments: There were no amendments.

Deviations: There were no deviations.

Results: The results of each participant are appended (Table 1).

Observations remained negative throughout the test interval.

Subject demographics are presented in Table 2.

Photograph of sample, sample receipt form and protocol are appended.

[redacted]

Summary: Under the conditions of this study, test material, [redacted] indicated no potential for dermal irritation or allergic contact sensitization.

[redacted]

[redacted]

Table 1

[redacted]

Individual Results

[redacted]

Subject Number	Day1*	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site Day 1*	Day 3
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0	---DNC---	
23	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0	0	0	0	0
27	0	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0	0

Day 1* = Supervised removal
DNC = Did not complete study

[redacted]

Table 1
(continued)
[redacted]

Individual Results

[redacted]

Subject Number	Day1*	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site Day 1*	Day 3
30	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0	0	0	0
36	----------DID NOT COMPLETE STUDY----------											
37	0	0	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0	0
44	0	0	0	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0	0
51	----------DID NOT COMPLETE STUDY----------											
52	0	0	0	0	0	0	0	0	0	0	0	0
53	0	0	0	0	0	0	0	0	0	0	0	0
54	0	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0	0	0	0	0

Day 1* = Supervised removal

Table 1
(continued)

[redacted]

Individual Results

[redacted]

Subject Number	Induction Phase									Virgin Challenge Site	
	Day1*	1	2	3	4	5	6	7	8	9	Day 1*	Day 3
[redacted]												
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	----------DID NOT COMPLETE STUDY----------									
11	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0	0
18	-†	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0	0	0	0
26	----------SUBJECT NUMBER NOT ASSIGNED----------											
27	0	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0[m]	0	0	0	0
[redacted]												

Day 1* = Supervised removal
† = Unsupervised removal
m = Additional makeup day granted at the discretion of the clinic supervisor

[redacted]

Table 1
(continued)

[redacted]

Individual Results

[redacted]

Subject Number	Day1*	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site Day 1*	Day 3
30	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0	0	0	0
36	0	0	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0	0
44	0	0	0	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0	0
51	0	0	0	0	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0	0	0	0	0
53	0	0	0	0	0	0	----------DID NOT COMPLETE STUDY--------					
54	0	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0	0	0	0	0
57	0	0	0	0	0	0	0	0	0	0	0	0

Day 1* = Supervised removal

Table 2

[redacted]

Subject Demographics

Subject Number	Initials	Age	Gender
1	[redacted]	47	F
2		73	F
3		62	F
4		39	F
5		37	F
6		74	M
7		77	M
8		49	F
9		73	F
10		43	M
11		52	F
12		65	F
13		24	M
14		34	F
15		62	M
16		47	M
17		47	F
18		33	M
19		33	F
20		66	F
21		74	F
22		51	F
23		27	F
24		48	F
25		52	F
26		47	F
27		34	M
28		37	F
29		64	F

[redacted]

[redacted]

Table 2
(continued)
[redacted]

Subject Demographics

[redacted]

Subject Number	Initials	Age	Gender
30	[redacted]	67	F
31		60	M
32		67	M
33		49	M
34		46	F
35		78	F
36		35	M
37		79	F
38		73	F
39		78	F
40		71	F
41		76	F
42		48	F
43		78	F
44		78	M
45		74	F
46		25	M
47		52	F
48		31	M
49		18	F
50		64	M
51		58	F
52		26	M
53		63	F
54		46	F
55		64	F
56		63	F

[redacted]

[redacted]

Table 2
(continued)
[redacted]

Subject Demographics

Subject Number	Initials	Age	Gender
1	[redacted]	66	F
2		39	F
3		33	F
4		51	F
5		64	F
6		44	F
7		63	M
8		58	F
9		67	M
10		50	F
11		61	F
12		69	F
13		59	F
14		62	M
15		49	F
16		69	F
17		41	M
18		69	M
19		43	F
20		26	F
21		50	M
22		57	F
23		39	F
24		68	F
25		64	F
26		-	-
27		66	M
28		22	F
29		24	M

- = Subject number not assigned

[redacted]

Table 2
(continued)
[redacted]

Subject Demographics

Subject Number	Initials	Age	Gender
30	[redacted]	66	F
31		21	F
32		58	F
33		28	F
34		56	F
35		66	F
36		41	F
37		49	M
38		58	F
39		52	F
40		63	F
41		54	F
42		20	M
43		62	F
44		59	M
45		69	F
46		18	F
47		61	F
48		48	F
49		31	F
50		37	M
51		51	F
52		24	F
53		30	M
54		56	M
55		56	M
56		67	F
57		56	F

2022 FDA VCRP DATA- OCTYLDODECYL STEAROYL STEARATE

OCTYLDODECYL STEAROYL STEARATE	03A	Eyebrow Pencil	2
OCTYLDODECYL STEAROYL STEARATE	03B	Eyeliner	3
OCTYLDODECYL STEAROYL STEARATE	03C	Eye Shadow	306
OCTYLDODECYL STEAROYL STEARATE	03G	Other Eye Makeup Preparations	11
OCTYLDODECYL STEAROYL STEARATE	05A	Hair Conditioner	1
OCTYLDODECYL STEAROYL STEARATE	07A	Blushers (all types)	72
OCTYLDODECYL STEAROYL STEARATE	07B	Face Powders	105
OCTYLDODECYL STEAROYL STEARATE	07C	Foundations	12
OCTYLDODECYL STEAROYL STEARATE	07E	Lipstick	48
OCTYLDODECYL STEAROYL STEARATE	07F	Makeup Bases	2
OCTYLDODECYL STEAROYL STEARATE	07G	Rouges	7
OCTYLDODECYL STEAROYL STEARATE	07I	Other Makeup Preparations	18
OCTYLDODECYL STEAROYL STEARATE	12A	Cleansing	2
OCTYLDODECYL STEAROYL STEARATE	12D	Body and Hand (exc shave)	5
OCTYLDODECYL STEAROYL STEARATE	12F	Moisturizing	7
OCTYLDODECYL STEAROYL STEARATE	12H	Paste Masks (mud packs)	1
OCTYLDODECYL STEAROYL STEARATE	12J	Other Skin Care Preps	3

Total 605